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From prevention to cure: ready for new challenges

Promosso da

SIMIT Società Italiana di Malattie Infettive e Tropicali

e da

INMI, Istituto Nazionale per le Malattie Infettive
ISS, Istituto Superiore di Sanità
AMCLI, Associazione Microbiologi Clinici Italiani
SIICA, Società Italiana di Immunologia, Immunologia Clinica e Allergologia
SIMaST, Società Interdisciplinare per lo Studio delle Malattie Sessualmente Trasmissibili
SITA, Società italiana per la Terapia Antinfettiva
SIV-ISV, Società Italiana di Virologia - Italian Society for Virology
ANLAIDS, Associazione Nazionale per la lotta all'AIDS
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LILA, Lega Italiana per la Lotta contro l'AIDS
MARIO MIELI, Circolo di Cultura Omosessuale
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NADIR, Associazione Nadir
NPS Italia Onlus, Network Persone Sieropositive
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Emerging immunological and virological concepts in viral hepatitis

OC 1 ULTRASENSITIVE HBV-RNA QUANTIFICATION AS A PROMISING BIOMARKER TO OPTIMIZE THE STAGING OF CHRONIC HBV INFECTION AND TO DETECT MINIMAL VIRAL ACTIVITY UNDER PROLONGED VIROLOGICAL SUPPRESSION AND OCCULT HBV INFECTION

L. Piermatteo[1,2], S. D'Anna[1], L. Duca[1], G. Torre[1], A.F. Guerra[3], C. Boarini[3], A. Tavelli[4], P. Ventura[3], F. Ceccherini-Silberstein[1], A. Pietrangelo[3], A. D'Arminio Monforte[4], G. Abbati[3], U. Gill[5], P. Kennedy[5], V. Svicher[1,2], R. Salpini[1]

[1]University of Rome "Tor Vergata", Department of Experimental Medicine, Rome, Italy, [2]University of Rome "Tor Vergata", Department of Biology, Rome, Italy, [3]Internal Medicine and Centre for Hemochromatosis, University Hospital of Modena, University of Modena and Reggio Emilia, Italy, [4]ICONA Foundation, Milan, Italy, [5]Barts Liver Centre, Blizard Institute, Barts and The London SMD, QMUL, London, United Kingdom

Background: Serum HBV-RNA reflects the burden of virions containing pre-genomic RNA (pgRNA) and is used as surrogate marker of cccDNA transcriptional activity. Here, we define HBV-RNA levels across the natural history of HBV infection, including the under studied phase of occult HBV infection (OBI) and after long-term NUC exposure.

Methods: This study includes 106 drug-naive patients (pts) categorized in 17 eAg+ with chronic infection (CI), 7 with eAg+ chronic hepatitis (CH), 50 with eAg- CI and 32 with eAg- CH based on EASL guidelines. 38 eAg- virologically suppressed pts under long-term NUC treatment and 68 Anti-HBc+/HBsAg- pts (28 HIV+, 18 HCV+ and 22 under iatrogenic immunosuppression) are also included. HBV-RNA is quantified by droplet digital PCR (LOQ:5 copies (cps)/ml).

Results: eAg+ CH and CI have elevated HBV-RNA levels (median[IQR]: 7.5 [5.7-8.3] and 7.1 [6.7-7.4] log cps/ml) in line with high HBV-DNA: 9.2[7.4-9.8] and 8.9 [8.7-9.2] log IU/ml) and HBsAg production (20,895 [10,696-67,693] and 52,518 [32,236-77,136] IU/ml).

HBV-RNA undergoes a significant decrease in eAg- phases, achieving the lowest levels in eAg- CI (median[IQR]: 1.1[0.5-1.5] in eAg- CI vs 2.5[1.4-2.4] log cps/ml in eAg- CH, P<0.001), paralleling the declining trend of HBV-DNA and HBsAg. In both eAg- phases, HBV-RNA correlates with HBV-DNA (Rho=0.49, P<0.001 for eAg- CI and Rho=0.33, P=0.06 for eAg- CHB) but not with HBsAg (Rho=0.2 and 0.12, p>0.2), consistent with HBsAg production from integrated HBV-DNA. Notably, by AUROC, HBV-RNA <50 cps/ml shows the best accuracy in predicting eAg- CI status (sensitivity: 87.5%, specificity: 71%).

In virologically suppressed pts (median[IQR] NUC duration: 6.0[4.1-9.1] years), HBV-RNA is positive in 78.9% of pts with a median of 1.7(1.3-2.0) log cps/ml. Notably, the rate of HBV-RNA positivity and HBV-RNA levels remain stable independently from NUC duration, suggesting no decline in intrahepatic HBV activity over prolonged therapy (73.3%, 75% and 90% for NUC duration of <5, 5-9 and >9 years, with median[IQR] HBV-RNA of 1.7[1.5-1.9], 1.4 [1.2-1.4] and 1.8[1.6-2.3] log cps/ml).

Finally, despite Anti-HBc+/HBsAg- status, HBV-RNA is positive in 31.8% of immunosuppressed, 32.1% of HIV+ and 22.2% of HCV+ pts, supporting occult viral activity. Notably, in HIV coinfection, HBV-RNA positive pts have a lower nadir CD4 T-cell count (median[IQR]: 181[69-242] vs 283[94-441] cells/µl, P=0.08), highlighting the role of immune-compromission in modulating HBV replicative activity.

Conclusions: The production of pgRNA-containing viral particles predominates during the initial phases of chronic infection and decreases after eAg-seroconversion. In this context, HBV-RNA can enhance the categorization of chronic HBV infection including the eAg- infection status. By detecting minimal viral activity in the setting of long-term NUC treatment or OBI, the ultra-sensitive HBV-RNA quantification can contribute to discriminate pts achieving or not functional cure.

Emerging immunological and virological concepts in viral hepatitis

OC 2 FUNCTIONAL AND TRANSCRIPTIONAL RESTORATION OF EXHAUSTED VIRUS-SPECIFIC T LYMPHOCYTES FROM PATIENTS WITH CHRONIC HEPATITIS B

C. Ceccatelli Berti[1], I. Montali[1], M. Morselli[2], C. Boni[3], A. Penna[3], D. Laccabue[1,3], A. Vecchi[3], M. Rossi[1], C. Tiezzi[1,3], V. Reverberi[3], A. Montali[1], S. Doselli[3], S. Schivazappa[3], C. Boarini[4], G. Abbati[4], G. Missale[1,3], C. Ferrari[1,3], P. Fisicaro[3]

[1]Department of Medicine and Surgery, University of Parma, Parma, Italy, [2]Laboratory of Biochemistry and Molecular Biology, Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy, [3]Laboratory of Viral Immunopathology, Unit of Infectious Diseases and Hepatology, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy, [4]Division of Internal Medicine 2 and Center for Hemochromatosis, University of Modena and Reggio Emilia, Modena, Italy

Background and Aims: The current therapy for chronic hepatitis B (CHB) is mainly based on direct acting antiviral drugs that efficiently suppress virus replication, but don't eradicate HBV and frequently require lifelong administration. Therefore, novel anti-HBV therapies should induce complete HBV cure in a short definite time of treatment. During CHB, HBV-specific T cells gradually lose their anti-viral functions in a process known as T cell exhaustion, which is associated with a deregulated CD8 transcriptional profile that underlies a number of altered biological processes. Among them, an impaired mitochondrial function with ROS overproduction as well as NAD depletion are believed to be crucial. These observations suggest that mitochondrial antioxidants, such as Mitoquinone, and NAD precursors, such as nicotinamide mononucleotide (NMN), perhaps in combination with inhibition of CD38, one of the principal NAD consumers, may represent possible therapeutic strategies aimed at restoring HBV-specific CD8 T cell functions.

Methods: HBV Core18-27- specific CD8 T cells from chronic HBV patients were expanded in vitro by HBV peptide stimulation in the presence or absence of Mitoquinone or NMN plus CD38 inhibitors (CD38i). Influenza(Flu)-specific CD8 cells from the same patients were expanded at the same experimental conditions without any treatment and used as controls for the definition of reference transcriptional features of memory CD8 T cells associated with control of infection. Virus-specific CD8 T cells were then sorted and subjected to low input RNA-Seq analysis by SMART-Seq. Differentially expressed genes were identified by DESeq2 v1.34.0, with the lfcShrink analysis (s value<0.05). The softwares Shinygo and GSEA were also used.

Results: HBV-specific CD8 cells from cultures treated with either therapy showed a significant reduction of PD1 expression and a trend towards a decreased CD38 expression. In addition, a number of differentially expressed genes were identified comparing cultures treated with immune-modulating strategies and untreated control cells. Interestingly, in parallel with antiviral function enhancement, both treatments induced the development of transcriptional memory T cell features. Among these, the down-regulation of several genes controlling intracellular Ca2+ uptake, which may be potentially responsible for reduced T cell activation, and regulating the glycolytic metabolism could be observed, with an enhancement of the fatty-acid β-oxidation. Interestingly, GSEA analysis showed a significant association of gene expression profiles in HBV-specific CD8 T cells from treated cultures with control fully functional FLU-specific CD8 T cells.

Conclusions: Administration of mitochondria-targeted antioxidant compounds and NAD supplementation represent strategies able to correct the deregulated transcriptional profile in exhausted HBV-specific CD8 T cells from CHB patients, by acting at several levels, including T cell metabolism.

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OC 3 HDV VIRAL DECLINE IN HIV-INFECTED AND UNINFECTED SUBJECTS WITH HBV/HDV-RELATED CIRRHOSIS DURING "REAL WORLD" BULEVIRTIDE COMPASSIONATE USE PROGRAM AT INMI SPALLANZANI IN ROME, ITALY

U.V. Comandini[1], C. Taibi[1], E. De Santis[2], F. De Maria[1], R. Lionetti[1], M. Montalbano[1], A. Rianda[1], P. Piccolo[3], C. De Ponte[4], S. Mazzotta[4], A.R. Garbuglia[5], F. Maggi[5], G. D'Offizi[1]

[1]Infectious Diseases and Hepatology Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome Italy (INMI), [2]La Sapienza University of Rome, Italy, [3]Internal Medicine Unit, Fatebenefratelli Isola Tiberina Hospital – Gemelli Isola, Rome, Italy, [4]Pharmacy Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome Italy, [5]Virology Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome Italy

Background: Hepatitis delta virus (HDV) infection is widespread globally, with estimated 10 to 20 million individuals currently infected. Until recently interferon alpha was the only licensed therapy for treatment of HDV. However, treatment success rates and tolerability were poor.
Bulevirtide (BLV) is the first entry inhibitor with specific antiviral activity in subjects with HBV/HDV co-infection. BLV specifically inhibits the sodium taurocholate co-transporting polypeptide, used by HDV to infect hepatocytes. BLV was recently approved in the EU for the treatment of HDV infection. BLV was prescribed at a dosage of 2 mg daily, as a self-administered subcutaneous injection.
Material and Methods: The aim of this study is to report the preliminary results of feasibility and efficacy of BLV in a small group of difficult-to-treat compensated cirrhotic patients with CSPH with and without HIV infection.
We describe preliminary results of bulevirtide compassionate use in 13 difficult-to treat HIV-infected (38%) and uninfected patients with HBV/HDV-related cirrhosis.
HDV-RNA level was assessed by EuroBioplex HDV-RNA real-time RT-PCR Quantification kit, with lower limit of quantification of 100 UI/ml.
Patients underwent clinical evaluation, blood testing, liver and spleen stiffness assessment at baseline (BL) and after treatment months 1, 2, 3, 4, 6 and 9. Blood tests included liver function, HDV-RNA load, HBV-DNA, quantitative HBsAg, HIV-RNA and CD4 count in HIV+ patients, and biliary salt dosage, to confirm self-reported adherence. Median follow-up time was 9.4 months. Efficacy of BLV was defined by virological response (HDV-RNA < 100 UI/ml) and/or ALT normalization.
Results: Overall, the mean HDV-RNA decline was 1.30 and 2.15 log UI/ml from baseline at 3 and 6 months, respectively; 23.1% had undetectable HDV-RNA (<100 UI/ml) at 3 months, 36.4% at 6 months and 50% at 9 months of treatment.
At month 6, compared to baseline, median AST and ALT levels fell by 46.5% and 71.3%, respectively; median liver stiffness decreased by -5.9 kPa (31%). HIV+ had higher median baseline HDV-RNA (5.66 log) than HIV-uninfected subjects (3.90 log), but a progressive mean decline was observed in both groups, -1.93 log and -2.06 log, respectively. A combined response was achieved in 40% of HIV+ and 66% of HIV-uninfected subjects.
Conclusions: Our preliminary results indicate that bulevirtide is feasible and safe in difficult-to-treat populations like HIV/HBV/HDV co-infected subjects and immigrants, when special attention is given to patient education. HIV+ patients showed high HDV-RNA values, but median declines during treatment were similar to HIV-uninfected subjects.

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Emerging immunological and virological concepts in viral hepatitis

OC 4 SUCCESSFUL TREATMENT OF RESISTANT HCV IN TEN PATIENTS, FAILED FOR OTHER DAA, WITH GLECAPREVIR/PIBRENTASVIR AND SOFOSBUVIR

M. Migliorati, L. Zeneli, F. Compostella, A. Cambianica, F. Pennati, F. Gottardi, S. Zaltron, F. Castelli, A. Spinetti

Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali di Brescia, Brescia, Italy

Background: The development of oral direct acting antiviral agents (DAAs) has significantly changed the management of HCV infections allowing to achieve a sustained virologic response (SVR) in more than 95% of cases. Nevertheless, a small portion of patients experiences HCV relapse after treatment.
Although rare, the failure to the latest-generation regimens represents a serious clinical problem since patients with virologic failure (VF) after treatment containing a NS5A inhibitors have limited retreatment options.
We evaluated the number of patients with sustained virologic response (SVR) after off-label regime with glecaprevir/pibrentasvir and sofosbuvir for 12 weeks as the guidelines require.
Material and Methods: We performed a retrospective observational study including patients with chronic HCV infection and past virologic failure to treatment containing at least one NS3 protease and/or NS5A/NS5B inhibitor.
These patients have been subsequently treated with glecaprevir/pibrentasvir and sofosbuvir for 12 weeks. We performed a descriptive analysis by collecting: virological data, previous DAA treatments and resistance-associated substitutions (RAS), found by resistance tests for the three target regions. Patients were tested for RAS after VF.
Results: In the table are depicted liver stiffness at the baseline, genotype distribution, previous treatments and resistance-associated substitutions (RAS).
Ten patients were enrolled: seven (70%) of them were male; seven (70%) had genotype 1 (of these 3 were 1a and 4 were 1b), two (20%) genotype 3 and one (10%) had genotype 4. Seven (70%) of the enrolled patients presented a stiffness value over F4, thus considered to be cirrhotic. Of all the patients four (40%) presented reduced susceptibility to sofosbuvir, one (10%) presented resistance and two (20%) reduced susceptibility to pibrentasvir, while everyone (100%) presented susceptibility to glecaprevir. Ten out of ten (100%) patients presented resistance in NS5A region, while only two patients (20%) presented resistance to voxilaprevir (both were genotype 1b) and received previous treatment with elbasvir/grazoprevir. One patient (10%) received two previous lines of treatment with DAA. All patients (100%) achieved SVR at 24 weeks after the end of treatment.
Conclusions: Treatment with glecaprevir/pibrentasvir and sofosbuvir for 12 weeks in patients with previous virologic failures to therapy containing a nonstructural protein 5A (NS5A) inhibitor, was well-tolerated and highly efficacious. Thus, it represents a valid therapeutic option in this setting. It is relevant to note that this combination therapy may retain its effectiveness even if the HCV presents RAS with resistance to sofosbuvir, voxilaprevir and NS5B inhibitors.

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Epidemiology trends in infections

OC 5 HIV-1 TRANSMITTED DRUG RESISTANCE IN NEWLY DIAGNOSED INDIVIDUALS IN ITALY OVER THE PERIOD 2015-2021

L. Fabeni[1], D. Armenia[2], I. Abbate[1], R. Gagliardini[1], V. Mazzotta[1], N. Orchi[1], A. Bertoli[3], W. Gennari[4], F. Forbici[1], G. Berno[1], L. Piermatteo[5], V. Borghi[4], S. Pittalis[1], C. Pinnetti[1], A. Vergori[1], A. Mondi[1], G. Parruti[6], F. Di Sora[7], M. Iannetta[3], M. Lichtner[8], A. Latini[9], C. Mussini[4], L. Sarmati[3], C.F. Perno[10], E. Girardi[1], A. Antinori[1], F. Ceccherini-Silberstein[5], F. Maggi[1], M.M. Santoro[5], The Italian Resistance group

[1]National Institute for Infectious Diseases L Spallanzani, IRCCS, Rome, Italy, [2]Saint Camillus International University of Health Sciences, Rome, Italy, [3]Polyclinic of Rome "Tor Vergata", Rome, Italy, [4]Policlinic of Modena, University of Modena and Reggio Emilia, Modena, Italy, [5]University of Rome "Tor Vergata", Rome, Italy, [6]Pescara General Hospital, Pescara, Italy, [7]S. Giovanni Addolorata Hospital, Rome, Italy, [8]Sapienza University, Latina, Italy, [9]San Gallicano Dermatological Institute, IRCCS, Rome, Italy, [10]Bambino Gesù Children's Hospital, Rome, Italy

Background: We evaluated transmitted drug-resistance (TDR) in HIV-1 infected individuals confirmed in different counselling and testing centres in North/Central Italy from 2015 to 2021, according to subtypes and transmission clusters (TCs).

Material and Methods: 2386 HIV-1 PR/RT sequences and 1831 INT sequences from drug-naïve individuals were analysed. TDR was evaluated over time by considering the list of Mutations for Drug Resistance Surveillance (https://hivdb.stanford.edu/). Phylogeny was generated by GTR model and 1000 bootstrap with maximum-likelihood method (MEGA6). TCs included small TCs (2-3 sequences, STCs), medium TCs (4-9 sequences, MTCs), large TCs (≥10 sequences, LTCs). Factors associated with TDR were evaluated by uni-multivariable logistic regression.

Results: Individuals were mainly male (79.1%) and Italian (56.2%), with a median (IQR) age of 38 (30-48) years. The main transmission route was sexual (MSM: 34.6%; heterosexual: 24.0%; transsexual and other unknown sexual behaviours: 8.1%). Non-B infected individuals accounted for 44.6% (N=1065) of the overall population (CRF02_AG=195; F=148; C=139; A=139; other=444) and increased over time (2015-2021: 42.1% to 51.0%, p=0.002). Overall, TDR prevalence to any class was 8.0% (9.5% in B subtype vs. 6.1% in non-B subtypes, p=0.002). In particular, TDR prevalence to NRTI was 2.6% (3.5% vs. 1.5%, p=0.003), to NNRTI 4.8% (5.5% vs. 3.9%, p=0.086), to PI 1.3% (1.7% vs. 0.8%, p=0.046), to INSTI 0.3% (0.2% vs. 0.5%, p=0.415). By evaluating the prevalence of TDR to any class over time, no significant changes were found from 2015 to 2021, though a slight increase was observed in 2020/2021 (2015: 6.4%; 2020: 11%; 2021: 8.8%, p=0.181) (See Table). Similarly, no significant changes in TDR prevalence were found by stratifying for subtype and considering the specific drug-classes.

Overall, 300 TCs were identified (B subtypes: 131 STCs, 49 MTCs, 8 LTCs; non-B subtypes: 70 STCs, 31 MTCs, 11 LTCs). These TCs involved 1155 (48.4%) individuals, with a similar proportion in B and non-infected individuals (49.7% vs. 46.8%, p=0.148). A similar prevalence of TDR among individuals in TCs and those out of TCs (8.2% vs. 7.8%, p=0.707).

By multivariable analysis, the time of diagnosis was the only factor significantly associated with a higher probability of TDR detection, while subtypes A, F, and CFR02_AG were negatively associated with TDR. No other factors, including to being part of TCs, were significantly associated with TDR.

Conclusions: Over the years 2015-2021, in Italy TDR prevalence was 8% and remained almost stable over time, even though a slight trend of increase was found in 2020-2021. TDR was mainly related to RTI. Resistant strains were found circulating regardless to be in TCs, but less likely in non-B subtypes. These results highlight the importance of a continuous surveillance of newly diagnosed individuals for evidence of TDR to inform clinical practice.

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Epidemiology trends in infections

OC 6 GENOMIC EPIDEMIOLOGY OF THE MAIN SARS-COV-2 VARIANTS CIRCULATING IN ITALY IN 2020 AND 2021 PERIOD

A. Bergna[1], A. Lai[1], C. della Ventura[1], A. Weisz[2], B. Bruzzone[3], F. Sagradi[4], G. Brindicci[5], D. Francisci[6], N. Clementi[7], I. Vicenti[8], A. Callegaro[9], S. Menzo[10], E. Venanzi Rullo[11], G. Giurato[2], F. Rizzo[2], T. Rocco[2], V. De Pace[3], C. Fraccalvieri[3], S. Testa[4], L. Lanfranchi[4], A. Saracino[5], S. Caucci[10], G. Nunnari[11], M. Clementi[7], M. Galli[1], A. Riva[1], S. Antinori[1], G. Zehender[1] and SARS-CoV-2 ITALIAN RESEARCH ENTERPRISE – (SCIRE) collaborative Group1

[1]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [2]Laboratory of Molecular Medicine and Genomics, Department of Medicine, Surgery and Dentistry 'Scuola Medica Salernitana', University of Salerno, Salerno, Italy, [3]Hygiene Unit, IRCCS AOU San Martino-IST, Genoa, Italy, [4]Unit of Infectious Diseases, Azienda Socio Sanitaria Territoriale Cremona, Cremona, Italy, [5]Infectious Diseases Unit, University of Bari, Bari, Italy, [6]Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy, [7]Laboratory of Microbiology and Virology, Università "Vita-Salute" San Raffaele, Milan, Italy, [8]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [9]Microbiology and Virology Laboratory, ASST Papa Giovanni XXIII, Bergamo, Italy, [10]Department of Biomedical Sciences and Public Health, Virology Unit, Polytechnic University of Marche, Ancona, Italy, [11]Unit of Infectious Diseases, Department of Experimental and Clinical Medicine, University of Messina, Messina, Italy

Introduction: The sustained transmission and replication, coupled with evolutionary pressures, contributed to the continuous evolution of SARS-CoV-2 and to the emergence of new variants, making their global monitoring and the study of their characteristics a priority. Aim of this work was to study the genomic heterogeneity, the temporal origin, the rate of viral evolution and the population dynamics of the main circulating variants (20E.EU1, Alpha and Delta) in Italy, in the period August 2020-January 2022.

Methods: 593 Whole Genome sequences of SARS-CoV-2 have been collected at the centres of the collaborative group SCIRE (SARS-CoV-2 Italian Research Enterprise). For each variant, two datasets were analyzed, the former including international genomes and the latter focusing on Italian sequences. Phylogenetic trees were estimated using IQ-TREE v.1.6.12. The Italian clusters were analyzed using BEAST v.2 to estimate tMRCA (time of the Most Recent Common Ancestor) and main epidemiological parameters.

Results: 20E.EU1 clade and Alpha variant, presented only mutations specific to the variant; differently, Delta variant sequences showed a high number of additional mutations, especially in the ORF1a region.

Among 20E.EU1 international clusters including more than 70% of Italian genomes, 6 pure Italian and 5 mixed (contained both Italian and non-Italian sequences) clusters were observed with a tMRCA between 13/06/2020 -28/09/2020; for the 15 pure Italian and 2 mixed clusters of Alpha variant we estimated a tMRCA between 10/11/2020-20/02/2021, while the 6 mixed and 2 pure Italian clusters of Delta variant presented a tMRCA ranging from 13/03/2021-27/07/2021. The annual growth rates estimated for each variant were 3.79, 2.85 and 5.9; while R0 resulted 1.07, 1.05 and 1.11, considering a duration of infectivity of 7 days. Re values showed the highest level between May and June 2020 in 20E.EU1 clade until autumn 2020. Starting from January 2021, it was observed a reduction of Re around the unit and the joining of the plateau. Re of Alpha variant was estimated above 1 since October 2020 when the highest mean value was estimated (1.18), remaining above 1 until March 2021, when it started to decrease until June 2021. For Delta variant, we observed two peaks: the first in March-May 2021 (1.34), and the second in June-July 2021 (1.14), while the decrease of Re to 1 matched with the achievement of the plateau in August remaining stable until 2022.

Conclusions: Our work highlighted a different evolutionary dynamic of studied lineages. A high concordance was observed between epidemiological parameters estimation and phylodinamic trends. When the Skyline Plot displayed an exponential increase in the viral population (indicating an increase in transmission events) the birth-death analysis showed Re values above 1, while Re periods below 1 corresponded to a decrease in the size of the epidemic.

Epidemiology trends in infections

OC 7 TRENDS OF TESTING FOR HIV AND SYPHILIS IN COMMUNITY BASED VOLUNTARY COUNSELLING AND TESTING (CBVCT) SERVICES IN THE PERIOD 2019-2022: ARE THERE PEOPLE MORE AT RISK?

A. Soria[1,2], D. Calzavara[2], R. Rossotti[2,3], R. Repossi[2,4], A. Bianchi[2,4], D. Zagato[4], N. Frattini[2,4], M. L. Cosmaro[2,5], P. Russo[2,6], S. Penon[5], S. Curridori[5], A. Antonino[2,4], D. Savarino[5], G. Lapadula[1,2], S. Bossolasco[2,7], A. De Bona[2,8], A. d'Arminio Monforte[2,9], M. Cernuschi[2,4,7]

[1]Fondazione IRCCS San Gerardo dei Tintori, Monza, [2]Milano Check Point ETS, Milano, [3]Grande Ospedale Metropolitano Niguarda, Milano, [4]ASA Milano ODV, Milano, [5]Fondazione Lila Milano Onlus, Milano, [6]CIG – Arcigay Milano ODV, Milano, [7]IRCCS Ospedale San Raffaele, Milano, [8]ASST Santi Paolo e Carlo, Milano, [9]Fondazione ICONA, Milano

Background: Screening of HIV in informal contexts is a cornerstone of preventive strategies to reduce HIV transmission, because it could be offered to a large number of individuals and it contributes to early detection and linkage to care. Community Based Voluntary Counselling and Testing (CBVCT) is a key to reach this target. Data on this informal activity, possibly penalized by COVID-19 pandemic in recent years, are lacking.

Methods: Rapid capillary tests of HIV and syphilis in different informal contexts (indoor screening sessions in the association site, outdoor offer during public events like Pride, amusement venues) have been offered between 2019 and 2022 by volunteers of different associations to at-risk populations, along with an anonymous questionnaire investigating attitudes and risks connected with sexual activity. Data were collected through a protected web platform (COBATEST network cobatest.org), and analysed with descriptive statistics.

Results: In the period 2019-2022, 9353 questionnaires have been administered by volunteers of three main associations, 543 (6%) by ASA Milano (ASA), 2631 (28%) by LILA, 6179 (66%) by Milano Checkpoint (MCP). Clients were predominantly men (72%); women and transgender women were 27% and 1%, respectively. The median (IQR) age was 32 (26-41), 27 (23-35), 29 (24-37) years for men, women, transgender women, respectively. In a 4-year period, there were 62 HIV positive out of 8952 tests (0.69%), and 194 syphilis positive out of 6518 tests (2.98%). The HIV positive rate dropped during COVID years (2020-2021), but raised again in 2022, while the syphilis positive rate increased significantly in the same time lag (p=0.001, Figure 1). HIV prevalence was higher in transgender women (5.08%), as well as in people reporting unprotected anal sex (1.06% vs 0.57%), subjects with concomitant diagnosis of syphilis (5.91% vs 0.43%), foreigners (1.59% vs 0.50%), subjects reporting previous sexually transmitted infections (STI) (1.76% vs 0.54%), sex workers (3.11% vs 0.61%), having been in prison (1.51% vs 0.63%), with intravenous drug use (6.34% vs 0.64%), being men having sex with men (MSM) (0.97% vs 0.40%), testing in needle exchange program or amusement venues with respect to CBVCT office or outdoor public events (1.27% vs 0.60%) (Table 1). No correlations were found between a positive HIV test and age, self-perceiving at-risk, reported condom use. In a multivariable logistic regression analysis, the only factors independently associated with a higher risk of positive HIV test were being MSM, foreigner, and with a concurrent positive syphilis test (Table 2).

Conclusions: CBVCT confirms a constant role in unveiling new HIV infections in people at risk, despite the decline in COVID years (2020-2021). Moreover, it is possible that the context of informal testing and outreach activities could head off even "the hardest to reach", in particular foreign MSM, thus favouring linkage to care of submerged populations.

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Epidemiology trends in infections

OC 8 EPIDEMIOLOGICAL AND PERCEIVED HEALTH STATUS DETERMINANTS OF EARLY ACCESS TO VACCINE IN LATIUM REGION MPOX VACCINATION (MPOXV) CAMPAIGN

G. Del Duca[1], A. Tavelli[2], I. Mastrorosa[1], V. Mazzotta[1], C. Aguglia[1], S. Lanini[1], A.C. Brita[1], R. Gagliardini[1], M.L. Giancola[1], S. Vita[1], A. Beccacece[1], A. Vergori[1], J. Paulicelli[1], G. Natalini[1], A. D'Urso[1], P. Piselli[3], C. Cimaglia[3], P. Galli[4], V. Mondillo[4], M. Ridolfi[5], G. D'Ettorre[5], E. Tamburrini[6], L. Coppola[7], A. Latini[8], M. Lichtner[9], V. Puro[1], M. Farinella[10], G.M. Corbelli[11], A. d'Arminio Monforte[2], F. Vairo[1], A. Barca[12], E. Nicastri[1], F. Vaia[1], E. Girardi[1], A. Antinori[1]

[1]Lazzaro Spallanzani National Institute for Infectious Diseases, Rome, Italy, [2]ASST Santi Paolo e Carlo, Unimi Milan, [3]Clinical Epidemiology, INMI Rome, [4]Health Management, INMI Rome, [5]Umberto I, Rome, [6]Clinical Infectious Diseases, A. Gemelli Rome, [7]Clinical Infectious Diseases, Tor Vergata Rome, [8]STD/HIV San Gallicano Dermatologic Unit IFO Rome, [9]Infectious Disease, La Sapienza University Santa Maria Goretti Hospital, Latina, [10]Circle of homosexual culture Mario Mieli Rome, [11]Plus Rome, Rome, [12]Regional Directorate of Health and Social Health Integration, Latium region

Background: Despite the efficacy of MpoxV, uncertainty to vaccination may have undermined the efforts to control the outbreak mainly in high-risk groups such as MSM. Herein, we aim to investigate vaccination attitudes, by analyzing empirical factors associated with vaccine acceptance in the MpoxV campaign in the Latium region.
Material and Methods: Among all the individuals referred to the Ministry of Health pathways provided for access to MpoxV in the Latium region, we included participants (pts) of the Mpox-VAC Study (EC approval:41-z 2022). All pts signed informed consent. Pts were asked to fill out an anonymous survey of 17 multiple-choice questions on demographics, perceived risk for Mpox infection, sexual behavior, vaccination attitude and perceived health status (SF-36 questionnaire). Two endpoints: 'delayed acceptance' and 'early acceptance' of MpoxV, defined as access for vaccination >60 and ≤30 days from vaccination compaign start (VCS), respectively. Pts characteristics and survey responses were compared in the 2 groups (vaccination ≤60 versus >60 days from VCS) by Chi-square and Wilcoxon rank-sum tests, as appropriate. The association between demographic/behavioral factors and the 2 endpoints was evaluated through logistic regression models.
Results: Over the study period, 1717 individuals underwent vaccination (Figure 1): 129 (7%) >60 and 676 (60%) ≤30 days from VCS. Table 1 shows characteristics and comparisons between the 2 groups. In the first adjusted model, a bisexual orientation [vs homosexual, adjusted odds ratio (AOR) 3.22; 95% confidence interval (CI) 1.77 -5.84], a lower education level (vs high school/university, AOR 3.65; 95%CI 1.83-7.28) and a worse perceived physical health (per 10 points lower SF-36 physical component summary, AOR 1.16; 95%CI 1.02-1.32) and mental health (per 10 points lower SF-36 mental component summary, AOR 1.13; 95%CI 1.02-1.23) were associated with delayed access to vaccination (Tab.2). In the second model, being PrEP users and, marginally, HIV positive (vs HIV negative not on PrEP, AOR 1.97; 95%CI 1.37-2.82 and AOR 1.24; 95%CI 0.99-1.57, respectively), having a high perceived risk for Mpox infection (AOR 1.43; 95%CI 1.13-1.82) and reporting high-risk behaviors like the use of recreational drugs/chems (AOR 1.49, 95%CI 1.11-2.00), sex under the influence of drugs and/or alcohol (AOR 1.78; 95%CI 1.36-2.34) and higher number of principal sexual partners (per 1 more, AOR 1.07; 95%CI 1.03-1.11), were associated with early access to vaccination (Tab.3).
Conclusions: Our data suggest that subjects with high-risk behaviors and with a high perceived risk for Mpox, show increased awareness of performing vaccination. Conversely, self-perception of worse health status and low educational level are critical factors for vaccination delay. This information could be a useful tool, at a public health level, for identifying strategies to encourage vaccine acceptance and address vaccine uncertainty or increase uptake.

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Immune response in SARS-CoV-2

OC 9 MONOCYTES AND NK CELL SUBSETS FREQUENCIES AFTER ANTI-S MONOCLONAL ANTIBODIES TREATMENT IN COVID-19 PATIENTS

L. Maddaloni[1], L. Santinelli[1], G. Bugani[1], A. Lazzaro[1], C.M. Lofaro[1], L. Sorrentino[2], M. Fracella[2], A. D'Auria[2], C. Ajassa[1], C. Leanza[1], A. Napoli[3], G. Antonelli[2], C.M. Mastroianni[1], G. Ceccarelli[1], C. Scagnolari[2], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, [2]Virology Laboratory, Department of Molecular Medicine, Sapienza University of Rome, Italy, [3]Laboratory of Microbiology and Virology, Department of Molecular Medicine, Sapienza University of Rome, Italy

Background: Non-classical and intermediate monocytes are known to be involved during viral infections and reduced frequencies were found in patients with severe COVID-19. Similarly, NK cells may have a role in the early immune response toward SARS-CoV-2. Despite treatment with neutralizing monoclonal antibodies (mAbs) against the Spike (S) of SARS-CoV-2 reduces COVID-19 severity in high-risk individuals, little is known regarding their impact on cellular innate immunity. Therefore, the aim of this study was to investigate monocytes and NK frequencies after mAbs treatment in COVID-19 patients.

Methods: High risk individuals with mild/moderate SARS-CoV-2 infection were enrolled and treated with mAbs. Peripheral blood was sampled before (T0) and twelve days after (T1) administration of mAbs. IgG against SARS-CoV-2 Spike protein at baseline were determined in infected patients' serum using a commercial assay. Frequencies of monocytes (classical, intermediate and non-classical) and NK (NKbright and NKdim) cell subsets were evaluated by multiparameter flow cytometry using the following anti-human monoclonal antibodies: CD3-PerCP, CD14-APC, CD16-PE-Vio770 and CD56-PE. Statistical analysis was performed using PRISM and $p<0.05$ were statistically significant. This research was supported by EU funding within the NextGeneration EU-MUR PNRR Extended Partnership initiative on Emerging Infectious Diseases (Project no. PE00000007, INF-ACT, Spoke 1, 2 and 4).

Results: 69 SARS-CoV-2 high-risk infected individuals with median age of 64 (55-74) years were enrolled; among them, 21 were not vaccinated, while 28 and 21 were vaccinated, exhibiting low (LAT) and high (HAT) vaccine-induced anti-S antibody titers at T0, respectively. Unvaccinated individuals had lower non-classical monocytes frequencies as compared to LAT and HAT groups at baseline ($p=0.019$ and $p=0.037$, respectively), but exhibited higher frequencies of intermediate monocytes compared to HAT group ($p=0.003$). After mAbs treatment, classical monocytes frequencies were increased in both vaccinated groups as compared to baseline (LAT: $p=0.002$; HAT: $p=0.0004$), while a decreasing trend was observed in the unvaccinated group ($p=0.168$). By contrast, non-classical monocytes frequencies were decreased in both groups of vaccinated subjects (LAT: $p=0.004$; HAT: $p=0.002$) and increased in unvaccinated ones ($p=0.008$). Moreover, unvaccinated individuals had lower percentages of classical monocytes as compared to LAT ($p=0.015$) and HAT ($p=0.0002$) groups, higher non-classical monocytes ($p=0.018$) and NKdim ($p=0.017$) frequencies than HAT group and higher NKbright frequencies than LAT one ($p=0.045$).

Conclusions: mAbs therapy in high-risk COVID-19 patients had a differential impact on monocytes and NK cell frequencies according to anti-SARS-CoV-2 vaccination status. The lack of anti-SARS-CoV-2 vaccination might be responsible for a delayed activation of cellular immunity among unvaccinated patients as compared to vaccinated ones.

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Immune response in SARS-CoV-2

OC 10 ERAPS CONTROL IN VITRO SARS-COV-2 INFECTION BY TRIGGERING NK AND NEUTROPHIL ACTIVATION

I. Saulle[1,2], M.L. Murno[2], F. Limanaqi[1,2], M. Garziano[1,2], S. Strizzi[2], C. Vanetti[2], S. Lo Caputo[3], M. Poliseno[3], T.A. Santantonio[3], M. Clerici[1,4], M. Biasin[2]

[1]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [2]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [3]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy, [4]Don C. Gnocchi Foundation, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Foundation, Milan, Italy

Introduction: ERAP1 and ERAP2 (ERAPs) are two endoplasmic reticulum aminopeptidases which control susceptibility as well as progression of different infectious disease. Beyond their canonical role in antigen processing and presentation, recent evidence suggests that following inflammatory stimuli ERAPs can be secreted and modulate several features of the acquired and natural immune response. In this frame, the present study aims to investigate if exogenous recombinant human (rh) ERAPs administration can control SARS-CoV-2 infection/replication by boosting the antiviral potential of different immunocompetent cells.

Methods: Peripheral blood mononuclear cells (PBMC) isolated from 10 healthy controls (HC) were stimulated with 300ng/mL of rhERAP1, rhERAP2 or rhERAP1+rhERAP2 (COMBO). After 24h, a mixed cell culture including rhERAP treated PBMC, granulocytes and in vitro SARS-CoV-2 infected A549-ACE2 expressing cell line was monitored to assess: 1) viral replication; 2) Neutrophils, NK and CD8 T cells activation; 3) cytokine secretion.

ERAP1 and ERAP2 mRNA levels were quantified in unstimulated and Spike-stimulated PBMC as well as in plasma from 10 mild (MD) and 10 severe (SD) COVID-19 patients.

Results: Notably, PBMC stimulation by rhERAPs significantly reduced SARS-CoV-2 replication in A549-ACE2 infected cells (rhERAP1 $p<0.05$; rhERAP2 $p<0.05$; COMBO $p<0.01$). This antiviral activity was associated with: 1) Neutrophil activation and degranulation (CD15+ CD16+CD66b++MPO) ($p < 0.05$); 2) an increase in the percentage of cytotoxic NK (CD56+CD16++107+) ($p < 0.05$) and CD8 T cells (CD8+CD107+Perforin+) ($p < 0.05$) and 3) a consistent release of several cytokine and chemokines mainly IL-8 ($p < 0.01$).

ERAPs antiviral activity is also correlated with COVID-19 progression. Indeed, ERAP1 and ERAP2 mRNA expression was drastically downregulated in both unstimulated ($p<0.05$ both ERAPs) and Spike-stimulated PBMC ($p<0.05$ both ERAPs) of SD compared to MD. Conversely, a higher concentration of both aminopeptidases was detected in plasma of SD compared MD (ERAP1 $p<0.05$; ERAP2 $p<0.05$).

Conclusions: ERAPs trigger several antiviral mechanisms in both Neutrophils and NK cells suggesting that their anti-SARS-CoV-2 potential is not limited to their canonical role in Ag presentation and CD8+ T cell activation. These findings pose the premise to further investigate the role of ERAPs in both innate and adaptive immunostimulatory pathways and suggest their potential use in novel preventive and therapeutic approaches against SARS-CoV-2 infection.

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Immune response in SARS-CoV-2

OC 11 A NOVEL ENHANCING EFFECT OF SARS-COV-2 MUTATIONS ON ANTI-VIRAL CD8 T CELL RESPONSES

C. Tiezzi[1,2], A. Vecchi[1], M. Rossi[2], D. Cavazzini[3], A. Bolchi[3,4], D. Laccabue[2], A. Penna[1], T. Meschi[2,5], A. Ticinesi[2,5], A. Nouvenne[5], G. Donofrio[6], P. Fisicaro[1], I. Montali[2], C.Ceccatelli Berti[1], V. Reverberi[1], A. Montali[2], S. Doselli[1], G. Pedrazzi[7], G. Missale[1,2], S. Ottonello[3,4], C. Ferrari[1,2], C. Boni[1]

[1]Laboratory of Viral Immunopathology, Unit of Infectious Diseases and Hepatology, Azienda-Ospedaliero-Universitaria di Parma, Parma, Italy, [2]Department of Medicine and Surgery, University of Parma, Parma, Italy, [3]Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy, [4]Interdepartmental Center Biopharmanet-Tec, University of Parma, Parma, Italy, [5]Geriatric-Rehabilitation Department, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy, [6]Department of Veterinary Science, University of Parma, Parma, Italy, [7]Department of Neuroscience - Biophysics and Medical Physics Unit, University of Parma, Parma, Italy

Background: Mutations carried by SARS-CoV-2 spike protein variants may promote viral escape from immune protection. Humoral immunity is sensitive to evasion by SARS-CoV-2 mutants, but the impact of viral evolution on the interplay between virus and host CD8 T cell reactivity remains uncertain. The aim of this study was to assess the impact of SARS-Cov-2 variant mutations on CD8-mediated responses induced by genetic mRNA vaccines or natural infection.

Material and Methods: SARS-CoV-2 spike-specific T cell responses were studied in vaccinated and convalescent patients by an ex-vivo FluoroSPOT assay based on PBMC stimulation with peptides of optimal length for CD8 T cell recognition containing most variant mutations reported so far. Ex-vivo intracellular cytokine staining was used to define the specific T cell sub-populations targeted by SARS-CoV-2 spike peptides and to characterize the overall breadth of the spike-specific CD8 T cell repertoire.

Results: Variant peptides were recognized by approximately half of the vaccinated subjects. As expected, most SARS-Cov-2 mutations were either inhibitory or neutral, meaning that the corresponding peptides elicited CD8-mediated responses lower than, or comparable to, those induced by the corresponding prototype epitopes. Surprisingly, 30% of the variant peptides were more immunogenic than the corresponding prototype epitopes. Similar effects were observed in convalescent patients, indicating that positive and negative modulation of CD8 responses also occurs during natural infection. By using overlapping peptides spanning the entire spike sequence, most vaccinated and convalescent donors exhibited widely multi-specific and powerful CD8-mediated T cell responses but a minor proportion of them showed much narrower and weaker responses.

Conclusion: Our results characterize a novel enhancing effect of SARS-CoV-2 mutations on CD8 T cell responses. These mutations are likely selected because able to provide the virus with a better capacity to spread in the infected host. Only when the mutant virus infects individuals with the appropriate HLA class I presenting molecule the mutated epitope could facilitate and improve CD8 T cell activation. Thus, this mechanism should not have a broad impact at the overall population level, but may have an effect on anti-viral protection only in the minor proportion of patients with the appropriate HLA haplotype, provided they express a narrowly focused CD8 T cell repertoire. Our data allow to clarify another unexpected facet of the complex interplay between host immune system and virus and highlight the existence of natural heteroclitic-like peptides that may be worth of consideration for the future development of new generation, more potent COVID-19 vaccines.

Immune response in SARS-CoV-2

OC 12 NEUTRALIZING ANTIBODIES RESPONSE TO NOVEL SARS-COV-2 OMICRON SUBLINEAGES IN LONG-TERM CARE FACILITY RESIDENTS AFTER THE FOURTH DOSE OF MONOVALENT BNT162B2 COVID-19 VACCINATION

I. Varasi[1], A. Lai[2], A. Bergna[2], L. Fiaschi[1], A. Gatti[3], B. Caimi[3], C. Balotta[3], C. Biba[1], A. Riva[2], G. Zehender[2], M. Zazzi[1], I. Vicenti[1]

[1]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [2]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [3]Azienda di Servizi alla Persona, Istituto Milanese Martinit e Stelline e Pio Albergo Trivulzio, Milan, Italy

Background: The dynamics of SARS-CoV-2 variants has transitioned from long-term dominance of a successful variant to a dynamic swarm of genetically related sublineages, carrying convergent aminoacidic mutations in the spike region. Aim of this work was to quantify the neutralizing antibodies (NtAb) titre against the recently predominant omicron sublineages BA.2.75.2, BQ.1.1, XBB.1 and CH.1.1 in a fragile population naïve for SARS-COV-2 infection and vaccinated with four doses of monovalent BNT162b2 COVID-19 mRNA vaccine.

Materials and Methods: Plasma samples were collected from 40 residents at Pio Albergo Trivulzio, the largest Italian long-term care facility, 71 [68-75] and 89 [80-91] median [IQR] days after the third (T3) and fourth (T4) BNT162b2 vaccine dose. The study group (91 [84-94] years, 5 males) had negative anti-nucleocapsid serology at first vaccine dose and was weekly screened by swab analysis to exclude subsequently SARS-CoV-2 infection. NtAb titers were measured at T3 and T4 against the wild type strain B.1 and at T4 against five Omicron sublineages (BA.5/BQ.1.1/BA.2.75.2/XBB.1/CH.1.1). Live virus microneutralization was performed in VERO E6 cells quantifying the cell viability by luminescence. The NtAb titer was defined as the reciprocal value of the sample dilution showing 50% protection of virus-induced cytopathic effect (ID50). SARS-CoV-2 IgG II Quant assay (Abbott) was used to quantify the anti-spike protein Ab at T3, T4 and after the first and the second vaccine dose (T1, T2).

Results: Prevalent comorbidities were dementia (59%), diabetes (31%), history of ictus (26%) or ischemic heart disease (23%). Thirty-four and 13 patients had at least 1 and 3 comorbidities respectively, and polypharmacy was common. NtAb titers to B.1 variant significantly increased ($p < 0.001$) at T4 (1094 [612-3252] ID50) with respect to T3 (518 [60-1515] ID50). A significant increase was also observed when comparing the anti-spike Ab median titers at T3 and T4 (9939 [4168-12,500] vs. 12,500 [6413-12,500], $p<0.001$). One patient never responded to the full vaccination cycle showing negative anti-spike Ab and NtAb titers at each time point analyzed. Overall, at T4 median NtAb titers to the B.1 strain correlated with those to each omicron variant ($p<0.001$ for all comparisons) but absolute values expressed as ID50 were significantly lower (B.1>BA.5>BA.2.75.2>BQ.1.1>XBB.1=CH.1.1; Figure 1). At each time point analyzed the anti-spike Ab and NtAb titers against B.1 and different variants, were not correlated to the different comorbidities when evaluated individually or stratified for increasing number ($p>0.05$).

Conclusions: In this elderly fragile population, circulating omicron sublineages BQ.1.1, BA.2.75.2, XBB.1 and CH.1.1 showed greater escape from monovalent BNT162b2 COVID-19 mRNA vaccine than the previously dominant BA.5 variant. It remains to be established whether the reduced NtAb titers still protect from incident infection with these and future variants.

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Inflammation: a major pathogenetic process

OC 13 EFFECTS OF CART ON RESIDUAL INFLAMMATION AND HIV RESERVOIRS IN PRIMARY AND CHRONIC HIV INFECTION

V. Bono[1], C. Tincati[1], M. Augello[1], R. Rovito[1], S. Rusconi[2], A. Gabrieli[2], S. Nozza[3], E. Bruzzesi[3], A. Gori[4], A. Calcagno[5], A. Giacomelli[6], G. Marchetti for the Inaction (Italian Network of Acute HIV Infection) Study Group

[1]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, [2]UOC Malattie Infettive, Ospedale Civile di Legnano, DIBIC, University of Milan, ASST Ovest Milanese, Legnano, [3]Vita-Salute San Raffaele University, Milan, [4]Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, [5]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin, [6]Clinic of Infectious Diseases, Department of Biomedical and Clinical Sciences, L. Sacco Hospital, University of Milan, Milan

Background: Inflammation during cART contributes to HIV persistence and is linked to the development of non-infectious comorbidities. While a greater decrease in HIV reservoirs is observed when starting cART in the acute stage of infection, little is known on the effect of early therapy on inflammation. We assessed inflammation and HIV DNA in HIV-infected subjects starting cART in primary HIV infection (PHI) and compared them to those introducing cART in chronic HIV (CHI).

Material and Methods: PHI individuals of the Italian Network of Acute HIV Infection (INACTION) cohort were studied prior to cART (T0), after 12 (T12) and 48 weeks (T48) of therapy and compared to those starting cART with high CD4+ T-cell counts in chronic HIV at T0 and T48 of treatment. Viro-immunologic parameters, HIV-DNA by Droplet Digital PCR (Biorad QX100), normalized to RPP30 reference gene and peripheral inflammation (sCD14, IL-4, IL-2, TNF-α, IFN-γ by ELISA and Luminex) were evaluated. Statistics: Friedman, Wilcoxon and Mann-Whitney tests.

Results: 55 PHI and 18 CHI individuals were included (Table1A). As expected, an increase of CD4 counts and CD4/CD8 ratio as well as a reduction of HIV-RNA was observed in both groups during cART (Table1B).

At T0, PHI and CHI displayed similar HIV DNA (Fig1A); a decrease of HIV-DNA during cART was observed in PHI (T0 vs T12: p=0.003; T12 vs T48: p=0.01; T0 vs T48: p<0.0001; Fig1A) yet not CHI (p=0.09; Fig1A) with a net result of lower HIV DNA in the former at T48 (p=0.007; Fig1A).

At T0, PHI displayed higher IL-4 (27.2pg/mL [19.8-42.7] vs 18.3pg/mL [11.5-28.1]; p=0.01) and IL-2 (5.8pg/mL [3.1-11] vs 2.5pg/mL [1.4-5.3]; p=0.0003) (Fig.2A-B) which decreased on cART reaching similar levels to those observed in CHI at T48 (IL-4: T0 27.2pg/mL [19.8-42.7], T48 15pg/mL [5.8-36.1], p=0.0004; IL-2: T0 5.8pg/mL [3.1-11], T48 3.4pg/mL [1.7-11.6], p=0.01). In contrast, no differences were observed in IFN-γ and TNF-α between groups, although at T48, PHI showed lower IFN-γ (0.5pg/mL [0-5] vs 4.9pg/mL [1.6-7.6]; p=0.01) and TNF-α than CHI (5pg/mL [3.5-7.6] vs 6.8pg/mL [5-9.5]; p=0.07) (Fig.2C-D). Of note, at T0, PHI showed lower sCD14 (1.6pg/mL [1.2-1.8] vs 2.8pg/mL [2.6-3.2]; p<0.0001), which further decreased on cART (T0 vs T48: 1.6pg/mL [1.2-1.8] vs 1.4pg/mL [1.2-1.6]; p=0.03); in CHI, cART had no effect on sCD14 levels (Fig.2E).

Conclusions: We show a decrease of HIV DNA in PHI, confirming the positive effect of early cART in reducing viral burden. Accordingly, the finding of lower sCD14 in PHI which further decreased on treatment, highlights the possible role of early cART in preventing microbial translocation-driven inflammation. In PHI, cART decreased cytokine levels and increased the CD4/CD8 ratio, yet did not account for significantly lower inflammation markers, with the exception of IFN-γ, in PHI than CHI. Our study suggests that even when started early in the course of infection, cART exerts only a partial control over inflammation.

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Inflammation: a major pathogenetic process

OC 14 SWITCHING TO DORAVIRINE REDUCES CHRONIC INFLAMMATION AMONG VIROLOGICALLY CONTROLLED PLWH: 48 WEEKS RESULTS FROM THE DORAGE COHORT

A. Lazzaro[1], R.A. Valia[1], G. Recchia[1], L. Battistini[1], S. Caruso[1], M. D'Amico[1], I. Mezzaroma[2], M. Falciano[1], C. Andreoni[1], C. Fimiani[1], L. Santinelli[1], L. Maddaloni[1], G. Bugani[1], G. Ceccarelli[1], C.M. Mastroianni[1], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Policlinico Umberto I of Rome, Rome, Italy, [2]Department of Translational and Precision Medicine; Sapienza University of Rome, AOU Policlinico Umberto I of Rome, Rome, Italy

Background: Doravirine (DOR) is a novel NNRTI with favourable resistance profile, high tolerability and low drug-drug interaction potential both for ARV-naïve and ARV-experienced PLWH. Nonetheless, whether DOR-based regimens might reduce the chronic immune activation/inflammation has not been fully addressed. Thus, we aimed to provide a real-life confirmation of the efficacy, safety and tolerability of DOR as a switching strategy among PLWH under virologic control and ongoing ARV; moreover, we assessed the effect of the switch to a DOR-based regimen on serum markers of chronic inflammation.

Materials and Methods: This was a longitudinal observational study on a real-life cohort of PLWH undergoing a therapeutic switch in conditions of virologic control (defined as HIV-RNA<50cp/ml) and ongoing ARV therapy, independently from the provenience ART regimen. Primary objective was the rate of virologic control at week 48 (w48) from the switch. Secondary objectives were to assess changes in immune, metabolic and inflammatory profile at w48; to describe safety and tolerability of DOR-based ARV regimens.

Baseline (BL) characteristics are described as median values ± interquartile range (IQR) or as simple frequencies (n) and percentages. Changes from baseline of continuous variables was assessed by the paired samples Wilcoxon test. All tests were two-sided and p-values (p) < 0.05 were considered statistically significant.

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Results: Overall, 150 PLWH were enrolled into the study. BL demographic, immunovirological and therapeutic data are shown in Figure 1.

Nineteen participants were discontinued from the study because of personal preference. A total of 131 PLWH completed the follow-up. Thus, the rate of virological control was 96.9% (127/131; CIs: 92.4% – 99.2%) in the per-protocol analysis, and in 84.7% (127/150; CIs: 77.9% – 90.0%) the intention-to-treat analysis.

After 48 weeks from the switch, we recorded a significant increase in both CD4+ (p<.001) and CD8+ (p .022), but not in CD4+/CD8+ (p 0.12); a significant decrease in serum fasting glucose (p .002), triglycerides (p. 0.003), total cholesterol levels (p .048), together with an increase in HDL cholesterol (p. 018); a significant slope in BMI (p .004). Interestingly, a subgroup of about 40 PLWH showed significant reduction in IL-6 (p .003) and PCR (p .036). No significant changes were detected for hepatic and renal profile.

Conclusions: DOR is an effective and safe choice for all PLWH, including those older than 50. The unexpected improvement in the markers of chronic inflammation warrants further study to investigate such promising immune modulatory effects.

Inflammation: a major pathogenetic process

OC 15 ANTIRETROVIRAL THERAPY PARTIALLY RESTORES PHENOTYPIC AND METABOLIC IMMUNOSENESCENCE FEATURES OF T CELLS IN HIV INFECTED INDIVIDUALS

B. Dallan[1], M. Campagnaro[1], E. Gallerani[1], D. Proietto[1], R. Cultrera[3], M. Libanore[4], L. Sighinolfi[4], F. Nicoli[1], A. Caputo[1], D. Segala[2]

[1]Laboratory of Biochemistry, Immunology and Microbiology (BIM), Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Ferrara, Italy, [2]Department of Translational Medicine, University of Ferrara, Italy Infectious Diseases Unit, Azienda Ospedaliero-Universitaria di Ferrara, Italy, [3]Department of Translational Medicine, University of Ferrara, Italy Infectious Diseases-Primary and Community Health Care Dept, Azienda Unità Sanitaria Locale di Ferrara, Italy, [4]Infectious Diseases Unit, Azienda Ospedaliero-Universitaria di Ferrara, Italy

Background: HIV causes premature ageing in infected individuals, hampering their immune system and increasing the risk of cardiovascular diseases. T cell phenotypes associated with HIV disease progression are indeed also described during the ageing process and include the expression of immune exhaustion and activation markers as well as the loss of naïve and the accumulation of late differentiated T cells. Studies in elderly subjects suggest that T cell senescence correlates with metabolic alterations observed at both the systemic and T cell levels. Advances in availability and effectiveness of ART has certainly prolonged life of HIV-infected individuals but senescence-associated problems occur at younger age even in ART-treated subjects. Biomarkers to monitor disease control and immunosenescence despite viral suppression are urgently needed. We identified measures of T cell metabolism/senescence as putative biomarkers.

Materials and Methods: We assessed activation and senescence features as the expression of activation (CD38, HLA-DR) and senescence (CD57) markers that has been analysed on CD4+ and CD8+ T cells. Metabolic properties as T cells lipid metabolism and mitochondrial functionality was evaluated on CD4+ and CD8+ T cells by means of fluorescent probes. All analyses were conducted on three different groups enrolled: 1. ART-treated HIV-infected adults (30-50 years old) on therapy since <5 years (n=19); 2. ART-treated HIV-infected adults (30-50 years old) on therapy since >10 years (n= 23); 3. healthy adults (30-50 years old) matched for age and sex with #1 and #2, (n= 21).

Results: We observed a comparable activation profile (CD38, HLA-DR) among CD4+ and CD8+ T cells from HIV-infected and healthy adults. Immunological restoration in ART-treated HIV-infected adults was also observed in T cell lipid metabolism, measured as fatty acid uptake (FA) and storage (NL), as well as glucose uptake (2-NBDG). However, despite ART-treatment, CD4+ and CD8+ T cells from HIV-infected subjects presented with altered mitochondrial functions, characterized as mitochondrial membrane potential (TMRM), a pattern previously associated with ageing. Indeed, features of HIV premature immunosenescence were observed also in higher CD57 expression among T cells from HIV-infected patients.

Conclusions: ART treatment restores immunological balance in T cells lipid metabolism and down-regulates abnormal basal T cells activation, both typical features of chronic inflammation. No restoration was detected on T cells mitochondrial functionality and CD57 expression whose detection may be used to monitor disease status and immunosenescence progression in ART-treated infected adults.

Inflammation: a major pathogenetic process

OC 16 HUMAN ENDOGENOUS RETROVIRUSES EXPRESSION CORRELATES WITH HIV RESERVOIR, LYMPHOCYTES ACTIVATION AND LOW CD4 COUNT IN VIROLOGICALLY SUPPRESSED PATIENTS

V. Petrone[1], R. Scutari[1], V. Malagnino[2,3], L. Piermatteo[1], M. Compagno[2,3], R. Salpini[1], E. Teti[2,3], M. Iannetta[2,3], A. Minutolo[1], M.M. Santoro[1], V. Svicher[1], M. Andreoni[2,3], Balestrieri[1], L. Sarmati[2,3], F. Ceccherini-Silberstein[1], S. Grelli[1,4], C. Matteucci[1]

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Italy, [2]Department of Systems Medicine, University of Rome Tor Vergata, Italy, [3]Infectious Diseases Clinic, Policlinic of Tor Vergata, Rome, Italy, [4]Virology Unit, Policlinic of Tor Vergata, Rome, Italy

Background: In the context of the long-term therapy in virologically suppressed HIV-1+ patients, the identification of new biomarkers associated with viro-immunological discordance and the risk of disease progression is needed. Human endogenous retroviruses (HERVs) are relics of ancestral exogenous retroviral infections and comprise 8% of the human genome. HERVs have been co-opted in physiological roles, but could be reactivated by exogenous viruses including HIV-1. We aimed to investigate HERVs expression in association with viro-immunological parameters for the identification of novel markers for the clinical monitoring of virologically suppressed HIV-1+ patients towards a personalized approach.

Material and methods: 40 HIV-1+ viral suppressed patients (HIV RNA<20cp/mL; CD4>400 cell/mm3) and 10 Healthy Donors (HD) were enrolled. Blood HIV-DNA levels and residual plasma viremia were quantified by droplet digital-PCR system (Biorad). The expression of the env gene of two elements of the HERV-K HML-2 group (HERV-K113 and HERV-K111), of pHERV-W, HERV-W Syncitin-1 (SYN-1) and HERV-H have been analysed by RT-Real time PCR. The immunophenotyping have been evaluated by flow cytometry. The non-parametric Mann-Whitney test and the Spearman Correlation analysis were used for statistical analysis.

Results: At HIV-1 diagnosis, viremia was 4.7 (4.3-5) Log10cps/mL and CD4+ were 469 (299-627) cells/μL; 27 (67.5%) patients had HIV-1 B subtype. At the study enrolment, median (IQR) CD4+ was 720 (583-1041) cells/μL and residual viremia was 3 (2-6) cps/mL. All patients were on 2 NRTI-regimen with a 3rd drug (20 INSTI, 15 NNRTI, 5 PI). The relative expression of pHERV-W, HERV-K113 and HERV-K111 was significantly higher in patients compared to HD ($p \leq 0.001$). Interestingly, the expression of HERVs directly correlated with HIV-DNA (HERV-K113: Rho=0.534, $p<0.010$; HERV-K111: Rho=0.706, $p<0.010$; SYN-1: Rho=0.623, $p<0.010$). Moreover, an inverse correlation was found between HERV-K111 and CD4 NADIR (Rho= -0.366, $p<0.050$), and HERV-K113 with absolute CD4 count at collection (Rho= -0.421, $p<0.050$). HIV-DNA values correlated directly with the percentage of CD8 T cells expressing the activation marker CD38 (CD8+CD38+) (Rho= 0.400; p=0.026). A significant direct correlation between CD8+CD38+ and HERV-K113 (Rho=0.526, $p<0.010$), HERV-K111 (Rho=0.513, $p<0.010$) and SYN-1 (Rho=0.403, $p<0.050$) was found. Activated B lymphocytes (CD19+CD38+) were also found to be positively correlated with pHERV-W (Rho=0.580, $p<0.010$), HERV-K113 (Rho=0.418, $p<0.050$) and HERV-K111 (Rho=0.382, $p<0.010$).

Conclusions: The analysis reveals a dynamic correlation between HERVs, HIV reservoir and lymphocytes activation. The correlation of HERVs with CD8+T and B lymphocytes activation provides new information on the involvement in modulating the immune response during HIV infection, potentially leading to new prognostic markers to monitor virologically suppressed patients. (Funded by Gilead Fellowship Program 2019)

Outcome in first-line regimens

OC 17 EFFECTIVENESS OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) IN REAL-WORLD SETTING IN ART-NAIVE PATIENTS: DATA FROM THE ICONA COHORT

A. Tavelli[1], G. Marchetti[2], A. Vergori[3], E. Quiros Roldan[4], V. Malagnino[5], F. Vichi[6], M. Lichtner[7], S. Nozza[8], R. Rossotti[9], L. Sarmati[5], F. Bai[2], A. Di Biagio[10], A. Antinori[3], A. d'Arminio Monforte[1] for the Icona Foundation Study Group

[1]Icona Foundation, Milan, Italy, [2]Department of Health Sciences, Unit of Infectious Diseases, ASST Santi Paolo e Carlo, 'San Paolo' Hospital, University of Milan, Milan, Italy, [3]Clinical Department, HIV/AIDS Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Roma, Italy, [4]Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili of Brescia, Brescia, Italy, [5]Unit of Clinical Infectious Disease, Department of System Medicine, Tor Vergata University, Rome, Italy, [6]Infectious Diseases Unit I, Santa Maria Annunziata Hospital, Azienda USL Toscana Centro, Florence, Italy, [7]Infectious Diseases Unit, Santa Maria Goretti Hospital, Sapienza University of Rome, Latina, Italy, [8]Infectious Diseases Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy, [9]Department of Infectious Diseases Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [10]Ospedale Policlinico San Martino IRCCS, University of Genoa, Genoa, Italy

Background: Use of BIC/FTC/TAF is based on several pivotal trials, but long-term real-world data, especially addressed to key-populations are still lacking. The aim of this study is to evaluate the effectiveness of BIC/FTC/TAF in ART-naïve people living with HIV (PLWH) focusing on sex, older age, late presenters and PLWH with advanced HIV disease.

Methods: Observational study including ART-naïve PLWH from Icona cohort who started BIC/FTC/TAF for the first time from Jan-2106 to Dec-2021. Primary endpoint: treatment failure 1 (TF1): virological failure (VF: 2 consecutive HIV-RNA >200 copies/ml or 1 >1000 copies/ml >6 months from initiation) or treatment discontinuation (TD) for any reason. Secondary endpoint: (i) treatment failure 2 (TF2): VF or TD only for toxicity/intolerance or for virological failure; (ii) VF ITT; (iii) VF OT.

Standard survival analysis (Kaplan–Meier curves and log-rank test) were used. Unadjusted and adjusted hazard ratios (HR) of the different endpoints were estimated by means of Cox regression models for the different exposure groups: ≥50 years old; female; late presenters (LP, CD4<350 cell/mm3 or AIDS) and advanced HIV disease (AD, CD4<200 cell/mm3 or AIDS). Sets of confounders were tailored for each of the exposure of interest.

Results: 416 ART-naïve included (17.5% female, 29.8% ≥50 years, 58.2% LP, 40.6% AD). Patients' characteristics are shown in Table1.

Over a median follow-up of 83.5 weeks (IQR 47.0-114.8), TF was observed in 81 PLWH (19.5%, 12 VF and 69 TD), TF2 in 34 (8.7%; 12 VF and 22 TD for toxicity or virological failure), VF OT in 12 (2.9%) and VF ITT analysis in 14 (4.0%) PLWH.

Reasons for TD: 16 toxicity/intolerance (3.8%), 25 simplification (6.0%), 6 virological failure (1.4%), 1 patient's decision (0.2%) and 21 other reasons for TD (2.2%). The estimated 96-week probability of TF1 by KM was 19.4% (95%CI 15.5-24.1). Probabilities of TF1, stratified by different subgroups and probabilities of TF2, VF ITT and VF OT are shown in Table2.

In the adjusted Cox regression models, only PLWH older than 50 years showed a higher risk of TF1 (vs <50 aHR=1.70, 95%CI 1.06-2.74). Also, according to the definition of TF2, the higher risk of failure was confirmed for the group >=50 years (vs. <50 yrs aHR=2.25, 95%CI 1.11-4.56). None of the other groups of interest had a higher risk of VF (Table 3).

Conclusions: BIC/FTC/TAF demonstrated high effectiveness in a real-world setting, including in immunosupressed PLWH (LP and AD). Overall, real-world data are similar to data from randomised trials showing an 88% efficacy at 96-weeks. In contrast to RCT data, PLWH older than 50 years had a higher risk of failure both, in the primary endpoint and in the alternative definition of failure (TF2). The reasons for such discordant results need to be further investigated.

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Outcome in first-line regimens

OC 18 EFFECTIVENESS OF FIRST-LINE LAMIVUDINE-DOLUTEGRAVIR (3TC-DTG) ANTIRETROVIRAL THERAPY (ART) IN PERSONS LIVING WITH HIV (PLWH): REAL-LIFE DATA FROM THE ICONA FOUNDATION COHORT

S. Lo Caputo[1], A. Cozzi-Lepri[2], R. Gagliardini[3], E. Schiaroli[4], G. Orofino[5], A. Vergori[3], F. Maggiolo[6], N. Gianotti[7], A. Castagna[8], A. Cingolani[9], A. Antinori[3], A. d'Arminio Monforte[10] for the Icona Foundation Study Group

[1]Clinic of Infectious Diseases, Department of Clinical and Surgical Sciences, University of Foggia, Foggia, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [3]Clinical and Research Department, National Institute for Infectious Diseases 'Lazzaro Spallanzani' IRCCS, Rome, Italy, [4]Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy, [5]Unit of Infectious Diseases, "Divisione A", Amedeo di Savoia Hospital, Torino, Italy, [6]UOC Infectious Diseases, ASST Papa Giovanni XXII, Bergamo, Italy, [7]Infectious Diseases Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy, [8]Infectious and Tropical Diseases Department, Vita-Salute San Raffaele University, Milan, Italy, [9]Infectious Diseases Unit, Fondazione Policlinico Universitario A.Gemelli IRCCS, Catholic University of the Sacred Heart, Rome, Italy, [10]Icona Foundation, Milan, Italy

Background: Week 96 data of the GEMINI-1 and GEMINI-2 trials showed that the efficacy of the 2-drug regimen (2DR) including 3TC-DTG is non-inferior to triple DTG-containing regimens as first-line therapy. However, concerns were expressed on the regimen efficacy in PLWH starting with CD4 counts <200/mm3. More in general, real-life long-term estimates of the effectiveness of first line treatment with 3TC-DTG are sparse.

Methods: We included PLWH enrolled in ICONA cohort who started first-line ART with 3TC-DTG. Primary endpoint: time to treatment failure (TF, i.e. time of the first of 2 consecutive viral load-VL>50 copies/mL after 6 months, or discontinuation of the regimen regardless of the reason). A sensitivity analysis was conducted in which only discontinuations due to toxicity/failure were counted as events. Main exposure of interest was CD4 count at ART initiation. We identified geographical location of attending site, age and HIV-RNA at ART initiation as time-fixed confounders. Participants' characteristics were compared according to CD4 count at ART initiation using non-parametric tests. Standard survival analysis by Kaplan-Meier curves and Cox regression model was used.

Results: A total of 281 PLWH started 3TC-DTG as first-line: 10.6% females, 27% born outside Italy, median CD4 458/mm3, 6% with CD4<200/mm3, 20.6% with HIV-RNA >100,000 copies/mL, only 2.0% with HIV-RNA >=500,000 copies/mL. PLWH with CD4<200/mm3 were more frequently males, older and with higher HIV-RNA copies (Table 1). Over a median follow-up of 19 months (IQR:3-30), 21 PLWH experienced TF (3 viral load>50 -of which 2 discontinuations- and other 18 discontinuations). Reported reasons for the latter were: allergic reactions (n=2), CNS toxicity (n=2), liver toxicity (n=1), switch to Long-acting regimens (n=2), patient's choice/simplification (n=5), other/unknown (n=4), lack of virological control (n=4). In the main analysis, the 2-year probability of TF was of 23% (00-46) in PLWH with CD4 <200/ mm3and 7.8% (3.7-11.9) in CD4>=200/mm3 (log-rank test p=0.04). This difference was attenuated after adjusting for age, HIV-RNA and geographical region (aRH=1.65 95% CI:0.42-6.48, p=0.47, Table2). In the sensitivity analysis including 12 true failure events, the 2 years estimate of the risk of TF was 4.0% (95% CI:1.4-6.7%). The results from the multivariable analysis showed an even larger aHR of TF according to CD4 count strata (>2-fold difference), although still with large uncertainty around the estimates (Table 2).

Conclusions: In our real-life setting, rate of TF of first line 3TC-DTG was even lower than that observed in randomized studies (<10% of individuals by 2 years, 4% in analysis excluding discontinuations for simplification). Also, after adjusting for potential confounders including HIV-RNA, we found little evidence that a CD4 count<200 cells/mm3 at ART initiation was associated with increased risk of TF, but longer follow-up is needed to obtain robust estimates.

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Outcome in first-line regimens

OC 19 BODY WEIGHT AND PLASMA LIPIDS CHANGES IN PERSON LIVING WITH HIV (PLWH) STARTING DOUBLE OR TRIPLE INSTI-BASED CART REGIMENS

F. Bai[1], M. Ponzano[2], F. Bovis[2], A. di Biagio[3], G. Guaraldi[4], A. Rodanò[5], C. Stingone[6], R. Marocco[7], D. Leoni[8], A. Cozzi-Lepri[9], A. d'Arminio Monforte[1], G. Marchetti[1]

[1]Clinic of Infectious Diseases, San Paolo Hospital, ASST Santi Paolo e Carlo, University of Milan, Milan, [2]Department of Health Sciences, University of Genoa, Genoa, [3]Infectious Diseases Unit, Ospedale Policlinico San Martino - IRCCS, Department of Health Sciences (DISSAL), University of Genoa, Genoa, [4]Department of Surgical, Medical, Dental and Morphological Sciences with Interest transplant, Oncological and Regenerative Medicine, University of Modena and Reggio Emilia, Modena, [5]Icona Foundation, [6]STI/HIV Unit, San Gallicano Dermatological Institute IRCCS, Rome, [7]Infectious Diseases Unit, SM Goretti Hospital, Sapienza University of Rome, Latina, [8]Infectious and Tropical Diseases Unit, Department of Medical Sciences, Padua University Hospital, Padua, [9]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, United Kingdom

Background: Data about associations between INSTI-based therapy, weight gain (WG) and lipids, as well as possible differences between dual and triple INSTI therapies are still limited. We aimed to compare WG and lipid modifications between first-line 3TC/DTG (2DR) vs FTC/TAF/BIC (3DR).

Material and Methods: Retrospective cohort study, including PLWH starting a 2DR or 3DR in ICONA (01/2016 -01/2023), having available weight measurements and/or plasma lipids at T0 (cART start) and T12 (12 +/-3 months after cART start). Patients who switched cART regimen during the first year were included; we excluded patients with lipid lowering therapy during study period. Linear regressions were fitted to compare T0-T12 WG and lipids change by 2DR vs 3DR, controlling for: (i) baseline weight/lipids; (ii) baseline weight/lipids and time fixed baseline variables (age, sex, mode of HIV transmission, CD4 count and log-transformed HIV-RNA at cART start, glycemia, hemoglobin, ALT, AST and hypertension); (iii) baseline weight/lipids and a propensity score (PS) adjustment. PS was calculated as a probability from a logistic regression that had 3DR vs 2DR as the dependent variable and the same variables as covariates. Logistic regression was also fitted to correlate BMI category change by 2DR vs 3DR, adjusted for the same confounders.

Results: During the study period, 164/472 (35%) patients started 2DR and 308 (65%) started 3DR. Patients who started 2DR were younger and showed higher CD4 counts and lower HIV-RNA, compared to 3DR; baseline weight, total cholesterol and LDL were higher in 2DR vs 3DR (Table 1). 3DR patients presented higher T0-T12 WG compared to 2DR, but the weight difference was lost after controlling for confounders and baseline characteristics [adjusted mean WG 2DR 3.18 (SD 10.35); 3DR 4.03 Kg (SD 5.26) Kg, Table 2]. Similarly, a higher proportion of normal weight 3DR patients became overweight (32% vs 15%), but no therapy effect on BMI category change was observed in multivariable analyses (Table 3/4). 3DR patients displayed a worse T0-T12 lipid profile and were characterized by a trend towards a higher LDL increase, also after adjustment for confounders and baseline parameters, without differences in the proportion of patients that reached T12 LDL ≥160 mg/dL (2DR 11/121, 9% vs 3DR 15/185, 8%); furthermore, no effect of 3DR vs 2DR was seen in total cholesterol/HDL ratio (Table 5).

Conclusions: PLWH starting 3DR showed higher WG after one year, compared with 2DR, but the association was largely attenuated after correction for baseline unbalanced characteristics. Despite proportion of patients who gained high LDL and total cholesterol/HDL ratio didn't differ between treatments after one year, LDL seems to increase more in patients starting 3DR, also in the weighted analyses, suggesting a possible effect of TAF on serum lipids that was independent of weight; future studies are needed to explore a possible effect of 2DR vs 3DR on cardiovascular risk and IMT.

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Outcome in first-line regimens

OC 20 HIV-DNA DECAY IN ART-NAÏVE PLWH STARTING DOLUTEGRAVIR PLUS LAMIVUDINE VS TRIPLE THERAPY: 48-WEEK RESULTS IN A REAL-LIFE SETTING

F. Lombardi[1,2], A. Sanfilippo[2], N. Bartolini[3], C. Paletti[3], I. Vicenti[3], P. Salvo[2], F. Lamanna[2], F. Saladini[3], A. Ciccullo[4], A. Borghetti[1], M. Zazzi[3], S. Di Giambenedetto[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma Italia, UOC malattie infettive, [2]Università Cattolica del Sacro Cuore, Roma Italia, Istituto di Clinica Malattie Infettive, [3]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [4]Unità di Malattie infettive, Ospedale San Salvatore, L'Aquila, Italia

Background: As an initial treatment strategy, dolutegravir (DTG) plus lamivudine (3TC) showed high efficacy and safety in people living with HIV (PLWH). However, data are lacking regarding the HIV-DNA decay in ART-naïve PLWH starting a DTG plus 3TC dual regimen. Aim of this work was to compare the HIV-DNA dynamics in a real-life setting of ART-naïve PLWH who start a triple regimen vs DTG+3TC dual regimen.

Methods: This prospective, longitudinal study enrolled participants who started either standard triple regimen with 2-NRTI backbone with an anchor drug (3-drug regimen group, 3DR), or dual regimen with DTG and 3TC either two-tablet (DTG 50mg plus 3TC 300mg once daily) or single-tablet regimen (2-drug regimen group, 2DR). We quantified the total blood-associated HIV-DNA by droplet digital PCR using a home-made protocol targeting the HIV-1 LTR region (detection limit: 32copies/106 leukocytes) at three time-points: before starting therapy (baseline, BL), at virological success (VS) (defined as the first HIV-RNA <50 copies/mL) and after one year (Week48, W48). Results were expressed as log10 HIV-DNA copies/106CD4. We used a GLM repeated measures ANOVA model to compare HIV-DNA levels over the study period within and between groups.

Results: We included 57 ART-naïve PLWH. Thirty participants started 3DR and 27 2DR: mostly males (84.2%), and Caucasians (82.1%), median age was 37 years (IQR 30-51). As compared to 3DR, participants in 2DR were younger (34 years, IQR 25-40 vs 40, IQR 35-52, p=0.012), with higher CD4 cell/mm3 (414, IQR 265-613 vs 232, IQR 71-511, p=0.008), and higher CD4/CD8 ratio (0.46, IQR 0.37-0.62 vs 0.25, IQR 0.12-0.46, p=0.003). No AIDS events were recorded in any group.

At BL, 2DR and 3DR groups displayed similar mean HIV-RNA [4.57 (4.24-4.90) and 4.87 (4.38-5.37) log10 copies/mL (p=0.298)] and HIV-DNA levels [3.83 (3.57-4.08) and 4.12 (3.65-4.59) log10 HIV-DNA copies/106CD4, p=0.283]; overall, BL HIV-DNA and pre-treatment HIV-RNA were correlated (r=0.530, p<0.001).

Median time to reach VS was similar between groups (2DR: 49 days, IQR 27-130 vs 3DR: 76, IQR 26-119, p=0.699). The frequency of participants with undetectable HIV-RNA was comparable between groups, about 60% at VS and 90% at W48 (p values 0.437 and 0.265, respectively). Whereas CD4 counts and CD4/CD8 ratio remained markedly higher in the 2DR group at VS (p values 0.011 and 0.015) and W48 (p values 0.008 and <0.001). Overall, a statistically significant reduction of HIV-DNA levels over 48 weeks was observed in both groups (both p values <0.001), with trends comparable between groups (p=0.385) (Figure 1).

Conclusions: In this clinical practice setting, treatment-naive PLWH who start either dual regimen or triple standard therapy showed a similar marked decay in HIV-DNA at both VS and after 48 weeks. Our results add important new data that support the effectiveness of the dual therapy approach on the cellular reservoir, which needs to be confirmed in larger cohorts.

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One size does not fit all

OC 21 SEXUAL AND REPRODUCTIVE UNMET CLINICAL NEEDS IN ITALIAN WOMEN LIVING WITH HIV: RESULTS FROM MARILYN STUDY

G.V. Calvino[1], M. Errico[2], A. Tavelli[3], M.L. Cosmaro[4], A. Perziano[5], A. Bove[6], L. Taramasso[7], I. Mastrorosa[8], M. Di Gaetano[9], M. Ferrara[10], M. Cernuschi[11], M. Lichtner[12], A.d'Arminio Monforte[3], A. Cingolani[13] for Icona Foundation Study Group

[1]Anlaids Onlus-ETS, Rome, Italy, [2]Network Persone Sieropositive Italia APS, Milan, Italy, [3]Icona Foundation, Milan, Italy, [4]Fondazione LILA Milano, Milan, Italy, [5]Associazione Arcobaleno AIDS ODV, Turin, Italy, [6]Circolo di Cultura Omosessuale "Mario Mieli", Rome, Italy, [7]Infectious Diseases Clinic, Policlinico San Martino Hospital, Genoa, Italy, [8]Clinical and Research Department, National Institute for Infectious Diseases 'Lazzaro Spallanzani' IRCCS, Rome, Italy, [9]Department of Infectious Diseases, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy, [10]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy, [11]Associazione Solidarietà AIDS ODV, Milan, Italy, [12]Infectious Diseases Unit, SM Goretti Hospital, Sapienza University of Rome, Latina, Italy, [13]Infectious Diseases Unit, Fondazione Policlinico Universitario A.Gemelli IRCCS, Catholic University of the Sacred Heart, Rome, Italy

Background: Women living with HIV (WLWH) face a unique variety of obstacles in their life and health-care journey with HIV : fear of disclosure, stigma-related and mental-related issues, sexual health management etc. Despite that, WLWH have been under-represented in many areas of HIV clinical research; therefore socio-structural barriers leading to gender-related health inequities still persist. Marilyn, a study promoted by Icona Foundation and community-based organizations, investigated for the first time the unmet needs of women living with HIV in Italy.

Methods: An anonymous nationwide web survey created by the Icona Community Advisory Board (CAB) was promoted by the clinical centers adhering to the Icona network and by Community websites and social media. The survey included 73 questions exploring several aspects such as socio-demographic characteristics (household composition and economic conditions), HIV-related health data, information on HIV disclosure, perceptions of stigma and self-stigma, and other female specific health aspect among which pregnancy, menopause, contraception and screening for cancer. The online RedCap survey was conducted from Jun2022 to March 2023.

Results: 210 women followed in 43 clinical centers of the Icona network and 11 other Italian infectious disease units participated to the survey. Median age is 52 (IQR 40-57); 33.5% were diagnosed in the last 10 years, 31.5% have a univerisity degree or equivalent. 21.1% plan to get pregnant and 40.3% initiated pregnancy after HIV diagnosis. They refer having received a less than acceptable medical (30%), psychological (13%) and social assistance (22%) respectively during pregnancy. 58.2% report being in menopause (median age of entry 49, IQR 47-52); 25% report depression soon after menopause, 68% refer not having received support from their clinical center with respect to menopause and 73.8% declare they have not received hormone replacement therapy. Only 18% received accurate informations regarding menopause and HIV. A total of 92% are using or have used contraceptives, 79.3% of them use condoms. 42.1% were advised to have periodic screenings for gynecological diseases, but only 26.3% received them at their HIV clinical center. Moreover, 46.9% felt they need more information on medications and body change, 32.4% on menopause, 23.4% on screenings, and 22.1% on gynecological conditions, while just 33.8% report to be sufficiently informed.

Conclusions: The Survey indicates that WLWH do not receive adequate support for their sexual health needs. These findings suggest (i) to continue investigation on the unexpressed and unmet needs of WLWH and (ii) to create HIV care pathways specifically designed for the female population and guidelines addressing menopause and its clinical management.

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One size does not fit all

OC 22 COVID PERCEPTIONS AMONG PREGNANT WOMEN LIVING IN A MALARIA HYPERENDEMIC RURAL REGION IN UGANDA: A CROSS-SECTIONAL STUDY

F.V. Segala[1], F. Di Gennaro[1], J. Ictho[2], M. L'Episcopia[3], E. Onapa[2], E. De Vita[1], R. Novara[1], N. Olung[4], V. Totaro[1], L. Olal[5], G. Patti[1], C. Bingom[2], U. Farina[6], R. Papagni[1], C. Agaro[7], J. Amone[4], G. Dall'Oglio[2], B. Ngole[5], C. Marotta[8], S. Okori[4], C. Severini[3], P. Lochoro[2], G. Putoto[8], A. Saracino[1]

[1]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy, [2]Doctors with Africa, CUAMM, Kampala, Uganda, [3]Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy, [4]St. John's XXIII Hospital Aber, Jaber, Uganda, [5]African Network for Change, Kampala, Uganda, [6]Hygiene Unit, Policlinico Riuniti Foggia Hospital, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy, [7]District Health Office, Oyam District Local Government, Loro, Uganda, [8]Operational Research Unit, Doctors with Africa CUAMM, Padua, Italy

Background: In Sub-Saharan malaria hyperendemic countries, COVID-19 poses a substantial challenge to health systems and community health. Indeed, although malaria and COVID-19 show an overlapping clinical presentation, they require a profoundly different approach in terms of community prevention, healthcare seeking and disease control. This challenge is particularly important for pregnant women, who are more vulnerable to both malaria and COVID-19 adverse clinical outcomes. So far, few studies have investigated the interplay between COVID-19 and malaria in terms of disease awareness in vulnerable population living in low-resourced communities, as well as the impact of dedicated educational programs. Aim of this study was to explore COVID-19 awareness among pregnant women living in a P. falciparum hyperendemic region in rural Uganda.

Methods: This cross-sectional, prospective study was conducted in one Hospital and two Health Centers (HC) in Lango region, Uganda, from 14th July, 2022, to 14th March, 2023. In Atipe and Aboke HC, dedicated COVID-19 meetings were organized during pandemic peaks. All pregnant women presenting to antenatal care visits were eligible for recruitment. Data about demographics, COVID-19 history and COVID-19 and malaria perceptions were collected by structured questionnaires using RedCap mobile app platform. Endpoint of the study was a context-specific COVID-19 knowledge score, which was developed with local community leaders, accounting for the most common disease misconceptions (Table 1). Association between study variables and good COVID-19 knowledge was assessed by chi-square and t-test, as appropriate, and variables found to be statistically significant were further explored in multivariate logistic regression analysis.

Results: As shown in Table 2, a total of 888 pregnant women were recruited, 719 (81%) in Aber Hospital, 97 (10.9%) in Aboke HC and 72 (8.1%) in Atipe HC. Median age was 24 (IQR 20-29) years, while 79% (n=704) attained only primary education and 66.6% (n=591) were employed in agriculture. SARS-CoV2 vaccination rate was 92%. In multivariate analysis (Table 3), variables associated with high COVID knowledge were presenting at antenatal care visit in Atipe HC (aOR 8.1, 95%CI 4.1 – 16.48), having attained at least upper secondary level of education (aOR 3.05, 95%CI 1.36 – 6.7), and having a previous good knowledge about malaria (aOR 1.76, 95%CI 1.21 – 2.56).

Conclusions: Among pregnant women living in rural Uganda, high COVID-19 awareness relies on the overall educational level and on active educational interventions. Among pregnant women living in P. falciparum endemic areas, good community-level malaria awareness might serve as a predictor for preparedness to future pandemics and emerging infectious diseases.

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One size does not fit all

OC 23 LIFE QUALITY AND PSYCHOLOGICAL HEALTH OF WOMEN LIVING WITH HIV: INSIGHT FROM A SINGLE CENTRE IN SASSARI, ITALY

A. Colpani[1], A. De Vito[1], C. Poggiu[1], F. Cherchi[1], A. Bitti[1], M.C. Meloni[1], B. Zauli[1], M. Fois[1], S. Bacciu[1], S. Ruiu[1], G. Moi[1], A. Nivoli[2], G. Madeddu[1], S. Babudieri[1]

[1]Unit of Infectious Diseases, Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy, [2]Psychiatric Unit, Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy

Background: The improvement of antiretroviral therapy(ART) has led to lengthening of life expectations of people with HIV(PWH). Several facets of PWH health must be carefully considered, including life quality and psychological health. Women living with HIV(WWH) can be even at higher risk of anxiety, depression and stress and can face worse life quality due to several aspects not yet entirely clarified. Several scores and questionnaires have been developed to screen psychological distress and life quality. We aimed to investigate this aspect among WWH attending our outpatient clinic.

Materials and Methods: We proposed a survey including the Depression anxiety stress scale(DASS-21), the Mini Sleep Quality test(MSQ), the quality of life assessment developed by WHO(WHOQOL), the EQ-5D scale and socio-demographic questions. The survey addressed all cisgender and transgender WWH, above 18 years old, attending the Unit of Infectious Diseases in Sassari. Additional data were retrieved from medical records. Logistic regression modelling was performed to determine factors associated with a low score in the different questionnaires. In addition, linear regression was performed to evaluate the correlation between WHOQOL and EQ-5D scales.

Results: Overall, 69 women were included. Characteristics of participants are reported in Table 1. Regarding DASS-21, few women reported concerning scoring, while more than half(65.2%) showed sleeping problems; in particular, 29(42%) had severe sleep problems. As for WHOQOL, considering a score<60/100 as poor, around one third reported poor scoring in the psychological, social, and environmental domains. Regarding sexual life, only 40.6% self-reported to be satisfied. From the logistic regression it appears that a poor sleep quality is significantly associated with lower score in the physical(p=0.002), psychological(p=0.003), and environmental domains (p=0.048); also, it is linked to a lower mean of the four domains at the WHOQOL(p=0.002). As for sexual life satisfaction, it is significantly associated with the physical(p=0.0035) and environmental domain(p=0.045) and with the mean score at the WHOQOL(p=0.004). On the other hand, no association between specific ART regimen and any domain examined has emerged. Regarding self-rate from 0-100 in the EQ-5D, the logistic regression reports a correlation with the score at each domain of the WHOQOL and with the MSQ score.

Conclusions: Our analysis shows that depression, anxiety, and stress are uncommon, while a poor quality of life is frequently reported, especially in the psychological, social, and environmental domains. Sleep quality and sexual life appear to be crucial determinants of quality of life. No association with specific antiretroviral regimens has emerged. However, this is a small sample size and a single centre experience. More attention should be dedicated to neuropsychological aspects of our patients and synergic strategies to improve life quality must be designed.

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One size does not fit all

OC 24 HIV IN PRISON SETTING: WHAT ABOUT INMATES? THE FOUR-YEARS EXPERIENCE INCLUDING SARS-COV2 PANDEMIC PERIOD IN FLORENCE

E. Salomoni[1], C. Tozzi[2], A. Gabbuti[1], L.G.Gragnoli[2], M. Pusceddu[2], M. Brogi[1], C.P. Rendo[3], M.A. Di Pietro[1]

[1]SOC Malattie Infettive I Firenze-Empoli, Azienda USL Toscana Centro, [2]SOS Infermieristica Firenze Nord-Ovest, Presidio Sanitario C.C. Sollicciano-Firenze, Azienda USL Toscana Centro, [3]SOC Salute in Carcere, Presidio Sanitario C.C. Sollicciano-Firenze, Azienda USL Toscana Centro

Background: Sollicciano Penitentiary Complex (SPC) is the most crowded prison of Tuscany Region, and the only one that holded both females and transgender women (TGW).
A service of Infectious Diseases specialistic visits is active 4-6 times a month.
Aim of the study was to describe the characteristics of all HIV patients in care at the Infectious Diseases Service in SCP from 2019 to 2022 (pre, during and post SARS-CoV2 pandemic), and to analyze the impact of imprisonment on viro-immunological assessment.
Material and Methods: All HIV patients who performed at least one specialistic visit from 1st January 2019 to 31st December 2022 were included in the study. HIV screening was offered to all new inmates. Demographic, imprisonment-related and HIV-related characteristics were collected (Table 1-2). We compared the viro-immunological inmates' features at the first detection from entrance with the last detection before release, or with the last available detection for the still imprisoned ones (Table 3).
Results: Sixty patients performed at least one visit: 31.7% females or TGW, median age 43.5 years, 48.3% foreigners, 28.4% with chronic hepatitis C, 3% with chronic hepatitis B, 25% exposed to Syphilis (Table 1). The 91.7% had a history of at least one previous incarceration, median lenght of current imprisonment was 259 days, 85% was released during the study period (Table 1). The 10% had first HIV positive diagnosis at imprisonment, 16.7% was naïve; in the study period 93.4% was on ART, initiation was missed in 6.6% of patients due to refusal or release. The 46.7% had an INSTI-based regimen, ART was switched during imprisonment in 25% of patients (Table 2). The median waiting period to perform the first viro-immunological assessment from the entrance was 19 days; at first detection 43.3% of patients had HIV-RNA > 200 cp/mL, median CD4/CD8 ratio 0.5, at the last detection 56.6% of patients had HIV-RNA < 20 cp/mL, median CD4/CD8 ratio 0.6% (Table 3).
Conclusions: HIV positive inmates of SCP were a difficult-to-treat population due to high rates of releases and reincarcerations and to a high percentage of foreigners and coinfections. Incarcerceration represented the moment of the first HIV positive diagnosis for a significant percentage ot patients. An organization based on a frequent access of the Infectious Diseases specialist that was maintained even during SARS-CoV2 pandemic, was essential and demonstrated a great impact on viral load improvement, that represents a major goal for a population returning to community.

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Early treatment for COVID-19

OC 25 INCIDENCE AND PREDICTORS OF CLINICAL PROGRESSION IN AN EARLY TREATED COVID-19 MULTICENTRIC COHORT OF AN ITALIAN REGION

V. Mazzotta[1,2], A. Cozzi Lepri[3], C. Del Borgo[4], S. Lanini[1], S. Meschi[1], S. Garattini[4], S. Rosati[1], V. Siciliano[5], A. Vergori[1], L. Coppola[6], A. Falletta[7], A. Carraro[4], G. Gramigna[1], A. Oliva[1], E. Matteini[5], A. Gasperin[4], G. Giannico[1], A. D'Abramo[1], R. Marocco[4], E. Milozzi[1], C. Cerva[1], F. Gavaruzzi[1], M. Rueca[1], C. Cimaglia[1], P. Piselli[1], E. Girardi[1], L. Sarmati[6], C. Mastroianni[7], M. Andreoni[6], M. Fantoni[5], F. Vaia[1], F. Maggi[1], E. Nicastri[1], M. Lichtner[4], A. Antinori[1]

[1]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]PhD course in Microbiology, Immunology, Infectious Diseases, and Transplants (MIMIT), University of Rome Tor Vergata, Rome, Italy, [3]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [4]Università La Sapienza Polo pontino, Latina, Italy, [5]Fondazione Universitaria Policlinico Agostino Gemelli, Rome, Italy, [6]University of Rome Tor Vergata, Rome, Italy, [7]Università La Sapienza Roma Italy

Background: Although the spread of vaccination and the lower pathogenicity of the current SARS-CoV-2 variants had drastically reduced the rate of COVID-19-related hospitalization/death, real-world evidence can help to identify categories still at risk of severe outcomes in order to tailor early treatment strategies.
Methods: Real-world evidence (RWE) study based on a large multi-center database including outpatients (pts) treated with monoclonal antibodies (mAbs) or antivirals for mild-to-moderate COVID-19 according to AIFA eligibility criteria from March 2021 to February 2023 in the Latium Region. The outcome was hospitalization due to severe COVID-19 or death by day 30 from treatment. We fitted a logistic regression analysis with this binary endpoint and 4 main exposures of interest measured at baseline: older age (>75 years old); vaccination status; calendar period corresponding to the main circulating variant of concern (VoC), and immunocompromised status. A separate model for each of these exposures, including a specific set of potential confounders, was fitted.
Results: 10,913 pts enrolled, female 46.4%, median age 69 yrs (IQR 57-79), unvaccinated 27%, previous infection 4.2%. Eligibility criteria were cardiovascular disease in 21.1%, cancer in 13.7%, immunocompromised status in 32.2%, COPD in 20.8%, neurological disorder in 8.5%, diabetes in 21.8%, renal impairment in 10%, and severe obesity in 19.6%. 4,045 (37%) pts were treated with mAbs and 6,868 (63%) with direct antiviral agents.
Prevalence according to calendar period is shown in Table 1A. The primary endpoint occurred in 134/10937 pts, with a day-30 incident risk of 1.2% (95% CI:1.0-1.4%). Tab.1B shows the unadjusted and adjusted odds ratios (OR) of hospitalization due to COVID-19 or death by day 30. After controlling for potential confounders, a higher risk was observed for older aged (OR 1.72; 95%CI 1.23-2.42), unvaccinated (1.91;1.17-3.11), and immunocompromised (1.68; 1.12-2.52). Using the "Delta period" as a reference, a decreased risk was observed across the periods when the various Omicron sublineages were circulating [BA.1 0.33 (0.21-0.52); BA.2 0.22 (0.12 -0.41); BA4/5 0.34 (0.19-0.61); BQ.1 0.53 (0.24-1.20)].
Conclusions: This RWE study confirmed the decrease in the risk of hospitalization/death across the calendar periods, consistent with data from the experimental arms of randomized studies. Despite the overall reduction observed during the Omicron waves, older aged, unvaccinated, and immunocompromised patients showed the highest risk of developing severe COVID-19, representing the most vulnerable categories on which to target future prevention and treatment approaches.

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Early treatment for COVID-19

OC 26 IMPACT OF ACTIVE AND PASSIVE SARS-COV-2 IMMUNIZATION ON CAR-T PATIENTS: AN ITALIAN EXPERIENCE

I. Pansini[1], F. Frondizi[2], E. Galli[3], A. Di Rocco[4], A. Cingolani[2,5], M. Di Palma[4], E. Metafuni[3], S. Hohaus[1,3], P. Chiusolo[1,3], A.P. Iori[4], S. Sica[1,3], M. Martelli[4], F. Sorà[1,3]

[1]Sezione di Ematologia, Dipartimento di Scienze Radiologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Rome (IT), [2]Dipartimento di Sicurezza e Bioetica, Università Cattolica del Sacro Cuore, Rome (IT), [3]Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome (IT), [4]Dipartimento di Medicina Traslazionale e di Precisione, Università di Roma Sapienza, Roma (IT), [5]Dipartimento di Scienze di Laboratorio e Infettivologiche, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome (IT)

Background: Since 2019 chimeric antigen receptor T-cells (CAR-T) became available for some relapsed/refractory B-cell malignancies, obtaining around 40% of persistent complete remission; this strategy requires complex logistics, including patient's referral, and lymphocyte collection and manipulation.
Pre-vaccine mortality among CAR-T patients who underwent SARS-CoV-2 infection stood at around 41%, while the overall mortality due to SARS-CoV-2 infection among patients treated with CAR-T stood at around 1.3%.
Patients and Methods: We valued clinical outcomes of CAR-T patients according to the availability of no, only active, or active and passive anti SARS-Cov-2 prophylaxis (ERA 1, 2, and 3, see Table 1).
Eighty-eight patients with aggressive B lymphomas or leukemias were eligible for CAR-T treatment from 2020 to December 2022 at the two CAR-T centers for adult patients in Lazio region (IT). In those patients, we considered the impact of prophylaxis in terms of time from referral to apheresis, time from apheresis to CAR-T infusion (vein-to vein), and cases of delayed or cancelled apheresis or infusions due to SARS-CoV-2 infections. Treatment efficacy outcomes were SARS-CoV-2 infections that occurred after CAR-T infusion and their related re-admissions or deaths.
We detected no differences among ERAs in the median time from referral to apheresis; indeed, we observed a trend for decreasing vein-to-vein time, as CAR-T cells were infused 66.5, 49, and 48.5 median days after apheresis in the three ERAs, respectively (p=0.096). SARS-CoV-2 infections influenced the CAR-T journey of 10/88 (11%) eligible patients: 1 delayed apheresis, 7 delayed CAR-T infusions, 2 deaths before infusion.
All 17 patients from ERA 1 alive at February 2021 subsequently received active immunization and 16 out of 36 alive patients from ERA 1 and 2 received passive prophylaxis with tixagevimab-cilgavimab after CAR-T infusion.
After CAR-T, at a median follow-up of 178 days, 31/86 (36%) patients experienced SARS-CoV-2 infection (8 cases of double infections for a total amount of 39 infections), with median time-to-infection of 201 days. In 21/39 (54%) cases SARS-CoV-2 infections received specific treatment, namely nirmatrelvir/ritonavir (n=8), remdesivir (n=7), paxlovid (n=2), remdesivir + paxlovid (n=2), molnupiravir (n=2), casirivimab/imdevimab (n=1), or tixagevimab/cilgavimab (n=1).
Only 4 cases required hospitalization and 1 patient died from SARS-CoV-2 pneumonia after CAR-T infusion, with concomitant progressive disease.
Conclusions: The 80% (69/86) of patients had received the highest available prophylaxis when CAR-T were administered. This aggressive prophylactic strategy, together with maximal available treatments, has lowered SARS-CoV-2 mortality among CAR-T treated patients, from 41% previously reported to 3% in our case series, suggesting the potentially fatal impact for SARS-CoV-2 being mainly reserved to patients who cannot be treated with CAR-T due to infection.

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Early treatment for COVID-19

OC 27 ORAL ANTIVIRALS AGAINST SARS-COV-2: A COMPARISON BETWEEN MOLNUPIRAVIR AND NIRMATRELVIR/RITONAVIR IN A REAL LIFE SETTING

N. Braccialarghe[1], R.A. Cavasio[1], D. Zaçe[1], L. Alborghetti[1], A. Cekrezi[1], A.C. Epifani[1], G. Montagnari[1], F. Nina[1], L. Coppola[2], M. Iannetta[1,2], L. Sarmati[1,2] and the Tor Vergata Hospital group

[1]Department of System Medicine Tor Vergata, University of Rome, Rome, Italy, [2]Infectious Disease Clinic, Policlinico Tor Vergata University Hospital, Rome, Italy

Background: After the massive vaccination campaigns for SARS-CoV-2 the risk of death and hospitalization has sensibly decreased. Despite being vaccinated, fragile patients can develop severe pneumonia if infected and are eligible for oral antiviral therapy to avoid hospitalization.

The lack of real-life studies about efficacy of Molnupiravir (M) has determined the suspension of its use in Europe in March 2023; Nirmatrelvir/Ritonavir (N/R) can still be prescribed but it presents major drug-drug interactions and needs renal adjustment.

The aim of this study is to compare the characteristics of two groups of patients who received M or N/R and the outcome of their SARS-CoV-2 infection.

Material and methods: We conducted a retrospective study including data from 602 outpatients who resulted positive for SARS-CoV-2 and were selected according to AIFA criteria to receive M or N/R in the Infectious Disease Clinic of the Tor Vergata Hospital from January 2022 to February 2023.

Results: Our cohort included 602 patients with a mean age of 69 years (SD ±14.9), 52% were males, 69% received M and 31% received N/R.

The group treated with N/R was younger with a mean age of 64 years (SD ±15.7), 52% were males and the most frequent risk factors were the presence of a primary or acquired immunodeficiency (39%), serious heart conditions (39%), active cancer (31%) and BMI ≥ 30 kg/m2 (20%). 51% of patients had at least two or more risk factors. 97% were vaccinated against SARS-CoV-2 and 80% resolved the infection without hospitalization and 20% of patients were lost at follow up.

Patients treated with M were older with a mean age of 71 years (SD ±14.0), 52% were males and the most frequent risk factors were the presence of a serious heart condition (74%), immunodeficiency (31%), active cancer (24%) and BMI ≥ 30 kg/m2 (22%). 62% of patients had at least two or more risk factors. Only 2% were not vaccinated, 94% were not hospitalized, 4% were lost at follow up and 4 patients died (mean age 83 years) with a positive nasopharyngeal swab (NPS) but in 3 of them the cause of death was not related to SARS-CoV-2 pneumonia, in 1 was unknown.

The mean time of negativization of the NPS was of 12.13 days (SD ±6.7) for patients treated with N/R, while patients treated with M had a mean time of negativization of 13.54 days (SD ±8.6).

Conclusions: Oral antivirals against SARS-CoV-2 are effective in reducing the risk of hospitalization and death in patients with risk factors.

N/R has major drug-drug interactions with chronic therapies for severe heart conditions, so the use of M is associated to older people with multiple comorbities.

The mean time of negativization of the NPS is longer in patients treated with M, but the outcome was favorable with both antivirals.

As the management of COVID-19 patients is evolving from a hospital setting to a home one, both M and N/R represent a valid treatment depending on comorbidities and chronic therapies.

Early treatment for COVID-19

OC 28 EFFICACY, TOLERABILITY AND PRESCRIBING CHOICE IN PATIENTS UNDERGOING EARLY THERAPY FOR COVID19: A SINGLE-CENTER 2-YEARS REAL LIFE EXPERIENCE

D. Di Trento[1], A. Gasperin[1], S. Garattini[1,2], A. Carraro[2], A. Grimaldi[1], S.G. De Maria[1], S. Corazza[1], G. Mancarella[1,2], F. Izzo[1], M. De Masi[2], B. Kertusha[2], A. Parente[1,2], T. Tieghi[2], P. Fabietti[2], C. Bortignon[1], O. D'Onofrio[1,2], G. Bagaglini[3], G. Bonanni[3], C. Del Borgo[2], M. Lichtner[1,2]

[1]Department of Public Health and Infectious Diseases, "La Sapienza" University, Rome, [2]Infectious Diseases Unit, SM Goretti Hospital Latina; 3 Pharmacy Service Unit, SM Goretti Hospital Latina

Background: During the pandemic emergency, the importance of early treatment for patients with underlying comorbidities became increasingly important. Nowadays, as reported by numerous studies in the literature, the two classes of drugs available, the neutralizing monoclonal antibodies (nMAbs) against SARS-CoV-2 and the antivirals (AV), have shown to have excellent efficacy in terms of reducing clinical progression and good tolerability by the patient, which is essential for adherence to treatment. An adequate evaluation of the patient remains fundamental in order to choose the best therapeutic option.

Materials and methods: Since March 2021, a dedicated service for prevention of severe COVID-19 disease was set up. Patients were enrolled after confirmation of a positive nasopharyngeal swab and the tailored therapy was chosen following the AIFA criteria, actual availability and considering VOC period. Data about clinical progression, hospitalization for pneumonia/ARDS and death (COVID or non-COVID related) were collected at 7, 14 and 30 days by telephone monitoring. The endpoint was defined as a composite outcome (hospitalization for pneumonia/ARDS and death for any cause). Comparison between groups was performed by chi square test or Mann Whitney t-test as appropriate. All tests were two-tailed, and a value of $p < .05$ was considered as statistically significant. Analyses were performed using Prism version v9.5.1.

Results: Until March 2023 a total of 6463 subjects were treated with nMAbs (1593; 24.6%) or antiviral (4870; 75.4%), 3878 (60.2%) of whom were female; median age was 68 years old (11-106); 2235 (35%) were vaccinated with one or more booster dose. At clinical evaluation, 184 subjects already presented COVID-19 pneumonia, so they were hospitalized and excluded from this analysis. Among patients with completed 30 days follow up (n=3691), 1850 (51%) were female, median age was 65 (51,5 -75,6) and rate of vaccination was 25%, as listed in table 1. At 30 days, 3598 patients (97.5%) were not hospitalized and did not have any clinical evolution; 10 patients (0,3%) died of non-COVID-19 related causes. 62 patients (1,6%) required hospitalization: 43 of them developed COVID related pneumonia, 4 ARDS, 10 died for any cause. Factors significantly related to clinical worsening was age (p value < 0.00001). No significant differences between treatments (nMabs and antivirals) were observed in terms of outcome.

Conclusions: The heterogeneity of the drugs available for the prevention of severe COVID19 infection represents a strength in patient management, offering the possibility of choosing the most suitable drug for the individual and being able to obtain similar outcomes from a clinical point of view, with significant containment of the progression of the disease. The follow up data is still ongoing but confirms the importance of an early treatment for high risk patient.

Clinical issues blinking to laboratory

OC 29 WEIGHT GAIN AND LOSS AND STABLE WEIGHT IN RELATION TO FAT AND LEAN MASS IN PWH

L. Taramasso[1], N. Barp[2], J. Milic[2], F. Bovis[1], F. Motta[2], G. Mancini[3], F. Medioli[2], J. Conti[2], M. Faltoni[2], G. Burastero[2], S. Volpi[2], M. Belli[2], A. Di Biagio[1], M. Bassetti[1], C. Mussini[2,3], G. Guaraldi[2,3]

[1]Infectious Disease Clinic, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [2]University of Modena and Reggio Emilia, Modena, Italy, [3]Infectious Diseases Unit, Policlinico di Modena, Università Degli Studi di Modena e Reggio Emilia, Modena, Italy

Background: Weight loss (WL) during ART has been associated with negative outcomes and mortality, but weight gain (WG) has been associated with poor metabolic health and obesity, thus either healthy WG and WL might be beneficial in different settings. The aim of this study was to investigate the impact of fat and lean mass on transitions from WG to WL and stable weight (WS) in people with HIV (PWH).

Methods: This was an observational longitudinal cohort study conducted at the multidisciplinary Modena HIV Metabolic Clinic, Italy, between January 2008 and 2021. Inclusion criteria was body composition assessment at each visit with DXA-derived appendicular skeletal muscle index (ASMI), trunk fat mass/height (m2) and visceral adipose tissue (VAT). People with cancers or active AIDS defining conditions were excluded. WG was defined as an increase of ≥ 5% body mass index (BMI), WL as a reduction of ≥ 5% and WS a change between -4.9 and +4.9%, each compared to BMI assessment at previous visit. A three-state continuous time homogeneous multi-state Markov model was used to evaluate body composition changes associated with state transitions (WL, WS and WG).

Results: 2620 PWH (71% males, median age 46.6 (±8) years) were included, contributing to 12.699 weight and body composition evaluation in a mean follow-up period of 6.27 (±4.05) years. People who experienced WL had 9% probability of continuing losing weight at subsequent visit, 69% of remaining WS and 23% of regain weight. People who were WS had 68% probability to remain stable, 8% to become WL and 15% to gain weight. Weight gainers had similar probability of WL (17%) or continuous WG (15%), while probability of WS was 68%. Their probability of subsequent WL was higher with higher protein intake (HR 1.6, 95%CI 1.03- 2.5), while the probability of becoming WS was favored by higher ASMI (aHR 1.1, 95%CI 1.04-1.2), physical activity (HR 1.1, 95%CI 1.01 -1.2) and protein intake (HR 1.6, 95%CI 1.3-2.0) and hampered by higher trunk fat (aHR 0.9, 95%CI 0.8-1.0) and smoking (HR 0.9 95%CI 0.8-1.0). Figure 1 depicts variables significantly associated with each weight state and weight transition.

Conclusions: Increase of ASMI may favor WS and prevent WG, suggesting the importance of physical activity and adequate protein intake on metabolic health. Anthropometric variables have less impact on WL.

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Clinical issues blinking to laboratory

OC 30 PREDICTING MAJOR CARDIOVASCULAR EVENTS IN PEOPLE LIVING WITH HIV: A PROSPECTIVE OBSERVATIONAL STUDY

E. Drappero, A. Bosio, M.C. Tettoni, M. Ferrara, F. Alladio, G. Accardo, S. Fantino, G. Trevisan, G. Di Perri, S. Bonora, A. Calcagno

Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino

Background: Despite significantly longer life expectancy People Living with HIV (PLHIV) on Highly Active Anti Retroviral Therapy (HAART) have a high burden of non infectious comorbidities. Major Cardiovascular Events (MACE) have a higher incidence in comparison to the general population (approximately 1.5 times higher). Given the poor prediction of cardiovascular risk (CVR) scores we aimed at estimating CVR in a cohort of prospectiveyl followed PLWH.

Material and Methods: From December 2012 to May 2018 patients were offered a screening visit and, after signing an informed consent, enrolled in a prospective cohort. A complete physical examination with cardiovascular screening tests and blood tests were performed. Patients were followed according to routine clinical practice until events or the last available visit. MACE included acute myocardial Infarction (AMI), unstable angina, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), stroke, heart failure, transient ischemic Attack (TIA) or death due to cardiovascular causes. Data are shown as average (± standard deviation). Event-free survival was assessed through Log-rank tests and Cox regression models.

Results: 320 participants were enrolled and 253 (79.1%) were male. At baseline average age was 50.3 years (±11.7) and CD4+ counts was 572 cells/mm3 (±280). HIV RNA was <50 copies/mL in 236 participants (73.8%) after an average of 15.5 (±7.1) years of treatment. FIB4 was >2.67 in 17 (5.6%).

Over a 7.1-year follow-up period we observed 12 MACE (5.28 per 1000 pts/years), mostly PCI (4, 33.3%) and CABG (3; 25%). Cardiovascular risk scores (ASCVD, DAD and CUORE) predicted MACE with a slightly better AUROC (0.722, p=0.013) for the CUORE risk score. Nt-proBNP and TMAO were not associated with MACE. Low HIV DNA was associated with a higher MACE incidence (HIV DNA <1.72 Log10 copies*106 PBMCs, Log-rank p=0.037) but it was inversely associated with treatment duration. After sensitivity analysis CUORE risk score (5% increase, aOR 1.70), PI use (aOR 9.59), FIB4 >2.67 (aOR 14.7) and treatment duration (5 year increase, aOR 0.48) were independent predictors of MACE.

Conclusions: In our cohort of middle aged PLWH, MACE incidence was 5.28 per 1000 persons*year. Besides CVR, PI use and advanced liver fibrosis were associated with CV events while longer treatment duration had a favorable effect.

Clinical issues blinking to laboratory

OC 31 LONG-TERM CD4+ CELLS RECOVERY IN PLWH ON ACTIVE ANTIRETROVIRAL TREATMENT

F. Maggiolo[1], L. Comi[1], D. Valenti[1,2], R. Teocchi[3], E. Di Filippo[1], S. Venturelli[1]

[1]UOC Infectious Diseases, [2]FROM foundation, [3]Informatics department, ASST Papa Giovanni XXII, Bergamo Italy

Background: In the era of potent antiretroviral therapy (ART), ongoing HIV replication is adequately suppressed to undetectable levels in appropriately treated individuals. However, up to 30% of ART–treated individuals fail to achieve CD4+ T cell counts to a normal level (> 500 cells/mcL). Most studies addressing CD4+ trajectories have, however, relatively short follow-ups. We explored CD4+ gains in PLWH treated for up to 40 years.
Methods: In this retrospective cohort study 2780 ART treated subjects were followed for up to 35 years. Immune recovery was defined as having the most recent CD4+ count > 500 cells/mcL. A probit model was applied to verify the impact of baseline and other variables on the immunologic outcome.
Results: They had a follow-up of (mean) 18 years (SD 10 years) but up to 40 years. Out of 2780 enrolled subjects, 25.8% were females and the overall median age was 53 years (IQR 45-59). Irrespective of the immunological picture at diagnosis, the median of last CD4+ counts was above 500 cells/mcL (figure panel A) although with significant differences (P < 0.0001) among groups. Median CD4+ was 666 cells/ mcL (IQR 425-917) for AIDS presenters, 659 (IQR 446-897) for PLWH with CD4+ < 200 cells/mcL, and 830 (IQR 651-1064), 927 (IQR 704 -1141) and 1109 (IQR 876-1368) for those with baseline CD4+ counts 200-349, 350-499 or ≥ 500, respectively. Despite this 413 (16.1%) PLWH showed a most recent CD4+ count < 500 cells/mcL and all groups contributed to this result. Several characteristics were associated with a reduced immune-reconstitution: advanced age (P = 0.001), male gender (P = 0.028), non- Italian ethnicity (P < 0.0001), risk factor for HIV (P = 0.011, lower baseline CD4+ (P < 0.0001), having at least a VL measure >200 copies/ml in the last 5 years (P<0.0001), having a concomitant neoplastic disease (P = 0.012) or cirrhosis (P < 0.0001). When entered in the multivariate probit model, however only the baseline CD4+ count, the Country of origin, the presence of a concomitant cirrhosis and having had, in the last 5 years a steady and complete suppression of HIV replication, retained a statistical significance (figure, panel B and panel C).
Conclusions: On the long run most PLWH effectively treated restore CD4+ T cell counts to a normal level. The proportion of subjects with an insufficient immunological response is about 16%. Beside the presence of concomitant diseases such an end-stage liver disease other factors significantly associated with the risk of insufficient immune-reconstitution appears to be closely related to antiretroviral therapy. A early diagnosis and therapy, to prevent pronounced immune-depression, the constant reinforcement of adherence, to prevent breakthroughs, the reduction of barriers to access to care, to include subjects of multiple ethnicities or to steadily engage difficult-to-treat subjects are the goals needed to improve the immunological outcome in all PLWH.

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Clinical issues blinking to laboratory

OC 32 A COMPREHENSIVE ANALYSIS OF TOTAL AND INTEGRATED HIV DNA, CD4 AND CD8 T CELL RESPONSE, AND SURVIVAL, QUIESCENCE, AND STEMNESS SIGNALING AT DIFFERENT STAGES OF HIV INFECTION

L. Santinelli[1], L. Maddaloni[1], Z. Michelini[2], M. Fracella[3], L. Sorrentino[3], M. Andreotti[2], G. Bugani[1], A. Lazzaro[1], F. Frasca[3], C. Lofaro[1], G. Antonelli[3], G. Ceccarelli[1], C. M. Mastroianni[1], C. Scagnolari[3], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, [2]National Center for Global Health, Istituto Superiore di Sanità, Rome, Italy, [3]Laboratory of Virology, Department of Molecular Medicine, affiliated to Istituto Pasteur Italia, Sapienza University, Rome

Background: The current inability to provide a cure for HIV infection despite ART is due to a persistent reservoir of latently infected CD4+ T cells harboring replication competent integrated HIV DNA. Recent evidence indicate that CD8+ T-cell-mediated cytotoxic but not cytolytic activity might play an important role in controlling HIV latency through the activation of survival, quiescence and stemness signaling pathways. Then, in order to provide insight into the relationship between CD8+ T cells and the establishment of latency, we analyzed total and integrated HIV DNA levels and assessed their relationship with the frequencies of CD4 and CD8 T cell activation, senescence, proliferation and WNT/β-catenin, TGF-β, BCL-2 and IFN-I pathways at different stages of HIV infection.
Methods: Blood samples were collected from PLWH ART naïve (n=15), ART treated for less (n=18) and longer (n=21) than 5 years and adults with HIV acquired from mother to child transmission (n=7). CD4+ and CD8+ T cell subsets (naïve, TCM and TEM), activation (CD38 and HLA-DR), senescence (PD-1) and proliferation (Ki-67) were evaluated by multiparametric flow cytometry. Total and integrated HIV-1 DNA (copies/10^6 PBMC) and mRNAs of WNT-1, β-catenin, SMAD2, SMAD3, SMAD4, GzmA, BCL2, IFNα, β and PKR were measured by Real Time PCR.
Results: ART naïve PLWH exhibited higher frequencies of CD38+HLA-DR+ CD8+ T cell subsets compared to treated PLWH and a total HIV DNA value of 274.4 (68.43-1970) copies/10^6 PBMC;among them, HIV-1 integrated DNA was detected in 72% of patients [44 (21.17-245.6) copies/10^6 PBMC]; although no differences were recorded between PLWH under ART for less and longer than 5 years regarding immune activation, senescence, and proliferation of CD8 T cells, in PLWH treated for less than 5 years the median of total HIV DNA was 409.3 (34.92-936.3) copies/10^6 PBMC (10.5% of cases < LD), while 37% of patients had detectable integrated HIV DNA [37.98 (20-101.6)]. PLWH treated for more than 5 years exhibited detectable total HIV-DNA among 90% of samples [183.8 (38.42-722.7) copies/10^6 PBMC], while among 43% of them integrated HIV DNA was not detected. Concerning vertical transmission group, only 1 patient had total HIV-DNA<50 copies/10^6 PBMC, but HIV-1 integrated DNA was undetectable in 33% of cases. However, both total and integrated HIV-DNA levels correlate with CD4+ and CD8+ T cells immune activation among all groups of PLWH ($p<0.05$). Also, higher levels of integrated HIV DNA were associated with higher mRNA expression of β-catenin, SMAD2, SMAD3, SMAD4, GzmA and BCL2 in CD4+ T cells and lower levels of WNT1 and IFNα, β and PKR in CD8+ T cells in treated PLWH, respectively.
Conclusion: Besides differences in immunophenotype and function of CD4+ and CD8+ T cells according viro-immunological status of PLWH, the association between integrated HIV-DNA levels and survival, quiescence and stemness pathways might significantly contribute to determining the HIV latency.

Viral infections old and new

OC 33 APRI AND FIB-4 SCORES PREDICT MORTALITY AND MORBIDITY IN HCV INFECTED SUBJECTS AFTER SUSTAINED VIROLOGIC RESPONSE OVER THE LONG-TERM

C. Costa, H. L. Morrone, B. Tassone, M.T. Tassone, G. Bruno, F. Valente, S. Rotundo, G. Marino, P. Fusco, A. Russo, E.M. Trecarichi, C. Torti

Department of Medical and Surgical Sciences, Chair of Infectious and Tropical Diseases, University "Magna Graecia", Catanzaro, Italy

Background: Current Direct Acting Antiviral (DAAs) treatments offer the unprecedented opportunity to significantly reduce HCV infection and related complications. Although Sustained Virologic Response (SVR) is associated with marked reduction of risk of hepatic and extrahepatic events, this risk is not eliminated by effective antiviral treatment. It would be crucial to predict the risk of clinical complications and death in patients undergoing SVR in order to tailor follow-up and treatment strategies. The aim of this prospective study is to evaluate whether APRI/FIB4 indexes are able to predict hepatic/extrahepatic events and death over long-term follow-up in patients who obtained SVR after DAA therapy.

Patients and Methods: Between March 1st, 2014 and September 30th, 2021, we enrolled all patients diagnosed with HCV infection who gained SVR defined as the undetectability of HCV-RNA in serum samples at 24 weeks from the end of therapy. Primary endpoints were hepatic (i.e. liver failure, hepatocellular carcinoma) and extrahepatic clinical events (i.e. bleeding oesophageal varices, hepatic encephalopathy, spontaneous bacterial peritonitis, other neoplasm, cardiovascular and cerebrovascular events). Secondary endpoint was death event. Statistical analysis was performed with IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). The values were expressed as frequencies or mean ± standard deviation. Event-free survival time analysis was conducted with log-rank test and Kaplan-Meier curves. Univariate and multivariable Cox regression analyses along with calculation of the Hazard Ratio (HR) was done to determine if liver cirrhosis (evaluated through APRI/FIB-4) could be an independent risk factor for event onset after 50 weeks.

Results: We followed 236 patients for a median of 4.16 years (84 subjects with liver cirrhosis and 152 subjects without liver cirrhosis). The analysis performed showed that, despite all patients having obtained SVR, 17.8% of the cohort studied developed at least one clinical event. The analysis of survival over the entire follow-up showed that the risk of developing hepatic and non-hepatic clinical events was significantly higher in patients with liver cirrhosis assessed using APRI and/or FIB-4 score (HR: 1.91, 95% CI 1.03-3.5; p=0.039). After adjusting for sex and comorbidities, estimated cirrhosis remained an independent predictor (HR: 1.94, 95% CI 1.04-3.60; p=0.036). Mortality was higher in the cirrhotic group as described by Kaplan Meier curves; the risk analysis showed a HR: 6.68 (p= 0.016) and this data was also confirmed by the multivariate analysis.

Conclusions: The results of our study show that cirrhosis assessed by APRI e FIB-4 score was predictive of risk of death and clinical manifestations in patients treated for HCV, suggesting their possible use in guiding and timing follow-up after SVR. These non-invasive, non-expensive prognostic scores could be especially useful in resource-limited settings.

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Viral infections old and new

OC 34 COMMON SEASONAL RESPIRATORY VIRAL INFECTIONS DURING NINE CONSECUTIVE SEASONS (2014 -2023), INCLUDING CORONAVIRUS DISEASE (COVID-19) PANDEMIC

I. Giberti[1], E. Costa[1], V. Ricucci[2], B. Galano[2], N. Nigro[2], G. Guarona[1,2], B. Bruzzone[2], A. Orsi[1,2], G. Icardi[1,2]

[1]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [2]Hygiene Laboratory Unit, IRCCS, Policlinico San Martino Hospital, Genoa, Italy

Background: This study aims to investigate the circulation of common pathogens recognized as etiological agents of acute respiratory infection (ARI) before and during the COVID-19 pandemic.

Materials and Methods: A retrospective single-centre study including admitted patients with acute respiratory infection (ARI) to IRCCS Ospedale Policlinico San Martino Genova (Italy) between October 1, 2014, and March 31, 2023 was performed.

Lower and upper respiratory tract specimens (nasal/oropharyngeal swabs, bronchoalveolar lavages and bronchial aspirates) were tested using the Allplex™ Respiratory Panel assays (Seegene Inc., South Korea) to detect 26 respiratory pathogens: Influenza A and B virus (Flu A and Flu B); Respiratory syncytial virus A and B (RSVA and RSVB); Adenovirus (AdV); Enterovirus (HEV); Metapneumovirus (MPV); Parainfluenza virus 1, 2, 3 and 4 (PIV1, PIV2, PIV3 and PIV4); Bocavirus 1, 2, 3 and 4 (HBoV); other Coronavirus (229E, NL63 and OC43); Human rhinovirus (HRV); Bordetella parapertussis (BPP); Bordetella pertussis (BP); Chlamydophila pneumoniae (CP); Haemophilus influenzae (HI); Legionella pneumophila (LP); Mycoplasma pneumoniae (MP) and Streptococcus pneumoniae (SP).

Results: Data from 16067 respiratory samples were analysed. In the pre-pandemic period, despite inter-seasonal differences, the number of samples was approximately 2000/season. In 2020-2021, this number was drastically reduced, with multiplex real-time PCR performed exclusively in non-Covid-19 patients hospitalized for acute respiratory disease. From the following season, the number of samples analysed returned to pre-pandemic levels.

Overall, in the period 2014-2023, 21.73% samples tested positive for at least a respiratory viral pathogen. Influenza viruses were the most frequently detected respiratory pathogens during the study period. The highest prevalences of Influenza A virus were found in 2016-2017 and 2018-2019 seasons (9.53% and 10.59% respectively), while an exceptional circulation of Influenza B virus was observed in the 2017-2018 season, reaching a prevalence of 8.17%.

During the first pandemic period (2020-2021), the circulation of both influenza viruses and other respiratory pathogens dropped out. The recovery of the circulation of influenza A and B viruses to pre-pandemic levels began with the discontinuation of non-pharmaceutical interventions against COVID-19 (after March 2021). Similarly, other viruses started to be isolated again, among which RSV stands out with a prevalence of type A in the 2021-2022 season (2.61%) and a total trend reversal with a prevalence of RSV-B in the current season (5%).

Conclusion: These data showed how the measures taken to manage the COVID-19 pandemic affected the circulation of the main respiratory pathogens in our setting.

This evidence, combined with continuous surveillance of ARI, could be a useful resource for planning effective preventive strategies in the event of new infectious threats.

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Viral infections old and new

OC 35 SEROPREVALENCE OF MONKEYPOX (MPX) IGG ANTIBODIES IN A COHORT OF PLWH IN ROME, DURING THE 2022 OUTBREAK

P.F. Salvo[1], D. Farinacci[2], R. Jo Steiner[1], V. Iannone[1], F. Lamanna[1], R.A. Passerotto[1], G. Placidi[3], A. Carbone[1], A. Borghetti[4], S. Di Giambenedetto[1,4], F. Lombardi[4]

[1]Dipartimento di Sicurezza e Bioetica, Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, [2]UOC Medicina Protetta - ASL Viterbo, Viterbo, [3]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, [4]UOC Malattie Infettive, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma

Background: In may 2022 one case of Monkeypox (MPX) virus infection was reported in UK. Since then, the number of cases have been increasing worldwide, outlining a new outbreak of MPX infection in non-endemic countries, with specific epidemiological and clinical characteristics. To date, 957 confirmed cases have been reported in Italy, the majority (410, 42.8%) in Lombardy.
Data from literature show that a small percentage of MPX infection could be asymptomatic. The aim of this study was to determine the proportion of people living with HIV (PLWH) with anti-MPX IgG antibodies in a sample from a single HIV referral center in Rome.
Materials and Methods: From October 2022 to February 2023 we serially collected serum sample from PLWH attending our outpatient clinic for their routine analysis. IgG against MPX have been assessed on stored cryopreserved serum samples with an enzyme-linked immunosorbent assay (ELISA). No significant cross-reactivity or interference between anti-MPX IgG and analogues were reported. For the purpose of this study, only people with no previous reported vaccine against smallpox nor previous clinical manifestations consistent with a MPX diagnosis were included.
Results: A total of 104 PLWH were tested. Nineteen participants reported a previous vaccination against smallpox and 1 participant reported a previous confirmed diagnosis of MPX infection. All the other 84 participants denied previous vaccination, infection or clinical manifestations consistent with a MPX infection. Men accounted for 81%, the median age was 43 (IQR 38–46) years, 66.7% were MSM. Median time since HIV diagnosis was 10 (IQR 6–14) years, the entire population was on antiretroviral treatment, with a median time of exposure to antiretroviral treatment of 9 (IQR 6–12) years. A previous AIDS-defining condition was present in 19 patients (22.6%). Our population had a median zenith of HIV-RNA of 5.04 (IQR 4.52 – 5.53) log10 cps/mL and a median nadir of CD4 cells count of 251 (102 – 409) cells/mmc.
Our analysis revealed a total of 6 patients who tested IgG positive for MPX. Seroprevalence was equal to 7.1%. Demographical and viro-immunological characteristics of the entire population and PLWH who tested IgG positive are shown in Table 1.
All of the positive patients were Caucasian male; 4 (66.7%) were MSM, 1 (16.7%) was heterosexual and 1 (16.7%) was a PWID. The median zenith of HIV-RNA was 4.85 (IQR 4.73–5.27) log10 cp/mL and median nadir of CD4 cells count was 60.5 (9.23–279.3) cells/mmc.
Conclusions: our findings from this setting showed a mildly high IgG MPX prevalence among PLWH with no previous clinical manifestations, suggesting the possibility of an asymptomatic course of the MPX virus infection. Therefore early detection and subsequent appropriate management of MPX infected people are of utmost importance for global public health.

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Viral infections old and new

OC 36 CASE SERIES OF MONKEYPOX IN A SEXUAL HEALTH CLINIC IN MILAN

G. Pozza[1], D. Moschese[1], A. Giacomelli[1], A. Chiesa[1], D. Mileto[2], G. Rizzardini[1], S. Antinori[1]

[1]Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [2]Clinical Microbiology, Virology and Bioemergency Diagnostics, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy

Background: As of 27 March 2023, a total of 86,724 laboratory confirmed cases including 112 deaths, have been reported. Since 13 May 2022, a high proportion of these cases have been reported from countries without previously documented mpox transmission. Transmission would appear to occur through contact during sexual intercourse, especially among MSM subjects. The primary objective of our study is to describe the clinical, epidemiological, and virological characteristics of mpox infection in the recent outbreak. Secondary objectives are to estimate healing time, estimate the incidence of complications, describe the reason and incidence of hospitalizations.

Material and Methods: Our study is a retrospective and prospective observational study. We include the confirmed cases of mpox infection carried out at the Luigi Sacco hospital in the period May-November 2022. Samples were collected from whole blood, oropharyngeal, skin or mucosal lesion, anal and urethral sites. virus detection by PCR at diagnosis (T0) and at 7 (T1), 14 (T2), 21 (T3), 28 (T4) days from the first sample. Data on the epidemiological, clinical and microbiological aspects of the infection were collected.

Results: A total of 87 subjects were diagnosed with mpox infection. The first diagnosis was performed on 24/05, the last on 01/10/2022. Of the 83 subjects only one was female. The median age was 39 years (IQR 34-44). The cases was MSM in 92.4%. 8 (9.6%) individuals reported having been vaccinated for smallpox. 37 (44.6%) subjects had HIV infection. In 18 (21.7%) cases mpox was accompanied by contextual diagnosis of at least one STI. The incubation period showed a median of 10 days (IQR 6-13). The symptoms lasted for a median of 25 days (IQR 18 -29). As regards the onset symptoms, 55% of cases the disease presented with mucocutaneous lesions, 45% with constitutional symptoms, 36% with fever and 24% with lymphadenopathy. The clinical manifestation was mild in 73 cases. All participants recovered from the disease. As regards lesions, 45 individuals (52.2%) showed lesions on the face and 9 (10.8%) in the oral cavity, 47 (56.6%) presented genital lesions, 35 (42.2%) anal lesions, in 18 (21.7%) on the palms of the hands and in 6 (7.2%) on the palms of the feet. 7 (8.4%) people were hospitalized for mpox infection. Fever occurred in 74.7% of cases, lasted an average of 4 days and started an average of 2 days after onset of the first symptom. The lymphadenopathy was reported in 56 subjects (67.5%) and began on average 3 days after onset of the first symptom.

Conclusions: From these elements we deduce the possibility of transmission during the close contact that occurs at the time of sexual intercourse is a typical aspect of the 2022 outbreak and the cohort we described is no exception: it is possible to hypothesize that there was a progressive adaptation of the mpox to the human species during repeated epidemics in an endemic area up to the definition of this new mode of transmission.

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Preferences limitations and long term outcomes

OC 37 REAL WORLD DATA ON PROS AND PHARMACOKINETICS IN PLWH STARTING LONG-ACTING INJECTABLE ANTIRETROVIRAL THERAPY (LAI-ART)

D. Tomasoni[1], L. Gazzola[1], R. Nardo[1], M. Sala[1], G. Brambilla[1], D. Cattaneo[2], T. Bini[1], G. Marchetti[1]

[1]Infectious Disease and Tropical Medicine, San Paolo University Hospital, Milan, [2]Unit of Clinical Pharmacology, L. Sacco University Hospital, Milan

Background: We hereby aim to describe safety, tolerability, and pharmacokinetic data in a small cohort of People Living With HIV (PLWH) switching to LAI-ART.

Materials and Methods: Since November 2022, we consecutively enrolled patients applying for LAI-ART with no prior virological failure, no documented INSTI or NNRTI-resistance, HBsAg negative and virologically suppressed for at least 6 months. Oral-lead in (OLI) was proposed to patients naive to INSTI or rilpivirine (RPV). Blood exams (CD4; HIV-RNA, biochemical) and metabolic parameters (BMI, waist-hip circumferences) were collected at baseline (Injection Visit 1, IV1) and at each following injection (IV2, IV3 etc.). At IV2 therapeutic drug monitoring (TDM) of RPV plasma levels was performed by chromatography. Tolerability and adverse events were collected by Perception of injection questionnaire (PIN) after 7 days from each injection. Treatment satisfaction was evaluated at IV1 and IV2 by HIV Treatment satisfaction questionnaire “status version” (HIVTSQs) and “change version” (HIVTSQc), respectively.

Results: Thirty-three patients underwent the first injection; clinical characteristics are shown in Table 1. High BMI was present in 10% of patients; historical genotype was unavailable in 40%; about 70% came from a dual INSTI-based therapy; oral lead-in was proposed in about half of the patients. In the subsequent follow-up, 25 patients reached the second injection and 9 patients the third one; with the limits of a short follow-up, no virological failure occurred, only two patients had viral blip at IV1, after OLI, not confirmed at further follow up. No toxicity at blood exams were evidenced at any follow-up time. The main symptom reported by PIN questionnaire was pain, followed by injection site reaction (ISR); both symptoms were mild or moderate, and judged very tolerable by 90% of patients (Figure 1). Nobody interrupted the treatment due to adverse event. Although patients applying for LAI-ART showed a high degree of satisfaction with their previous oral therapy (HIVTSQs 94%, IQR 87%-100%), after 4 weeks from switching to LAI-ART (IV2) all patients reported an improvement in treatment satisfaction (Figure 2 A and B). RPV plasma levels at IV2 were available in 15 patients: the median plasma level was 28 ng/mL (IQR 38 -19). Despite at IV2 5/15 (33%) had RPV plasma level below the threshold of 20 ng/mL, only one patient maintained RPV plasma level below 20 ng/mL at IV3. No correlation between BMI and RPV plasma levels was observed.

Conclusions: In our experience the introduction of LAI-ART has been appreciated by patients as a new opportunity, and well tolerated, with no evidence of toxicity. Despite a high prevalence of mild pain and injection site reaction, patients reported great improvement in treatment satisfaction.

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Preferences limitations and long term outcomes

OC 38 PERCEIVED HEALTH DISCRIMINATION AND NORMATIVE STIGMA: HEALTH CONSEQUENCES IN A COHORT OF PEOPLE LIVING WITH HIV

V. Massaroni[1], V. Iannone[1,2], V. Delle Donne[1], A. D'Angelillo[1,2], G. Baldin[2], R. Passerotto[1,2], F. Sangiorgi[1,2], R. Jo Steiner[1,2], E. Visconti[2], S. Di Giambenedetto[1,2], A. Ciccullo[3]

[1]Infectious Diseases Institute, Department of Safety and Bioethics, Catholic University of Sacred Heart, Rome, Italy, [2]UOC Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [3]UOC Infectious Diseases, Ospedale S. Salvatore, L'Aquila; Italy

Background: People living with HIV (PLWH) may have stigmatizing experiences within the family or social community, but also in a healthcare setting by healthcare providers. Discrimination in the healthcare setting may lead PLWH to drop out of their clinical care, with negative effects on their psychological wellbeing and with severe consequences on comorbidities prevention and treat. The aim of this study is to describe the stigmatizing situation in the healthcare setting experienced by a cohort of PLWH.

Material and Methods: Infectious disease physicians administered a 17-item anonymous questionnaire to 100 PLWH during outpatient visits. Exclusion criteria were age < 18 years and difficulties with the Italian language. Clinical data collected investigated an history of diabetes, dyslipidemia, hypertension, mental health issues and gynaecological issues. PLWH were asked whether they usually prefer that the HIV-related exemption not be indicated on prescriptions for specialist visits, whether they happened to reunite using the exemption by opting for a paid visit or to forgo specialists visits outside the infectious disease setting to avoid disclosing their HIV, and whether this affected their health. In addition, some vicarious stigma scale questions were administered to probe patients' perceptions of subjective stigmatizing experiences.

Results: Many of PLWH were male (67%) and aged 41 to 55 years (44%). In the past two years, 29% of patients reported that they had no specialist visits, while 19% had cardiology and gynaecology visits. Overall, 34% of PLWH always ask their infectious disease physician not to indicate their HIV-related exemption when they need a prescription for a specialist visit, while 36% of them always prefer a paid visit for fear of feeling stigmatized and when they can avoid specialist visits altogether. Moreover 26% of patients felt unwelcome because of HIV during a specialist medical visit. The biggest problems encountered by patients for avoiding specialist medical visits were dental problems (16%). Overall, 38% of PLWH sometimes heard stories of a healthcare provider not wanting to touch someone because of their HIV and of people being mistreated by hospital staff because of HIV. Furthermore, 32% of respondents sometimes heard stories of people being refused medical care or denied hospital services because of HIV and 35% of them sometimes heard stories of a health care provider speaking publicly about a HIV patient.

Conclusions: In conclusion, our results suggest in our patients the presence of stigmatizing experience within the care setting. Stigma is an important variable to consider in the care of PLWH in order to build interventions to help healthcare providers know HIV disease and to allow the patient to access freely to clinical care setting. Patient interventions will also be needed to promote positive coping with their illness and to lead a reduction of comorbidities in clinical follow up.

Preferences limitations and long term outcomes

OC 39 OUTCOME OF TENOFOVIR AND INTEGRASE INHIBITORS-INCLUDING ART IN PLWH AND HBV: DATA FROM THE SCOLTA COHORT

L.A. Nicolini[1], B. Menzaghi[2], E. Ricci[3], N. Squillace[4], G.V. De Socio[5], P. Maggi[6], S. Piconi[7], G. Orofino[8], G. Madeddu[9], B.M. Celesia[10], G.F. Pellicanò[11], L. Valsecchi[12], E. Sarchi[13], F. Vichi[14], F. Lagi[15], K. Falasca[16], R. Gulminetti[17], A. Bandera[18,19], L. Calza[20], P. Bonfanti[4,21], A. Di Biagio[1,21]

[1]Unit of Infectious Diseases, IRCCS Ospedale Policlinico San Martino, Genoa, Italy, [2]Unit of Infectious Diseases, ASST Della Valle Olona-Busto Arsizio (VA), Busto Arsizio, [3]Fondazione ASIA Onlus, Milan, Italy, [4]Unit of Infectious Diseases, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [5]Unit of Infectious Diseases, Department of Medicine, Azienda Ospedaliera di Perugia, Santa Maria Hospital, Perugia, [6]Infectious and Tropical Diseases Clinic, AORN Sant'Anna and San Sebastiano, Caserta, Italy, [7]Infectious Diseases, Azienda Ospedaliera di Lecco, Lecco, Italy, [8]Unit of Infectious Diseases, "Divisione A", Amedeo di Savoia Hospital, Torino, Italy, [9]Unit of Infectious Diseases, Department of Medicine, Surgery and Pharmacy, University of Sassari, Italy, [10]Unit of Infectious Diseases, University of Catania, Catania, Italy, [11]Department of Human Pathology of the Adult and the Developmental Age 'G. Barresi', Unit of Infectious Diseases, University of Messina, [12]Infectious Disease Unit (I Division), ASST Fatebenefratelli Sacco, Milan, Italy, [13]Infectious Diseases Unit, SS. Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy, [14]Infectious Diseases Unit, Santa Maria Annunziata Hospital, Bagno a Ripoli, Florence, Italy, [15]SOD Malattie Infettive e Tropicali AOU Careggi, Florence, Italy, [16]Clinic of Infectious Diseases, Department of Medicine and Science of Aging, University 'G. d'Annunzio' Chieti-Pescara, Chieti, Italy,[17]Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia Italy, [18]Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy, [19]Department of Pathophysiology and Transplantation, University of Milano, Milan, Italy, [20]Unit of Infectious Diseases; Unit of Microbiology; and Hospital Pharmacy, S. Orsola Hospital, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, [21]University of Milano-Bicocca, Milan, Italy, [22]Department of Health Science (Dissal), University of Genoa, Genoa, Italy

Background: HBV infection in people living with HIV (PLWH), has been reported to negatively impact on CD4-T cell count recovery during antiretroviral treatment (ART). According to current guidelines, PLWH coinfected with HBV should receive tenofovir disoproxil (TDF) or tenofovir alafenamide (TAF) including ART unless history of tenofovir intolerance. In the present study, we aimed to evaluate effectiveness, safety and durability of tenofovir and integrase inhibitor-including ART in HBsAg positive PLWH.

Methods: Consecutive PLWH enrolled in an integrase inhibitor (TAF/emtricitabine/bictegravir, TDF/emtricitabine/elvitegravir/cobicistat or dolutegravir) cohort in the SCOLTA project, on a TDF or TAF-based regimen, were included if at least a follow-up visit was recorded. The CD4-T cell count recovery and HIV virological success were evaluated according to HBsAg status up to 3 years of follow-up. Categorical variables were compared using the Chi-square test, and continuous variables by Anova or Mann-Whitney test as appropriate.

Results: Of 1050 evaluated PLWH, 79 (7.52%) were HBsAg positive. See Table 1 for patients' details at baseline. Of them, 48.1% were on TAF-based ART. HBsAg positive PLWH were older (49.8±9.3 vs 46.4±11.9 years, p<0.015), more frequently males (93.7% vs 75.2%, p<0.0001) and affected by metabolic syndrome (42.9% vs 33.4%, p=0.041) and/or diabetes mellitus (19.1% vs 4.6%, p=0.025) than HBsAg negative. Although not statistically significant, less HBsAg positive PLWH were previously ART naïve (21.5% vs 27.4%, p=0.058). The median duration of ART before study inclusion was similar between groups (4.8, IQR 0.9-15.2, vs. 4.2, IQR 0-13.3, years, p=0.17).

Durability of tenofovir and integrase inhibitor-including ART was similar in HBsAg positive and negative PLWH (median 33, IQR 20-40, vs 26, IQR 14-36, months, p at log-rank 0.86). In spite of similar baseline CD4-T cell count, CD4-T cell recovery was slightly lower in HBsAg positive PLWH, even if not statistically significant (Figure 1). On-treatment HIV virological suppression rates did not differ according to HBsAg status in ART naïve (p=0.22) and previously experienced PLWH (p=0.096 and p=0.13 for PLWH with baseline detectable and undetectable HIV-RNA, respectively).

HIV viral suppression rates in PLWH with previously detectable HIV-RNA did not differ between groups (p at log-rank 0.53) (Figure 2). During the study period, 4 (5%) HBsAg positive and 65 (6.7%) HBsAg negative PLWH changed ART for side effects (p=0.75).

Discussion: HIV virological suppression, durability and safety of tenofovir and integrase inhibitor-including ART seem to be not affected by chronic HBV infection. Although slightly lower, CD4-T cell count recovery was not statistically different between groups.

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Preferences limitations and long term outcomes

OC 40 MISSING DATA GENERATE MISSING OPPORTUNITIES: FRAILTY PHENOTYPE ASSESSMENT IN THE GEPPO COHORT

E. Focà[1], S. Arsuffi[1], S. Calza[2], J. Milic[3], C. Mussi[4], A. Marengoni[5], M. Ferrara[6], B.M. Celesia[7], G. Madeddu[8], A.M. Cattelan[9], G. Di Perri[6], A. Calcagno[6], G. Guaraldi[3]

[1]Department of Clincal and Experimental Sciences, Unit of Infectious Diseases, University of Brescia and Spedali Civili Hospital, Brescia, Italy, [2]Unit of Biostatistics and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy, [3]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, [4]Department of Biomedical, Metabolic and Neural Sciences, Center for Gerontological Evaluation and Research, University of Modena and Reggio Emilia, Modena, Italy, [5]Department of Clincal and Experimental Sciences, Unit of Geriatrics, University of Brescia and Spedali Civili Hospital, Brescia, Italy, [6]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy, [7]Division of Infectious Diseases, ARNAS Garibaldi, Catania, Italy, [8]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Science, University of Sassari, Sassari, Italy, [9]Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, Italy

Background: The clinical importance of diagnosing frailty in older people living with HIV (OPWH) relates to it being an independent risk factor for developing new co-morbidities, falls, cognitive decline, polypharmacy, hospitalization, loss of independence and increased mortality.
The objective of this study was to highlight the missing data in frailty evaluation in OPWH aged >65 years included in the GEPPO cohort. Secondary objective was to describe clinical characteristics of OPWH according to phenotype classification.
Methods: This was a cross sectional study including all clinical assessment of OPWH in the GEPPO cohort.
Frailty was operationalized in the frailty phenotype (FP) tool, which objectively assesses five specific parameters: self-reported weight loss, self-reported exhaustion, low levels of physical activity as measured by a standardized questionnaire, measured 15 feet walk time, and measured grip strength. The presence of 3 or more factors defines frailty, with 1-2 denoting a pre-frail state and the absence of any being considered as non-frail.
The subjects were divided into two groups: fit and pre-frail/frail and clinical and HIV characteristic were analysed.
Results: 5842 clinical evaluations were analysed out of 1945 OPWH. 266 (4.6%) observations were classified as Fit phenotype and 933 (17%) as pre-frail/frail, having at least one positive FP criteria. 4583 (78.4%) it was not possible to evaluate FP. In detail: unintentional weight loss was missing in 4035 (69%) observations, low physical activity in 4249 (73%), exhaustion in 4392 (75%), grip strength in 4750 (81%) and gait speed in 4820 (83%).
146 OPWH were classified as fit and 551 as pre-frail/frail. Table 1 compares clinical and HIV characteristics of Fit vs pre-frail/frail OPWH. Interestingly, Pre-frail/fit phenotype was not associated with any single comorbidities, but rather with multimorbid and polypharmacy.
Conclusions: This study highlights difficulties in collecting frailty phenotype in both clinical and research setting.
Educational and clinical activities should be placed in the collection of all the 5 FP items.
Pre-frail/frail phenotype helps to identify OPWH with multimorbidity and polypharmacy who require dedicated interventions and resources.

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Immune response to viruses

OC 41 HUMORAL AND CELL-MEDIATED IMMUNITY AGAINST SARS-COV-2 IN DIALYSIS PATIENTS AFTER THE VACCINATION WITH MRNA-1273 AND BNT162B2 VACCINES

M. Tarkowski[1], N. Landriani[2], C. Costanza[1], C. Airaghi[2], E. Sabadini[3], R. Gingis[3], C. De Salvo[3], A. Gabrielli[1], M. Gallieni[1], A. Riva[1] *CoVICIS EU Horizon grant nr 101046041*

[1]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [2]L. Sacco Hospital, Milan, Italy, [3]Fattebenefratelli Hospital, Milan, Italy

Background: Patients requiring dialysis were recognized as one of the groups at high risk of contracting SARS-CoV-2 infection and to develop severe form of the disease. For that reason, they were included in the first line of people to receive vaccine against COVID-19. The protective efficacy of the vaccination in this group however remains of high concern. The goal of our study was to evaluate the humoral and cell-mediated immune response to SARS-CoV-2 vaccination in patients on dialysis.

Material and Methods: 99 patients attending the Nephrology Clinic in 2 hospitals in Milan requiring dialysis participated in the study. 57 men and 42 women at median age of 60 years were enrolled. They received 3 or 4 doses of anti-SARS-CoV-2 vaccine. IgG anti-SARS-CoV-2 levels were evaluated by multi-antigen Luminex kit. Cell mediated responses were measured by activation-induced markers test (AIM) in which PBMCs were stimulated with Spike BA.1 (BA.1-S) variant specific and the reference wild type Spike peptides (WT–refS1). The responses were evaluated by means of flowcytometry. The levels of IFN-g released during activation were measured by Luminex.

Results: In the studied group anti-SARS-CoV-2 IgG levels against spike S1 subunit and receptor binding domain (RBD) were significantly ($p<0,001$) increased after all doses of the vaccination in comparison to the pre-vaccination. Infection with SARS-COV-2 significantly augmented anti-SARS-CoV-2 IgG titers. In a group of 71 subjects without previous SARS-COV-2 infection, mRNA-1273 induced significantly higher in comparison to BNT162b2 vaccine. Steroid treatment did not significantly affect IgG anti-SARS-CoV-2 titers. Age was inversely correlated with anti-S1 IgG titers 3 months after the vaccination. Anti-RBD IgG titers at 30 days and 3 months after vaccination were significantly lower in those with diabetes. CD8 T cells responses to WT-refS1 were significantly augmented 30 days after 2nd dose of vaccination, correlated positively with released IFN-g levels. However, this effect was not observed in case of T cells stimulated with BA.1-S peptides at the same time. At 3 months after the 2nd dose of vaccination, CD8 T cell responses to WT-refS1 were still significantly higher than in pre-vaccination time and not significantly lower in comparison to 2 months earlier. A significant inverse correlation between the CD8 T cells response and age ($p=0.033$) was identified in vaccinated patients including those with previous infection.

Conclusions: Dialysis patients appear able to respond to the vaccination with a significant increase of the levels of anti-SARS-Cov-2 IgG and to develop cell mediated immunity. Age and diabetes may significantly, negatively, affect the immune responses in this group of patients. The cell mediated immunity after the vaccination is weak against SARS-CoV-2 omicron variants rendering this group vulnerable to the potential infection.

Immune response to viruses

OC 42 IMMUNE RESPONSE TRIGGERED BY A CANDIDATE VACCINE BASED ON A CLONE OF LEISHMANIA TARENTOLAE EXPRESSING THE SARS-COV-2 SPIKE PROTEIN

M. Garziano[1,2], I. Varotto-Boccazzi[3,4], C. Conforti[1], G.M. Cattaneo[3], M. Clerici[2,5], C. Vanetti[1], S. Epis[3,4], M. Biasin[1], C. Bandi[3,4], D. Trabattoni[1]

[1]Department of Biomedical and Clinical Sciences "L. Sacco", University of Milan, Milan, Italy, [2]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [3]Department of Biosciences, University of Milan, Milan, Italy, [4]Pediatric CRC 'Romeo ed Enrica Invernizzi', University of Milan, Milan, Italy, [5]IRCCS Fondazione don Carlo Gnocchi, Milan, Italy

Background: Leishmania tarentolae is regarded as a non-pathogenic species, already developed as a biofactory for protein production, and explored as a candidate vaccine or vaccine vehicle. Indeed, these microorganisms are characterized by their capacity to target macrophages and dendritic cells (DC) sand could thus be exploited for the delivery of antigens to immune cells. However, results on the type of immune polarization determined by L. tarentolae are still inconclusive.

Methods: DCs were derived from human monocytes and exposed to live non-engineered L. tarentolae P.10 strain (Lt-wt) as well as the same strain engineered for SARS-CoV-2 spike protein expression (Lt-spike). Then DCs were cultured with autologous lymphocytes to mime antigen presentation. We analyzed: 1) DC parasite internalization, 2) DC activation by the assayed strain, and 3) T lymphocyte polarization.

Results: Both L. Tarantolae strains were internalized by DCs triggering their full maturation, in terms of MHC class II and costimulatory molecule expression (CD80, CD83). In addition, Leishmania from both strains induced a Th1-like polarization profile, characterized by TNF-α, IL-6, IL-9, IFN-ɣ, MCP-1 production. Moreover, IL-12p70 release was higher in Lt-spike-stimulated DC supernatants while MIP and IP-10 secretion was enhanced following Lt-wt stimulation. In T-DC co-cultures, IFN-γ and IL-10 secretion were up- and down-regulated respectively suggesting a TH1 polarization outline.

Conclusion: Our data suggest that L. tarentolae behaves as a vaccine vehicle able to trigger DC activation and Th1 differentiation. This peculiar profile could be exploited in the setting up of vaccinal strategies to counteract viral infections.

Immune response to viruses

OC 43 SPECIFIC T-CELL RESPONSES TO VARICELLA ZOSTER VIRUS GLYCOPROTEIN E ARE ELICITED AFTER VACCINATION WITH A RECOMBINANT ADJUVANTED SUBUNIT VACCINE IN PATIENTS WITH MULTIPLE SCLEROSIS ON IMMUNE MODULATING TREATMENTS

M. Iannetta[1,2], L. Benedetti[1], D. Landi[3], F. Napoli[3], I. Fato[1], G. Alessio[1], A. Di Lorenzo[1], A. Imeneo[1], B. Massa[1], V. Barchi[1], C. Picarelli[1], F. Angelone[1], A.C. Epifani[1], G. Mataluni[3], C.G. Nicoletti[3], E. Teti[2], G.A. Marfia[3,4], L. Sarmati[1,2]

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Infectious Diseases Unit, Fondazione PTV, University of Rome Tor Vergata, Rome, Italy, [3]University of Rome Tor Vergata, Multiple Sclerosis Clinical and Research Unit, Department of Systems Medicine, Rome, Italy, [4]IRCCS Neuromed, Unit of Neurology, Pozzilli (IS), Italy

Background: The reactivation of varicella-zoster virus (VZV) causes herpes zoster (HZ). VZV-specific T-cell–mediated immunity (CMI) is considered fundamental to prevent HZ. Age and immunomodulating drugs can impair VZV-specific CMI and contribute to HZ occurrence. A new adjuvanted recombinant subunit vaccine (HZ/su) has been recently approved for the prevention of HZ in adults >50 years or <18 years with immunosuppression. Our study aimed to investigate VZV-specific immunity in multiple sclerosis (MS) patients on immune modulating treatments after HZ/su vaccination.

Material and Methods: Patients on active follow-up in the MS Unit of Policlinico Tor Vergata were enrolled in the study.

Two doses of HZ/su were administered 2 months apart (T0 and T1 respectively), with a follow-up visit 1 month after the second dose (T2). T-cell responses were assessed at T0, T1 and T2 with an in-house Interferon Gamma Release Assay (IGRA), consisting of heparin whole blood stimulation with VZV glycoprotein E (gE) and Immediate Early (IE)-63 peptide libraries. Each test included a negative (NC) and positive (phytohemagglutinin, PHA) control. Interferon (IFN)-γ production was measured with the automated ELLA platform. Anti-gE specific antibodies (Abs) were also assessed at each timepoint by ELISA. Statistical analysis was performed with Prism8.2.1.

Results: 11 patients with MS (55% females) have completed the vaccination schedule, so far. Median age is 46 years (IQR 41-53), median Expanded Disability Status Scale (EDSS) is 1,5 (IQR 1-3). All patients but one were on immunosuppressive drugs at the time of vaccination. Treatments were distributed as follows: dimethyl fumarate (4/11, 36%), glatiramer acetate (2/11, 18%), natalizumab (2/11, 18%), fingolimod (1/11, 32%), ocrelizumab (1/11). Median IFN-γ production after gE stimulation was 11.39 pg/ml, 22.26 pg/ml and 174.4 pg/ml at T0, T1 and T2, respectively (Friedman p<0,0001). Median IFN-γ production after IE-63 stimulation was 0.59 pg/ml, 0.55 pg/ml and 0.80 pg/ml at T0, T1 and T2, respectively (Friedman p=0,63) (Figure 1). An effective vaccinal response was defined as a 4-fold increase in IFN-γ production in the gE stimulated condition, from T0 to T2. Accordingly, 2/11 patients (18%) were considered as non-responder (one on fingolimod and one on dimethyl fumarate). As for VZV specific anti-gE Abs, all patients had detectable pre-vaccination titers (T0). Noteworthy, anti-gE levels were reduced in the MS patient on ocrelizumab (Fig1).

Conclusions: VZV gE IGRA is a sensitive and specific tool to assess CMI after HZ/su vaccination. HZ/su elicited a significant T-cell response in more than 80% of MS patients on immune modulating therapies. However, 2 patients had a limited or absent increase in IFN-γ production from T0 to T2. This aspect highlights the importance of assessing VZV-specific CMI in patients receiving immune modulating treatments after HZ/su vaccination to verify protection from VZV reactivation.

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Immune response to viruses

OC 44 INTERFERON AND INFLAMMATORY RESPONSE IN SARS-COV-2 INFECTED PATIENTS TREATED WITH ANTI-S MONOCLONAL ANTIBODIES

L. Maddaloni[1], L. Santinelli[1], G. Bugani[1], A. Lazzaro[1], E. Gentilini Cacciola[1], C.M. Lofaro[1], A. D'Auria[2], F. Frasca[1], C. Leanza[1], C. Ajassa[1], G. Antonelli[2], C.M. Mastroianni[1], G. Ceccarelli[1], C. Scagnolari[2], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, [2]Virology Laboratory, Department of Molecular Medicine, Sapienza University of Rome, Italy

Background: Treatment with neutralizing monoclonal antibodies (mAbs) against the Spike of SARS-CoV-2 reduces the risk of hospitalization and mortality in high-risk individuals with mild to moderate disease. During viral infections, type I interferon (IFN-I) are cytokines required for the induction of early innate immune response; however, distinct SARS-CoV-2 proteins are able to cause dysregulation on the IFN-I production and IFN related pathways, allowing virus to escape from such host defenses. One of the hallmarks of severe COVID-19 is an alterated and delayed IFN-I production along with an overexpression of pro and anti-inflammatory cytokines such as IL-1β, IL-6 and IL-10, TNF-α and TGF-β. On the light of these considerations, the aim of this study was to find out differences in the innate immune response to mAb treatment between vaccinated and unvaccinated COVID-19 patients.

Methods: High risk individuals with mild/moderate SARS-CoV-2 infection were enrolled and treated with mAbs. Peripheral blood was sampled before (T0) and twelve days after (T1) mAbs administration. The mRNA levels of IFN-α, IFN-ω, IFN-α and -β receptor subunit 1 (IFNAR1) and 2 (IFNAR2), IFN regulatory factor 9 (IRF9), IFN-stimulated gene 15 (ISG15) and ISG56, IFN-α-inducible protein 27 (IFI27), IL-1β, IL-6, IL-10, TNF-α and TGF-β and were evaluated using RT/real-time quantitative PCR. Statistical analysis was performed using PRISM and $p<0.05$ were statistically significant. This research was supported by EU funding within the NextGeneration EU-MUR PNRR Extended Partnership initiative on Emerging Infectious Diseases (Project no. PE00000007, INF-ACT, Spoke 1, 2 and 4).

Results: 103 SARS-CoV-2 infected high-risk individuals with median age of 64 (55-73) years were enrolled. Participants were stratified according to their vaccination status against SARS-CoV-2: 72 were vaccinated, while 31 were not vaccinated. Unvaccinated patients had lower mRNA expression levels of IFN-α ($p = 0.006$) and IFN-ω ($p=0.034$) as compared to vaccinated subjects before receiving mAbs therapy, but exhibited increased mRNA levels of IFNAR1 ($p=0.009$), IFNAR2 ($p=0.033$), IRF9 ($p<0.0001$), ISG15 ($p=0.0008$), ISG56 ($p=0.036$), IFI27 ($p=0.004$), IL-6 ($p=0.047$), IL-10 ($p=0.034$) and TGF-β ($p=0.044$). After mAbs treatment, the vaccinated group did not show any significant variation in IFN-α, IFN-ω, IFNAR1, IFNAR2 and IRF9 mRNA expression; by contrast, unvaccinated individuals showed higher mRNA expression levels of IFN-α ($p=0.0006$) and IFN-ω ($p=0.003$), as compared to baseline, as well as reduced levels of IFNAR1 ($p=0.009$), IFNAR2 ($p=0.017$) and IRF9 ($p<0.0001$). Also, a reduction in ISG15, ISG56, IFI27 and IL-10 mRNAs was observed in both vaccinated and unvaccinated patients after mAbs therapy.

Conclusions: In high-risk, unvaccinated COVID-19 patients, treatment with mAbs was associated with a modulation of IFN response and reduction in the expression of inflammatory genes as compared to vaccinated individuals.

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COVID-19 outcome in special population

OC 45 EFFICACY OF TIXAGEVIMAB/CILGAVIMAB PRE-EXPOSURE PROPHYLAXIS OF COVID-19 IN SEVERELY IMMUNOCOMPROMISED INDIVIDUALS: DATA FROM THE OCTOPUS STUDY

A. Vergori[1], G. Matusali[2], E. Cimini[3], L. Bordi[2], P. Borrelli[4], S. Lanini[1], R. Palazzi[5], J. Paulicelli[1], D. Mariotti[2], V. Mazzotta[1], S. Notari[3], R. Casetti[3], M. Francalancia[2], S. Rosati[6], A. D'Abramo[6], C. Mija[2], P. Mencarini[7], S. Sica[8], E. Metafuni[8], F. Sorà[8], A. Rago[9], A. Siniscalchi[9], E. Abruzzese[10], M.G. Garzia[11], G. Luzi[11], R. Battistini[11], L. Prosperini[12], E. Girardi[13], F. Vaia[14], A. Cingolani[15], F. Maggi[2], E. Nicastri[6], A. Antinori[1] on behalf of the Octopus Study group

[1]HIV/AIDS Unit, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [2]Laboratory of Virology, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [3]Laboratory of Cellular Immunology and Pharmacology, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome , Italy, [4]Laboratory of Biostatistics, Department of Medical, Oral and Biotechnological Sciences, University "G. D'Annunzio" of Chieti- Pescara, Chieti, Italy, [5]Accettazione e Teleconsulto Rete Regionale Malattie Infettive, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [6]Emerging Infectious Diseases Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [7]Respiratory Infectious Diseases Unit, National Institute for Infectious Diseases 'L. Spallanzani', IRCCS, Rome, Italy, [8]Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica e Ematologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome Italy, [9]UOSD Ematologia ASL Roma 1, San Filippo Neri Hospital, Rome, Italy, [10]UOC Ematologia, Sant'Eugenio Hospital, Rome, Italy, [11]UOC Ematologia e Trapianto di Cellule Staminali, San Camillo-Forlanini Hospital, Rome, Italy, [12]UOC Neurologia e Neurofisiopatologia, San Camillo-Forlanini Hospital, Rome, Italy, [13]Scientific Direction, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [14]General Direction, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome , Italy, [15]Infectious Diseases Institute, Policlinico A. Gemelli, Rome, Italy

Background: We report the clinical efficacy, antibody persistence, neutralizing activity, and specific T immunity over time in severely immunocompromised patients undergoing pre-exposure prophylaxis (PrEP) with tixagevimab/cilgavimab (T/C).

Methods: Observational study, including participants (pts) who received T/C for PrEP at the dosage of 300 mg intramuscularly (IM) in Mar22-Feb23 and stratified according to SARS-CoV-2 infection, No COVID19 (NoC), Hybrids if occurred before PrEP (H) and breakthrough infections (BTIs) if occurred after PrEP.

At the time of the administration of T/C (T0), 3 (T1), 6 (T2), and/or 9 (T3) months after, anti-RBD IgG and omicron BA.5 neutralizing antibodies (nAbs) were measured by chemiluminescent assay and live-virus microneutralization test (MNA90), respectively. Saliva samples were tested by immunofluorescence for mucosal IgG. T cell-specific immunity was assessed by IFN-γ production (ELISA test). Mann-Whitney test was used to compare markers levels in each group across timepoints, Poisson regression model to calculate specific BTIs incidence rate ratios (IRRs) considering sex, age, anti-RBD IgG at T0 and number of COVID-19 vaccine doses received.

Results: 231 pts: mean age 62+13 y, 84% hematological disease (43% Non-Hodgkin Lymphoma, 25% Multiple Myeloma, 12% Chronic Lymphocytic Leukemia), 57% >1 comorbidity; median vaccine doses received 3. N=82 NoC and 109 H, BTIs were diagnosed in 17% with an IR of 3.6 BTIs/100 patients-months. Anti-RBD IgG at T0 were significantly associated to a reduced rate of BTIs (IRR: 0.99, 95%CI:0.99-0.99). No adverse events to T/C were observed. 85% of the BTIs were mild/moderate (according to WHO criteria), 1 severe resulted in a not COVID-19-related death, 85% of BTIs occurred in Jul22-Feb23 (BA.5 predominant).

On available samples, at T0, significantly higher levels of anti-RBD and nAbs were observed in the H group vs. others; a significant increase of both humoral markers after PrEP (T1) was observed in all the groups, with a decline at T2. Anti-RBD IgG retained levels above the cut-off until T3, while the mean nAbs titers were low at T1 for all the groups and below the cut off at T2 and T3 in NoC and H (Fig1A,B). IFN-γ was found variably around the cut-off in all groups at T0 with a significant slight increase, from T0 to T2 (Fig.1C). Detection of anti-SARS-CoV-2 IgG in saliva are reported in Fig.1D.

Conclusion: Overall, an incidence of 17% of mild/moderate BTIs under PrEP with T/C was observed. Anti-RBD IgG levels persistence was ensured while the neutralizing activity measured against the currently predominant omicron variant BA.5 was low to undetectable. Conversely, baseline cellular T immunity has been shown to be variable likely dependent on the underlying disease with a small increase over time probably due to recovery of immunological status. The salivary-ab response was mainly observed at T1 in all the groups, albeit quantification of mucosal IgA might better clarify this issue.

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COVID-19 outcome in special population

OC 46 OUTCOMES AND CLINICAL FEATURES OF COVID-19 PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES IN THE OMICRON ERA

A. Oliva[1], S. Valeri[1], G. Savelloni[1], F. Cogliati Dezza[1], F. Iannazzo[1], F. Infante[1], A. Iacovelli[2], F. Cancelli[1], M. Venditti[1], P. Palange[2], C.M. Mastroianni[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome

Background: Patients with haematological malignancies (HM) and SARS-CoV-2 infection present a higher risk of severe COVID-19, higher mortality, longer hospitalization, prolonged viral shedding and delayed respiratory worsening (>10 days). The aim of the study was to investigate clinical features and outcomes of HM patients hospitalized with COVID-19 after Omicron variant appearance. Outcomes included i) overall and 30-day in-hospital mortality; ii) respiratory worsening; iii) Intensive Care Unit (ICU) admission; iv) hospitalization length; v) viral shedding duration.

Materials and Methods: This is a single-centre retrospective study in HM patients hospitalized due to SARS-CoV -2 infection from March 2020 to October 2022. Patients were divided into PRE-OMICRON group (patients hospitalized before the appearance of Omicron variant) and OMICRON group (patients hospitalized after the appearance of Omicron variant). A total of 218 patients were included (106 PRE-OMICRON and 112 OMICRON). Cut-off was established on February 1st when Omicron variant became dominant in Italy.

Results: PRE-OMICRON patients showed a higher overall and 30-day in-hospital mortality (36.8% PRE-OMICRON vs 21.4% OMICRON, p =0.003; 27.4% PRE-OMICRON vs 8.9% OMICRON p <0.001, respectively) and a significantly higher risk of intensive care unit (ICU) admission (21.7 % vs. 7.4%, p =0.003). In PRE-OMICRON group a respiratory worsening occurred more frequently (62.3% vs 38.4%, p <0.001) and more rapidly (6 days [2-14] vs 11 days [5-33]), also requiring high-level of oxygen support. Nevertheless, both hospitalization length and viral shedding duration did not significantly differ between the two groups. Patients in the PRE-OMICRON had 13.2% Rate of superinfections compared to OMICRON. CAPA (COVID-19 associated pulmonary aspergillosis) was found in 5.5% of patients [2.8% PRE-OMICRON vs 8% OMICRON, p =0.093].

A significantly higher mortality emerged in patients who received a diagnosis of severe and/or critical illness at admission (p <0.001), in patients who received corticosteroid (p =0.000) or previous antibiotic therapy (p =0.000) and in patients who developed secondary infections (p =0.003).

At the multivariable analysis, home steroid therapy (p =0.042), respiratory worsening during hospitalization (p =0.039), ICU admission (p <0.001) and development of nosocomial infections (p =0.042) were independently associated with in-hospital mortality, while partial or complete remission of the hematologic malignancy was a protective factor (p = 0.038).

Conclusions: Omicron variant had a positive impact on the clinical evolution and outcomes of HM patients. Nevertheless, they continue to present high mortality, especially if had received corticosteroids, worsened during hospitalization and developed secondary infections.

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COVID-19 outcome in special population

OC 47 COVID-19 IN PLWH: CLINICAL OUTCOMES, A SINGLE CENTER ANALYSIS

C. Grillo, A. Narducci, M. Caggese, E.P. Drago, C. Muscatiello, S. Ferrara, T.A. Santantonio, S. Lo Caputo

Infectious Disease Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy

Background: COVID-19 pandemic had a great impact on our society and a severe health risk in immunocompromised patients. People living with HIV (PLWH) could have a higher risk of developing clinical complications for their fragility and their higher frequency of comorbidities. Our study aims to evaluate the prevalence and clinical outcome of SARS CoV-2 infection in PLWH>50 years in relation to the respond to the vaccine campaign for COVID-19.

Methods: This is a single center retrospective observational study performed from March 2020 to December 2022. Socio-demographic data, comorbidities, clinical stage HIV disease at onset, were collected from medical records. Data on Covid-19 were retrieved from the GIAVA Puglia vaccine platform and the IRIS Puglia platform. In addition, clinical evolution of COVID-19 (asymptomatic, mild, moderate and severe) was investigated with a survey. Comorbidities were assessed in patients with moderate or severe COVID-19 disease.

Results: 193 PLWH>50 years were included in the analysis. 87 (45%) HIV-infected individuals were diagnosed with COVID-19, 60 (68,97%) of them were male.

Among the COVID-19 patients, 14 (16,09%) were asymptomatic, 51 (58,6%) had mild disease, 20 (22,9%) moderate disease, 2 (2,3%) with severe disease were hospitalized.

Among patients with moderate and severe COVID-19, 14 (63,6%) had > 2 comorbidities, 7 (31,8%) had > 3 comorbidities. About COVID-19 vaccination status, 166 (86,01%) HIV patients were vaccinated with at least one dose, 15 (7,7%) PLWH are still not vaccinated, in 12 (6,2%) PLWH no data were available.

Among unvaccinated PLWH, 4 (26,67%) have never been infected, 10 (66,6%) were infected: 2 (20%) had moderate COVID-19 disease, none with severe manifestations.

In unvaccinated group, 10 (66,6%) PLWH had advanced HIV disease at diagnosis (CD4+<200), 3 (30%) was AIDS.

Conclusions: Despite the immunocompromission, most PLWH had asymptomatic or mild COVID-19 related symptoms. Patients who had moderate or severe COVID-19 had at least 2 or more comorbidities that impacted the clinical outcome of the disease. Most of PLWH got vaccinated for COVID-19 but we must encourage PLWH to all type of vaccination and improve the vaccination rate for their intrinsic immunological clinical risk. Additional data should be added and studied in the non-pandemic phase.

COVID-19 outcome in special population

OC 48 MOLECULAR CHARACTERIZATION OF SARS-COV-2 OMICRON CLADE AND CLINICAL PRESENTATION IN CHILDREN

R. Scutari[1,2], V. Fox[1,2], V. Fini[2], A. Granaglia[2], P. Bernaschi[3], C. Russo[3], A. Campana[4], S. Bernardi[4], A. Villani[4], C. F. Perno[2,3], C. Alteri[1,2]

[1]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy, [2]Multimodal Research Area, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [3]Microbiology and Diagnostics in Immunology, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [4]Academic Department of Pediatrics, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

Background: Since its emergence, SARS-CoV-2 Omicron clade showed marked degree of variability and different clinical presentation compared with previous clades. Here, the genomic characteristics and impact on COVID-19 presentation of this clade were evaluated in children.

Material and Methods: 657 Omicron whole sequences were obtained from patients aged ≤12 years referred for SARS-CoV-2 diagnosis at Bambino Gesù Children Hospital from December 2021, to early November 2022. Phylogenetic structure of the paediatric epidemic and evolutionary rate of Omicron clade were evaluated by maximum likelihood and Bayesian coalescent methods. Constitutive (intra-patient prevalence >70%, according to https://covariants.org/) and non-constitutive (intra-patient prevalence 2-70%) mutations defining Omicron lineages were evaluated. Logistic regression was performed to assess factors associated with disease severity.

Results: 347 (52.8%) children were male, with a median age of 0.56 (Interquartile range, IQR: 0.23-1.66) years. Mild infections were the most prevalent (82.0%), followed by asymptomatic (9.8%), and moderate/severe infections (8.2%). One-hundred and twenty-three (18.7%) patients had comorbidities. At least four Omicron lineages circulated widely in children: 40.5% of sequences belonged to BA.2, followed by BA.1 (33.6%), BA.5 (23.7%) and BQ.1 (2.1%) (Figure 1). The Omicron mean evolutionary rate (subs/site/year) was 9.8x10^-4 (95% HPD, 8.8x10^-4 -1.1x10^-3) and no differences were observed among Omicron lineages.

Constitutive mutations increased from 46 (45-46) of BA.1 to 66 of BQ.1 (P<0.001). Of note, 4 non-constitutive mutations characterized by a median intra-patient prevalence of 7.6% (IQR: 6.2-11.5) (Nucleocapside-L221F, nsp6-L260F, RdRp-G678G, Spike-A694S) also increased their frequencies across lineages, with the exception for Spike-S686R, close to furin-cleavage-site, that decreased from 82% of BA.1 to 10% of BA.5 (P<0.001).

Logistic regression showed that BA.5 and age <1 year were negatively associated with moderate/severe COVID -19 presentation (adjusted odds ratio, AOR: 0.26 [0.07-0.90] P=0.034; 0.45 [0.23-0.89] P=0.021), while positive association were observed with BA.1 and comorbidity (AOR [95% CI]: 2.2 [1.2-4.1] P=0.014; 2.6 [1.3-5.1] P=0.006).

Conclusions: These results highlighted the extensive SARS-CoV-2 Omicron circulation in children, mostly aged <1 year, and provided insights on non-constitutive mutations and their role in evolutionary processes. Our findings also suggested a milder phenotype of BA.5 compared to other Omicron lineages, letting suppose the potential contribution of viral diversification in affecting disease severity.

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Antiviral treatment in COVID-19

OC 49 PROLONGED ANTIVIRAL THERAPY COMBINED WITH NEUTRALIZING MONOCLONAL ANTIBODIES AS A TREATMENT STRATEGY FOR COVID-19 IN SEVERELY IMMUNOCOMPROMISED PATIENTS DURING THE OMICRON WAVE: A QUASI-EXPERIMENTAL MULTICENTRE COHORT STUDY

D.F. Bavaro[1], C. Pellegrino[1], F. Balena[1], A. Belati[1], L. Diella[1], G. Metrangolo[1], V. Totaro[1], L. Frallonardo[1], E. Pallara[1,3], G. Bruno[2], C. Muscatiello[3,4], F. Di Gennaro[1], N. Giovine[5], F. Pomarico[5], M. Dell'Aera[5], G.B. Buccoliero[2], S. Carbonara[3], A. Saracino[1]

[1]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University Hospital of Bari, Bari, Italy, [2]Infectious Diseases Unit, "San Giuseppe Moscati" Hospital, Taranto, Italy, [3]U.O.C. Malattie Infettive, ASL BAT, P.O. V. Emanuele II, Bisceglie, Italy, [4]Department of Medical and Surgical Science, University of Foggia, Foggia, Italy, [5]Pharmacy Unit, University Hospital Polyclinic of Bari, Bari, Italy

Background: COVID-19 is a serious threat in immunocompromised hosts, who show low response to vaccination and low capacity to control disease progression. Additionally, persistent infection can hamper access to care and further antineoplastic treatments in these patients. Aim of this study is to evaluate efficacy and safety of a prolonged antiviral treatment strategy compared with standard of care (SOC) in immunocompromised COVID-19 patients.

Materials and Methods: This is a quasi-experimental multicentric cohort study carried out in three referral COVID -19 Hospitals. Severe (based on NIH definition) immunocompromised in- and outpatients with SARS-CoV-2 infection were included. Two different cohorts were compared [Fig. 1]: SOC group, treated with standard antiviral therapy (AT) from February to October 2022, and Interventional Group (IG), treated with prolonged AT up to antigenic and/or molecular negative nasal swab (NS) from November 2022 to February 2023. In IG, first line AT was remdesivir (REM) for inpatients and nirmatrelvir/ritonavir (NIR/r) for outpatients. In case of drug interactions or hepato-renal impairment, molnupiravir (MOL) was the second line in both cases. If anti-Spike antibodies were below the protective titre (according to different laboratory thresholds), a single therapeutic dose of tixagevimab/cilgavimab (TGM/CGM) was administered. All patients underwent a monitoring swab every 5 days until negative NS.

Results: A total of 784 patients were screened [Fig. 1], of whom 320 immunocompromised. Of these, 171 were eligible: 102 (59.6%) in SOC and 69 (40.4%) in IG. Baseline features were similar between the two groups [Tab. 1]. Overall, NIR/r, MOL, and REM were prescribed in 81 (47%), 47 (27%), and 43 (26%) cases, respectively. In IG, the median therapy duration was 10 (5-39) days; 33 (48%) patients also received TGM/CGM. Interestingly, in IG a significant lower incidence of COVID-19 related lung failure [9% vs 25%, p=.006], mortality [4% vs 14%, p=.044], and 60-day recurrences [3% vs 17%, p=.007] was noted, along with a shorter time to negative NS [10 (4-46) vs 14 (4-210) days, p=.002]. However, a higher risk of adverse events to AT was observed (4% vs 0%, p=.034), including a renal failure and two bradycardia severe events leading to drug discontinuation. By performing a uni- and multivariate logistic regression, independent predictors of COVID-19 related lung failure were age (aOR=1.04, 95%CI=1.00-1.07), persistent positive NS (aOR=1.02, 95%CI=1.00-1.04), while protective IgG anti-spike title (aOR=0.26, 95%CI=0.09-0.72) and prolonged AT (aOR=0.33, 95%CI=0.11-0.98) were associated with better outcome.

Conclusions: Prolonged antiviral therapy combined with mAb could represent a valid therapeutic approach for severe immunocompromised patients with COVID-19 to reduce disease progression and obtain faster viral clearance, even if a strict clinical monitoring is warranted. Validation of this strategy on larger cohorts is needed.

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Antiviral treatment in COVID-19

OC 50 ANTI-SPIKE MONOCLONAL ANTIBODIES TO PREVENT HOSPITALIZATION IN MILD COVID-19: FINAL ANALYSIS OF AN OBSERVATIONAL MULTICENTER STUDY (CONDIVIDIAMO)

G. Ghilardi[1], A. Soria[1], F. Graziano[1], G. Lapadula[1,2], D. Dalla Gasperina[3], S.V. Benatti[4], M.E. Quiros Roldan[5], P. Brambilla[6], F. Bai[7], M. Merli[8], D. Minisci[9], M. Franzetti[10], E. Asperges[11], D. Pocaterra[12], A. Pandolfo[13], F. Zanini[14], D. Lombardi[15], A. Cappelletti[1], A. Rugova[1], M. L. Borghesi[1], L. Pusterla[15], S. Piconi[13], P. Morelli[12], P. Rovere[16], R. Bruno[11], S. Rusconi[10], S. Casari[9], A. Bandera[17], F. Franzetti[18], M. Puoti[2,8], A. d'Arminio Monforte[7], G. Marchetti[7], M. Milesi[6], F. Castelli[5], M. Rizzi[4], F. Dentali[3], M. Mallardo[2], E. Rossi[2], M. G. Valsecchi[2], S. Galimberti[2], P. Bonfanti[1,2]

[1]IRCCS San Gerardo dei Tintori, Monza, [2]University of Milano-Bicocca, Monza, [3]ASST Sette Laghi, Varese, [4]ASST Papa Giovanni XXIII, Bergamo, [5]University of Brescia, Brescia, [6]ASST Cremona, Cremona, [7]ASST Santi Paolo e Carlo, [8]ASST Grande Ospedale Metropolitano Niguarda, Milan, [9]ASST Mantova, Mantova, [10]ASST Ovest Milano, Legnano, [11]IRCCS Policlinico San Matteo, Pavia, [12]IRCCS Humanitas, Rozzano, [13]ASST Lecco, [14]ASST Nord Milano, Cinisello Balsamo, [15]ASST Lariana, Como, [16]IRCCS San Raffaele, Milan, [17]IRCCS Ca' Granda Policlinico, Milan; 18ASST Valle Olona, Busto Arsizio

Introduction: Anti-SARS-CoV-2 monoclonal antibodies (mAbs) reduce COVID-19 hospitalizations in clinical trials. Large multicenter data on real world use in daily practice, with a long observation period, are scanty.

Methods: CONDIVIDIAMO is a multicenter observational study approved by Lazzaro Spallanzani National Ethics Committee, enrolling patients treated with mAbs in different Infectious Diseases and Internal Medicine centers in Lombardy. All patients were treated as outpatients and followed for 28 days since mAbs treatment. Rates of death, hospitalization or emergency room visit were evaluated. Characteristics of those who were/were not hospitalized within 28 days of treatment were compared by Mann-Whitney U test for continuous data and $\chi 2$ test for categorical data.

Results: Between March 2021 and December 2022, in 17 centers, 1578 subjects received mAbs: 647 (41.0%) bamlanivimab (631 in combination with etesevimab), 234 (14.8%) casirivimab/imdevimab, 589 (37.3%) sotrovimab, 108 (6.8%) tixagevimab/cilgavimab. Median (IQR) age was 67 (53-75) years, 710 (45%) were women. All patients had at least 1 risk factor for COVID-19 progression, the most common being age >65 years (700 [44.4%]), immunodeficiency (644 [40.8%]), cardiovascular disease (541 [32.6%]), obesity (292 [18.5%]), kidney failure 246 (246 [15.6%]), lung disease (202 [12.8%]). 319 (20.2%) patients had >=3 risk factors simultaneously. 1168 (75.5%) patients were fully vaccinated for COVID-19 before mAbs treatment. The median (IQR) time between onset of symptoms and mAbs receipt was 4 (3-6) days. After 28-day follow-up, 129 out of 1556 (8.3%) subjects were hospitalized, of whom 69 (54%) had a COVID-19 progression and 60 were admitted for other causes; 6 (4.7%) were hospitalized twice. We recorded 14 deaths (0.9%), of which 5 were due to COVID-19.

Table 1 shows the characteristics of the patients according to hospitalization outcome by 28 days. Hospitalized patients were older and had more frequently >=3 risk factors for clinical progression than those who were not hospitalized.

Discussion: Hospitalization rate in mAbs recipients with mild COVID-19 in a large multicenter real-life cohort was generally low, although higher than what seen in randomized clinical trials, probably because of a higher age and comorbidity in real world than in controlled settings. Patients who progressed to hospitalization despite mAbs had a higher morbidity burden. Differences of outcomes between mAbs could be influenced by many factors, notably the calendar period and the shift of SARS-CoV-2 variants to the less pathogenic Omicron, thus they should be interpreted cautiously.

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Antiviral treatment in COVID-19

OC 51 CLINICAL EFFICACY OF TIXAGEVIMAB/CILGAVIMAB PRE-EXPOSURE PROPHYLAXIS IN IMMUNOCOMPROMISED PATIENTS TREATED DURING OMICRON SUBLINEAGES DIFFUSION. REAL LIFE EXPERIENCE FROM ASST LECCO

V. Morena[1], S. Pontiggia[1], F. Alberton[2], F. Badalucco[2], C. Molteni[1], L. Bradanini[1], F. Conti[1], A. Pandolfo1, A. Castagna[2], S. Piconi[1]

[1]Infectious Diseases Unit, Alessandro Manzoni Hospital, Lecco, Italy, [2]University Vita-Salute IRCCS San Raffaele Hospital, Milan, Italy

Background: In March 2022 Italian Agency of Drug (AIFA) approved pre-exposure prophylaxis with tixagevimab/cilgavimab (Evusheld) for immunocompromised patients with an increased risk of severe form of COVID-19. The recommended dose of tixagevimab/cilgavimab was increased from 150 mg + 150 mg to 300 mg + 300 mg because of spreading of new SARS-COV-2 Omicron sub-lineages and data from real-life studies suggested a better protection with a double dose of monoclonal antibodies. The aim of this study was to evaluate the incidence of SARS COV -2 infection after pre-exposure prophylaxis using tixagevimab/cilgavimab at dose of 150 mg + 150 mg in immunocompromised patients attending at Infectious Diseases Unit of A. Manzoni Hospital, Lecco (Italy).

Materials and Methods: We retrospectively collected data from all adult patients who received pre-exposure prophylaxis with tixagevimab/cilgavimab according to AIFA guidelines between June and December 2022. After 3 -6 months from the prophylaxis, patients were called in order to get information about eventual SARS-COV-2 infection. Only SARS-COV-2 infections diagnosed at least 5 days after pre-exposure prophylaxis were included in the analyses.

Patients' characteristics were described as median, interquartile ranges (IQR) for quantitative variables or count and percentage for qualitative variables.

Results: 269 patients received tixagevimab/cilgavimab. Demographic carachteristcs, comorbidities and information on previous SARS-COV-2 vaccinations were reported in Table 1. 33/233 (14,1%) patients had confirmed SARS-COV-2 infection after pre-exposure prophylaxis. Of them, 86.2% had onco-hematological disease and 97% had completed anti-SARS-COV-2 vaccination cycle (at least three doses). Median time between pre-exposure prophylaxis and SARS-COV-2 infection was of 88 days (IQR 52-154). Antiviral treatments were prescribed to only 8/33 (24,2%) patients: 6 were treated with nirmatrelvir/ritonavir and 2 with molnupiravir. 4 (12,2%) patients were hospitalized and 1 (3%) of them died for COVID19 complications (Table 2). Median time of negativization of nasopharyngeal swab was 8 days (IQR 5-14).

Conclusions: Our study reported a higher incidence of SARS-COV-2 infection after pre-exposure prophylaxis compared to data available in literature. These results may depend on longer follow up time (3-6 months versus 73 days), low monoclonal dosage and the spreading of BA.2, BA.4, and BA.5 SARS-COV-2 Omicron sublineages during study period. These data could suggest that monoclonal antibodies used for pre-exposure prophylaxis should be promptly updated against the new emerging variants in order to maintain their clinical efficacy.

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Antiviral treatment in COVID-19

OC 52 VACCINATION AND ANTIVIRAL TREATMENT REDUCE THE TIME TO NEGATIVE SARS-COV-2 SWAB: A REAL-LIFE STUDY

A. De Vito[1] , G. Moi[1], L. Saderi[2], M. Puci[2], A. Colpani[1], B. Zauli[1], V. Fiore[1], M. Fois[1], A. Bitti[1], B. Zauli[1], I. Maida[1], S. Babudieri[1], G. Sotgiu[2], G. Madeddu[1]

[1]Unit of Infectious Diseases, Department of Medicine, Surgery, and Pharmacy, University of Sassari, Sassari, Italy, [2]Clinical Epidemiology and Medical Statistics Unit, Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy

Background: Clinical trials demonstrated that vaccines and antiviral therapies against SARS-CoV-2 can reduce the risk of disease progression and death. However, few data on time to negativity of those treated are available. Therefore, aim of the study was to assess clinical characteristics of SARS-CoV2 patients and time to negativity of vaccinated and treated persons.

Material and methods: SARS-CoV-2 infected persons while being hospitalized for other reasons were recruited. According to the hospital protocol, patients were tested every 24-48h to assess their contagiousness. Patients who died or were discharged with a positive swab were excluded.

Sample characteristics were described with median and interquartile range (IQR) for quantitative variables and with absolute and relative (percentages) frequencies for qualitative ones.

Kaplan–Meier curves were plotted to describe time to negativity after 14 days, stratifying by vaccination status and antiviral therapies. Statistical significance was set at p-values less of 0.05, data analysis was carried out through STATA17 software.

Results: We included 175 people;97 (55.4%) were male, with a median (IQR) age of 77 (68-83) years. The most prevalent comorbidity was chronic heart failure (37.1%), followed by neurological diseases (29.1%), obesity (28.6%), diabetes (26.3%, with 74% with decompensated diabetes), neoplasia (24.6%, with 11.4% with metastasis), and COPD (21.7%). In addition, 91.4% were vaccinated with at least two doses.

Regarding symptoms, 41.7% complained of fever, 28.6% cough, and 20% dyspnoea; gastrointestinal symptoms (6.3%), pharyngodynia (10.9%), headache (8.6%) were less incident.

Radiological consolidations and GGO were found in 31 (17.7%), with 3 showing pulmonary embolism.

Sixty-five (37.1%) patients received a 3-day cycle of remdesivir, 37 (21.1%) monlupiravir, 12 (6.9%) nirmatrelvir/ritonavir. Forty-four (25.1) were treated with monoclonal antibodies (sotrovimab or Casirivimab/Imdevimab).

Median (IQR) time to negativity of unvaccinated and vaccinated patients was 18 (17-22) and 10 (7-13) days, respectively (Fig.1 and 2). Patients exposed to antiviral therapy had a shorter median (IQR) time to negativity (14 days): those treated with remdesivir 9 (7-12) days, those with molnupiravir 10 (7-14) days, and those with nirmatrelvir/ritonavir 10.5 (7-14) days (Figures 3 and 4).

Conclusions: Prompt administration of antiviral therapies can shorten SARS-CoV-2 clearance, reducing the risk of viral transmission and hospital stay.

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HIV: much left to do

OC 53 HIV AND HOSPITALS: AN EVOLVING RELATIONSHIP

L. Brogonzoli[1], M. Cascio[2], E. Sala[1], C. Crepaldi[1], R. Iardino[1], A. d'Arminio Monforte[3]

[1]Fondazione The Bridge, Milano, [2]European AIDS Treatment Group (EATG), Palermo, [3]University of Milan, Milano, Fondazione Icona, Milano

Background: This work is the result of a research conducted by HIV Outcomes Italia, the Italian spin-off of the European initiative that aims to improve the HRQoL (health-related quality of life) of PLWH (People living with HIV).

PLWH have the possibility to live longer, but with the risk of long-term problems related to the chronic state of activation and latent inflammation of the immune system. Moreover, the stigma that PLWH still face impacts their quality of life, and their possibility to access healthcare services.

For these reasons, HIV Outcomes has decided to investigate the knowledge on HIV and the level of stigma in hospitals, to better grasp the training needs and gaps, and the prejudices that might exclude PLWH from the healthcare system, in order to inform future actions towards education.

Material and Methods: The research was conducted using a self-compiled survey including 29 questions, divided into 4 items: knowledge, stigma, actions, and personal data. A sample of 33 hospitals was selected, belonging to one to three medium/big cities, in order to have a qualitative representation of the territory.

The survey was sent out to general or medical directors of selected hospitals, asking them to disseminate it to all personnel (excluding infectious diseases departments), to be filled on-line.

Only three Regions (Emilia Romagna, Veneto, Toscana), and therefore 6 hospitals, compiled a significant number of questionnaires, that were then analyzed, for a total of 870 respondents among nurses (59%), doctors (7.1%), licensed practical nurses (LPNs) (13.6%), obstetricians (20.2%), lab technicians (0.1%). All medical departments were represented: Surgery (25.9%), Emergency (20%), Internal medicine (31.7%) and services (22.4%).

Results: The results show that the knowledge related to HIV among hospital workers is not adequate: all responded to have a good knowledge, but 9.5% declared that HIV is a disease (13% in LPNs). Around half of the sample responded that life expectancy of PLWH is inferior to the general population. Most respondents affirmed that it's possible for a PLWH to give birth to uninfected children, but around 10-15% said no.

The results relating to stigma also show in a number of questions around 7% that report a worst treatment towards PLWH and people belonging to key populations, with cases of PLWH being refused treatment or treated with less care. The analysis by macro areas and by assigned tasks highlighted differences regarding both the knowledge and the stigma, with obstetricians being the ones with both more knowledge and less stigma. Indeed, a correlation is clear between knowledge and stigma, even though it is not possible to understand its consequentiality.

Conclusions: The gaps in knowledge and the ongoing stigma underline the need for training on HIV, with the objective of decrease, and even eliminate, HIV related stigma within the healthcare system.

HIV: much left to do

OC 54 ACHIEVING THE THIRD 95 IN OUR HIV CLINICS: IT IS POSSIBLE, BUT THERE IS STILL A LOT TO DO

E. Teti[1], A. Crea[1], B. Rossi[1], D. Checchi[1], M. Compagno[1], L. Sarmati[2], A.M. Geretti[2]

[1]Clinical Infectious Diseases, Tor Vergata Hospital, Rome, Italy, [2]Clinical Infectious Diseases, Department of System Medicine, Tor Vergata University, Rome, Italy

Background: In December 2020, UNAIDS released a new set of ambitious targets calling for 95% of all PLWH to know their status, 95% of all people with diagnosed HIV to receive antiretrovirals, and 95% of all people receiving antiretrovirals to have viral suppression by 2025. In order to concretely contribute to the sustainability of these aims, especially the third one, it is advisable to carry out a systematic review of PLWH of each of our clinics and the clinical audit is undoubtedly a tool for this purpose. Clinical audits allow clinicians to evaluate the quality of services, identify their deficiencies and adopt countermeasures aimed at improving the health care provided to patients.

Methods: The main outcome was to verify that a sample of PLWH followed in our HIV clinic had reached the third UNAIDS target. Based on our out-patient population size (n=750), reliable audit estimates required a random sample of 100 people retrospectively identified among those who had their visit appointment as of 30th September 2021. Patients on treatment for less than 6 months were excluded. Viral suppression was defined as HIV-RNA<50 copies/ml. After one year, a re-audit was conducted on the same population to verify a change by implementing certain identified action points.

Results: PLWH (n. 100) evaluated within the audit were predominantly males (68%), Italian (73%), who contracted HIV sexually (89%), with a three-drug regimen (86%); moreover, 73% of the regimens were INI-based, 11% PI-based and 10% NNRTI-based. Viral suppression was observed in 85%. Based on this result, the population covered by the audit did not achieve the third 95. Table 1 shows the characteristics of PLWH not virologically suppressed (n=15) of which the main cause was poor adherence to treatment and follow-up. Comparing the suppressed population with the non-suppressed one in a descriptive way, women, foreigners, injecting drug users and patients taking PI-based regimens showed predominantly detectable viraemia. Actions points have been proposed and implemented such as guaranteeing only one doctor of reference for the most fragile patients, analysing the barriers to access to treatment, recalling patients who missed appointments, strengthening the psycho-social network for a better awareness and sharing of the infection, optimizing the pill-burden and guaranteeing a proactive attitude on the management of long-term toxicity, organizing complex case review meetings. The re-audit one year later, in September 2022, documented the achievement of viral suppression in 10/15 patients.

Conclusions: We recommend that to achieve the third 95%, HIV clinics implement a capillary, structured and ongoing review of all the clinical, psychological and social indicators that impact HIV treatment outcomes. Clinical audit has proved a valuable tool for improving the quality of HIV care in our centre. The care of people who report IDU continues to pose challenges and requires enhanced efforts.

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HIV: much left to do

OC 55 IMPLEMENTATION OF THE REGIONAL DCA 401/2016 IN LATIUM: AN EXAMPLE OF A COORDINATED, MULTIDISCIPLINARY AND INDIVIDUALIZED APPROACH TO PLWH TERRITORIAL HEALTHCARE, FORERUNNER OF THE NATIONAL RECOVERY AND RESILIENCE PLAN (PNRR) INDICATIONS

A. Faticoni, A. Agresta, R. Casa, R. Esvan, V. Puro, N. Orchi

INMI L. Spallanzani - IRCCS, Roma

Background: The recent PNRR calls for the implementation of new models of territorial healthcare (THC), close to the real needs of chronic persons, especially if vulnerable and disabled, to ensures multidisciplinary, integrated, tailor-made interventions. Similar objectives guided the THC model for persons with HIV (PLWH) in the metropolitan area of Rome, Latium, the Italian region with the highest incidence of HIV. A consolidated hospital-based home care (HC) scheme, based on integration between public and private sectors, and coordinated by a public centre (CCTAD) was updated by the Regional DCA 401 issued on December 2016.

To fit the changed HIV disease profile after the introduction of ART, the new model reshapes the relationships between HIV clinical centers (CC) and all the District's territorial services (DTS). In particular, it complementarily includes HIV-dedicated THC for people with AIDS/advanced HIV disease (at home or in HIV facilities), and integrates generic THC provided by DTS to persons with asymptomatic HIV chronic disease.

Materials and methods: We revised data from CCTAD activity, and compared the 2012-2016 period (pre-DCA) to the 2017-2022 period (post-DCA), to estimate the impact of the introduction of the DCA on the amount and the type of THC provided to PLWH. Interrupted Time Series Analysis using Poisson segmented regression model with Newey-West standard errors to account for autocorrelation and heteroskedasticity were used, as appropriate.

Results: During the eleven years considered, 1579 requests of THC were taken in charge: 1018 in pre-DCA and 561 in post-DCA (Table). A significant increase in the proportion of THC provided by DTS was observed in post-DCA period, compared to pre-DCA (14.4% vs 3.9%), at the expense of HIV-dedicated Home Care (76.1% vs 88.1%) ($p<0.001$). Disease severity in persons taken in charge was significantly lower in the post-DCA (p 0.004).

As shown in the figure, the number of requests showed a decreasing trend of 14.9% per year in pre-DCA period (incidence rate ratio [IRR] 0.851 [95% confidence interval, 0.840-0.861]), reaching a reduction of 29.7% (compared with the counterfactual) in 2017, the year of the DCA (IRR 0.703 [0.658-0.750]), and then increased of 3.5% per year in the post-DCA period (IRR 1.035 [1.021-1.048].

Conclusions: After the progressive decrease of the PLWH taken in charge from 2012 to 2017, the trend reversal in the post-DCA could be put in relation to the widening of the generic DTS offered and utilized by patients. The increase of PLWH cared in non-HIV-dedicated DTS suggests that even in this population, often stigmatized and marginalized, the integrated approach between HIV CC and territory under the CCTAD coordination, with Territorial Operations Center (COT in PNRR) functions, allows a tailored and multidisciplinary response, able to answer the person's needs, according to PNRR objectives.

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HIV: much left to do

OC 56 BELONG – WHY PEOPLE LIVING WITH HIV MUST BE INCLUDED IN NON-HIV CLINICAL TRIALS. A COMMUNITY-LED INITIATIVE FOR AN INCLUSIVE APPROACH TO CLINICAL RESEARCH

R. Pignata, R. Tatoud, G. Barbareschi, F. Greenhalgh

European AIDS Treatment Group, Brussels

Background: HIV is now considered a chronic and manageable condition when appropriate treatment is available. Consequently, people living with HIV (PLHIV) live longer lives and may experience non-HIV-related health conditions. However, safety and efficacy data of drugs and treatments for these illnesses in PLHIV are lacking due to their historical exclusion from clinical research of not-HIV drugs and therapeutic strategies and despite the evidence that the participation of PLHIV in clinical research is feasible and beneficial. The HIV community is concerned with eligibility criteria excluding PLHIV solely based on serological status and there has been an ongoing discussion, exacerbated by COVID-19 vaccine trials, that restrictive and unjustified eligibility criteria prevent PLHIV from receiving effective treatment. Therefore, the European AIDS Treatment Group (EATG) developed a position paper detailing why people living with HIV must be included in non-HIV clinical trials.

Material and Methods: A position paper was developed based on a review of eligibility criteria used in non-HIV clinical studies, mapping and review of existing clinical research guidelines and a consultation with community experts representing the HIV community in Europe.

Results: Systematic data on the participation of PLHIV in non-HIV clinical research remains limited. Exclusion of PLHIV from participating in clinical research often occurs despite evidence that drugs are safe and effective for PLHIV. The decision to exclude PLHIV is often arbitrary. When there is a potentially viable explanation for exclusion, efforts to address safety concerns are rarely made. Existing guidelines are limited geographically and to certain conditions.

Conclusions: Improving access of PLHIV to the best healthcare available requires systematically addressing current research thinking and practice. EATG calls for European health regulatory authorities to adopt clinical research guidelines mirroring those of US FDA for the inclusion of PLHIV and/or hepatitis B/C in cancer trial applications. It also recommends extending the scope of the guidelines to other illnesses and health conditions that affect PLHIV. EATG is implementing the BELONG project to encourage and support the development and implementation of inclusive clinical research guidelines toward improving health outcomes for PLHIV and other comorbidities. In addition, EATG aims to contribute to discussions in Europe and elsewhere towards the revision of Good Clinical Practice Guidelines and inspire other communities of people living with different health conditions to advocate for a more inclusive approach to clinical research, whose outcomes may benefit their treatment and care. The early engagement of PLHIV in clinical research is an opportunity to build a trusted relationship between patients, researchers and health professionals and contribute to a global patient empowerment effort, as well as an overall improvement of the R&D process.

Cardiovascular and malignancies

OC 57 MALIGNANCIES AND MACES IN THE PRESTIGIO REGISTRY

T. Clemente[1,2], D. Pontillo[2], D. Minisci[3], A. Di Biagio[4], A. Galli[2], L. Attala[5], G. Cenderello[6], V. Malagnino[7], S. Lo Caputo[8], M. Tavio[9], A. Giacomelli[10], A. Castagna[1,2], V. Spagnuolo[2] on behalf of the PRESTIGIO Study Group

[1]Faculty of Medicine and Surgery, Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [3]University Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili, Brescia, Italy, [4]Unit of Infectious Diseases, IRCCS Ospedale Policlinico San Martino, Genoa, Italy, [5]Infectious Diseases Unit, Santa Maria Annunziata Hospital, Bagno a Ripoli, Italy, [6]Infectious Disease Unit, Sanremo Hospital, Sanremo, Italy, [7]Infectious Disease Clinic, Policlinico Tor Vergata University Hospital, Rome, Italy, [8]Clinic of Infectious Diseases, Department of Clinical and Surgical Sciences, University of Foggia, Foggia, Italy, [9]Infective Diseases, AOU Ospedali Riuniti, Ancona, Italy, [10]III Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy

Background: Aim of the current study was to explore the incidence of malignancies and major adverse cardiovascular events (MACEs) in people living with 4-class drug-resistant HIV (4DR-PLWH).
Methods: Cohort study on PLWH with documented resistance to NRTIs, NNRTIs, PIs, and INSTIs, from the PRESTIGIO Registry.
The primary outcome was to evaluate the incidence rates (IRs) of malignancies and MACEs occurred after 4DR evidence (baseline, BL). Malignancies included both AIDS- and non-AIDS-related cancers. MACEs included stroke, acute myocardial infarction, coronary or peripheral artery disease requiring revascularization, and acute congestive heart failure.
Follow-up accrued from BL until death/loss-to-follow-up/freezing date (28th February, 2023).
Descriptions by median (interquartile range, IQR) or frequency (%). Poisson regression modelled IRs and 95% confidence intervals (95%CIs). Kaplan-Meier curves estimated cumulative probabilities of the first incident: 1) cancer; and 2) MACE.
Results: Overall, 229 4DR-PLWH included: BL characteristics reported in Table 1.
During a median follow-up of 7.7 (4.8-10.3) years [1760 person-years-of-follow-up (PYFU)], 28 (12.2%) 4DR-PLWH developed ≥1 incident cancer (n=30, Figure 1): IR=1.7 (95%CI=1.1-2.3)/100 PYFU. Specifically, 24 (80%) malignancies were non-AIDS-related: 7 HPV-related anal neoplasms, 4 Hodgkin lymphomas, 4 skin cancers, 2 hepatocellular carcinomas, 2 laryngeal carcinomas, 1 breast cancer, 1 lung cancer, 1 urothelial carcinoma, 1 cholangiocarcinoma, 1 conjunctival squamous cell carcinoma. Only 6 (20%) tumors were AIDS-defining: 4 high-grade non-Hodgkin lymphomas, and 2 Kaposi's sarcomas. Notably, 2 individuals developed 2 different incident malignancies: one person developed Hodgkin lymphoma followed by non-Hodgkin lymphoma, the other a skin cancer followed by an HPV-related anal neoplasm. Furthermore, an individual who developed Kaposi's sarcoma, had a prevalent HPV-related anal cancer at baseline.
Twenty-two (9.6%) 4DR-PLWH developed ≥1 MACE (n=31, Figure 1): IR=1.8 (95%CI=1.1-2.4)/100 PYFU. In particular, 15 myocardial infarctions, 8 acute congestive heart failures, 4 coronary diseases requiring revascularization, 3 strokes, and 1 peripheral artery disease requiring revascularization occurred. Remarkably, 5 individuals developed ≥2 incident MACEs: 2 events occurred in 2 individuals, 3 events in 2, 4 events in 1.
Cumulative probabilities of the first incident cancer and the first incident MACE reported in Figure 2.
Among 4DR-PLWH who experienced ≥1 incident malignancy or ≥1 incident MACE, 11 died: 8 after ≥1 tumor, 2 after ≥1 MACE, and 1 after both 1 malignancy and 1 MACE (Figure 1).
Conclusions: Due to high incidence of malignancies and MACEs in people living with multidrug-resistant HIV, screening and prevention strategies are strongly recommended in this fragile population.

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Cardiovascular and malignancies

OC 58 CARDIOVASCULAR EVENTS ON INTEGRASE STRAND-TRANSFER INHIBITORS TREATMENT

P. Bonfanti[1], E. Ricci[2], G.V. De Socio[3], P. Maggi[4], N. Squillace[1], L. Taramasso[5], L.A. Nicolini[5], G. Orofino[6], M.B. Celesia[7], G. Madeddu[8], B. Menzaghi[9], F. Vichi[10], A. Di Biagio[5] on behalf of CISAI Study Group

[1]Fondazione IRRCS San Gerardo dei Tintori-University of Milano-Bicocca, Monza, [2]Fondazione ASIA Onlus, [3]Santa Maria Hospital, Perugia, [4]AORN Sant'Anna e San Sebastiano - University L.Vanvitelli, Caserta, [5]IRCCS Policlinico San Martino Hospital - University of Genova, Genova, [6]Amedeo di Savoia Hospital, Torino, [7]A. Garibaldi Hospital, Catania, [8]Università di Sassari, Sassari, [9]Busto Arsizio Hospital, Busto Arsizio (VA), [10]Sant'Annunziata Hospital, Firenze

Background: The issue of HIV- and antiretroviral (ART)-related risk factors for cardiovascular disease (CVD) events is of utmost importance, given the progressive aging of people living with HIV (PLWH). Since they receive chronic therapy, it is crucial to analyse to what extent certain drugs or classes of ART drugs are associated with increased CVD risk. A recent study reported on the exposure to integrase strand-transfer inhibitors (INSTI) as a risk factor for the increased incidence of CVD in PLWH. Although unmeasured confounding and channelling bias cannot be excluded, starting an INSTI was associated with an early onset, excess incidence of CVD in the first 2 years of exposure. Aim of this study is to evaluate the impact of starting InSTI-based compared to other ART on cardiovascular events among people with HIV in the SCOLTA Cohort.

Methods: SCOLTA project is a prospective study reporting adverse reactions to newly marketed ART drugs, currently involving 30 Italian infectious disease centres. The study collected demographical information, risk factors for HIV infection, viral-immunological data and the causes of treatment interruption. Discontinuation was defined as PLWH stopping the use of the cohort drug. Since 2002, cohorts for lopinavir, atazanavir, darunavir, raltegravir, rilpivirine, elvitegravir, dolutegravir, bictegravir and doravirine enrolled and followed-up prospectively both naïve and experienced PLWH.

Results: Excluding 1069 INSTI-experienced PLWH, 4603 PLWH naïve to INSTI were eligible for the analysis (see table). We found 17 acute myocardial infarctions, five strokes, one sudden cardiac death, over a median follow-up time of 2.1 years (interquartile range, IQR, 1.0-3.4). The PY of observation were 11325.8, for a crude incidence rate (IR) of 2.03 (95% CI 1.32-3.00) for 1000 PY. IRs were 2.68 (95% CI 1.54-4.14) for INSTI and 1.35 (95% CI 0.59-2.67) for non-INSTI (crude rate ratio, cRR, 2.39, 95% CI 0.97-6.61). As expected, a strong channelling bias was present, as traditional cardiovascular risk factors were different: 25.8% on INSTI vs. 15.0% on non-INSTI regimens had at least one CVD risk factor (previous CVD event, diabetes, hypertension, dyslipidaemia). Excluding them, 14 CVD events occurred in 9050.9 PY (IR 1.55, 95% CI 0.88-2.53). IRs were 1.97 (95% CI 0.90-3.74) in INSTI and 1.15 (95% CI 0.36-2.60) in non-INSTI group (cRR 1.77, 95% CI 0.59-5.82).

Conclusions: Our data confirm the signal of increased risk, albeit with all the potential confounding factors inevitably existing in cohort studies. INSTIs are currently the most widely prescribed ART class, recommended by current guidelines for PLWH at high CVD risk, thus we believe that the findings of the RESPOND study deserve to be discussed and further verified, as previously occurred about other drugs.

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Cardiovascular and malignancies

OC 59 MULTIDIMENSIONAL EVALUATION OF SWITCHING FROM A FIRST GENERATION 3 DRUG (DR) INSTI REGIMEN TO A SECOND GENERATION 3DR- OR 2DR INSTI REGIMEN: A SINGLE CENTER RETROSPECTIVE DESIRABILITY OF OUTCOME RANKING (DOOR) ANALYSIS

N. De Gennaro, F. Balena, D. Fiordelisi, L. Frallonardo, G. Guido, D. Cassano, V. Guerra, V. Spada, A. Dargeni, G. Romito, G. Manco Cesari, V. Totaro, C. Pellegrino, D.F. Bavaro, A. Saracino

Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy

Background: Integrase strand transfer inhibitors (INSTI) represent key components of antiretroviral therapy (ART) in naïve and experienced people who live with HIV (PLWH). Currently, many new generation INSTI-based regimens are available in fixed dose combinations: bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF), dolutegravir/lamivudine (DTG/3TC) or /rilpivirine (DTG/RPV). Herein, potential advantages of switching from a first generation INSTI-based regimen to a new INSTI-based triple drug (3DR) regimen or to a dual drug (2DR) were evaluated.

Material and Methods: All PLWH on first generation 3DR INSTI-based ART, virologically suppressed for at least one year, switching to an INSTI-based 3DR or 2DR from June 2019 to March 2022 at our Clinical Centre were evaluated. Demographic, clinical, biochemical and immunovirological data were retrieved at baseline and 48 weeks after switch. The two ART strategies (before and after switch) were compared through a specific Desirability of Outcome Ranking (DOOR) analysis. At 48 weeks after switch, PLWH were assigned a mutually exclusive rank 0 or 1 if virologically suppressed (VS); one additional point was assigned to VS PLWH if the following endpoints were achieved: CD4/CD8 ratio increase ≥0.05; body mass index (BMI) increase ≤0.5kg/m2; decrease of total/high density lipoprotein cholesterol (TC/HDL-c) ≥0.10 mg/dl, and of creatinine ≥0.11 mg/dl; absence of any adverse event to ART. Descriptive statistic and logistic regression models were performed on the real-life population. To match baseline PLWH features, an inverse probability of treatment weighting (IPTW) was built. Then, the analyses were repeated on the matched pseudo-population.

Results: Overall, 309 PLWH (84 females at birth, 27%) were enrolled, with median age of 54 (45-59) years; 33% in AIDS stage, with median CD4-nadir of 307 (204-469) cell/uL; 182 patients (58.9%) had at least one comorbidity; 37 were HIV-HCV-coinfected; before switch, 77% were in TAF/FTC and 53.4% were in elvitegravir (EVG). A total of 210 PLWH switched to 3DR-INSTI whereas 99 to 2DR-INSTI; no significant baseline differences were found between the two groups.

In the DOOR analysis at 48 weeks after the switch a better ranking distribution was noticed for 2DR-INSTI (p=.026) (Fig 1). In fact (Table 1), the univariate unadjusted analysis showed a reduced risk of weight and creatinine increase in the group switching to 2DR-INSTI compared to 3DR. However, at the IPTW-adjusted analysis, the effect on creatinine (aOR 0.32 [0.14-0.72] p=.006) was confirmed while the weight change resulted non-significant. In addition, an increased probability of lower CT/HDL-c ratio was observed (aOR 2.09 [1.07-4.09] p=.031.) .

Conclusions: Based on this DOOR analysis, the switch from a first generation INSTI regimen to a 2DR INSTI seems to offer potential advantages compared to 3DR INSTI in terms of improving metabolic outcomes, particularly on lipid profile and renal function.

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Cardiovascular and malignancies

OC 60 SELECTED COMORBIDITIES AND THE RISK OF ART SWITCH IN THE CONTEXT OF HIV-RNA SUPPRESSED TO ≤50 COPIES/ML

A. Cozzi-Lepri[1], A. Tavelli[2], L. Taramasso[3], D. Barbanotti [4], G. Lapadula[5], N. Bobbio[6], S. Piconi[7], G. Guaraldi[8], A. Di Biagio[3], C. Muccini[9], A. Antinori[10], A. d'Arminio Monforte[2], on behalf of the Icona Foundation Study group

[1]IGH University College London, CREME Center, London, United Kingdom, [2]Icona Foundation Study, Milano, Italy, 3San Martino Hospital, Genova, Italy, [4]San Paolo Hospital, Milano, Italy, 5Fondazione IRCCS "San Gerardo" and Bicocca University, Monza/Milano, Italy, [6]Galliera Hospital, Genova, Italy, [7]Unità Operativa Complessa ASST Lecco, Lecco, Italy, [8]University of Modena and Reggio Emilia, Modena, Italy, [9]San Raffaele Hospital, Milano, Italy, [10]INMI Lazzaro Spallanzani, Roma, Italy

Background: Although HIV-associated mortality has been greatly reduced by ART, the incidence of deaths due to non-communicable diseases remains high in PLWH. Clinical decisions regarding whether to modify ART regimens in the context of a HIV-RNA≤50 copies/mL may be guided by current ART and the development of specific comorbidities.

Methods: Cohort data analysis of the risk of ART switch (RTS) in PLWH of the Icona Foundation Study with a stable VL≤50 copies/mL according to the development in course of follow-up of a set of a priori chosen co-morbidities (i.e. becoming overweight (OW, BMI>26), developing dyslipidaemia (DP), kidney disease (KD, eGFR<60) and diabetes mellitus (DM)). At the time of their first ever episode of >6 months with VL≤50 copies/mL after January 2017 (baseline) participants had to be free from the comorbidity of interest. After baseline they were followed-up until they developed the event (if there was a ART switch) or their follow-up was censored (if ART remained unchanged or if VL went >50 copies/mL). Four separate standard Cox regression models with baseline confounders were fitted (one for each of the time-varying exposures, see footnote of the Table for exact specifications). Models were repeated after stratification by anchor drug class received at the beginning of the episode.

Results: In the model with diabetes as the time-varying exposure, we included 1,146 PLWH with a median (IQR) age of 41 (32-50) years, 18% females, 51% MSM, 60% of foreign nationality with a median of 642 (447-869) CD4 count at baseline. Estimated incidence of RTS was 0.29 (95% CI: 0.27-0.31) per 100 person-years of follow-up. The Table shows unadjusted and adjusted hazard ratios (HR) of RTS from fitting the four separate models. In the main analysis controlling for confounders, DM was the only co-morbidity associated with an increased risk of RTS (approximately 6-fold higher risk in exposed vs. unexposed, although not significant p=0.15). For DP, there was weak evidence that the risk varied by anchor drug class received at baseline (interaction p=0.31), with participants receiving PIs , however, showing a higher risk of RTS (aHR=2.23, 95% CI:1.02-4.87) vs. inconclusive results in the overall analysis (aHR=1.12, 95% CI:0.87-1.45, p=0.39, Table). Finally, there was no evidence that BMI had a different prognostic role in predicting RTS after restricting to participants currently receiving INSTI-based regimens (interaction p=0.60).

Conclusions: Overall, modern regimens appeared to be relatively safe and well tolerated with low incidence of RTS even in participants with co-morbidities. Among the conditions evaluated, only the development of DM (and of DP in those receiving PIs) appeared to be associated with a greater risk of modification of participants' ART regimen composition in the setting of VL≤50 copies/mL. The analysis, which is slightly underpowered, needs to be repeated when a larger number of RTS cumulates.

Analysis sponsored by Gilead Srl

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Severe clinical issues in HIV-1 infection

OC 61 LOWER AIDS-RELATED HOSPITALIZATIONS IN WOMEN LIVING WITH HIV MULTIDRUG RESISTANCE: RESULTS FROM THE PRESTIGIO REGISTRY

R. Papaioannu Borjesson[1], L. Galli[2], R. Lolatto[2], B. Menzaghi[3], M. Feasi[4], R. Gulminetti[5], C. Fornabaio[6], A.M. Cattelan[7], S. Bonora[8], F. Lagi[9], M. Zazzi[10], A. Castagna[1,2], on behalf of PRESTIGIO Study Group

[1]San Raffaele Vita-Salute University, Milan, Italy, [2]Infectious Diseases Department, San Raffaele Scientific Institute, Milan, Italy, [3]Unit of Infectious Diseases, ASST della Valle Olona, Busto Arsizio, Italy, [4]Ente Ospedaliero Ospedali Galliera, Genova, Italy, [5]Department of Medical Sciences and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [6]ASST Cremona, Cremona, Italy, [7]Azienda Ospedale-Università Padova, Padova, Italy, [8]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Torino, Italy, [9]Infectious and Tropical diseases Unit, Azienda Ospedaliera Universitaria Careggi, Florence, Italy, [10]Department of Medical Biotechnologies, University of Siena, Siena, Italy

Background: We explored the incidence of hospitalization in male and female people living with 4-drug class resistant HIV (4DR-PLWH) enrolled in the PRESTIGIO study.

Methods: We included PLWH with a documented resistance to NRTIs, NNRTIs, PIs and INSTIs. Hospitalization was defined as a hospital admission for any reason with ≥1 overnight stay. Follow-up started from the date of the first 4DR evidence (baseline) until death/loss-to-follow-up/freezing date (December 31st, 2022). Data were reported as median (IQR) or frequency (%). Poisson regression was used to model incidence rates (IR) with 95% confidence intervals (CI).

Results: Overall, 178 4DR-PLWH were included; baseline characteristics, according to gender, are reported in Table 1.

During 1294 PYFU, 122 hospitalizations (28 in females) occurred in 60 4DR-PLWH: 29/60 (48.3%) had >1 hospitalization.

The overall IR for hospitalization was 9.43/100 PYFU (95%CI=7.76-11.10), without a significant difference between males and females (Incidence rate ratio (F/M)=0.77, 95%CI=0.51-1.17, p=0.223). At 7 years after baseline, 34.7% were estimated to have had >=1 hospitalization.

The median duration of hospitalization was 8 days (IQR 4-20). The most frequent causes were non-AIDS-defining infections (n=28, 23%) and major adverse cardiovascular events (MACEs, n=19, 15.6%). Females had no hospitalizations for AIDS-defining events compared to males (0% vs 11.7% (n=11), p=0.049); gender differences appeared with regard to hospitalizations for non-AIDS-defining events (MACEs: 17 (18.1%) and 2 (7.1%) in males vs females, p=0.097; non-AIDS-defining infections: 19 (20.2%) and 9 (32.1%) in males vs females, p=0.084; Figure1).

Conclusion: Women living with HIV multidrug resistance seem to have a lower incidence of AIDS-defining events hospitalizations; women tended to have fewer hospitalizations for MACEs and more hospitalizations for non-AIDS-defining infections than males.

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Severe clinical issues in HIV-1 infection

OC 62 MALIGNANCIES IN PLWH: A 20-YEAR EXPERIENCE IN PERUGIA AND ANCONA HOSPITALS

L. Curci, C. Papalini, L. Brescini, F. Barchiesi, A. Giacometti, D. Francisci

Infectious Diseases Clinic, Santa Maria della Misericordia Hospital, University of Perugia, Perugia, Italy, Biomedical Sciences and Public Health Department, University Politecnica delle Marche, Ancona, Italy

Background: It is known that HIV infection predisposes to some malignancies (AIDS-defining diseases), but given the prolonged survival of people living with HIV (PLWH) due to antiretroviral treatment (ART), an increased incidence of non-AIDS-defining malignancies has been observed.
The aim of this study is to describe the epidemiology of PLWH affected by malignancies in two Italian hospitals and to analyse differences in patients' characteristics depending on the type of neoplasms: solid tumor, blood cancer, Kaposi Sarcoma (KS) and HPV-related precancerous lesions (cervical and anal intraepithelial neoplasms).
Materials and Methods: A retrospective observational study was conducted on PLWH ever affected by neoplasms in their life, visited in the Infectious Diseases Clinics of Santa Maria della Misericordia Hospital in Perugia and Torrette Hospital in Ancona from January 2001 to December 2022. We evaluated: sex, country of origin, age at diagnosis of malignancy, immunological and viral status at the time of diagnosis of cancer, CD4+ nadir, HIV-RNA zenith, CD4+/CD8+ ratio at neoplasm diagnosis, risk cofactors for neoplasms (positive PCR for HPV on anal and/or genital swab, HBV and/or HCV co-infection).
Results: We evaluated 367 patients, whose clinical and epidemiological features are summarized in Table 1: 199 patients were diagnosed with solid tumors, 62 with KS, 76 with blood cancer and 92 with precancerous lesions. Furthermore 26 were diagnosed with a second tumor: 8 patients with solid tumors also had a second one, 2 had precancerous lesions, and 2 had blood cancer; 5 patients with SK also had another solid tumor, 2 had precancerous lesions, and 1 had blood cancer; 5 patients with blood cancers also had a solid tumor and 1 had precancerous lesions. Analyzing differences in patients' characteristics between the 4 aforementioned groups we found that patients with solid tumors were older while those with precancerous lesions were the youngest. Concerning immune and viral status at HIV diagnosis, patients with KS presented a lower CD4+ nadir compared to patients with precancerous lesions and solid tumors; on the other hand, mean HIV RNA zenith, was similar in all the groups. Similarly, at tumor diagnosis patients with KS had higher viremia and lower CD4+ count and CD4+/CD8+ ratio in comparison to the other groups. Moreover, also individuals affected by blood cancers showed lower CD4+ count and CD4+/CD8+ ratio at neoplasm diagnosis compared to those of the ones affected by solid tumors or precancerous lesions.
Conclusions: Malignancies are a common co-morbidity in PLWH. The study revealed patients affected by solid tumors are older, but those affected by KS and blood cancers had the worse immune-viral status.

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Severe clinical issues in HIV-1 infection

OC 63 CLINICAL PRESENTATION AND NEUROIMAGING IN NEWLY DIAGNOSED AIDS PATIENTS IN THE LAST 6 YEARS

L. Carani[1], A. Calcagno[1], G.C. Orofino[2], G. Calleri[2], P. Busolli[3]

[1]Dipartimento di Scienze Mediche, Università degli Studi di Torino, Torino, [2]Divisione A Malattie Infettive e Tropicali, Ospedale Amedeo di Savoia, Torino, [3]SS Imaging Neuroncologico, Ospedale Giovanni Bosco, Torino

Background: In a significant proportion of patients living with HIV the infection is not discovered early: they are classified as late presenters (CD4<350/uL) or AIDS presenters (CD4<200/uL).
Aware of the effects of COVID19 outbreak on HIV services for prevention and treatment some studies have shown an increasing number of late-presenting patients in recent years.
Aim of this study was to assess the clinical presentation and neuroimaging abnormalities in AIDS presenters in the last 6 years.
Methods: An observational retrospective study was conducted including all hospitalized AIDS-presenters at the Amedeo di Savoia Hospital in Turin (Italy), from 2017 to 2022. Data are shown as median (IQR) and compared through non-parametric tests.
Results: We included 173 patients, 89 in the 2017-2019 years and 84 in 2020-2022. Baseline features and p values for differences are shown in the tables below.
Patients mainly presented to medical attention for fever (45.7%), weight loss (39.9%) and weakness (32.9%).
Cytomegalovirus-related conditions, candidiasis (invasive or not) and Pneumocystis jirovecii pneumonia were the principal opportunistic infections (OIs) followed by Mycobacterium avium complex diseases and tuberculosis.
58 patients (33.5%) presented at least one neurological symptom; the commonest central nervous system (CNS) disease was neurotoxoplasmosis (13.3%) followed by HIV encephalopathy.
In 126 patients (72.8%) brain MRI or CE-CT was performed: in 33 (56.9%) patients with and 2 (1.7%) without neurological symptoms CNS opportunistic infections (OIs) were seen.
In 58 asymptomatic patients with less than 100 CD4/uL and available neuroimaging 2 neurotoxoplasmosis were diagnosed (prevalence 3.4%).
Conclusions: AIDS presenters during or after COVID-19 pandemic presented higher HIV-1 RNA (viral load) at baseline compared with the 2017-2019 period. Despite not showing neurological symptoms AIDS presenters with less than 100 CD4/uL have a 3.4% risk of CNS OIs.

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Severe clinical issues in HIV-1 infection

OC 64 PROLONGED SURVIVAL IN HIV-ASSOCIATED PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML) TREATED WITH PEMBROLIZUMAB: A CASE SERIES ON TREATMENT AND LONG-TERM FOLLOW-UP

M. Chiuchiarelli[1], F.V. Segala[2], G. Giuliano[3], P. Del Giacomo[4], A. Dusina[4], G. Maiuro[4], E. Matteini[1], F. Frondizi[1], S. Gaudino[5], E. Cimini[6], R. Santangelo[4,7], C. Agrati[6], A.Cingolani[4]

[1]Department of Bioethics and security, Università Cattolica del Sacro Cuore, Rome, Italy, [2]Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari, Bari, Italy, [4]Dipartimento Scienze di Laboratorio e Infettivologiche - Fondazione Policlinico Gemelli IRCCS, Roma, Italy, [5]Department of Radiological Sciences, Catholic University, School of Medicine, Rome, Italy, [6]Laboratory of Cellular Immunology and Clinical Pharmacology, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Roma, Italy, [7]Department of Basic Biotechnological, Clinical Intensivological and Perioperative Sciences, Catholic University of the Sacred Heart, Rome, Italy

Background: PML is a disease typically associated with a history of immunosuppression, including PLWH (persons living with HIV), which allows reactivation of the polyoma JC virus causing a demyelinating illness, with a wide range of clinical manifestations and an annual mortality rate around 30% a year. Treatment option for this disease remain limited so in recent years the use of immune therapy has been explored. Pembrolizumab is an immune checkpoint inhibitor targeting PD-1 receptors on T lymphocytes, which normally decrease the immune response of T cells. The expression of PD-1 seems increased in PML patients' CSF; therefore this therapy seems promising, and a treatment approach based on pembrolizumab was implemented in our center for HIV-infected with a diagnosis of PML.

Materials and Methods: We present here the first 3 consecutive HIV-infected patients who were admitted to our ward presenting with clinical and radiological MRI findings suggestive of PML, who were included in the pembrolizumab protocol. All of them underwent LP with chemical tests, cultural exam, HIV-RNA quantitative test, PCR for JC virus and essay to determine JCV-specific PD-1 activity in CSF and whole blood. All of them were treated with monthly IV administration of Pembrolizumab at 2mg/kg for at least four times. All of them continued HAART and underwent follow-up blood and CSF tests and radiological assessment.

Results: The three described patients are 2 males and one female. Demographic, clinical and disease-specific characteristics are reported in Table 1. All three of them showed a clinical and neurological presentation suggestive for PML and a CSF with detected JCV-DNA virus. The radiological findings on MRI defined a complex picture for all three patients with multifocal signal alterations in the white substance. All of them performed treatment with Pembrolizumab at the overmentioned dose (patient 1 had 8 infusions instead of four). Clinically all three patients showed an improvement on neurological deficits reacquiring partially the lost functions and they are alive at 3.5 years, 14 months, and 9 months respectively. Follow-up MRI were performed in patient 1 and 3 showing stability of the kind and number of lesions (figure 2), without reactivation evidence.

Conclusion: A prolonged survival was observed in these patients treated with pembrolizumab, with radiological findings show a consistent response. The decrease of JCV-specific PD-1 activity in LCR and WB, suggest a correlation between clinical and immunomediated response to pembrolizumab. Due to the conflicting literature reports, further research is needed to assess the effectiveness of this treatment on a large scale and its persisting effect.

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Oral or injectable 2-drug regimens

OC 65 "WITH AGE COMES WISDOM": EFFICACY AND TOLERABILITY OF DOLUTEGRAVIR+LAMIVUDINE IN VIROLOGICALLY-SUPPRESSED PLWH

G. Baldin[1], A. Ciccullo[2], R. Passerotto[3], A. Dusina[1], V. Iannone[3], A. Lamanna[3], A. Carbone[3], I. Mozzetta[1], E. Visconti[1], S. Di Giambenedetto[1,3], A. Borghetti[1]

[1]UOC Malattie Infettive, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [2]Malattie Infettive, Ospedale San Salvatore, L'Aquila, Italy, [3]Dipartimento di Sicurezza e Bioetica, Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Rome, Italy

Background: Results from clinical trials and observational studies suggest that dolutegravir plus lamivudine is a well-tolerated option for simplification in PLWH. We aimed to assess long-time efficacy and safety in our cohort.
Material and methods: This was an observational study enrolling HIV-1-infected, virologically suppressed from at least 6 months patients, switching to dolutegravir plus lamivudine. Exclusion criteria were HBV-coinfection and the presence of the M184V mutation before the simplification. We performed survival analysis to evaluate time to virological failure (VF, defined by a single HIV-RNA ≥200 copies/mL or by two consecutive HIV-RNA ≥ 50 copies/mL) and treatment discontinuation (TD, defined as the interruption of either 3TC or DTG). We selected variables associated with VF at a p-value <0.100 at univariable analysis to build a multivariable Cox regression model.
Results: Six hundred thirty-one patients were considered for the analysis: 446 were males (70.7%), with a median age of 51.1 years (IQR 42.6-57.6). Full characteristics at baseline are presented in Table 1. Estimated probabilities of maintaining virological suppression at 48 and 96 months were 95.1% (95%CI 92.0-96.2) and 91.5% (95%CI 87.1-94.4), respectively. At multivariable analysis, including zenith HIV-RNA, time of virological suppression before switch, risk factors for HIV infection and age, only IDU (versus other risk factors, aHR 3.58, 95%CI 1.38-9.28, p=0.009) independetely predicted VF. A border-line significant association with VF emerged for age (per 10-years more, aHR 0.72, 95%CI 0.51-1.01, p=0.058) and zenith HIV-RNA > 500000 cps/mL (versus <500000 cps/mL, aHR 2.31, 95%CI 0.98-5.46, p=0.056).
In our cohort, 67 pts interrupted the study-regimen due to virological failure (3), toxicity (2 for hypersensitivity reaction, 7 for GI, 10 for neurological, 9 for other toxicities), pregnancy (2), simplification (7), other or unknown reasons (28). Estimated probabilities of remaining on study regimen at 48 and 96 months were 87.8% (95%CI 84.5 -90.5) and 85.1% (95%CI 81.0-88.5), respectively.
Conclusions: Our findings confirm the long-term efficacy and tolerability of dolutegravir plus lamivudine in virologically suppressed patients.

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Oral or injectable 2-drug regimens

OC 66 ASSESSING LONG-TERM RISK OF VIROLOGICAL FAILURE IN PLWHIV STARTING DOLUTEGRAVIR +LAMIVUDINE AS A SWITCH STRATEGY

A. Ciccullo[1], G. Baldin[2], F. Lombardi[2], A. Carbone[3], D. Farinacci[4], G. Placidi[2], A. Dusina[2], E. Visconti[2], A. Borghetti[2], S. Di Giambenedetto[2,3]

[1]UOC Malattie Infettive, PO San Salvatore, L'Aquila, Italia, [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italia, [3]Università Cattolica del Sacro Cuore, Roma, Italia, [4]UO Medicina Protetta - Malattie Infettive, ASL Viterbo, Italia

Background: Results from clinical trials and observational studies suggest that dolutegravir plus lamivudine (DTG +3TC) could be an effective and well-tolerated option for simplification in People Living With HIV (PLWHIV). We aimed to assess the long-term safety of this switch strategy, searching for predictors of treatment failure.
Methods: This was an observational study enrolling HIV-1-infected, virologically suppressed PLWHIV switching to DTG+3TC. Criteria for eligibility were: patient's informed consent to data collection, being at least 18 years-old, being on stable (i.e. at least 6 months) antiretroviral therapy (ARV) with viral suppression (HIV-RNA<50 copies/mL) at time of switch to DTG+3TC (baseline) and being HBsAg negative. We collected data on clinical history and viro-immunological status at baseline and during follow-up. We performed survival analyses to evaluate time to virological failure (VF, defined as a single HIV-RNA determination ≥1,000 copies/mL or two consecutive determinations ≥ 50 copies/mL), assessing predictors via Cox regression analyses.
Results: We analyzed data from 726 PLWHIV: 510 were males (70.2%), with a median age of 51.4 years (IQR 43.2-57.7), a median time from HIV diagnosis of 18.0 years (10.2-25.0) and a median time from ARV initiation of 15.0 years (9.0-23.0). Full population characteristics are shown in Table 1. During 2332.2 PYFU we observed 39 VF, a rate of 1.7 VF per 100 PYFU; median time to VF was 29.6 months (20.2-54.3), with 10 VF (25.6%) occurring in the first 12 months after switching to DTG+3TC. Estimated probabilities of maintaining virological suppression were 94.1% (SD±1.0), 92.6% (SD±1.3) and 90.0% (SD±2.0) at 144 weeks, 240 weeks and 336 weeks, respectively. Individuals who reached virological suppression in the 24 months before starting DTG+3TC had a higher risk of VF compared with PLWHIV with a longer time of virological suppression before baseline: probability of maintaining suppression at 240 weeks was 88.2% (SD±4.1) in those with less than 24 months of suppression at baseline and 92.7% (SD±1.4) in those with a longer time of suppression before switch (log-rank p=0.014). At a multivariate analysis, a longer time of virological suppression before switching to DTG+3TC resulted protective against VF (aHR 0.991, 95%CI 0.984-0.997, p=0.007), after adjusting for peak HIV-RNA and the presence of the M184V resistance mutation. Among the 39 PLWHIV that experienced VF, 15 (38.5%) discontinued DTG+3TC, while the others maintained the 2DR and re-achieved virological suppression subsequently. We did not observe any acquired resistance mutation in the 39 failed PLWHIV at a subsequent genotypic test.
Conclusion: Our data confirm the high efficacy and safety of a 2DR with DTG+3TC as a switch strategy. In our cohort the role of the M184V mutation was minimal regarding the risk of VF while a correlation was observed with time of virological suppression before baseline.

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Oral or injectable 2-drug regimens

OC 67 CHARACTERISTICS AND CLINICAL FEATURES OF PATIENTS RECEIVING LA CAB/RPV IN A LARGE CLINICAL CENTRE

M.V. Cossu[1], D. Moschese[1], M. Piscaglia[1,3], F. Caruso[2,3], C. Fusetti[2,3], M. Matone[1,3], C. De Luca[1], M. Faenzi[1], S. Sportoletti[1], A.F. Capetti[1], P.R. Meraviglia[2], A. Gori[2,3], G. Rizzardini[1]

[1]I Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [2]II Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [3]University of Milano, Milan, Italy

Background: Cabotegravir and rilpivirine is the first long-acting injectable cART approved for virologically suppressed adults with HIV-1.
Since Dec 2016, our center was involved in 4 pivotal randomized controlled trials: FLAIR, ATLAS, ATLAS-2M and SOLAR. FLAIR and ATLAS trials investigated LA CAB/RPV every 4 weeks as maintenance therapy in comparison to standard cART in virally suppressed PLWH, while ATLAS-2M and SOLAR trials investigated this regimen at a reduced dosing frequency (every 8 weeks).
Aim of this study is the clinical characterization of the patients involved in the CAB/RPV trials.
Material and methods: We collected clinical features of all patients enrolled in the CAB/RPV trials at our Division of Infectious Disease from Dec 2016 to Nov 2020. All patients involved in this analysis have received at least one dose of LA injectable CAB/RPV.
Data for continuous variables are showed as means or median (and ST or IQR where appropriated) and categorial variables as frequencies and percentages.
Results: Among the 68 patients enrolled, 49 were less than 50 yrs (72%), 17 were females (25%), with relatively few comorbidities (Table 1). In addition, 5 PLWH (7.35 %) were classified as obese (BMI greater 30 kg/m2), while 22 (32.5%) were overweight (25-30 BMI kg/m2). Median duration of infection was 2 years (IQR 2-8 yrs) and mean CD4 count was 727,5 cell/mmc (SD 340 cell/mmc), while 6 subjects had a history of AIDS (8%).
34 patients were enrolled in both FLAIR/ATLAS and ATLAS-2M/SOLAR trials (50% in each group). When not mandatory, oral lead-in was refused by 3 patients that started the IM regimen directly. Comedications were recorded, with 16.2 % of patients having 2 or more comedications; none was
considered likely to cause DDIs.
Oral bridging with CAB/RPV during the Maintenance Phase was necessary for 8 patients with a median duration of 2 months [IQR 1,75-4].
The most common adverse event was injection-site reactions reported in 38 PLWH (56 %).
Only 4 patients are currently no longer part of our cohort: one moved to another country, one experienced an Non-Hodgkin Lymphoma, while one decided to interrupted the therapy due to uncomplete satisfaction.
Although few viral blips occurred, only one virologic failure (HIV-RNA >200 cp/mL) was recorded in our cohort: the patient did not present any contraindication, risk factor or RAM for CAB/RPV.
Conclusions: Overall, our experience demonstrates that heterogeneous characteristics observed in our cohort do not interfere with the efficacy and tolerability of this long-awaited promising regimen.

Oral or injectable 2-drug regimens

OC 68 3-MONTH OUTCOME OF LONG-ACTING CABOTEGRAVIR AND RILPIVIRINE: PRELIMINARY RESULTS FROM THE SCOHOLART STUDY

C. Candela[1,2], V. Gordo[1], L. Galli[1], T. Clemente[1,2], B. Trentacapilli[1,2], M.F. Lucente[1,2], R. Monardo[1,2], F. Alberton[1,2], R. Lolatto[1], M. Lavall[1], A. Lettieri[1], R. Melzi[1], P. Striglia[1], D. Zandonà[1], S. Bagaglio[1], E. Carini[1], A. Castagna[1,2], N. Gianotti[1]

[1]Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milano, Italy, [2]Vita-Salute San Raffaele University, Milano, Italy

Background: The primary aim of the SCohoLART Study is to collect clinical data on people living with HIV (PLWH) treated with long-acting regimen of cabotegravir and rilpivirine in our center, in order to optimize their clinical management, during a long-term follow-up. Aim of the present preliminary analysis is to evaluate the 3-month outcome of long-acting cabotegravir and rilpivirine in people enrolled in this study.

Methods: SCohoLART (NCT05663580) is a single-center, prospective, cohort study of PLWH treated with long-acting cabotegravir and rilpivirine.

Individuals with HIV-RNA <50 copies/mL, starting for the first time long-acting cabotegravir and rilpivirine (with or without oral lead-in) are consecutively enrolled, after giving written informed consent. They are followed-up, according to national guidelines. HBsAg-/HBcAb+ people are monitored by HBV-DNA quantification.

Treatment failure (TF) is defined as (a) switch to another regimen for any reason or (b) virological failure (VF); virological failure is defined as HIV-RNA ≥50 copies/mL at two consecutive measurements or a single measure of HIV-RNA ≥1000 copies/mL.

The primary endpoint of the present analysis is the cumulative probability of treatment failure within 3 months of follow-up, estimated by Kaplan-Meier curve.

Results: At March 15, 2023, 374 people started the study regimen; 301 started before February 1, 2023 and were included in the present analysis. Most relevant baseline (BL) characteristics were: male gender: 269 (89.4%); median (IQR) age: 48.62 (39.6 - 57.05) years; years since HIV diagnosis: 13.95 (8.76 - 20.87); years since ART start: 11.55 (7.9 - 17.87); nadir CD4+ count: 331 (212 - 508) cells/μL, with 77 (25.6%) with ≤200 cells/μL; current CD4+ count: 775 (588.5 - 945.5) cells/μL; years with virological suppression: 9.14 (5.51 - 12.96); on a NNRTI-based regimen: 83 (27.6%); on a PI-based regimen: 15 (5%); on an INSTI-based regimen: 203 (67.4%).

The median follow-up was 3.78 (2.86 - 5.1) months. We observed 15 TFs, including two VFs (pending resistance testing and drug concentrations results at failure; both underwent injections within the scheduled window). The 3-month probability of TF was 3.5% (95%CI: 1.9%-6.5%, figure); the main reason of TF was central nervous system (CNS) toxicity (5 cases, 1.7%), followed by injection site reaction (ISR; 3 cases, 1%); causes of treatment withdrawal are detailed in the figure. A HBV-relapse was observed in one individual HBsAg-/HBcAb+ at BL; in this case TAF/FTC was promptly reintroduced.

Conclusions: The 3-month probability of TF with the long-acting regimen of cabotegravir and rilpivirine was low, with few VFs. CNS toxicity was the leading cause of discontinuation. HBsAg-/HbcAb+ people should be strictly monitored by HBV-DNA. VFs are currently under investigation to understand possible reasons leading to this event.

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Prevention, access and engagement

OC 69 A NURSE-LED HIV/STI PREVENTION PROGRAM IN A VOLUNTARY COUNSELLING AND TESTING SITE IN THE METROPOLITAN AREA OF ROME

E. Gennaro, R. Esvan, O. Bruzzi, A. Faticoni, G. Iannicelli, A. Navarra, N. Orchi, E. Piscitelli, S. Pittalis, D. Tonnini, V. Puro

Centro di Riferimento AIDS, Istituto Nazionale per le Malattie Infettive "Lazzaro Spallanzani", Roma

Background: Implementing evidence-based combination HIV prevention programs is key to ending the HIV epidemic. We here describe the impact of the implementation of a service led by appropriately trained registered nurses to counselling and testing for HIV and Sexually Transmitted Infections (STI), and linkage to prevention care. This service is offered at the Voluntary Counseling and Testing Site (VCTs) of the AIDS Regional Reference Center in the National Institute for Infectious Diseases “L. Spallanzani”.

Materials and methods: In 2022, a new nurse-led service for free HIV/syphilis/HCV rapid point-of-care testing and HIV/STI prevention counseling for adults ≥18 years was introduced. All persons attending the service were offered risk reduction counselling, information on HIV post-exposure prophylaxis (PEP), Pre-Exposure Prophylaxis (PrEP), vaccinations (including Mpox since August 2022) or care, as appropriated. Determine™ HIV Early Detect (Abbot), Determine™ Syphilis TP (Abbot) and OraQuick® HCV (OraSure Technologies) were used. In case of preliminary test reactivity, a confirmatory test was carried out immediately after to ensure a prompt linkage to care. Moreover, attenders received a risk assessment questionnaire to identify high-risk behaviours in the previous 3 months: unprotected receptive sex with an HIV serostatus unknown partner, STI, and/or chemsex. Demographics, behavioral and clinical data, test results and preventive measures prescribed were collected from 1st May 2022 to March 31 2023. Persons were considered linked to prevention and/or care if attended the center at least one time after the first access (i.e. repeating test, PEP, PrEP, ART, vaccinations, dermatology/STI services).

Results: In the study period, a total of 612 persons referred to the nurse-led service: 506 were males at birth; median age was 36 years (IQR 29-47); 89 were non-Italians; 76 were first-testers; 339 self-identified as men who have sex with men (MSM) or Transgender Women (TGW).

Nineteen persons were tested HIV positive and promptly linked to care; 6 turned out to be already aware of the positivity, all not-Italians TGW asking for care in Rome. Among the 13 newly diagnosed HIV infection, 5 were early (one acute, four recent), while 3 were advanced infections (CD4 cell count< 350/mmc).

Moreover, 11/369 syphilis and 1/254 HCV tests were reactive, all confirmed, and persons promptly referred to care.

Of the remaining 580 who tested HIV/syphilis/HCV negative, 150 were identified as at high-risk (126 MSM/TGW), 120 of whom attended the center at least one time after the first access.

Conclusions: Expanding the offer by setting up easy and qualified nurse-led services could represent an important chance for diagnosis of new infections and referral to care, or enrollment of key populations in continuum of prevention. Larger studies are needed to confirm the effectiveness of this offer as an additional resource for the HIV/STI prevention programs.

Prevention, access and engagement

OC 70 EPIDEMIOLOGICAL IMPACT OF PRE-EXPOSURE PROPHYLAXIS IN HIV PREVENTION: A SINGLE CENTER OBSERVATIONAL EXPERIENCE IN PRE AND POST PROPHYLAXIS ERA

L.F. Rezzonico[1,2], C. Baiguera[1], A. Raimondi[1], C. Rogati[1], L. Baldassari[1,3], F. Peracchi[1,3], F. D'Amico[1], D. Calzavara[4], M.C. Moioli[1], L.G. Chianura[1], M. Puoti[1,3], R. Rossotti[1]

[1]Department of Infectious Disease, ASST Grande Ospedale Metropolitano Niguarda, Milan, [2]School of Medicine, University of Pavia, Pavia, [3]School of Medicine, University of Milano-Bicocca, Milan, [4]Associazione Milano Check Point, Milan

Background: HIV transmission is decreasing globally and especially in high-income countries: in 2021, for instance, Milan showed a small number of new cases ranking below the other major Italian cities. Such trend is due to more effective treatments and implementation of infection control measures. Among those, treatment as prevention (TasP) and pre-exposure prophylaxis (PrEP) are major players. While PrEP is recognized as an effective approach, his net effect on epidemiology has not been clearly proven yet. Aim of this analysis is to address the potential PrEP role on the trajectory of new HIV infections.

Materials and Methods: This monocentric retrospective study included all new HIV infections from 2012 to 2022 stratified into 3 different historic periods: pre-TasP (2012-2015), TasP (2015-2018) and PrEP (2019-2022). Demographic and clinical features were retrieved from regional disease notification forms. Descriptive statistics and non-parametric tests were used to depict study population. Linear regression analysis was applied to predict the trajectories of diagnoses in different subgroups including patients eligible to PrEP, defined as MSM with CD4+ count >500 cell/mmc (with/without Italian origin).

Results: We included 501 patients (228 pre-TasP, 151 TasP, 122 PrEP) with a new HIV diagnosis: demographic and clinical features are summarized in Table 1. MSM were the largest group (50.5%) while PrEP candidates represented only a small portion of those (11.0%). The Italian origin was predictably more consistent (58.1%) followed by latin American (18.7%). No differences in the characteristics emerged throughout historic periods. New HIV diagnosis decreased significantly over time (b-coefficient: -1.325, p<0.001; Fig.1). This decrease happened without substantial changes in terms of CD4+ count (b-coefficient: 0.002, p=0.72; Fig. 2), log10 viral load (b-coefficient: 0.104, p=0.486; Fig. 3) or CDC stage C at diagnosis (b-coefficient: -0.383, p=0.237). The linear regression applied to risk factors showed a similar reduction in all groups (Fig. 4). Patients eligible to PrEP had a prominent new diagnosis decrease at the limit of significance (b-coefficient: -2.789, p=0.065). Adding Italian origin to PrEP eligibility definition confirmed a decreasing trend (b-coefficient: -2.699, p=0.075).

Conclusions: The overall number of new HIV diagnosis showed a progressive reduction during the last decade: the most consistent downward trend was observed among PrEP candidates suggesting this preventive approach may be a protective factor for HIV transmission even at population level. Although the sample size it was not sufficient to reach full statistical significance, the decremental trajectory shown by PrEP potential candidates was evident. The relationship of this trend with Italian origin could underline that access to PrEP is still depending on socio-economic factors. Enlarging PrEP availability could lead to a more prominent decrease of new HIV diagnosis.

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Prevention, access and engagement

OC 71 LATE HIV DIAGNOSIS: THE NEW CONSENSUS DEFINITION REDUCES THE PROPORTION OF LATE PRESENTATIONS

V. Regine, L. Pugliese, B. Suligoi

Istituto Superiore di Sanità, Rome

Background: Late HIV diagnosis remains a key indicator for evaluating the effectiveness of HIV infection prevention programs. Since 2010 in Europe, a new HIV diagnosis with a CD4 count <350 cells/μL or with a concomitant AIDS diagnosis has been defined as a late presenter. ECDC, the WHO Regional Office for Europe and the European AIDS Clinical Society (EACS), recently proposed a new definition that includes markers of recent infection to allow for better classification and reduce HIV late diagnosis overestimate. This study aims at evaluating the impact of the new definition using data from the Italian HIV Surveillance System.

Materials and Methods: According to the new definition, late HIV diagnosis is defined as a first diagnosis with a CD4 count <350 cells/μL or with an AIDS-defining event, regardless of the CD4 cell count. People with CD4 count <350 and evidence of recent infection were classified as 'not late', based on any of the following criteria, hierarchically: (i) a positive test for recent infection; (ii) a last negative HIV test within 12 months of diagnosis; (iii) clinical evidence of acute infection. We applied this new definition on HIV surveillance records reporting requested data (CD4 count, recent infection test, date of last negative test, information on acute infection). The proportion of late diagnoses based on new definition was compared with that obtained using previous definition.

Results: In 2012-2021, 31,467 new HIV diagnoses were reported. Among these, 81.4% reported CD4 cell count, 17.5% reported a recent infection test result, 20% reported the date of last negative test, and 30.8% reported information on acute infection. Overall, 13,569 new diagnoses reporting data on any of the three mentioned criteria were analyzed. Using the previous definition (CD4 count <350 cell/μL), late diagnoses were 7,076 (52.1%). Using the new definition, late diagnoses were 6,408 (47.2%). The 4.9% re-classification was composed of 1.7% diagnoses identified by a test for recent infection, 2.8% by a negative HIV test <12 months, and 0.4% were acute infections. Misclassification was significantly higher in males than females (5.4% vs. 3.3%), in people aged 25 to 50 compared to other ages (5.2% vs. 4.2%), in Italians compared to foreigners (5.4% vs. 3.6%), in MSM compared to other modes of transmission (MSM 5.9%, heterosexual male 4.4%, heterosexual female 3.2%, IDU 4.2%, Other/not reported 5.8%).

Conclusions: The new definition yielded a 5% reduction in the proportion of late diagnoses, especially among MSM and Italians. However, our analysis included less than half of all the diagnoses reported to the Surveillance system due to the lack of data needed for re-classification. Therefore, routine testing for recent HIV infection should be promoted, enhancing also data collection on last negative HIV test and evidence of acute infection.

Prevention, access and engagement

OC 72 IMPACT OF COVID-19 PANDEMIC ON RETENTION IN CARE OF NATIVE AND MIGRANT PLWH IN THE ICONA COHORT

R. Gagliardini[1], A. Giacomelli[2], G. Bozzi[3], A. D'Arminio Monforte[4], A. Tavelli[4], V. Mazzotta[1], E. Bruzzesi[5], A. Cervo[6], A. Saracino[7], C. Mussini[6], E. Girardi[8], A. Cozzi-Lepri[9], A. Antinori[1], on behalf of COVID-19 ICONA study group

[1]Clinical and Research Infectious Diseases Department, National Institute of Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]III Infectious Disease Unit, ASST-Fatebenefratelli Sacco, Milan, Italy, [3]Infectious Diseases Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, [4]Icona Foundation, Milan, Italy, [5]UO Malattie Infettive, IRCCS Ospedale San Raffaele, [6]Division of Infectious Diseases, University of Modena, Modena, Italy, [7]Clinic of Infectious Diseases, University Hospital, University of Bari, Bari, Italy, [8]Scientific Direction, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [9]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, University College London, London, UK

Background: COVID-19 pandemic had a negative impact on all HIV epidemic goals. However, little is known about the impact of the pandemic on HIV retention in care in Italy and whether the disruption of health service may have had a more profound effect in the migrant population.

Methods: All PLWH enrolled in Icona Foundation Cohort with active follow up (FU, defined as at least one among HIV-RNA, CD4 cells count, visit, clinical event except for death) were included in the study: those in FU from 01/09/2019 to 29/02/2020 constituted the pandemic period population, those in FU from 01/03/2018 to 31/08/2018 the historical period population (Figure 1a). Primary outcome was temporary LTFU, defined as no laboratory exams, ART modification, clinical visit or clinical event for ≥1 year. Logistic regression analysis was performed with LTFU as binary outcome and migrant status as the main exposure of interest. The model was controlled for gender, age, geographical location of site, AIDS diagnosis, maximum level of education and employment. Difference in difference (DID) analysis approach was also used, to estimate the potential impact of the pandemic to exacerbate the difference in risk of LTFU between migrants and natives. A sensitivity analysis restricted to centres with electronic data import was performed, to minimise potential bias due to delays in data reporting.

Results: A total of 8,847 and 8,135 PLWH were included in the pandemic and in the historical period population, with migrants accounting for 17% in both populations. In the unadjusted Cox regression model, during the pandemic period a higher risk of LTFU was observed for migrants when compared to native PLWH (odds ratio, OR, 1.96, 95%CI 1.70, 2.26, p<0.001), confirmed after adjustment for potential confounders (aOR, 1.78, 95%CI 1.49, 2.12, p<0.001) and partially even in the sensitivity analysis (aOR 1.54, 95%CI 0.97, 2.42, p=0.07).

DID analysis was performed in 6,659 PLWH who contributed to both periods (population characteristics, Figure 1b). In historical period (2018-2020), proportion of PLWH with LTFU was 1.2% (95%CI 0.9, 1.5) in natives vs 2.2% (95% CI, 1.3, 3.1) in migrants. In pandemic period, proportion of PLWH with LTFU was 10.9% (95% CI, 10.1, 11.7) in natives vs 19.2% (95% CI, 16.8, 21.7) in migrants, with a resulting DID of 7.4% (95% CI, 4.6; 10.1, p<0.0001). In the sensitivity analysis, lower risk of LTFU was detected for all groups, with migrants in pandemic period retaining the highest proportion of LTFU (7.2%, 95% CI, 4.3, 10) and a DID of 1.6 % (95% CI,-1.7, 4.9, p=0.36).

Conclusion: A higher proportion of LTFU in migrants compared to native PLWH was detected both in historical period and in pandemic period, although some of this effect appeared to be due to a delay in data reporting. Dedicated interventions to minimize LTFU of migrants are needed as the COVID-19 pandemic seemed to have exacerbated their risk of discharge from care even after one year from the first wave hit.

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The increasing burden of STIs

OC 73 A CROSS SECTIONAL STUDY OF SEXUALLY TRANSMITTED INFECTIONS IN A NORTHERN ITALY STI CLINIC

G. Mulè[1], D. Tesoro[1], A. De Bona[1], L. Biasioli[1], M. Mazzoccoli[1], A. Copes[1], L. Albertini[1], A. Tavelli[1], S. Cianciola[1], E. Limoj[1], M. Settembrese[1], F. Miraglia[1], F. Bai[2], C. Tincati[2], A. d'Arminio Monforte[1], G.C. Marchetti[2]

[1]ASST Santi Paolo e Carlo, Milano, [2]Università Statale di Milano, Milano

Background: Key populations [adolescents, men having sex with men (MSM), transgender, pregnant women, intravenous drug users, prisoners and members of other closed communities, migrants] are disproportionally affected by or particularly vulnerable to sexually transmitted infections (STIs) and they often lack adequate access to health services. This study analyses the epidemiology, characteristics and sexual behaviour of our STI clinic clients, at San Paolo Hospital, Milan, to better define risk groups and to tailor treatment and prevention strategies.
Methods: In our cross-sectional study, we enrolled subjects accessing by self-presentation or by doctor's referral from November 2021 to March 2023; we excluded people living with HIV or taking Prep. Each subject filled a survey about demographics and sexual behaviors and received tests for STI. Primary endpoint was prevalence of any STI. Secondary endpoints were: prevalence of HIV, HAV, HBV, HCV, Syphilis, Chlamydia, Gonorrhea; prevalence of symptomatic STIs, risk factors for STIs and testing for screening (no symptoms). We compared subgroups by sexual orientation using Kruskal Wallis and chi-square tests and we calculated odds ratios with logistic regression.
Results: Table 1 shows demographics, sexual behaviors and STI history. We enrolled 252 subjects, of which 51% MSM (no transgender, nor adolescents) and 10% non-Caucasian. MSM were tested more than women and heterosexual. In the study period, 52/252 (21%) was the prevalence of any STI; 3% syphilis, 11% chlamydia, and 12% gonorrhea, no cases of HIV/hepatitis. 58% of STI were symptomatic; 8/10 (80%) of STI were asymptomatic in women. Female gender positively correlated, while physician's referral and history of any STI negatively correlated with testing for STI without symptoms (table 2). Referral to our center by a physician's vs-referral by internet, friend or partner, and symptoms, positively correlated with STI in multivariable logistic regression (table 3).
Conclusions: STI prevalence with a higher proportion of gonorrhea was in line with international data. Almost half cases of IST were asymptomatic, mainly in women. MSM were the only key population adequately reached, showing more risky behaviors but maybe higher awareness on sexual health than others (higher frequency in testing and U=U knowledge). Spreading prevention-oriented culture also among general practitioners and reducing barriers to STI services is strongly needed to guarantee sexual health at all population levels.

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The increasing burden of STIs

OC 74 SEXUALLY TRANSMITTED INFECTIONS IN MEN WITH MULTIDRUG-RESISTANT HUMAN IMMUNODEFICIENCY VIRUS: DATA FROM THE PRESTIGIO REGISTRY

T. Clemente[1,2], R. Lolatto[2], R. Papaioannu Borjesson[1,2], M. Fabbiani[3], E. Manzillo[4], E. Fronti[5], S. Di Giambenedetto[6,7], R. Gagliardini[8], S. Rusconi[9,10], M.M. Santoro[11], A. Castagna[1,2], V. Spagnuolo[2], on behalf of the PRESTIGIO Study Group

[1]Faculty of Medicine and Surgery, Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [3]Department of Medical Sciences, Infectious and Tropical Diseases Unit, University Hospital of Siena, Siena, Italy, [4]Ospedale dei Colli, Napoli, Italy, [5]Unit of Infectious Diseases, AO-Universitaria, Parma, Italy, [6]Department of Safety and Bioethics, Catholic University of the Sacred Heart, Rome, Italy, [7]Infectious Diseases Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [8]National Institute for Infectious Diseases 'L. Spallanzani' IRCCS, Rome, Italy, [9]Infectious Diseases Unit, Ospedale Civile di Legnano, ASST Ovest Milanese, Legnano, Italy, [10]DIBIC Luigi Sacco, University of Milan, Milan, Italy, [11]Department of Experimental Medicine, University of Rome 'Tor Vergata', Rome, Italy

Background: Individuals with 4-class drug-resistant (4DR) HIV constitute a fragile population with an elevated risk of AIDS- and non-AIDS-defining events or death for any cause and a high inflammatory burden. No data on the occurrence of sexually transmitted infections (STIs) in people living with 4DR HIV (4DR-PLWH) are currently available. Therefore, aim of this study was to explore the incidence of bacterial sexually transmitted infections (STIs) in men with 4DR HIV.

Methods: Cohort study on male PLWH with documented resistance to NRTIs, NNRTIs, PIs, and INSTIs, from the PRESTIGIO Registry. Follow-up accrued from the date of first 4DR evidence (baseline) until death/loss-to-follow-up/freezing date (December 31th, 2022).

Incident bacterial STIs included: Neisseria gonorrhoeae, Chlamydia trachomatis, including lymphogranuloma venereum, or Mycoplasma genitalium infection or syphilis. We also evaluated the occurrence of Trichomonas vaginalis, mpox, and first diagnoses of genital HPV and genital HSV infections in male 4DR-PLWH. Descriptions by median (interquartile range, IQR) or frequency (%). Poisson regression modelled incidence rates (IR) and 95% confidence intervals (95%CI) for bacterial STIs.

Results: Overall, 132 male 4DR-PLWH [48/132 (36.4%) men who have sex with men (MSM)] evaluated: characteristics reported in Table 1.

During a median follow-up of 6.7 (4.4-9.8) years with a viremia copy-years of 1133 (302-34520) copy per years/mL, 6/132 (4.5%) male 4DR-PLWH, all MSM [6/48 (12.5%)], developed ≥1 bacterial STI. Twelve bacterial STIs were diagnosed during 933 person-years-of-follow-up (PYFU), for an IR=1.29 (95%CI=0.56-2.01)/100 PYFU in the overall male population [only MSM: IR=3.54 (95%CI=1.54-5.55)/100 PYFU during 339 PYFU]: 5 syphilis, 2 Chlamydia trachomatis, 1 gonorrhea, and 4 Mycoplasma genitalium infections. Specific characteristics of individuals with ≥1 bacterial STI are reported in Table 2. No bacterial STIs occurred when VL ≥200 copies/mL.

HSV was first diagnosed in 5/132 (3.8%) males, all MSM [5/48 (10.4%)], and HPV in 11/132 (8.3%) males, specifically 9/48 (18.8%) MSM. No Trichomonas vaginalis or mpox cases occurred.

Conclusions: Men living with multidrug-resistant HIV showed a non-negligible incidence of bacterial STIs, especially after virological suppression. Intriguingly, a good control of HIV infection, even in case of multidrug resistance, might lead to an improvement in life quality, with a consequent impact on sexual behaviors. However, considering the risk of virological failure in this population with limited treatment options, close HIV viremia monitoring and careful STI prevention counselling are required, also in order to prevent the possible transmission of a multiresistant virus.

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The increasing burden of STIs

OC 75 TEMPORAL TRENDS IN INCIDENCE OF BACTERIAL SEXUALLY TRANSMITTED INFECTIONS AMONG PREP USERS OF MILANO CHECKPOINT

A. Tavelli[1,2], R. Rossotti[2,3], D. Calzavara[1], A. Soria[1,4], E. Caruso[1], R. Repossi[1,5], N. Frattini[1,5], P. Vinti[1], C. Muccini[1,6], D. Tesoro[1,7], G. Mulé[1,7], D. Moschese[1,8], A. Foschi[1,8], L. Biasioli[1,7], G. Lapadula[1,2], S. Bossolasco[1,6], A. De Bona[1,7], A. d'Arminio Monforte[1,2], M. Cernuschi[1,5,6]

[1]Milano Check Point ETS, Milano, Italy, [2]Fondazione Icona, Milano, Italy, [3]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy, [4]Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [5]ASA Milano ODV, Milano, Italy, [6]IRCCS San Raffaele Scientific Institute, Milan, Italy, [7]ASST Santi Paolo e Carlo, Milano, Italy, [8]ASST Fatebenefratelli Sacco, Milano, Italy

Background: Pre-exposure prophylaxis (PrEP) prevents HIV acquisition, but is ineffective against other sexually transmitted infections (STIs): thus, increased STIs screening is required. Few data are available on temporal trends of STIs in recent years in PrEP users Italy. Herein we describe trends in bacterial STIs incidence in PrEP users of a community-based service in the last 4 years.

Methods: Analysis of samples from PrEP users attending Milano Checkpoint (MCP), prospectively collected from 2019 to 2022. At each PrEP visit, point of care tests (POCT) for C. trachomatis (Ct), N. gonorrhoeae (Ng) and syphilis were performed. Demographics, clinical, sexual and behavioural information were also collected through a self-administered questionnaire at every visit.

Patients were included if they had at least one POCT to investigate prevalence of each STI overall and by year. Repeated tests after first visit were counted to calculate incidence rates (IR) over time. Incidence rate ratios (IRRs) to estimated changes in STIs incidence per calendar year period were calculated using Poisson regression, adjusted also for age and nation of birth (Italian vs non-native). Differences in IR over calendar years between Italian-born and non-native have been further investigated.

Results: 878 PrEP users of MCP have been included (163 had a follow-up in 2019, 278 in 2020, 518 in 2021 and 693 in 2022): 97.7% male, 96.4% MSM, median age 36 (IQR 31-44), 79.3% born in Italy, 68.6% with a university degree.

83 syphilis were diagnosed in 72 patients during the study period: prevalence was 8.2% (95%CI 6.5-10.2). Syphilis IR remained low during the study period, but raising from 4.6 x 100 PYFU in 2019 to 7.7 x 100 PYFU in 2022) [Tab1A, Fig1]. No significant difference per year identified in the Poisson regression model [Tab2A].

329 Ct cases were found in 234 users, with an overall prevalence of 26.6% (95%CI 23.7-29.7) and Ct IR of 27.0x 100 PYFU, 95%CI 23.8-30.6) [Tab1B, Fig1]. Again, no significant difference per year emerged in the Poisson regression model [Tab2B].

318 Ng positive tests for 227 users were found, with an overall prevalence of 25.8% (23.0-28.9) and IR 25.5 x 100 PYFU (22.4-29.0). IR raised from 17.4 x 100 PYFU (9.5-29.2) in 2019 to 34.4 x 100 PYFU (28.8-40.9) in 2022 [Tab1C, Fig1]. In the adjusted Poisson regression model, 2022 was associated with a 2-fold higher incidence of Ng diagnosis compared to 2019 (aIRR 1.95, 95%CI 1.12-5.64)[Tab2C]. Ng incidence by calendar year was also different according to nation of birth (p-value for interaction 0.004) with a higher increase in recent years in non-Italians compared to Italians [Fig2].

Conclusions: Ct and Ng incidence among MCP PrEP users was high: in 2022 a significant increase in Ng was observed, especially among non-Italians. Monitoring sexual behaviours/compensation in this Ng ongoing outbreak is an essential task of PrEP services given the high contagiousness and increasing reports of resistance.

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The increasing burden of STIs

OC 76 TRENDS OF ANTIMICROBIAL SUSCEPTIBILITY OF NEISSERIA GONORRHOEAE ISOLATES BETWEEN 2012 AND 2023: A SINGLE-CENTER EXPERIENCE IN MILAN, ITALY

M.F. Lucente[1], A.R. Raccagni[1], L. Galli[2], R. Lolatto[2], M. Ripa[1,2], G. Ponta[1], R. Monardo[1], F. Gona[3], N. Clementi[1,3], R. Burioni[1,3], S. Carletti[3], A. Castagna[1,2], S. Nozza[1,2]

[1]Vita-Salute San Raffaele University, Milan, [2]Infectious Diseases Unit, San Raffaele Scientific Institute, Milan, [3]Laboratory of Microbiology and Virology, San Raffaele Scientific Institute, Milan

Background: The European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) recommended in the 2021 report active surveillance of antimicrobial susceptibility of Neisseria gonorrhoeae (Ng), monitoring isolates with decreased drug susceptibility/resistance (DS/R) to ceftriaxone (CRO). Aim of this study were to present trends of antimicrobial susceptibility of genital, anal and pharyngeal Ng strains.

Material and methods: Retrospective, single-center study on Ng strains collected from outpatients at San Raffaele Scientific Institute, from September 2012 to February 2023. Ng testing was performed in double with nucleic acid amplification test and gonococcal-specific cultures at urethral, pharyngeal and anal sites; positive cultures were included. Minimum inhibitory concentrations (MICs) for benzyl-penicillin (PenG), tetracycline (TET), ciprofloxacin (CIP), azithromycin (AZM) and CRO were determined by gradient-test strips. Susceptibility (S) and resistance (R) profiles were based on EUCAST criteria v 13.0; all MIC values were classified according to these criteria. AZM-R was defined according to the epidemiological cut-off value (ECOFF) of >1mg/L; CRO-DS as MIC>0.032mg/L. Geometric means of MICs per year were estimated to assess trend over time; bivariate linear regression models, including calendar year and HIV status, were also calculated on continuous logarithmic MICs values. The Cochran-Armitage test was calculated to test for linear trend on proportions of resistant strains.

Results: Overall, 436 Ng isolates in 352 individuals were analysed (308 at rectal site, 105 urethral and 20 pharyngeal). Overall, 205 (58%) were PLWH and 97 (27.6%) PrEP users; main Characteristics according to HIV status in Table 1. MICs geometric means of included antibiotics over years are presented in Table 2. CRO and PenG logarithmic MICs reduced over time (β=-0-08, p<0.0001 and β=-0.03, p=0.030), whereas AZM increased (β= +0.05, p=0.001), with no trend differences according to HIV status (p=0.193, p=0.673 and p=0.708). CIP and TET logarithmic MICs did not change over time (p=0.473 and p=0.272). Overall, the percentages of susceptible strains were: PenG 44 (10.1%), TET 40 (9.2%), CIP 226 (51.8%), AZM 417 (95.6%); CRO-DS strains were 37 (8.7%) and 1 CRO-R strain was identified [Figure 1]. The proportion of resistant strains increased over time for AZM (p=0.007), TET (p=0.001) and CIP (p<0.0001), whereas decreased for PenG-R (p<0.0001). The proportion of CRO-DS/R strains also decreased over time (p<0.0001).

Conclusions: In line with Euro-GASP data, Ng strains showed high susceptibility to ceftriaxone, although cases of DS/R were identified. High levels of susceptibility to azithromycin were observed, although a shift towards higher MICs above the ECOFF was noted. The primary regimen with ceftriaxone and azithromycin keeps its effectiveness. The high percentage of resistance to tetracycline confirms the expected low effectiveness of DoxyPEP against Ng.

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The increasing burden of STIs

OC 77 PREDICTORS OF MPOX DURATION AND SEVERITY IN AN ITALIAN MULTICENTER COHORT (MPOX-ICONA)

V. Mazzotta[1], A. Tavelli[2], D. Moschese[3], A. Cozzi Lepri[4], F.M. Fusco[5], F. Colavita[6], L. Biasioli[7], A. Mondi[1], F. Carletti[6], A. Di Biagio[8], D. Mileto[9], G. Baldin[10], S. Nozza[11], L. Pipitò[12], D. Tesoro[7], N. Sangiovanni[5], E. Nicastri[1], G. Rizzardini[3], F. Maggi[6], A. d'Arminio Monforte[7], A. Antinori[1], S. Lanini[1]

[1]Clinical and Research Department, INMI Lazzaro Spallanzani IRCCS, Roma, Italy, [2]Icona Foundation, Milan, Italy, [3]I Division of Infectious Diseaeses, Luigi Sacco Hospital, ASST Fatebenefratelli Sacco, Milano, Italy, [4]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [5]UOC Infezioni Sistemiche e dell'Immunodepresso, P.O. "D. Cotugno", Azienda Ospedaliera dei Colli, Napoli, Italy, [6]Laboratory of Virology, INMI Lazzaro Spallanzani IRCCS, Roma, Italy, [7]Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [8]Infectious Diseases Clinic, Policlinico San Martino Hospital, Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [9]Laboratory of Clinical Microbiology Virology and Bioemergencies, Luigi Sacco Hospital, ASST Fatebenefratelli Sacco, Milano, Italy, [10]Fondazione Universitaria policlinico Gemelli, Roma, Italy, [11]Infectious Diseases Unit, San Raffaele Hospital, Vita-Salute San Raffaele University, Milano, Italy, [12]Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties "G. D'Alessandro", University of Palermo, Palermo, Italy

Background: Mpox is a pivotal example of how old viral pathogens can cause new outbreaks with novel clinical presentation and new routes of transmission. This analysis explores potential predictors of mpox severity and duration, and mpox virus (MPXV) persistence in relevant biological fluids after healing.

Method: Italian multicenter cohort study in the network of Icona Foundation. Severe cases were defined as those hospitalized or with proctitis, pharyngotonsillitis, ocular lesion, or >20 skin lesions, and recovery as the resolution of all mucocutaneous lesions. Predictors of mpox duration and severity were assessed by multivariable linear and logistic models, respectively. A stepwise backward process was fitted for the selection of variables in both multivariate models, using HIV status as a priori predictor. Assessment of early MPXV viral load (VL) as a predictor of severity was done by Student T-Test and logistic regression model.

Results: Between 11 May 2022 and 28 Jan 2023, 352 pts were enrolled (Fig A), 350 male, mean age 39 yrs (range 19-75), 158 (45.02 %) PLWH. The mean time to mpox resolution, in 319 pts with complete follow-up, was 23.15 days (95% CI 21.54-24.77): duration (Fig B) was significantly longer in pts with proctitis (+7.62 days), pharyngitis (+5.98 days), lymphadenopathy (+3.47 days), age >46 years (+4.40 days) and in PLWH with <350 CD4 (+14.29 days). Multivariable analysis for severity predictors (Fig C) showed that presentation with fever (OR 2.91; p<0.001), lymphadenopathy (OR 1.88), diarrhea (OR 4.43), peri-anal (OR 1.92) and face lesions (OR 1.92) were significantly associated with severe mpox. Quantitative determination of VL in the upper respiratory tract (URT) was available for 118 pts (74 mild and 44 severe). Mean Ct-value was 36.00 (95%CI 34.28-37.73) and 29.68 (95%CI 27.47-31.87) in mild and severe cases, respectively (P<0.001; Fig D). By logistic model the probability of developing severe disease had a strong inverse association with Ct-value, dropping by 10% per Ct (OR 0.90 95%CI 0.85-0.95; p<0.001; Fig E). Finally, we found that MPXV persists in body fluids despite clinical recovery: a detectable amount of MPXV was found in sperm (12/28 pts), urine (3/47), anorectal (8/38), and URT (18/73) specimens in recovered pts with a minimum Ct value of 26.

Conclusion: Clinical presentation with systemic symptoms (fever and lymphadenopathy), diarrhea, peri-anal and face lesions could predict the development of severe mpox. The occurrence of proctitis/pharyngitis implies a longer disease duration, as does an advanced HIV infection with a low CD4 count, consistent with literature data. Remarkably, our results suggest that MPXV is a virulent pathogen with a direct association between VL and disease severity and with viral shedding that may persist even after clinical recovery in several anatomical sites. Urgently need to assess whether the persistence of MPXV in biological samples after clinical recovery may lead to a status of persistent infectivity.

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Vaccine in frail patients

OC 78 PNEUMOCOCCAL VACCINATION COVERAGE AMONG PEOPLE LIVING WITH HIV BEFORE AND AFTER THE IMPLEMENTATION OF AN ON-SITE VACCINATION SERVICE AT AN HIV CLINIC: A RETROSPECTIVE OBSERVATIONAL STUDY

M.L. Colombo[1,2], A. Giacomelli[1], M.V. Cossu[3], G. Carrozzo[1,2], A. Poloni[1,2], G. Casalini[1,2], B. Caloni[1,2], S. Pagano[1,2], M. Beltrami[1,2], L. Oreni[1], S. Antinori[1,2], A.L. Ridolfo[1]

[1]III Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [2]Università degli Studi di Milano, DIBIC Luigi Sacco, Milan, Italy, [3]I Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy

Background: People living with HIV (PLWH) are at increased risk of invasive pneumococcal diseases when compared to the general population. Although current guidelines recommend pneumococcal vaccination with a 13-valent conjugate vaccine (PCV13) followed by a 23-valent polysaccharide vaccine (PPSV23) to all PLWH, vaccine uptake is far from satisfactory. To promote vaccination into routine practice, an on-site vaccination service dedicated to all PLWH was implemented at L. Sacco Hospital. We assessed the pneumococcal vaccination uptake before and after the implementation of this service.

Material and Methods: This was a retrospective observational study conducted at III Infectious Disease Unit, L. Sacco Hospital (Milan, Italy) between 28th October 2017 and 31st December 2022. All PLWH who had at least one visit in the 12 months before the start of our vaccination service (28th October 2018) were enrolled in the study and followed up until 31st December 2022. Their demographic and epidemiological characteristics and date of uptake of PCV13 and PPSV23 were collected. The main outcome of interest was the pneumococcal vaccination uptake with a dose of PCV13 and the completion of the vaccination schedule with a dose of PPSV23. A descriptive statistical analysis was performed.

Results: A total of 2003 PLWH were included in the study. They were prevalently males (72.7%) with a median age of 51 years (Inter Quartile Range 43-56); sexual transmission was the main route of HIV acquisition, with men having sex with men accounting for the 34%, and heterosexuals for the 43.8%; Most of the subjects were Italians (84.1%) and employed (79%) (Table 1).

Overall, 760 (37.9%) subjects started the vaccination schedule and underwent PCV13, 94 (12%) before October 2018 and 666 (88%) thereafter. Of these subjects, 522 (68%) completed the vaccination schedule with the dose of PPSV23. At the end of the study period, the rate of pneumococcal vaccination completion was 26%.

As shown in Figure 1 pneumococcal vaccination uptake increased consistently after the start of on-site vaccination service. Males had higher odds of completing the vaccination schedule than females (OR 1.43 95% CI 1.13-1.81) as did MSM compared to other risk categories (OR 1.47 95% CI 1.19-1.8). Moreover, non-Italians showed lower odds of completing the vaccination schedule than Italians (OR 0.49 95% CI 0.35-0.67). Finally, of the 173 subjects aged over 65 years, 21% completed the vaccination schedule.

Conclusions: Pneumococcal vaccination coverage among PLWH attending our clinic consistently increased after the implementation of an on-site vaccination service, with males and MSM subjects presenting higher odds of completing the vaccination schedule. However, the overall vaccination uptake remains suboptimal, and this is particularly concerning for subjects aged > 65 years. Thus, additional strategies are needed to promote vaccination uptake, particularly among older subjects and non-Italians.

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Vaccine in frail patients

OC 79 SARS-COV-2 MRNA VACCINATION AND VIRO-IMMUNOLOGICAL CHANGES IN PLWH

A. Vergori[1], A. Cozzi-Lepri[2], G. Marchetti[3], A. Tavelli[4], R. Gagliardini[1], G. Lapadula[5], N. Caroccia[6], L. Taramasso[7], A.M. Azzini[8], S. Lanini[1], F. Ceccherini-Silberstein[9], M. Giannella[6], E. Tacconelli[8], A. d'Arminio Monforte[4], A. Antinori[1] on behalf of the VAX-ICONA Study Group

[1]HIV/AIDS Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [3]Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [4]Icona Foundation, Milan, Italy, [5]Clinic of Infectious Diseases, Foundation IRCCS San Gerardo dei Tintori -University of Milano Bicocca, Monza, Italy, [6]Infectious Diseases Unit, IRCCS Azienda Ospedaliero Universitaria di Bologna, Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy, [7]Infectious Disease Clinic, IRCCS Policlinico San Martino Hospital, Genova, Italy, [8]Division of Infectious Diseases, Department of Diagnostics and Public Health, University of Verona, Verona, Italy, [9]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy

Background: Despite anecdotal reports describing a transient increase in HIVRNA viral load (VL) and decrease of CD4 count after SARS-CoV-2 mRNA vaccination in people living with HIV (PLWH), whether vaccination has an impact on viro-immunological parameters remains to be investigated.

Methods: PLWH of the VAXICONA-ORCHESTRA cohort who received ≥1 dose of SARS-CoV-2 mRNA vaccine and for whom paired measures of immuno-virological markers [VL, CD4, CD8 count 1 month before and after the dose] were available, were included, stratified according to the time elapsed from ART initiation: less than 6 months (L6m) vs. more than 6 months (M6m). Paired t-test was used to verify whether a change in CD4, CD8 count (natural scale) or VL (log10 scale) occurred over + 1 month around vaccine dose (VD). Subgroup analyses were performed according to i) VL and CD4 count 1 month before vaccination, ii) time of ART initiation. In addition, we conducted a sensitivity analysis restricted to participants with no evidence of natural infections at any time during the follow-up (established by anti-N+ result or recorded clinical evidence).

Results: N=473 PLWH were included, contributing 684 marker pairs: N=176 (26%) started ART L6m and 508 (74%) M6m; 17% were female, median age 55 y(IQR 46-60), CD4 count before VD was 480 cells/mm3 (286,711), CD8 790 (597,1103), 90% of participants had VL<50 cps/mL, 42% had ≥1 comorbidity, time since HIV diagnosis 9 years (4-18), 17% and 83% received 2 and 3 VDs, respectively. Pooling together all the VDs, over a median of 28 days (3-53) between pre- and post-VD value, CD4 count significantly increased by a mean of +18 cells/mm3 (SD 124; p<.001), CD8 by +13 (SD 360; p=0.345). VL decreased by -0.10 Log10 (0.87; p=0.002), among PLWH with VL<50cps/mL pre-VD only 2% had VL>50 cps/mL and in 35% of those with VL >50 cps/mL pre-VD post-VD VL became ≤50 copies/mL. Similar results were observed when the analysis was restricted to those with VL ≤50 cps/mL pre-VD and to those with CD4 count ≤200/mm3 (Tab. 1A). In this latter analysis we observed larger changes, possibly due to the regression to the mean. Results were also similar among participants who started ART M6m, thus minimizing the potential confounding effect of ART (Tab.1B) and after excluding those with evidence of natural infection at any time in follow-up (Tab.1C).

Discussion: Contrary to previous observations in PLWH, SARS-CoV-2 mRNA vaccination was not associated neither with a CD4 drop nor with transient increases in HIVRNA If anything, a significant increase in CD4 count and a drop in HIV-RNA were observed, although the magnitude of the changes were of negligeable clinical significance. In addition, there was no evidence of any effect on CD8 count. Our findings are consistent with the hypothesis that SARS-CoV-2 mRNA vaccine is able to rapidly prime CD4 T spike specific cells independently from ART also in immuno-suppressed participants, emphasizing the usefulness of vaccination in advanced PLWH.

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Vaccine in frail patients

OC 80 SPECIFIC HUMORAL AND T-CELL RESPONSE TO THREE DOSES OF SARS-COV-2 MRNA VACCINE IN SOLID ORGAN TRANSPLANT RECIPIENTS

M. Guardiani[1], M.A. Zingaropoli[1], E. Tortellini[1], F. Cogliati Dezza[1], F. Dominelli[1], P. Pasculli[1], M. Garofalo[2], A. Centofanti[3], C. Carillo[3], A. Gaeta[4], C. Del Borgo[5], A. Napoli[4], F. Mengoni[1], V. Vullo[1], M.R. Ciardi[1], G. Russo[1], C.M. Mastroianni[1], M. Lichtner[5,6]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome - Rome (Italy), [2]General Surgery and Organ Transplantation Unit, Sapienza University of Rome - Rome (Italy), [3]Division of Thoracic Surgery and Lung Transplant, Sapienza University of Rome - Rome (Italy), [4]Department of Molecular Medicine, Sapienza University of Rome - Rome (Italy), [5]Infectious Diseases Unit, Santa Maria (SM) Goretti Hospital, Sapienza University of Rome - Rome (Italy), [6]Department of Neurosciences, Mental Health, and Sense Organs, NESMOS, Sapienza University of Rome - Rome (Italy)

Background: In solid organ transplant recipients (SOTR), COVID-19 vaccine is strongly recommended as high-risk patients due to their immunocompromised status. Therefore, we investigated specific humoral and T-cell response to the third dose of mRNA vaccine in this population.

Materials and Methods: Humoral and T-cell responses were evaluated in SOTR before (T0) and after 2 months (T1) from the third dose of vaccine. By intracellular cytokine flow cytometry assay, upon S peptide libraries stimulation in peripheral blood mononuclear cells, we identified T-cells producing all possible combinations of IFNg, IL2 and TNFa. We named those producing any of them as “responding” T-cells and those simultaneously producing all 3 as polyfunctional. SOTR were stratified according to transplant into Lung Transplant Recipients (LuTR) and Kidney Transplant Recipient (KTR). As control group, healthy donors (HD) were enrolled. For a subgroup of SOTR, the humoral response was further assessed at 6(T2) and 12(T3) months.

Results: Thirty-two SOTR and 12 HD were enrolled (Table 1).

Overall, 44% (14/32) and 81% (26/32) of SOTR showed a specific humoral response at T0 and T1, respectively, with an increase of over 30% maintained over-time (T2: 87% [19/22] and T3 89%[16/18]). Collectively, at T0 and T1, significant a lower percentage of “responding” T-cells (CD4 T0:p<0.0001,T1:p=0.0005; CD8 T0:p=0.0007,T1:p=0.0457) and polyfunctional T-cells (CD4 T0:p<0.0001, T1:p=0.0005; CD8 T0:p=0.0075, T1:p<0.0001) were found in SOTR compared to HD.

SOTR were stratified into LuTR and KTR. 11%(1/9) of LuTR and 48%(13/23) of KTR and 45%(4/9) of LuTR and 96%(22/23) of KTR developed a specific humoral response at T0 and T1, respectively. In both groups, at T0, anti-S levels were significantly lower compared to HD (p<0.0001 and p=0.0069, respectively), while at T1, only in LuTR group (p=0.00062). At T0 and T1, significant a lower percentage of “responding” T-cells (CD4 T0:p<0.0001,T1:p=0.0119; CD8 T0:p<0.0001,T1:p=0.0221) and polyfunctional T-cells (CD4 T0:p=0.0012, T1:p=0.0093; CD8 T1:p=0030) were found in LuTR compared to HD, as well as in KTR (responding: CD4 T0:p=0.0004,T1:p=0.0002; CD8 T0:p=0.0073,T1:p=0.0691; polyfunctional: CD4 T0:p<0.0001, T1:p=0.0002; CD8 T0:p=0.0002, T1:p<0.0001).

Conclusions: Overall, in SOTR, the booster dose increased the rate of seroconversion, particularly in KTR. However, specific T-cell response remained significantly lower compared to HD. These data support that in this population different strategies aimed at increasing the immunogenicity of COVID-19 vaccination are needed.

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Vaccine in frail patients

OC 81 HUMORAL AND CELL-MEDIATED IMMUNE RESPONSES IN ELDERLY RESIDING IN A RETIREMENT HOUSE AFTER 4 DOSES OF ANTI-SARS-COV-2 BNT162B2 VACCINE

M. Tarkowski[1], A. Bergna[1], C. della Ventura[1], A. Gabrielli[1], B. Caimi[2], A. Gatti[2], C. Balotta[1], A. Riva[1], A. Lai[1] CoVICIS EU Horizon grant nr 101046041

[1]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [2]Azienda Servizi alla Persona, Istituti Milanesi Martinitt e Stelline e Pio Albergo Trivulzio, Milan, Italy

Background: SARS-CoV-2 pandemic determines significant risk of severe disease and death, especially in elderly. Older adults due to their ageing immune system are also at risk of not developing sufficient protection after vaccination. The main goal of this study was to assess the humoral and cell-mediated immunity after anti-SARS-CoV-2 vaccination in residents of long-term care facility Pio Albergo Trivulzio.

Material and Methods: 116 subjects were enrolled. Humoral and cell mediated immunity to SARS-CoV-2 were assessed in 38 women and 5 men with an average age of 89 before and after 4th dose of the vaccine. Antibody responses were evaluated by measurement of anti-Spike IgG levels using Elecsys Anti-SARS-CoV-2 S (Roche). Cell mediated responses were measured by activation-induced markers test (AIM) in which PBMCs were stimulated with Spike BA.5 (BA.5-S) variant specific and reference wild type Spike peptides (WT-refS) and response was evaluated by means of flowcytometric analyses of the expression of activation markers on CD4 and CD8 T cells. Additionally, cell mediated response was measured by IFN-γ release from T cells in response to two sets of SARS-CoV-2 antigens .

Results: Enrolled subjects had received 2 doses of BNT162b2 vaccine in December 2020/January 2021, 3rd dose in October 2021, and 31 subjects received 4th dose in April/August 2022. Out of 43 people studied, 12 had COVID-19 post 3rd dose of the vaccine and 10 of them did not receive the 4th dose . After 4th dose all the subjects presented anti-Spike IgG levels above the threshold but also those with only 3 doses demonstrated elevated levels of SARS-CoV-2 specific IgG. For CD4 T cells mediated response, out of 43 people, 10 did not respond to WT-refS and 11 to BA.5-S. The responses to CD8 T cells were absent in 4 and 6 subjects, respectively. Negative AIM test for both T cell subpopulations and antigens was observed in 1 person. For those whose AIM test was positive, responses to BA.5-S peptides were 31% and 25% lower in comparison to the WT-refS for CD4 and CD8 T cells, respectively. SARS-CoV-2 S1 subunit peptides , targeting CD4 T cells caused elevated release of IFN-γ (>0,15 IU/ml) in 20, whereas stimulation with S1+S2 subunit peptides recognised by CD4 and CD8 T cells, determined similar effect in 22 out of 43 people tested. Among those paired samples for which IFN-γ was elevated, its release was significantly ($p<0.001$) higher after stimulation with Ag2 than Ag1. In the same paired samples, the frequency of WT-refS activated CD8 T cells was significantly higher than WT-refS CD4 T cells ($p=0.035$).

Conclusions: Our data demonstrate that in elderly, 4 doses of BTN162b2 vaccine induced elevated levels of the anti-SARS-CoV-2 IgG but T-cell mediated responses were present only in 50-75% of them and even lower when tested against SARS-CoV-2 BA.5 omicron variant. In those who responded, virus activated CD8 T cells and elevated release of IFN-γ were present.

Vaccine in frail patients

OC 82 ASSESSMENT OF SARS-COV-2 SPECIFIC T-CELL RESPONSES USING AN IN-HOUSE INTERFERON-G RELEASE ASSAY (IGRA) IN PEOPLE WITH HIV

L. Benedetti[1], L. Ferrari[2], A. Ruggiero[3], C. Stefani[3], N. Braccialarghe[1], A. Imeneo[1], C. Piubelli[4], A. Matucci[4], E. Teti[2], L. Sarmati[1,2], A.M. Geretti[1,2,5], M. Iannetta[1,2]

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Infectious Diseases Unit, Fondazione PTV, University of Rome Tor Vergata, Rome, Italy, [3]Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy, [4]Department of Infectious, Tropical Diseases and Microbiology, IRCCS Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy, [5]School of Immunity and Microbial Sciences, King's College London, London, United Kingdom

Introduction: In people living with HIV, immune dysfunction may persist despite virological suppression on ART, with a possible effect on SARS-CoV-2 antigen-specific immune responses. Interferon (IFN)-y release assays (IGRAs) may provide a practical tool to measure T-cell activation in response to SARS-CoV-2 specific antigens. The aim of the study was to explore the use of a SARS-CoV-2 IGRA to measure cell-mediated immunity (CMI) after SARS-CoV-2 vaccination and natural infection in a diverse cohort of people with HIV.

Methods: This prospective study is enrolling stably treated patients in active follow up at the Infectious Diseases Outpatient Clinic of Policlinico Tor Vergata in Rome. Demographic, clinical, and viro-immunological data were collected from the medical records. SARS-CoV-2 specific CMI was assessed with an in-house IGRA. Heparin whole blood was stimulated with SARS-CoV-2 specific peptide libraries, covering the Spike (S) and nucleocapsid (N) protein sequences (Miltenyi Biotec). For each patient a negative (non-stimulated, NS) and positive (phytohemagglutinin, PHA) control were also included. IFN-y production was assessed through the Ella platform and expressed as antigen or PHA stimulated condition minus NS condition. Prism8 was used for the statistical analysis.

Results: To date, 17 participants were enrolled, comprising 11 males and 6 females, with a median age of 55 years (IQR 42-59), a median nadir CD4 count of 121 cells/µl (IQR 34-377), a median current CD4 count of 727 cells/µl (IQR 472-078), and a median CD4/CD8 ratio of 0.96 (IQR 0.56-1.38); 14/17 (82%) had HIV-RNA<50 copies/ml. All patients were vaccinated with the Pfizer-BioNTech BNT162b2 vaccine; 2/17 (12%) received 2 doses; 12/17 (71%) 3 doses and 3/17 (18%) 4 doses. Overall, 8/17 (47%) had a diagnosis of SARS-CoV-2 infection. Median time from last vaccination or infection was 395 days (IQR 252-451). Median IFN-y production was 163 pg/ml (IQR 334-535) to S peptide stimulation and 9.1 pg/ml (IQR 55-117) to N peptide stimulation. IFN-y production to SARS-CoV-2 (but not to PHA) was reduced at CD4 counts <350 cells/µl (Fig 1). IFN-y production after S and N peptide stimulation was correlated with the nadir CD4 count (Spearman's rho 0.54; p=0.033) (Fig 1). No correlation has so far emerged with age, pre-ART and current viral load, number of vaccine doses, and time from last vaccination or infection.

Conclusions: IGRA provides a promising tool to explore SARS-CoV-2 CMI in people with HIV and thus potentially guide strategies for vaccination and management of infection. Antiviral responses were reduced at CD4 counts <350 cells/µl. Conversely, in people with CD4 counts >350 cells/µl SARS-CoV-2 specific CMI was conserved, even one year after last known antigenic exposure. Our initial observations also indicate that a low nadir CD4 count may predict reduced CMI responses to SARS-CoV-2. The study is ongoing to confirm and extend these preliminary results.

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Clinical outcome of SARS-CoV-2 infection

OC 83 ASSOCIATION BETWEEN VACCINATION STATUS AND DISEASE SEVERITY IN PATIENTS (PTS) HOSPITALIZED FOR COVID-19: DATA FROM A NATIONAL REFERENCE HOSPITAL

A. Mondi, I. Mastrorosa, A. Navarra, S. Lanini, A. D'Annunzio, P. Gallì, C. Cimaglia, A. Agresta, F. Vaia, E. Girardi, A. Antinori

National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy

Background: The aim was to compare the clinical profile and hospital outcomes of pts hospitalized for COVID-19 according to vaccination status over an 18-month period.

Methods: Retrospective observational study including all pts admitted to INMI, from Jan1, 2021, to June30, 2022, with confirmed COVID-19 diagnosis and SARS-CoV-2 vaccination data available from medical records and/or regional vaccine registry. Main characteristics at hospital admission and clinical outcomes were compared among pts unvaccinated (NV =no vaccine doses or only the first of a 2-dose series<14 days before), fully vaccinated (FV=complete primary vaccine schedule>14 days before), and who received a booster dose (FV&B=complete primary vaccine schedule and received a booster dose>14 days before).FV and FV&B pts were further stratified according to the distance since the last dose (>or ≤120 days). Predictive factors of clinical progression (admission to Intensive Care Unit [ICU]/death) and death within 28 days from hospital admission were assessed both in the total population and in vaccinated pts by multivariable logistic regression.

Results: Overall 2,988 pts were included: 1,984NV (66.4%), 523 FV(17.5%), and 481 FV&B(16.1%). Among the vaccinated pts, 79.5%of FV and 53.2%of FV&B received their last dose >120 days from hospitalization. NV pts were more likely to be younger, non-Italian, without comorbidities and to have pneumonia at hospital admission compared to FV and FV&B pts. Within 28 days from admission, 434(14.9%) pts were admitted to ICU and 243 (8.1%) died. The three groups did not significantly differ in 28-day mortality rate and median length of hospital and ICU stay. A higher proportion of NV compared to vaccinated pts required intensive care during hospitalization [Table1]. By multivariable logistic regression, FV and FV&B pts had a significantly lower risk of both clinical progression and death within 28 days from hospitalization compared to NV pts. Similarly, female gender was associated with a lower risk of 28-day clinical progression. On the contrary, older age and having more than one comorbidity predicted a higher chance of severe clinical outcomes[Table2a]. Restricting the analysis to vaccinated pts, being FV, regardless of the distance since the last dose, was associated with a higher risk of 28-day clinical progression compared to having received a booster dose ≤120 days before admission. Older age and multi-comorbidities were also associated with a higher risk of severe outcomes whereas female gender lowered the chance of clinical progression[Table2b].

Conclusions: Our data confirm the efficacy of vaccination in preventing severe clinical outcomes of COVID-19. In vaccinated pts, subjects with a recent booster dose had a lower risk of clinical progression compared to those vaccinated only with the primary schedule. Efforts to promote SARS-CoV-2 vaccination and increase the uptake of booster doses are critical to prevent COVID19–associated severe outcomes.

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Clinical outcome of SARS-CoV-2 infection

OC 84 ANTI-SPIKE SARS-COV-2 ANTIBODY TITER AND RISK OF CLINICAL PROGRESSION IN PATIENTS WITH COVID19-RELATED PNEUMONIA

L. Mezzadri[1], G. Lapadula[1,2], G. Lo Cascio[1], L. Antolini[1], S. Malandrin[2], P. Columpsi[2], A. Rugova[2], S. Limonta[2], A. Cavallero[2], P. Bonfanti[1,2]

[1]School of Medicine and Surgery, University of Milano Bicocca, Milan, Italy, [2]Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy

Background: Antibodies against SARS-CoV-2 spike-protein (anti-S Ab), either elicited by natural infection or by vaccination, correlate with protection from symptomatic infection. Whether Ab level predicts the outcome of patients with severe COVID19 is still unclear. We aimed at assessing whether anti-S Ab titer is associated with the risk of death or mechanical ventilation in patients hospitalized for COVID19 pneumonia.

Material and Methods: We conducted a retrospective cohort study on adults hospitalized for COVID19 pneumonia (defined as radiological evidence of lung involvement or presence of respiratory failure) between July 2021 and July 2022, provided their anti-S Ab titer (LIAISON® SARS-CoV-2 TrimericS IgG assay) had been measured within 72 hours. Uni- and multivariable logistic regression was used to explore the association between the occurrence of death or mechanical ventilation (MV) and the following variables: Ab titer, age, gender, immunosuppressive conditions (i.e., hematological or solid malignancies, diabetes, renal failure, cirrhosis, HIV infection, immunosuppressive therapy), days since symptoms' onset and use of monoclonal Ab (mAb). Separate analyses were conducted for vaccinated and unvaccinated individuals.

Results: Among 534 patients, 63% were male, 61% were vaccinated and 42% had ≥1 immunosuppressive condition; mean age was 71.5 years (SD 14.4). The median Ab titer was 1370 BAU/ml (IQR 116-2080) among vaccinated and 15.5 (IQR 0-107) among unvaccinated individuals. Overall, 42 patients underwent MV and 92 died, corresponding to 28.9% vaccinated and 21.8% unvaccinated subjects meeting the outcome.

Table 1 shows the results of the logistic regression assessing predictors of death/MV. Among vaccinated individuals, increasing anti-S Ab titer was significantly associated with a lower risk of death/MV (per log2 BAU/ml increase, OR 0.90, 95%CI 0.84-0.97). Using multivariable analysis, Ab titer (per log2 BAU/ml increase, aOR 0.88, 95%CI 0.81-0.97), age (aOR 1.03, 95%CI 1.01-1.06) and solid malignancies (aOR 3.01, 95%CI 1.33-6.79) were significantly associated with the outcome, independently of each other and of symptoms' duration and hematological malignancies.

Among unvaccinated individuals, anti-S Ab titer was marginally protective against the outcome (per log2 BAU/ml, aOR 0.86, 95%CI 0.73-1.01), independently of age (aOR 1.04, 95%CI 1.01-1.07), immunosuppressive therapy (aOR 16.3, 95%CI 2.2-119.5) and diabetes (aOR 3, 95%CI 1.24-7.48). In an additional model adjusted for mAb treatment (aOR 0.31, 95%CI 0.10-0.97), the association between Ab titer and outcome was strengthened (per log2, aOR 0.81, 95%CI 0.68-0.96).

Conclusion: Higher anti-S Ab titer was a protective factor against critical disease in patients hospitalized for COVID-19 pneumonia, regardless of vaccination status. Thus, Ab titer could be used to guide patients' risk stratification and inform on the need for vaccination boosters.

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Clinical outcome of SARS-CoV-2 infection

OC 85 VACCINATION AGAINST SARS-COV-2 AFTER THE NATURAL INFECTION, IS ASSOCIATED WITH A REDUCED RISK OF LATE-ONSET THROMBOTIC AND CARDIOVASCULAR EVENTS (18-MONTHS ANALYSIS, ON THE "SURVIVING-COVID" COHORT, BERGAMO)

S.V. Benatti[1], S. Venturelli[1], G. Crotti[2], A. Ghirardi[3], F. D'Aloia[5], F. Binda[1], M. Savardi[4], M. Seghezzi[1], G. Previtali[1], P.A. Bonaffini[1], A. Zucchi[2], M. Rizzi[1]

[1]ASST Papa Giovanni XXIII, Bergamo, [2]ATS Bergamo, Ufficio Epidemiologico, [3]Fondazione per la Ricerca Ospedale di Bergamo (FROM) - ETS, [4]Università degli Studi di Brescia, Facoltà di Informatica, [5]Università degli Studi di Milano-Bicocca, Scuola di Specializzazione in Malattie Infettive e Tropicali, Monza

Background: Thrombosis induced by infection-related endothelial activation, is a known complication of acute infection by SARS-CoV-2. An increased risk of late-onset thrombotic and cardiovascular events seems to persist for months, after recovery, sustained by yet unknown mechanisms. Following natural SARS-CoV-2 infection, COVID-19-vaccination protects towards reinfections, but any potential effect on those thrombotic and cardiovascular late events is unknown.

Methods: "Surviving COVID" is a large cohort of patients from the first epidemic wave in our institution. All the patients got infected in the 6 months before the first COVID-19 vaccines were introduced. Each patient was followed-up once, at about three months into recovery; blood tests and chest X-ray were obtained.

For each patient, we searched the provincial healthcare (ATS Bergamo) data-base, for details and ICD-9 codes of each hospital admission or Emergency Department consultation, eventual SARS-CoV-2 reinfections and vaccinations.

We defined a composite outcome ("outcome events", OEs) including ICD-9 codes for: cerebral o cardiac ischemia, venous or arterial thrombosis of any site, pulmonary embolism, cardiac arrhythmia, heart failure. We tracked the occurrence of OEs, from the day of follow-up, until 18 months after infection. To investigate if the receipt of any COVID-19 vaccine was protective towards OEs, we matched each vaccinated patient to one unvaccinated control (by age, gender and previous history of any OE). A multivariable Cox proportional hazard model (including vaccine as a time-dependent variable) was fitted, adjusting for potential confounders as assessed at follow-up (radiographic damage by Brixia score, serum Brain-Natriuretic-Peptide, circulating Neutrophil/Lymphocytes ratio, presence of severe renal failure).

Results: Among 1515 patients, we identified 84 OEs occurring to 75 patients (5%). Patients meeting any OE were more often unvaccinated (28.9% of the 166 unvaccinated, versus 2.0% of the 1349 vaccinated, $p < 0.001$). The number of doses received was inveersely associated to OEs (no doses versus 1, 2 or 3 doses – p for trend < 0.001), also after matching (see Figure). Despite the apparent homogeneity of clinical characteristics among cases and controls, the Cox model we have adopted doesn't prove the effect of vaccines to be independently associated with a reduced risk of OEs (HR=0.81, 95% CI 0.24-2.66, p=0.72). In fact, due to the retrospective nature of the study, other non-identified confounding factors may have prevented from vaccination the individual more at risk for OEs. Nonetheless, the possibility of shaping the immuno-thrombosis by means of vaccines deserves further research.

Conclusions: COVID-19 vaccination might be beneficial in preventing late-onset thrombotic and cardiovascular events, also in individuals recovering from natural infection. The type of immunity enhanced by vaccination could be beneficial in reducing or preventing immuno-thrombosis.

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Clinical outcome of SARS-CoV-2 infection

OC 86 LONG-TERM ASSESSMENT OF ANTI-SARS-COV-2 IMMUNOGENICITY AFTER A MRNA VACCINE IN PLWH

A. Vergori[1], A. Cozzi-Lepri[2], G. Matusali[3], S. Cicalini[1], E. Cimini[4], S. Meschi[3], V. Mazzotta[1], F. Colavita[3], M. Fusto[1], S. Notari[4], S. Lanini[1], D. Lapa[3], R. Gagliardini[1], D. Mariotti[3], G. Giannico[1], E. Girardi[5], F. Vaia[6], C. Agrati[4,7], F. Maggi[3], A. Antinori[1]

[1]HIV/AIDS Unit, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome , Italy, [2]Institute of Global Health, University College London, CREME Center, London, United Kingdom, [3]Laboratory of Virology, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [4]Laboratory of Cellular Immunology and Pharmacology, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [5]Scientific Direction, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [6]General Direction, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [7]Oncoematologia e Officina Farmaceutica, Ospedale Pediatrico Bambino Gesù, IRCCS, Rome, Italy

Background: Waning of neutralizing and cell-mediated immune response after the primary vaccine cycle (PVC) and the first booster dose (BD) is of concern, especially for PLWH with a CD4 count ≤200 cells/mm3.

Material and Methods: PLWH who completed the two-dose PVC with a mRNA vaccine received the BD and had repeated measurements of immune-response parameters in 4 sequential time points: 2 months post-PVC (T1), 4 months post-PVC (T2), 2 weeks (T3), and 5 months after the third dose (T4) were included. nAbs titers by microneutralization assay (MNA90) and IFN-gamma production by ELISA assay were assessed, with optimal neutralizing response defined as nAbs ≥1:40 and IFN-gamma >12 pg/mL. Participants were stratified by CD4 count at the time of first vaccination dose (Low CD4, LCD4, ≤200/mm3; intermediate, ICD4, 201-500/mm3 and high, HCD4, >500/mm3). Mixed linear models were used to estimate the longitudinal mean nAbs against WD614G (in a subgroup also vs. Omicron BA.1) and IFN-gamma values over T1-T4 and compared across exposure groups adjusting for age and CD4 count nadir.

Results: We studied 314 PLWH on ART (LCDR=56; ICDR =120; HCDR =138): median age 56 y(IQR 50, 61), 95% had HIV-RNA <50 cps/mL, median time since HIV diagnosis of 9 y (4-21), with a median of 1 comorbidity (1 -2). The distribution of response markers over T1-T4 is shown in Fig.1A-C). Concerning nAbs against WD614G, at all the time points identified, values in HCDR were larger than those in ICDR which were larger than those seen for LCDR (Fig1A); after controlling for potential confounding factors, there was evidence for a difference in nAbs trajectories over time by CD4 count group (p=0.04; Tab. 1A). The predictions from the multivariable mixed linear model also showed that the BD was crucial for increasing the average nAbs levels against WD614G above the suboptimal neutralization threshold, a status which was maintained up to T4 in all CD4 count groups;. In contrast, nAbs response against Omicron BA.1 was suboptimal and stable over T1-T2 in all CD4 count groups (Fig.1B). Receiving BD again was pivotal for increasing these levels above the suboptimal threshold at T3 but the waning over T3-T4 was more severe leading to levels back below the threshold at T4 in all exposure groups (Tab1B). At all the time points identified, IFN-gamma levels were above the threshold for T-cell mediated response, regardless of CD4 count (Fig.1C) with no evidence for a difference in time trajectories by CD4 count groups (p=0.31, Tab.1C).

Conclusions: A CD4 count ≤500 cells/mm3 was associated with persistent levels below optimal neutralization titers prior to the BD, regardless of the VoC. The BD was pivotal for increasing the nAbs above the threshold for all CD4 count groups, although failed to provide a sustained long-term response against BA.1. Conversely, PVC alone appeared to induce an IFN-gamma production sufficient to protect all PLWH from severe COVID-19 disease, regardless of their CD4 count.

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Bench studies of viral infections

OC 87 PREVALENCE AND PHENOTYPIC SUSCEPTIBILITY TO DORAVIRINE OF THE HIV-1 REVERSE TRANSCRIPTASE V106I POLYMORPHISM IN B AND NON-B SUBTYPES

F. Giammarino[1], A. de Salazar[2], A. Fuentes[2], L. Viñuela[2], F. Saladini[1], N. Bartolini[1], C. Charpentier[3], S. Lambert-Niclot[4], G. Sterrantino[5], G. Colao[6], V. Micheli[7], A. Bertoli[8], L.Fabeni[9], I. Malet[10], E. Teyssou[10], R. Delgado[11], I. Falces[12], A. Aguilera[13], P. Gomes[14], D. Paraskevis[15], M.M. Santoro[16], A.G. Marcelin[10], F. Ceccherini-Silberstein[16], M. Zazzi[1], F. García[2]

[1]University of Siena, Department of Medical Biotechnologies, Siena, Italy, [2]Hospital Universitario Clinico San Cecilio, Clinical Microbiology, Granada, Spain, [3]AP-HP, Hôpital Bichat-Claude Bernard, Laboratoire de Virologie, Paris, France, [4]AP-HP, Hôpital Saint-Antoine, Laboratoire de Virologie, Paris, France, [5]University of Florence, Department of Clinical and Experimental Medicine, Florence, Italy, [6]Careggi Hospital, Laboratory of Virology, Florence, Italy, [7]Sacco University Hospital, Department of Clinical Microbiology, Virology and Bioemergencies, Milan, Italy, [8]University Hospital "Tor Vergata", Laboratory of Virology, Rome, Italy, [9]"Lazzaro Spallanzani"-IRCCS, National Institute for Infectious Diseases, Virology and Biosafety Laboratories Unit, Rome, Italy, [10]AP-HP, Hôpitaux Universitaires Pitié-Salpêtrière - Charles Foix, Laboratoire de Virologie, Paris, France, [11]Hospital 12 de Octubre, Clinical Microbiology Service, Madrid, Spain, [12]Hospital La Paz, Clinical Microbiology Service, Madrid, Spain, [13]Complejo Hospitalario Santiago, Clinical Microbiology Service, Santiago de Compostela, Spain, [14]CiiEM. IUEM. Almada, Portugal and Centro Hospitalar Lisboa Ocidental – HEM, Laboratório de Biología Molecular, LMCBM, SPC, Lisboa, Portugal, [15]National and Kapodistrian University of Athens, Department of Hygiene, Epidemiology and Medical Statistics, Athens, Greece, [16]University of Rome "Tor Vergata", Department of Experimental Medicine, Rome, Italy

Background: This study aimed to evaluate prevalence and the in vitro susceptibility to doravirine of the HIV-1 RT V106I polymorphism detected in samples collected among the MeditRes HIV consortium.

Methods: MeditRes HIV includes ART naïve people living with HIV newly diagnosed in France, Greece, Italy, Portugal, and Spain during the years 2018-2021. We evaluated the impact of V106I on susceptibility to doravirine (a) in site directed mutants containing V106I, V106A, V106M & Y188L mutations in subtype B (NL4-3, HXB2) and CRF02_AG background and (b) in a subset of recombinant viruses with clinically derived RT-RNAseH coding region harboring V106I and no other major NNRTI RAMs. Phenotypic susceptibility to doravirine was determined through a TZM-bl cell-based assay and expressed as fold-change (FC) with respect to the reference wild type virus.

Results: MeditRes HIV includes 2705 patients. Viral subtypes were B in 1523 cases (56.3%), CRF02_AG 441 (16.3%), A 160 (5.9%), C 141 (5.2%), F 124 (4.6%), others 316 (11.7%). The prevalence of V106I was 2.9%, 3.2% and 2.5% in the overall dataset, in B and non-B subtypes, respectively. Among non-B subtypes, the prevalence of V106I was 3.1%, 0.7%, 8.1%, 3.6%, 14.3%, 0.9%, and 3.1% in subtype A, C, F, G, D, CRF02_AG and CRF06_cpx, respectively. FC values for site directed mutants in the NL4-3, HXB2 and CRF02_AG background were 0.7, 2.0 and 2.5 with V106I, respectively; 3.4, 19.9 and na (not available) with V106A; 9.4, 27.3 and 13.5 with V106M; >100, na, and >100 with Y188L. The panel of clinically derived viruses tested includes 22 subtypes B and 28 non-B subtypes (2 A1, 2 CRF02_AG, 4 CRF06_cpx, 1 CRF44_BF, 3 D, 14 F1, 1 G and 1 URF). The median doravirine FC values were 1.3 (IQR 0.9-2.2) in the whole data set, while the susceptibility in B subtype is slightly lower than non-B subtypes (1.2 [IQR 0.9-1.6] vs. 1.8 [IQR 0.9-3.0]), and particularly than F1 subtype (2.6 [IQR 1.0 -4.0]). Eight out of 50 (16%) viruses showed FC values equal or higher than the doravirine biological FC cutoff (3.0), one subtype B (FC 3.0) and seven non-B subtypes (A1, FC 5.5; CRF06_cpx, FC 3.7; F1, FC 7.9, 6.5, 3.1, 3.0, 3.0).

Conclusions: The prevalence of the HIV-1 RT V106I polymorphism in the MeditRes database remains low and comparable to previous studies. V106I appeared to minimally decrease the susceptibility to doravirine in site directed mutants and most of clinical isolates. Reduced susceptibility has been observed with increased frequency in non-B subtypes, especially subtype F1, however the clinical impact remains to be investigated.

Bench studies of viral infections

OC 88 THE IN VITRO EFFECTS OF DOLUTEGRAVIR AND BICTEGRAVIR ON MUSCULOSKELETAL CELLS

A. Cazzaniga[1], J.A.M. Maier[1], S. Rusconi[1,2]

[1]Department of Biomedical and Clinical Sciences (DIBIC), University of Milan, [2]Infectious Disease Unit, Legnano General Hospital, ASST Ovest Milanese

Background: Integrase strand transfer inhibitor (INSTI) are safe, effective and highly recommended in ART regimens for HIV treatment. Long term administration of antiretrovirals might result in osteoporosis and decline of musculoskeletal function, with consequent increase of frailty. To look into the cellular basis of musculoskeletal impairment, we evaluated the effects of two 2nd generation INSTI, dolutegravir and bictegravir, on the performance of cultured osteoblast and myoblasts/myotubes.

Materials and Methods: C2C12 murine myoblasts were cultured in Dulbecco Modified Eagle's Medium with high glucose (4.5 mg/l) and 2% fetal horse serum for 6 days to induce myoblast differentiation. Dolutegravir and bictegravir were used at the maximal concentration of [2xIC90] on C2C12 before (C2C12) and after (myoblasts) differentiation. Dichlorofluorescin (DCFH) and Mitochondrial Superoxide Indicators (Mitosox) fluorescent assays were performed. The slow and fast fibers were detected by western blot. The mitochondrial content was investigated by Mito Tracker stain. The amount of neutral lipids was measured using the Bodipy fluorescent dye. Dolutegravir and bictegravir were also used on cultured human osteoblasts. Alkaline Phosphatase Assay (ALP) was evaluated using a fluorimetric Kit and their transition into osteoblasts was followed by RTPCR.

Results: In myotubes, dolutegravir, but not bictegravir, triggers the accumulation of reactive oxygen species (ROS) as detected by DCFH, while no increase of mitochondrial ROS emerged (Figure 1). Mito Tracker stain reveals that only bictegravir increases mitochondrial mass in myoblasts (C2C12) and myotubes (Figure 2). Moreover, both dolutegravir and bictegravir increase neutral lipid deposition as evaluated by Bodiby staining (Figure 3) and enhance the amounts of slow fibers as demonstrated by western blot. Turning to osteoblasts, only dolutegravir impairs the synthesis of ALP and the conversion to osteocytes.

Conclusions: These results contribute to the understanding of some effects of two widely used INSTI. Unlike dolutegravir, bictegravir had no effects on osteoblasts. Both impact on myoblasts and myotubes. Our results are potentially useful to promote further investigations on the metabolic impact of INSTI.

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Bench studies of viral infections

OC 89 PHARMACOKINETICS OF FIRST-LINE ANTITUBERCULAR DRUGS IN PEOPLE LIVING WITH HIV AND CONTROLS IN A THERAPEUTIC DRUG MONITORING REGISTRY

V. Pirriatore[1], J. Cusato[2], E. De Vivo[2], P. Piccioni[3], G. Rossi[3], A. Trentalange[4], G. Calleri[1], S. Audagnotto[4], G. Di Perri[4], S. Bonora[4], A. D'Avolio[2], A. Calcagno[4]

[1]Unit of Infectious and Tropical Diseases Divisione A, Ospedale Amedeo di Savoia, ASL Città di Torino, Torino, [2]Laboratory of Clinical Pharmacology and Pharmacogenetics, Department of Medical Sciences, University of Torino, [3]Unit of Pneumology at Ospedale Amedeo di Savoia, ASL Città di Torino, Torino, [4]Infectious Diseases, Department of Medical Sciences, University of Torino at Ospedale Amedeo di Savoia, ASL Città di Torino, Torino

Background: Tuberculosis (TB) is the leading cause of death worldwide among infectious diseases and particularly among people living with HIV (PLWH). Inadequate concentrations of first line anti-TB drug (FLDs) could lead to lower cure rates and the selection of resistant strains. Therapeutic drug monitoring (TDM) of FLDs has been suggested in order to improve treatment outcomes. Despite poorer efficacy in PLWH, the impact of HIV infection on the pharmacokinetics of FLDs is controversial. The aim of the study is comparing FLD plasma concentrations in PLWH and controls.

Materials and Methods: We searched our TDM registry database for plasma concentrations of FLDs from 2011 to 2023. Plasma concentrations of rifampicin (RFP), isoniazid (INH), ethambutol (ETB) and pyrazinamide (PZA) were measured through a validated chromatographic (LC-MS/MS) method. Maximum plasma concentrations (Cmax) were considered those withdrawn ≤4 hours and Ctrough those 22-24 hours post-dose. Cmax threshold were 8000 µg/mL (RFP), 3000 µg/mL (INH), 2000 (ETB) µg/mL and 20000 µg/mL (PZA). Results are given as medians (interquartile ranges) and compared through non-parametric tests.

Results: 1084 plasma samples were studied: median age was 40 (27-51) years and 793 (73.2 %) from male patients. 42 participants (3.9%) were living with HIV. Sex and gender were similar while weight was significantly higher in PLWH (78 vs. 61 Kg, p<0.001). 604 (55.7%) samples were considered Cmax and sample were withdrawn 2 hours (2-3) post-dose: the other samples were obtained 24 hours (6-24) post-dose. A significantly lower dose of RFP was recorded in PLWH (9.5 vs. 10.3 mg/Kg, p=0.005).

PLWH showed similar RFP (6387 vs. 6710 ng/mL, p=0.551), INH (2138 vs. 2133 ng/mL, p=0.755), ETB (1992 vs. 1876 ng/mL, p=0.866) and PZA Cmax (24976 vs. 28956 ng/mL, p=0.190) Cmax as compared to controls. Subtherapeutic Cmax were observed in 61.6% (RFP), 67.3% (INH), 21.3% (PZA) and 53% (ETB): only PZA Cmax <20000 ng/mL were border-line more common in PLWH (45.5% vs. 20.8%, p=0.062). Ctroughs samples showed higher INH (113 ng/mL vs. <LOQ, p=0.013), EMB (793 ng/mL vs. 233 ng/mL, p=0.009) and PZA (13799 vs. 4604 ng/ml, p=0.002) concentrations in PLWH.

Conclusions: With the limitations of a TDM Registry we observed lower RFP dose in PLWH but no major difference in first-line antitubercular Cmax was observed. The finding of higher trough concentrations in PLWH deserves additional analysis.

Bench studies of viral infections

OC 90 EXTRACELLULAR VESICLES DESIGNED TO DECOY OR COMPETE WITH SPIKE BINDING TO THE HUMAN ACE2 RECEPTOR OF SARS-COV-2 HIGHLIGHT THE DIVERSITY OF OMICRON SPIKE

I. Pagani[1], M. Schürz[2], M.M. Neto[3], N. Temperton[3], N. Meisner-Kober[2], E. Vicenzi[1]

[1]Viral Pathogenesis and Biosafety Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy, [2]Chemical Biology and Biological Therapeutics, Department of Biosciences and Medical Biology, University of Salzburg, Austria, [3]Medway School of Pharmacy, University of Kent, United Kingdom

Introduction: Extracellular vesicles share multiple mechanistic parallels to viruses including their biogenesis, cellular uptake, and trafficking routes. This makes EVs an attractive agent for the development of antiviral applications. To interfere with the entry of SARS-CoV-2, we investigated either an EV decoy expressing the human Angiotensin-converting-enzyme 2 (hACE2) receptor (ACE2-EVs) or EVs expressing the spike protein (S-EVs) aimed at competing with the virion spike.

Materials and Methods: EVs were isolated from HEK293T cells transfected with plasmids expressing either the spike protein (Wuhan isolate) or the hACE2 receptor by ultrafiltration and size exclusion chromatography. EVs were analysed by quantitative single vesicle imaging and super resolution microscopy. After characterisation, EVs and control medium were tested for inhibition of viral entry in Vero cells and in the human epithelial Calu-3 cell line in a dose-dependent manner with different SARS-CoV-2 variants. Furthermore, both ACE2-EVs and S-EVs were tested in the infection of primary human 3D bronchial (HBE) and nasal epithelia (HNE) with either SARS-CoV-2 D614G or Omicron BA.1 variants. Viral replication was quantified by Plaque Forming Unit Assay (PFA) in culture supernatants collected at 24-48-72 and 144 h post-infection and immunofluorescence analysis with specific antibodies.

Results: Immunostaining with antibodies and sera from Covid patients confirmed expression and steric accessibility of the spike or hACE2 proteins on the EV surface. Cotreatment of cells with SARS-CoV-2 and either S-EVs or ACE2-EVs significantly reduced viral entry and replication in all cellular models. The inhibition was more efficient with the ACE2-EVs than the S-EVs as a 4-log10 as compared to 1-log10 decrease of viral replication was reached in infected HBE treated with ACE2-EVs and S-EVs, respectively. Immunofluorescence analysis confirmed the reduction of viral Nucleocapsid and dsRNA signals in EV-treated epithelial cells. Surprisingly, while the inhibition of both ACE2-EVs and S-EVs was maintained across the SARS-CoV-2 variants up to Delta, the ACE2-EVs activity was completely lost against the Omicron clade.

Discussion: Our data demonstrate that SARS-CoV-2 infection can be inhibited by both ACE2-EVs decoy and by competitive S-EVs. However, the adaptation of SARS-CoV-2 renders ACE2-EVs ineffective in inhibiting the Omicron variant. This finding highlights the impact of the increased affinity of Omicron spike to hACE2 and its preferential endosomal over the plasma membrane entry route.

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Liver, vessels and lipids

OC 91 TO TAF OR NOT TO TAF? WHAT IS THE DIFFERENCE? DATA FROM A REAL-LIFE SETTING

N. Squillace[1], L. Taramasso[2], E. Ricci[3], B. Menzaghi[4], G. De Socio[5], G. Orofino[6], B.M. Celesia[7], E. Sarchi[8], S. Piconi[9], G. Pellicano'[10], S. Rusconi[11], F. Vichi[12], A. Di Biagio[2], P. Bonfanti[1], for the CISAI Study Group

[1]Infectious Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, University of Milano-Bicocca, Monza, [2]Infectious Diseases, San Martino Hospital Genoa, University of Genoa, Genoa, [3]Fondazione ASIA Onlus, Buccinasco (MI), [4]Unit of Infectious Diseases, ASST della Valle Olona – Busto Arsizio (VA), [5]Unit of Infectious Diseases, Santa Maria Hospital, Perugia; [6]Division I of Infectious and Tropical Diseases, ASL Città di Torino, [7]Unit of Infectious Diseases, Garibaldi Hospital, Catania, [8]Infectious Diseases Unit, S.Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, [9]Unit of Infectious Diseases, A. Manzoni Hospital, Lecco, [10]Infectious Diseases, G. Martino Hospital -University of Messina, Messina, [11]Infectious Diseases Unit, ASST Ovest Milanese, Legnano (MI) - DIBIC, University of Milan, [12]Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Florence

Background: Our aim was to investigate the role of switching from Emtricitabine/Tenofovir Alafenamide (FTC/TAF) based regimen to a dolutegravir (DTG) containing two-drug regimen (2DR) vs continuing FTC/TAF on metabolic and anthropometric parameters.

Material and Methods: Consecutive people living with HIV infection (PLWH) enrolled in a multicenter observational cohort (SCOLTA) project, on a stable FTC/TAF based regimen (at least 24 weeks) with HIV-RNA<40 copies/ml were included. The baseline was considered as the time of the switch to a 2DR regimen or to a different third drug maintaining FTC/TAF. Changes from baseline (T0) to follow-up (T1, week 24) were analyzed

Results: Four hundred forty-one PLWH met the inclusion criteria, 340 (77.1%) were males, 28 (6.4%) diabetics.

At T0 main characteristics were (mean ± standard deviation [SD]) the following: age 48.9 ± 11.9 years, body mass index (BMI) 25.6 ± 4.2 kg/m2, total cholesterol (TC) 196 ± 41 mg/dL, HDL cholesterol (HDL-c) 52 ± 16 mg/dL, LDL-cholesterol (LDL-c) 117 ± 36 mg/dL, glucose 93 ± 17 mg/dL in non-diabetic PLWH. CD4+ cell count (CD4) median value was 687 cell/μL (interquartile range [IQR] 504-901), triglycerides (TGL) 120 mg/dL (IQR 86-161). Antiretoviral regimen before switching were predominantly: FTC/TAF/ELV/COBI [197 PLWH , (44.7%)] , FTC/TAF/DTG [75, (17.1%)], FTC/TAF/RPV [48, (10.9%], FTC/TAF/DRV/COBI [31, (7.1%)], FTC/TAF/RAL [27, 6.1%), FTC/TAF/BIC [26, (5.9%)], Other PI-boosted based regimens [25, (5.7%)], other NNRTI-based regimens [6, (1.4%)].

Three hundred six PLWH switched to FTC/TAF/BIC, fourteen to FTC/TAF/DTG, Ninety-eight to DTG/lamivudine (3TC) and twenty-three to DTG/rilpivirine (RPV).

PLWH switching to 2DR or continuing FTC/TAF differed in term of risk factor for HIV acquisition (intravenous drug use 5.0% vs 18.4%, p<0.0001), HCV coinfection (9.3% vs 24.6%, p=0.0005), median baseline CD4 (744 vs 652, p=0.0002) and CDC stage (B 16.5% vs 27.9% and C 6.6% vs 20.1%, p<0.0001). The previous regimen included cobicistat (COBI) in 245 PLWH (36.4% in 2DR vs 62.8% in TAF, p<0.0001).

Mean change in cholesterol, TG and weight from baseline are shown in Table 1. No significant difference from baseline or between groups was observed in the overall sample. After checking for the presence of COBI in the previous regimen, we observed that PLWH with a previous COBI-including regimen showed a significant decline in CT, LDL and TGL in both 2DR and FTC/TAF groups.

Conclusions: No difference was found in weight , TC, LDL-c and TG in PLWH continuing an FTC/TAF regimen vs those switching to 2DR. Switching from a previous COBI-including regimen was associated with a significant decrease of blood lipids.

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Liver, vessels and lipids

OC 92 LDL-C TARGET ACHIEVEMENT IN PEOPLE LIVING WITH HIV ACCORDING TO INDIVIDUAL CARDIOVASCULAR RISK: A RETROSPECTIVE SINGLE CENTER OBSERVATIONAL STUDY

G. Carrozzo[1,2], B. Caloni[1,2], A. Poloni[1,2], S. Pagano[1,2], M.L. Colombo[1,2], M. Beltrami[1,2], G. Casalini[1,2], C. Gervasoni[1], A.L. Ridolfo[1], A. Giacomelli[1], S. Antinori[1,2]

[1]III Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [2]Università degli Studi di Milano, DIBIC Luigi Sacco, Milan, Italy

Background: People living with HIV (PLWH) have a higher rate of cardiovascular disease (CVD) compared to general population.
The last European AIDS Clinical Society (EACS) guidelines of October 2022 confirm the goals for calculated low density lipoprotein (LDL-c) in PLWH according to individual CVD risk, as reported in the previous update. We aimed to assess LDL-c target achievement in a cohort of PLWH according to the individual CVD risk.
Methods: We conducted a retrospective, observational, single center study. Consecutive PLWH accessing the outpatient service of the III Infectious Disease Division L. Sacco Hospital (Milan) from January 1st to 31st 2023 were included. We collected demographic, clinical and laboratory characteristics. According to EACS and European Society of Cardiology (ESC) guidelines, we assessed patients' 10-year CVD risk through ESC app calculators (SCORE-2, SCORE-2OP, ADVANCE, SMART, ASCVD) or other defining criteria (i.e. atherosclerotic CVD, diabetes, chronic kidney disease). Patients were classified into three risk levels: very high risk (VHR), high risk (HR) and no-HR, including moderate and low risk. Since these scores were validated for people older than 40 years old, we considered a low CVD risk for otherwise healthy younger PLWH. By using the last available laboratory data performed within 12 months from study start, we investigated if they reach LDL-c target according to their CVD risk: <55 mg/dL in VHR, <70 mg/dL in HR, <100 mg/dL in moderate and <116 mg/dL in low risk.
Results: Among 246 patients, mostly were male (77%) and caucasian (85%); the median age was 51 (inter quartile range (IQR) 46-60) (Table 1). 95% of patients had HIV RNA <50 copies/mL and the median CD4 count was 715 (IQR 561-911) cells/μL. Twenty-one (8.5%) patients had a previous CVD and 84 (34%) took lipid lowering therapy, of which 64 (26%) were statins. A complete lipid profile was available for 230 patients (93.5%) with a median LDL-c of 119 (IQR 97-171) mg/dL [114 (IQR 93-138) mg/dL in VHR, 129 (IQR 94-156) mg/dL in HR, 114 (IQR 97-132) mg/dL in no-HR)].
About 10-year CVD risk assessment, 8 patients did not have sufficient data to calculate the risk. Among the remaining 238 patients, 55 (23%) were at VHR, 80 (34%) at HR and 103 (43%) at no-HR (Figure 1). Overall, LDL-c target was not achieved in 178 PLWH (75%). Fifty three out of 55 (96%) patients in the VHR group who were not on LDL-c target although 26 (47%) were on statin treatment; 69/80 (86%) were not on LDL-c target in the HR group of whom 18 (22%) were on a statin treatment (Figure 2).
Conclusions: After more than one year from the publication of the updated EACS treatment goals for LDL-c in PLWH, we found out that we are far away from reaching an adequate LDL-c target especially in VHR and HR subjects. Considering the aging PLWH with a consequent expected increased risk of CVD urgent interventions are warranted to raise awareness of physicians to achieve a correct CVD prevention.

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Liver, vessels and lipids

OC 93 EVALUATION OF INTIMAL THICKNESS AND ATHEROMATOUS PLAQUES IN HIV-EXPERIENCED VS HIV-NEGATIVE PATIENTS: DATA FROM THE ARCHIPREVALEAT COHORT

S. Martini[1], E.D. Ricci[2], A. Masiello[3], S. Zacà[4], A. Castagna[5], C. Muccini[5], L. Galli[5], B.M. Celesia[6], S. Ferrara[7], A. Tartaglia[8], D. Angiletta[4], P. Maggi[1,3]

[1]Università della Campania Luigi Vanvitelli, Naples, Italy, [2]Fondazione ASIA Onlus, Milan, Italy, [3]AORN Sant'Anna e San Sebastiano, Caserta, Italy, [4]Chirurgia Vascolare ed Endovascolare"Aldo Moro", Università di Bari, Bari, Italy, [5]Università Vita e Salute San Raffaele, Milan, Italy, [6]Azienda Ospedaliera ARNAS Garibaldi, Catania, Italy, [7]Università degli Studi, Foggia, Italy, [8]Azienda Ospedaliera Foggia-Italy, Foggia, Italy

Background: Antiretroviral therapy has allowed patients with HIV a marked improvement in prognosis and quality of life, but metabolic problems still remain, mainly characterized by dyslipidemia. Over time, this can lead to a progressive myointimal thickening of the supra-aortic trunks up to the formation of atheromatous plaques, which determine a greater cardiovascular risk for the affected patients1. The aim of our study is to evaluate whether HIV+ patients actually present, once the age factor is excluded, greater evidence of high myointimal thickness (IMT) and atheromatous plaques (IMT>1.20 mm) compared to a control group of seronegative patients for HIV.

Materials and Methods: To evaluate the association between HIV infection in antiretroviral treatment and vascular pathology, we performed a cross-sectional study, retrospectively observing 872 patients, 277 HIV+ present in the Archiprevaleat cohort and 595 HIV- as control group. All patients had a Doppler scan of the supra-aortic trunks performed between 2009 and 2022. We analyzed and compared the comorbidities in the 2 groups of patients with and without HIV infection. The comparison between the two groups was carried out using logistic regression, considering age, gender and calendar year as confounding factors.

Results: HIV- patients had a significantly higher mean age than the HIV+ group and were less frequently male. Regarding comorbidities, HIV+ patients have less incidence of diabetes and more dyslipidemia than HIV-negative patients (Table 1). Plaque frequency was higher in the HIV- group (44.7% vs 33.8%, p=0.003) in general, since these were older patients and therefore more at risk. However, this figure was reversed if the age difference was excluded from the statistical analysis. Thus, the risk of vascular damage, in terms of IMT and the presence of plaques, was higher in the group of HIV+ patients. In fact, logistic regression analysis showed a clear increase in risk in the HIV+ group for both IMT between 1.0 and 1.2 mm (odds ratio, OR, 2.15, 95% confidence interval, CI, 0.98-4.75) and for plaques (OR 1.92, 95% CI 1.16-3.18) compared to HIV- subjects. Figure 1a shows the increased risk of plaque in all HIV-infected people: this damage was more evident with the increase in the years of antiretroviral therapy (figure 1b), as if it were linked to a cumulative drug toxicity.

Conclusions: Our real-life study on a large sample of patients, although still awaiting complete comorbidity data, shows that HIV+ patients treated with antiretroviral regimens are more at risk of developing IMT and atheromatous plaques than HIV- subjects . They are to a greater extent if they have been treated for longer and if they are older. To our knowledge, there is no such data in the literature. This may stimulate better monitoring of patients with Doppler to prevent cardiovascular risk which is one of the main causes of death of HIV+ patients.

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Liver, vessels and lipids

OC 94 RISK FACTORS FOR LIVER FIBROSIS PROGRESSION IN HIV: A MULTI-CENTER LONGITUDINAL STUDY

J. Milic[1], S. Renzetti[2], F. Motta[1], J. Bischoff[3], G. Besutti[1], G. Mancini[4], S. Esperti[1], V. Menozzi[1], D. Kablawi[5], S. Calza[2], C. Mussini[1,4], J. Rockstroh[3], G. Sebastiani[5], G. Guaraldi[1,4]

[1]University of Modena and Reggio Emilia, Modena, Italy, [2]University of Brescia, Brescia, Italy, [3]University of Bonn, Bonn, Germany, [4]Clinic of Infectious Diseases, University Hospital of Modena, Modena, Italy, [5]McGill University, Montreal, Canada

Background: People with HIV (PWH) are at high risk for metabolic dysfunction-associated fatty liver disease (MAFLD). Liver fibrosis (LF) is the most significant predictor of liver disease progression and mortality. We aimed to investigate the effect of MAFLD and antiretroviral exposure on LF progression in PWH.
Methods: This was a longitudinal study of three large prospective cohorts of PWH in Italy, Germany and Canada. Patients with at least two transient elastography with controlled attenuation parameters (CAP) exams were included. LF progression was defined as development of significant LF (defined as liver stiffness >8 kPa), or transition to cirrhosis (defined as liver stiffness >13 kPa for those with liver stiffness >8 but < 13 kPa at baseline). MAFLD was defined according to Eslam criteria: presence of hepatic steatosis (CAP>248 dB/m), plus any among type 2 diabetes, overweight (BMI>25 Kg/m2) or two other metabolic abnormalities. Other longitudinal predictors included co-infection with HBV or HCV, weight gain (WG), defined as a 5% BMI increase in two consecutive visits, and current exposure to ART classes. A multi-state Markov model was used to describe the process in which PWH moved through the next LF state. Cox regression model was used to identify predictors for LF progression event.
Results: A total of 1183 PWH were included (median age 52.9 years, 77% males, median duration since HIV diagnosis 18 years). Prevalence of MAFLD was 46.8%. Coinfections with HBV and HCV were present in 3.6% and 21.9%, respectively. At baseline, liver stiffness was <8 kPa in 85.6%, 8-12.9 kPa in 8.6%, and >13 kPa in 5.7% of PWH. During a median follow-up period of 2.5 years, a minimum of two and maximum of six yearly LF assessments were performed. In Markov model, WG was positively associated with progression of LF (OR=3.107, 95% CI 1.588, 6.078) while it prevented LF regression (OR=0.304, 95% CI 0.037, 2.514). The incidence rate of LF progression was 3.4 per 100 persons-year. Comparing 128 (9.6%) LF progressors with 1212 (90.4%) of non LF progressors, significant differences included mean BMI (26.3 vs 24.5), duration of HIV (16.7 vs 18.6 yrs), MAFLD (66.7 vs 48.3), HBV co-infection (7.8 vs 3.5%), ALT (36 vs. 25 UI) and WG (32.4 vs 21.9%). On multivariable analysis, predictors of LF progression were WG and MAFLD (see Table 1).
Conclusion: LF progression occurs in a significant proportion of PWH, higher than reported in literature for the general population. Its main drivers include metabolic health variables, while ART exposure does not seem to impact LF progression. PWH should be routinely screened for liver fibrosis, regardless of viral hepatitis co-infection.

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PACS: what to asses

OC 95 ASSESSING HEALTH STATUS DYNAMICS IN PEOPLE WITH POST-ACUTE COVID-19 SYNDROME COMPARING PATIENT REPORTED OUTCOME MEASURES WITH PHYSICAL FUNCTIONING, SARCOPENIA AND FRAILTY

J. Milic, M. Caccamo, F. Motta, M. Belli, L. Sighinolfi, V. Menozzi, M.D. Di Trapani, S. Esperti, C. Mussini, A. Montis, S. Caselli, G. Guaraldi

University of Modena and Reggio Emilia, Modena, Italy

Background: Acute COVID-19 and subsequently post-acute COVID-19 syndrome (PACS) are often associated with frailty, loss of physical function and muscle mass which may impact health related quality of life (HR-QoL) and self-perceived health status. The primary objective was to describe changes of the objective measures of physical health status, depicted by physical functioning, sarcopenia and frailty in people with PACS. The secondary objective was to explore: (1) correlations among these objective measures, (2) correlations among subjectively estimated health status, assessed by two questionnaires evaluating HR-QoL and (3) relationships between the two.

Methods: This was an observational retrospective longitudinal single center study including patients who were previously hospitalized for COVID-19 or referred by the general practitioner to the Modena PACS clinic. Patients were evaluated at 2 time points: at least 3 months after hospital discharge or acute COVID-19 and at approximately 1-year follow-up after. The outcomes of the study were objective and subjective measures of physical health status. Physical functioning was assessed by 6-minute walking test, short physical performance battery (SPPB) including balance test, chair stand test and gait speed. Sarcopenia was defined as (1) weak hand grip or as (2) appendicular skeletal muscular index (ASMI) score <7.26 /<5.45 kg/m2 for men/women or (3) as a combination of the two. Frailty was assessed with frailty phenotype (FP). HR-QoL was assessed by EQ-5D-5L and SF-36 questionnaire. Spearman correlation coefficient was used to explore correlations described in the secondary objective.

Results: In the period July 2020–July 2022, a total of 161 patients with at least two follow-up visits at Modena PACS clinic were evaluated. At baseline, median age was 63, 69.6% were males, median BMI was 30 kg/m2. Overweight and obesity were present in 85.3% and 45.6% patients, respectively. Frailty prevalence reduced from 34.3% to 15.6% (p<0.001). Sarcopenia, defined as hand grip only (38.6% vs. 27.3%, p=0.03) and as both ASMI and hand grip (22.4% vs. 13.9%, p<0.001) reduced significantly. SPPB and HR-QoL measured with both EQ-5D -5L and SF-36 did not vary. Figure 1 depicts heat maps with Spearman coefficients among objective measures of physical health status (Figure 1A), subjective measures of health status (Figure 1B), and between the two (Figure 1C). SF-36 physical functioning domain had similar or superior performance as SF-36 total score in association with objective measures.

Conclusions: Partial recovery of objective and subjective physical health status was observed in people with PASC. Moderate correlations were observed between objective and subjective measures of health status. SF-36 physical functioning domain could be assessed alone for quick estimation of physical health status. Multiple objective and subjective measures should be collected to identify clinical evolution of people with PACS.

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PACS: what to asses

OC 96 FRAILTY TRANSITIONS IN PEOPLE WITH POST-ACUTE COVID SYNDROME

J. Milic[1], A. Spadoni[1], S. Renzetti[2], F. Motta[1], A. Fisce[1], F. Medioli[1], A. Dessilani[1], J. Conti[1], A. Verduri[1], B. Beghe'[1], E. Clini[1], C. Mussini[1], S. Calza[2], G. Guaraldi[1]

[1]University of Modena and Reggio Emilia, Modena, Italy, [2]University of Brescia, Brescia, Italy

Background: Frailty has been an important predictor of clinical outcomes in the acute phase of COVID-19, but the impact of frailty in the post-acute COVID syndrome (PACS) is largely unknown. The objective of the study is to describe longitudinal transitions of frailty phenotype (FP) states in relation to symptoms' clusters and health-related quality of life (HRQoL) in people with PACS.

Methods: This was an observational single center study including patients followed at Modena PACS clinic (MPC) from July 2020 to May 2022. MPC is a referral center established after the first wave of the COVID-19 pandemic to screen patients for signs and symptoms of PACS along with comprehensive geriatric assessment including frailty. Patients with at least two follow-up visits were included in the study. The diagnosis of PACS was based on ≥1 cluster of symptoms: respiratory, neurocognitive, musculoskeletal, psychological, sensory, dermatological. HRQoL was evaluated with EQ-5D-5L questionnaire. Optimal quality of life was defined as score >89.7%. The outcome was frailty transition, assessed by frailty phenotype criteria. Probability of frailty phenotype changes over time was explored in mixed effect model for ordinal data. Multivariable logistic regression models were used to explore the relationship among PACS symptoms, quality of life and frailty.

Results: 823 patients were included, 60.3% were males, with the mean age of 60.3 years. At baseline, overweight and obesity were present in 333 (40.5%) and 301 (36.6%), respectively. Frailty was diagnosed in 30.5% (203) of patients. Among PACS clusters, musculoskeletal cluster was present in 575 (72.5%), neurocognitive in 398 (50.7%), respiratory in 399 (49.7%), psychological in 374 (47.8%), sensory in 363 (47.5%), and metabolic in 202 (31.4%) One-hundred seventy (32.1%) patients had optimal quality of life (>89.7%), assessed by EQ-5D-5L. Musculoskeletal, neurocognitive, and sensory significantly decreased over time, while QoL did not substantially change. Prevalence of frailty decreased over time: in the first 6 months after COVID-19 symptoms' onset, frailty was present in 220 (30.3%), from 6 to 12 months in 34 (23.6%), and >12 months in 10 (17.9%). The probability of frailty reduced over time (OR=0.98, p<0.001). Figure 1 shows multivariate logistic regression for metabolic, musculoskeletal, neurocognitive, psychological, respiratory and sensory cluster.

Conclusions: This longitudinal study showed that trends of frailty decreased over time, indicating that frailty in COVID-19 survivors might be reversable. Burden of musculoskeletal, neurocognitive, and sensory PACS clusters reduced over time, but without changes in other PACS clusters and overall QoL. However, both frailty and QoL were strongly associated with musculoskeletal, neurocognitive, and respiratory PACS, suggesting that self-reported PACS symptoms were indicative of overall vulnerability and well-being in COVID-19 survivors.

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PACS: what to asses

OC 97 12-MONTH FOLLOW-UP OF THE LONG COVID DURING THREE PANDEMIC YEARS

I.F. Bottalico, M. Poliseno, D. Capruzzi, G.A. Minafra, D.C. Cibelli, M. Rizzo, L. Barbera, F. De Gregorio, T.A. Santantonio, S. Lo Caputo

Infectious Disease Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy

Background: Long COVID syndrome is described as the persistence of symptoms even months after the initial COVID-19 infection. Since the introduction of vaccines worldwide and the spread of the omicron variant, the chance of developing long COVID has been significantly reduced and these symptoms tend to be milder and resolve more quickly. Our study aims to examine, over a one-year- follow-up (FU), long-COVID symptoms in terms of prevalence, risk, and protective factors.

Methods: Prospective observational clinical study performed in the Long COVID Infectious Diseases Outpatient Clinic of "Policlinico Riuniti" in Foggia. Data of all outpatients consecutively received from July 1st, 2020, to December 31st, 2022 were retrieved from medical records. Long COVID-related symptoms were collected at the 1 -3 (T1), 6 (T2), and 12 months (T3) FU visits performed after primary Sars-CoV2 infection. The study population was stratified according to the year of infection: the chi-square test and Mann-Whitney U test were used as appropriate to compare the groups. Survival analysis with Kaplan-Maier (KM) curves was used to assess the risk of persistence of Long-COVID symptoms at 12 months according to the year of infection, vaccine status, and history of hospitalization due to COVID-19. Multivariate Cox regression analysis was conducted to identify, among patients variables (sex, age, co-morbidities, vaccine status, hospitalization, pneumonia, and Intensive Care Unit admission), predictors of persistence of Long-COVID symptoms at 12 months.

Results: Of 1446 outpatients visited in the study period, 744 had 12-month FU available. Of these, 237 (31.9%) had been infected in 2020, 394 (53%) in 2021, and 113 (15.1%) in 2022. Their clinical features are reported in Table 1. Long COVID symptoms were reported by 540 patients at T1 (72.6%), 429 patients at T2 (57.7%), and 312 at T3 (41.9%). In the last case, asthenia, brain fog, dyspnea, and chest pain were most frequently complained about, even though a significant reduction in their prevalence was observed over the years 2020-2022. At survival analysis, while subjects infected in 2021 showed a reduced risk of having Long-COVID symptoms at 12 months compared to those infected in 2020 (HR 0.76, 95% CI 0.60-0.97, p=.02), patients who had been hospitalized due to COVID-19 had an almost double risk of symptoms persistence (HR 1.81, 95% CI 1.44-2.27, p<.001) (Fig. 2). No significant relation with vaccine status was observed. At multivariate analysis, female sex and history of hospitalization due to COVID-19 were associated with a higher risk of persistence of Long COVID symptoms at 12 months.

Conclusion: Although symptoms related to Long-COVID19 could still be observed even after 12 months from the primary infection, their prevalence has decreased over the years. A higher risk of Long-COVID-19 is observed in patients with a history of hospitalization due to COVID-19. In the post-vaccination era, the demand to perform examinations has decreased, maybe in correlation with the reduce perception of COVID symptoms.

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PACS: what to asses

OC 98 A PICTURE OF PSYCHOLOGICAL SYMPTOMS AND COPING STRATEGIES WITHIN POST COVID-19 POPULATION

A.C. Brita[1], G. Del Duca[1], A. Lonigro[2], M. Camici[1], A. Vergori[1], I. Mastrorosa[1], A. Mondi[1], C. Caligiuri[1], V. Mazzotta[1], S. Lanini[1], C. Pinnetti[1], A. Antinori[1]

[1]Clinical department, Lazzaro Spallanzani National Institute for Infectious Diseases, IRCCS, Rome, Italy, [2]Department of Education, University of Roma Tre, Italy

Background: SARS-CoV-2 infection can affect psychological state. The aim of the following study is to assess the prevalence of psychological symptoms, perception of health status (HS) and coping strategies (CS) in post Covid -19 population, stratified by gender (G) [male (MG), female (FG)], age (A) and previous hospitalization (pH). Moreover, the role of CS in mental HS was investigated.

Materials and Methods: We enrolled patients (pts) in a observational, cohort study (NeuroCOVID Study) evaluated at any time at post-COVID-19 service, from Mar20 to Oct22. Coping Orientation to the Problems Experiences-new Italian version (COPE-NVI), Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI-II), Pittsburgh Sleep Quality Index (PSQI), and Visual Analogue Scale of the EQ5D (EQ-VAS) were administered at each pts. ANOVAs for each study variable were performed to verify G and A differences, whereas bivariate correlations were computed to examine potential relations between variables. Chi-square test was used to ascertain the relation between pH, Gender and Age, respectively.

Result: N=466 pts included: median age 54 y (IQR 47-61), 53% female, 45% pH. ANOVAs showed a main effect of G for low-functional CS: COPE-SS [F (1.380) =10.78 (p<0.01)], COPE-AS [F (1.380)=9.27 (p<0.05)], COPE-TR [F (1.379)=4.89 (p<0.05)] and psychopathological scales: PSQI [F (1.466)=12.91 (p<0.01)], BDI-C [F (1.463)=3.84 (p=0.05)], BBDI-SA [F (1.463)=4.80 (p<0.05)], BDI-T [F(1.63)=6.63 (p<0.01)], BAI [F(1.462)=13.17 (p<0.001)] and EQ-VAS [F (1.465) =10.71 (p<0.01)]. Except for the EQ-VAS, in which MG obtained higher mean scores, for all other measures FG outperformed MG. A main effect of A was found for COPE-SS [F (1.380)=4.16 (p<0.05)], in which pts aged ≤54 yrs presented significantly higher mean scores, and COPE-TR [F (1.379)=6.35 (p<0.05)], in which those aged >54 yrs presented significantly higher mean scores than youngers. No Gender x Age interaction effect was found. Regarding pH, Pearson's Chi-square test showed a higher hospitalization rate in pts aged >54 [χ2 (1.461) =28.55; p <0.001] and in MG [χ2 (1. 461) =6.86, p<0.01]. Additionally, FG correlates with worse psychopathological scores, worse perception of HS and lower functional CS (COPE SS/SE). COPE PA (functional CS) correlates positively with better HS; COPE SS, SE and TR correlate with worse psychopathological scores and worse perception of HS, while COPE SE correlates negatively with HS perception. The correlation coefficients range from a minimum of -0.253 (p < 0.01) to a maximum of 0.374 (p < 0.01). Correlations are shown in Table 1.

Conclusions: Our results found that female gender presents worse psychopathological outcomes within post COVID-19 population. In addition, less performing CS were implemented in this population, correlating to a worse perception of health and mental status.

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Innovative tools for diagnosis and monitoring of viral infections

OC 99 PRELIMINARY EVALUATION ON THE RELEVANCE OF CSF CELL-FREE MITOCHONDRIAL DNA IN DIFFERENT SETTING OF VIRAL NEUROINFLAMMATORY DISEASES

G. Chimienti[1], A. Zingaropoli[2], T. Latronico[1], L. Trisolini[1], P. Pasculli[2], C.M. Mastroianni[2], M.R. Ciardi[2], G.M. Liuzzi[1]

[1]Department of Biociences, Biotechnology and Environment, University of Bari Aldo Moro, Bari, Italy, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Background: SARS-CoV-2 infected cells release damage-associated molecular patterns (DAMPs) able to activate the innate responses. In the severe forms of COVID-19, instead of being a bridge between immune and non-immune cells for resolution of damages, DAMPs play a pivotal role in the dysregulated immune response. Circulating cell-free mitochondrial DNA (cf-mtDNA), together with cardiolipin, cytochrome C and N-formylated peptides belongs to mitochondrial DAMPs Elevated levels of cf-mtDNA have been found in plasma of COVID-19 patients and increasing evidence supports the role of this circulating molecule as a risk factor for severe illness (doi: 10.1172/jci.insight.143299).

Although COVID-19 presents mainly as a pulmonary disease, it also causes injury to other organ systems, including the central nervous system. At the best of our knowledge, no study has focused on cf-mtDNA in cerebrospinal fluid (CSF) of neuro-COVID patients.

Aim of this study was to evaluate cf-mtDNA levels in paired samples of CSF and plasma of neuro-COVID patients, as well as in patients suffering from neurological manifestations of different viral origin, namely PML in multiple sclerosis (MS) and in HIV. Plasma of healthy subjects (HD) (n=5) was also analyzed as control.

Methods: Paired plasma and CSF samples were collected from neuro-COVID (n=6), MS (n=4), and HIV (n=6) patients at the hospitalization.

Copies of cf-mtDNA were measured in 2 µL of CSF or 2 µL of 10 fold diluted plasma by digital droplet PCR (ddPCR) multiplex assay on a QX200 ddPCR system using hydrolysis probes and conditions as reported in Podlesniy et al. (doi: 10.1007/978-1-4939-7778-9_7).

Droplets were read on Q×200 droplet reader and data were analyzed using QuantaSoft software. Results were expressed as copies/uL.

Results: cf-mtDNA CSF levels were 10.7±49.9, 11.6±27.2, and 2.6±0.3 copies/uL in neuro-COVID, MS and HIV patients, respectively (Median±SEM). A statistically significant difference was found in the three groups (p: 0.0017, Kruskall-Wallis test) . Statistically significant increase in CSF levels of cf-mtDNA were detected in samples from neuro-COVID and MS compared with HIV ($p<0.05$) (Dunn's multiple comparison post-test). No statistically significant difference was observed between plasma levels of neuro-COVID (101.9±94.6), MS (49.5±46.7), HIV (34.5±77) and HD (37.5±6.7) (Median±SEM). In order to investigate on the origin of CSF cf-mtDNA, the Q-cfmtDNA (CSF cf-mtDNA/plasma cf-mtDNA) was calculated. Median values±SEM were 0.16±0.36; 0.31±0.09; 0.08±0.04, respectively in neuro-COVID, MS and HIV patients. No statistically significant difference was evident.

Conclusion: These preliminary data indicate the presence of increased amount of CSF cf-mt DNA in neuro-COVID and MS in comparison with HIV suggesting a higher activation of the innate immune response. Further studies are needed to explore the origin of CSF cf-mtDNA in the neuroinflammatory pathologies of different viral ethiology.

Innovative tools for diagnosis and monitoring of viral infections

OC 100 SERUM ANTIBODY FINGERPRINTING FOR SARS-COV-2 VARIANTS BY LABEL-FREE MICROARRAY BIOSENSOR

T. Carzaniga[1], L. Casiraghi[1], G. Nava[1], G. Zanchetta[1], T. Inzani[1], M. Chiari[2], V. Bollati[3], S. Epis[4], C. Bandi[4], A. Lai[5], G. Zehender[5], T. Bellini[1], M. Buscaglia[1]

[1]Department of Medical Biotechnologies and Translational Medicine, Università degli Studi di Milano, Segrate, Italy, [2]Istituto di Scienze e Tecnologie Chimiche "Giulio Natta", National Research Council of Italy (SCITEC-CNR), Milano, Italy, [3]Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milano, Italy, [4]Department of Biosciences, Università degli Studi di Milano, Milano, Italy, [5]Department of Biomedical and Clinical Sciences, Università degli Studi di Milano, Milano, Italy

Background: From the early days of the pandemic, several strategies to detect and monitor SARS-CoV-2 infection have been developed. Among these, accurate serological testing, although not suitable to determine the protection from further infection, help assessing past exposure and the response derived from vaccines. Rapid serological tests are commonly directed against only one or two targets. Affordable methods to assess more complex multiplex serological profiling are currently missing.

Material and Methods: We developed an innovative label-free microarray based on an optical biosensor, named "Reflective Phantom Interface" (RPI), which enables real-time quantification of molecular binding without fluorescent or colorimetric markers. Different SARS-CoV-2 antigens were immobilized on the RPI surface and their binding to antibodies from plasma of infected patients and vaccinated volunteers was quantified within minutes (Figure 1). The antigens panel included trimeric spike of SARS-CoV-2, five different variants of the spike Receptor Binding Domain (RBD) and nucleocapsid protein (N).

Results: We measured the amount of antibodies binding to the antigens immobilized on the label-free microarray in real-time and quantified the rate of increase of the signal on each antigen. This enabled to reduce the measuring time down to a few minutes. We extracted individual serum antibody fingerprints of both total immunoglobulins (Ig) and IgA fraction. For convalescent subjects, Ig profiles showed a peak of response to the antigen corresponding to the variant of infection (Wuhan, delta, gamma or omicron), hence indicating a larger amount of specific antibodies (Figure2). As expected, vaccinated subjects provided a fingerprint similar to subjects infected with Wuhan variant. In contrast, no clear correlation was observed for IgA response patterns. Overall, vaccinated subjects without evidence of previous virus infection showed larger amount of Ig anti-SARS-CoV-2 and smaller amount of IgA (Figure 3). This was confirmed by comparing the fingerprint of vaccinated subjects before and after a symptomatic infection that showed an increase of Ig corresponding to the virus variant and a non-specific increase of overall IgA amount.

Conclusions: We demonstrated a proof of concept of a rapid, antigen microarray enabling serum antibody fingerprinting. The method is cost-effective and easy to use, thus suitable for point-of-care testing. We found that anti-SARS-CoV-2 Ig fingerprints are strongly correlated with the specific virus variant that caused the infection, hence potentially enabling accurate population screening in a condition of multiple coexisting variants. In contrast, IgA fraction profiles are overall largely variable among persons, although non-vaccinated convalescent subjects have a larger fraction of IgA in average. Moreover, we observed that a change of both Ig and IgA profiles of a person can reveal a recent infection from a specific variant.

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Innovative tools for diagnosis and monitoring of viral infections

OC 101 MOLECULAR DIAGNOSIS OF HUMAN MONKEYPOX VIRUS IN THE 2022 OUTBREAK: PRELIMINARY EVALUATION OF NOVEL REAL-TIME QUALITATIVE PCR ASSAYS

V. De Pace[1], G. Guarona[2], G. Garzillo[2], M. Ferraris[1], V. Chessa[1], S. Varesano[2], M. Lucente[1], A. Di Biagio[2,3], E. Costa[2], A. Orsi[1,2]

[1]Hygiene Laboratory Unit, IRCCS, Policlinico San Martino Hospital, Genoa, Italy, [2]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [3]Infectious Diseases, IRCCS San Martino Hospital-IST, Genoa, Italy

The emerging outbreak of Monkeypox (MPX), a rare zoonotic disease caused by human monkeypox virus which spreads strongly with close/intimate contact, is a new challenge for global public health. Since early May 2022, several human MPX cases were identified in non-endemic countries.

The aim of this study is to compare the diagnostic performances of four real-time PCR assays with a home-made PCR test, for MPX laboratory diagnosis, during the 2022 outbreak.

In the Hygiene Unit laboratory at San Martino Hospital (Genoa), 27 positive and 10 negative specimens (swabs from lesions, crusts and exudates), harvested from 25 patients with a clinical picture suggestive for MPX disease between July to August 2022, were retrospectively tested with different multiplex real-time qualitative PCR assays, according to the manufacturer's instructions: RealCycler MONK-UX/-GX (Progenie Molecular), STANDARD M10 MPX/OPX (SD Biosensor) and Novaplex - MPXV Assay (Seegene Inc.) and RealStar Orthopoxvirus PCR Kit 1.0 (Altona Diagnostics) which they are recognized as "Research use only (RUO)". All the specimens have been previously tested with a home-made real-time PCR for generic MPX virus DNA detection (MPXV generic G2R_G). Like the home-made test, turn-around-time (TAT) of these assays was 3 hours, excluding STANDARD M10 MPX/OPX that is categorized as a one-hour TAT point-of-care test. Furthermore, STANDARD M10 MPX/OPX MPX differentiated West-African and Congo-Basin strains. The diagnostic characteristics of these different commercial tests were evaluated.

The accuracy and sensitivity of these molecular RUO MPX assays ranged from 97.3% (86.2-99.5) to 100% (90.6 -100) and 96.3% (81.72-99.34) to 100% (72.25-100), respectively. RealCycler MONK-UX and STANDARD M10 MPX/OPX did not detect a positive sample with low viral load [cycle threshold (ct) of 36]. The overall specificity was 100% (72.25-100). Furthermore, these tests had Cohen's k values ranging from 1 (0.67-1) to 0.93 (0.61–1). The diagnostic performances data were reported in table 1. All MPX patients were affected by West African strain.

In-house and RUO molecular tests showed a different ct distribution for high viral load (ct ≤ 30) specimens (Wilcoxon's test: $p < 0.05$) (Figure 1, panel A). However, overall the interpretation of these results as positive unchanged. Instead, skin swabs with low viral load (ct of 31–35) had ct values which they were similarly distributed, among reference and RUO tests, even if the sample size of this group were low (N = 7) (Wilcoxon's test: $p > 0.05$) (Figure 1, panel B).

Furthermore, RUO MPX assays showed no cross-reactivity testing a HSV1, HSV2 and VZV pool.

As they are very accurate, reliable and user-friendly, these tests are highly recommended for daily or rapid laboratory discrimination of MPX infections from other rash illness.

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Innovative tools for diagnosis and monitoring of viral infections

OC 102 KINETIC OF TTV DNA LOAD IN PERIPHERAL BLOOD LYMPHOMONOCYTES IN EARLY TREATED ACUTE HIV INFECTIONS

I. Abbate[1], G. Rozera[1], E. Cimini[2], F. Carletti[1], E. Tartaglia[2], M. Rubino[2], S. Pittalis[3], R. Esvan[3], R. Gagliardini[4], A. Mondi[4], V. Mazzotta[4], A. Antinori[4], V. Puro[3], E. Girardi[5], F. Vaia[6], F. Maggi[1]

[1]Virology Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Laboratory of Cellular Immunology, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [3]AIDS Referral Center, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [4]Clinical and Research Infectious Department, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [5]Scientific Direction, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [6]General Direction, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy

Background: Torque teno virus (TTV) is a ubiquitous, non-pathogenic virus and, in allogeneic hematopoietic stem cell transplantation, its viral load directly correlates with the degree of immune reconstitution. In HIV infection, immune reconstitution is a hallmark of effective ART and is characterized mainly by an increase of CD4 T cells. Cells involved in TTV replication, in particular in the immune compartment, are still not identified. In this study, we investigated the kinetics of TTV titers in a group of early treated acutely infected HIV patients, trying to evaluate the correlation between the presence of the virus and the different immune cells involved in immune reconstitution.
Methods: Seventeen acute HIV infections (Ab/Ag positive with immune-blot test negative) were evaluated at serodiagnosis (T0), at 3 (T0.5), and 12 (T1) months after early treatment with FTC/TDF associated with either DRV/RTV and RGV or DLG. TTV DNA and HIV-1 DNA quantifications in PBMC were performed by in-house Real-time PCR. Plasma HIV-1 RNA was measured by Aptima™ HIV-1 Quant Dx Assay (Hologic). Differentiation profile, activation, senescence, and exhaustion markers in CD4 and CD8 T cells were analyzed by multiparametric flow cytometry: 7 healthy donors (HD) were added as a control group. Statistical analysis was performed by Mann-Whitney, Wilcoxon matched-pairs signed rank and Spearman tests.
Results: At T0, median (IQR) HIV-1 RNA copies/ml, and HIV-1 DNA copies/million PBMC were 7.00 (6.16-8.04) and 4.18 (3.88-4.94) respectively, with median (IQR) CD4 T of 594 (329-824) cell counts/ul and a CD4/CD8 ratio of 0.72 (0.45-1.23). At T0, TTV DNA was detected in 12 out of 17 subjects with a median (IQR) copies/million PBMC of 4.20 (3.39-5.03). A statistically significant increase in TTV DNA load was observed between T0 and T1, whereas HIV-1 RNA and HIV-1 DNA significantly declined (Fig. 1A). The increase of TTV DNA paralleled with the statistically significant CD4 and CD4/CD8 increase (Fig. 1B), although no direct correlation between TTV and total CD4 T cells or CD4/CD8 ratios was observed. Immunological analysis, conducted on a subgroup of HIV patients, showed at T0 a significantly lower amount of both CD4 and CD8 naïve cells and a higher amount of effector memory (EM) cell CD8 T cells as compared to HD (HIV+ naïve CD4: 2.1(1.2-22.7) vs HD naïve CD4 30.5(18.1 -35.1) $p<0.01$; HIV+ naïve CD8: 1.2(0.3-7.9) vs HD naïve CD8 17.7(6.3-30.8) $p<0.01$; HIV+ EM CD8: 78.1(56.6 -88.9) vs HD EM CD8 52.1(38.6-62.8) $p<0.03$; respectively). During immune reconstitution of HIV patients, a direct correlation between TTV DNA load and central memory CD8 cells ($n=10$, $r= 0.66$, $p=0.04$) was found.
Conclusions: As for transplanted patients, TTV DNA load may represent a parameter to functionally evaluate immune reconstitution in HIV patients receiving ART. However, the mechanisms underlying this phenomenon remain to be clarified, in particular the different CD4 and CD8 T cell involvement.

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The experience of PrEP in Italy

OC 103 PREP IN ITALY: INCREASED COVERAGE DESPITE SIGNIFICANT BARRIERS TO ACCESS

M. Falaguasta[1], M. Stizioli[1], P. Vinti[1], F. Leserri[2], G.M. Corbelli[2]

[1]PrEP in Italia, [2]Plus Roma

Background: PrEP is an effective tool to reduce new HIV infections but in Italy it is not reimbursed yet. Currently no official statistics on people using PrEP and its accessibility are available. To address this issue, a first community-led survey of PrEP centres was conducted in 2019, with a follow-up in 2022.

Materials and Methods: In February 2023 a survey was sent to the 72 PrEP centres currently mapped by PrEP in Italia. The research is aimed at understanding which populations use PrEP, its accessibility and the costs related to PrEP use. The data collected are estimates and have a margin of error attached.

Results: 47 centres responded to the survey, 19 in Northern Italy, 19 in Central Italy, 9 in Southern and Insular Italy. As of December 2022, at least 6444 people are on PrEP in Italy, with an increase of 77.0% compared to 2021 (71.8% considering only centres participating also in 2021 or established in 2022). 6158 of them are MSM (95,6% vs. 94.6% in 2021). Uptake has been slower in other populations, such as cis heterosexual men (2.3% vs. 2.2% in 2021), trans women (1.3% vs. 1.3% in 2021), cis women (0.8% in 2022, 0.6% in 2021) and 1 trans man (regional distribution in Table 1). 39.1% of the centres follow at least one chemsex user and 40.4% at least one sex worker. At least 537 users discontinued PrEP during 2022 (main reasons for discontinuation in Figure 1). In 2022 12 new HIV infections were detected at baseline and 4 incident infections during PrEP use, all due to suboptimal adherence. STIs cases in 2022 are presented in Table 2. In addition to the out-of-pocket cost to buy PrEP, remaining in care often involves other costs: while visits are free in 65.3% of clinical centres, through the use of fee exemption codes (B01 mainly), costs can exceed €150 for mandatory blood panels and STIs screenings at each visit, with an average cost of €60. As for future prospects for PrEP: 87.5% centres are in favour of introducing long-acting injectable cabotegravir, and 68.8% of introducing telemedicine for PrEP. Despite the fact that 83% of the centres do not have links with local organisations to refer PrEP users to in cases of problematic chems use or intimate partner violence, all have expressed an interest in establishing such partnerships. 43.8% of PrEP centres administered mpox vaccinations directly, while 37.5% referred eligible PrEP users to another health centre.

Conclusions: Costs continue to be a notable barrier to PrEP access and there is a need to simplify procedures for access and continuation. There is also an ongoing and very significant territorial divide in PrEP access, with 44% of Italian PrEP users being followed in Milano, and still few centres in Southern and Insular Italy. The vast majority of PrEP users continue to be MSM. It is therefore still necessary to continue outreach efforts to all key populations about PrEP, and build partnerships between public health institutions, clinical centres and community-based organisations.

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The experience of PrEP in Italy

OC 104 DAILY OR ON DEMAND ORAL HIV PRE-EXPOSURE PROPHYLAXIS: A COMPARISON OF USERS' CHARACTERISTICS AND SEXUALLY TRANSMITTED INFECTION FEATURES

C. Quarta[1], I. Miglio[1], C.M. Tettoni[1], M. Quaranta[1], S. Taurian[1], G. Di Perri[1], S. Bonora[1], A. Calcagno[1], M. Tutone[2], P. Sales[2], A. Lucchini[2]

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin, [2]Sexual Health Clinic, ASL Città di Torino, Italy Affiliation

Introduction: Pre-exposure prophylaxis for HIV (PrEP) is based on the use of antiretroviral therapy for preventive purposes in high-risk HIV negative individuals. Therapy is taken orally, daily (D) or on demand (onD). The only drug available in Italy since 2017 is a combination of emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF).
Materials and Methods: In this observational study were enrolled 458 patients affering to multidisciplinary centre for sexual health of Turin for PrEP, from 2018 to the end of 2022, with a medium follow-up duration of 9.5±13 months. The aim of the study was to evaluate real life efficacy, tolerability, safety, adherence, risk compensation and comparison between pre- and post-PREP STIs onset. At preliminary visit, data on general health and sexual history were collected to assess the risk of contracting HIV (SIMIT-approved questionnaire, PrEP indicated if >10 points), then blood count, renal and liver function, urine, serology for HIV, T. pallidum, and viral hepatitis; PCR analysis for Chlamydia and Gonorrhea were performed on genital and pharyngeal swabs as well as on urine. At every scheduled visit (three subsequent controls: T1,T2,T3) were repeated blood chemistry, HIV test and screening for STIs . Data were collected anonymously and processed by SPSS software.
Results: Mean age of the population was 38±10 years, 99.3% male (95% MSM, 3% bisexual, 1.5% heterosexual,0.5% transgender). The medium score of the risk questionnaire was 17.03±7.47. 72% of patients chose the onD regimen and 28% the D regimen. Choice of D regimen was associated with female sex, transgender, sex workers, alcohol use, higher number of partners in life and in the last 6 months. Two HIV infections occurred during follow-up. 5% of patients changed regimen during the study and 9% had expected side effects. Renal function parameters remained within normal limits. The percentage of use of pre-T1 condom decreased for all types of intercourse, but the difference was statistically significant only for versatile anal sex; there were no significant differences between onD and D treatment. The mean number of partners increased using PreP but no significant differences emerged in the pre-T1,T1-T2,T1-T3,pre-T3 comparisons.The prevalence of STIs remained high throughout the study, without significant differences of STIs during scheduled visit.
Conclusions: In this subgroup of patients at high risk of contracting HIV, PrEP was found to be well tolerated and effective (only two cases of HIV at T1), despite a high prevalence of STIs. We observed a preferential use in MSM people, even if this prevention treatment should be suggested to other risk groups as well. We believe that the possibility to choose and modificate the regimen over time according to the needings and habits of the PrEP candidate subjects enhance the adherence to this therapy.

The experience of PrEP in Italy

OC 105 CONFIDENCE IN THE "UNDETECTABLE EQUALS UNTRANSMITTABLE" (U=U) PARADIGM AMONG PREP USERS

S. Venturelli[1], D. Ripamonti[1], A.S. Tran[2], L. Comi[1], F. Borghi[1], F. Maggiolo[1], M. Rizzi[1]

[1]UOC Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy, [2]University of Milan, Milano, Italy

Background: The risk of acquiring or transmitting HIV by sex is estimated to be zero when HIV infected patients have undetectable plasma HIV RNA (longer than 6 months) following treatment. This paradigm, known as "Undetectable=Untransmittable", supported the worldwide Prevention Access Campaign, also endorsed by the WHO. Confidence and misunderstanding of the U=U paradigm among sexuals minorities, clinicians and PreP users are variable.

Methods: PrEP users, attending a single centre in northern Italy, have been consecutively interviewed (cross-sectional analysis) about the knowledge of the U=U paradigm and on their level of confidence in having sex without using PrEP with persistently "undetectable" HIV infected partners. Participants also answered questions regarding the number of partners in the previous three months and the use of condom for penetrative sex. For each participant we also collected data on time of starting PrEP and type of regimen, demographics and past and intercurrent STIs. The first 77 questionnaires (out of 146 ongoing PrEP users with at least a 3-month follow-up visit) have been collected since 19th January 2023.

Results: A total of 77 users completed the interview (99% men and 1% transgender woman). Among male users, 86% were MSM, 5% heterosexual and 9% bisexual. Median age was 36 years (IQR 29-44). On interview date, 59 out of 77 (77%) declared having started PrEP more than 4 months earlier and 47 users (61%) being on "on-demand" regimen.

A total of 58 users (75%) had past or current STIs at their first visit at PrEP clinic and 38 of them (49%) intercurrent STIs since they started PrEP (rectal chlamydia was the most frequent).

A total of 26 users (34%) declared having sex with less than 5 partners in the previous 3 months, 30 users (39%) with 5-10 and 21 users (27%) with more than 10. A total of 34 users (44%) declared using condom in ≤30% of their sexual encounters.

Among the 77 participants, 68 users (88%) declared they heard about the U=U paradigm. However, when asked if they would continue to use PrEP with a known HIV-RNA undetectable partner, 86% of them (59/68) answered they would, despite 59% (35/59) being on "event-driven" regimen.

Conclusions: Despite the majority of PrEP users are aware about the U=U paradigm, they would not be confident in not using PrEP with a known HIV-RNA undetectable partner. This suggests some degree of skepticism about the HIV transmission risk in the U=U setting. Clearer messaging on the U=U paradigm should be empowered by PrEP providers to increase confidence in zero risk in HIV transmission and decreasing HIV stigma.

The experience of PrEP in Italy

OC 106 MDPV AWARENESS AND PREPAREDNESS AMONG PREP USERS: A COMMUNITY SURVEY

A. Bianchi[1,2], D. Moschese[1,3], D. Calzavara[1], R. Rossotti[1,4], D. Zagato[2], A. Antonino[1,2], A. Tavelli[5], E. Caruso[1], I. Khattat[1], P. Vinti[1], P. Testoni[1,2], M. Cernuschi[1,2,6]

[1]Milano Check Point ETS - Milan, Italy, [2]ASA Milano ODV - Milan, Italy, [3]ASST Fatebenefratelli Sacco - Milan, Italy, [4]ASST Grande Ospedale Metropolitano Niguarda - Milan, Italy, [5]Fondazione ICONA - Milan, Italy, [6]IRCCS Ospedale San Raffaele - Milan, Italy

Background: 3,4-methylenedioxypyrovalerone (MDPV or PV) is a novel synthetic cathinone that emerged in the last few years in the chemsex scene in Milan. It has rapidly gained popularity due to its psychostimulant and empathogenic effects. Along with its positive subjective effects such as increased self-esteem, sociability, and libido, PV abuse also produces alarming neurologic, cardiovascular, and psychiatric adverse effects which often undermine social and working life and leads to health impairment and fatalities.
As its use is considerably increasing, we aimed to investigate the level of awareness and preparedness of PrEP users when it comes to MDPV as a chemsex and recreational drug.
Methods: An anonymous survey was sent to PrEP users who regularly attend our community-based service. This survey was built by our psychology team featuring skilled therapists in the field of sexual identity, HIV stigma, chemsex and drug harm reduction.
Socio-demographic and PrEP-use features, PV knowledge, type of use, possible discontinuation, and its emotional, physical, social complications and relapses were collected.
Results: Among the 467 respondents to the survey, only 186 (40%) ever heard about PV: 93% of them were MSM between 30s-40s, mainly Italians living in Milan, with high education and employment. 87% reported a previous experience with recreative drugs. Nearly half of them (48%) have been on PrEP for at least 2 years.
The most well-known effects were subjective positive ones like increased libido (67%) and euphoria (54%), followed by negative ones such as sleep deprivation (54%) and paranoia (47%).
The choice of not using it was mainly due to the fear of adverse effects and addictive potential. Notably, one third of respondents do not use any type of drugs and never engaged in chemsex.
Fifty-four subjects (12%) were PV-experienced, but 42 consider themselves as former users. The most popular contexts of consumption are chemsex and chill parties and sexual intercourse with casual partners (94%). Frequency of practice is mostly reported as sporadic (92%). The majority (61%) stated to feel worried after PV use. , even more significant if considered that 87% report a precedent experience with drugs. Only 10 reported a need for help to quit PV and were satisfied with the help received from their network. Possible fear-for-judgment and self-stigma biases must be taken in consideration for such a low number of help-seeking consumers. 70% reported quitting PV due to concern about psycho-physical adverse effects.
Conclusions: Our survey shows the lack of information about MDPV among the community that showed a significant level of unpreparedness. It thus underlines the need in actions of education and counseling about the oustanding risk of use. The fast increase in consumption of this cathinone marks these interventions as urgent.

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Virological topics in SARS-CoV-2 infection

OC 107 A HEPARAN SULFATE PROTEOGLYCAN BINDING TETRAPEPTIDE SUCCESSFULLY INHIBITS SARS-COV -2 OMICRON REPLICATION

C. Biba, L. Depau, L. Fiaschi, J. Brunetti, I. Varasi, C. Falciani, M. Zazzi, I. Vicenti, L. Bracci

Department of Medical Biotechnologies, University of Siena, Siena

Background: The emergence of the SARS-CoV-2 Omicron variant has led to increased transmissibility and immune escape, due to the high number of mutations in the Spike (S) region, particularly in the receptor binding domain (RBD) responsible for the interaction with the Angiotensin Converting Enzyme 2 (ACE2). At the same time, the mechanism of Omicron entry has evolved into endocytic dependent internalization, as opposed to membrane fusion dependent internalization, which was predominant with previous variants. In addition, a possible interaction of membrane Heparan Sulfate Proteoglycans (HSPG) with SARS-CoV-2 during virus internalization has been recently suggested. The aim of this work was to determine the role of HSPG in the infectivity of the Omicron variant, and the efficacy of an HSPG binding tetrapeptide (LB-1) in inhibiting Omicron entry in a live virus cell-based model.

Materials and Methods: LB-1 was synthesized in a tetra-branched form on a multiple automated synthesizer by standard Fmoc chemistry. The infection model was set up with Omicron BA.1 and Delta SARS-CoV-2 strains in the adherent human intestinal Caco-2 cell line with 24h incubation followed by transfer of the virus supernatant to a highly permissive reporter cell line (VERO E6 monkey kidney cells). The half-maximal Tissue Culture Infectious Dose was determined after 24h in VERO E6 measuring the viral nucleocapsid expression by ELISA assay. The experiments were performed in quadruplicate, with and without treatment with heparinase to remove the HSPG chains. The half-maximal cytotoxic concentration of LB-1 was determined by luminescence. To determine the antiviral activity, serial dilutions of LB-1 starting from the not-toxic dose, were incubated with a fixed amount of BA.5, BA.1 and Delta strains (MOI=0.01) for 1h at 37°C on pre-seeded Caco-2 cells. After incubation, the virus-peptide mixture was removed, and fresh LB-1 was added. Viral supernatants were transferred in VERO E6 as previously described. The half-maximal inhibitory concentration of LB-1 (IC50) was measured by SARS-CoV-2 nucleocapsid ELISA. Each experiment included a mock infection control, a virus control and two reference inhibitors with known IC50 (remdesivir and a previously tested human immune serum).

Results: LB-1 inhibited cell infection by BA.1 and BA.5 with 21.5 ± 2.8 and 19.5 ± 1.7 μM IC50, respectively. By contrast, LB-1 had no effect against delta variant (Figure 1) indicating a crucial role for HSPG in cell infection by Omicron but not by Delta. Heparinase treated cells were not permissive to Omicron infection, confirming the role of HSPG, while a modest impact was measured on Delta (4.6-fold reduction).

Conclusions: The prototype HSPG binding tetrapeptide LB-1 selectively inhibited the replication of SARS-CoV-2 Omicron. The role of HSPG in Omicron infection and this proof-of-concept results support further development of HSPG targeting agents as a novel strategy to block SARS-CoV-2 infection.

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Virological topics in SARS-CoV-2 infection

OC 108 SYNERGISTIC EFFECTS OF ANTIVIRALS AND MONOCLONAL ANTIBODIES IN VITRO AGAINST SARS-COV-2 WILD TYPE B.1 STRAIN AND BQ.1.1 OMICRON SUBLINEAGE

L. Fiaschi, C. Biba, I. Varasi, N. Bartolini, C. Paletti, F. Giammarino, F. Saladini, M. Zazzi, I. Vicenti

University of Siena, Department of Medical Biotechnologies, Siena, Italy

Background: Combination regimens can enhance antiviral potency, limit emergent drug resistance, and lower drug dosage. Aim of this work was to determine, in a live virus cell-based assay, the potential synergistic effects of (i) the combination of approved Directly Acting Antivirals (DAAs) against SARS-COV-2 wild type strain B.1 (WT) and omicron BQ.1.1 and (ii) the combination of remdesivir (RDV) with licensed monoclonal antibodies (mAbs) against WT.

Materials and Methods: The toxicity of the active form of molnupiravir (EIDD-1931), RDV, nirmatrelvir (NRM), cilgavimab (CIL), tixagevimab (TIX), bebtelovimab (BEB) and sotrovimab (SOT) was determined by luminescence in VERO-E6 treated with CP-100356 P-gp inhibitor. Scalar dilutions of each DAA were incubated in a 36 pairwise concentration matrix on VERO-E6 infected with WT and BQ.1.1 (MOI=0.01). After 72h cytopathic effect was quantified. The same experiments were performed with RDV plus each mAb. The synergistic score (SC) was calculated by SynergyFinder3.0 using Bliss/Loewe model and confirmed by Multi-dimensional Synergy of Combinations (MuSyC) post-analysis option. SC>10 was scored as synergistic, -10≥SC≤10 as additive, SC<-10 as antagonist.

Results: Half-maximal inhibitory concentrations (IC50) for EIDD-1931, RDV and NRM were 2.40±0.40/1.59±0.44, 0.06±0.03/0.03±0.01 and 0.10±0.03/0.10±0.01 μM against WT/BQ.1.1, respectively. CIL, TIX, BEB and SOT were active only against WT (IC50 of 0.20±0.13, 0.07±0.04, 0.03±0.01, 0.81±0.32 μg/ml, respectively). Global weighted SCs for all DAAs combinations showed additivity against WT (-0.96±1.69 EIDD-1931+RDV, -6.71±0.89 EIDD-1931 +NRM and 0.02±0.33 RDV+NRM) and BQ.1.1 (-0.33±4.10 EIDD-1931+RDV, -0.47±0.37 EIDD-1931+NRM and -2.12±3.8 RDV+NRM). Additivity was also observed for all mAbs/RDV combos against WT (-5.9±4.4 SOT+RDV, -5.5±1.6 RDV+BEB, 0.88±2.1 RDV+CIL and –4.3±1.6 TIX/RDV). SC >10 was observed for a few DAAs combos at specific concentrations including EIDD-1931 0.05-0.19-0.75 μM + RDV 0.4 μM, EIDD-1931 0.075-1.5 μM + NRM 0.05 μM and RDV 0.02 μM + NRM 0.01 μM against both viral strains. Similarly, SC >10 was observed against WT for the following RDV+mAbs combos: RDV 0.06 μM + SOT 0.09-0.04-0.1 μg/ml, RDV 0.016-0.06 μM + BEB 0.04 μg/ml, RDV 0.016-0.06 μM + TIX 0.04-0.009 μg/ml. As a proof of concept, IC50 shifts were measured in infected cells treated with 3 fixed NRM concentrations plus scalar EIDD-1931. The IC50 of EIDD-1931 with the addition of 0.1, 0.05, 0.025 μM NRM was reduced by >61-, 8- and 1-fold against WT and by >41-, 10- and 3-fold against BQ.1.1 (Figure1).

Conclusions: Global weighted SCs indicated additive effects. However, each DAAs combination induced synergistic potency shifts against WT and BQ.1.1 at specific concentrations' combination. We observed the same effects for RDV in combination with SOT, BEB or TIX against WT, but it was not possible to evaluate these combos against the BQ.1.1 strain due to its resistance to all tested mAbs.

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Virological topics in SARS-CoV-2 infection

OC 109 IN VITRO MODELLING TO MONITOR PATHOGENIC IMPLICATIONS OF RSV AND SARS-COV-2 CO-INFECTION

C. Vanetti[1], S. Zecchini[1], G. Cappelletti[1], M. Garziano[2], I. Saulle[2], S. Strizzi[1], F. Limanaqi[1], C. Fenizia[2], M. Clerici[3], D. Trabattoni[1], M. Biasin[1]

[1]Università degli Studi di Milano, Department of Biomedical and Clinical Sciences, Milan, [2]Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Milan, [3]IRCCS, Fondazione Don Carlo Gnocchi, Milan

Background: Concurrent infections with two or more pathogens are common and can seriously affect the course of each infection from its own natural history. Co-infecting pathogens with an analogous tropism, such as RSV and SARS-CoV-2, may antagonize or facilitate each other modulating host disease outcomes and microbe transmission relative to a single infection. Clinically, a severe phenotype has been reported in children with RSV/SARS-CoV-2 co-infections. However, experimental models to study the molecular and immunological dynamics of co-infections are extremely limited. Herein, we propose an in vitro co-infection model to assess RSV/SARS-CoV-2 immune and viral evolution.

Materials and Methods: RSV/SARS-CoV-2 co-infection model (Figure 1): 0.7×105 A549-ACE2 expressing cells were co-infected with RSV and SARS-CoV-2 (MOI=0.01 each). SARS-CoV-2 and RSV replication was determined at 24, 48 and 72 hours post infection (hpi) by RT-qPCR, immune-fluorescent (IF) and transmission electron microscopy (TEM) analyses. Secretome analyses (17 Multiplex Cytokine ELISA) on cell culture supernatants and anti-viral/immune gene expression (RT-qPCR) were assessed as well. All the experiments were performed in the BSL3 facility.

Results: The RSV/SARS-CoV-2 co-infection was characterized by a significant increase in the replication rate of RSV (co-infection vs single RSV $p<0.001$) (Figure 2). Notably, it was accompanied by a significant rise in the expression of ACE2 ($p<0.01$), IFNb and the main Interferon Stimulated Genes (ISG) (co-infection vs single RSV: MX1 $p<0.05$; MX2<0.01; IFITM3<0.05; IFNβ<0.05) (co-infection vs single SARS-CoV-2: MX2 $p<0.001$), along with pro-inflammatory genes. The secretome analysis revealed an enhanced inflammation in the co-infected condition as well, with increased levels of the main pro-inflammatory cytokines compared to single infections (co-infection vs single RSV: IL-1b $p<0.01$, IL-2 $p< 0.01$; IL-4 $p<0.01$; IL-5 $p<0.001$; IL-6 $p<0.05$; IL-17 $p<0.001$; G-CSF $p<0.05$; GM-CSF $p<0.05$; IFN-g $p<0.001$; MIP-1b $p<0.01$; TNF-a $p<0.01$) (co-infection vs single SARS-CoV-2 : IL-1b $p<0.05$, IL-2 $p< 0.05$; IL-5 $p<0.05$; IL-10 $p<0.05$; GM-CSF $p<0.05$; IFN-g $p<0.05$; MIP-1b $p<0.05$; TNF-a $p<0.01$).

Conclusion: The RSV/SARS-CoV-2 co-infection model displays a unique and specific viral and molecular fingerprint. In particular, the co-infected condition is characterized by an increased replication rate of RSV, together with an enhanced pro-inflammatory profile, giving clues of augmented severity upon RSV infection in the context of a concomitant SARS-CoV-2 co-infection. The in vitro co-infection model may represent an attractive cost/effective approach to mimic both viral dynamics and host immune responses, providing readily-measurable targets predictive of co-infection progression.

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Virological topics in SARS-CoV-2 infection

OC 110 EFFICACY AND SARS COV-2 VIRAL DECAY IN NASOPHARYNX, SALIVA AND PLASMA IN HIGH-RISK VACCINATED PATIENTS TREATED WITH MONOCLONAL ANTIBODIES (MAB)

F. Bai[1], T. Beringheli[1], R. Rovito[1], M. Marsiglia[2], V. Bono[1], S. Bianchi[2], E. Borghi[2], G. Marchetti[1]

[1]Clinic of Infectious Diseases, San Paolo Hospital, ASST Santi Paolo e Carlo, University of Milan, [2]Microbiology Laboratory, Department of Health Sciences, University of Milan

Background: mAb are currently recommended in patients diagnosed with a mild-moderate infection at high risk of clinical progression and contraindications to antivirals. Given the efficacy of COVID-19 vaccination in protecting from severe disease, the additional clinical and virological value of mAb in high risk vaccinated people needs further investigation. We aimed to investigate the efficacy of mAb and the viral load in nasopharynx (NP), saliva and plasma according to vaccination.

Materials and Methods: Prospective cohort study including patients diagnosed with SARS CoV-2 infection, at high risk of clinical progression and treated with mAb as either outpatients or hospitalized patients (03/2021 -05/2022). Risk factors for progression were: age >65 years, chronic diseases or immunodeficiencies. Patients underwent NP, saliva swabs and plasma collection at T0 (mAb treatment), T1 and T2 (7 and 14 days after mAb, respectively); efficacy (clinical recovery vs hospitalization after treatment or death), virological clearance at T1 (antigenic or molecular NP swab) and median time from symptoms' onset to first negative NP swab were collected. Primary endpoint was efficacy; secondary endpoint was comparison of NP, saliva and plasma viral load between unvaccinated (unvax) and vaccinated patients (vax). In a subgroup viral variant was available. Mann-Whitney, Chi-square and Wilcoxon test were used for statistics.

Results: 247 patients received mAb (3.2% Bamlanivimab, 34.4% Bamlanivimab/Etesevimab, 48.2% Casirivimab/Imdevimab, 14.2% Sotrovimab) during the study period: 55.8% had received ≥1 dose of any COVID -19 vaccine platform (10.1% one dose, 60.1% primary cycle, 29.7% first booster; 52.3% received mAb ≥120 days from the last vaccine dose). Vax were older, presented more frequently chronic diseases or immunodeficiencies/cancers and were more commonly hospitalized, compared to unvax (Table 1). Vax were infected more commonly by Delta and Omicron variants, Alpha variant was predominant in unvax. A shorter duration from symptoms' onset to mAb therapy was shown in vax. Median NP and saliva viral load were similar at T0 between vax and unvax and presented a similar decay at T1-T2 (Graph 2). Conversely, vax displayed higher median SARS-COV2 plasma viremia and a lower proportion of negative plasma viral load at T0 (31.2% vs 46.9%, p=0.020), that was maintained at T1 (36.9% vs 69.2%, p<0.001) and T2 (39.3% vs 72.9%, p=0.003) (Graph 2). Interestingly, vax were characterized by a higher proportion of efficacy and a shorter time to virological clearance vs unvax (Table 1).

Conclusions: Despite featuring higher risk factors and higher plasma SARS-COV-2 viremia, vax receiving mAb were significantly more protected toward severe outcomes as compared to unvax. These results emphasize the importance of prompt and early mAb treatment in high-risk patients with comorbidities even when vaccinated and need to be confirmed in future studies on current viral variants and mAb.

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Education and knowledge to reduce the burden of HIV and STIs

OC 111 COMMUNITY BASED VOLUNTARY COUNSELLING AND TESTING (CBVCT) SERVICES FOR HIV AND OTHER SEXUAL TRANSMISSED DISEASES OFFERED DURING THE PANDEMIC

A. Nappo[1], P. Piselli[1], C. Cimaglia[1], L. Cosmaro[2], M. Farinella[3], L. Rancilio[4], M. Stagnitta[5], S. Mattioli[6], V. Calvino[7], D. Calzavara[8], P. Testoni[9], D. Masci[10], P. Meli[11], J. Testa[12], I. Pennini[13], M. Errico[14], A. Caraglia[15], E. Girardi[1] for the Working Group of the project "The impact of COVID -19 on the processes and outcomes of care of people with HIV"

[1]INMI L. Spallanzani, Rome, [2]LILA Milano, Milan, [3]Circolo di Cultura Omosessuale "Mario Mieli, Rome, [4]CARITAS Ambrosiana, Milan, [5]CNCA, Rome, [6]PLUS, Bologna, [7]ANLAIDS Onlus-ETS, Rome, [8]Milano Checkpoint, Milan, [9]Associazione Solidarietà AIDS, Milan, [10]Villa Maraini, Rome, [11]CICA, Bergamo, [12]Italian Society of Migration Medicine - SIMM, Rome, [13]Arcigay, Bologna, [14]NPS Italia, Naples, [15]Ministero della Salute, Rome

Background and Objectives: The pandemic of COVID-19 has led to a drastic re-organization of healthcare settings and opportunities of testing for Sexual transmitted diseases (STDs) as well a profound rearrangement of Community Based Voluntary Counseling and Testing (CBVCT) activities. Our aim was to assess Counselling and Testing (CT) activities in the last four years (2019-2022) in order to evaluate the impact of COVID-19 on counselling and testing activities offered in non-healthcare setting.

Material and Methods: A survey was proposed to national non-governmental organizations (NGOs) and third-sector Associations involved in the fight against HIV/AIDS. Information relating to services offered for HIV testing and/or other STDs was collected, in terms of number of accesses to CT for HIV or other STDs, the number of HIV rapid tests performed and proportion of reactive results, as well as the percentage of subjects with a reactive result linked to a clinical center.

Results: Overall, twenty-nine organizations from all over Italy participated to the survey, of which 25 (86.2%) offered HIV testing and/or other STDs. When considering accesses to CT, during the first lockdown period (Mar-May 2020) there was a strongly decreased of the testing activity both in the number of organizations still offering the possibility to be tested, as well as the number of monthly tests, slowly recovering from September 2020, and steadily reaching the pre-pandemic levels (about 750 monthly/tests) in 2021 and exceeding up to 1300 monthly tests at the end of 2022 (Fig.1). Considering, the median monthly tests performed by the single association a strong decrease of median monthly tested was observed for the entire 2020 after COVID-19 pandemic up to Oct 2021 when pre-pandemic figures were reached (26 tests/association per month) and steadily showing exceeding pre-pandemic levels mainly in the last months of 2022 (Fig.2). Overall, out of 31666 tests recorded, 225 (0.71%) were those who resulted preliminary positives, substantially all linked to a clinical center.

Conclusions: The COVID-19 pandemic has shown to have an extremely negative impact on CBVCT activities especially during the first months of pandemic and consequent lockdown where CBVCT were practically halted. However, already at the end of 2020 a gradual growth was observed in the number of Associations that resumed testing activity, as well as in the number of monthly tests offered, exceeding, in the first months of 2022, pre-pandemic levels.

Project funded by the Minister of Health (ref 4023).

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Education and knowledge to reduce the burden of HIV and STIs

OC 112 KNOWLEDGE, ATTITUDES AND PRACTICES REGARDING HIV AND OTHER SEXUALLY TRANSMITTED INFECTIONS AMONG HIGH SCHOOL STUDENTS IN SOUTHERN ITALY: A CROSS-SECTIONAL SURVEY

A. Belati[1], F.V. Segala[1], C.R. Santoro[1], I. Bottalico[2], C. Pellegrino[1], R. Novara[1], G. Guido[1], L. Frallonardo[1], L. De Santis[1], M. Cormio[1], M. Camporeale[1], S. Cotugno[1], S. Di Gregorio[1], V. Totaro[1], N. Catucci[3], A. De Giosa[3], R. Giusto[3], F. Di Gennaro[1], S. Lo Caputo[2], A. Saracino[1]

[1]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy, [2]Infection Diseases Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy, [3]CAMA LILA Bari

Background: Adolescents represent a crucial population in the fight towards the spread of HIV and other sexually transmitted infections (STIs) and poor knowledge, unfavourable attitudes, and dangerous behaviours pose major obstacles to achieving this goal. This study aimed to explore the knowledge, attitude, and practices (KAP) among high school students regarding HIV and other STIs.

Materials and Methods: A prospective cross-sectional design was adopted. After acquisition of informed consent of both students and parents, data were collected through an anonymized structured questionnaire on RedCap platform. All high school students attending the educational meetings in 14 schools in Abruzzo and Apulia from 22nd February to 28th March 2023 were eligible for inclusion. A score 0-27 points was created (0-14 for knowledge, 0-7 for attitude, and 0-6 for practice) and used as a dependent variable for analysis. High KAP score was assigned to people who attained above the third quartile (>14 points). Association between study variables and high KAP score was assessed by chi-square and t-test, as appropriate, and variables found to be statistically significant were further explored in multivariate logistic regression analysis.

Results: A total of 1,955 students were eligible for the study. Of them, 1,702 students gave the consent. General characteristics and stratification for KAP score is shown in Tab.1. Median age was 17 (IQR: 16-17) years, and the majority were females (971, 57.1%). 1,350 (79.3%) declared to be heterosexual and cis-gender. Most students attended the technical institute (806, 47.4%). Median (q1-q3) KAP score obtained was 10 (IQR 5-14); 459 (26.9%) participants were above the third quartile and were classified as "high KAP score". At univariate analysis, the likelihood of having a high KAP score was associated with female sex at birth, sexual and gender identity, lower number of sexual partners, being vaccinated against HPV, being aware of the HBV status. Moreover, 1,583 (87.1%) had already heard of STIs, and it was associated with a higher KAP score, regardless the source of knowledge. Finally, 38 (2.2%) students declared to have used injective drugs (ID), variable that showed significant association with a low KAP score. At multivariable logistic regression (Tab.2), confirmed predictors of a high KAP were: reporting previous sexual intercourses (aOR 2.27, p<.001, CI95% 1.6-3.1) and being vaccinated against HPV (aOR 1.37, p<.04, CI95% 1.01-1.8). Conversely, refusing to answer to questions about ID use (aOR 0.39 p=.02, CI95% 0.16-0.83), and declaring to be cis-gender and heterosexual (aOR 0.49, p<0.014, CI95% 0.32-0.76) were predictors of a low KAP score.

Conclusions: Many teenagers have inadequate knowledge regarding HIV and other STIs. Our results underline the need to adopt interventions aimed at increasing the awareness on these issues in young population groups, in order to improve their practices and reduce the spread of HIV and STIs.

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Education and knowledge to reduce the burden of HIV and STIs

OC 113 KNOWLEDGE REDUCES STIGMA AND GENERATES AWARENESS. THE EXPERIENCE OF THE #CHIVUOLECONOSCERE PROJECT IN BERGAMO

I. Mercurio[1], P. Meli[1], D. Meli[1], F. Maggiolo[2], E. Zanetti[3], C. Pellegris[3], I. Fontana[4], S. Zuppardo[5], F. Tognoli[6]

[1]Don Giuseppe Monticelli Società Cooperativa Sociale, [2]ASST Papa Giovanni XXIII, [3]Associazione Comunità Emmaus, [4]Ufficio Scolastico Territoriale di Bergamo, [5]Istituto Istruzione Superiore Caterina Caniana, [6]Liceo Don Lorenzo Milani

Background: Don Giuseppe Monticelli Società Cooperativa Sociale promotes in the high schools of Bergamo and its Province the project #cHIVuoleconoscere, which aims to inform students about HIV/AIDS scientifically (what, how it is transmitted and can be prevented), relational (which reasons make communicating the positivity status difficult) and socio-cultural (as the theme of HIV has evolved and presented over the years).

Materials and Methods: Students have to complete a pre- and post-intervention questionnaire which investigates scientific knowledge and personal perceptions on HIV themes. Twenty-three questions investigate their scientific knowledge and are transformed into a binary score (yes or no) totalling 23 at the most with highest scores indicating better knowledge. Five questions (on a scale 1 to 10) deal with personal perception of HIV and stigma; again a comprehensive score (max 50) measures their attitude (higher scores = worse attitude).

The research aimed to verify if the intervention would increase knowledge and change perception about HIV reducing preconceptions towards PLWHIV.

Results: From October 2019 to February 2023, 5589 students were involved and 4210 compiled both pre and post questionnaires. Of them 1900 were females, 2021 attended a prep high-school, 1910 a technical one and 277 a professional high school. The mean score of the knowledge index pre-intervention was 17.7 (95%CI 17.6-17.7) and it was significantly different (P<0.0001) for type of school (prep> technical> professional) and gender (female>male) (Panel A). It significantly increased post-intervention (mean 20.7; 95%CI 20.6-20.7) indicating a better knowledge. The discrimination index, on the contrary, lowered (P<0.0001) from a mean of 17.6 (95%CI 17.4 -17.9) pre, to 12.4 (95%CI 12.2-12.6) post, indicating a better attitude and reduced stigma (Panel B). There was both pre and post intervention a strict correlation (P<0.0001) between the individual level of knowledge and the personal attitude toward HIV problems and PLWHIV.

Despite the age limit for the access to the test, among students attending the training course at schools in 2022, 79 did the test either at the Bergamo Fast Track City check point or during an awareness-raising event organized by students in two institutes (Panel C).

Conclusions: Our results indicate how training leads to a spread of correct and appropriate knowledge about HIV also in younger people. The increased awareness has a positive impact on the stigma towards people living with HIV, reducing fear and judgment.

In addition, knowledge allows people to take care of their own health approaching sexual health in a more comprehensive and active way as testified by the good number of students who approached for the first time an HIV screening test.

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Education and knowledge to reduce the burden of HIV and STIs

OC 114 JUST LILA - A PILOT PROJECT AND PROMOTIONAL CAMPAIGN TO PROMOTE SELF-TESTING

M.L. Cosmaro[1], G. Dessi[2], G. Di Pasquale[3], G. Giupponi[2], M. Oldrini[1], S. Penon[1], C. Perone[4], P. Perone[2], D. Savarino[1]

[1]Fondazione LILA Milano, Milano, [2]LILA Nazionale Onlus, Como, [3]Diversity Lab, Milano, [4]Cliccaquì, Roma

Background: In Italy self-test kits have been available in pharmacies since Dec 2016 but few people know about it; access remains limited. In May 2022 LILA launched "JustLILA" (JL), a pilot project and promotional campaign part of a larger European program funded by Gilead Grants. Objectives are to promote importance of HIV testing, availability of self-tests, the opportunity to receive at home free OraQuick kits on oral fluid and, if needed, remote counselling offered by trained staff. The project will end in June 2023.

Materials and Methods: A promotional campaign was launched in May 2022, still ongoing: tone of voice is easy, untroubled and optimistic, to normalize HIV testing. A video (https://youtu.be/_aa2vD9yHJU), brochure and materials were developed for wide dissemination mostly on social media. The dedicated website https://www.lila.it/it/just-lila gives information on self-testing and pilot service, includes a pre-order questionnaire for collection of anonymous demographic/behavioral data and a separate order form. Permission is asked for sending a follow-up questionnaire 15 days after kit delivery, to derive information about test results, ease of use, etc. Clients wishing to receive support can book remote counselling through a phone call or Zoom connection with LILA staff.

Results: In 1st 10 months 2.213 pre-order questionnaires were completed (sociodemographic data enclosed). Main reasons for interest in service: it is free of charge (59,5%), easy to use (47,4%), it ensures privacy (35%). First time testers were 44,7%. 47.4% reported having engaged in active unprotected fellatio, 45,9% in unprotected vaginal intercourse, 37,9% in unprotected anal intercourse.

Out of the 2.213 respondents, 1.850 ordered and received the kits. 16.4% did not proceed probably feeling uncomfortable when filling-in personal data in the order form.

366 people (19.8%) completed the post-test survey: two of them had a reactive result, 9 had an invalid one. Data indicate a high degree of acceptability of self-tests: 98.9% clients would use them again; 83% declared to prefer self-testing rather than testing at healthcare facilities (9.3%) or community settings (7.2%). 91.2% declared no need for remote support services and 6.2% relied on the assistance of a close person. Only 14 people benefited of the remote counselling service: their results were negative. Ease of use of self-test kits was evaluated as excellent (89.5%) or good (9.3%).

Conclusions: Stigma surrounding HIV testing – implying engagement in risky, socially unaccepted behaviors – likely still prevents some people from even ordering a self-test kit; data collected on testing history indicate self-tests might bring people who have never tested before for HIV to do so. Efforts should therefore be made to lower cost of self-tests, promote such testing option and normalize testing, in order to improve access for those who presently do not access healthcare or community facilities.

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Real world evidence in different treatment setting

OC 115 ADHERENCE TO AND FORGIVENESS TO IMPERFECT ADHERENCE OF FTC/TAF/RPV

F. Maggiolo[1], L. Taramasso[2], L. Comi[1], G. Brucci[2], D. Valenti[1,3], E. Di Filippo[1], A. Di Biagio[4]

[1]UOC Infectious Diseases1 ASST Papa Giovanni XXII, Bergamo, [2]IRCCS Ospedale Policlinico San Martino di Genova, Genova, [3]FROM foundation, Bergamo, [4]Department of Health Sciences, Clinic of Infectious Diseases, University of Genoa, Genoa, Italy

Background: When applied to ART, forgiveness refers to the ability of a given regimen to maintain complete viral suppression despite imperfect adherence. Forgiveness lacks an established, quantitative measure, but, despite this, the medical community has embraced the concept that some regimens are more forgiving than others, basing on this assumption therapeutic choices. We explored adherence and forgiveness of FTC/TAF/RPV (rilpivirine/emtricitabine/tenofovir alafenamide).

Methods: In this retrospective study, pharmacy drug refills were used to calculate PDC as a proxy of adherence. PDC is the number of days with medication available divided by the number of days in a specified time interval. If excess medication is collected or refills are made early, the excess is applied toward subsequent absences of drugs. Forgiveness was defined as achieving a sensitive therapeutic success (e.g. selected HIV-RNA threshold) under a given level of imperfect adherence. Three different virologic cut-offs were used: target not detected (TND), that is a value of HIV-RNA current standard methods do not detect; HIV-RNA < 50 copies/ml as the gold standard to define therapeutic efficacy; HIV-RNA < 200 copies/ml as the value that prevents HIV transmission by sexual contacts. A probit model was used to verify the impact of baseline variables and adherence on the virologic outcomes.

Results: 542 adult PLWH were included, 76.2% were males with a median age of 52 years (IQR 44-57). The median follow-up of the cohort under FTC/TAF/RPV was longer than 4.5 years (1727 days, IQR 554-903) totaling 2408 patient/years. Adherence was high with a median of 97.8% (IQR 92.6-99.7%). Consequently, the virologic response was sustained: 59.2% of PLWH had HIV-RNA TND throughout the study period; 81.9% showed constant HIV RNA < 50 copies/ml and 95.6% of subjects had an HIV-RNA always < 200 copies/ml (U=U level). Considering the < 200 copies/ml cut-off for HIV-RNA, a PDC (adherence) of at least 90% was needed to steadily maintain the desired virologic outcome in > 95% of subjects and the same level of adherence obtained a constant TND level of HIV-RNA in > 50% of patients for the whole follow-up (figure, panel A). Probit analysis indicated that PDC significantly correlated with all the pre-defined virologic outcomes. The only other factor significantly associated with the risk of virologic failure in multivariate analysis was being of non-Italian origin (VL < 50 copies/ml endpoint only)(figure, panel B).

Conclusions: Adherence dynamics under FTC/TAF/RPV indicate that most patients steadily take the drug correctly with adherence rates > 97%. This high adherence rate seems to be maintained even over very long periods of time. The long-term effectiveness of the regimen seems to rely mostly on tolerability, friendliness and low intrusiveness of the patient's lifestyle, factors associated to high adherence rather than on its forgiveness that is in line with other NNRTI-based regimens.

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Real world evidence in different treatment setting

OC 116 ADHERENCE TO AND FORGIVENESS TO IMPERFECT ADHERENCE OF B/F/TAF

F. Maggiolo[1], L. Taramasso[2], L. Comi[1], G. Brucci[2], D. Valenti[1,3], E. Di Filippo[1], A. Di Biagio[4]

[1]UOC Infectious Diseases1 ASST Papa Giovanni XXII, Bergamo, [2]IRCCS Ospedale Policlinico San Martino di Genova, Genova, [3]FROM Foundation, Bergamo, [4]Department of Health Sciences, Clinic of Infectious Diseases, University of Genoa, Genoa, Italy

Background: When applied to ART, forgiveness refers to the ability of a given regimen to maintain complete viral suppression despite imperfect adherence. Forgiveness lacks an established, quantitative measure, but, despite this, the medical community has embraced the concept that some regimens are more forgiving than others, basing on this assumption therapeutic choices. We explored forgiveness of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF).

Methods: In this retrospective study, pharmacy drug refills were used to calculate PDC as a proxy of adherence. PDC is the number of days with medication available divided by the number of days in a specified time interval. If excess medication is collected or refills are made early, the excess is applied toward subsequent absences of drugs. Forgiveness was defined as achieving a sensitive therapeutic success (e.g. selected HIV-RNA threshold) under a given level of imperfect adherence. Three different virologic cut-offs were used: target not detected (TND), that is a value of HIV-RNA current standard methods do not detect; HIV-RNA < 50 copies/ml as the gold standard to define therapeutic efficacy; HIV-RNA < 200 copies/ml as the value that prevents HIV transmission by sexual contacts. A probit model was applied to verify the impact of baseline variables and adherence on the virologic outcomes.

Results: 493 adult PLWH were included, 72.8% were males with a median age of 51 years (IQR 43-58). The median follow-up of the cohort under B/F/TAF was 764 days (IQR 554-903) for a total of 991 patient/years. Adherence was very high with a median of 96.2% (IQR 90-100%). Consequently, the virologic response was sustained: 45.2% of PLWH had HIV-RNA TND throughout the study period; 86.8% showed constant HIV RNA < 50 copies/ml and 96.3% of subjects had an HIV-RNA always < 200 copies/ml (U=U level). Considering the < 200 copies/ml cut-off for HIV-RNA, a PDC (adherence) as low as 85% was sufficient to steadily obtain the desired virologic outcome in > 95% of subjects and a PDC > 90% was associated with a 100% success rate (figure, panel A). Probit analysis indicated that PDC significantly correlated with all the pre-defined virologic outcomes. Other factors significantly associated with the risk of virologic failure were: time with HIV infection (TND endpoint only) and nadir value of CD4 cells (TND endpoint and VL steadily < 200 copies/ml endpoint)(figure, panel B).

Conclusions: Adherence dynamics under B/F/TAF indicate that most patients steadily take the drug correctly with adherence rates > 96%. Moreover, this regimen is highly forgiving and obtains desired virologic outcomes for adherence levels as low as 85%. Long-term success of ART needs well tolerated, effective regimens that are the least intrusive of the patient's lifestyle. In this context, an elevated forgiveness may be considered as an additional feature that can further improve long-term outcomes.

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Real world evidence in different treatment setting

OC 117 ANTIRETROVIRAL THERAPY PRESCRIPTION IN OLDER PEOPLE LIVING WITH HIV: CROSS-SECTIONAL STUDY ON MULTIDRUG REGIMENS (MDR) AND LESS DRUG REGIMENS (LDR) IN GEPPO COHORT

S. Nozza[1], B. Fioretti[2], S. Calza[3], G. Guaraldi[4], J. Milic[4], G.V. De Socio[5], A. Riva[6], G. Orofino[7], G. Di Perri[8], A. Calcagno[8], E. Focà[2]

[1]Department of Infectious Diseases, San Raffaele Scientific Institute, Milano, Italy, [2]Department of Clincal and Experimental Sciences, Unit of Infectious Diseases, University of Brescia and Spedali Civili Hospital, Brescia, Italy, [3]Unit of Biostatistics and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy, [4]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, Modena e Reggio Emilia, Italy, [5]Department of Infectious Diseases, Azienda Ospedaliero-Universitaria di Perugia, Perugia, Italy, [6]3rd Division of Infectious Diseases, University of Milano, Ospedale L. Sacco, Milano,Italy, [7]Unit of Infectious Diseases,Ospedale Amedeo di Savoia, ASLTO2,Torino, Italy, [8]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy

Background: Older people living with HIV (OPLWH) are commonly exposed to several comorbidities and to polypharmacy, which could affect the antiretroviral therapy (ART), most of all in a real-life setting. However, no data concerning ART prescribing criteria are present regarding this population, underrepresented in clinical trials. Aim of this study is to characterize ART prescribing criteria the in people living with HIV aged ≥65 years.

Methods: This is a cross-sectional study describing the current ARV regimens in the GEPPO cohort, an observational multi-centric cohort including OPLWH, and community-dwelling controls aged ≥65 years (OPW/oH). Antiretroviral treatments are classified as multidrug regimens (MDR), described as triple or mega ART, and less drug regimens (LDR), described as fewer than three ART compounds. Multimorbidity (MM) was defined as the presence of ≥3 non-communicable diseases, and polypharmacy (PP) as ≥5 chronic medications. We divided our cohort according to their current ART regimen in LDR and MDR. In a multivariate regression model, we analysed age, gender, duration of HIV infection and presence of MM and PP to investigate the association with the current LDR vs MDR.

Results: We included 1693 OPLWH: 547 in the LDR and 1146 in the MDR subgroup. Females were 18% and 17% of the two groups, respectively. The mean age was 73 years old. LDR subgroup showed longer duration of HIV infection (mean 21 vs 20 years, p-value <0.001) and ARV therapy (18 vs 17 years, p-value 0.012). Evaluating ART combinations, INSTI-based (n=336, 61% vs n=495, 43%; p-value<0.001), PI-based (n=188, 34% vs n=169, 15%; p-value<0.001) and NRTI-sparing (n=348, 64% vs n=2419, 21%; p-value<0.001) regimens were prevalent in LDR group, while NNRTI-based (n=122, 22% vs n=355, 31%; p-value<0.001) were more common in MDR group. Complete descriptions of ART regimens are showed in figure 1. Considering the comorbidities, in LDR group there was a higher prevalence of chronic kidney disease (n=200, 44% vs n=281, 29%; p-value<0.001), cancer (n=67, 16% vs n=101, 11%; p-value=0.013), arterial hypertension (n=337, 74% vs n=637, 66%; p-value=0.004), type 2 diabetes mellitus (n=148, 33% vs n=236, 25%; p-value=0.002), and cardiovascular diseases (n=115, 25% vs n=176, 18%; p-value=0.003). After adjustment for age, gender and duration of HIV infection, the combination of MM and PP had a higher prevalence in LDR group (OR 1.86 95%IC, p-value<0.001). This was confirmed also for the presence of MM without PP (OR 1.68 95%IC, p-value<0.001), but not for PP without MM.

Conclusions: Our data evidenced that LDR regimens are more frequent in OPLWH with long duration of HIV infection and ART. The presence of comorbidities, of PP and most of all of MM appears to be associated with higher prevalence of LDR. The use of geriatric deprescription tools could be one of the possible approaches to manage the complexity of an ageing population, to tailor ART therapy and reduce the polypharmacy.

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Real world evidence in different treatment setting

OC 118 REASONS FOR CHOOSING A DORAVIRINE (DOR) BASED VERSUS AN INSTI-BASED REGIMEN IN ART-NAÏVE AND ART-EXPERIENCED PATIENTS IN REAL-WORLD SETTING: DATA FROM THE ICONA COHORT

A. Saracino[1], M. Ponzano[2], F. Bovis[2], E. Quiros-Roldan[3], M. Fabbiani[4], N. Squillace[5], S. Rusconi[6], M. Ferrara[7], S. Lo Caputo[8], A. Tavelli[9], A. Antinori[10], A. d'Arminio Monforte[9]

[1]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy, [2]Biostatistics Unit, Department of Health Sciences, University of Genoa, Genoa, Italy, [3]Clinic of Infectious Diseases, University of Brescia, Brescia, Italy, [4]Clinic of Infectious Diseases, Azienda Ospedaliera Universitaria Senese, Siena, Italy, [5]Infectious Diseases Clinic, Fondazione IRCCS San Gerardo dei Tintori, University of Milano-Bicocca, Monza, Italy, [6]Infectious Diseases Unit, Ospedale Civile di Legnano, ASST Ovest Milanese, and DIBIC Luigi Sacco, Università degli Studi di Milano, Legnano, Italy, [7]Department of Infectious Diseases, University of Torino and "Amedeo di Savoia" Hospital, Turin, Italy, [8]Infectious Diseases Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy, [9]Icona Foundation, Milan, Italy, [10]Clinical and Research Infectious Diseases Department, National Institute of Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy

Background: Doravirine (DOR), the most recent antiretroviral drug of the NNRTI lass, demonstrated to overcome limitations of previous NNRTIs including low genetic barrier, CNS toxicity, food requirement, and showed a favourable safety profile, especially on metabolic side effects. However, as a direct comparison of DOR versus INSTI regimens in randomized trials is lacking, the clinical characteristics of PLWH assigned to different regimens is crucial and could affect outcomes in real world.

Aim of the study was to investigate the sociodemographic and clinical drivers of starting or switching to a doravirine (DOR) versus an INSTI-based regimen.

Methods: All PLWH enrolled in the Icona cohort, who after January 2020 (date of DOR availability in Italy) started a first line DOR- or INSTI-based 3 drug regimens (DR) (Naïve Group) or switched for the first time to DOR or a 3DR/2DR INSTI-based regimen while on virological suppression (Experienced Group), were included in this observational study. Demographic and clinical data were compared according to different groups. Chi-square or U-Mann-Whitney or one-way ANOVA tests were used to compare baseline characteristics. A logistic regression model was used to explore factors associated with DOR start and a multinomial logistic analysis was used to explore factors associated to switch to INSTI vs DOR regimen.

Results: The baseline characteristics of 62 naive PLWH starting 3DR DOR and 1,341 starting 3DR INSTI were compared; features associated with DOR use were intravenous drug use, smoking, higher CD4 count and CD4: CD8 ratio, lower HIV-RNA and nadir CD4 count, higher BMI and LDL levels, and a longer disease duration (Table 1). In adjusted multivariate models, higher CD4 (AOR 1,43, 95%CI1,09-1,86,) and not Italians remained significantly associated with DOR use (Italians vs non Italian DOR use: AOR 0,20, 95%CI 0,05-0,91).

In the experienced group, DOR, 2DR INSTI and 3DR INSTI regimens were initiated in 308, 1,594 and 1,134 PLWH, respectively, whose characteristics were differently distributed as shown in Table 2.

12.8% of DOR group were switching from a PI-based, 18.3% from an INSTI-based, and 64.0% from another NNRTI-based regimen, 4.9% from other regimens.

Independent factors of prescribing DOR were being females and diabetes (only vs 2DR-INSTI), older age (vs 3DR-INSTI), high tryglicerides, high HDL and disease duration (vs both 2DR-and 3DR-INSTI).

Conclusions: DOR is preferentially used by clinicians for ART-naïve PLWH with less advanced HIV disease, and, in case of switching with suppressed viral load, in females and older dyslipidemic PLWH. Overall, clinicians' choices were in agreements with guidelines and were in line with the lower toxicity of doravirine-regimen.

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Body and mind

OC 119 BMI VS BODY COMPOSITION CHANGES TO PREDICT METABOLIC OUTCOMES IN PEOPLE WITH HIV

L. Taramasso[1], M. Simion[2], J. Milic[1], F. Bovis[1], F. Motta[2], G. Besutti[3], G. Mancini[4], A. Dessiliani[2], M. Del Monte[2], A. Mazzocchi[2], L. Sighinolfi[2], M. Ponzano[1], A. Di Biagio[1], M. Bassetti[1], C. Mussini[2,4], G. Guaraldi[2,4]

[1]Infectious Disease Clinic, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [2]University of Modena and Reggio Emilia, Modena, Italy, [3]Radiology Unit, Azienda USL-IRCCS di Reggio Emilia, [4]Infectious Diseases Unit, Policlinico di Modena, Universita Degli Studi di Modena e Reggio Emilia, Modena, Italy

Background: Body mass index (BMI) is commonly used to describe weight changes in people with HIV (PWH). However, BMI fails to depict changes in body composition which may differently affect metabolic outcomes including diabetes mellitus (DM) and metabolic syndrome (MetS). The aim of the study was to compare changes in BMI, vs bone, lean and fat body composition components in the prediction of DM and MetS.

Methods: This was an observational prospective study that comprised ART-experienced PWH attending Modena HIV metabolic clinic from 2008 to 2021. Inclusion criteria was body composition assessment performed with DEXA including trunk fat mass/height2, lumbar T-score, appendicular skeletal muscle index (ASMI), visceral adipose tissue (VAT, also assessed with CT). Study outcomes were incidence of DM, MetS or the composite of the two. The association between anthropometric variables and study outcomes was explored with Cox proportional hazards models, with exposure represented by time-varying. The performance of each body composition measure to predict study outcomes was assessed using c-index. Possible effect modification of the associations of each body mass measure with the outcomes of interest by sex was investigated by including a statistical interaction term.

Results: A total of 1895 PWH (70% males) were included, with a median follow-up of 5.8 (range 0.5-14.3) years and a median of 5 repeated measurements (range 2-17). Mean age was 46.6 (± 8.0) years, CD4 625/mmc (± 286) and HIV-VL was undetectable in 88% PWH at the first visit. In the follow up, incidence of DM was 1.5/100 PYFU (95% CI: 1.3-1.7) (219 cases), incidence of MetS 3.7/100 PYFU (95% CI:3.3-4.1) (377 cases), incidence of composite DM/MetS 4.1/100 PYFU (95% CI: 3.9-4.7) (417 cases). Predictors of composite outcome and performance comparison are presented in Table 1. At multivariable Cox analysis, BMI (aHR 1.06, 95%CI 1.02 -1.10), trunk fat (aHR 1.16, 95%CI 1.03-1.29), VAT (aHR 77.5, 95%CI 17.1-350.9) and ASMI increase (aHR 1.39, 95%CI 1.18-1.65) were significantly correlated to the composite risk of DM/MS, without significant interaction with sex. VAT and ASMI were the best predictors of composite study outcome (c-index 0.702 for both), however, also BMI showed a similar performance (c-index 0.699).

Conclusions: The study of body composition (VAT and ASMI) changes offered the best indicator of DM/MetS risk in our study. In the absence of possibility to perform DXA or CT, BMI may be a reliable alternative in relation to DM/MetS risk estimation.

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Body and mind

OC 120 PREVALENCE, INCIDENCE AND RISK FACTORS FOR SARCOPENIC OBESITY IN PEOPLE WITH HIV

J. Milic[1] , S. Cantergiani[1], S. Renzetti[2], F. Motta[1], C. Mussini[1], S. Calza[2], G. Sebastiani[3], G. Guaraldi[1]

[1]University of Modena and Reggio Emilia, Modena, Italy, [2]University of Brescia, Brescia, Italy, [3]McGill University, Montreal, Canada

Background: Sarcopenic obesity (SO) is defined as contemporary presence of sarcopenia (low muscle mass and/or reduced muscle strength) and obesity and it is an indicator of patient's vulnerability to adverse outcomes. The objective of the study was to describe 4 different definitions of SO, using 2 definitions of sarcopenia and obesity, and to determine incidence and risk factors of each SO definition.
Methods: This was a longitudinal study of PWH attending Modena HIV Metabolic Clinic, Italy. PWH with at least two visits who met at least one of SO definition were included. Sarcopenia was defined as (1) weak hand grip, adjusted for sex and age, assessed by dynamometer or as (2) appendicular skeletal muscular index (ASMI) score <7.26 /<5.45 kg/m2 for men/women, assessed by Dual-energy X-ray absorptiometry (DEXA). Obesity was defined as (1) accumulation of visceral adipose tissue (VAT) >=160 cm2, assessed by DEXA or computed tomography; or as (2) body mass index (BMI) >= 30 kg/m2. Four SO definitions were used: SO1 (hand grip + VAT), SO2 (hand grip + BMI), SO2 (ASMI + VAT), SO4 (ASMI + BMI). Cumulative incidence over the years was calculated. Cox regression models were used to explore risk factors for each SO definition and were adjusted for age, sex, years since HIV diagnosis, nadir CD4, current exposure to INSTI, NNRTI and PI.
Results: A total of 3195 PWH were included (median age 48.7 years, 76% males, years since HIV diagnosis 18.2, current CD4 612). At last visit, SO1 was present in 34 (12.1%) out of 280, SO2 in 63 (3.8%) out of 1652, SO3 in 191 (8.9%) out of 2144, SO4 in 27 (0.8%) out of 3195 PWH. The cumulative incidence rates for SO1, SO2, SO3 and SO4 were 1.2, 0.4, 1.5 and 0.1 per 100 person-years (Figure). Exposure to NNRTI (OR=7.7, 95%CI: 1.7-12.8) was negatively associated with SO1. Age (OR=1.06, 95%CI:1.03-1.09) and years since HIV diagnosis (OR=0.996, 95%CI: 0.992-0.999) were associated with SO2. Age (OR=1.06, 95%CI: 1.04-1.08) and male sex (OR=4.01, 95% CI: 2.36-6.84) were associated with SO3. Age (OR=1.08, 95%CI: 1.03-1.12), years since HIV diagnosis (OR=0.994, 95%CI: 0.989-0.999) and exposure to INSTI (OR=2.9, 95%CI: 1.13-7.46) were associated with SO4.
Conclusion: Incidence and prevalence of 4 SO definitions had great variability, which may identify diverse metabolic phenotypes of PWH. INSTI were related to SO using BMI as obesity definition, but not VAT. Further studies are needed to explore the relationship between antiretroviral therapy and SO.

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Body and mind

OC 121 PLASMA AND CSF BIOMARKERS OF CNS INVOLVEMENT DURING PRIMARY HIV INFECTION

A. Calcagno[1], M. Antonucci[2], P. Cinque[3], G. Marchetti[4], D. Bernasconi[5], M. Trunfio[1], E. Bruzzesi[6], S. Rusconi[7,8], A. Gabrieli[8], A. Muscatello[9], A. Antinori[10], D. Ripamonti[11], R.Gulminetti[12], J. Cusato[13], S. Nozza[3] for the INACTION Study Group

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin, [2]ASL Città di Torino, Amedeo di Savoia Hospital, Turin, Italy, [3]Unit of Infectious Diseases, IRCCS Ospedale san Raffaele, Milan, Italy, [4]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, [5]Bicocca Bioinformatics Biostatistics and Bioimaging Centre - B4 School of Medicine and Surgery, University of Milano-Bicocca, Monza, [6]Vita-Salute San Raffaele University, Milan, [7]UOC Malattie Infettive, Ospedale Civile di Legnano, ASST Ovest Milanese, Legnano, [8]Dipartimento di Scienze Biomediche e Cliniche (DIBIC), University of Milan, Milan, [9]Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, [10]INMI L. Spallanzani, Rome, [11]Papa Giovanni XXIII Hospital, Bergamo, [12]Infectious Diseases Unit, Department of Medical Science and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, [13]Laboratory of Clinical Pharmacology and Pharmacogenetics, Department of Medical Sciences, University of Turin, Turin, Italy

Background: Soon after infection, HIV penetrates into the central nervous system (CNS) and neurological disorders may occur during primary HIV infection (PHI). Despite combination antiretroviral treatment some patients develop neurocognitive disorders supporting the investigation of CNS cells damage and inflammation. Aim of the study was to measure plasma (p) and cerebrospinal fluid (CSF) biomarkers of CNS Involvement in patients treated during PHI.

Material and Methods: Participants with PHI were enrolled in a randomized, open-label, multicentric study and they were randomized to one of three regimens including TAF/FTC plus either darunavir, dolutegravir or both. All patients were offered to enter a neurological substudy in which lumbar punctures were performed at baseline and week 12. In addition, plasma was stored at baseline (BL), W12 and W48 from all participants. Available CSF and plasma specimens were analysed through Single Molecule Array (Simoa SR-X, Quanterix®) for markers of neuronal damage (NFL, tau), signaling and plasticity (BNDF), astrocyte activation (GFAP) and ubiquitin-proteasome involvement (UCHL-1). Data are described as medians (interquartile ranges) and compared through non-parametric tests.

Results: Plasma was examined from 50 participants: 96% male, median age of 33 years (27-43) and most frequently enrolled at Fiebig stages V (40%) and II (22%). Thirteen participants were enrolled in the neurological substudy with CSF available for 7/13 at W12. BL serum and CSF HIV RNA were 5.70 (4.55-6.62) and 3.38 (2.23 -3.60) Log10 copies/mL; HIV DNA was 4.34 (4.07-4.68) Log10 copies/10^6 PBMCs.

Plasma and CSF biomarkers are shown in the Table. At BL we observed significant correlations between plasma and CSF biomarkers (NFL, GFAP and BDNF). Patients in early Fiebig stages (I/II) had higher pNFL (p=0.047).

pGFAP and pNFL showed significant changes over time (Friedman's p <0.05). We observed no association between biomarker changes and immunovirological parameters except for higher BL CSF HIV RNA, associated with a greater decrease in plasma NFL, GFAP and UCH-L1 (all p values <0.05). Patients with higher decrease in plasma HIV RNA showed higher decrease in pUCHL-1 (R=0.32, p=0.033). When stratifying for Fiebig stage or symptoms during PHI we observed no difference over time in plasma or CSF biomarkers. Nevertheless, patients in the dolutegravir arm showed a greater decrease in pNFL (p=0.006) and GFAP (p=0.006).

Conclusions: In patients treated during PHI, we observed a decrease in plasma levels of biomarkers of axonal damage (NFL) and astrocyte activation (GFAP) after cART introduction with a greater reduction in those receiving TAF/FTC plus dolutegravir. Monitoring plasma biomarkers of CNS involvement in PLWH may help understanding the pathogenesis of CNS disorders.

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Body and mind

OC 122 THE EFFECTS OF SWITCHING FROM DOLUTEGRAVIR/ABACAVIR/LAMIVUDINE TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE IN VIROLOGICALLY SUPPRESSED PEOPLE LIVING WITH HIV ON NEUROPSYCHIATRIC SYMPTOMS: 3-MONTHS FINDINGS FROM A RANDOMIZED STUDY

B. Rossetti[1,2], M. Ferrara[3], L. Taramasso[4], F. Bai[5], F. Lombardi[6], N. Ciccarelli[7], M. Durante[8], F. Alladio[3], I. Rancan[1,8], F. Montagnani[1,8], A. Di Biagio[9], A. d'Arminio Monforte[5], M. Zazzi[8], M. Fabbiani[1] for DOBINeuro study group

[1]Infectious and Tropical Diseases Unit, University Hospital of Siena, Siena, Italy, [2]Infectious Disease Department, USL SUDEST Toscana, Misericordia Hospital, Grosseto, Italy, [3]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy, [4]Infectious Diseases Clinic, Department of Internal Medicine, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [5]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy, [6]Infectious Diseases Unit, UOC Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [7]Department of Psychology, Catholic University, Milan, Italy, [8]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [9]Infectious Diseases Clinic, Department of Health Sciences, University of Genoa, San Martino Hospital-IRCCS, Genoa, Italy

Background: Central nervous system adverse events (AE) have been a cause of discontinuation of dolutegravir-containing therapy, especially in combination with abacavir. The main aim of the study was to evaluate whether the switch to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) was associated with a reduction in severity and incidence of neuropsychiatric symptoms compared to continue dolutegravir/abacavir/lamivudine (DTG/ABC/3TC). Quality-of-life, suicide risk and self-reported symptoms were also evaluated using validated questionnaires.

Materials and Methods: DOBINeuro is a 12-month, randomized trial enrolling people living with HIV (PLWH) treated with DTG/ABC/3TC for >6 months and with HIV-RNA <50 cps/ml for >12 months. Exclusion criteria were previous AIDS, alcohol or substance abuse, major psychiatric disorders, history of virological failure with InSTI, and positive HBsAg. At baseline (BL), PLWH are randomized to continue DTG/ABC/3TC or switch to B/F/TAF. The original sample size was 50 PLWH per arm, but the enrollment was prematurely stopped due to a delayed recruitment process. Here, we describe findings at 3 months (3M) in the enrolled PLWH (primary endpoint).

Results: We included 41 PLWH (78% males, median age 53 years, median CD4 673 cells/mm3): 20 were randomized to continue DTG/ABC/3TC and 21 to switch to B/F/TAF (Table). At BL, clinical and laboratory characteristics were homogeneous in the two arms; overall, 12.8% of PLWH had cognitive impairment (def. global Z score ≤-1) with no difference between arms.

At 3M, among the primary symptom dimensions of symptom check list-90 (SCL-90), anxiety was less frequently reported with B/F/TAF than with DTG/ABC/3TC (mean 0.15, standard deviation, SD, 0.50 vs 0.42, SD 0.51, p=0.04). No significant differences were observed between arms regarding self-reported adherence, treatment satisfaction and quality-of-life.

The following primary symptom dimensions of SCL-90 were less frequently reported with B/F/TAF at 3M compared to BL: depression (p=0.001), obsessive-compulsive behaviour (p=0.008), anxiety (p=0.013), phobic anxiety (p=0.05), sleep disturbance (p<0.001) and global severity index (p=0.034). Similarly, with DTG/ABC/3TC depression (p=0.021), obsessive-compulsive behaviour (p=0.005), anxiety (p=0.023) and sleep disturbance (p=0.029) were less frequently reported at 3M respect to BL, while psychoticism was more frequently reported (p=0.020). In quality-of-life assessment, trouble concentrating was less frequently reported with B/F/TAF (p=0.042), while sadness (p=0.040), fear for health (p=0.027), impact on sex life (p=0.027) were less frequently reported with DTG/ABC/3TC at 3M compared to BL. VL was confirmed <50 cp/mL for all PLWH in both arms.

Conclusions: Switch to B/F/TAF in virologically suppressed PLWH was associated with short term improvement in some self-reported neuropsychiatric symptoms and anxiety was less frequently reported with B/F/TAF than with continuing DTG/ABC/3TC.

PACS: clinical outcome

OC 123 LONG COVID PHENOTYPES AND ASSOCIATION WITH SARS COV-2 VARIANTS IN THE EUCARE-POSTCOVID STUDY

F. Bai[1], S. De Benedittis[1], A. Tavelli[1], M.M. Santoro[2], F. Ceccherini-Silberstein[2], M. Iannetta[3], Y. Shimoni[4], S. Ravid[4], T. Kozlovski[4], F. Köning[5], N. Pfeifer[5], E. Shamsara[5], M.Parczewski[6], A. Cozzi-Lepri[7], A. d'Arminio Monforte[1], G. Marchetti[1]

[1]Clinic of Infectious Diseases, San Paolo Hospital, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Italy, [2]Department of Experimental Medicine, University of Rome Tor Vergata, Roma, Lazio, Italy, [3]Infectious Disease Unit, Department of System Medicine, Tor Vergata University and Hospital, Rome, Italy, [4]Healthcare Informatics, IBM Research-Haifa, Mount Carmel Haifa, Israel, [5]Institute for Bioinformatics and Medical Informatics, University of Tübingen, Tübingen, Germany, [6]Department of Infectious Tropical Diseases and Immune Deficiency, Pomeranian Medical University in Szczecin, Szczecin, Poland, [7]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK

Background: The EUCARE-POSTCOVID study is a multicenter study enrolling recovered COVID-19 patients to investigate the prevalence and predictors of long COVID. The prevalence, risk factors and clinical presentation of long COVID aren't well understood yet; first data showed a reduced probability of long COVID during the Omicron era compared to Delta. We aimed to investigate the association between viral variants and long COVID.

Materials and methods: Long COVID was defined according to WHO (symptoms at 3 months after the COVID -19, that last at least 2 months without an alternative diagnosis). We included patients hospitalized for acute COVID-19 in San Paolo Hospital, Milan and Policlinico Tor Vergata, Rome (24/02/2020-07/01/2022). An unselected group of hospitalized patients underwent post COVID-19 evaluations at 1-3, 6-9 and 12-15 months after the acute phase; patients with ≥1 visit have been included. At the post COVID evaluation patients filled in questionnaires about ongoing symptoms. Viral variants were approximated by country variant surveillance data that allowed to assign a predominant variant over time. Logistic regression analyses were fitted to calculate propensity scores (PS) using predictors of undergoing a post COVID visit; PS were then used to evaluate the role of viral variants in developing long COVID by means of Inverse Probability Weighting.

Results: Among 2802 hospitalized patients, 772 (27.5%) underwent at least one post COVID visit; 84.6% patients had a post COVID visit at 1-3 months visit, 13.6% at 6-9 months and 1.8% at 12-15 months. 530/772 (68.7%) had long COVID (65.4% and 29.7% had physical and psychological symptoms, respectively). Most frequent symptoms were Myalgic Encephalomyelitis, defined by fatigue, post exertional malaise and unrefreshing sleep and ≥1 symptom between impaired memory and orthostatic intolerance (57.8%), brain fog (31.5%), respiratory symptoms (30%) and musculoskeletal symptoms (25.4%). Long COVID was independently associated with female gender; no association with comorbidities or disease's severity was found (Table 1). Omicron variant was available in 35/2802 (1.2%) patients. We did not observe any association between viral variants and long COVID, even using the weighted model; a borderline association between Delta variant (vs wild strain) and fatigue or brain fog was shown, but the association was largely attenuated in the weighted analysis (Figure 1).

Conclusions: Long COVID seems a common complication after acute COVID-19 at least during Delta circulation and is characterized more frequently by myalgic encephalomyelitis. Compared to the primary viral strain, Delta variant was slightly associated with a higher probability of fatigue and brain fog, but no association between long COVID and variants was found after adjustment for baseline unbalanced characteristics. Although there was no evidence for an association with Omicron subvariants, this needs to be reassessed as more events cumulate.

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PACS: clinical outcome

OC 124 IMPLICATION OF HUMAN ENDOGENOUS RETROVIRUSES IN DEVELOPMENT, PROGRESSION AND LONG-TERM SEQUELAE OF COVID-19: TOWARDS A PERSONALIZED MEDICINE

A. Minutolo[1], V. Petrone[1], M. Fanelli[1], C. Maracchioni[1], M. Giudice[1], R. Chirico[1], C. Cipriani, L. Coppola[2], E. Teti[2], C. Sorace[2], M. Zordan[2,3], P. Vitale[2,3], V. Malagnino[2,3], M. Iannetta[2,3], M. Andreoni[2,3], H. Perron[4], S. Grelli[1,5], E. Balestrieri[1], L. Sarmati[2,3], C. Matteucci[1]

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Infectious Diseases Clinic, Policlinic of Tor Vergata, Rome, Italy, [3]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, [4]Geneuro – Innovation, Lyon-France, [5]Virology Unit, Policlinic of Tor Vergata, Rome, Italy

Introduction: The human coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated not only with elevated morbidity and mortality, but with long-term complications. Recent evidences highlight Human Endogenous Retroviruses (HERVs) can be activated in response to infectious agents leading to immune-pathological effects and the present study aims to evaluate HERVs in the immune-pathogenesis of COVID-19, for the identification of new biomarkers for the diagnosis, prognosis, and follow-up of COVID-19 patients and their prioritization for targeted therapy.
Methods: Blood samples were collected at Tor Vergata University Hospital of Rome from Acute COVID-19 patients (COV) and Healthy Donors (HD). Blood from Post-Acute Sequelae of SARS- CoV-2 individuals (PASC) was also collected (range: 7-48 weeks post-infection). The expression of the envelope (ENV) of HERV-K and HERV-W have been analyzed by flow cytometry and correlated with clinical signs, immunophenotyping, inflammatory markers, and disease progression. The T cell differentiation markers were also analysed.
Results: HERV-W and HERV-K ENV proteins have been found expressed in blood samples from COV but not in HDs. Despite the percentage of Lymphocytes recovery, even after several weeks post-infection the expression of HERVs remained elevated in PASC. Among leukocytes, lymphocytes displayed the highest percentage of HERV-W ENV positive cells in COV, which correlated with T cell differentiation, exhaustion, and senescence markers. Instead, HERV-K ENV resulted in highly expressed in granulocytes and directly correlates with senescence markers CD57. HERV-W ENV positive CD4+ T cells significantly correlated with coagulopathy and biochemical parameters associated with COVID-19 severity. In PASC, HERVs protein expression remained high, especially in granulocytes. Notably, despite restoration of the normal distribution of leukocyte subpopulation in PASC, the percentage of CD4 naïve cells and CD8 terminal effector memory resulted altered suggesting a persistent immune dysfunction in PASC. To date, long-term health problems, including neurological symptoms such as headache, fatigue, dizziness, memory loss, confusion, and difficulty focusing, are associated with post-COVID-19 infection. Notably, HERVs expression was found modified in patients with specific neurological symptoms such as paraesthesia and tremors, suggesting their involvement in neurological alterations related to COVID-19.
Discussion and Conclusion: These data suggest HERVs as contributing factors in the development, progression, and long-term complications of COVID-19 describing disease evolution and opening avenues for novel therapeutic strategies for personalized medicine.
Funded by HERVCOV project (GA101057302) HORIZON-HLTH-2021-DISEASE-04 Personalised medicine and infectious diseases: understanding the individual host response to viruses.

PACS: clinical outcome

OC 125 IMPACT OF LONG-COVID ON DAILY WORKING ACTIVITY IN NON-ELDERLY PATIENTS: A CROSS SECTIONAL STUDY

A.I. Ritacco, D.F. Bavaro, F.V. Segala, L. Piccolomo, V. Giliberti, A. Amendolara, A. Lugli, D. Cassano, G. Manco Cesari, G. Romita, M. De Filippis, G. Brindicci, F. Di Gennaro, A. Saracino

Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy

Background: COVID-19 pandemic had devasting effects on lives and world economy. A huge number of infected patients developed the so called "long covid" defined by WHO as the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, lasting for at least 2 months with no other explanation. Anyway, the real incidence and risk factors of long-COVID in young people, and its impact on normal working activity, are still unknown. We aimed to evaluate the incidence and predictors of working activities impairment associated with long-COVID in non-elderly people (age ≤60 years according to the WHO definition).

Materials and Methods: This is a cross-sectional study carried out in March 2023 on a retrospective cohort of patients aged 60 or younger hospitalized for COVID-19 from 1st March 2020 to 31st December 2022 in a COVID -19 hospital. The study was conducted by phone interview, after consent, with a structured questionnaire. It consists of 50 questions, including items impacting on work capacity, divided into 3 sections: general symptoms, anxiety/depression, post-traumatic stress disorder (PTSD). Data were recorded on a datasheet. The primary endpoint was being "unable to work" after COVID-19, defined as loss of physical and cognitive performance that hampered re-initiation of previous working activities, which was used as a measurable proxy of long-COVID-9 effect on everyday activity.

Results: Out of 513 called patients, 326 answered the phone and provided consent to the questionnaire. The final population was composed of 192 males (59%) with a median (q1-q3) age of 47 (37-56) years.

Median time since hospitalization was 106 (66 - 129) weeks. At least one long-Covid symptom was reported in 97% of cases (316 patients); however, this percentage dropped to 28.8% (94 patients) if considering those "Unable to work" (Table 1). Factors associated with inability to restore previous working activity after COVID-19 were: hypertension, diabetes, infection during Omicron wave, low educational/occupational level and economical/social status at hospitalization, and new onset of mental disorders (anxiety/depression/PTSD) after infection. As the only variables newly occurring after COVID-19 were mental disorders, a post-hoc uni- and multivariate logistic regression for predictors of anxiety/depression/PTSD was performed [Table 2]. Male sex resulted protective (aOR 0.61, CI 95% 0.38-0.99, p = 0.048), while the need of oxygen during hospitalization (aOR 1.78, CI 95% 1.10-2.86, p = 0.018) and the lowest working level (vs higher occupations) were associated with an increased risk of developing mental disorders.

Conclusions: Long-COVID-19 was more frequent in young patients with metabolic comorbidities and occurrence of mental health disorders after the infection. Interestingly, these latter were associated with severe COVID-19, female sex, and low occupational status. Further studies should be directed on this target population.

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PACS: clinical outcome

OC 126 SYMPTOM CLUSTERS AND RISK FACTORS FOR LONG COVID SYNDROME IN HOSPITALIZED PATIENTS AT 6 MONTHS OF FOLLOW UP

V. Cogliandro[1], N. Squillace[1], E. Rossi[2], M.C. Ferrara[3], A. Monzani[4], M. Pozzi[5], V. Salvarani[6], L. Valagussa[7], I.C. Caramma[1], A. Cappelletti[1], L. Bonaffini[1], C. Ferrarese[8,9], G. Foti[5,9], M. Lettino[7,9], F. Luppi[4], M.G. Strepparava[6,9], G. Bellelli[3,9], P. Bonfanti[1,9]

[1]Infectious Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [2]Bicocca Center of Bioinformatics, Biostatistics and Bioimaging, University of Milano-Bicocca, Monza, Italy, [3]Acute Geriatric Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [4]Respiratory Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [5]Anesthesia and Intensive Care Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [6]Clinical Psychology Unit, Department of Mental Health, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [7]Cardiology Division, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [8]Neurology Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [9]School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy

Background: Long COVID is a multiorgan syndrome that persists for more than 3 months from the onset of COVID-19 infection. Risk factors for this condition are not well established. The aim of this study was to characterize the syndrome and establish any association between symptoms' persistence and clinical and socio-demographic variables.

Methods: A multidisciplinary Long COVID clinic was created in 2020 at the San Gerardo Hospital in Monza. In this analysis we evaluated patients who were discharged from the hospital with the diagnosis of SARS-CoV-2 infection, describing symptoms present at discharge or appeared after discharge and still present at follow up visit. We grouped symptoms in four clusters: respiratory (RC; dyspnea, cough), neurological (NC, peripheral neuropathies, headache, impaired mobility, behavioral disorders, cognitive disorders), psychological (PC; sleep disorders, mood disorders), and muscular (MC; arthromyalgia, fatigue). We described their prevalence and the risk factors associated with their persistence at follow up.

Results: 672 patients were evaluated (median age 61 years old, 68.1% male), including 174 patients (25.9%) discharged from the Intensive Care Unit (ICU). The median time from discharge to follow up visit was 179 days (98.5 days for ICU group; 286 days for non-ICU group). 68,3% of patients (372/672) had required non-invasive ventilation during hospital admission. The commonest persisting symptoms were dyspnea (30%), sleep disorders (30%), fatigue (29%) and mood disorders (22%). RC and MC were most prevalent at discharge, respectively 54,3% (365/672) and 59,2% (398/672); whereas PC appeared more frequently during follow up (+11.2%) and they were the most persistent at follow up visit (40,2%, 270/672). In a multivariate regression, persistence of any symptom cluster was associated with female sex and disease severity (ICU admission and length of hospital stay). Additionally, obesity was associated with the persistence of RC and the presence of comorbidities was associated with MC. In another multivariate regression, including the Clinical Frailty Score (CFS) at follow up and all variables included in the previous model, CFS was independently associated with any symptom cluster.

Conclusions: We confirmed the association between female sex and severity of disease with the persistence of symptoms at 6-month follow up. In addition, CFS was independently associated with the persistence of any symptom cluster, regardless the type. These data suggest that frailty could be a good predictor of Long COVID syndrome, able to identify all its multifaceted manifestations.

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Viruses, resistance and drugs

OC 127 DOES NGS ON HIV-1 DNA IMPROVE RESISTANCE ASSESSMENT IN HIGHLY TREATMENT-EXPERIENCED AND MULTI-RESISTANT INDIVIDUALS UNDER VIROLOGICAL CONTROL? AN EXPERIENCE FROM THE PRESTIGIO REGISTRY

D. Armenia[1], V. Spagnuolo[2], M.C. Bellocchi[3], L. Galli[2], L. Duca[3], G. Marchegiani[3], T. Clemente[2], L. Carioti[3], R. Lolatto[2], L. Calza[4], B.M. Celesia[5], A. Cascio[6], D. Francisci[7], A. Saracino[8], C. Torti[9], M. Zazzi[10], A. Castagna[2], M.M. Santoro[3] on behalf of the PRESTIGIO Registry

[1]Saint Camillus International University of Health Sciences, Rome, Italy, [2]Clinic of Infectious Diseases, Istituto Scientifico San Raffaele, Milano, Italy, [3]Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy, [4]Policlinico Sant`Orsola-Malpighi, Bologna, Italy, [5]Unit of Infectious Diseases, Garibaldi Hospital, Catania, Italy, [6]Infectious and Tropical Diseases Unit -Department of Health Promotion, Maternal and Infant Care, Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy, [7]Clinic of Infectious Diseases, Department of Medicine and Surgery, University of Perugia, Perugia, Italy, [8]Clinic of Infectious Diseases, University of Bari, Bari, Italy, [9]Department of Medical and Surgical Sciences, University "Magna Graecia", Catanzaro, Italy, [10]Department of Medical Biotechnologies, University of Siena, Siena, Italy

Background: This study aimed to clarify whether NGS might be useful for resistance assessment in virologically suppressed highly treatment-experienced (HTE) individuals with multidrug resistance (MDR).

Methods: Ninety-one HTE MDR individuals from the PRESTIGIO registry were analysed. HIV-1 DNA PR/RT/IN and V3 sequences were obtained through NGS on MiSeq platform. Major resistance mutations (MRM) and APOBEC editing estimation (APOBEC mutations [APO-M]; stop codons) were evaluated through HIVdb algorithm. NGS cut-offs at ≥1%, ≥5% and ≥20% were tested. Minority MRM with frequency ranging 1-5% (mV1%) and 5-20% (mV5%) and majority MRM (frequency >20%, mV20%) were compared to historical-GRT (H-GRT). Variants distribution was compared between individuals who experienced virological rebound after NGS-GRT and those who maintained virological control.

Results: At NGS-GRT, individuals had a median (IQR) cART exposure of 23 (21-25) years, had been virologically suppressed since 3 (2-5) years and had a total HIV-DNA of 2,377 (1,274-4,949) copies/106 CD4+ cells. X4 tropism was detected in 61.5% of individuals.

A total of 1,772 MRM were detected. Around half of MRM detected by NGS were already found in H-GRT; on the other hand, NGS-GRT detected a considerable number of additional mutations never observed before (Figure 1). The highest detection rate of historical MRM was obtained by setting NGS at 1% (Figure 2).

NGS set at 1% showed poor reliability, although associated with the highest detection rate of historical MRM. In fact, mV1% (N=337) were frequently detected in samples with stop codons (94.4%) or APO-M (97.4%) providing potential misleading resistance assessment.

Differently, among mV5% (N=370), a substantial proportion of cases was not affected by APOBEC editing and contributed in expanding detection of historical MRM (25.9%) or detecting new MRM (18.6%).

Regarding majority variants, mV20% (N=704) were marginally detected in samples with stop codons (2.9%) or APO-M (5.3%), and mostly contributed to detect (69.4%) historical MRM or detect new MRM (25.4%).

After NGS-GRT, 21 individuals underwent virological rebound with a median (IQR) viremia of 365 (98-7,840) copies/mL. Among them, only the median (IQR) number of mV5% detected exclusively by NGS-GRT was higher (2 [1-3]) compared to those who maintained virological control (1 [0-2], p=0.030, Figure 3). The number of mV5% newly detected by NGS in failing individuals positively correlated with plasma HIV-RNA levels detected at virological rebound (Spearman test, Rho=0.474, P=0.030).

Conclusions: In HTE MDR virologically suppressed individuals, NGS-GRT on HIV-1 DNA allows detection of around 60-70% historical MRM and detects considerable new resistance. Our results confirm that setting NGS at 5% might be a good choice to obtain reliable sequence data. At this setting, an increased number of minority species correlates with loss of virological control and with viremia levels at virological rebound.

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Viruses, resistance and drugs

OC 128 HIV-1 PERSISTENCE IN PEOPLE LIVING WITH HIV WHO STARTED ANTIRETROVIRAL THERAPY IN ACUTE OR CHRONIC INFECTION: INSIGHT INTO MOLECULAR MECHANISMS

E. Bruzzesi[1], G. Spinozzi[2], L. Rudilosso[2], P. Gallina[2], G. Amodio[2], A. Castagna[1], S. Gregori[2], E. Montini[2], A.Calabria[2], S. Nozza[1], D. Cesana[2]

[1]Vita-Salute San Raffaele University, [2]San Raffaele Telethon Institute for Gene Therapy (Sr-TIGET), San Raffaele Scientific Institute, Milan, Italy

The early establishment of a proliferating reservoir of infected cells harboring infectious proviruses represents the major obstacle to HIV eradication. Long-lived infected cells persist either in a latent state or undergo clonal expansion following homeostatic or antigenic stimulation or because of an insertional mutagenesis mechanism. Regulatory T cells (Tregs) were demonstrated to play a role in favouring viral persistence in people living with HIV (PLWH), taking advantage of insertional mutagenesis mechanisms. Indeed, the expression of chimeric transcripts containing viral HIV-1 sequences fused to the first protein-coding exon of STAT5B and BACH2 cellular genes was specifically enriched in Tregs and in central memory T cells.

Aims of the study are to characterize the composition of the lymphocytic and myeloid regulatory compartment in 13 PLWH with undetectable viremia and with CD4+ T cell count > 500 cell/uL who started antiretroviral treatment either in acute (n=4) or in chronic infection (n=2 receiving ART >15 years and n=7 receiving ART >5 years) and to evaluate if genes other than BACH2 and STAT5B can be activated by insertional mutagenesis mechanisms.

By cytofluorimetric analysis, no significant difference in the percentage of classical Foxp3-expressing Tregs, non-classical T regulatory cells (as referred to Tr1) (Fig. 1, A-E) and in myeloid cells with regulatory functions (such as DC-10) (Fig. 1, F-M) were observed among the different groups of HIV patients and respect to healthy controls. However, an increase in HLA-G-expressing CD8+ T cells was observed in PLWH, as compared to healthy controls.

Viral integration sites (IS) were retrieved from CD4+ T cells by Sonication Linker Mediated PCR, yielding 4559 IS A high variability in the number of IS retrieved were retrieved among the different patients and no correlation has been observed with IPDA values, considering both intact and defective provirus and presence of chimeric transcripts. Moreover, no differences emerged in the quantification of both intact and defective provirus copies in subjects who started therapy in chronic infection, as assessed by IPDA (Fig. 2).

Although the vast majority of infected clones were represented by few cells, in 3 subjects clones were detected with high relative abundance, reaching 65% (Fig. 3). Although HIV integrations in BACH2 and STAT5B were identified only in 3 patients of our cohort, we confirmed the expression of HIV/STAT5B and HIV/BACH2 chimeric transcripts in 83% and 38% of the subjects enrolled, respectively (Fig. 4).

In conclusion, these results show that the composition of the regulatory lymphoid and myeloid compartments was not different from healthy donors and provide a better understanding of the complex mechanism of HIV persistence and show that the retrieval of the chimeric transcripts is more efficient than integration site analysis in the identification of putative culprits of integration, paving the way for future studies.

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Viruses, resistance and drugs

OC 129 COMPARISON OF DIFFERENT INTERPRETATION TOOLS FOR HIV-1 RESISTANCE DETECTED THROUGH NEXT GENERATION SEQUENCING IN ITALIAN CLINICAL ROUTINE

D. Armenia[1], L. Carioti[2], V. Micheli[3], T. Allice[4], C. Bonura[5], B. Bruzzone[6], F. Bracchitta[3], F. Cerutti[4], G. Giammanco[5], N. Randazzo[6], A. Bonifacio[7], I. Bon[8], A. Bertoli[9], M. Vatteroni[10], G. Ibba[11], F. Novazzi[12], M.R. Lipsi[13], N. Cuomo[14], I. Vicenti[15], F. Ceccherini-Silberstein[2], B. Rossetti[16], A. Bezenchek[17], F. Saladini[15], M. Zazzi[15], M.M. Santoro[2], on behalf of the NGS Network

[1]UniCamillus, Saint Camillus International University of Health Sciences, Rome, Italy, [2]University of Rome "Tor Vergata", Rome, Italy, [3]Laboratory of Clinical Microbiology, Virology and Bioemergencies, ASST Fatebenefratelli Sacco - University of Milan, Milan, Italy, [4]Laboratory of Microbiology and Virology, Amedeo di Savoia Hospital, Turin, Italy, [5]Azienda Ospedaliera Universitaria Policlinico "P. Giaccone" - Universita' degli Studi di Palermo, Palermo, Italy, [6]Hygiene Unit, Ospedale Policlinico San Martino, Genoa, Italy, [7]Section of Experimental and Clinical Pathology, Department of Precision and Regenerative Medicine and Jonic Area, University of Bari, Bari, Italy, [8]Microbiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy, [9]Virology Unit, Polyclinic of "Tor Vergata", Rome , Italy, [10]Virology Unit, AOU Pisana, Pisa, Italy, [11]Microbiology and Virology Unit, Diagnostic Department, AOU Sassari, Sassari, Italy, [12]Department of Medicine and Surgery, University of Insubria, Varese, Italy, [13]Microbiology and Virology Unit, Policlinico Riuniti Foggia Hospital, Foggia, Italy, [14]U.O.C. Microbiologia e Virologia, P. O. "D.Cotugno" - AO dei Colli - Napoli, Italy, [15]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [16]Infectious Disease Department, USL SUDEST, Toscana, Misericordia Hospital, Grosseto, Italy, [17]IPRO-InformaPRO S.r.l., Rome, Italy, EuResist Network GEIE, Rome, Italy

Background: HIV genotypic drug resistance testing through next generation sequencing (NGS-GRT) is gradually replacing Sanger sequencing. This work aimed at evaluating the concordance in resistance detection among different interpretation systems for NGS data obtained from real-life settings.

Material and Methods: Routine NGS-GRT data from viral RNA generated through the HIV-1 Solution v2 kit (Arrow Diagnostics, Illumina MiSeq/iSeq100 platforms) and Sentosa® SQ HIV-1 Genotyping Assay (Ion torrent platform) was collected from 13 Italian laboratories. The interpretation of NGS results was performed by three online tools (Paseq, Hydra, HIVdb Stanford) and the SmartVir standalone software. FastQs were considered reliable for NGS-GRT when the coverage was >100 reads (100X) for at least three tools at each PR/RT/IN resistance associated position listed in the HIVdb algorithm ver.9.4. Mutations detected were classified as follows: unreliable (frequency <5% by all tools), minority variants (mV: frequency 5%-20% by all tools), majority variants (MV: frequency >20% by all tools), unclassified5% (U5%: frequency <5% by at least one tool), unclassified20% (U20%: frequency 5%-20% by at least one tool). The coefficient of variation (CV) of mutation's frequency was calculated to estimate variability among interpretation tools.

Results: 738 NGS-GRT were evaluated. About 40% of samples were from individuals infected with non-B subtypes and the majority of samples (78.5%) had contextual viremia >10,000 copies/mL.

Reliable 100X coverage was obtained for 471 NGS-GRT (63.8%). The proportion of reliable samples was affected by non-B subtypes and viremia levels <10,000 copies/mL (Figure 1).

In reliable samples, 7452/9640 (77.3%) mutations detected were excluded as unreliable minority variants. Among the 2188 mutations evaluated (PR:703; RT:835; INT:650), 77.8% (MV: 59.9%; mV: 17.9%) were concordantly detected by 4, 3 or 2 tools (87.2%, 8.1% and 4.7%, respectively). Median (IQR) CV related to these mutations was low (1.3% [0.6%-4.6%]). The highest CV was found in INT region (Figure 2 Panel A) compared to PR/RT, and it was slightly higher in case of viremia ≤1,000 copies/mL (Figure 2 Panel B).

Overall, 492 (22.5%) mutations were considered as unclassifiable, 428 as U5% (19.6%) and 64 as U20% (2.9%). Median (IQR) CV was high both for U5% (34.0% [18.3%-52.2%]) and U20% (46.2% [18.3%-62.2%]). For these unclassifiable mutations, the median of maximum frequency detected among interpretation tools was 6.7% (5.7% -9.7%); the third quartile of this distribution (9.7%) suggests that results of NGS are more likely to be discordant for mutations with frequency below 10% across interpretations tools (Figure 3).

Conclusions: This first survey on NGS resistance testing suggests that the reliability of NGS-GRT is negatively affected by viremia <10,000 copies/mL and non-B subtypes. At frequency >10%, mutations were detected with acceptable concordance among different interpretation tools.

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Viruses, resistance and drugs

OC 130 PHARMACOKINETIC OF TECOVIRIMAT IN PLASMA AND SEMEN OF MPOX PATIENTS

M. Tempestilli[1], A. Mondi[1], C. Pinnetti[1], A. D'Avolio[2], V. Mazzotta[1], G. Matusali[1], D. Mariotti[1], O. Forini[1], A. Beccacece[1], A. De Nicolò[2], P. Faccendini[1], E. Cimini[1], F. Maggi[1], E. Girardi[1], E. Nicastri[1], F. Vaia[1], A. Antinori[1]

[1]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]University of Turin, Turin, Italy

Background: During the current multi-country outbreak, Mpox was driven by human-to-human transmission. Peculiar epidemiological characteristics and the detection of Mpox virus (MPXV)-DNA and infectious virus in rectal swabs and semen, suggested an important role of sexual transmission. Tecovirimat is the only antiviral drug authorized for the treatment of severe Mpox but no pharmacokinetics (PK)/pharmacodynamic (PD) data in real-life patients are available. The aim of this study was to investigate Tecovirimat PK in people with Mpox and its penetration and efficacy into seminal fluid.

Methods: Monocentric, prospective, observational study enrolling Mpox patients who received oral tecovirimat (600 mg twice daily for 14 days). Plasma samples for PK assessment were collected at steady state, before and 3, 5, 7, and 12 hours after Tecovirimat administration. In the same day, seminal samples at Ctrough were collected from available patients. Plasma and semen drug concentrations were determined by validated liquid chromatography coupled with tandem mass spectrometry. MPXV-DNA load in seminal fluid was evaluated at baseline, during and after Tecovirimat treatment, by a real-time polymerase chain reaction.

Results: Overall, 14 male patients hospitalized for severe Mpox, were enrolled. Six were HIV positive, all of them on antiretroviral therapy and with undetectable HIV viral load. Significant differences in Tecovirimat PK parameters were observed between subjects with and without HIV infection (figure1). Particularly, Tecovirimat Cmin, Cmax, and Area Under Curve0–12 were 37%, 39%, and 42% lower in HIV-positive versus HIV-negative subjects, respectively. Apparent systemic clearance of Tecovirimat was increased by 42% in HIV-positive patients versus controls. However, these differences in tecovirimat PK were not associated with treatment failure in people living with HIV. In a subgroup of three Mpox patients, Tecovirimat PK/PD in the seminal fluid was evaluated showing concentrations of Tecovirimat above the 50% inhibitory concentration MPXV in vitro and a sustained clearance of MPXV-DNA approximately after the first week of treatment.

Conclusions: In this study, we observed a significant decrease in plasma exposure of Tecovirimat in Mpox patients with HIV compared to those without HIV infection, with no apparent impact on clinical outcome. Additionally, we found Tecovirimat levels in the seminal fluid that could be adequate for viral suppression in this compartment. Further studies on a larger population are needed to determine whether Tecovirimat concentrations in plasma and in body compartments are sufficient to suppress MPXV replication, especially in the early phase of the disease, in order to improve decisions on Tecovirimat use for infection prevention (reducing the sexual MPXV transmission) and control (to avoid viral reservoir establishment and viral resistance development).

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Mpox and Immunopathogenic mechanisms

OC 131 HUMORAL AND CELLULAR IMMUNE RESPONSE AFTER EIGHT MONTHS FROM MPOX VIRUS INFECTION

V. Mazzotta[1], G. Matusali[2], E. Cimini[3], F. Colavita[2], R. Casetti[3], C. Pinnetti[1], A. Mondi[1], A. Bettini[2], Bordoni[4], G. Grassi[3], G. Prota[5], S. Vita[6], N. Nicastri[6], E. Girardi[7], C. Agrati[4], F. Vaia[8], F. Maggi[2], A. Antinori[1]

[1]HIV/AIDS Unit, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [2]Laboratory of Virology, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [3]Laboratory of Cellular Immunology and Pharmacology, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [4]Unit of Pathogen Specific Immunity Department of Pediatric Hematology and Oncology, IRCCS, Ospedale Pediatrico Bambino Gesù, Rome, Italy, [5]Laboratory of Microbiology, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [6]Emerging Infectious Diseases Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [7]Scientific Direction, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [8]General Direction, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy

Background: Immunological signature of mpox was described in the early stages of infection. Analysis of its persistence could have implications for decision-making on the need and timing of vaccination in mpox virus (MPXV) infected subjects. We described the kinetics of humoral and cellular immune response from symptoms onset (FSO) up to 8 months after infection.

Material and Methods: 16 patients (pts) with confirmed mpox were enrolled in a cross-sectional study from May to July 2022, and blood samples collected in the early phase of infection, at 3-4 and 6-8 months post-infection. Anti-MPXV IgM, IgA, IgG, and neutralizing antibodies (nAb) titers were measured by immunofluorescence assay and by 50% plaque reduction neutralization test (PRNT50). Interferon-γ producing specific T-cells to MVA peptides was assessed by ELISpot assay. In all pts, we analysed the proportion of naïve (N), central memory (CM), effector memory (EM), and terminally differentiated (TEMRA) CD4+ and CD8+ T-cells and their expression of activation and exhaustion markers (CD38/CD57/PD-1) by flow cytometry. Kinetics of the cellular response were compared with eight healthy donors matched by sex and age. Kruskal-Wallis, Dunn's, Mann-Whitney, and Wilcoxon tests were used for statistics, as appropriate.

Results: All were MSM with a median age of 38 years (IQR 34-44). 7 were PLWH, all on ART with good viro-immunological status (median CD4 count 686 cells/mm, 525-856). Only one received smallpox vaccine during childhood.

Anti-MPXV IgM, IgA, IgG, and nAbs were detected as early as 4 days FSO and peaked during the third week. At 3 -4 and 6-8 months FSO, lower levels of all the humoral markers were observed: IgM became undetectable; IgA were detected in 30% and 25% of patients, and IgG and nAb in all samples (Fig1A). Regarding T-cells differentiation profile, a significant expansion of CM and EM cells was observed after T3-4 months by decreasing at 6-8 months post-infection (Fig1B). Exhaustion and activation markers (PD-1, CD57, CD38) were increased at the beginning of infection and resulted lower after 3-4 and 6-8 months (Fig 1C). No differences were observed between PLWH and not. MVA-specific T-cells response significantly increased from T0-4 days to 3-4 months and decreased at T6-8 months after infection (Fig1D). Preliminary data showed the persistence of memory pox-specific T cells at 6-8 months, able to expand after in vitro stimulation.

Conclusions: In all the patients tested, markers of humoral immunity have been observed in the acute phase of infection, specific IgG and nAbs were still detectable in the 6-8 months follow-up. Analysis of cellular immune response in the early phase of mpox, until 3-4 months post-infection showed increased CM, EM, and MVA-specific responding T-cells. These markers decreased and stabilized after 6-8 months post-infection suggesting the maintenance of the protective memory/effector T cells expansion observed at 3-4 months post-infection.

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Mpox and Immunopathogenic mechanisms

OC 132 NEUTRALIZING AND T CELL IMMUNOGENICITY AFTER MVA-BN VACCINATION FOR MPOX ACCORDING TO PREVIOUS SMALLPOX VACCINATION, HIV STATUS, AND ADMINISTRATION ROUTE

V. Mazzotta[1,2], A. Cozzi Lepri[3], G. Matusali[1], E. Cimini[1], S. Lanini[1], C. Aguglia[1,4], F. Colavita[1], S. Notari[1], R. Gagliardini[1], S. Meschi[1], A. Oliva[1], S. Vita[1], P. Piselli[1], V. Mondillo[1], G. Montagnari[1,4], E. Nicastri[1], A. Siddu[5], G. Rezza[5], A. Barca[6], E. Girardi[1], F. Vaia[1], F. Maggi[1], A. Antinori[1] and the Mpox Vaccine Lazio Study Group

[1]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]PhD course in Microbiology, Immunology, Infectious Diseases, and Transplants (MIMIT), University of Rome Tor Vergata, Rome, Italy, [3]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK; [4]University of Rome Tor Vergata, Rome, Italy, [5]Italian Ministery of Health, [6]Department of Health of Lazio Region

Background: A massive vaccination campaign with MVA-BN was undertaken worldwide to stop the mpox multi-country outbreak. However, data on humoral and cellular immunogenicity are still limited, and how historical smallpox vaccination, HIV infection, and administration route impact immune response remains to be clarified.
Materials: Persons eligible for MVA-BN vaccination according to Italian Ministry of Health recommendations were included. Blood samples were collected at baseline and one month after the last dose (T1-T2-T3) and tested for MPXV-specific nAbs by 50% plaque reduction neutralization test (PRNT50, starting dilution 1:10) and for IFN-γ-producing specific T cells by ELISpot assay. Paired or unpaired t-tests for nAbs and Wilcoxon or Mann-Whitney test for T-cell response were fitted. Average Treatment Effect (ATE) of the difference from baseline to vaccine completion by priming and administration route was estimated after weighting for HIV status.
Results: 171 pts, 90 (53%) smallpox-primed. Median age 48 yrs (IQR 40-54), 82 (48%) PLWH. All pts received the second dose intradermically, with 88 (51%) receiving the first (or single) dose subcutaneously. A significant increase of nAbs titers (Fig. 1a) and of T-cell response to MVA-peptides (Fig. 1b) after two-shot (not primed) or single-shot (primed) was observed. ATE estimating average changes from baseline to the completion of a full cycle showed no difference between primed and not primed for nAbs and a significantly higher T cell response in those receiving two-shot than single-shot (Table 1A). In the subset of those not reactive at T1, the probability of the whole population becoming reactive to nAbs was not influenced by previous smallpox vaccination (60% vs. 61%), whereas in PLWH, a reduced proportion of those becoming reactive for nAbs (48% vs. 61%) was observed in primed, with a lower estimated probability of seroconversion (Fig 2). ATE weighted for HIV and previous vaccination showed comparable immunogenicity between the subcutaneous and intradermal routes of administration of the first dose (Table 1B).
Conclusions: Two-shot MVA-BN vaccination significantly increased both MPXV-nAbs and T-cell response in smallpox, non-primed individuals. The T-cell response was consistently lower in primed than in non-primed, and, in PLWH, a single-shot cycle also elicited a lower rate of nAb seroconversion in primed, suggesting that a two-shot course should be considered for all people, regardless of previous smallpox vaccination status, and in any case recommended in PLWH. The intradermal route proved to be immunogenic as the subcutaneous one.

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Mpox and Immunopathogenic mechanisms

OC 133 INTERFERON-GAMMA (IFN-G), BUT NOT TUMOR NECROSIS FACTOR-ALPHA (TNF-A) INDUCES THE POLARIZATION OF HUMAN MONOCYTE-DERIVED MACROPHAGE (MDM) INTO M1 CELLS RESTRICTING HIV-1 REPLICATION

C. Mazzei[1], V.S. Ibba[1], S. Ghezzi[1], G. Poli[1,2]

[1]San Raffaele Scientific Institute, Division of Immunology, Transplantation and Infectius Deseases, Human Immuno-Virology Group, Milano, [2]Vita-Salute San Raffaele University, School of Medicine, Milano

Background: We have previously reported that M1-polarization of human MDM by short-term (18h) stimulation with IFN-g+TNF-a leads to a partial restriction of HIV-1 replication. Furthermore, restimulation of infected M1-MDM with the same cytokines several days after infection drives HIV-1 to a state of reversible latency. We have here investigated whether the contribution of both cytokines is required to obtain this restricted profile of HIV-1 replication.

Material and Methods: Human monocytes from 7 independent healthy donors were purified by Ficoll-derived PBMC by Percoll density gradient and allowed to differentiate into MDM for 5-7 days. MDM were then incubated or not with either IFN-g or TNF-a or their combination for 18h. Cytokines were then removed and both unstimulated (CTRL) and stimulated MDM were incubated with CCR5-dependent (R5) HIV-1BaL at the MOI of 0.1. Both stimulated and unstimulated MDM were re-exposed or not to the same cytokines 7 days after infection. HIV-1 replication was monitored by RT activity released in culture supernatants.

Results: MDM polarized as M1 cells by IFN-g+TNF-a significantly decreased the levels of virus production in comparison to CTRL cells; furthermore, when these M1-MDM were restimulated with the same cytokines the levels of virus production became almost undetectable, as published. This pattern was fully reproduced when MDM were stimulated with IFN-g alone, whereas cells incubated with TNF-a did not demonstrate any restriction in HIV-1 replication.

Conclusions: IFN-g induces a state of restriction of HIV-1 replication in human MDM that is superimposable to that observed with cell stimulation by IFN-g+TNF-a. We are currently investigating whether latency-reversal could also be accomplished M1-MDM polarized by IFN-g alone, which would imply a surprising dispensability of TNF-induced activation of NF-kB in driving proviral transcription.

Mpox and Immunopathogenic mechanisms

OC 134 EFFECT OF SERA FROM HIV-1-EXPOSED SERONEGATIVE SUBJECTS, LONG TERM NON PROGRESSORS, HIV-1+ AND HIV-1- INDIVIDUALS ON CCR5 EXPRESSION AND R5 HIV-1 INFECTIVITY IN HUMAN PRIMARY MACROPHAGES AND CD4+ T LYMPHOCYTES

I. Farina[1], C. Pastori[2], R. Bona[1], C.M. Galluzzo[1], R. Amici[1], C. Purificato[1], M.C. Gauzzi[1], M. Andreotti[1], L. Lopalco[2], L. Fantuzzi[1]

[1]National Center for Global Health, Istituto Superiore di Sanità, Rome, Italy, [2]Division of Immunology, Transplantation and Infectious Diseases, San Raffaele Scientific Institute, Milan, Italy

Background: CCR5 is the main coreceptor for HIV-1 entry in target cells. Natural antibodies (Abs) against the first extracellular loop of CCR5 were found in several cohorts of HIV-1-exposed seronegative (HESN) subjects and of long-term non-progressors (LTNP), suggesting a role for such Abs in controlling viral replication in vivo. These Abs do not interfere with virus binding but determine sustained CCR5 internalization and inhibit HIV-1 infection in CD4+ T lymphocytes. The aim of this study was to assess the effect of sera from HESN, LTNP, HIV-1+ and HIV-1- individuals, characterized for the presence or absence of natural anti-CCR5 Abs, on CCR5 membrane expression and HIV-1 infection in monocyte-derived macrophages (MDMs).

Materials and Methods: Serum samples were obtained from 3 HESN and 2 LTNP subjects with anti-CCR5 Abs, and from 3 HESN, 2 HIV-1+ and 3 HIV-1- subjects without anti-CCR5 Abs. CCR5 membrane expression was measured in subject's autologous CD4+ T lymphocytes. The effect of sera on CCL4 binding and CCR5 internalization was evaluated in CD4+ T lymphocytes from healthy donors, and the neutralizing activity of isolated immunoglobulins (Ig) was measured in PBMCs from healthy donors infected with an R5 primary isolate. MDMs were obtained from CD14+ monocytes isolated from the peripheral blood of 12 healthy donors by immunomagnetic selection and cultured in vitro for 6 days. MDMs were exposed to appropriate dilutions of sera for 48 h and then infected with HIV-1BaL. Membrane CCR5 expression was evaluated by flow cytometry at the time of infection. HIV -1 Gag and Env genes expression was assessed 72 h post infection by qPCR.

Results: CCR5 was expressed by most of control subject's autologous CD4+ lymphocytes (mean value 98.6%, range 95-100%), but only in a low percentage of lymphocytes from subjects with anti-CCR5 Abs (mean value 14.5%, range 10-25%). Sera containing anti-CCR5 Abs caused a partial internalization of CCR5 and inhibition of CCL4 binding, and Ig isolated from these sera neutralized the infectivity of R5 HIV-1 primary isolate in PBMCs. Unlike lymphocytes, a variable and low percentage of MDMs express CCR5 on the membrane (mean value 11.2%, range 3.8-22%). Correlation analysis highlighted a lack of correlation between viral DNA copies and CCR5 expression in MDMs. Exposure to sera determined a variable reduction of CCR5 membrane expression and of viral DNA copies in almost all donors MDMs, with a trend dependent on the donor tested but independent of the type and dilution of the serum used.

Conclusions: Overall, these results suggest that the percentage of CCR5 membrane expression is not a major determinant of MDMs infection level and that the observed modulation of CCR5 and R5 HIV-1 infectivity might depend on the interaction between factors other than anti-CCR5 Abs present in sera and/or intrinsic to the donors on which sera were tested.

This work was supported by the Italian Ministry of Health (RF-2018-12365208 to LF).

Outcomes in treatment experienced PLWH

OC 135 EFFECTIVENESS OF SWITCH TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) IN VIROLOGICALLY SUPPRESSED PERSONS LIVING WITH HIV (PLWH): 96-WEEK DATA FROM THE ICONA COHORT

A. d'Arminio Monforte[1], A. Tavelli[2], A. Cingolani[3], L. Taramasso[4], C. Mussini[5], S. Piconi[6], A. Calcagno[7], G. Orofino[8], S. Cicalini[9], A. Castagna[10], F. Ceccherini-Silberstein[11], A. Gori[12], G. Guaraldi[5], A. Antinori[9] for the Icona Foundation Study Group

[1]Icona Foundation, University of Milan, Milan, Italy, [2]Icona Foundation, Milan, Italy, [3]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Department of Safety and Bioethics, Infectious Diseases Unit, Rome, Italy, [4]Ospedale Policlinico San Martino IRCCS, University of Genoa, Unit of Infectious Diseases, Genoa, Italy, [5]Azienda Ospedaliero Universitaria di Modena, University of Modena and Reggio Emilia, Infectious and Tropical Diseases Unit, Modena, Italy, [6]ASST Lecco, Infectious Diseases Unit, Lecco, Italy, [7]Ospedale Amedeo di Savoia, University of Turin, Unit of Infectious Diseases, Department of Medical Sciences, Turin, Italy, [8]Ospedale Amedeo di Savoia, ASL Città di Torino, Division A of Infectious Diseases, Turin, Italy, [9]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS,Clinical Deparment, HIV/AIDS Unit, Rome, Italy, [10]IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Infectious Diseases Unit, Milan, Italy, [11]University of Rome Tor Vergata, Department of Experimental Medicine, Rome, Italy, [12]IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Department of Pathophysiology and Transplantation, Clinic of Infectious Diseases, Milan

Background: Real-world clinical data on BIC/FTC/TAF, especially from key-populations, are still lacking. The aim of this study is to evaluate the effectiveness of switching to BIC/FTC/TAF in ART-experienced virologically suppressed (VS) people living with HIV (PLWH), focusing on females and PLWH older than 50 years.

Methods: Observational study including ART-experienced VS PLWH from the Icona cohort who switched to BIC/FTC/TAF for the first time from Apr-2018 to Dec-2021. Primary endpoint: treatment failure (TF1) defined as virological failure (VF: 2 consecutive HIV-RNA > 200 copies/ml or 1 HIV-RNA>1000 cps/ml) or treatment discontinuation (TD) for any reason. Secondary endpoints: (i) treatment failure excluding TD for pregnancy (ii) treatment failure 2 (TF2): VF or TD only for toxicity/intolerance or for virological failure; (iii) VF in ITT and (iv) VF OT.

Standard survival analysis (Kaplan–Meier curves) were used. Unadjusted and adjusted hazard ratios (HR) of the different endpoints were estimated by means of Cox regression models for the different exposure groups: ≥50 years old and females. Sets of confounders were tailored for each of the exposure of interest.

Results: 1,233 PLWH were included (44.0% >50 years, 18.6% female). Patients' characteristics are shown on Table1.

Over a median follow-up of 125.2 weeks from BIC/FTC/TAF switch (IQR 52-88.7), 179 PLWH had TF1 (14.5%; 19 VF, 159 TD); TD due to pregnancy/planned pregnancy was observed in 8 out of 229 (3.5%) women. 56 PLWH had TF2 (4.8%; 37 TD for toxicity/failure and 19 VF); VF-ITT occurred in 23 (1.9%), VF-OT in 19 (1.6%) PLWH.

Reasons for BIC/FTC/TAF discontinuation among 159 PLWH were: 88 TD for simplifications (7.1% of total population, 55% of total discontinuations), 34 TD for toxicities/intolerance (2.6%, 21.4%), 3 TD for virological failures (0.3%, 1.9%), 3 TD for patient's decision (0.3%, 1.9%) and 31 (2.5%, 19.5%) for other reasons (including the 8 pregnancies/planned pregnancy).

The 96-week probability of TF1 estimated by KM was 10.3% (95%CI 8.7-12.2-), KM probabilities by subgroups are shown in Table2, together with KM probabilities of TF excluding pregnancies, TF2, VF-ITT and VF-OT.

In the adjusted Cox regression models, PLWH ≥50 years did not have a different risk of TF1 compared to those <50 years (aHR 0.88, 95%CI 0.64-1.2), while females had a 42% higher risk (aHR 1.42, 95%CI 1.00-2.04) (Table3). However, after excluding 8 TD for pregnancy or planned pregnancy as events, treatment failure risk in women was comparable to that of men (aHR 1.13, 95%CI 0.77-1.68).

Neither age nor sex was associated with risk of treatment failure according to the TF2 definition.

In the Cox regression models PLWH older than 50 did not have a higher risk of VF OT and ITT, while females had a significant 2.78-fold higher risk of VF in the ITT analysis (aHR=2.78, 95%CI 1.19-6.5), witha marginally significant aHR of 2.38 (95%CI 0.91-6.2) in the OT analysis (Table 3).

Conclusions: Switching to BIC/FTC/TAF demonstrated high long-term effectiveness, including also in PLWH older than >50, consistent with data from RCTs. Higher risk of treatment failure in females is mainly related to planned or ongoing pregnancies. Reasons for higher risk of VF for females have to be further investigated.

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Outcomes in treatment experienced PLWH

OC 136 EFFECTIVNESS OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE(BIC/FTC/TAF) AS SWITCH STRATEGY IN VIROLOGICALLY SUPPRESSED: REAL WORLD DATA FROM MONOCENTRIC COHORT

R.A. Passerotto[1], F. Lamanna[1], D. Farinacci[2], A. Dusina[3], A. D'Angelillo[1], A. Ciccullo[4], G. Baldin[3], I. Mozzetta[3], E. Visconti[3], S. Di Giambenedetto[1,3], A. Borghetti[3]

[1]Dipartimento di Sicurezza e Bioetica, Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Rome, Italy, [2]UOC Medicina Protetta - Malattie Infettive - ASL Viterbo, Viterbo, Italy, [3]UOC Malattie Infettive, Fondazione Policlinico Universitario A.Gemelli IRCCS, Rome, Italy, [4]Malattie Infettive, Ospedale San Salvatore, L'Aquila, Italy

Background: BIC/FTC/TAF showed efficacy and tolerability in randomized trials as a switch strategy in virologically-suppressed people living with HIV (PLWH). We evaluated its effectiveness in a real-life setting.
Material and methods: A retrospective monocentric cohort study was performed by including patients switching to TAF/FTC/BIC after reaching virological suppression (VS, HIV-RNA<50 cp/mL) in the period 2018-2022. Patients with no follow-up visits were excluded. Probabilities of virological failure (VF, i.e. 2 consecutive HIV-RNA>50 cp/mL or a single HIV-RNA≥200 cp/mL) and of regimen discontinuation were estimated by Kaplan-Meier, and predictors of both outcomes were identified through multivariable Cox regression, with a backward stepwise selection of covariates. Analysis of variance for repeated measures was used to examine changes in CD4 count and CD4-to-CD8 ratio from baseline (BL) up to 36 months, and predictors of variation in both CD4 and CD4-to-CD8 at 12 months were analyzed through linear regression.
Results: Overall, 431 PLWH were included, with 54 years of median age. At least one VF before switch was reported in 52% of patients, 4% of whom with an INSTI-based regimen. Most of the patients switched from 2NRTI-based regimen + INSTI or NNRTI or PI. The main reason to switch was pro-active. Patients' characteristics at baseline are shown in table 1.
19 VF occurred during 22 months of median follow-up time. Estimated probabilities of VF at 1, 2 and 3 years were 2.2% (95% CI 1.1-4.4%), 4.0% (95% CI 2.2-7.0%), 6.5% (95% CI 4.0-10.5%), respectively.
Time of VS before BL (per 1 year more, aHR 0.85, 95% CI 0.76-0.95; p= 0.005) and a history of previous VF (versus none, aHR 14.91, 95% CI 1.98-112.30; p = 0.009) independently predicted VF.
Discontinuation occurred in 40 cases: 21 (52.5%) for simplification to dual therapy, 15 (37.5%) for toxicity (predominantly from central nervous system, 3 cases, and gastrointestinal tract, 4 cases), 1 pregnancy and 1 death, 2 (5%) for other/unknown reasons. No discontinuation due to VF was reported. No predictors of BIC/FTC/TAF discontinuation were identified.
An increasing trend in CD4 count over 3 years was evidenced (p=0.095). A nadir CD4 count<200 cell/μL (compared with nadir>200, B: -55, 95%CI -96 - -13; p=0.011), injection drug users as a risk factor of HIV infection (versus others, B: -47, 95% CI -87 - -8; p=0.019) and a higher CD4 count at switch (per 100 cells/mL more, B: -15, 95% CI -22 - -9; p<0.001) were associated with a reduction in delta CD4 count at 12 months.
An increase in CD4-to-CD8 ratio over 3 years was evidenced (p<0.001). A history of AIDS (versus none, B: -0.10, 95% CI -0.18 - -0.01; p=0.037) and longer time of virological suppression (per 1 year more, B: -0.02, 95% CI - 0.02 - -0.01; p<0.001) were associated with a reduction in delta CD4-to-CD8 at 12 months.
Conclusions: BIC/FTC/TAF as switch strategy demonstrated high effectiveness, tolerability and safety in real-life.

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Outcomes in treatment experienced PLWH

OC 137 USE OF TENOFOVIR ALAFENAMIDE/EMTRICITABINE/BICTEGRAVIR (B/F/TAF) IN TREATMENT-EXPERIENCED PEOPLE LIVING WITH HIV. REAL-LIFE DATA FROM INFECTIOUS DISEASE UNIT OF ALESSANDRO MANZONI HOSPITAL IN LECCO

V. Morena, F. Conti, S. Pontiggia, C. Molteni, L. Bradanini, A. Pandolfo, S. Piconi

Infectious Diseases Unit, Alessandro Manzoni Hospital, Lecco (LC), Italy

Background: B/F/TAF represents a first choice combination for PLWH. Randomized clinical trials (RCTs) have demonstrated efficacy and tolerability of switching to B/F/TAF in virologically suppressed patients. Recent studies have also shown the maintenance of virological suppression even in patients with resistance mutations affecting the NRTI backbone of the regimen (including M184V or other thymidine analogue associated mutations). Here, we present the experience of our Unit with B/F/TAF switching in experienced PLWH with a complex treatment history.

Materials and Methods: This is an observational retrospective study. We included all treatment-experienced PLWH who had been treated with B/F/TAF for at least six months at time of data collection (23rd March 2023). We defined treatment-experienced all patients who received at least one other antiretroviral combination before switching to B/F/TAF. Aim of the study was to describe characteristics of study population, durability of B/F/TAF regimen and gaining or maintaining virological suppression after switch, especially in PLWH with an history of previous virological failures (VF)and resistance associated mutations (RAMs) at genotype resistance test (GRT). For patients with previous failures we considered GRT done at time of VF while for the others we considered GRT done before starting ART.

Results: Across all PLWH attending our Unit (n=767), 124 patients were included. Characteristics of study population are shown in Table 1. Median duration of HIV infection was 18 years (IQR 12-28) with a median duration of ART of 16 years (IQR 10-24). 111/124 patients had VL <50 cps/ml at time of switch to B/F/TAF. They received a mean of 2 different regimens (IQR 1-4) before switching and 26 of them were treated also with non-HAART regimens like zidovudine or didanosine in monotherapy. 39 (31%) experienced at least one VF and 9 of them failed to 2 or more regimens. GRT was available for 75 (60%) subjects. 23 showed RAMs affecting at least one drug class and 17 affecting 2 or more classes. No patients had INSTI resistance mutations. Timidine-associated mutations (TAMs) conferring resistance to NRTIs were seen in 21 cases with M184V in 17 of them.

Mean duration of B/F/TAF regimen was of 30 months (IQR 13-40). 120 PLWH (97%) gained or maintained virological suppression 6 months after switch. 4 patients showed HIV-RNA >50 cps/m l (3/4 with HIV-RNA between 50 and 200 cps/ml); 3 of them had a VL >50 cps/ml also before switching. 6 patients discontinued B/F/TAF; one because of viral failure, 2 for drug simplification and 3 for adverse events.

Discussion: Our data show that switching to B/F/TAF is well tolerated and effective in treatment-experienced PLWH, with a long and complex treatment history and also with RAMs and TAMs at genotype analyses. This results are in line with data from other studies. Prospective studies with a bigger study population and a longer follow-up time are needed in order to confirm these results.

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Outcomes in treatment experienced PLWH

OC 138 SAFETY AND EFFICACY OF DORAVIRINE-BASED REGIMENS IN PEOPLE LIVING WITH HIV: A REAL-LIFE MULTICENTRIC STUDY

C. Micali[1], Y. Russotto[2], G.F. Pellicanò[3], L. Panella[4], A. Albanese[5], L. Santoro[2], S. Sofia[6], G. Pantò[6], M. Coco[2], A. Guarneri[2], C. Iacobello[6], M.S. Paternò Raddusa[2], M. Ceccarelli[7], A. Marino[7], B.M. Celesia[8], B.S. Cacopardo[7], A. Montineri[9], C. Frasca[9], A. Colpani[10], A. De Vito[10], G. Madeddu[10], A. Alibrandi[11], E. Venanzi Rullo[2], G. Nunnari[2]

[1]Unit of Infectious Diseases, Department of Biomedical, Dental, Morphological and Functional Imaging Sciences, University of Messina, Messina, Italy, [2]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy, [3]Department of Human Pathology of the Adult and the Developmental Age "G. Barresi", University of Messina, Messina, Italy, [4]"Cutroni Zodda" Hospital, Barcellona Pozzo di Gotto, Messina, Italy, [5]"Papardo" Hospital, Messina, Italy, [6]"Azienda Ospedaliera per l'Emergenza Cannizzaro", Unit of Infectious Diseases, Catania, Italy, [7]Unit of Infectious Diseases, ARNAS Garibaldi, Nesima Hospital, Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy, [8]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy, [9]"G. Rodolico - San Marco" Hospital, Catania, Italy, [10]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [11]Unit of Statistical and Mathematical Sciences, Department of Economics, University of Messina, Messina, Italy

Background: Pivotal studies on Doravirine (DOR) showed its high tolerability and effectiveness, even on resistant strains. Therefore, DOR has been referred to as a cardiovascular-safe drug. However, data from real-life studies on safety and efficacy of DOR are lacking.

Methods: Retrospective multicenter cohort study, including 6 Italian HIV centers, evaluated adult treatment-experienced PLWH who switched to DOR-based regimens from June 2020 to June 2022. PLWHs with known resistance mutations to DOR were excluded. Clinical and laboratory data were collected 24 weeks before the switch, at the time of the switch and after 24 and 48 weeks.

Results: A total of 126 PLWHs were switched to a DOR-based regimen. 96 (76.2%) PLWHs were male, the median age was 51.59 ± 11.74 years. The main reasons for switching to DOR-based regimens were proactive switch (33.3%) and simplification (27.1%). 88.4% of PLWHs were switched to DOR/lamivudine (3TC)/tenofovir disoproxil fumarate (TDF), while in 11.6% of cases DOR was administered as a dual therapy with INSTIs [(6.1% with dolutegravir (DTG) and 5.2% with raltegravir (RAL)]. Of importance, a reduction of VL was observed, although it did not reach statistical significance, as well as a significant reduction in total cholesterol and triglycerides ($p < 0.004$ and 0.009, respectively). A slight increase in AST and ALT serum levels in two PLWHs was observed. No differences were observed in CD4+ and CD8+ count, CD4+/CD8+ ratio, azotemia and serum creatinine levels. We also observed an LDL serum levels reduction. Adverse events (AEs) were reported in 2 PLWHs and were characterized by the onset of a nodular rash in both arms and legs after 2 weeks of therapy in one PLWH and by the onset of a progressive paresthesia in both extremities of arms after one week of treatment in the other PLWH. In both cases the treatment with DOR was interrupted.

Conclusions: The present real-life study showed that DOR based regimens significantly reduced lipid levels. The virological efficacy of DOR along with its immunological, metabolic and safety profile are key elements for a proactive management of the cardiovascular risk.

Clinical approach to COVID in vulnerable populations

OC 139 EFFICACY AND SAFETY OF THERAPIES FOR COVID-19 IN PREGNANCY: A SYSTEMATIC REVIEW AND META-ANALYSIS

G. Guido[1], F. Di Gennaro[1], L. Frallonardo[1], F. V. Segala[1], R. De Nola[2], G.R. Damiani[2], E. De Vita[1], V. Totaro[1], M. Barbagallo[3], G. Liuzzi[4], E. Nicastri[4], A. Vimercati[2], E. Cicinelli[2], N. Veronese[3], A. Saracino[1]

[1]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area - (DiMePRe-J), University of Bari "Aldo Moro,"70124 Bari, Italy, [2]Clinic of Obstetrics & Gynaecology, University of "Aldo Moro," Bari, Italy, [3]Geriatrics Section, Department of Internal Medicine, University of Palermo, Palermo, Italy, [4]National Institute for Infectious Diseases 'Lazzaro Spallanzani' (IRCCS), Rome, Italy

Background: Clinical evidence suggests that pregnant women are more vulnerable to COVID-19, since they are at increased risk for disease progression and for obstetric complications such as premature labor, miscarriage, preeclampsia, cesarean delivery, fetal growth restriction, and perinatal death. Despite this evidence, pregnant women are often excluded from clinical trials, resulting in limited knowledge on COVID-19 management. Aim of this systematic review and meta-analysis is to provide better evidence on the efficacy and safety of available COVID-19 treatment in pregnant women.

Methods: Four authors searched major electronic databases from inception until 1st November-2022 for controlled trials/observational studies, investigating outcomes after the administration of anti-SARS-CoV-2 treatments in pregnant women affected by COVID-19. The analyses investigated the cumulative incidence of delivery and maternal outcomes in pregnant women, comparing those taking active medication vs standard care. Risk ratios (RRs) with 95% confidence intervals were calculated. Statistical significance was assessed using the random effects model and inverse-variance method. This systematic review and meta-analysis was conducted in accordance with the updated 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol has been registered in Prospero (number registration: CRD42023397445).

Results: From initially 937 non duplicate records, we assessed the full texts of 40 articles, finally including ten studies. In six studies, including 1627 patients, the use of casirivimab/imdevimab (CAS/IMD), remdesivir, and IFN-alpha 2b significantly decreased the need of cesarean section ((RR=0.665; 95%CI: 0.491-0.899; p=0.008; I 2 =19.5%;) (Table1, Figure 1). Treatments did not decrease the risk of preterm delivery, admission to neonatal ICU, or stillbirth/perinatal loss (p-values>0.50 for all these outcomes) and did not prevent the progression of disease towards severe degrees (k=8; 2,374 pregnant women; RR=0.778; 95%CI: 0.550-1.099; p=0.15; I 2 =0%). Moreover, the use of medications during pregnancy did not modify the incidence of maternal death in two studies. (Table 2).

Conclusions: To our analysis, CAS/IMD, remdesivir, and IFN alpha 2b reduced the number of cesarean sections but demonstrated no effect on disease progression and other obstetric and COVID-19 related outcomes. Unfortunately, due to lack of data, it was not possible to assess the impact of viral load in disease progression among pregnant women. In our systematic review, no major side effects were reported. Though, it is essential for the medical community to focus more on clinical trials and less on episodic case reports and case series, with standardization of fetal and maternal outcomes.

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Clinical approach to COVID in vulnerable populations

OC 140 SARS-COV2 INFECTION IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES IN THE OMICRON ERA: HOSPITALIZATION, NEED FOR MECHANICAL VENTILATION AND MORTALITY IN SERONEGATIVE AND SEROPOSITIVE POPULATION

V. Todisco[1], V. Menozzi[1], M. Pellegrino[1], S. Cantergiani[1], A. Spadoni[1], F. Romani[1], F. Bettelli[2], A. Santoro[1], C. Mussini[1], E. Franceschini[1]

[1]Malattie Infettive - Azienda Ospedaliero Universitaria Policlinico di Modena, [2]Ematologia - Azienda Ospedaliero Universitaria Policlinico di Modena

Background: Patients with hematological malignancies (HM) have a higher risk of developing a severe COVID-19 in terms of morbidity, hospitalization and mortality, regardless of their vaccination status. The aim of the study was to describe HM patients with SARS-CoV2 infection who were evaluated for anti-COVID-19 treatment comparing patients responder to vaccination to non-responders. The second aim was to identify risk factors for mechanical ventilation (MV).

Material and methods: Retrospective single-center study including patients with HM and SARS-CoV2 infection at AOU Policlinico of Modena from January 2022 to March 2023. Patients were evaluated for antiviral or monoclonal antibodies (mABs) treatment, according to national criteria. Independent sample T-test. Chi-square test and Fisher's test were used to evaluate the association of variables with the outcomes of interest. The Cox regression model was performed for survival analysis to identify risk factors associated with mortality.

Results: A total of 231 patients were included in the study. Baseline, clinical, SARS-CoV2 infection characteristics of the whole cohort and of seronegative and seropositive patients are described in table 1.

Overall, 83% were treated with at least one drug among antivirals or mABs. 33% of patients were hospitalized, 17% developed respiratory failure and 10% needed MV. Mortality rate was 3%, 8% and 10% at 30, 60 and 90-days, respectively. Serological status for SARS-CoV2 was available for 115 patients. 44 patients (19%) showed at least one negative serology test for SARS-CoV2 (< 33.8 BAU/ml) in the 3 months before the infection and were defined "non-responders".

Non-responder group were older, had a higher proportion of patients with a diagnosis of lymphoid neoplasm and were more frequently treated with anti-CD20 agents.

Moreover, a statistically significant difference between the two groups was found with regards to need of oxygen treatment and administration of MV. Furthermore, factors associated with MV at the univariate analysis were hypertension (OR 3.47; CI 1.32-9.09; p. 0.011), diagnosis of lymphoid neoplasm at the baseline (OR 2.75; CI 1.04 -7.23; p 0.041), anti-CD20 treatment (OR2.76; CI 1.17-6.51; p. 0.02), seronegative status(OR 3.19; CI 1.07-9.51; p. 0.038). 90-days mortality rate was two-fold higher in non-responders (21%) compared to the whole cohort (10%) but the difference did not reach statistical significance.

Conclusions: Hematological patients with SARS-CoV2 infection continue to have an high hospitalization and mortality rate also in the Omicron era. Furthermore, patients non-responder to vaccine showed an higher rate of oxygen need and mechanical ventilation compared to responder patients. At the univariate analysis a seronegative status increased threefold the risk of mechanical ventilation. At the multivariate analysis this result did not reach statistical significance probably due to the small sample size.

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Clinical approach to COVID in vulnerable populations

OC 141 ANTIBODY RESPONSE IN WOMEN VACCINATED AGAINST SARS-COV-2 DURING PREGNANCY AND RESPECTIVE BABIES AT BIRTH AND AFTER A NINE-MONTHS FOLLOW-UP

A. Proto[1], S. Agliardi[2], S. Renica[3], A. Pani[2], G. Gazzaniga[2], R. Giossi[2], M. Senatore[2], F. di Ruscio[3], C. Vismara[4], D. Campisi[4], F. Scaglione[2], S. Martinelli[1]

[1]Neonatology and Neonatal Intensive Care Unit, Niguarda Hospital, Milan, Italy, [2]Postgraduate School of Clinical Pharmacology and Toxicology, Department of Medical Biotechnology and Translational Medicine, Università degli Studi di Milano, Milan, Italy, [3]Postgraduate School of Microbiology and Virology, Department of Biomedical, Surgical and Dental Sciences, Università degli Studi di Milano, Milan, Italy, [4]Microbiology Unit, Niguarda Hospital, Milan, Italy

Background: The risk of severe disease and mortality in pregnant women and newborns is greater if compared to non-pregnant adults' risk, in case of SARS-CoV-2 infection. Vaccination against SARS-CoV-2 has been demonstrated to be safe during gestation. Nevertheless, there are no robust data about the antibody transmission from the mother to the newborn, its entity, and the persistence of the antibodies in babies' serum.
Methods: Participants were recruited at Niguarda Hospital of Milan, from May to November 2021.
We included pregnant women having received an anti-SARS-CoV-2 vaccination with mRNA vaccines during pregnancy and their newborns.
Serological IgG antibodies anti-S1-RBD were evaluated through a quantitative chemiluminescent-assay (Abbott) and information about vaccination timing was obtained.
Results: 98 women were included in the analysis. 24 mothers out of 98 received just one dose, while 74 received two doses. The geometric mean titer (GMT) of anti-S IgG is 417.8 AU/ml for babies and 746.5 AU/ml for mothers in the group of subjects who received just one dose. In the group of those who received two doses, the GMT was 5825.94 AU/ml for babies and 4979.00 AU/ml for mothers. A significant positive correlation ($p<0.001$) was found between maternal and neonatal serum levels at birth.
The relation between the gestational age and the serological titer of the newborn at birth is significant ($p<0.001$): the higher the gestational age when mothers received vaccination, the higher the serological titers of the respective newborns at birth (Tobit mixed-models regression).
Data for children over time were available for 79 babies at 3 months of life, 61 babies at 6 months, and 45 babies at 9 months. The birth antibody level decreases significantly over time ($p<0.001$).
During the follow-up, 34 children were infected with SARS-CoV-2. If we compare antibodies kinetics in the two groups of infants (infection vs no-infection), we observed that antibody titers decline was significantly slower in the infection-group ($p<0.001$).
Moreover, if we consider lactating women only in the no-infection group, we observed a slower decline in antibody titers in totally/partially breastfed babies if compared to formula-fed babies.
Conclusions: Our data suggest that:
1 The birth titer in children of mothers who received two doses of vaccine during pregnancy results equal to or higher than the mothers' titer.
2 There is a correlation between gestational age at vaccination and serological titer at birth.
3 SARS-CoV-2 infection can lead to an increase in the antibody titer even in the youngest.
4 The antibody titer reduction is progressive, but it seems to be slightly lower in breastfed babies.

Clinical approach to COVID in vulnerable populations

OC 142 SAFETY OF ANTIVIRAL THERAPY IN FRAGILE SARS COV 2 PAEDIATRIC PATIENTS

S. Bernardi[1], M. Di Giuseppe[1], L. Romani[1], F. Calo' Carducci[1], L. Cursi[1], L. Lancella[1], S. Mercadante[1], C. Tripiciano[1], M. De Luca[1], S. Chiurchiu'[1], A. Krzsyztofiak[1], R. Adorisio[1], A. Amodeo[1], G. Paglietti[1], L. Colagrossi[1], R. Scutari[1], C. Di Maio[1], C. Russo[1], P. Palma[1], V. Santilli[1], E. Manno[1], B. Rivalta[1], A. Campana[1], D. Perrotta[1], A. Antinori[2], E. Nicastri[2], P. Merli[1], B. Lucarelli[1], F. Galaverna[1], M. Becilli[1], T. Corsetti[1], F. Tangari[1], C.F. Perno[1], Villani[1], M. Raponi[1], F. Locatelli[1], L. Vallesi[1]

[1]Bambino Gesù Children's Hospital, [2]INMI National Institute Infectious Disease Lazzaro Spallanzani

Background : After three years of Pandemic it is now established that the use of antiviral therapy in SARS COV 2 infection is indicated for populations at risk of developing severe disease and persistence of viral replication.
In the paediatric age, treatment data relate to a few limited experiences with the use of both monoclonal Ab and antivirals.
Material and methods: From March 2021 to date, 520 fragile patients with SARS COV 2 infection have been treated at the Bambino Gesù Children's Hospital. 70 % of the categories treated were patients with primary or secondary immunodeficiency due to onco haematological pathology or post organ transplant treatment; 30 % were patients with congenital heart disease or chronic bronchopneumopathy or severe obesity.
344 patients were treated with monoclonal Ab: 79 (23%) were treated with Casirivimab- Imdevimab, 26 (7.5%) with Bamlaminiivab-Etesevimab , 94 (27.%) with Sotrovimab , 145 (42.5%) with Tixagevimab-Cilgavimab
176 patients were treated with antiviral therapy: 103 (58.5%) with Nilmatrevir/Ritonavir and 73 (41.5%) with Remdesivir.
Ab Monoclonal therapy was discontinued in two cases for rash and pruritus, and antiviral injection therapy with Remdesivir was discontinued in three cases: in one case for heart rhythm disturbances and in two cases for hypertransaminasemia. Nilmatrevir Ritonavir therapy was interrupted in three cases for nausea and vomiting
Conclusion: The antiviral therapy now available for SARS COV 2 infection has been shown to be safe in a group of paediatric patients. Cohort studies are needed to establish the true efficacy and paediatric-specific PK data will be needed.

Emerging issues in HIV-1 infection

OC 143 IMPACT OF COVID-19 IN TIME TO LINKAGE TO CARE (LTC) AND ART INITIATION IN THE ICONA COHORT

P. Piselli[1], A. De Vito[2], A. Tavelli[3], C. Cimaglia[1], A. Nappo[1], M. Farinella[4], L. Rancilio[5], L. Cosmaro[6], C. Muccini[7], C. Santoro[8], D. Segala[9], M. Trizzino[10], A. Caraglia[11], A. d'Arminio Monforte[3], A. Antinori[1], E. Girardi[1], G. Madeddu[2] for the ICONA Foundation Study Group and for the Working Group of the project "The impact of COVID-19 on the processes and outcomes of care of people with HIV"

[1]INMI L. Spallanzani IRCCS, Rome, [2]University of Sassari, Sassari, [3]Icona Foundation, Milan, [4]Circolo Mario Mieli, Rome, [5]Caritas Ambrosiana, Milan, [6]LILA, Milan, [7]IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, [8]University of Bari, Bari, [9]AOU di Ferrara, University of Ferrara, Ferrara, [10]AOU Policlinico "P. Giaccone", Palermo, [11]Minister of Health, Rome

Background and Objectives: SARS-CoV-2 pandemic heavily affected healthcare systems, potentially altering care for other relevant diseases, including HIV. Our objective was to analyse the trend of time from HIV diagnosis to linkage to care (LtC) and from LtC to ART initiation among people with HIV (PWH) enrolled in the ICONA cohort in 2010-2022, evaluating the impact of COVID-19.

Methods: Time to LtC was defined as the time from HIV diagnosis to first CD4, HIV-RNA determination or ICONA enrolment; time to ART was defined as the time from LtC to ART initiation. We consider rapid LtC (rLtC) a period of time ≤14 days from HIV diagnosis to LtC and rapid ART initiation (rART) a period of time ≤14 days from LtC to ART start. For PWH diagnosed after 2016 (universal ART), we performed a logistic regression analysis to investigate the association of year of diagnosis with rLtC and rART, adjusting for gender, age, nationality, area of residence, mode of HIV transmission, concurrent STD diagnosis (and CD4 and HIV-RNA at diagnosis for ART initiation).

Results: Among 12,310 patients considered, 81.2% were males, 74.7% Italians, 48.4% men-who-have-sex-with-men and 6.3% drug users; 710 (5.8%) with AIDS or acute infection at HIV-diagnosis were excluded in the final analysis. Therefore, among 11,600 PWH analysed, we observed a significant decrease over time to LtC, with less than 40% of PWH linked to care within 14-days in 2010-2012 and more than 65% in the last years (Fig.1A). Among 5,241 PWH diagnosed from 2016 onwards, a progressive increase of rLtC was observed over time up to 2019, slower in the first period of COVID-19 pandemic (Mar-Jun 2020) and recovered in 2022 (Fig.1B).

Similarly, we observed a progressive reduction of time to ART, with less than 30% in 2010-11 starting ART within 30-days from LtC to >90% in the last period (Fig.2A). In the analysis considering the period of universal ART, time to ART was progressively shortened with some fluctuations in 2021, fully recovered in 2022 with the higher chance of rART (aOR=5.26 vs 2016, Fig.2B).

Conclusions: A progressive reduction in time to LtC and time to ART initiation was observed over time from the introduction of universal ART. COVID-19 does not appear to have a major impact on LtC except in the period March-June 2020, with no relevant effect on the shortening of time to therapy starting. Monitoring COVID-19 indirect effects on health systems and preparing specific organization plans to reduce the impact of future waves or other pandemics on HIV management remains remarkable.

Project partially funded by Minister of Health (ref 4023). Associations involved in the project (in alphabetic order): ANLAIDS, Arcigay, Caritas, CICA, Circolo Mario Mieli, CNCA, Fondazione Villa Maraini, LILA, NPS Italia, PLUS, SIMM.

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Emerging issues in HIV-1 infection

OC 144 RISK OF COVID-19 IN-HOSPITAL MORTALITY IN PEOPLE LIVING WITH HIV COMPARED TO GENERAL POPULATION ACCORDING TO AGE AND CD4 STRATA: DATA FROM THE ICONA NETWORK

A. Giacomelli[1], R. Gagliardini[2], A. Tavelli[3], S. De Benedittis[4], V. Mazzotta[2], G. Rizzardini[5], A. Mondi[2], D. Barbanotti[4], S. Antinori[1], A. Vergori[2], A. Gori[6], M. Menozzi[7], L. Taramasso[8], F.M. Fusco[9], A. De Vito[10], G. Mancarella[11], G. Marchetti[4], A. d'Arminio Monforte[3], A. Antinori[2], A. Cozzi-Lepri[12] on behalf of COVID-19 ICONA study group

[1]III Infectious Disease Unit, ASST Fatebenefratelli Sacco, Milan, Italy, [2]Clinical and Research Infectious Diseases Department, National Institute of Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [3]Icona Foundation, Milan, Italy, [4]ASST Santi Paolo e Carlo, San Paolo Hospital, Unit of Infectious Diseases, Department of Health Sciences, University of Milan, Milan, Italy, [5]I Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [6]II Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, University of Milan, Milan, Italy, [7]Infectious Diseases Unit, Azienda Ospedaliero-Universitaria di Modena, University of Modena and Reggio Emilia, Modena, Italy, [8]Infectious Disease Clinic, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [9]UOC Infezioni Sistemiche e dell'Immunodepresso, AORN Ospedali dei Colli, P.O. "D. Cotugno", Naples, Italy, [10]Unit of Infectious Diseases, Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy, [11]Infectious Diseases Unit, SM Goretti Hospital, Sapienza University of Rome, Latina, Italy, [12]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, University College London, London, UK

Background: Some evidence suggests that people living with HIV (PLWH) are at higher risk of COVID-19 mortality when compared to the general population (GenPop). Our aim was to assess whether PLWH with COVID -19 had an increased risk of in-hospital mortality compared to the GenPop in the Italian setting, according to CD4 cell count (<vs ≥200 cell/mm3) and age strata (<vs ≥65 years).

Methods: A retrospective observational study was conducted in 19 Italian ICONA centers (February 2020-November 2022). Hospitalized PLWH and GenPop with a confirmed SARS-CoV-2 infection, matched by calendar period of enrolment were included. The main outcome of interest was in-hospital mortality. A competing risk unadjusted and adjusted by Fine-Gray Cox regression model with discharge as the competing event have been used to estimate the association between a 5 levels' exposure (GenPop <65 years vs GenPop ≥65 vs PLWH <65 and CD4 ≥200 vs PLWH <65 and CD4 <200 vs PLWH ≥65 years) and in-hospital mortality. Besides the calendar period, the model was further adjusted for age, sex, ethnicity, lung disease, and region of the enrolling site. A subanalysis including only patients with lung disease or PO2/FiO2<300 ad admission was also performed.

Results: 7,401 COVID-19 patients have been included in the study, 240 (3.2%) PLWH, and 7,161 (96.8%) GenPop. Characteristics of the study population are reported in Table 1. PLWH were younger [55 (IQR 46-62) vs 68 (55-80) years, p<0.001)] and more frequently male (77.7% vs 60.1%, p<0.001) when compared to the GenPop. PLWH showed a median CD4 cell count of 397 (IQR 154-626) cell/mm3 with 30.2% <200 cells/mm3 and 23.8% had an HIV-RNA >50cp/mL. The crude in-hospital mortality was higher in the GenPop group when compared to PLWH [1,283/7,161 (17.9%) vs 34/240 (14.2%)]. The unadjusted estimates of in-hospital mortality according to age and CD4 strata are reported in Figure 1. In the final Fine-Gray regression model (Table 2A), after adjusting for potential confounders, when compared to the GenPop <65 years a significantly higher risk of in-hospital death was observed for the GenPop ≥65 years [adjusted Subdistribution Hazard Ration (aSHR) 1.92 (95% CI 1.48-2.49)], PLWH <65 years with CD4 <200 [aSHR 5.90 (95% CI 3.49-9.98)] and PLWH ≥65 years [aSHR 1.99 (95%CI 1.05 -3.77)], whereas PLWH <65 with CD4 ≥200 did not [aSHR 1.13 (95%CI 0.53-2.39)]. Data were confirmed in the sub-analysis including only patients with documented pneumonia or PO2/FiO2<300 at admission (Table 2B).

Conclusions: PLWH with low CD4 count have an increased risk of COVID-19 in-hospital mortality. We found that in PLWH aged <65 with a CD4 cell count <200 cell/mmc, COVID-19 in-hospital mortality was 6-fold higher than GenPop, after controlling for the key confounding factors. The effect of low CD4 cell count seems to be mitigated in those aged ≥65 where the COVID-19 course is mainly age-drive.

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Emerging issues in HIV-1 infection

OC 145 PATIENT REPORTED OUTCOMES IN OLDER PEOPLE LIVING WITH/WITHOUT HIV IN THE GEPPO COHORT

A. Calcagno[1], M. Sandri[2], J. Milic[3], M. Ferrara[1], S. Nozza[4], S. Arsuffi[5], T. Lucchi[6], G.V. De Socio[7], G. Orofino[8], C. Mussi[9], A. Riva[10], G. Guaraldi[3], S. Calza[2], G. Di Perri[1], E. Focà[5]

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin; 2. Unit of Biostatistics and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, [3]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, [4]Unit of Infectious Diseases, San Raffaele Scientific Institute, Milan, [5]Unit of Infectious and Tropical Diseases, Department of Clinical and Experimental Sciences, ASST Spedali Civili di Brescia, University of Brescia, Brescia, [6]Geriatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, [7]Unit of Infectious Diseases, Department of Medicine and Surgery, University of Perugia, Perugia, [8]Unit of Infectious Diseases, "Divisione A", Amedeo di Savoia Hospital, ASL Città di Torino, [9]Centro di Valutazione e Ricerca Gerontologica, Chair of Geriatrics, University of Modena and Reggio Emilia, Modena, [10]Division of Infectious Diseases, Luigi Sacco Hospital, University of Milan, Milan

Introduction: A good health related quality of life (HRQoL) for people living with HIV (PLWH) is the ultimate goal for patients' care. Patient reported outcomes (PROs) are useful to explore factors associated with HRQoL, particularly in older PWH (OPWH) in whom these data are missing. The objective was to evaluate anxiety, depression and HRQoL in OPWH and older people without HIV (OPW/oH).

Material and Methods: This was a cross sectional study of participants of the GEPPO cohort including OPWH and community-dwelling controls aged ≥65 yrs (OPW/oH), enrolled between 2018 and 2021 and evaluated at yearly visit and with comprehensive geriatric assessment (including physical performance battery or SPPB). Inclusion criteria was availability of self-administered questionnaires including Center for Epidemiologic Studies Depression Scale (CES-D, ≥17 probable depression), Hamilton anxiety scale (HAM-A, <7 no, 8-14 mild, 15-23 moderate, ≥24 severe anxiety symptoms) and EQ-5D-5L. Data were described as average (± standard deviation) and compared through parametric-tests. The association between PROs and potential predictors were investigated using multivariable mixed-effect linear models: the covariates found significant in univariate analysis were entered into the multivariable models of Table 1.

Results: 289 OPWH and 76 OPW/oH patients were included: 224 and 24 (78% and 32%) males and mean age was 70 (±4.8) and 80 (±6.5) years, respectively. In OPWH the mean CD4 cell count was 655/mm3 (±260) and 220 patients (99%) had HIV RNA <50 copies/mL. The mean value of EQ-5D-5L score was significantly lower in OPWH compared to OPW/oH [729 (±319) vs. 884 (±128), respectively; p<0.001]; similar scores were found in CES-D [13.1 (±9.7) vs 13.8 (±8.5); p=0.6] and in HAM-A [8.4 (±7.6) vs. 7.7 (±5.7), p=0.5]. The results of multivariate analysis are shown in the Table.

Poorer physical function (lower grip strength and SPPB) was associated with worse quality of life (p values <0.001 and 0.011, respectively) and depressive symptoms (p values <0.001 for both) while a high number of falls was associated with poorer quality of life and higher anxiety.

Conclusions: Depressive and anxiety symptoms are commonly reported by OPWH that also show poorer quality of life as compared to age-matched controls. Virological control, comorbidities management and physical exercise are among the critical aims of optimal care in OPWH.

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Emerging issues in HIV-1 infection

OC 146 IMPLEMENTING AN ELECTRONIC PATIENT-REPORTED OUTCOMES (EPROS) SYSTEM IN PLWH MANAGEMENT: EXPERIENCE OF ICONA COHORT

A. Tavelli[1], L. Cosmaro[2], N. Gianotti[3], R. Gagliardini[4], V.G. Calvino[5], F. Bai[6], G. Guaraldi[7], F. Vichi[8], I. Fanti[1], M. Cernuschi[9], A. Antinori[4], A. d'Arminio Monforte[6], A. Cingolani[10]

[1]ICONA Foundation, Milano, [2]Fondazione LILA Milano, Milano, [3]Hospital San Raffaele, Milano, [4]INMI "L.Spallanzani", Roma, [5]Anlaids Onlus-ETS, Roma, [6]San Paolo Hospital, Milano, [7]University of Modena and Reggio Emilia, Modena, [8]Santa maria Annunziata Hospital, Firenze, [9]Associazione Solidarietà Aids, Milano, [10]Fondazione A. Gemelli IRCCS, Roma

Background: Care for people living with HIV (PLWH) passes towards the ability to collect individual's health and well-being reported directly by the patients (patient reported outcomes, PROs). Here we describe implementation of a mobile app (e-QoL) to collect PROs in ICONA cohort, in order to integrate the longitudinal data collection of the cohort and patients self-reported measurement.

Materials and Methods: e-QoL is a mobile app developed with Flutter framework for Android and iOS to provide a tool for collecting ePROs and integrating the data collection with the pre-existing Icona web application. Pts specific login credentials, are centrally set in the Icona dataset. No questionnaire data is saved on the mobile device of PLWH. Each patient that agrees to participate, receives the login credentials and a brochure with instructions. The app is structured in 3 areas: 1) informative section on the importance of PROs, 2) main section collecting 9 validated questionnaires: EQ-5D-5L, PHQ-9, GAD-7, ADH, AUDIT-C, HIVDQoL, HIVTSQ, HIVSRQ, W-BQ16, 3) a "Daily" section for reporting weight, blood pressure, waist circumference and smoking status. All questionnaires should be complete once year, the EQ-5D-3L every 6 months. In this analysis, the results from the first year of implementation were reported.

Results: From 2.2022 to 2.2023 10 ICONA centers started the recruitment of PLWH in the Icona eQoL app. 106 out of 4012 PLWH followed in the 10 centers filled at least 1 questionnaire, for a total of 718 questionnaires. 11.9% of participants were female, median age 45 y (IQR 36-56), 76% MSM, 13% previous AIDS diagnosis, 93% suppressed HIV-RNA, median CD4 cell count 674 cell/ccm (526-979). To be ART experienced (p=0.02), MSM (p<0.001), and university education level (p=0.001) were associated with higher probability of downloading eQoL App. 53% of PLWH reported a very good/optimal general QoL and 47% very good/optimal health status (HIVDQoL questionnaire). The treatment satisfaction score was 95.3% (IQR 88.9-98.6) (HIVTSQs). A moderate/severe depression was reported in 21% of PLWH (PHQ-9) and a moderate/severe anxiety in 17% (GAD7). An analytical description of the results for the questionnaire collected is shown in table 1.

Conclusions: ePROs can be an important tool for management of PLWH, and their implementation in observational research setting could identify specific profile of PLWH, providing causal pathways to clinical outcomes, but it needs more specific efforts for adequate implementation. People with technological or language barriers may be ones with higher burden of unmet needs and may need assistance to complete them. The first year of the electronic collection of PROs in ICONA cohort documented mental health disorders despite high level of general QoL and health status. These data can help to inform interventions that ensure long-term retention in care and maintenance of good physical and emotional health.

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Novel clinical and epidemiological aspects of viral hepatitis

OC 147 HDV REPLICATIVE ACTIVITY PARALLELS THE PRODUCTION OF THE THREE HBSAG FORMS (LARGE, MIDDLE AND SMALL HBSAG) AND ITS PATHOGENETIC IMPACT IS EXACERBATED BY CONCOMITANT HBV REPLICATION

L. Duca[1], A. Olivero[2], L. Piermatteo[1,3], S. D'Anna[1], G.Torre[1], E. Teti[4], A. Di Lorenzo[4], V. Malagnino[4], M. Iannetta[4], L. Baiocchi[5], S. Francioso[5], I. Lenci[5], F. Ceccherini-Silberstein[1], M. Milella[6], A. Saracino[6], A. Ciancio[2], L. Sarmati[4], M. Rizzetto[2], G.P. Caviglia[2], V. Svicher[1,3], R. Salpini[1]

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Department of Medical Sciences, University of Turin, Turin, Italy, [3]Department of Biology, University of Rome Tor Vergata, Rome, Italy, [4]Department of Systems Medicine, Infectious Disease Clinic, Tor Vergata University, Rome, Italy, [5]Hepatology Unit, Policlinico Tor Vergata, Rome, Italy, [6]Clinic of Infectious Diseases, Department of Biomedical Sciences and Human Oncology, University of Bari "Aldo Moro," Bari, Italy

Background: HBV surface proteins (HBsAg) enable the morphogenesis of HDV progeny and entry into hepatocytes. Total HBsAg is composed by 3 different forms: Large-HBs (L-HBs), Middle-HBs (M-HBs), and Small-HBs (S-HBs). Here, we investigate the still unexplored levels of the different HBs forms in the setting of HDV coinfection and their correlation with the interplay between HDV and HBV.

Methods: This study includes 160 plasma samples from patients with HDV-HBV chronic infection (92.5% HBeAg negative, 31.3% drug-naïve) Total HBsAg is measured by COBAS HBsAgII assays (Roche Diagnostics) while ad-hoc designed ELISAs are used to quantify L-HBs, M-HBs, S-HBs (Beacle Inc).

Results: Patients have a median (IQR) serum HDV-RNA and total HBsAg of 5.1 (3.4-6.1) log IU/ml and 5,716 (1,372-10,887) IU/ml, respectively. ALT >40U/L is observed in 76.9% (median [IQR]: 87 [67-136) U/L] and 63.8% is cirrhotic. The median (IQR) levels of S-HBs, M-HBs and L-HBs are 3,984 (637-6,993), 1,147 (141-2,299) and 2.3 (0.2-6.5) ng/ml, respectively. A positive correlation is revealed for serum HDV-RNA with the levels of the 3 HBs forms (Rho=0.42, 0.46 and 0.39 for S-, M- and L-HBs, respectively; P<0.001 for all), supporting a direct correlation between HDV replicative activity and HBs form production.

Focusing on 50 drug-naïve patients, 35 are characterized by HDV+HBV codominance (median [IQR] serum HDV-RNA and HBV-DNA of 5.2 [4.5-5.9] and 2.3 [3.1-4.0] logIU/ml), while 15 have an exclusive HDV replication despite no treatment (median [IQR] serum HDV-RNA: 5.2 [4.0-5.9] logIU/ml and HBV-DNA <LLOD for all). Patients with HDV+HBV codominance show higher levels of S-, M- and L-HBs than patients with exclusive HDV replication (median [IQR]: 5123 [3863-8066] vs 2155 [563-6274] for S-HBs; 1606 [465-3001] vs 982 [55-2666] for M-HBs and 2.8 [0.2-6.3] vs 1.4 [0.1-5.5] ng/ml for L-HBs). Notably, a more intensive cytolytic activity is revealed in patients with exclusive HDV replication (median [IQR] ALT: 109 [63-222] vs 71 [48-97] U/L, P=0.03) corroborating the key role of HDV replication in driving pro-inflammatory stimuli. Conversely, a higher proportion of patients with cirrhosis is observed in HBV+HDV codominance group, highlighting the contribution of HBV replication (even at low level) in accelerating liver disease progression (68.8% vs 20%, P=0.04). Result confirmed by multivariable analysis after adjusting for demographic and virological parameters (OR [95%CI]: 22.2 [1.7-291], P=0.02).

Conclusion: In chronic HDV coinfection, abundant levels of the 3 HBs forms support an enhanced burden of HDV replication and their composition varies according to the interplay existing between HDV and HBV. Such interplay can modulate the progression of liver disease and its definition is critical to identify patients in whom antiviral treatment should be prioritized.

Novel clinical and epidemiological aspects of viral hepatitis

OC 148 MANAGEMENT OF ANTIVIRAL PROPHYLAXIS IN PATIENTS WITH RESOLVED HBV INFECTION RECEIVING IMMUNOSUPPRESSIVE TREATMENT

C. Sorace[1], L. Campogiani[1], G. De Simone[1], N. Braccialarghe[1], C. Aguglia[1], E. Teti[1], L. Sarmati[2], A.M. Geretti[2]

[1]Clinical Infectious Disease, Tor Vergata Hospital, Rome, Italy, [2]Clinical infectious disease, Department of System Medicine, Tor Vergata University, Rome, Italy

After resolution of active infection,HBV persists as covalently closed circular DNA (cccDNA) in the nucleus of hepatocytes. Immunosuppression may cause HBV reactivation(HBV-R) in people who are HBSAg negative with positive anti-HBc,with or without detectable anti-HBs.Risk of HBV-R is related to the underlying condition and immunosuppressive regimen and may be classified as high(>10%),moderate (1-10%) or lo (<10%).Antiviral prophylaxis alongside laboratory monitoring is recommended to reduce the risk of HBV-R.However, European guidelines recommend the use of entecavir (ETV) or tenofovir (TDF) over lamivudine (LAM). Indications on how to screen,monitor and treat immunosuppressed patients with risk of HBV reactivation lack consistency.The aim of this study was to audit the clinical practice of our outpatient clinic for HBV prophylaxis.Our current practice is that patients typically receive LAM and undergo blood tests every 3 months and a clinical visit every 6 months.

Based on our population size, we calculated that a random sample of 100 patients would provide reliable audit estimates. We retrospectively identified the last consecutive 100 visits scheduled from October 2022 backwards at the Infectious Diseases Clinic of Policlinico Tor Vergata.Data were collected from clinical charts and the hospital electronic platform for laboratory tests.

Among 100 patients,mean age was 67 years;60% were males;88% were born in Italy.The most common cause of immunosuppressive treatment was hematological disease (81%):18/81 (22.2%) patients received hematopoietic stem cell transplantation (HSCT, 13 allogenic , 5 autologous). At baseline, 47% had positive anti-HBc and anti-HBs,11% had isolated anti-HBc, and 15% had isolated anti-HBs. HBV-R risk was classed as high in 38%, moderate in 53%, and low in 9%.

A total of 95 patients received antiviral prophylaxis,92% with LAM and 6% with ETV;a further 2% switched from LAM to ETV, one because of baseline HBV-DNA <10 U/ml and the other because of poor gastrointestinal tolerability of LAM.During follow-up, 2 patients in the high-risk HBV-R group experienced a single detection of HBV-DNA (target detected <10 UI/ml) while receiving LAM.In one case LAM was continued, in the other LAM was switched to ETV, both had undetectable HBV-DNA during follow-up.

Prophylaxis was discontinued in 12 patients,a median of 2 years after discontinuation of immunosuppressive therapy in the HBV-R high-risk group and 1 year in the moderate-risk group. During subsequent follow-up, after 4 months,one patient had a single HBV-DNA detection (target detected <10 UI/mL), which resolved without treatment.

In our outpatient clinic,no HBsAg reactivation were detected in patients receiving antiviral prophylaxis with LAM and after scheduled suspension of prophylaxis.Data from this audit were used to improve our clinical practice in relation to the frequency of follow-up to produce updated internal guidelines, tailoring treatment strategy to HBV-R risk.

Novel clinical and epidemiological aspects of viral hepatitis

OC 149 HDV INFECTION IS STABLE IN CENTRAL ITALY ACROSS THE LAST TWO DECADES AND IS CHARACTERIZED BY THE CIRCULATION OF MULTIPLE HDV SUB-GENOTYPES 1 WITH A DIFFERENT PRO-INFLAMMATORY POTENTIAL

R. Salpini[1], L. Piermatteo[1,2], G. Torre[1], S. D'Anna[1], S. Khan[1], L. Duca[1], A. Bertoli[1,3], V. Malagnino[4], P. Paba[3], M. Ciotti[3], I. Lenci[5], S. Francioso[5], C. Paquazzi[6], M. Lichtner[7], C. Mastroianni[7], F. Santopaolo[8], G. De Sanctis[9], M. Marignani[6], A. Pellicelli[10], G. Galati[11], A. Moretti[12], G. Colucci[13], K. Casinelli[14], L. Caterini[15], N. Iapadre[16], G. Parruti[17], I. Vecchiet[18], M. Paoloni[19], S. Grelli[3], F. Ceccherini-Silberstein[1], L. Sarmati[4], V. Svicher[1]

[1]Tor Vergata University, Department of Experimental Medicine, Rome, Italy, [2]Tor Vergata University, Department of Biology, Rome, Italy, [3]Tor Vergata University Hospital, Virology Unit, Rome, Italy, [4]Tor Vergata University Hospital, Infectious Diseases Unit, Rome, Italy, [5]Tor Vergata University Hospital, Hepatology Unit, Rome, Italy, [6]S.Andrea Hospital, Rome, Italy, [7]La Sapienza University, Rome, Italy, [8]Internal Medicine and Gastroenterology-Hepatology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [9]"Umberto I" University Hospital, Rome, Italy, [10]Liver and Transplant Unit, San Camillo Forlanini Hospital, Rome, Italy, [11]Internal Medicine and Hepatology Unit , University Campus Bio-Medico, Rome, Italy, [12]San Filippo Neri Hospital, Rome, Italy, [13]Nuovo Regina Margherita Hospital, Spaziani Hospital, Rome, Italy, [14]Infectious Disease Unit, Spaziani Hospital, Frosinone, Italy, [15]Belcolle Hospital, Viterbo, Italy, [16]San Salvatore Hospital, L'Aquila, Italy, [17]Pescara General Hospital, Pescara, Italy, [18]Clinic of Infectious Diseases, Department of Medicine and Science of Aging, University "G. d'Annunzio" Chieti-Pescara, Chieti, Italy, [19]Infectious Diseases Unit, Avezzano General Hospital, Avezzano, Italy

Background: In Italy, HDV-prevalence and its fluctuations over time are controversial while an extensive characterization of HDV-infected patients (pts) is missing. Here, we assess HDV-seroprevalence in a large cohort of HBsAg-positive pts, followed in Central Italy over time, and the epidemiological/virological features of HDV-infected pts.

Methods: This study included 1579 consecutive and well-characterized HBsAg-positive pts, followed in different clinical centers of Central Italy from 2005 to 2022. Factors (demographics, transaminases, HBeAg status) correlated with the lack of HDV screening were defined by multivariable model. HBV genotypes and HDV sub-genotypes were defined by phylogenetic-analysis.

Results: Most HBsAg-positive pts were male (67%) and Italian (59.4%) with a median (IQR) age of 47 (35-60) years. 75% of pts were HBeAg-negative, median (IQR) serum HBV-DNA and HBsAg were 3.1 (2.8-4.1) IU/ml and 3499 (618-11662) IU/ml, while median ALT was 42 (26-78) U/L.

Overall, 45.3% (715/1579) received HDV-screening with an increasing temporal-trend: 17.1% (2005-2010), 43.2% (2011-2015), 56.5% (2016-2019), 75.8% (2020-2022), suggesting higher awareness for HDV-screening in recent years. By multivariable model, normal ALT was the only independent factor significantly correlated with the lack of HDV-screening (OR [95%CI]: 1.71 [1.29-2.30], P<0.001).

Notably, 13.4% (96/715) of HDV-screened pts resulted anti-HDV+ with a stable temporal trend: 10.7% (2005 -2010), 15.6% (2011-2015), 10.8% (2016-2019), 10% (2020-2022). Among them, 80.5% had detectable HDV-RNA (median [IQR]: 4.6 [3.6-5.6] log copies/ml) with altered ALT in 89.3% (median [IQR]: 92 [62-177] U/L) and cirrhosis in 75%.

Anti-HDV positivity was higher in pts from East Europe than from Italy (23.6% vs 12.9%, P=0.002) and stable over time in both groups. Notably, anti-HDV+ pts from East Europe were younger (44 [37-54] vs 53 [47-62] years, P<0.001) with higher HDV-RNA (4.8 [3.6-5.8] vs 3.9 [1.4-4.9]copies/ml, P=0.016) and HBsAg (9,461 [4,159 -24,532] vs 4,447 [737-13,336] IU/ml), P=0.032), indicating more intense HDV replicative activity.

By phylogenetic analysis, we found a more marked dominance of HBV genotype D in Anti-HDV+ respect to Anti-HDV negative pts (82.8% vs 59.5%, p<0.001), supporting a preferential circulation of HDV in association with HBV D-genotype in Italy. Even more, phylogenetic analysis revealed the circulation of HDV sub-genotype 1a (25.9%), 1b (33.4%), 1c (25.9) and 1d (14.8%). Notably, sub-genotype 1a and 1c correlated with 3xULN ALT compared to 1b and 1d (75% versus 27.3%, P=0.039).

Conclusions: The awareness to request HDV-screening is increasing over time even if some gaps persist to achieve HDV-screening in all HBsAg-positive pts. The prevalence of HDV infection remains stable in both foreign and Italian pts over time. The detection of different sub-genotypes, triggering variable inflammatory stimuli, supports the need to expand HDV molecular characterization.

Novel clinical and epidemiological aspects of viral hepatitis

OC 150 PREVALENCE AND OUTCOME OF HEPATITIS DELTA VIRUS (HDV) INFECTION AMONG PERSONS LIVING WITH HIV (PLWH) IN ITALY: THE DELTA-ICONA STUDY

M. Puoti[1,2], R. Salpini[3], A. Tavelli[4], L. Piermatteo[3], S. D'Anna[3], S. Carrara[5], V. Malagnino[6], V. Mazzotta[7], G. Brancaccio[8], G.B. Gaeta[9], G Marchetti[10,11], E. Rosselli Del Turco[12,13], C.F. Perno[14], V. Svicher[3], A. d'Arminio Monforte[4] for Icona Foundation Study Group

[1]University of Milano Bicocca, School of Medicine, Milan, Italy, [2]ASST GOM Niguarda, Infectious Diseases, Italy, [3]University of Rome Tor Vergata, Department of Experimental Medicine, Italy, [4]Icona Foundation, Milano, Italy, [5]INMI, Unity of Microbiology and Biobank, Roma, Italy, [6]University of Rome Tor Vergata, Department of Medicine of Systems, Clinical Infectious Diseases, Rome, Italy, [7]INMI, Clinical and Research Infectious Diseases Department , Rome, Italy, [8]University of Padua, Department of Molecular Medicine, Padua, Italy, [9]University L. Vanvitelli, Infectious Diseases Unit, Naples, Italy, [10]ASST Santi Paolo e Carlo, Clinic of Infectious Diseases, Milano, Italy, [11]University of Milano, Department of Health Sciences, Milano, Italy, [12]Alma Mater Studiorum Bologna University, Department of Medical and Surgical Sciences, Bologna, Italy, [13]IRCCS Azienda Ospedaliero Universitaria S. Orsola- Malpighi, Infectious Diseases Unit, Bologna, Italy, [14]Bambino Gesu Pediatric Hospital, Rome, Italy

Background: The prevalence and outcome of Delta infection among PLWH in different geographical and behavioral settings is poorly studied. Further, HDV-RNA pos PLWH may undergo clinical progression faster than HIV neg patients. We studied the prevalence and outcome of HDV infection with and without HDV viremia in HBsAg pos PLWH in the ICONA cohort.

Methods: All HBsAg-pos PLWH with a stored plasma sample were included. Anti-HDV was detected by Liaison XL Murex Anti-HDV assay; in case of anti-HDV positivity, HDV-RNA was quantified by Robogene v.2 assay. We compared demographic and clinical data between different groups:

1- HBsAg-pos /anti-HDV neg vs. HBsAg-pos/anti-HDV pos

2- anti-HDV pos/HDV-RNA neg vs. anti-HDV pos/HDV-RNA pos.

Baseline was the date of the first HDV serology/virology test. The time to and predictors of Liver Related Hard Outcome (LRHO; decompensated cirrhosis, HCC, liver transplantation, liver-related death) according to HDV status were identified. Chi-squared test and Wilcoxon rank sum test were used to compare clinical and demographical variables between groups. Cox multivariable analyses were fitted to identify the risk of LRHO according to 4 groups of HBsAg pos PLWH: anti-HDV neg vs. Anti-HDV pos/HDV-RNA pos vs. Anti-HDV pos/HDV-RNA neg vs. Anti-HDV pos/HDV-RNA unknown.

Results: A total of 1,028 out of 18,285 PLWH (5.6%) displayed at least 1 HBsAg-pos test. Among these, 809 were screened for anti-HDV: 152 (18.8%) showed anti-HDV reactivity. HDV viremia was detected in 63/95 (68%) tested anti-HDV pos PLWH.

Anti-HDV pos were less frequently female (7,9% vs 18,1%), more frequently IDU (67,1 vs 15,8%), more frequently anti HCV pos (66 vs 16%), less frequently HCV-RNA pos (11 vs 15%) and more frequently showed FIB-4 >3,25 (25 vs 11%) than HBsAg pos/anti-HDV neg PLWH (Table 1).

HDV-RNA pos were more frequently Italian (97% vs 72%) and more frequently with a FIB4 >3,25 (34 vs 9.7%) compared with HDV-RNA neg (Table 2).

Over a median follow-up of 5.1 (2.0-9.9) years, a total of 37 LRHO occurred in 736 HBsAg pos patients with >=1 follow-up after first HDV-screening.

By Kaplan-Meier curves, the 5- years overall cumulative probability of LRHO was 4.2% (95%CI 2.8-6.3); 2.0% (1.0 -3.9) for anti-HDV neg, 11.0% (4.1-27.6) for anti-HDV pos / HDV-RNA missing, 12.0% (4.0-32.8) for anti-HDV pos / HDV-RNA neg and 14.8% (7.3-28.7) for anti-HDV pos / HDV-RNA pos (log-rank p<0.01).

Anti-HDV pos/HDV-RNA pos PLWH showed an unadjusted 6.60 (95%CI 3.08-14.14) fold higher risk than anti-HDV neg HBsAg pos PLWH.

After controlling for baseline factors at time-fixed covariates, alcohol consumption, baseline CD4 count, anti-HCV status, this association was attenuated but the effect size was still remarkable: aHR = 4.08 (95%CI 1.69-9.86) (Table 3).

Conclusions: Even if HDV circulation among PLWH is not so extended, HDV screening is mandatory, as its presence is associated with severe liver outcomes, and new therapies are approaching.

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Antiretroviral therapy

P 1 HIV-1 RNA LEVELS IN SEMEN OF PEOPLE ON "SHORT-CYCLE" ANTIRETROVIRAL THERAPY

M. Lanzafame[1], A. Delama[1], D. Fait[1], L. Collini[2], S. Vento[3]

[1]Unit of Infectious Diseases,Ospedale Santa Chiara, Trento, Italy, [2]Unit of Microbiology, Ospedale Santa Chiara,Trento, Italy, [3]Faculty of Medicine, University of Puthisastra, Phnom Penh, Cambodia

Background: Short-cycle antiretroviral therapy (ART), whereby virally suppressed people living with HIV (PLWH) switch to 4 or 5-days-on and 3 or 2-days-off maintenance treatment, has been shown to be a safe and effective alternative to standard daily treatment in a randomised clinical trial and other small, not randomised,studies. Pharmacokinetic analyses showed low or undetectable plasma drug levels in the "off" period in some participants, without virological failure.

PLWH on daily ART with suppressed plasma HIV RNA are advised that they can have unprotected sexual intercourse without transmitting the virus. To the best of our knowledge, no data have been reported about seminal HIV RNA shedding in people on short-cycle ART.

Material and Methods: We evaluated HIV RNA levels in the seminal fluid of seven virologically suppressed PLWH (all males),after a written informed consent, on different short-cycle antiretroviral regimens (Table 1). They were on short cycle therapy for a mean of 33.4 months (range 9-43 months). At the time of sample collection, four patients were taking ART from Monday to Thursday while three from Monday to Friday. Semen samples (collected through masturbation) and blood samples were collected on Monday, the day after the off period 1 to 12 hours before pill's oral intake. All people were asymptomatic for sexually transmitted infections (STI) and screening tests for STI were negative at the same time of plasma and seminal HIV RNA quantification.All patients had avoided sexual intercourse for 48 hours before sample collection, and samples were processed within one hour of collection. To obtain seminal plasma, semen was centrifuged at 2,800 rpm for 10 min. HIV RNA in seminal plasma was measured in copies/mL using the Xpert® HIV-1 Viral Load assay manufactured by Cepheid (Milan, Italy). The analysis was performed twice for each individual at interval of three months.

Results: All patients had plasma HIV RNA <20 copies/ml and undetectable HIV RNA in seminal fluid at both time points.

Conclusions: HIV shedding in genital fluids despite plasma viral suppression has been reported and can be partially explained by HIV replication in locally infected cells. The presence of an STI or local inflammation has been associated with HIV shedding in the genital tract. It may be that, similarly to blood, HIV rebound in genital fluids could observed after an eclipse phase of 1-7 days or even longer after the interruption of an effective therapy; this is particularly evident in subjects with a long history of virological suppression. In fact, in ART interruption studies the resumption of viral replication occurred after a 5-8 day latency. Our results, limited by the low number of individuals studied and the fact that they were all males, could prompt further studies on this important issue.

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Antiretroviral therapy

P 2 EFFICACY AND SAFETY OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE IN PEOPLE LIVING WITH HIV-1 AGED OVER 65 YEARS

L. Calza[1], V. Colangeli[1], D. Riccucci[1], C. Rigamonti[1], D. Marzolla[1], I. Bon[2], P. Viale[1]

[1]Unit of Infectious Diseases, [2]Unit of Microbiology, IRCCS S.Orsola Hospital, University of Bologna, Bologna, Italy

Clinical trials of triple regimen Bictegravir/Emtricitabine/Tenofovir Alafenamide (BIC/F/TAF) demonstrated potent efficacy and favourable safety in both antiretroviral therapy-naïve and -experienced patients, but data about older people are still lacking.

Methods: Retrospective cohort study evaluating records from HIV-infected patients aged ≥65 years at our HIV Clinic who started BIC/F/TAF between January 2019 and December 2021. Eligible patients were antiretroviral therapy-naive or -experienced PLWHIV with 48 weeks of follow-up data and no known resistance mutations for bictegravir, emtricitabine and tenofovir. The primary endpoint was virological efficacy at week 48. The impact of switching to BIC/F/TAF on drug-drug interactions (DDIs) and safety parameters was also assessed.

Results: Inclusion criteria were met by 69 patients: 38 naive and 31 experienced. Mean age was 74.6 years (range, 65-88), 86% were men, and 95% were Caucasian, In naive patients, mean CD4+ T lymphocyte count was 317 cells/mm3, mean log10 HIV RNA was 4.25, and 15 (39%) had an AIDS diagnosis. In experienced patients, mean CD4+ T lymphocyte count was 577 cells/mm3, 28 (90%) had HIV RNA <50 copies/mL, 10 (32%) had an AIDS diagnosis. The most common reason for switch in experienced patients was simplification (in 44% of cases), followed by toxicity (30%), and DDIs (26%). After 12 months, 62 patients (89.8%) had HIV RNA <50 copies/mL: 33 (86.8%) naive and 29 (93.5%) experienced. Seven patients discontinued BIC/F/TAF: two for virological failure, three for adverse events and two for missing data. A genotype resistance testing was performed in both patients with virological failure (HIV RNA 1095 and 4470 copies/mL) and did not show any resistance mutations for NRTIs or integrase inhibitors. Fourty-six potential DDIs were identified in 39 (57%) patients at baseline and were resolved after switching to BIC/F/TAF. Treatment-related adverse events occurred in 18 (26%) patients (all grade 1-2) but there were only three cases (4.3%) of treatment discontinuation because of anxiety and sleeping disturbances (in two cases) or gastrointestinal symptoms (in one case).

At month 12, mean change (+ SD) in CD4+ T lymphocyte count was +156 (+104) cells/mm3 in naive patients and +49 (+27) cells/mm3 in experienced patients. Overall, mean variations (+SD) in creatinine, total cholesterol and triglycerides were +0.18 (+0.11) mg/dL, -19 (+10) mg/dL, and -32 (+27) mg/dL, respectively. At month 12, mean change (+SD) in body weight was +2.23 (+1.67) Kg (p=0.209) in naive patients and +1.47 (+0.92) Kg (p=0.447) in experienced patients.

Conclusion: In this real-world cohort, BIC/F/TAF was associated with high virological efficacy, good tolerability profile, and avoidance of DDIs among antiretroviral therapy-naive or -experienced PLWHIV aged over 65 years. These data support use of BIC/F/TAF as a treatment option in older patients with HIV infection.

Antiretroviral therapy

P 3 REAL-WORLD DATA ON THE EFFECTIVENESS AND SAFETY OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (B/F/TAF) IN PEOPLE LIVING WITH HIV (PLWH): 24-MONTH RESULTS OF THE ITALIAN BICSTAR COHORT

A. Saracino[1], S. Rusconi[2], D. Canetti[3], V. Esposito[4], E. Quiros-Roldan[5], B. Candelaresi[6], G. Marchetti[7], M. Andreoni[8], A. Antinori[9], A. Marongiu[10], L. Albini[11], R. Caldera[11], G. Forcina[11], G. Di Perri[12]

[1]Division of Infectious Diseases, Bari University Hospital, University of Bari, Bari, Italy, [2]Infectious Diseases Unit, ASST Ovest Milanese - University of Milan, Milan, Italy, [3]Clinic of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [4]Infectious Diseases and Gender Medicine Unit D. Cotugno Hospital-A.O. dei Colli, Naples, Italy, [5]Division of Infectious and Tropical Medicine, ASST Spedali Civili, Brescia, Italy, [6]Infectious Diseases Clinic, Department of Biological Sciences and Public Health, Marche Polytechnic University, Ancona, Italy, [7]Clinic of Infectious Diseases, Department of Health Sciences, University of Milan, "ASST Santi Paolo e Carlo", Milan, Italy, [8]Infectious Diseases Clinic, University Hospital "Tor Vergata", Rome, Italy, [9]HIV/AIDS Department, National Institute of Infectious Diseases, L. Spallanzani, IRCCS, Rome, Italy, [10]Gilead Sciences Europe Ltd, Stockley Park, Uxbridge, UK, [11]Gilead Sciences Srl, Milan, Italy, [12]Department of Medical Sciences, Infectious Diseases, University of Turin, Turin, Italy

Background: BICSTaR (GS-EU-380-4472) is a prospective, multi-country, observational cohort study evaluating the effectiveness and safety of B/F/TAF in routine clinical care in antiretroviral therapy (ART)-naive (TN) and ART-experienced (TE) PLWH. Here we present the month 24 (M24) results from the Italian cohort.

Material and Methods: The analysis set consisted of PLWH initiated on B/F/TAF in routine care with at least one follow-up. Outcomes of interest were viral suppression (HIV-1 RNA <50 cp/mL; missing/discontinuation=excluded [M=E] and discontinuation=failure [D=F] analyses), treatment persistence, weight change, and drug-related non-serious/serious adverse events (DRAEs/DRSAEs).

Results: Of 94 PLWH (88 TE, 6 TN), 79% were male, 41% ≥50 years of age. Baseline (BL) characteristics are shown in Table 1. Comorbidities were documented for 69% of participants (pts) (those occurring in ≥10% of pts were hyperlipidemia [34%], musculoskeletal disorders [21%], hypertension [16%], and cardiovascular disorders [11%]); 49% received concomitant medication (taken by ≥10%: lipid-modifying agents [16%], and agents acting on the renin-angiotensin system [13%]).

22% of TE had a history of virologic failure, 14% of major resistance-associated mutations (RAMs); 99% were virologically suppressed. Most common regimens prior to B/F/TAF were elvitegravir/cobicistat/F/TAF [55%], dolutegravir+F/TAF [11%], and rilpivirine/F/TAF [8%]).

In the M=E analysis, HIV-1 RNA was <50 cp/mL in 97% (76/78) of TE and 100% (5/5) of TN. In the D=F analysis, rates were 93% (76/82) in TE and 100% (5/5) in TN. Only one resistance test was documented during follow-up, with no emergent B/F/TAF-specific RAMs.

At M24, 5% had discontinued B/F/TAF (all TE: 2 pts due to doctor's discretion, 2 due to DRAEs (incl. anxiety [n=2], depression, loss of libido, alopecia), 1 participant decision). Two pts discontinued the study without B/F/TAF discontinuation, 3 were lost to follow-up.

Overall, no DRSAEs and 9 DRAEs (insomnia [n=2], anxiety [2], depression [1], loss of libido [1], tongue disorder [1], paraesthesia [1] and alopecia [1]) were reported in 6 (6%) pts.

In TE (n=69 with weight data at BL and M24), median BL weight was 76kg (Q1, Q3 [68, 82]); median relative weight change at M24 was +0.8% (Q1, Q3 [-3.5%, +3.2%]). Relative weight gains of >5% and >10% in TE were reported in 16% (11/69) and 3% (2/69), respectively. Weight loss of >5% and >10% in TE was reported in 14% (10/69) and 0% (0/69), respectively.

Conclusion: During the 2-year observation period of the Italian BICSTaR cohort, B/F/TAF maintained high rates of viral suppression without emergence of resistance. Persistence on B/F/TAF was high with no discontinuation due to virologic failure and only 2 discontinuations due to DRAEs. Weight gain and loss of >5% occurred with similar frequency. Real-world data support the safety and effectiveness of B/F/TAF, including TE PLWH with comorbidities and a history of multiple treatment regimens.

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Antiretroviral therapy

P 4 PROBABILITY OF STARTING 2DR VS 3DR REGIMENS IN ART-NAÏVE AND ART-EXPERIENCED PLWH BEFORE AND AFTER THE COVID-19 PANDEMIC

A. Vergori[1], N. Gianotti[2], A. Tavelli[3], C. Tincati[4], A. Giacomelli[5], E. Matteini[6], G. Lapadula[7], F. Bai[4], L. Sarmati[8], A. d'Arminio Monforte[3], A. Antinori[1], A. Cozzi-Lepri[9], on behalf of the ICONA Foundation Study Group

[1]HIV/AIDS Unit, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, Roma, Italy, [2]Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milano, Italy, [3]Icona Foundation, Milano, Italy, [4]Clinica di Malattie Infettive, Dipartimento di Scienze della Salute, ASST Santi Paolo e Carlo-Presidio Ospedaliero San Paolo, Università degli Studi di Milano, Milano, Italy, [5]III Infectious Disease Unit, ASST-Fatebenefratelli Sacco, Milano, Italy, [6]Dipartimento di Sicurezza e Bioetica - Università Cattolica del Sacro Cuore, Roma, Italy, [7]IRCCS Fondazione San Gerardo, Monza, Università di Milano Bicocca, Milano, Italy, [8]Clinical Infectious Diseases, Department of System Medicine, Tor Vergata University, Roma, Italy, [9]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, University College London, London, UK

Background: COVID19 pandemic temporarily disrupted and reduced HIV services. In May 2020 BHIVA issued an interim pragmatic statement to recommend the use of B/F/TAF in all circumstances, unless contraindicated. Whether lockdown and interim guidelines statements impacted ART prescriptions has not been evaluated.

Material and Methods: PLWH enrolled in the ICONA cohort (HBsAg-), ART-naïve who started their first-line ART between Jan2019-Dec2022 and ART-experienced who started new ART with a HIV RNA <50 cps/mL in the period Jan2016-Dec2022. The endpoint of the analysis was the proportion of PLWH starting/switching to a dual (2DR) or a triple (3DR) ART regimen. Participants' characteristics at time of starting/switching by calendar period were compared by chi-square and/or Kruskal-Wallis tests. A logistic regression (LR) model was used to evaluate the association between calendar period of starting/switching and type of regimen (2DR vs. 3DR) after adjusting for sex and age (line of therapy in the ART-experienced group). Moreover, we investigated whether the effect of calendar period on ART prescriptions varied by use of INSTI, sex and CD4 count at initiation/switch.

Results: Of 2,483 ART-naïve included (N=871 in 2019, 522 in 2020 and 1,090 in 2021/22) 17% were female, had a median age of 40 (IQR 32, 51) years, 66% had a CD4 count >200/mm3 and 78% a HIVRNA <100,000 cps/mL; 9% started a 2DR in 2019, 18% in 2020, 13% in 2021,10% in 2022. Using 2020 as the comparator (the lockdown year), odds ratio (OR) from fitting a LR showed a reduced probability of prescribing 2DR both before and after 2020 (Fig1A). Of 12,659 ART-experienced (N=7266 in 2016/18, 3389 in 2019/20 and 2004 in 2021/22) 20% were female, had a median age of 47 (38,55) years, 3% had CD4 <200/mm3 at switch. 24% switched to a 2DR in 2016, 10% in 2017, 13% in 2018, 25% in 2019, 37% in 2020, 61% in 2021, 64% in 2022. The estimated ORs showed an inverse trend of 2DR prescription before and after 2020, with a >3- fold higher probability to be switched to 2DR than 3DR in recent years (2021-2022) (Fig1B). Results were similar in the analysis stratified by sex and CD4 count at time of switch (interaction p=0.75). After restricting the analysis to INSTI-sparing regimens, we estimated a probability of 22.3% in 2016 followed by a drop to approximately 8-9% of switch to 2DR which remained stable over time [aOR 1.63 (1.18, 2.25) in 2016/2018 vs. 0.99 (0.60, 1.63); in 2021/22, interaction p<0.0001].

Conclusions: In our cohort of ART-naive PLWH we did not detect reduced odds of initiating 2DR vs 3DR during 2020, which however occurred over the following years; our analysis cannot clarify whether this reflects a true pragmatic change in clinical practice or was due to difficulties in resuming full HIV services. In contrast, in ART-experienced PLWH, we observed an increasing frequency of 2DR vs 3DR regimens initiation over time, especially INSTI-based in recent years.

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Antiretroviral therapy

P 5 PHYSICAL ACTIVITY, OXIDATIVE STRESS AND ANTIRETROVIRAL THERAPY IN PEOPLE LIVING WITH HIV: A MULTIDISCIPLINARY PILOT STUDY IN PEOPLE SWITCHING TO DOUBLE THERAPY

J. Cusato[1], A. Mulasso[2], M. Ferrara[3], A. Palermiti[1], A. Manca[1], M. Antonucci[3], G. Bianco[1], D. Maiese[1], F. Chiara[4], J. Mula[1], E.D. De Vivo[1], M.G. Maddalone[1], G. Accardo[5], M.C. Tettoni[3], S. Cuomo[2], L. Marinaro[3], S. Bonora[5], G. Di Perri[5], C. Lupo[2], A. Rainoldi[2], A. D'Avolio[1]

[1]Laboratory of Clinical Pharmacology and Pharmacogenetics, Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, Italy, [2]Department of Medical Sciences, NeuroMuscolarFunction | Research Group, University of Turin, Italy, [3]ASL Città di Torino, Amedeo di Savoia Hospital, Turin, Italy, [4]Laboratory of Clinical Pharmacology S.Luigi A.O.U., Department of Clinical and Biological Sciences, University of Turin, Regione Gonzole, Orbassano, Turin, Italy, [5]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, Italy

Background: Increased oxidative stress and HAART could impact on lipid and muscle metabolism in PWH. Physical activity could increase the production of oxidative stress biomarkers (OSB), including reactive oxygen species, affecting the expression of drug transporters involved in antiretrovirals disposition and clinical response.
Evidence is also available that vitamin D (VD) can affect cell signaling components, such as calcium and OSB, modulating the expression of proteins functioning in a number of cellular processes.
The potential relationship between physical activity, oxidative stress and antiretroviral drug exposure is presently ill defined. Accordingly, this study aims at investigating if OSB, VD and drug exposure were different in PWH switching from triple to dual HAART.
Materials and Methods: PWH were evaluated just before (baseline, treated with triple therapy) and 6 months after the switch to dual therapy. Their lifestyle habits (sedentary versus non-sedentary) were also considered. WHOQoL-brief questionnaire was used for the quality of life assessment. Physical function was measured using validated tools such as the Tapping test for dexterity and the Sit to Stand test for leg strength. Plasma and intracellular (PBMCs) anti HIV drug concentrations and mitochondrial and cytosol OSB levels were evaluated through liquid chromatography tandem mass spectrometry.
Results: 30 patients (10 sedentary and 20 non-sedentary) were included in the study: median (IQR) age and BMI were 42 (34-48) years and 23.2 (21.9-25.3) Kg/m2, respectively. As shown in Table 1, the following biomarkers resulted statistically different when comparing triple versus dual anti-HIV therapy: mitochondrial cysteine, cytosol taurine, cytosol S-adenosilmethionine, AST, calcium and VD levels. Also dominant tapping test, sit to stand and physical pain resulted statistically different considering the switch. Weight and HIV-RNA were not different before versus after the switch to dual HAART.
Significant differences were found on cytosol N-formylmethionine, alkaline phosphatase and vitamin D levels for triple therapy, cytosol glutathione and hemoglobin for dual therapy, when comparing inactive versus physically active PWH. No significant associations were found between anti-HIV drug plasma/intracellular concentrations and the studied biomarkers.
Conclusions: Our study documented, for the first time, a different pattern of expression of OSB, particularly with a reduction in terms of protective OSB in PWH switched from triple to dual antiretroviral therapies. Remarkably, such differences were significantly affected by physical activity. The clinical relevance of the present findings should be investigated in larger cohort of patients.

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Antiretroviral therapy

P 6 BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) IN A PREGNANT WOMAN WITH DRUG RESISTANT HIV-1 INFECTION: A CASE REPORT

A. Giaccone[1], A. Maddaloni[1], P. Bellopede[1], M. Talamo[1], S. Parente[1], A. Gallicchio[1], S. Susini[2], I. Gentile[2], A. Franco[1]

[1]AORN Ospedali dei Colli, Ospedale D. Cotugno, U.O.C. Malattie Infettive dell'Età Geriatrica, Napoli, [2]AOU Federico II, U.O.C. Malattie infettive, Napoli

Background: All the current guidelines recommend that all pregnant women with HIV should receive antiretroviral therapy (ART) regardless the CD4+ T lymphocytes count and the viral load, for their own health and that of the sexual partners and to prevent perinatal HIV transmission. For women who get pregnant while already receiving ART, regimens that result in viral suppression are likely to maintain their benefits during pregnancy and should not be withheld unless there is sound evidence that they may cause harm to the woman or the foetus or that the PKs changes in pregnancy might impact on the drug plasma level. Integrase strand transfer inhibitors (INSTIs) are a preferred component of ART regimens during pregnancy, being associated with higher rates of viral suppression, faster viral load decline and higher genetic barrier to drug resistance: nonetheless, BIC/FTC/TAF is not currently recommended given the lack of efficacy and safety data on bictegravir (BIC) and tenofovir alafenamide (TAF) in pregnancy. We present here the case of a seropositive woman treated with BIC/FTC/TAF during pregnancy with a physiological pregnancy course and no mother-to-child transmission.

Case Presentation: A 35-year-old caucasian woman with perinatally acquired HIV-1 infection (CDC 1993 category C3 at nadir), with an history of low compliance to previous ART regimens leading to virological failure and development of drug resistance (NRTIs, NNRTIs, INSTIs), switched to BIC/FTC/TAF 16 months before conception. Notably, despite a low-level resistance to bictegravir, the patient achieved sustained virological suppression. As she got pregnant, she decided to maintain the same regimen even after accurate counselling about the potential risks for the fetus. The patient was fully adherent to ART during pregnancy, with undetectable viral load and CD4+ T lymphocytes >700 cells/mm^3 at all the pregnancy control visits. A vaginal delivery was performed at 38 weeks of gestation without complications. The baby was healthy, with normal vital signs, physical examination and blood tests, and undetectable HIV RNA at birth and after a 4-week course of prophylaxis with iv zidovudine.

Conclusions: A BIC-containing regimen might be an effective choice for pregnant women with HIV, especially those with a history of drug resistance (including a low-level resistance to INSTIs) and previous treatment failures. Although no specific concerns have been raised regarding potential teratogenicity so far, large scale studies are mandatory to assess the safety profile of BIC/FTC/TAF in pregnancy.

Antiretroviral therapy

P 7 TO ENDORSE DORAVIRINE USE IN ANTIRETROVIRAL TREATMENT?

C. Papalini[1], B. Canovari[2], F. Lagi[3], G. Formica[4], K. Sterrantino[4], F. Barchiesi[2], D. Francisci[1]

[1]Clinica Malattie Infettive, Ospedale Santa Maria della Misereicordia, Università degli studi di Perugia, Perugia, [2]Clinica Malattie Infettive, Ospedale San Salvatore, Ospedali Riuniti Marche Nord, Pesaro, [3]SOD Malattie Infettive e tropicali, AOU Careggi, Firenze, [4]Dipartimento medicina sperimentale e clinica, Università degli studi di Firenze, Firenze

Introduction: Doravirine (DOR) is the last licensed Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI), available singly or co-formulated with Tenofovir diproxil fumarate (TDF) and Lamivudine (3TC) in a single tablet (STR).

The most recent EACS guidelines included DOR in the first line antiretroviral regimens (ART) due to its barrier resistance and metabolic profile.

The aim of this study is to compare immune, viral and metabolic parameters collected 6 months after DOR starting to those collected just before its introduction.

Materials and Methods: Prospective study focused on persons living with HIV (PLWH) visited at Infectious Diseases Clinics of Santa Maria della Misericordia Hospital (Perugia, Umbria, Italy), San Salvatore Hospital (Pesaro, Marche, Italy) and Careggi Hospital (Florence, Tuscany, Italy).

We collected epidemiological (gender; nationality; age; CDC classification, ART), immune (HIV RNA and CD4+ cell count) and metabolic (glycaemia; creatinine; gamma-glutamyl transpeptidase (GGT); glutamate pyruvate transaminase (GPT); triglycerides; total, LDL and HDL cholesterol) information about all the PLWH before and 6 months after DOR introduction.

Results: Patients included in this study were 153 whose data are reported in Table 1: 120 (78.4%) assumed STR (Delstrigo®) and 33 (21.5%) doravirine (Pifeltro®) with other antiretroviral drugs. The principle reason for DOR introduction was ART optimization followed by dyslipidemia and adverse effects to previous ART. About 50% of ART assumed before switching to DOR was Tenofovir alafenamide (TAF) and/or Integrase Inhibitors (IN)-based. Six months after DOR starting, viral suppression was stable, as weight, renal and hepatic parameters with the exception of GPT increase keeping anyway within normality range.

Regarding metabolic aspects, we found a statistically relevant decrease of triglycerides, total and LDL cholesterol after DOR introduction while no glycaemia and HDL levels' modification resulted.

Four patients have been lost to follow up while 9 (5.9%) persons discontinued DOR: 1 died for respiratory failure, 1 migrated in the country of origin, 1 had documents problems, 2 had detectable viremia, 3 complained for pruritus and/or rash and 1 for abdominal pain.

Conclusion: DOR introduction contributed to lower triglycerides, total and LDL cholesterol levels guaranteeing stable viral suppression, renal and hepatic function. No differences were noticed in weight, glycaemia and HDL cholesterol.

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Antiretroviral therapy

P 8 EFFECTIVENESS OF DOLUTEGRAVIR/LAMIVUDINE VERSUS TENOFOVIR ALAFENAMIDE/EMTRICITABINE/BICTEGRAVIR IN A REAL-LIFE COHORT OF HIV-1 VIROLOGICALLY SUPPRESSED TREATMENT EXPERIENCED PATIENTS

S. Tordi, G. De Socio, D. Altobelli, S. Benedetti, A. Gidari, A. Zoffoli, D. Francisci

Clinica di Malattie Infettive, Dipartimento di Medicina e Chirurgia, Università degli Studi di Perugia

Background: The aim of the study is to evaluate the effectiveness of two-drug regimen (2-DR) with dolutegravir/lamivudine (DTG/3TC) versus a three-drug regimen (3-DR) with tenofovir alafenamide/emtricitabine/bictegravir (TAF/FTC/BIC) in a real-life cohort of HIV-1 virologically suppressed treatment-experienced (TE) patients.

Material and Methods: A single-centre, retrospective, observational study analysing adult (≥18 years) TE patients who started the 2-DR single tablet regimen (STR) or 3-DR STR between January 2018 and January 2023, according to the physician's decision. All patients with a viral load (VL) <50 copies/mL at the time of switch and with a follow-up of more than 6 months were included. We excluded lost to follow-up patients. We investigated the baseline characteristics and clinical outcomes for both groups. The primary endpoint was the maintenance of VL <50 copies/mL. Secondary endpoints were the rate of patients with VL <20 copies/mL and VL undetectable. Plasma HIV-1 RNA was measured with a limit detection of 20 copies/mL. A univariate statistical analysis was conducted by Mann Whitney test or $\chi 2$ test, as appropriate. Statistical analyses were performed with SPSS.

Results: A total of 324 virologically suppressed individuals were included; their baseline characteristics are shown in Table 1. From these, 110 (34%) were on 2-DR and 214 (66%) were on 3-DR. The median age of the 2-DR cohort was 56.0 [IQR 44.0-63.0], 3-DR 56.5 years [IQR 48.0-61.5] (p=0.653); male individuals were 82 (74.5%) in the 2-DR group and 172 (80.4%) in 3-DR. Comorbidities were more represented in 2-DR patients (median number 2 [IQR 1-5] in 2-DR versus 1 [IQR 0-2] in 3-DR, p<0.0001); hypertension (p=0.011), cardiovascular diseases (p<0.0001), dyslipidaemia (p<0.0001) and chronic kidney disease (p<0.0001) were more frequent. Patients in 3-DR shown lower baseline CD4 (585 cells/μL on 3-DR versus 781.5 cells/μL on 2-DR, p<0.0001), CD4 nadir (214 cells/μL on 3-DR versus 297 cells/μL on 2-DR, p=0.015) and a less favourable genotype resistance test. The median follow-up was 19.6 months [IQR 14.2-26.4] in 2-DR and 27.5 months [IQR15.3-32.6] in 3-DR (p<0.0001). Most of the patients remained on therapy in both groups (92.7% 2-DR versus 90.2% 3-DR), while virological failures occurred in 1.8% 2-DR versus 0.9% 3-DR (p=0.495). Overall, 99.1% achieved VL<50 copies/mL in 2-DR versus 97.2% in 3-DR (p=0.260) (difference: 1.9%; 95% CI 0.37 to 2.64). 2-DR provided high rates of VL<20 copies/mL compared with 3-DR (respectively, 96.4% versus 86.7%, p=0.006), as well as undetectable VL (88.2% 2-DR versus 68.2% 3-DR, p<0.0001) (Table 2). **Conclusion:** Our study shows a similar effectiveness profile in virologically suppressed TE patients who switch to DTG/3TC or TAF/FTC/BIC. In clinical practice, physicians tend to prescribe 2-DR in patients with better immunological profile and more comorbidities and 3-DR in patients with worse drug resistance profile and immunologic status.

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Antiretroviral therapy

P 9 IMMUNO-VIROLOGICAL STABILITY IN PATIENT WITH MULTI-DRUG-RESISTENT HIV AND HISTORY OF POLIALLERGY AND INTOLERANCE TO SEVERAL ANTIRETROVIRAL DRUGS

R. Riccardi, D. Riccucci, L. Calza

Infectious Disease Unit, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy IRCCS S.Orsola Hospital

We report a case of a 62 years-old female with HIV diagnosed since 1989.
Her medical history is relevant for poor immuno- virological control because of several intolerances and allergies to various AntiRetroviral Therapies (ART) regimens (including RAL,TPV/r, DRV/r, T20, MVC). This problem led to lack of adherence to ART and, consequently, to various virological failures with the accumulation of multiple mutations in all the main classes of ART drugs (PI, INSTI, NRTI, NNRTI).
During the course of the years, the patient reported several allergic reactions. The most relevant of which we report below:

- Cutaneous rash with prurigo to T20
- Erythema localized to face and torso during trimethoprim/sulfamethoxazole (TMP/SMX) therapy for Pneumocystis Jiroveci Pneumonia (PJP) in september 2014
- Fever and diffuse cutaneous rash during cART with TDF/FTC + DRV/r + MVC and PJP prophylaxis with atovaquone in october 2014
- Cutaneous rash with prurigo and facial edema during TMP/SMX desensitization in december 2014

The most relevant mutations described in the latest Genotypic Drug Resistance Test (GDRT), performed on 09/01/2014, are:

- K70R, M184V which allow for the use of 3TC/FTC in association with TDF
- M46I, I54A, L90M in combination to V82T which make DRV/r the only therapeutic option in the PI class; however the patient had exhibited rash to DRV/r which excluded the drug from a possible regimen
- N155H with accessory V151I which are predicted to decrease susceptibility to RAL and EVG while having minimal effect on DTG and 2nd gen INSTI
- R5 tropism with a FPR of 30.1%, in addition to the history of allergy to MVC

After the interruption of the ART regimen with TDF/FTC + DRV/r + MVC due to allergic reaction, treatment with ETV+TDF/FTC was introduced with optimal compliance. After that, in december 2014, in consideration of the necessity to start a secondary prophylaxis for PJP in a patient who manifested a severe allergy to atovaquone, we performed TMP/SMX desensitization. The process was complicated by the onset of cutaneous rash with prurigo and facial edema, so we decided to start steroid therapy and to stop both the ART with ETV+TDF/FTC and TMP/SMX.
Finally, on 02/23/2015, we started a new ART regimen with DTG BID (increased dosage due to resistance to first generation INSTI in the latest GDRT) + TDF/FTC which was well tolerated and with no evidence of allergic reactions. This regimen was able to achieve HIV-RNA suppression and CD4+ count rose above 200/mmc in about a year.
In 11/17/2017, TDF/FTC was shifted with TAF/FTC because of the development of osteoporosis with multiple vertebral fractures (T7,T10,T12) with no variation on adherence to ART or development of new allergic reactions. The case is interesting because it was possible to achieve immunovirological control despite numerous allergic reactions and intolerances to several cART regimens over the years.

Antiretroviral therapy

P 10 LONG-ACTING CABOTEGRAVIR-RILPIVIRINE IN HIGHLY EXPERIENCED PLWHIV: THE ROLE OF DIRECTLY OBSERVED TREATMENT (DOT) IN OVERCOMING BARRIERS TO ADHERENCE

A. Ciccullo[1], M. Petrucci[2], F. Onorati[2], V. Iannone[3], A.Borghetti[2], E. Visconti[2], S. Di Giambenedetto[2,3]

[1]Infectious Diseases Unit, San Salvatore Hospital, L'Aquila, [2]Infectious Diseases Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, [3]Dipartimento di Sicurezza e Bioetica, Università Cattolica del Sacro Cuore, Infectious Diseases Unit, Roma

Background: A lack of adherence to daily dosing of antiretroviral treatment is one of the main reasons of treatment failure in both treatment-naïve and experienced individuals and thus, being able to reduce "treatment fatigue" may play a key role towards a better control of viral replication and reducing morbidity and mortality of PLWHIV. Recently, FDA approved the parenteral, long-acting formulation of a 2-drug regimen (2DR) of cabotegravir (CAB) plus rilpivirine (RPV) for the treatment of virologically-suppressed PLWHIV with no known resistance mutations towards either of the two molecules; also, compassionate, off-label use of this combination has been reported, with good results in terms of efficacy and tolerability. Despite potentially eliminating pill burden and "treatment fatigue", non-compliant PLWHIV may not be able to attend scheduled visits and thus scheduled administrations of CAB+RPV, becoming at risk of having sub-par plasma levels of drugs. For this reason, in particularly difficult-to-treat individuals, a personalized Directly Observed Treatment (DOT) approach may be beneficial. In this study, we aimed to describe a cohort of PLWHIV switched to long acting CAB+RPV administered at home by a dedicated "home-based care unit".

Methods: We analyzed data from a cohort of PLWHIV followed in our Infectious Diseases Unit in Rome, assisted via an "home care assistance unit", with a dedicated teams of doctor and nurses who visit PLWHIV twice per week. We analyzed treatment-experienced individuals started the long-acting combination of CAB+RPV in clinical practice, with a every-4-weeks parenteral administration. We collected individuals' clinical history and viro-immunological parameters at time of switch (baseline) and during follow-up. We used non-parametric tests to compare variables.

Results: We collected data from 15 PLWHIV: 8 were females (53.3%), with a median age of 53 years (IQR 42-64) and a median time from HIV diagnosis of 10.9 years (IQR 5.9-21.1). Three individuals started a month of oral lead-in of CAB+RPV; 2 of them decided to discontinue treatment after the lead-in month. At the time of the first parenteral administration, 1/13 (7.7%) had an HIV-RNA of 86 copies/mL, while all other individuals had a HIV-RNA below the threshold of 50 copies/mL; median CD4+ cell count at baseline was 619 cell/mm3 (IQR 239-740). At week 8 of follow-up, all analyzed PLWHIV had an HIV-RNA < 50 copies/mL. Regarding immunological parameters, we did not find any significant change in absolute CD4+ cell count or CD4/CD8 ratio during follow-up. As to reported side-effects, one individual reported the onset of fever after the first administration, while 2 PLWHIV reported pain at injection site after each administration.

Conclusions: Our results confirm the efficacy and tolerability of CAB+RPV as a switch strategy in experienced PLWHIV while also highlighting how useful a DOT strategy may be in selected difficult-to-treat PLWHIV.

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Antiretroviral therapy

P 11 SATISFACTION, CLINICAL AND LABORATORY OUTCOMES OF LONG ACTING CABOTEGRAVIR AND RILPIVIRINE IN A REAL-LIFE COHORT OF PEOPLE LIVING WITH HIV

M. Mazzitelli, L. Sasset, D. Leoni, S. Gardin, E. Agostini, A.M. Cattelan

Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, Italy

Background: Data from clinical trials granted efficacy and safety of long acting (LA) cabotegravir and rilpivirine (CAB/RPV) that were recently added to the therapeutical armamentarium of the HIV treatment. Real life data are currently scarce. Our objective is to describe the preliminary real-life experience with injectable CAB/RPV at Padua University Hospital.

Methods: We included all people living with HIV (PLWH) who started a LA treatment in our center and with at least 12 weeks of follow-up. We collected demographics, clinical data, and laboratory parameters (HIV-RNA, CD4+ T cell count, total cholesterol, LDL, HDL, HDL/LDL radio, triglycerides, weight, BMI), and any side effects. Treatment satisfaction was assessed by HIV treatment satisfaction questionnaire (HIVTSQ).

Results: To March 2023, 42 PLWH were included (71.4% males, median age 48 [IQR: 43-56] years). Median length of HIV infection was 10 (IQR: 6-17) years; 54.7% PLWH had multimorbidity. Most of PLWH (85.7%) received LA on their own request. The most common regimens at the baseline were TAF/FTC/RPV (38.1%), DTG/3TC (30.9%), DTG/RPV (10%), other single tablet regimens, STR (10%). Table 1 shows changes of the study parameter from baseline to 12-week follow up. A woman experienced virological failure after two doses (with no resistance mutation and despite serum concentration of CAB/RPV were above the therapeutical target). A patient stopped because of severe pain in the injection site after the first injection. Impact on body weight and metabolic biomarkers at 12 weeks of follow-up (40 patients) was neutral, with no statistically significant changes. Three patients had a mild increase of liver function tests after the first injections. Injection site reactions (ISRs), myalgia, and fever (post the first administration) were reported by 80.9%, 40.5%, and 16.7% cases, respectively. As for treatment satisfaction questionnaire, 90.5% PLWH reported a median score of 51.6 at week 12 of follow-up and disclosed to be happy not to take oral therapy anymore, despite side effects. 1 PWH was completely unsatisfied, three patients were thinking to stop treatment due to pain in the injection site and radiating down the leg.

Discussion: LA treatment showed a good clinical efficacy and a neutral effect on body weight, lipids, and immunological parameters. Despite 89% PLWH were on a STR for many years, with a well-controlled HIV infection, most of them was very attracted and satisfied by this new route of administration. In addition, even though 85% of patients experienced side effects, only a patient discontinued the drugs. These data may suggest that PLWH still suffer from stigma, also linked to the simple antiretroviral intake. However, in a future perspective of large implementation of this strategy in the real-life setting, further prospective studies with a longer follow-up are needed to better characterized patients' selection and to assess long term effect of this new combination.

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Antiretroviral therapy

P 12 CLINICAL AND ECONOMIC EVALUATION OF DUAL THERAPIES IN CART-EXPERIENCED HIV POSITIVE PATIENTS

S. Palantone[1], M. Allegrini[2], T. Calamia[1], S. Minniti[2]

[1]Pharmacy, P.O. Perrino (ASL BR), Brindisi, Italy, [2]Infectious Diseases Unit, P.O. Perrino (ASL BR), Brindisi, Italy

Background: The optimization of antiretroviral therapy with two drug regimens (2DR) is crucial in reducing medication burden, preventing long-term toxicity, reducing adverse drug interactions (ADR) and improving patients' quality of life. Furthermore, the reduction in the number of drugs, may represents an opportunity to cut antiretroviral costs. The aim of the study is to evaluate the reasons for the switch and tolerability of 2DR in cART-experienced HIV patients and relative costs.

Material and Methods: Clinical data were screened from medical records of those patients who underwent therapeutic simplification to an INSTI-based dual regimen with 3TC+DTG, RPV+DTG and CAB+RPV long-acting between January 1st 2020 and March 1st 2023. We took into account only drug costs (ex-factory prices, included all discounts and VAT) from the perspective of the Italian NHS. For each enrolled patient, we compared annual cost of previous cART to annual cost of 2DR.

Results: Overall 27 patients were included in the study: 21 male (78%) and 6 female (22%), median age 51 years and all of them were Italian. The mean time between the start of ART and switch to 2DR was 5 years. All of them presented at least one comorbidity. 13 (48.1%) individuals were switched to RPV+DTG, 9 (33.3%) to 3TC+DTG and 5 (18.5%) to CAB+RPV long acting. All previous cART included triple-drug regimens: NNRTI for 5 patients, PI for 3 patients and INSTI for 19 patients. Principal reasons for the switch were: preventing long-term toxicity 9 (33%), reducing pill burden 5 (19%), ADR to cART 6 (22%), avoiding drug interactions 2 (7%), patient's choise 5 (19%). All 5 patients switched to CAB+RPV, asked themselves to change cART in order to avoid taking pills. It was reported only 1 case of ADR to 2DR consisting in pyrexia, injection site reaction and muscular pain after the first CAB+RPV injection. Compared with previous cART regimen switching to 2DR allowed cost saving in 20 patients (74%) instead it involved major cost in 7 patients (26%). Overall annual average saving per patient with 2DR was 912.68 €.

Conclusions: The results of this study confirmed potential benefits of dual therapies in improving tolerability and reducing antiretroviral costs in most of cases. Although the small number of patients, long acting therapy could be considered a cost effective option often requested by patients in order to improve quality of life and reduce HIV-related stigma. In this framework, the future challenge is to optimize, when possible, stable virologically suppressed HIV-infected patients currently undergoing treatment with cART regimens in order to reduce toxicities, personalize cART and improve quality of life and best optimize economic resources.

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Antiretroviral therapy

P 13 HIV-DNA TREND IN ART-EXPERIENCED PLWH SWITCHING TO INJECTABLE LONG-ACTING ANTIRETROVIRAL THERAPIES WITH CAB+RPV: 12-WEEK RESULTS IN A REAL-LIFE SETTING

F. Lombardi[1], F. Onorati[1], M. Petrucci[1], A. Sanfilippo[2], V. Iannone[2], D. Farinacci[2], A. Dusina[1], A. Carbone[2], A. Borghetti[1], A. Ciccullo[3], S. Di Giambenedetto[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma Italia, UOC malattie infettive, [2]Università Cattolica del Sacro Cuore, Roma Italia, Istituto di Clinica Malattie Infettive, [3]Unità di Malattie infettive, Ospedale San Salvatore, L'Aquila, Italia

Background: The long-acting antiretroviral therapies (LA-ART), the novel drug delivery approach, is about to revolutionize the way people living with HIV (PLWH) are treated. This promising strategy can simultaneously improve convenience and reduce social stigmas associated with HIV. In this context, the current injectable LA formulation with CAB+RPV (CAB+RPV LAI) is optimized for the maintenance of HIV suppression in treatment-experienced patients, and has been demonstrated to ensure 2 month-long effective plasma concentrations. However, it has yet to be determined whether this strategy affects the viral reservoir. The aim of this work was to closely monitor the blood-associated total HIV-DNA level, as a biomarker of the HIV cellular reservoir, over 12 weeks in a real-life setting of ART-experienced PLWH who switched from standard ART to CAB+RPV LAI.
Material and Methods: This prospective, longitudinal study enrolled participants who switched from their daily oral ART to CAB+RPV LAI. We quantified total HIV-DNA in the blood by droplet digital PCR at several time-points over 12 weeks: before starting CAB+RPV LAI (baseline, BL, right before the first injection), after two weeks (2W), after 4 weeks (4W, right before the second injection) after 6 weeks (6W) and after 12 weeks (12W, right before the third injection). Results were expressed as log10 HIV-DNA copies/106 leukocytes.
Results: We enrolled 18 participants: 7 were currently attending our outpatient clinic, 10 were currently being followed by our home-based care unit, and one participant was hospitalized for chemotherapy administration for neoplasia. More than half were males (56%), mostly Caucasians (89%), with a median age of 56 (IQR 46-63) years; 83% were viro-suppressed (with HIV-RNA <50 cps/mL). The participants' characteristics at the time of the switch are summarized in Table 1. Interestingly, the trend of HIV-DNA levels decreased two weeks after the first injection, changing from 2.36 down to 2.11, and then there was a slight and steady upward trend up to 2.22 at 12W, which, however, was below the BL level (Figure 1). When we divided participants into suppressed (n=15) and non-suppressed (n=3), the former showed a comparable trend with respect to the entire population, starting from 2.35 at BL, 2.07 at 2W and up to 2.16 at 12W. The non-suppressed PLWH started from a higher BL HIV-DNA level, 2.58, and they remained stable until 6W and displayed an increase of up to 2.75 at 12W.
Conclusions: Overall, in this clinical practice setting of ART-experienced PLWH we observed that the first injection of CAB+RPV LAI had a beneficial effect on the control of the reservoir, which was more marked in suppressed PLWH, and that lasted until the one-month second injection. However, this effect appeared to fade at 12W before the bimonthly third administration. These exploratory data need to be confirmed in a larger cohort and with a longer follow-up.

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Antiretroviral therapy

P 14 EFFICACY AND SAFETY OF A SWITCH TO DORAVIRINE AND DOLUTEGRAVIR COMBINATION IN HIV-1-INFECTED PATIENTS IN A SINGLE ITALIAN CENTER: A COHORT DATA ANALYSIS

F. Lagi[1], G. Formica[2], F. Ducci[2], S.T. Kiros[2], M. Pozzi[1], M. Meli[1], M. Pittorru[3], A. Bartoloni[1,2], G. Sterrantino[2]

[1]Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, Italy, [2]Department of Experimental and Clinical Medicine, University of Florence, Florence Italy, [3]Dipartimento del Farmaco - Azienda ASL Toscana Centro

Background: Doravirine (DOR) is a recently approved antiretroviral belonging to the class of non-nucleoside reverse transcriptase inhibitors (NNRTI). The DOR/dolutegravir (DTG) combination has not been studied in clinical studies, is not recommended in the guidelines for the treatment of HIV and limited real-life data are available. The study aims to evaluate the effectiveness and safety of a switch to DOR and DTG in a cohort of people living with HIV (PLWH) in a single center in Florence, Italy.
Methods: This is a retrospective-monocentric cohort study. From 01/01/2020 to 31/12/2022, we included all HIV-1 positive, ART-experienced persons switching to DOR+DTG with at least one visit of follow-up. Study entry was the date of drug initiation; exit was the date of discontinuation, virologic failure (VF), or the end of FU (31/03/2023).
Results: We included 26 patients. The median follow-up was 1.1 years [IQR 0.7-1.8]. The majority were male (n=16; 61.5%) with a median age of 60 years [IQR 54-72] and a long history of HIV [median: 26 years (14-30)]. We show the pre-switch regimens and reasons to switch in Figures 1 and 2, respectively. Seven patients had HIV RNA >50 cp/mL at baseline: 3 of 7 switched to DTG + DOR for virologic failure, 4 of 7 after having viral blips. Baseline characteristics are summarized in table 1. All patients included had at least one comorbidity and 20 (67.9%) patients were taking at least one concomitant medication. The most common comorbidity was dyslipidemia (n=8; 30.8%), followed by hypertension (n=7; 26.9%) and diabetes (n=5; 19.2%). Historical genotype was available in 22 out 26 patients.
Twenty PLWH (76.9%) had a virus with at least one major resistance mutation in the historical genotype. According to Stanford HIV drug resistance database, two patients had a virus with mutations conferring potential low-level resistance to DOR (K101P), 1 patient had high-level resistance to DOR (K101E, V108I, Y181C, H221Y).
Overall, we observed 2 discontinuations: 1 for sleep disturbance and 1 because lack of virological suppression in a patient with detectable viremia at the time of the switch and the high-level resistance to DOR [Table 1]. All other patients had HIV-RNA <50 cp/mL at the end of follow-up. The overall discontinuation rate due to all causes was 5.92 x 100 py [1.48-23.63].
Conclusions: DOR + DTG proves to be an effective and well tolerated regimen even in patients with a long previous therapeutic history, history of virological failure, presence of comorbidities and resistance mutations.

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Antiretroviral therapy

P 15 COMPARING EFFICACY, SAFETY, AND TOLERABILITY OF 3TC/DTG, TAF/3TC/DOR, AND TAF/FTC/BIC IN SWITCH STRATEGY OF VIROLOGICALLY SUPPRESSED HIV-INFECTED PEOPLE

D. Farinacci[1], A. Ciccullo[2], A. D'angelillo[1,3], V. Iannone[3], A. Carbone[3], E. Visconti[4], G. Baldin[4], A. Borghetti[4], S. Di Giambenedetto[3,4]

[1]UOC Medicina Protetta-Malattie Infettive, ASL Viterbo, Italy, [2]Ospedale San Sebastiano, L'Aquila, Italy, [3]Università Cattolica del Sacro Cuore, Roma, Italy, [4]Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Roma, Italy

Background: Antiretroviral therapies have reached a higher efficacy and tolerability compared to older regimens and this is very important because of the progressive lengthening of life expectancy of patients with HIV (PLWH). [1]
Single tablet regimens (STR) are now the cornerstone of treatment as a first-line and switch therapy. [2]
In this study, we wanted to compare the viro-immunological and metabolic characteristics of patients treated with the main STRs regimens.
Methods: We collected data from HIV-infected patients followed at a single center, with viremia < 50 copies/mL for at least 6 months who switched therapy to 3TC/DTG, TAF/3TC/DOR or TAF/FTC/BIC, analyzing immunovirological data and metabolic parameters.
Results: We analyzed data from 1372 PLWH: 1006 in the DTG group, 319 in the BIC group, and 47 in the DOR group. The 3 groups significantly differed for peak HIV-RNA, CD4+ cell count nadir, years of virological suppression, CDC stage, previous virological failures (VF), and CD4+ cell count at baseline, as shown in Table 1.
Regarding the risk of VF, we found no difference between groups (log-rank p=0.363) after 48 weeks. Similarly, we found no difference regarding the risk of treatment discontinuation (TD) (log-rank p=0.156).
In the immunological aspects, patients in 3TC/DTG showed an increase in CD4/CD8 ratio of +0.03 (p<0.001) after 48 weeks. In patients treated with TDF/3TC/DOR, we found an increase of +11 CD4+ cells (p=0.035) while in the BIC group, we saw an increase of both CD4+ cells (+0.9 cells, p=0.001) and CD4/CD8 ratio (+0.02, p<0.001).
Analyzing changes in metabolic parameters after 48 weeks, in the DTG group we observed a reduction in total cholesterol (-4.5 mg/dL, p<0.001), LDL cholesterol (-3.0 mg/dL, p=0.017) and triglycerides (-9.2 mg/dL p<0.001), while also registering an increase in serum creatinine (+0.06 mg/dL, p<0.001). In the BIC group, we observed an increase in serum creatinine (+0.02 mg/dL, p=0.010). Finally, in the DOR group, we observed a reduction in total cholesterol (-17.2 mg/dL, p=0.013) and triglycerides (-20.6 mg/dL, p=0.027). In the DTG group, male sex (vs. female, B 13.4, p=0.019) and baseline triglycerides values (per 10 mg/dL more, B -6.1, p<0.001) were predictors of changes after 48 weeks. Similarly, in the DTG group baseline total cholesterol (per 10 mg/dL more, B-3.3, p<0.001) and male sex (B-7.7, p=0.003) were correlated to changes in cholesterol levels during follow-up. Finally, in the DTG group baseline serum creatinine predicted significant change at week 48 (B 0.2, p<0.001).
Discussion: Treatment regimens show an excellent ability to maintain virological suppression, with no differences between groups in VF. 3TC/DTG and TAF/FTC/BIC confirmed the CD4/CD8 ratio increase.
DTG and DOR show an improvement in lipids for the metabolic parameters, which is more evident in the DOR group. DTG and BIC confirm an effect on creatinine increase.

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Antiretroviral therapy

P 16 RISK OF FAILURE IN DUAL THERAPY VERSUS TRIPLE THERAPY IN VIRO-SUPPRESSED HIV PATIENTS SWITCHED TO CAB OR DTV DUAL REGIMENS: A SYSTEMATIC REVIEW AND META-ANALYSIS

V. Zollo[1], S. Martini[1], M. Pisaturo[1], L. Onorato[1], A. Russo[1], M.G. Palamone[1], M. Russo[1], P. Maggi[1,2], N. Coppola[1]

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [2]Infectious Diseases Unit, A.O. S Anna e S Sebastiano, Caserta, Italy

Background: The objective of this meta-analysis was to evaluate the relative risk (RR) of failure of dual therapies compared to triple therapies in HIV-virosuppressed patients.
Methods: We searched MEDLINE, Google Scholar and the Cochrane Library. The following criteria were used: present data from original articles comparing the two treatment regimens; published from January 2007 up to March, 2023. No language or study design restriction was applied. Subjects were HIV- positive virosuppressed patients switched to dual (CAB+RPV or DTV+RPV or DTV+3TC) or triple antiretroviral therapy (ART) showing data of follow up at 96 weeks. A systematic review and meta-analysis was performed. Treatment failure (TF) was the primary outcome evaluated; hetero-geneity was assessed using the Q statistic and I2.
Results: Four studies were included(Figure 1), allowing a meta-analysis on 2040 patients. The meta-analysis performed showed that the Relative Risk(RR) of Treatment failure(TF) (RR > 1 favouring tri-ple therapy) in 4 studies was 0.73 (95% confidence interval (CI): 0.55-0.95, I2: 0%)(Figure 2); the RR of viro-logical failure (VF) in four studies was 0.79 (95% CI: 0.39-1.61, I2: 0%)(Figure 3); the RR of adverse drug reaction leading to discontinuation of the regimen at 96 weeks in three studies was 0.28 (95% CI: 0.05-1.56, I2: 0%)(Figure 4).
Conclusion: Dual therapies are as effective as those with three drugs, showing no difference according to the different dual therapies, considering VR and adverse drug reaction, leading to discontinuation. Studies included showed that patients who performed dual regimen showed a lower treatment failure.

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Antiretroviral therapy

P 17 SIGNIFICANT CD4+ T-CELL INCREASE IN WOMEN LIVING WITH HIV (WLWH) SWITCHING TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (B/F/TAF): MULTI-CENTER REAL-WORLD RETROSPECTIVE LONGITUDINAL STUDY

M. Ceccarelli[1,2,3], A. De Vito[4], G. Pantò[5], A. Albanese[6], G.F. Pellicanò[7,8], M.C. Frasca[9], M.S. Paternò Raddusa[2,10], A. Colpani[4], A.E. Campanella[5,10], L. Santoro[6,10], Y. Russotto[10,8], L. Todaro[9,10], E. Venanzi Rullo[8,10], M. Coco[5,10], S.A. Sofia[5], C. Micali[3,8], A. Marino[1,2,11], C. Iacobello[5], A. Montineri[9], B.S. Cacopardo[2,1], G. Madeddu[4], B.M. Celesia[2], G. Nunnari[2,1]

[1]University of Catania, Department of Clinical and Experimental Medicine, Catania, Italy, [2]ARNAS "Garibaldi", "Nesima" Hospital, Unit of Infectious Diseases, Catania, Italy, [3]University of Messina, Department of Biomedical and Dental Sciences and of Morphological and Functional Imaging, Messina, Italy, [4]University of Sassari, Medical, Surgical, and Experimental Sciences, Sassari, Italy, [5]AOE "Cannizzaro", Unit of Infectious Diseases, Catania, Italy, [6]"Papardo" Hospital, Unit of Infectious Diseases, Messina, Italy, [7]University of Messina, "G. Barresi" Department of Human and Pediatric Pathology, Messina, Italy, [8]"G. Martino" University Hospital, Unit of Infectious Diseases, Messina, Italy, [9]"G. Rodolico - S. Marco" University Hospital, Unit of Infectious Diseases, Catania, Italy, [10]University of Messina, Department of Clinical and Experimental Medicine, Messina, Italy, [11]University of Catania, Department of Biomedical and Biotechnological Sciences, Catania, Italy

Background: Despite B/F/TAF has been available for more than 5 years, there are not many data about its safety and effectiveness in women living with HIV (WLWH). This study aims to fill this knowledge-gap with real-world data.

Methods: We collected data about viro-immunological and metabolic parameters, at baseline and after 48 weeks, of the WLWH in follow-up at 6 different clinics in Eastern Sicily and Northern Sardinia, beginning treatment with B/F/TAF during the period September 2019 – December 2021.

Results: We collected data about 83 WLWH, 11 (13.3%) naïve to treatment and 72 (86.7%) experienced ones. 48.6% of the experienced WLWH were taking EVG/c/FTC/TAF before switch. At baseline, median age was 50 years (IQR 41-56). Experienced WLHW were diagnosed for a median of 16 years (IQR 5-26.5), were on a median of 3 ART lines before B/F/TAF (IQR 2-6) and median durability of the previous regimen was 131 weeks (IQR 90 -193). Our data show that B/F/TAF has high virological and immunological effectiveness both in naïve and experienced WLWH (figures 1 a-d), leading to persistent undetectable viremia (figures 1 a-b) and to a significant increase in CD4+ T-cell count after 48 weeks (figures 1 c-d). B/F/TAF has a positive effect on lipid metabolism in experienced WLWH, but not in naïve ones, with a significant decrease of low-density lipoprotein cholesterol at 48 weeks (p = 0.0312). There is no difference in triglycerides, total cholesterol, and high-density lipoprotein cholesterol. Creatinine increased significantly in naïve WLWH (p = 0.0117) at 48 weeks. No significant weight change was highlighted.

Conclusions: Switching to B/F/TAF significantly increases CD4+ T-cells in experienced WLWH, showing an excellent virological and metabolic profile. Interestingly, we did not find any significant weight change.

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Antiretroviral therapy

P 18 VIROLOGICAL REBOUND AND THE USE OF DIETARY SUPPLEMENTS IN PEOPLE LIVING WITH HIV: RESULTS OF A SURVEY

S. Esperti, M. Del Monte, B. Fontana, I. Baldisserotto, A. Dessilani, A. Cervo, V. Borghi, C. Mussini

Malattie Infettive, Azienda Ospedaliera-Universitaria di Modena, Università di Modena e Reggio Emilia Modena

Background: One of the possible reason of virological rebound in people living with HIV (PLWH) is the presence of drug interactions with antiretroviral therapy (ART). Some supplements could interfere with ART absorption among different mechanisms; in particular, interaction between integrase strand transfer inhibitors (INSTI) and cations has been well documented. However, the use of supplements is often underestimated and not always self-reported among PLWH. We aimed to investigate the potential correlation between abnormal virological response and supplements intake in PLWH attending as outpatients the HIV Clinic of Modena.

Material and Methods: A survey concerning supplements intake was randomly submitted in PLWH at the same time of blood check during the period August to December 2022. Data on typesetting (cations, amino acids, vitamins, or herbs) and frequency (daily or occasionally) of supplements intake were collected. All subjects were on stable ART. Virological rebound (VR) was defined as blip if the baseline HIV viral load (VL), at the time of survey, was >50 copies/ml in previously undetectable HIV-VL; persistent low level viremia (pLLV) if HIV-VL between 50 and 200 before and after baseline. Univariable analysis by supplements intake was performed. Multivariable analysis was used to investigate predictor factors of virological rebound.

Results: Two-hundred PLWH completed the survey, 206 (77.2%) were males, with median age of 55 years (IQR 48-61), ART duration was 13 years (IQR 8-23). INSTIs were used in 166 (62.2%) subjects; dual regimen (2DR) in 130 (48.7%). One-hundred twenty (44.9%) PLWH reported the use of any kind of supplements: 49 (40.8%) had daily intake and 13 (10.8%) more than one. Cationic intake was reported in 74 (61.7%) subjects (Table 1). PLWH taking supplements had longer duration of HIV infection (20 vs 16 years, p=0.044).

VR was observed in 15 (5.6%) PLWH: 7 (2.6%) and 8 (3%) had blips and pLLV, respectively. One third (33.3%) of PLWH with virological rebound reported to take supplements: all of those used cations. In multivariable analysis, the use of three-drug based regimen instead of a 2DR resulted the only protective factor for VR (aOR 0.14, 95% CI 0.03-0.65, p 0.01) (Table 2). No association was found between VR and supplements intake (aOR 1.54, 95% CI 0.18-1.68, p= 0.29) (Model I in Table 2), neither considering only cations use (aOR 1.16, 95% CI 0.37-3.62, p=0.79) (Model II).

Conclusions: Supplements intake was reported in almost one half of the questioned outpatients; cations were used in one third. While three-drugs regimens reduced the risk of virological rebound in a random sample of HIV outpatients, cations intake was not associated with virological rebound. Further analysis on bigger cohorts and pharmacokinetics data are needed.

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Antiretroviral therapy

P 19 INSTI RESISTANCE MUTATIONS EMERGING WHILE ON DTG/3TC DUAL THERAPY

F. Conti, V. Morena, C. Molteni, L. Bradanini, A. Pandolfo, S. Pontiggia, S. Piconi

Infectious Diseases Unit, Alessandro Manzoni Hospital, Lecco (LC), Italy

Dolutegravir (DTG) plus lamivudine (3TC) is recommended by main international guidelines for the treatment of ART-naïve adults living with HIV and as switch strategy for virologically suppressed persons. GEMINI-1 and GEMINI-2 demonstrated the non-inferiority of DTG+3TC versus DTG + TDF/FTC in treatment-naïve adults at 96 weeks. 11 participants in the DTG+3TC group met confirmed virologic withdrawal criteria through week 96, but none reported treatment-emergent resistance mutations. The TANGO study demonstrated the non-inferiority of DTG+3TC compared to continuing TAF-based regimen in virologically suppressed persons at 144 weeks, and non-inferiority of switching to DTG+3TC versus continuing current antiretroviral regimen was demonstrated also in the SALSA study. No cases of virological failure were reported in those study. In a systematic literature review published in 2021 summarizing real world data of DTG+3TC use, treatment emerging resistance were reported only in two individuals failing DTG+3TC. One reported M41ML substitution, associated with low-level resistance to zidovudine, and one reported the S147G integrase substitution, conferring high level resistance to elvitegravir but with little impact on DTG.

We present the case of a 58-years-old HIV-positive Cameroonian woman attending our HIV clinic in Lecco (Lombardy, Italy), who developed resistance to both DTG and 3TG while on therapy with DTG/3TC single tablet regimen despite no previous history of viral failure nor resistance to integrase strand transfer inhibitors (INSTI) or nucleoside reverse transcriptase inhibitors (NRTI). The patient's medical history included a treatment for latent tuberculosis and syphilis, osteopenia, previous hepatitis B and a surgical intervention of reductive mastoplasty. Her CD4 nadir was 139 cells/mmc, HIVRNA zenith was 154.000 copies/ml. At diagnosis, genotypic resistance test (GRT) showed no resistance mutations to NRTI, NNRTI and protease inhibitors. INSTI resistance was not assessed. In 2017, she started her first ARV regimen with DTG/ABC/3TC, being successfully virologically suppressed for almost 5 years. In November 2021, her ARV regimen was simplified to DTG/3TC. After 4 months HIV RNA was 30 copies/ml. Approximately one year after the switch her viral load was 12.700 copies/ml. The patient did not reported assumption of any new licit or illicit drug and declared unremarkable compliance. Two months later her viral load was 6.550 copies/ml. A GRT was performed and showed high level resistance to 3TC (mutation M184V) and all INSTI (mutations E138K, G140A, S147SG, Q148R). The patient was switched to DRV/c/TAF/FTC. Approximately one month later HIVRNA was 120 copies/ml.

To our knowledge this is the first case report of major INSTI resistance mutation emerging after failing DTG/3TC. This case report highlights the importance of GRT at viral failure even among people on high barrier antiretroviral regimens.

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Antiretroviral therapy

P 20 REAL-LIFE EXPERIENCE OF DORAVIRINE-BASED REGIMENS IN A COHORT LIVING WITH HIV

N. Braccialarghe[1], L.V. Rindi[1], L. Ansaldo[1], D. Zaçe[1], M. Compagno[2], E. Teti[2], A.M. Geretti[1,2,3], L. Sarmati[1,2]

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Infectious Diseases Unit, Fondazione PTV, University of Rome Tor Vergata, Rome, Italy, [3]School of Immunity and Microbial Sciences, King's College London, London, United Kingdom

Background: Doravirine (DOR), a non-nucleosidic transcriptase inhibitor (NNRTI) with improved genetic barrier, was approved in 2018 for the treatment of HIV-1 in Europe and North America. It is available alone or coformulated with Tenofovir Disoproxil Fumarate (TDF) and lamivudine (3TC) as single tablet regimen. ART-naive and switch studies demonstrated the non-inferior efficacy of DOR-based regimens and an overall favorable adverse event profile including improved blood lipids.

Methods: We retrospectively studied patients of the HIV Clinic of Tor Vergata Hospital who received a DOR-based regimen between 2016, with patients enrolled to clinical trials, to March 2023. We collected demographic, lifestyle, clinical data and results of blood tests performed at the start of DOR (T0) and 12 (T12) and 24 (T24) weeks later. Statistical analysis was performed with JASP.

Results: We identified 37 patients with a mean age of 51 years (SD+13); 81% were males and 78% were Italian. The transmission group was largely MSM (16/37, 43%) or heterosexual (12/37, 32%); 12/37 (32%) had a prior AIDS diagnosis. At T0, 30/37 (81%) patients were virologically suppressed, 4 patients were experiencing virological failure and 3 were ART-naïve. The median CD4 count was 770 cells/uL (IQR 488-1052). None of the patients had a prior history of NNRTI failure or documented NNRTI resistance. 8 patients were dyslipidemic and receiving lipid-lowering agents. DOR-based regimens comprised DOR/TDF/FTC (n=32), DOR+TAF/FTC (n=3), DOR+BIC/TAF/FTC (n=1) and DOR+DTG/3TC (n=1). The most frequent reasons to start DOR were a switch for dyslipidemia or weight gain (n=12, 32%), followed by proactive switch to avoid long-term toxicity (n=9, 24%) or due to toxicity (n=5, 14%). Overall, 5 patients (14%) discontinued DOR after starting (mean time 16 weeks): 2 developed paradoxical dyslipidemia, 1 could not swallow the pill and 2 had gastrointestinal symptoms. Over a mean time of follow-up of 58 weeks all 32 patients achieved or maintained virological suppression.

Between T0 and T24, there were significant decreases in total cholesterol by mean-33mg/dL (SD +36.5, p<0.001), LDL cholesterol by mean-15 mg/dL (p<0.015) and in weight by mean-2.2 kg (p<0.041). There was also a reduction in the DAD score (F-5 years) of mean 3.2%, but this difference could be influenced by a limited group of patients with extreme T0 values. No patient started or modified lipid-lowering therapy during the period of observation. eGFR values remained stable both in the overall cohort and in the subgroup who started TDF. There were no apparent differences in triglyceride levels, Framingham Risk Score, FRAX Score, blood pressure, BMI or HDL cholesterol.

Conclusions: DOR-based regimens offer a valid switch option in suppressed patients with dyslipidemia, reducing total cholesterol, LDL and cardiovascular risk while maintaining virological suppression. Larger scale studies in real-life settings are needed to confirm these results.

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Antiretroviral therapy

P 21 EFFICACY AND SAFETY OF DOLUTEGRAVIR/LAMIVUDINE IN A PATIENT WITH HIV FOLLOWING SLEEVE GASTRECTOMY

G. De Simone[1], M. Tempestilli[3], E. Teti[1], M. Compagno[1], L. Sarmati[1], A.M. Geretti[2]

[1]Infectious Diseases Unit, Tor Vergata Hospital, Rome, Italy, [2]Infectious Diseases Unit, Department of System Medicine, Tor Vergata University, Rome, Italy, [3]Laboratory of Cellular Immunology and Clinical Pharmacology, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy

Background: Bariatric surgery to address obesity is becoming increasingly common among people living with HIV. Resulting changes in the upper gastrointestinal tract physiology may alter the pharmacokinetics of antiretrovirals (ARVs) and potentially lead to suboptimal plasmatic concentrations.
Case Report: We report the case of a 56-year-old male patient with HIV (CDC B3) who started antiretroviral treatment (ART) in 2009, had good adherence, and showed excellent immune-virological responses to therapy. His most recent regimen, started in 2019 was BIC/F/TAF. Medical history included marked obesity (BMI 43.8 kg/m2), metabolic syndrome, and multiple endocrine neoplasia type 2A (MEN2). In November 2022, he decided to undergo sleeve gastrectomy. Two weeks before surgery, the ART regimen was simplified to single-tablet dolutegravir (50 mg) plus lamivudine 300 mg (DTG/3TC) once daily. The patient was instructed to assume only liquids in the 4 days post-surgery and during this time he took DTG/3TC crushing the tablet. The patient was seen in clinic at 1, 2 and 3 months after surgery. At each visit, plasma HIV RNA remained below <20 copies/mL and no variations in CD4 cell count were observed (Table 1). Plasma concentrations of DTG measured 12 weeks post-surgery using a validated HPLC-UV method showed a Ctrough of 845 ng/mL, well above the recommended therapeutical concentration of 300 ng/mL.
Discussion: Available data suggest that bariatric surgery does not substantially alter the bioavailability of most ARVs, although a drop in plasma concentrations has been described for some ARVs such as atazanavir, raltegravir and rilpivirine. There are conflicting data on DTG and some authors suggest a temporary dose increase to 50 mg twice daily in the first months after surgery. Our therapeutic drug monitoring test revealed optimal plasma levels three months after surgery and no dose adjustment was made. This was based on the consideration that the main site of DTG absorption is the proximal small intestine. In addition, DTG is a weak acid and more soluble in its ionized form in the elevated post-surgery gastric pH.
Conclusions: These are the first reported data on the efficacy of single-tablet DTG/3TC after bariatric surgery. The data suggest that the regimen represents an effective and safe choice in this context, maintaining good plasmatic DTG concentrations and stable viral suppression with no adverse events.

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Antiretroviral therapy

P 22 A RETROSPECTIVE COHORT ANALYSIS TO EVALUATE THE BARRIERS AND FACILITATORS ENCOUNTERED BY HIV-POSITIVE PATIENTS UNDERGOING HAART REGIMEN AND CLINICAL OUTCOMES

D. Cicetti, R. Caprara, G. Pierfelice, L. Appolloni, G. Pensalfine, S. Vitale, A. Stancari

IRCCS University Hospital Company - S.Orsola-Malpighi Polyclinic - Clinical Pharmacy, Bologna

Thanks to the significant advances made in recent decades with the development of once-daily combination therapies, with increased duration of action and efficacy, it has been possible to lower the acceptable threshold of adherence to therapy from ≥95% to 80-85%, while still guaranteeing the estimated viral suppression a <50copies/ml.This study aims to evaluate the correlation between self-reported adherence therapy, obtained through the compilation of specific questionnaires, and the clinical outcomes of patients, trying to demonstrate whether a correct intake of the antiretroviral drugs could be or not an indication of a contained viremia load. The second aim was to understand whether complex therapeutic regimens or other variables could impact non-adherence to therapy. The analysis have been developed in March 2023 at the distribution center of the pharmacy, through dispensing of questionnaires to patients who went to the hospital to collect antiretroviral therapy. The data collection was done using Excel spreadsheets, through which it was also possible to carry out analyses that made it possible to correlate adherence to therapy with clinical outcomes.The study involved 159 patients of which 37% (n.59) aged between 50-60 years and about half (n.71) in treatment for 2-10 years. It emerged that 88% (n.139) of the patients have no one to remind them to take the therapy, moreover more than 63% are subjected to a poly therapeutic regimen. Of all the patients analysed, 32% take 1 or 2 drugs in addition to antiretroviral therapy and 20% more than three. Of 159 patients, 62% (n.99) reported never skipping therapy in the past month. Within the group of patients who skipped therapy (n.60), 72% said it was due to forgetfulness, 14% due to impossibility and 14% attributable to other causes. 89% of patients declare that they do not experience side effects when taking the drugs. Considered the last immunovirological evaluation of the 159 patients in 99% of them an HIV-RNA <50copies/mL is observed and only in 1% an HIV-RNA >50copies/mL. Regarding the assessment of TCD4 count in 86% of patients it is >400 cells/μL.The adherence file proposed to patients proved to be suitable for the assessment of adherence. The main cause of non-intake is forgetfulness (27%) followed by impossibility (6.9%), regardless of the number of tablets and/or frequency of intake. Taking other concomitant drugs does not significantly affect adherence. However, non-optimal adherence is not related to an alteration of the immunological values probably determined by the choice of therapeutic regimens that allow good viremic control. It will be useful to deepen these data by continuing to propose to patients who belong to the clinic the compilation of the adherence form and then discuss it with a multidisciplinary team to intervene promptly and take actions aimed at improving retention in care.

Antiretroviral therapy

P 23 FOSTEMSAVIR, A NEW ANTIRETROVIRAL MOLECULE FOR THE TREATMENT OF HEAVILY TREATMENT-EXPERIENCED (HTE) PLWH WITH MULTI-DRUG RESISTANT (MDR) HIV-1 INFECTION: DATA FROM CLINICAL PRACTICE

P.F. Salvo[1], R. Jo Steiner[1], A. Sanfilippo[1], G. Baldin[2], E. Visconti[2], A. D'angelillo[3], A. Ciccullo[4], F. Raffaelli[2], A. Dusina[2], S. Di Giambenedetto[1,2], A, Borghetti[2]

[1]Dipartimento di Sicurezza e Bioetica, Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, [2]UOC Malattie Infettive, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, [3]UOC Medicina Protetta - ASL Viterbo, Viterbo, [4]Malattie Infettive, Ospedale San Salvatore, L'Aquila

Background: Fostemsavir is a new antiretroviral agent approved by FDA and EMA for the treatment of HIV-1 infection. It is the first attachment inhibitor approved for the treatment of heavily treatment-experienced (HTE) PLWH with multi-drug resistant (MDR) HIV-1 infection. The aim of the study was to evaluate viro-immunological efficacy and clinical tolerability of this new antiretroviral molecule in clinical practice.

Materials and Methods: We selected HTE-PLWH with MDR HIV-1 infection and detectable viremia. Participants switched to fostemsavir in combination with an optimized background therapy (OBT) with at least 2 active antiretroviral molecules. We collected clinical and viro-immunological data at baseline (BL, time of switch) and after 4 weeks (4W). Moreover, for 75% of patients we quantified the total blood-associated HIV-DNA, as a biomarker of the HIV cellular reservoir, by droplet digital PCR at BL and 4W.

Results: We enrolled 8 HTE-PLWH. For 4 patients a previous genotypic resistance testing (GRT) was available, documenting resistance to at least 3 antiretroviral classes; for the other 4 patients the GRT was not available at BL, but resistances were deducible from previous documented virological failures with antiretroviral agents belonging to 3 different classes. All the enrolled patients were Caucasian; men accounted for 75%. Median age was 62 (IQR 54–64) yrs. Two patients (25%) were MSM, 3 (37.5%) were heterosexuals and 3 (37.5%) were people who inject drugs (PWID). Median time since HIV diagnosis was 32 (IQR 30–34) yrs and median exposition to antiretroviral therapy was 28 (IQR 27–31) yrs. A previous AIDS-defining event was present in 75% of the population. The median zenith of plasma HIV-RNA was 5.7 (IQR 5.4–5.8) log10 cps/mL, the median nadir CD4 cell count was 39 (7–182) cells/μL and the median levels of HIV-DNA were 2.72 (IQR 2.5–3.0) log10 copies/106 leukocytes. Demographical and viroimmunological characteristics of each patient are shown in Table 1.

At 4W one patient (12.5%) achieved virological suppression with target non detectable (TND), two patients achieved HIV-RNA levels <30 cps/mL. HIV-DNA decreased in all 6 patients with available data (-0.57 log10 x 106 leukocytes; 95% CI -0.79/-0.35; Wilkoxon matched-pairs signed-rank test p=0.001). A decrease in CD4 cell count was observed, but non-statistically significant (-108 cells/μL, 95% CI -242/+26; Wilkoxon matched-pairs signed-rank test p=0.093).

Three discontinuations occurred during the study period, due to treatment-related gastrointestinal side effects in two cases and headache and insomnia in the third one.

Conclusions: In line with clinical trials, fostemsavir seemed to show good antiviral potency against MDR HIV-1. However, observations from our experience in clinical practice raise concern due to the apparently unfavorable immunological profile and tolerability, prompting the need for further evaluations.

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Antiretroviral therapy

P 24 EXPERIENCE WITH THE USE OF PROLONGED-RELEASE INJECTABLE CAB/RPV IN OUTPATIENTS

N. Bobbio[1], E. Blasi Vacca[1], S.Boni[1], F. Del Puente[1], M. Feasi[1], A. Parisini[1], R. Prinapori[1], D. Fiorellino[2], S. Puppo[2], A. Zunino[3], C. Fraguglia[3], F. Filauro[3], B. Mainero[3], E. Pontali[1]

[1]MD Department of Infectious Diseases, E.E.O.O. Galliera, Genoa, [2]Professional Nurse Department of Infectious Diseases, E.E.O.O. Galliera, Genoa, [3]Pharmacists of the Hospital Pharmacy, E.E.O.O. Galliera, Genoa

Background: Since 9 May 2022 the first antiretroviral (ARV) drugs by intramuscular injection (IM) cabotegravir + rilpivirine (CAB/RPV) entered the market in Italy. Since November 2022 these drugs have been present in our Hospital Pharmacy and are in use in our Outpatient clinic. The aim of the work is to describe the cases observed in 5 months of use of these drugs.

Material and Methods: We prospectively collected data of patients who, since November 2022, underwent CAB/RPV administration, initially orally (28 days) and subsequently by the IM route. For each patient (pts), the following were collected: epidemiological data, evaluation of immunovirological staging and blood chemistry tests, possible onset of adverse events.

Results: 23 pts were observed, 19 males (83%) and 4 females (17%) whose mean age was 46 years, mean BMI 25.4; risk factor for HIV: 11 ES (48%), 11 MSM (48%), 1 TD (4%). 13 pts (65%) had metabolic risk factors such as diabetes, overweight, arterial hypertension, dyslipidemia; 16 pts (69.5%) previously recevied triple ARV therapy, 7 pts (30.5%) previously took oral dual ARV therapy. All pts performed immunovirological staging on the first day of oral CBV/RPV administration, on the day of the first IM administration (28 days after the start of oral CBV/RPV), on the second administration IM of CAB/RPV 21-35 days after the first, and at subsequent bimonthly administrations. All pts in the study showed CAB/RPV HIV RNA <14 cp/ml at the time of oral intake. On the day of the first IM administration of CAB/RPV on 23 pts we recorded HIV RNA <14cp/ml (92%) in 21 pts, 2 pts with viraemic blips (HIV RNA <40cp/ml). 1 pt discontinued treatment due to fever and arthralgias that appeared three days after the first IM administration of CAB/RPV (Injection Site Reactions, ISR). Of the 23 pts in the study, 18 pts performed the second IM administration of CAB/RPV, all viraemias performed showed HIV RNA <14 cp/ml (4 pts will perform the second administration in the next month).

Three days after the second IM administration of CBV/RPV, 1 pt discontinued treatment due to the onset of fever and intense arthralgias lasting for 5-6 days (ISR).

1 pt suspended the therapy due to the appearance of acute pancreatitis; the patient was hospitalized in a Medicine Department of a city hospital, 4 days before admission the patient had been given the second IM injection of CAB/RPV.

9 pts performed the third IM administration of CAB/RPV, 8 pts showed HIV RNA <14 cp/ml, 1 pt with viraemic blip < 70 cp/ml.

Conclusions: Despite the need for a larger series and with a longer observation time, our work shows that the injection therapy with CBV/RPV has excellent virological efficacy while maintaining the suppression of the viraemia. We also observed 3 cases of therapy interruption (2 ISRs), greater experience with these drugs will be essential to better evaluate their tolerability.

Antiretroviral therapy

P 25 EFFICACY, TOLERABILITY, SAFETY AND ADHERENCE TO DOLUTEGRAVIR/LAMIVUDINE AS FIRST-LINE REGIMEN IN THE REAL LIFE SETTING

M. Quaranta[1], M. Ferrara[1], M.C. Ottino[1], A. Serra[1], V. Maccario[1], E. Drappero[1], G. Orofino[2], O. Bargiacchi[3], P. Bigliano[4], D. Vitullo[5], G. Di Perri[1], A. Calcagno[1], S. Bonora[1]

[1]Unit of Infectious Diseases, Department of Medical Sciences Infectious Diseases, University of Turin, Torino, [2]Amedeo di Savoia Hospital Divisione A, Turin, Italy, [3]Infectious Diseases Unit, University Hospital Maggiore della Carità, Novara, Italy, [4]Unit of Infectious Diseases, Cardinal Massaia Hospital, Asti, Italy, [5]Division of Infectious and Tropical Diseases, Department of S. Croce e Carle Hospital, Cuneo, Italy

Background: Dolutegravir/lamivudine (DTG/3TC) in single tablet regimen (STR) has been approved in all main International HIV guidelines as first-line antiretroviral (ARV) regimen for naïve people living with HIV (PLWH). Efficacy and tolerability have been already assessed by GEMINI-1 and GEMINI-2 data at 96 weeks, however few reports are available in literature in the real life setting. Aim of our study was to evaluate efficacy, safety and tolerability and adherence to DTG/3TC in the clinical setting.

Methods: Naïve PLWH on DTG/3TC regimen were enrolled in a multicentre study including four Hospital Centers in Piedmont region from 2018. At W48, a snapshot analysis was performed based on the primary outcome of virological efficacy (HIV-RNA<20 cp/mL) and safety (discontinuation to treatment). Metabolic assessment and adherence to treatment were explored as secondary outcome. Data regarding adherence, expressed as proportion of days covered (PDC) based on the refill from the Hospital Pharmacy was collected in a subset of participants. Study population characteristics were analysed by Mann-Whitney and Wilcoxon, as appropriate. All data are expressed as geometric mean (CI95) and HIV-RNA and cumulative adherence as median (IQR).

Results: 48 PLWH were included, 19% were female, age and BMI were 41 years (38-45) and 23.4 kg/m2 (21.7 -25.2) respectively, with CD4+ nadir of 461.8 cells/μL (397.0-526.6). 1 (2%) participant had BL viral load (VL) more than 500.000 cp/ml and 5 (10.4%) CD4+ T cell count less than 200 cell/μL. At W48, 44 out of 48 participants (92%) resulted to have VL<20 cp/mL with a mean time to virological suppression of 2.5 (1.8-3.3) months, while 2 (4%) resulted to have a detectable VL, respectively 33 and 154 cp/mL and 2 (4%) were early discontinuations due to lost to follow-up. Longer time to suppression was observed in participants with CD4+<200 than CD4>200 cells/μL, respectively 6 (1.3-10.6) and 2.2 (1.5-2.9) months (p=0.004). A concomitant increase of CD4+ T cells and CD4/CD8 ratio (p<0.001) was found in the overall population. Moreover, after one year, no modification of lipid assessment from BL, but a significative increase of creatinine and reduction of eGFR (p<0.001) was observed. In a subset of 36 participants, median cumulative adherence to the regimen was observed to be 99.8% (97.9-100.0) through time of observation.

Conclusions: DTG/3TC showed high efficacy at 48 week (92%) an in our real-life setting, coupled with a high level of adherence and comparable to previous randomized clinical trial. Rate of discontinuation was low (4%) and not related to safety. DTG/FTC confirmed, even in the clinical setting, to be an option in naïve patients.

Antiretroviral therapy

P 26 ACCEPTABILITY OF LONG-ACTING INJECTABLE ANTIRETROVIRAL THERAPY (LAI-ART) IN PEOPLE LIVING WITH HIV

S. Arsuffi[1], C. Mazzi[2], S. Calza[3], I. Izzo[1], I. El Hamad[1], R. Fazio[4], G. Piccardi[4], C. Anzoni[1], M. Migliorati[1], D. Laurenda[1], I. Polesini[1], E. Quiros-Roldan[1], F. Castelli[1], E. Focà[1]

[1]Clinica di Malattie Infettive e Tropicali, Università degli Studi di Brescia e ASST Spedali Civili di Brescia, [2]Università degli Studi di Brescia, [3]Unità di Biostatistica e Biomatematica e Unità di Bioinformatica, Dipartimento di Medicina Molecolare e Traslazionale, Università degli Studi di Brescia, [4]Unità Operativa Farmacia Aziendale, ASST Spedali Civili di Brescia

Background: Long-acting injectable antiretroviral therapy (LAI-ART) was recently approved for the treatment of people living with HIV (PLWH) with a persistent undetectable viral load. The introduction of LAI-ART could change the perception of the patients regarding long-life treatment. The aim of this study is to evaluate the acceptability of LAI-ART in a cohort of PLWH.

Methods: This is a monocentric prospective study. An anonymous, multiple-choice self-completion questionnaire was offered to all the PLWH in care at the Clinic of the Infectious and Tropical Diseases Clinic of the ASST Spedali Civili of Brescia from June 2022 to March 2023.

Results: The questionnaire was administered to 433 subjects: 317 (73.2%) were males, 403 (93.1%) Italians, with a mean age of 53.4 years old. Evaluating the current ART regimen, 385 (88.9%) were single-tablet regimen, 53 (12.2%) two-tablet regimen, 21 (4.8%) regimen were of 3+ tablets. 14 subjects (3.2%) declared to not have correctly taken their ART during the last year. A mean of 2.9 concomitant medication were declared. Considering ART perception, 388 (89.6%) described it as essential, 32 (73.9%) as hard to bear, 23 (5.3%) as a limitation of their liberty. Evaluating knowledge of LAI-ART, 249 (57.5%) haven't ever heard about it, 24 (5.5%) were informed by acquaintances, 73 (16.9%) from the media, 93 (21.5%) at the hospital. Overall, 280 (64.7%) subjects would be favorable to administration at the hospital. Main doubts were the fear of the injections (n=20, 4.6%) and the consuetude to oral ART (n=69, 15.9%). Once-a-week administration at the hospital would be acceptable for 9 (2%) subjects, fortnightly for 25 (5.8%), monthly 110 (25.4%), every two months for 124 (28.6%), at least every three months for 180 (41.6%) subjects. Overall, 198 (45.7%) individuals would prefer administration at home, 156 (36%) at the hospital, 74 (17.1%) in the general practitioner's office, 52 (12%) at the pharmacy or near home.

Conclusions: Our study evidenced that patients aware of the availability of LAI-ART are still few. Subjects seem to favorably accept the perspective, with limitations mainly due to the consuetude to oral ART and to the increment in the number of accesses to the hospital. A precise selection of patients strongly motivated to this therapeutic change, appear to be crucial for the correct implementation of this new treatment strategy.

Patients reported outcomes will be fundamental to evaluate the patients' satisfaction regarding ART and for the proper management of these therapies.

Antiretroviral therapy

P 27 WILL LENACAPAVIR SAVE US? COMPASSIONATE USE IN HEAVILY TREATMENT-EXPERIENCED PATIENTS WITH MULTI-DRUG RESISTANT HIV INFECTION: A NARRATIVE DESCRIPTION OF THE ITALIAN EXPERIENCE

M.C. Ottino[1], G. Orofino[1], A. Soria[2], A. Ranzani[2], M. Feasi[3], G. De Socio[4], G. Lapadula[5], E. Teti[6], S. Martini[7]

[1]Osp. Amedeo di Savoia, Torino, [2]IRCCS Fondazione San Gerardo dei Tintori, Monza, [3]EO Ospedali Galliera, Genova, [4]AO di Perugia, [5]Università di Milano, Bicocca, [6]Policlinico Tor Vergata, Roma, [7]Università degli studi della Campania, Luigi Vanvitelli

Background: Lenacapavir is a first-in-class capside inhibitor, it is emerging as a highly effective drug in heavily treatment-experienced (HTE) patients living with HIV (PLWH) with limited therapeutic strategies. CAPELLA study shows evidence of efficacy and safety in this kind of complex patients, it has already been licensed in the EU, while in Italy is under review by AIFA. Due to the peculiarity of the patients and limited real life experience, the use of this drug is tailored with different strategic choices, as needed in a multy-drug resistant (MDR) HIV infection: as a drug on top of the optimized background regimen (OBR) with fostemsavir or ibalizumab or with an active or partial active backbone RT or INI based, or even in desire for an injective strategy. Currently in Italy, 7 patients are being treated with this drug, we collected their data and first results.

Material and Methods: Italian physicians could ask for the expanded access program for HTE patients with virologic failure and limited treatment options. Each request was separately reviewed and approved by an ethical committee. Key criterias for the request were: virological failure, demonstrated MDR to at least 2 drugs of at least 3 of the main classes (PI, NRTI, NNRTI, INI), inability to take other antiretrovirals (ARV) for intolerance, drug-drug interaction or adverse reactions (AE), absence of other active therapeutic possibilities.

Data were collected by Italian treating physicians from 6 different clinics: genotipic resistence test (GRT), prior ARV lines, risk, comorbidities, polytherapy, baseline data, follow-up (FU) on viral load and CD4 count and AE were collected.

Results: Each HTE patient has a peculiar clinical situation but all of them show a complex GRT profile and a previous use of numerous ARV lines. Although currently the FUs are in most cases very short, therefore not evaluable on the CD4 level, all patients demonstrate viral suppression (VS) already 2 months after the first injectable administration (after a different oral load in period). Lenacapavir was used with a new optimized background regimen (OBR) in most of the cases (mostly with fostemsavir andor ibalizumab), in one case the therapy already in place was maintained with the achievement of the VS. Each case reflects different therapeutic needs despite sharing the common problem of MDR such as to provide a complete injective therapy, to manage a vertical infection in a young adult, or even as a resource after an AE related to another rescue ARV.

Conclusion: Even in the absence of long FUs, Lenacapavir demonstrated good tolerability, immediate achievement of VS in patients with long history of virological failure and exposure to many ARV lines, and great versatility which is useful in the treatment of HTE patients with MDR issue.

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Antiretroviral therapy

P 28 REAL LIFE EFFICACY AND SATISFACTION OF LONG-ACTING ART CABOTEGRAVIR-RILPIVIRINE: NEW ERA OF ART

S. Spampinato[1], A.G. Saia[1], Y. Russotto[1], C. Micali[1], M. Ceccarelli[2], E. Venanzi Rullo[1], G.F. Pellicanò[3], G. Nunnari[2]

[1]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy, [2]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Catania, ARNAS Garibaldi Hospital, Catania, Italy, [3]Unit of Infectious Diseases, Department of Human and Pediatric Pathology "Gaetano Barresi", University of Messina, Messina, Italy

Background: Treatment of HIV infection has historically consisted in daily oral antiretroviral therapy (ART). The introduction of long-acting formulations of cabotegravir + rilpivirine (CAB+RPV) association administered by intramuscular injection allows to treat people living with HIV (PLWH) without pills for the first time in history. Clinical trials showed that switching from oral ART to injectable CAB+RPV is effective and safe, reduces pill burden, increases patients' satisfaction, and improves the adherence.

Methods: Our observational study was carried out at the "G. Martino" University Hospital in Messina (Italy). PLWH switched to an IM ART with CAB+RPV were virologically suppressed for at least 6 months, were taking the same oral regimen for at least 6 months, had no reported or alleged resistance mutation affecting susceptibility to either CAB or RPV. All PLWH on IM CAB+RPV regimen were consecutively enrolled in this study.

Data about viro-immunological effectiveness (HIV-RNA plasma viral load, pVL; CD4+ T-cell count and percentage; CD4/CD8 ratio) and metabolic safety (creatinine, LDL) were collected at baseline, at the end of the lead-in phase with oral CAB+RPV (2 pills) and one month after the first injection. The end of the lead-in phase corresponded with the day of the first IM injection, while the second one was performed one month later, as per protocol. After each administration, we asked PLWH about their satisfaction and pain experience.

Results: We included a total of 14 PLWH, 13 males (92.9%), with a median age of 36 years (30.25-39.75). Twelve PLWH (85.7%) switched from an integrase strand transfer inhibitor (INSTI)-based regimen, 1 (7.1%) from a non-nucleosidic reverse transcriptase inhibitor (NNRTI)-based regimen and 1 PLWH (7.1%) from a protease inhibitor (PI)-based regimen. pVL remained undetectable at both time points. Pain was moderate to severe in 78.5% of cases after the first IM injection and 57.1% of cases after the second injection.

Although not statistically significant, we highlighted an upward trend in CD4+ percentage ($p = 0.641$) and CD4/CD8 ratio ($p = 0.368$), although the CD4+ T-cell count decreased ($p = 0.882$). Low-density lipoprotein cholesterol (LDLc) was not affected by the switch to IM CAB+RPV ($p = 0.417$).

When interviewed about their happiness with the new regimen, 10 out of 14 PLWH (71.4%) answered that they were happy about it, while 3 (21.4%) said they would rather not respond.

Conclusions: Although including a small number of PLWH, our real-life experience shows that switching to IM CAB+RPV is appreciated by PLWH. This regimen is highly effective with persisting undetectable pVL. The upward trend in CD4+ T-cell percentage and CD4/CD8 suggests that IM CAB+RPV might help improving inflammation in PLWH, thus leading to a decrease in cardiovascular disease and metabolic consequences. Pain was the major side effect, as reported in the trials, with a downward trend in its severity.

Antiretroviral therapy

P 29 BICTEGRAVIR VERSUS DOLUTEGRAVIR-BASED REGIMEN IN THE SETTING OF RAPID ART INITIATION: 48-WEEK ANALYSIS IN A ONE CLINICAL CENTER

A. Cervo, V. Borghi, M. Menozzi, M. Digaetano, M.D. Di Trapani, I. Baldisserotto, G. Cuomo, C. Mussini

Infectious Diseases Unit, Hospital University of Modena

Background: Guidelines recommend the use of 2nd generation INSTI in case of rapid start of antiretroviral regimen. We aimed to investigate efficacy and durability of bictegravir (BIC) versus dolutegravir (DTG)-based antiretroviral therapy given to people with new diagnosis of HIV infection in the context of Rapid ART Initiation.

Methods: This is a retrospective study included treatment-naïve people with HIV (PWH) infection from 1st Jan 2017 to 31st Jan 2022 who started a three-drug regimen with DTG or BIC within 7 days from the baseline viro-immunological exams. Hospitalized patients were included too, except those with mycobacterial or criptococcal infection. Virological suppression (VS) was defined as viral load(VL) <50 cp/ml. Virological failure (VF) was defined as HIV RNA >200 cp/ml after undetectable VL. Time and reasons for discontinuation were collected. Durability was defined as time to INSTI discontinuation. Univariable analysis was performed to compare patients by anchor drug, using Fisher-exact test and Mann-Withney-U test as appropriate.

Results: Of 111 naïve PWH who rapidly initiated ART, 46 (41%) and 65 (59%) were on BIC and DTG, respectively. Baseline viro-immunological characteristics were similar between the two groups (Table 1). Median time of ART initiation was 0 day (IQR 0-1). No resistance associated mutations (RAMs) to INSTI and NRTI were found at baseline. During 48-week follow-up, 25/65 (38.5%) subjects in DTG group and 10/46 (21.7%) in BIC group discontinued the treatment (p=0.062) after a median of 6.0 weeks (IQR 2.0-22.5) and 15.5 weeks (IQR 4.5 -32.0), respectively (p=0.380). Switch to a simplified regimen (52.0%) and toxicity (40.0%) were the main reasons for DTG discontinuation; neurological (5/10) and gastrointestinal (3/10) symptoms were the most represented side effects in DTG group. Conversely, being lost to follow-up (60.0%) mainly led to BIC discontinuation (p=0.004). VS at 48 weeks was achieved in 77.5%. Among 76 patients who maintained the same anchor drug, 61 (80.2%) achieved VS: 36/40 (90%) and 25/36 (69.4%) in DTG and BIC group, respectively (p<0.01). Of the 11 subjects in BIC group who did not reach VS, missing data and suspected or confirmed loss of adherence were recorded, in particular during biennial 2020-2021. Two patients experienced VF (1 in DTG group and 1 in BIC group): genotypic resistance test did not show the emergence of new RAMs. There was no difference in trend of immunological parameters (CD4+), creatinine, lipidic profile from baseline to 24 and 48 weeks of follow-up (data not showed).

Conclusion: In the context of Rapid ART Initiation, BIC-based regimen was favored in terms of durability compared to DTG. Patients who started with DTG experienced more toxicities and were more frequently switched to a single tablet regimen. The overall non-optimal rate of VS, in particular in BIC group, may be due to missing data, lower adherence and lost to follow-up during COVID pandemia.

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Antiretroviral therapy

P 30 OUTCOME OF DRV/COBICISTAT-BASED REGIMENS IN HIV-INFECTED PEOPLE WHO EXPERIENCED VIROLOGICAL FAILURE

F. Alberton[1,2], L. Galli[1], R. Lolatto[1], C. Candela[1,2], N. Gianotti[1], D. Canetti[1], M. Chiurlo[1,2], M. Ranzenigo[1,2], M. Strano[1,2], A. Uglietti[3], A. Castagna[1,2]

[1]Infectious Disease, IRCCS San Raffaele Scientific Institute, Milano, Italy, [2]Vita-Salute San Raffaele University, Milano, Italy, [3]Medical Affairs, Janssen-Cilag Italy

Background: Fixed-dose formulations of darunavir/cobicistat showed high efficacy and tolerability in both treatment-naive and treatment-experienced HIV-infected people: DRV/c could represents a choice for HIV-infected people showing virological failure (VF) because of absence of cross-resistance with, non-nucleoside reverse transcriptase inhibitor (NNRTI), integrase strand transfer inhibitor (InSTI) and most protease inhibitors (PIs). The aim of this study was to describe the virological outcome of DRVc−based regimens in HIV−infected patients who experienced VF on any previous drug combination.

Material and methods: Retrospective cohort study (CSLHIV Cohort) of adults living with HIV, who started a DRVc−based regimen with HIV−RNA >50 copies/mL after VF on any previous drug combination. For each patient we recorded data about demographics, ARTs since HIV diagnosis with numbers of previous regimens failure, metabolic and immunological parameters from baseline to 48 weeks to assess cumulative proportion of patients who achieved virologic success (VS), defined as at least one HIV−RNA values <50 copies/mL within 12 months. Kaplan-Meier curve were used for cumulative probabilities of VS and discontinuation, compared by log-rank test. Univariable and multivariable Cox proportional hazard regression models have been performed to identify baseline factors associated with the achievement of VS.

Results: One-hundred seventy six patients were included in this study and their characteristics were reported in table 1. 120 out of 176 people [68.2%; 95% confidence interval (CI): 61.0% - 74.6%)] achieved <50 HIV−RNA copies/mL within 12 months since the start of the DRVc−based regimen. Figure 1 shows cumulative probability of VS. At multivariable analysis, baseline HDL- cholesterol was independently associated to the risk of VS (adjusted hazard ratio=1.021 (95%CI: 1.004-1.038), p=0.014; Table 2). Among the 120 people with VS, 27 (22.5%, 95%CI: 15.9% - 30.8%) had VF during a median follow-up (FU) of 20.8 months since first undetectable HIV-RNA (IQR: 9.1 – 46.4). Resistance testing after VF was available for 2 people: in 1 the following PI resistance mutations were detected: D30N, I50V, N88D; in the second case, no PI resistance mutation were detected. During a median FU of 38.4 months (IQR: 16.4 – 50.5), 65/176 (36.9%, 95%CI: 30.2% - 44.3%) individuals discontinued DRV/c for any reason [37/120 (30.8%) people who achieved VS vs 28/56 (50%) people without VS, p=0.019; median time to discontinuation was longer in people with VS: 41.5 months (IQR: 20.0 – 60.6) vs 23.0 months (IQR: 7.2 – 44.5), p=0.0007]. No statistically significant changes were observed in lipid profile during the DRV/c based regimen treatment period.

Conclusions: The majority of people included in this study achieved VS within 12 months from the beginning of DRV/c based-regimen. DRV/c based-regimens are a viable option for people with VF who were previously treated with different regimens.

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Antiretroviral therapy

P 31 THE IMPACT OF DORAVIRINE ON LIPID METABOLISM: A REAL-LIFE STUDY

G. Valenti, M. Trizzino, L. Pipitò, M. Alfonso, A. Mancuso, A. Cascio

Infectious and Tropical Diseases Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy

Background: Doravirine is the newest NNRTI, recommended as a first-line drug in the treatment of HIV-1 infection. Its use in clinical practice is increasingly widespreading, as several clinical studies have repeatedly demonstrated its efficacy in terms of viral suppression, as well as an excellent safety profile, in particular regarding to lipid metabolism. The purpose of this study is to provide further real-life datas, analyzing the population in therapy with DOR, evaluating the therapeutic efficacy of the drug, and its impact on lipid parameters and hepatic metabolism.

Material and Methods: Starting from January 2021 to March 2023, both naive patients and PLWH treated with DOR at the UOC of Infectious Disease of Palermo AOUP have been enrolled in the trial. The demographic characteristics of the cohort were analyzed, their blood chemistry results were collected and their level of compliance to therapy was tracked. T1 and T2 were respectively defined as: the start of an ART regimen containing Doravirine and the 24-week follow-up.

Results: Our population consisted of 42 patients including 30 men (71%) and 12 women (29%), the mean age was 51.3 years, 90.5% were caucasian. Patients in STR with DOR/TDF/3TC were 6 (14.3%), the rest of the cohort was under other regimens: 71.4% (30) DOR + DTG, 9.5% (4) DOR + TAF/FTC, 4.7% (2) other regimens containing PIs. During the study only two patients were in virological failure: one of these achieved viremia undetectability maintaining the same therapy, the other patient had not yet performed the control sample one month after failure. Comparing the laboratory data at T1 and T2, a statistically significant increase in AST was described, from a mean value of 25.37 U/l to 26.68 U/l (p 0.028); parallel to this, a reduction was observed in the average levels of total cholesterol, LDL, triglycerides, ALT as well as in indices used in clinical practice such as the TyG-index, although none of these has statistical relevance in progress. However, documenting the variation of the mean value of triglycerides in the subpopulation in therapy with DOR + DTG, it was found that this reduction was at the limits of significance: from 141 mg/dl at T1 to 108mg/dl at T2 (p 0.056).

Conclusions: Despite the limitations due to the small number of patients examined, this real-life study confirms the datas already present in the literature regarding the efficacy of Doravirine-based regimens and its neutral effect on lipid metabolism. Once the sample has increased, it could also be useful to further stratify the population, analyzing any comorbidities present and other drugs taken, with particular reference to lipid-lowering drugs.

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Antiretroviral therapy

P 32 CARDIOVASCULAR RISK AND ARV: AN OBSERVATIONAL STUDY OF PLWH WITH PI BASED REGIMEN VERSUS INSTI AND NNRTI BASED REGIMENS

N. Leoni, A. Leonardi, S. Perra, L. Matta, M.F. Nurchi, S. Bergamin, M. Buffa, G. Caligaris, G. Sanna, F. Cabras, A. Bolliri, M. Garau, G. Angioni

UOC Malattie Infettive e Tropicali, SS Trinità, Cagliari

Background: People living with HIV have several classes of available drugs to be taken for life in order to achieve virus-suppression. Comorbidities currently represent an important aspect of virus-suppressed patient, especially in aging experienced patients and naïve patients at an advanced age (on average 40 years in 2021). According to current literature, cardiovascular (CVD) risk deserves more attention.

Materials and methods: In our HIV clinic we selected 90 stably virologically suppressed patients, divided into 3 cohorts of 30 patients each, according to the class of taken drugs: protease inhibitors with boosters, second generation integrase inhibitors without boosters (both triple and dual), and non-nucleoside inhibitors (triple therapy). Each patient followed a therapeutic regimen for at least 3 years. On average, our selected patients were 51.6 years old and had 10.5 years of antiretroviral therapy. 26.6% of the patients were women. The immune profile of all patients was excellent (average 751.6 CD4/mcl). The lipid level was characterized by mean total cholesterol of 190 mg/dl and HDL values of 49.1 mg/dl. CVD risk was assessed with the Framingham score and the DAD full score, specific for HIV patients on antiretroviral therapy. Both scores of all the three patient cohorts were compared. The distribution of each cohort, given the size of the sample, was considered non-normal. The median CVD risk of patients taking PIs were 9.4% (Framingham) and 11.8% (DAD), 8.6% (Framingham) and 6.7% (DAD) in patients with INSTIs, and finally 9.9% (Framingham) and 6.3% (DAD) in patients with NNRTIs. Jasp software was used for statistical analysis, performing the Kruskal-Wallis test and Dunn's test.

Results: Regarding the DAD score, a statistical significance was reached (p=0.049). In particular, the comparison between PIs-based cohort versus both INSTIs-based (p=0.045) and NNRTIs-based (p=0.026) regimens was statistical significant. However, the comparison between INSTIs and NNRTIs was not statistically significant. Regarding the Framingham score, no statistical significance was achieved in any of the possible comparisons.

Discussion: The use of scores such as the DAD, which take into consideration parameters related to the infection (such as the number of CD4s, the years of ART and the exposure to specific drugs), leads to a more precise assessment of the risk.

Conclusions: PLWHs constitute a special population, whose comorbidities, related to ART, infection, and senescence, acquire greater importance now than in the past. Cardiovascular risk assessment should be an important routine in the management of the HIV patient and could influence therapeutic approaches. In fact, the physician should propose a "tailored" therapeutic regimen, with a lower cardiometabolic impact such as INSTIs and NNRTIs, in the face of a lasting virosopression, common to the three classes of antiretrovirals.

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P 33 LONG-ACTING INJECTABLE CAB/RPV VS DTG/RPV: TWO SIDES OF SIMILAR TWO-DRUGS REGIMENS

C. Bartalucci[1,2], F. Baldi[1,2], E. Ricci[3], G. Orofino[4], B. Menzaghi[5], N. Squillace[6], F. Vichi[7], G.F. Pellicanò[8], S. Ferrara[9], E. Sarchi[10], E. Pontali[11], G. V. De Socio[12], G. Cenderello[13], O. Bargiacchi[14], M.A. Carleo[15], F. Lagi[16], S. Piconi[17], S. Martini[18], B.M. Celesia[19], A. Cascio[20], R. Gulminetti[21], G. Madeddu[22], P. Bonfanti[23], A. Di Biagio[1,2]

[1]DISSAL - University of Genova – Genoa, Italy, [2]IRCCS Ospedale Policlinico San Martino – Genova, Italy, [3]Fondazione Asia Onlus, Buccinasco (MI), [4]Division I of Infectious and Tropical Diseases, ASL Città di Torino, Italy, [5]Unit of Infectious Diseases, ASST della Valle Olona – Busto Arsizio (VA), Italy, [6]Infectious Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [7]SOC 1 USLCENTRO FIRENZE, Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Florence, Italy, [8]Unit of Infectious Diseases, Department of Human Pathology of the Adult and the Developmental Age 'G. Barresi', University of Messina, Messina, Italy, [9]Malattie Infettive Univ. AOU Policlinico Foggia, [10]Infectious Diseases Unit, S. Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy, [11]Department of Infectious Diseases, Galliera Hospital, Genoa, Italy, [12]Unit of Infectious Diseases, Santa Maria Hospital, Perugia, Italy, [13]SC Malattie Infettive, ASL1 Imperiese, Sanremo, Italy, [14]Unit of Infectious Diseases, Ospedale Maggiore della Carità, Novara, Italy, [15]Department of Infectious Diseases, Galliera Hospital, Genoa, Italy, [16]Infectious and Tropical Disease Unit, AOU Careggi, Florence Italy, [17]Infectious Diseases, Azienda Ospedaliera di Lecco, Lecco, Italy, [18]UOC Malattie Infettive - Università degli studi della Campania, Luigi Vanvitelli, [19]Unit of Infectious Diseases, Garibaldi Hospital, Catania, Italy, [20]Unit of Infectious Diseases, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy, [21]Infectious Diseases Unit, Department of Medical Science and Infectious Diseases - Fondazione IRCCS Policlinico San Matteo - University of Pavia - Italy, [22]Unit of Infectious Diseases, Department of Medicine, Surgery and Pharmacy, University of Sassari, Italy, [23]Infectious Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza - University of Milano-Bicocca, Monza, Italy

Background: Switch to a two-drug antiretroviral therapy (ART) regimen is a consolidated practice in the management of People Living with HIV (PWH). Injectable cabotegravir (CAB) and rilpivirine (RPV) long-acting offers an alternative to the oral combination of dolutegravir (DTG) and RPV. The aim of this study is to compare clinical and demographic characteristics of two real-life cohort of PWH on these two regimens.

Material and methods: This was an observational prospective study from SCOLTA multi-center observational prospective database. Treatment-experienced PWH who started CAB/RPV or DTG/RPV regimen from July 2014 to 15th March 2023 were included. Data were described using mean and standard deviation (SD) for normally distributed continuous variables, median and interquartile range (IQR) for not normally distributed continuous variables and percentage for categorical and ordinal variables. Differences between the two groups were described using Chi-square and Kruskal-Wallis tests.

Results: 340 PWH were included: 198 PWH (58.24%) in CAB/RPV and 142 (41.8%) in DTG/RPV. Male sex was predominant in both groups, while PWH in CAB/RPV were younger (p=0.0009). The main risk factors for acquiring HIV infection were significantly different in the two groups: prevalently man who have sex with man (MSM) (47.9%) in CAB/RPV group and heterosexual exposure (30.9%) in DTG/RPV group (p=0.0031). Median CD4+T cells were lower in DTG/RPV group (p=0.0044). Five of 198 (2.53%) and 7/142 (4.93%) PWH had HIV-RNA>40 copies/mL. No one had HBsAg positive, while more PWH had HCV-coinfection in DTG/RPV group (p=0.0050). Body mass index (BMI) was lower DTG/RPV group (p=0.0123). PWH in DTG/RPV had higher mean total cholesterol and triglycerides (p<0.0001). No statistically significant differences were found between the two groups regarding comorbidities and comedications. All PWH were treatment-experienced, with higher median time of ART exposure in DTG/RPV group (p=0.0002), more frequently coming from PIs (p<0.0001) and NNTIs regimen (p= 0.0038), while PWH in CAB/RPV were coming more frequently from an INSTIs based regimen (p<0001). In DTG/RPV group a higher median time of previous exposure to PIs (p<0.0001) and NNRTIs (p=0.0307) was observed.

Conclusions: Many differences have been observed in the two groups, showing that although ART regimen consist of similar drugs, injective administration is more likely to be prescribed in young and MSM PWH. In DTG/RPV group, PWH has lower CD4+T cells and more years of ART exposure with higher exposure to PIs and NNRTIs. Surprisingly, the higher BMI in the CAB/RPV group does not represent a limiting factor for its prescription. The number of comorbidities and comedications, seems not a factor in favor of the choice of injective administration.

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Antiretroviral therapy

P 34 DUAL THERAPY VS TRIPLE THERAPY IN EXPERIENCED PLWH: A MULTICENTRE ONE-YEAR LONG OBSERVATIONAL STUDY

Y. Russotto[1], A. G. Saia[1], E.V. Rullo[1], G. F. Pellicanò[2], G. Nunnari[1,3]

[1]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy, [2]Department of Human Pathology of the Adult and the Developmental Age "G. Barresi", University of Messina, Messina, Italy, [3]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, ARNAS Garibaldi Nesima Hospital, University of Catania, Catania, Italy

Introductrion: The introduction of new antiretroviral drugs with increased viral potency, especially integrase inhibitors (INI), has drastically changed the history of HIV. The higher potency has brought to light the necessity to reduce drug adverse effects, drug-drug interaction and costs and two-drug combination therapy has been compared to other three or more drug regimens.

We conducted a multicentre observational study and we observed a group of people living with HIV (PLWH) from four different hospitals who had switched to a two drugs regimen (2DR) for a year, comparing it with a group of similar PLWH who maintained the 3DR regimen, focusing on inflammation markers.

Materials and Methods: We did a multicentre parallel-group, observational study, from four Sicilian hospitals: "Gaetano Martino" hospital of Messina, "Cutroni-Zodda" hospital of Barcellona Pozzo di Gotto, "Papardo" hospital of Messina, "Cannizzaro" hospital of Catania. First group comprehends PLWH aged 18 years or older, with no distinction in sex or race, who switched from a 3 or more drugs antiretroviral therapy (ART), of any class, to a 2DR ART, of any class excluding new long acting treatment, between 2020 and 2022. Second group comprehends PLWH aged 18 or older, who maintained their 3DR, of any class. We observed the two groups through blood analyses that we performed at three time-points (time 0, 6 months and 12 months).We considered the following items: HIV viral load, CD4+, CD4+/CD8+, platelets (PLT) count, C reactive protein (CRP) and lactate dehydrogenase (LDH). We performed a statistical analysis using the student T test.

Results: Group one comprehends 81 individuals, 69 males and 12 females, with a mean age of 54 ± 8 years old. Group two comprehends 97 individuals, 55 males and 43 females, with a mean age of 49 ± 11 years old. During the observation, no statistically significant difference between 2DR group and 3DR group was found in terms of HIV viral load (p-value 0.203), CD4+ count (p-value 0.238), CD4+/CD8+ (p-value 0.556), PLT count (p-value 0.631), LDH (p-value 0.295) and CRP (p-value 0.558). No adverse effects to the therapy, in individuals who had switched, were reported.

Discussion: The major concern in switching to 2DR has been the diminished pressure on HIV and the possibility of viral blips and increase of inflammation factors. Recent studies have reported no changes in activation and inflammation markers in HIV-suppressed people, who switch to 2DR, compared to those who maintain the 3DR. Similarly to the other studies, we did not observe statistically significant changes in inflammation markers.

Conclusion: Considering the brief time of observation as main limitation to our study, we did not observe changes in inflammation markers in people who switched to 2DR and those in 3DR, in a year-long observation.

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P 35 SAFE SWITCH TO DUAL THERAPY IN HIV VERTICALLY TRANSMITTED YOUNG PATIENTS

G. Meraviglia[1], C. Russo Artimagnella[2], A. Sala[1], L. Taramasso[2], S. Rusconi[3], A. Di Biagio[2], V. Giacomet[1]

[1]Pediatric Infectious Diseases Unit, Department of Pediatrics, ASST Fatebenefratelli-Sacco, Luigi Sacco Hospital, Università degli Studi di Milano, Italy, [2]Infectious Diseases Unit, Department of Internal Medicine, IRCCS Policlinico San Martino Hospital, Genova, Italy, [3]Infectious Diseases Unit, ASST Ovest Milanese, Legnano General Hospital and DIBIC "Luigi Sacco", Università degli Studi di Milano, Italy

Background: People living with HIV are exposed to antiretroviral drugs throughout their lives, especially in case of vertical transmission. Dual therapy regimens based on dolutegravir (DTG), the first integrase inhibitor with a high genetic barrier, are becoming increasingly popular for the treatment of HIV-1 infected people, showing excellent safety and efficacy in several observational cohorts. These regimens have been effectively used also in highly experienced patients, giving the opportunity to reduce toxicity and drug burden. However, studies reporting experience of dual therapy in vertically infected people are still lacking.

Material and methods: We analysed data about 27 patients with vertical HIV-1 infection followed in two reference centres of Northern Italy (13 in Milan and 14 in Genova) who switched from a combination antiretroviral therapy (cART) regimen to a maintenance dual therapy with DTG variably associated with lamivudine (3TC), non-nucleoside reverse transcriptase inhibitors (NNRTIs – Doravirine or Rilpivirine) or boosted protease inhibitors (PIs) depending on eventual resistances.

Results: Patient ages ranged from 3 to 37 years (median 31, IQR 21.1-34.3 yrs). Most subjects had a long cART history (median 21, IQR 15.5-26 yrs) and experienced multiple lines of therapy. The resistance testing showed resistance to 2 or more drug classes in 55% of patients. All patients were virologically suppressed at the moment of the switch except two (one for resistances and one for poor compliance), with CD4+ lymphocyte count >200 cell/mcl. Depending on the resistance profile, 10 patients switched to DTG+3TC, another 10 to DTG+boosted PI (DRN/c or ATZ/c) and the remaining 7 to DTG+NNRTI (DOR or RPV). No virologic failure was detected after the switch except for one patient with poor compliance and there was no significant difference in CD4+ lymphocyte counts during the previous regimen and dual therapy (p=0.179, Table 1). One patient had an isolated viral blip (300 copies/ml). Renal function (eGFR) and lipid profile (total cholesterol, HDL-cholesterol, and triglycerides) were not influenced by the switch (p=0.084, p=0.733, p=0.474, p=0.281 respectively, Table 1). No side effects have been registered during the dual regimen. Patient compliance was good or excellent in all cases except for the one. The median follow-up under dual therapy was 28 months.

Conclusions: Our experience supports the switch to dual therapy with dolutegravir for the treatment of HIV-vertically transmitted young patients, being safe and effective in maintaining virologic suppression and an adequate CD4+ lymphocyte count. This implementation addresses the need of more manageable and less impactful regimens. However, due to the pharmacokinetic profile of these drugs, a decisive factor in the success of dual therapy is the patient compliance, being necessary an exhaustive counselling before switch especially in the age of adolescence.

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Antiretroviral therapy

P 36 PWH PIONEERS OF CABOTEGRAVIR AND RILPIVIRINE LONG-ACTING THERAPY IN SCOLTA: WHO ARE THEY?

C. Bartalucci[1,2], F. Baldi[1,2], E. Ricci[3], G. Orofino[4], B. Menzaghi[5], S. Ferrara[6], G.F. Pellicanò[7], N. Squillace[8], E. Sarchi[9], E. Pontali[10], G. Cenderello[11], O. Bargiacchi[12], F. Vichi[13], M.A. Carleo[14], A. Cascio[15], G.V. De Socio[16], P. Bonfanti[17], A. Di Biagio[1,2]

[1]DISSAL - University of Genova – Genoa, Italy, [2]IRCCS Ospedale Policlinico San Martino – Genova, Italy, [3]Fondazione ASIA Onlus, Buccinasco (MI), [4]Division I of Infectious and Tropical Diseases, ASL Città di Torino, Italy, [5]Unit of Infectious Diseases, ASST della Valle Olona – Busto Arsizio (VA), Italy, [6]S.C. Malattie Infettive Universitarie AOU OO.RR. Foggia, [7]Unit of Infectious Diseases, Department of Human Pathology of the Adult and the Developmental Age 'G. Barresi', University of Messina, Messina, Italy, [8]Infectious Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [9]Infectious Diseases Unit, S.Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy, [10]Department of Infectious Diseases, Galliera Hospital, Genoa, Italy, [11]SC Malattie Infettive, ASL1 Imperiese, Sanremo, Italy, [12]Unit of Infectious Diseases, Ospedale Maggiore della Carità, Novara, Italy, [13]SOC 1 USL CENTRO FIRENZE, Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Florence, Italy, [14]Infectious diseases and gender medicine Unit - PO Cotugno, AO dei Colli, Napoli, [15]Unit of Infectious Diseases, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy, [16]Unit of Infectious Diseases, Santa Maria Hospital, Perugia, Italy, [17]Infectious Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza - University of Milano-Bicocca, Monza, Italy

Background: Injectable cabotegravir (CAB) and rilpivirine (RPV) long acting is a revolutionary new antiretroviral treatment (ART) option for HIV infection in virologically suppressed adults on a stable antiretroviral regimen. The aim of this study is to describe the first People Living with HIV (PWH) who started this regimen in Italy, assessing adherence to eligibility criteria.

Material and methods: This was an observational prospective study from SCOLTA multi-center observational prospective database. PWH who started CAB/RPV long-acting injectable regimen from July 2022 to 15th March 2023 were included. Data were described using mean and standard deviation (SD) for normally distributed continuous variables, median and interquartile range (IQR) for not normally distributed continuous variables and percentage for categorical and ordinal variables.

Results: 198 PWH were included: 148 (74,8%) were male, mean age was 48.4 (SD 11.2) years, 187 (94.4%) were Caucasians. The main risk factor for acquiring HIV infection was male-to-male sexual exposure in 95/198 cases (47.9%), and CDC stages was C in 35/195 (17,9%) cases. At the time of enrolment median CD4+T cells were 824 (IQR 580-1070) cells/mm3, and 5/198 (2.5%) PWH had HIV-RNA >40 (range 45.0-314.0) copies/mL. All PWH had negative HBsAg, while 26 PWH (26/197, 13.2%) had HCV-coinfection. Mean BMI was 25.4 kg/m2 (SD 4.1), with 14/164 PWH having BMI >30 kg/m2, mean glomerular filtration rate was 84.8 (SD 19.0), and all PWH had normal liver function with median ALT value of 23 (IQR 17-31) U/L. In the study population, 71/198 (35.8%) and 37/198 (18.6%) have 1 to 2 and ≥3 comorbidities, respectively. Regarding comedications, 79/198 (39.9%) and 28/198 (14.1%) were on 1 to 2 and ≥3 comedications, respectively. All PWH were treatment-experienced, with median time of antiretroviral treatment exposure of 9.9 (IQR 5.9-15.2) years. The previous regimen included PIs in 6/198 (3.0%), NNRTIs in 87/198 (43.9%) and INSTIs in 162/198 (81.8%) cases. Ninety-two PWH were previously exposed to PIs, 125/198 to NNRTIs and 158/198 to NSTIs, with median time of exposure of 42 (IQR 22-96), 69 (IQR 25-118) and 62 (IQR 36.0-81.0) months, respectively. In the study population 64/168 (38.1%) PWH performed the oral lead-in phase with CAB+RPV in tablets before starting CAB/RPV long-acting by injection.

Conclusions: Our real-life data show slight differences from baseline characteristics of PWH in the registration studies. Our population was older, predominantly male, with a higher BMI, and the main previous regimen was INSTIs-based. The appropriateness of prescription was not met in a minority of cases, such as detectable HIV-RNA and BMI higher than 30 kg/m2. Additionally, a consistent proportion of PWH were taking comedications, which could represent a limited benefit of the injectable treatment on the person's pill-burden.

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Antiretroviral therapy

P 37 CD4 AND CD4/CD8 RATIO GAIN IN PLWH TREATED WITH FOSTEMSAVIR: RESULTS FROM THE PRESTIGIO REGISTRY

R. Papaioannu Borjesson[1], L. Galli[2], R. Gagliardini[3], M. Feasi[4], M. Ferrara[5], S. di Giambenedetto[6,7], F. Lagi[8], G. Marchetti[9], M. Malena[10], A. Cervo[11], A.M. Cattelan[12], F. Maggiolo[13], M. Fabbiani[14], V. Spagnuolo[2], A. Castagna[1,2]

[1]Faculty of Medicine and Surgery, Vita-Salute San Raffaele University, Milan, [2]Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, [3]National Institute for Infectious Diseases 'L. Spallanzani' IRCCS, Rome, [4]Ente Ospedaliero Ospedali Galliera, Genova, [5]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, [6]Department of Safety and Bioethics, Catholic University of the Sacred Heart, Rome, [7]Infectious Diseases Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, [8]Department of Clinical and Experimental Medicine, University of Florence, [9]Clinic of Infectious Diseases and Tropical Medicine, San Paolo Hospital, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, [10]Infectious Diseases Unit, AULSS9 Scaligera, Verona, [11]Department of Infectious Diseases, Azienda Ospedaliero-Universitaria di Modena, [12]Azienda Ospedale-Università Padova, [13]Department of Infectious Diseases, Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, [14]Department of Medical Sciences, Infectious and Tropical Diseases Unit, University Hospital of Siena

Background: In the BRIGHTE trial the overall rate of virologic response to fostemsavir (FTR) was 53% at week 96 with a mean increase of 205 (SD 191) and 119 (SD 202) CD4+/μL in non-randomized and randomized cohort, respectively.

Our aim was to describe the immunological recovery of FTR in people living with 4-drug class resistant HIV (4DR-PLWH) in a real-life setting.

Material and Methods: We included PLWH from the PRESTIGIO Registry, with a documented resistance to NRTIs, NNRTIs, PIs and INSTIs (if no INSTI genotypic resistance test was available, a virological failure to an INSTI-regimen was accepted as inclusion criterion), who started a FTR-including regimen with HIV-RNA>50 copies/mL.

Follow-up (FU) started from the date of FTR start (baseline; BL) until discontinuation of FTR/death/freezing date (28 Feb 2023). Discontinuation of FTR was defined as interruption of the drug for any cause.

Descriptions by median (IQR) or frequency (%). Genotypic susceptibility score for the optimized background therapy introduced with FTR (OBT-GSS) was estimated according to the cumulative data of the available plasma genotyping resistance tests recorded for each patient at baseline.

Results: Overall, 21 4DR-PLWH were included; the overall baseline characteristics are reported in Table 1.

After a median FU of 25.2 months (IQR: 3.9-80.5), 15 (65.2%) 4DR-PLWH maintain the FTR-including regimen [FTR treatment ongoing since 25.3 months (2.7-81.9)] and 8 (34.8%) discontinued FTR after 8.6 months (4.7 -30.6). Virological failure was the most common cause of discontinuation (n=6, 75%); the median HIV-RNA at time of discontinuation was 4.56 (2.67-5.28) log10cp/mL.

At last FU visit, the overall median CD4+ change (estimated in 19/21 people due to recent FTR start) was +35 cells/μL (IQR: -15/+176), the median CD4/CD8 ratio change was +0.04 (IQR: -0.008/+0.23) and 9/19 (47%) people had HIV-RNA < 50 copies/mL.

Characteristics of PLWH who experienced a greater (≥176 cells/μL, third quartile of CD4+ change) vs lower immunological recovery (<176 cells/μL) at the end of FU were evaluated; no significant differences were found, however, PLWH with a greater CD4+ recovery tended to be infected with HIV more recently, less treated with ART, to have a higher nadir CD4, a lower HIV-RNA at the start of FTR and a higher OBT GSS (Table 1). The maximum values of CD4+ and CD4/CD8 ratio changes per patient achieved during FTR treatment are reported in Figure 1; among PLWH with CD4+ change≥ 176 cells/μL, some individual achieved very high increases as illustrated in Figure 1.

Conclusions: In our preliminary study a quarter of PLWH treated with FTR had a strong CD4+ cell count gain with a heterogeneous CD4+/CD8+ increase. Studies are needed to identify predictive factors of immunological recovery.

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Antiretroviral therapy

P 38 CLINICAL TRIALS VERSUS REAL-LIFE: SIMILARITIES AND DIFFERENCES OF PATIENTS RECEIVING LA CAB/RPV IN A LARGE CLINICAL CENTRE

M. Piscaglia[1,4], D. Moschese[1], G. Pozza[2,4], A. Giacomelli[2], A. Ridolfo[2], F. Caruso[3,4], F. Petri[3,4], L. Galli[3,4], C. Atzori[3], P.R. Meraviglia[3], A.F. Capetti[1], S. Antinori[2,4], A. Gori[3,4], G. Rizzardini[1], M.V. Cossu

[1]I Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [2]III Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [3]II Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [4]University of Milano, Milan, Italy

Background: Cabotegravir/rilpivirine is the first long-acting injectable cART approved for virologically suppressed adults with HIV-1.
As this novel administration route present a high degree of acceptance and anticipation from PLWH, its safety, efficacy and tolerability data only come from clinical trials.
Aim of this study was to compare clinical features of our cohorts of patients from clinical trials and real-life setting.
Material and methods: As this combination started to be commercially available from October 2022, we retrospectively analyzed and compared the characteristics of patients enrolled in clinical trials (FLAIR, ATLAS, ATLAS-2M and SOLAR) with those of patients prescribed with this LA regimen in real life.
Data for continuous variables are showed as means or median (and SD or IQR as appropriate) and categorial variables as frequencies and percentages. For comparison of the 2 groups indipendent T-test, Mann-Whitney and Chi square test were used where adequate.
Results: 68 patients were included in the Trial Cohort while 63 patients were included in the Real Life Cohort. Patients' characteristics are summarized in Table 1.
Among demographic characteristics, differences in sex at birth, race, ethnicity, BMI and HIV risk factors were not statistically significant, although of note Is the high involvement of female PLWH in both cohorts.
Yet the Real Life Cohort shows some statistically significant peculiarities featuring a median older age ($p<0.001$) and a longer history on ART (127 months [IQR 79-213] vs 36 months [IQR 23-68]). Also, the Real Life group featured a slightly higher number of patients with history of AIDS.
As expected, patients with an longer infection present a more heterogeneous cART history: interestingly, patients in the Real Life Cohort show a significantly higher exposition to NNRTI in their history. These data was expected due to less stringent selection criteria in every-day practice.
No differences in comorbidities rates and in daily comedications therapies were identified in the 2 groups.
Follow up time is still too short to permit any other comparison between the two groups but at the moment no patient discontinued this regimen due to safety, clinical or personal reasons the Real Life Cohort.
Conclusions: CBV/RPV present the potential to become a valid option for a larger population than thought. In fact, our experience from real life shows that also older patient with multiple morbidities and medications as well as those with a longer HIV history and experience on NNRTI drugs have accessed and can benefit from it. Still, further studies are needed to better understand safety, efficacy and tolerability on special populations in the long term.

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Antiretroviral therapy

P 39 "TEST AND TREAT STRATEGY": EVALUATION DATA FROM A MULTICENTER ITALIAN COHORT

A. Carbone[1], V. Iannone[1], L. Oreni[2], P. Fusco[3], M. Fabbiani[4], V. Borghi[5], A. Giacomelli[2], S. Antinori[2], C. Mussini[5], C. Torti[3], M. Tumbarello[4], S. Di Giambenedetto[1,6], G. Baldin[6]

[1]Istituto di Malattie Infettive, Dipartimento di Sicurezza e Bioetica, Università Cattolica del Sacro Cuore, Roma, [2]Infectious Diseases Unit, DIBIC Luigi Sacco, University of Milan, [3]Unit of Infectious and Tropical Diseases, Department of Medical and Surgical Sciences, "Magna Graecia" University, Catanzaro, [4]Department of Medical Biotechnologies, University of Siena, Siena, [5]Azienda Ospedaliero Universitaria di Modena, Clinica Malattie Infettive e Tropicali, Modena, [6]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, UOC Malattie Infettive, Roma

Background: Antiretroviral therapy (ART) has been shown to dramatically reduce the viral load, leading to a strongly reduction in transmission risks. Test-and-treat and rapid-ART-start strategies show promise in the progress toward the HIV care,testing and initiating antiretroviral therapy upon diagnosis.Our aim is to evaluate effectiveness of "Test and treat" approach in term of achieving virological suppression and probability of maintaining the first ART regimen at 6 months.

Methods: In this multicenter, retrospective, observational cohort study involving five Italian centers we enrolled ART-treatment naïve PLWHIV from 2018 to 2022.We recorded the first antiretroviral regimen and collected the viro-immunological parameters both at baseline (BL, time of ART initiation) and after 6 months from the diagnosis. Then we calculated the elapsed time between HIV diagnosis and ART initiation,based on that participants were divided into 4 groups.Survival analysis of the first ART regimen was performed using Kaplan Mayer curves.

Results: We enrolled 273 participants:216 were male (79,1%), with a median age of 41 (IQR 33-51) yrs, with an AIDS-defining-illnesses registered in 59 participants (21,6%). Median CD4 cell count was 204 cell/mm3 (IQR 45 -450). Patients' characteristics at baseline are summarized in Table 1.Regarding the first line regimen (or initial ART) 215 patients received a triple therapy with a two-NRTI backbone (TAF/FTC) combined with an integrase inhibitor as anchor drug (i.e., 114 DTG, 74 BIC, 25 RGV and 2 EVG) and 17 received a triple therapy with a two-NRTI backbone (TAF/FTC) combined with boosted protease inhibitor (Darunavir).Twenty-four started a dual regimen containing 3TC/DTG.Median time from HIV diagnosis to the ART initiation was 8 (IQR 3-21) days,11 in 2018, 8 in 2019, 7 in 2020, 8.5 in 2021 and 3 in 2022.Forty-four participants started ART within a day from the diagnosis (0-1 dd, first group);88 participants started ART within 7 days (2-7 dd, second group);52 included participants who started ARV within 15 days (8-15 dd, third group);89 participants started ART over than 15 days after diagnosis (>15 dd, fourth group).Virological suppression was achieved in 139 patients (71%) within 6 months and no statistically significant differences between the four groups was found.The probability of maintaining the first ART regimen at 6 months was 78.4% (SD 2.5%);no differences were found between groups.Reasons for treatment discontinuation were simplification (21 PTS, 36,2%),hypersensitivity reaction (6 PTS, 10,3%), neurological toxicity (6 PTS, 10,3%),renal toxicity (2 PTS, 3,4%),gastroenteric toxicity (1 PT, 1,7%),dyslipidemia (1 PT, 1,72%),DDI (3 PTS, 5,2%),other (18 PTS, 31,0%).

Conclusions: In our cohort, we did not observe an advantage in using one day treatment approach, compared to a delayed ART initiation. Further evaluations are needed to define the optimal timing of ART initiation, leading to improve efficacy of antiretrovirals regimen.

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Antiretroviral therapy

P 40 ANTIRETROVIRAL THERAPY IS ASSOCIATED WITH SEXUAL DYSFUNCTION AND PARESTHESIAS

V. Vola, E. Gentilini Cacciola, P. Vassalini, A. Lazzaro, G. d'Ettore, C.M. Mastroianni

Policlinico Umberto I, Università La Sapienza, Roma

Background: There is a lack of data In literature about the impact of cART and symptoms due to adverse drug reactions (ADRs). In particular, Sexual Dysfunction is often unaddressed in routine clinical consultation, and important symptoms like Erectile disfunction (ED) in men are often neglected. While some studies suggest that cART, particularly protease inhibitors (PIs), is associated with ED, other studies fail to show any association. Moreover these data were collected from old cART regimens. In this research we administrated in PLWH the PRO-CTCAE questionnaire, used in several clinical studies to capture symptomatic toxicities due to therapy in patients. Aim of the study is investigate association of currently cART regimens and general ADRs and symptoms associated with them, in particular ED. Second end point is to evaluate the frequency of ED and its association with other symptoms due to cART intake.

Material and methods: This is an observational retrospective real life cohort describing data from patients currently under ART. The following information were extracted from the database of the Department of Public Health and Infectious Diseases of Sapienza University of Rome: demographics (age, sex), smoking, risk factors for HIV infection, time from HIV-1 diagnosis, history of AIDS diagnosis, HCV co-infection, HBV co-infection, presence of comorbidities, number of comedications, time with HIV-1 RNA < 50 copies/mL before switch, BMI, renal function, HDL- and LDL-cholesterol, HIV-RNA, CD4+, CD8+, CD4/CD8 ratio. We interviewed 137 patients.

Results: The vast majority of PLWH enrolled in the current study receive an INSTI-based regimen (56 %), while 33 (30%) partecipants receive an NNRTI-based regimen, followed by PI-based ART (23%). The PRO-CTCAE Item Library includes 124 items representing 78 symptomatic toxicities drawn from the CTCAE.

Items can be summarized as followed: GI problems, reported by 63%; respiratory problems, reported by 22%; cardio/circulatory problems reported by 25%; cutaneous problems reported by 34%; Neurological problems reported by 30%; concentration and memory problems, reported by 34%; pain reported by 36%; insomnia, fatigue in sleep and awake problems reported by 42%; mood problems reported by 24%; Achieve and maintain erection (34%), Ejaculation problems (10%), Decreased libido (22%), Delayed orgasm (14%), Unable to have orgasm (7%), Painful sexual intercourse (3%), into SD reported by 42%.

Conclusions: A correlation has been seen between ART and the following side effects: erectile dysfunction and paresthesia. This result increases in a consistent manner with increasing age. We divided the > 55 and < 55 patients, observing that the Side effect remains correlated with a higher prevalence in the over 55s, probably due to the presence of comorbidities. These data have statistical significance and our aim is to increase the number of patients observed.

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Antiretroviral therapy

P 41 RESCUE THERAPY WITH IBALIZUMAB IN HIV MDR PATIENT

S. Martini[1], N. Cuomo[2], M. Pisaturo[1], A. Cascone[1], N. Coppola[1]

[1]UOC Malattie infettive Università degli studi della Campania Luigi Vanvitelli, Napoli, [2]AORN dei COLLI, Unità di Malattie Infettive ospedale Cotugno, Napoli

Background: Advances in antiretroviral therapy have improved efficacy,tolerability and adherence,but some patients remain more difficult to manage.These are patients who have changed many therapeutic regimens developing multidrug resistance(MDR).The guidelines in this case suggest setting up a therapy that contains new generation drugs associated with residues that are still effective.One such new generation drug is Ibalizumab,a monoclonal antibody that blocks the CD4 cell receptor thus preventing interaction with the viral gp1201.

Materials and Methods: Our clinical case concerns a patient who presents over the years a range of multiple mutations to all classes of antiretrovirals,evident in resistance tests performed on plasma and HIV-DNA.On the basis of these tests,a rescue therapy was set up with the combination of Etravirine+Tenofovir/Emtricitabine +Dolutegravir+Ibalizumab.At the time of introduction of this therapy,the patient had HIV-RNA of 37,800 copies/ml and CD4+ of 147 cells/µL(14%),CD4/CD8 0.25.He started therapy with ibalizumab a year ago,first as monotherapy with a loading dose of 2000 mg,then after 7 days an 800 mg dose associated with drugs chosen according to the resistance test.

Results: The viro-immunological data were progressively evaluated showing efficacy of the rescue therapy.After 7 days,ibalizumab alone had already reduced the HIV viral load by 2 logs.At 3 weeks,after combining other drugs with residual antiviral activity,the viraemia was reduced by 1 log more and after 4 weeks viral suppression was achieved.The CD4 count improved progressively from 147(14%) to 230 cells/µL(19.3%).The patient experienced no adverse events except an increase in blood pressure after ibalizumab infusions.In the last 3 months,the patient temporarily discontinued ibalizumab,without losing viro-immunological efficacy.During the follow-up we also noticed a progressive reduction in the detectability of viral mutations in the reservoir.The latest HIV-DNA genotyping test shows no viral mutations.This could explain the efficacy of rescue therapy even without ibalizumab for the last 3 months.

Conclusions: In conclusion,our case report shows that ibalizumab was highly effective in lowering viral load,both alone and subsequently in combination with other antiretrovirals with residual efficacy.The persistent virological suppression was accompanied by a good immunological recovery,never previously obtained by the patient.The efficacy of the therapy was also highlighted in the reservoir with a progressive reduction of HIV-DNA and the impossibility of detecting initially present mutations.In fact,the patient showed virological suppression even after discontinuing ibalizumab in the last 3 months.The overall safety profile was good,despite the onset of hypertension following ibalizumab infusions,requiring pharmacological treatment.Our data confirm the efficacy of ibalizumab in salvage therapies of MDRs.

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Antiretroviral therapy

P 42 ANALYSIS OF DETERMINANTS OF C-ART SWITCH STRATEGIES IN PLWH IN POST-COVID-19 ERA: RESULTS FROM A REAL-LIFE RETROSPECTIVE STUDY FROM A TERTIARY UNIVERSITY CENTER IN ITALY

E. Zappulo, N. Esposito, A. Truono, M.E. Forte, G. Di Filippo, M. Cotugno, S. Mercinelli, I. Gentile

Department of Clinical Medicine and Surgery, Section of Infectious Diseases, University of Naples "Federico II", Naples, Italy

Background: In people living with HIV(PLWH) on combination-antiretroviral-therapy(c-ART), therapeutic switch is imperative in case of treatment failure and optional in virologically suppressed adult patients in order to reduce or prevent drug toxicity, ease treatment of comorbidities, enhance patient satisfaction and finally improve its quality of life. In this study, we provided updated real-life data of the status of switch rates and determinants of c-ART switch in a population of PLWH in southern Italy in post-COVID-19 era.

Methods: All PLWH who experienced a c-ART switch between Oct.2020-Jan.2023 at the Infectious Diseases Unit of "Federico II" University Hospital in Naples, Italy, were retrospectively recruited. Data were collected from charts and electronic medical records review.

Results: A total of 108 patients (69% male) were enrolled, 52% switched to two-drug regimens (2DR), 48% to three-drug regimens(3DR). Patients baseline characteristics stratified according to main regimen are reported in Table.1. Overall annual switch rates were 10.5% (60/569) from Oct.2020-Oct.2021, and 9%(54/598) from Oct.2021-Oct.2022. Patients in 3DR were more often diagnosed HIV infection before 1996 (21%vs 10%,p=0,044). Patients with concomitant obesity and steatosis were the more commonly switched to 3DR (12% vs 2%,p= 0,043 and 33% vs 16%,p= 0,038 respectively). In 2DR arm, switch was predictably quite always due to reduction of components (81% vs 2%, p<0,001) followed by the prevention of long-term toxicity (39% vs 13%, p= 0,008); in 3DR group the main determinant was simplification(18%)(Table2). Significant differences were reported in terms of sleep problems and pregnancy, indications for exclusive switch to 3DR (9%,p=0,023; and 14%,p=0,002, respectively). At switch, median CD4/CD8 ratio and CD4 cell counts were significantly higher in patients in 2DR (1,49 vs 1,10, p=0,005; 821 vs 648 cells/mm3, p=0,013; respectively)(Table2). Univariate analysis showed that the switch to 3DR was performed more often in female patients, exposed to multiple prior c-ART, with HIV-RNA > 20 copies/mL, on PI-based regimen and with CD/CD8<1 (Table 3). At multivariate model, female sex, multiple cART lines, CD4/CD8 ratio <1 and HIV-RNA >20 copies/mL remained strongly correlated with the choice of a 3DR (OR:1,012, 95%CI: 1,05-7,19, p=0,039; OR:1,155, 95%CI:1,22-8,29,p=0,018; OR:1,406,95%CI:1,54-10,78, p=0,005; OR:0,985,95%CI:1,077-6,658,p=0,034, respectively). No impact of the CDC '93 class at the diagnosis, disease duration, age or presence of comorbidity was observed.

Conclusions: Over the study period, the annual switch rate in our cohort was approximately 10%: prescription of 3DR was carried out significantly more often in patients with lower CD4/CD8 ratios and higher rates of HIV-RNA>20 cp/ml at the time of switch. Female sex and multiple c-ART regimen were a priori factors associated with the choice of a 3DR.

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Antiretroviral therapy

P 43 IMMUNE RECONSTITUTION AND SAFE METABOLIC PROFILE AFTER THE SWITCH TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE FUMARATE AMONG VIROLOGICALLY CONTROLLED PLWH: A 96 WEEK UPDATE FROM BICTEL COHORT

J. Morcos[1], A. Lazzaro[1], D. Bianchini[1], E. Gentilini Cacciola[1], I. Mezzaroma[2], M. Falciano[1], C. Andreoni[1], C. Fimiani[1], L. Santinelli[1], L. Maddaloni[1], G. Bugani[1], G. Ceccarelli[1], C.M. Mastroianni[1], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Policlinico Umberto I of Rome, Rome, Italy, [2]Department of Translational and Precision Medicine; Sapienza University of Rome, AOU Policlinico Umberto I of Rome, Rome, Italy

Background: The single tablet regimen based on bictegravir/emtricitabine/tenofovir alafenamide fumarate (BIC/FTC/TAF) is a recommended regimen for the treatment of people living with HIV (PLWH).Our previous observations on the immunological profile of PLWH switching to BIC/FTC/TAF under virological control and ongoing antiretroviral therapy (ART) showed un unexpected immune reconstitution after 48 weeks (w48) from the switch [1]], which was confirmed at week 96 (w96) [2].

Thus, we aimed to confirm efficacy, safety and tolerability on larger sample size after w96 from the switch; and to assess whether the improvement in the immune profile observed after the switch to BIC/FTC/TAF was associated with baseline (BL) features.

Methods: The BICTEL cohort is an observational retrospective real-life cohort describing data from PLWH who switched their current ART to BIC/FTC/TAF, independently from the previous ART regimen. The following data were retrospectively collected from medical records: virologic control (HIV-RNA <50 copie/ml), immune (CD4+ T cells, CD8+T cells and CD4+/CD8+ ratio) and metabolic changes from BL. Statistics used are described in Figure 1.

Results: The per protocol analysis (treating missing as excluded) showed a virologic suppression rate of 95.2% (118/124; CIs: 89.8%–98.2%). At BL, 2 participants had M184V mutation and 3 had at least one thymidine analogue mutations. None of them showed virologic failure at both w48 and w96 and all completed the follow-up. A significant increased (p<.001) in CD4+ and CD4+/CD8+ ratio as compared to BL was confirmed at w96, with a median increase in CD4+ by 136 cells/µl. CD4+/CD8+ ratio at w96 were significantly higher tan w48 values (p.014). Such immune reconstituition showed to be associated to BL immune status. Both the w96 versus BL (p .004) and w48 versus BL (p. 001) comparison showed a negative relationship between the increase in CD4+T cells count and the CD4+/CD8+ ratio on one side, and the BL CD4+ Tcells count, on the other, as showed in Figure.

Conclusions: We confirmed BIC/FTC/TAF as an effective, safe and tolerated choice for all PLWH, including women and older tan 55.. Beyond the unexpected and promising effect of BIC/FTC/TAF on immune reconstitution observed in participants with sustained virological suppression prior to the switch, we demostrated an inverse association between the degree of immune impairment at BL and immune reconstitution following the switch. Further studies are needed to better understand the impact of BIC/FTC/TAF on immunity.

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Antiretroviral therapy

P 44 CMV RE-ACTIVATION IN PATIENTS ON TRIPLE ART SWITCHING TO B/F/TAF OR DTG/3TC: A SUBSTUDY OF THE DEBATE TRIAL

A. Cossarizza[1], A. Cozzi-Lepri[2], A. Paolini[1], A. Neroni[1], S. De Biasi[1], M. Mattioli[1], D. Lo Tartaro[1], R. Borella[1], L. Fidanza[1], L. Gibellini[1], E. Santacroce[1], B. Beghetto[3], E. Roncaglia[3], G. Nardini[3], J. Milic[3], M. Menozzi[4], G. Cuomo[4], M. Di Gaetano[4], G. Orlando[4], M. Sarti[5], M. Lichtner[6], V. Borghi[4], G. Guaraldi[3,4], C. Mussini[3,4]

[1]Chair of Pathology and Immunology, University of Modena and Reggio Emilia School of Medicine, Modena, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [3]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy, [4]Clinic of Infectious Diseases, Azienda Ospedaliero-Universitaria Policlinico of Modena, Italy, [5]Clinical Pathology Department, Virology Section, Azienda Ospedaliero-Universitaria Policlinico of Modena, Italy, [6]Clinic of Infectious Diseases, University La Sapienza, Rome, Italy

Background: The aim of the DEBATE randomized clinical trial was to compare the immunophenotype and inflammatory biomarkers in virally-suppressed PLWH switching from a three-drug regimen (3DR) to a B/F/TAF vs. the combination DTG/3TC. CMV previous infection has been related to poor prognosis in people living with HIV. This sub-study had the aim of analyzing the effects of such switch on the amount of cytomegalovirus (CMV) reactivation and on the specific, anti-CMV T cell immune response.

Methods: This was an open-label, prospective RCT enrolling PLWH receiving a 3DR who switched to B/F/TAF or DTG/3TC. Blood was taken at time 0 (T0) and after 6 (T6) and 12 months (T12); peripheral blood mononuclear cells (PBMC) and plasma were isolated and frozen until used, using well standardized protocols. The amount of CMV-DNA in PBMC was quantified by digital PCR, plasma levels of anti-CMV IgM and IgG were measured by CLIA and the functionality of specific CD4+ T cells was assessed by the intracellular cytokine staining assay after stimulation with the CMV peptide pp65 (measuring CD107a, IFN-gamma, TNF, IL-2 and IL-17 by polychromatic flow cytometry). CMV re-activation was defined as the presence of anti-CMV IgM in a patient previously IgG+ and/or the presence of CMVDNA.

Findings: We enrolled 66 PLWH (33 per arm). All patients had positive CMV IgG at baseline. In the group of PLWH who switched to DTG/3TC (arm “A”) we found one patient positive to CMV-DNA at T0 and one positive at T12, and two other different patients showing detectable IgM plasma levels at T12. Thus 3 patients showed CMV re-activation (9.1%). In the group of those who switched to B/F/TAF (arm “B”, that had 2 dropouts after 6 months) we found one patient who had detectable plasma levels of IgM at T0, T6 and T12 and who also had detectable CMV DNA at T12. Thus, no patient had re-activation (0%). Among patients who displayed plasma IgM, the analysis of T cell polyfunctionality revealed that throughout the study the patient in arm B had less anti-CMV polyfunctional CD4+ T cells (expressing both a marker of cytotoxicity such as CD107a and TNF) in comparison with those IgM+ or CMV+ present in the arm A.

Interpretation: The presence of CMV re-activation either in arm B/F/TAF and at baseline, thus on triple therapy in arm DTG/3TC confirms that the re-activation of this virus could happened also during suppressive triple therapy. Nevertheless, our study showed that in patients switching to DTG/3TC CMV re-activation was frequently detected while that was no cases among patients switching to B/F/TAF. In conclusion, switching to DTG/3TC could increase the risk of CMV reactivation. More studies are needed to confirm these data.

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Clinical HIV

P 45 CLINICAL/THERAPEUTIC CORRELATES OF ANXIETY AND DEPRESSION IN PEOPLE LIVING WITH HIV

A. Calcagno[1], M. Trunfio[1], F. Portesani[1], E. Vuaran[1], D. Vai[1], G. Guastamacchia[2], M.C. Tettoni[1], M. Ferrara[1], G. Di Perri[1], S. Bonora[1]

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Ospedale Amedeo di Savoia, Turin, Italy, [2]Unit Of Neurology, Ospedale Maria Vittoria, Turin, Italy

Background: A high prevalence of anxiety and depressive disorders have been reported in people living with HIV (PLWH). Since both affect cognitive function and quality of life it would be important to better characterize contributing factors besides genetics background and psychosocial features.

Material and Methods: PLWH on cART undergoing neurocognitive tests were enrolled after signing a written informed consent. Anxiety and depression symptoms were assessed through the self-filled Hamilton Anxiety Rating Scale (HAM-A) and the Beck Depression Inventory II (BDI-II). The severity of anxiety symptoms was graded as none (≤7), mild (8-14), moderate (15-23) and severe (≥24) while depression as none (≤13), mild (13-19), moderate (20-28) and severe (≥29). Variables are described as average values (± standard deviation); stepwise multivariate analysis were conducted both for continuous variables (linear regression) and for categorical ones (binary logistic regression).

Results: We enrolled 405 patients: mostly male (340, 83.9%) and aged 53.7 (+/-10.1) years. Current and nadir CD4 were 607 (307) cells/mm3 and 200 (157) cells/mm3. HIV RNA was <20 copies/mL in 343 (84.7%) participants; cART contained integrase ("INSTI", 197, 48.6% with 92 receiving dolutegravir), protease ("PI", 164, 40.5%) and non-nucleoside reverse transcriptase inhibitors (120, 29.6%). Average HAM-A score was 5.2 (+/-5.4) with 19%, 6.2% and 1.2% showing mild, moderate and severe anxiety symptoms. Average BDI-II score was 7.8 (+/-8.0) with 21.5%, 5.9% and 2.7% showing mild, moderate and severe depression symptoms. The correlation between the two scores was fair (R2=0.42, p<0.001): among 14 participants with either severe anxiety or severe depression only two had both. At linear regression analysis HCV-positivity (p=0.007), non-Italian-born (p=0.010) and female gender (p=0.044) were independently associated with anxiety symptoms; HCV-positivity (p=0.017), non-Italian born (p=0.0280) and PI use (p=0.044) were independently associated with depressive symptoms. At multivariate analysis dolutegravir use was associated (p=0.048) with severe anxiety. Severe depression was observed only in Italian-born participants and it was less prevalent with HIV RNA<20 copies/mL (p=0.056) and INSTI use (p=0.061).

Conclusions: Anxiety and depressive symptoms are frequently reported by PLWH. Besides sex, age and ethnicity, comorbidities (including HCV-positivity) and therapeutic (PI and dolutegravir use) factors need to be considered in the management of these disorders.

Clinical HIV

P 46 HBCAB POSITIVITY IS A RISK FACTOR FOR FAILURE TO ACHIEVE COMPLETE VIROLOGIC SUPPRESSION OF HIV-RNA AFTER ANTIRETROVIRAL SWITCH TO 3TC+DTG

V. Malagnino[1,2], T. Mulas[1], M. Basso[4], Y. Abi Aad[3], J.P. Vincensini[3], M. Brucker[3], G. Battagin[6], E. Teti[1], M. Iannetta[1,2], S.G. Parisi[4], K. Lacombe[3,5], L. Sarmati[1,2]

[1]Infectious Diseases Unit, Policlinico Tor Vergata Of Rome, [2]Department of Medicin of Systems, Tor Vergata University of Rome, [3]GHU APHP. Sorbonne Université, Service des Maladies Infectieuses et Tropicales, Hôpital Saint-Antoine, Paris, France, [4]Dipartimento di Medicina Molecolare, Università degli Studi di Padova, [5]Sorbonne Université, INSERM, Institut Pierre Louis d'Épidémiologie et de Santé Publique, Paris, France, [6]UOC Malattie Infettive, Ospedale di Vicenza

Background: HBV anti-HBc antibody positivity (HBcAb+) may be a surrogate marker for hepatitis B occult infection (OBI), but is not a contraindication to switch to two-drug therapy (2DR).
Methods: A European multicentre retrospective study was conducted to investigate the impact of HBcAb positivity on HIV-RNA suppression in patients switched to 2DR consisting of Lamivudine and/with Dolutegravir (3TC/DTG). All patients on 3TC/DTG therapy with available anamnestic and immunovirological data at 6, 12, 18, 24 and 36 months after switch to 2DR were included. The following definitions were adopted: (1): Target Not Detected (TND) <20 cp/ml; (2) Target Detected (TD) <20 cp/ml; and (3) Detectable >20 cp/ml <50 cp/ml. A comparison analysis was conducted between HBcAb-positive and HBcAb-negative patients by means of Fischer's chi2 or exact test for categorical variables or mann-whitney test for continuous variables.
Results: 267 patients on 2DR with 3TC-DTG were included, predominantly male (181, 67.8%), with a median age of 41 years (IQR 32-52). From combined antiretroviral therapy (cART) initiation to switch there was a recovery of CD4+ cell number (306 [203-442] and 754 [562-961] respectively). Another indicator of cART efficacy, pre- and post-switch to 2DR, was the rate of patients with HIV-RNA <20 c/ml (TND or TD) above 90% at all timepoints from the switch. In contrast, during the first 24 months after switch to 2DR only 149 patients (66.8%) were TND at each observation, 42 (52.5%) at 48 months. Between HBcAb-positive and HBcAb-negative patients, the following differences were found: HBcAb-positive patients were older (45 years [35-54]) and had a lower CD4+ nadir (248 vs 349 cells/mmc, p=0.007), whereas at the time of switch there was no significant difference in CD4+cell number between the two groups (767 vs 741, p=0.84). HBcAb-positive and negative patients did not differ in maintenance of virological suppression at pre-switch timepoints (p=0.35 at 24 months pre-switch; p=0.30, at 12 months pre-switch and p=0.15 at the time of switch).
Differently, at 12 months post-switch 23 HBcAb-positive patients (30,6%) presented detectable HIV-RNA (10 with HIV-RNA >20 cp/ml [13,3%]), compared to 21 (14,9%) HBcAb-negative (12 with HIV-RNA >20cp/ml [9,8%]) (p=0.004), as well as at 24 months where 19 HBcAb-positive patients (27,5%) presented detectable HIV-RNA (4 with HIV-RNA >20 cp/ml [5,8%]), compared to 16 (10,1%) HBcAb-negative (10 with HIV-RNA >20cp/ml [6,2%]) (p=0.004). Data confirmed at 36 months after 3TC-DTG switch: 25 (33,5%) HBcAb-positive patients were HIV-RNA detectable (3 [6,7%] with HIV-RNA >20 cp/ml), while HBcAb-negative patients maintained an acceptable virological suppression and only 7 (7,2%) were HIV-RNA detectable (2 [2,1%] >20 cp/ml). During the 36-month of follow-up 16 (18%) HBcAb-positive patients were HIV-RNA TND at all timepoints, compared to 73 (59,9%) HBcAb-negative (p<0.0001).
Conclusions: In a group of PLWH switched to 2DR containing 3TC-DTG, HBcAb positivity does not appear to influence treatment efficacy (HIV-RNA below 50 cp/ml), however signs of less virological control (detectable viremia above 20 cp) seem to be detected, hence closer monitoring of HIV-RNA and of HBV-DNA could be suggested.

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Clinical HIV

P 47 PREVALENCE AND RISK FACTORS FOR SLEEP DISTURBANCES IN PLWH: PRELIMINARY RESULTS FROM AN OBSERVATIONAL STUDY

G. Bruno[1], M. Giotta[2], S. Perelli[1], V. Spada[3], M.A. Purgatorio[1], N. Bartolomeo[2], G.B. Buccoliero[1]

[1]Infectious Diseases Unit, San Giuseppe Moscati Hospital, Taranto, Azienda Sanitaria Locale Taranto, Italy, [2]Interdisciplinary Department of Medicine, University of Bari Aldo Moro, Italy, [3]Clinic of Infectious Diseases, University of Bari, Bari, Italy

Introduction: Sleep disorders have been described in patients living with HIV (PLWH) occurring in over 50% of cases. It is not yet clear which are the main risk factors involved in the onset of this event. We aim to assess the prevalence and risk factors for significant sleep disturbances in a population of PLWH receiving antiretroviral therapy (ART).

Methods: The Pittsburgh Sleep Quality Index (PSQI) was used to evaluate the prevalence of altered sleep quality in all consecutive PLWH attending our Outpatient Clinic between October 2022 and March 2023. A higher PSQI score than 5 indicated impaired sleep quality whereas a score > 10 revealed severe sleep disturbances compromising quality of life. A logistic regression model was carried out to assess risk factors associated with an altered PSQI score.

Results: A total of 106 PLWH (76.4% males) who received ART for at least one month were included in this study. Median age was 56. Among all, 32 (30.1%) had a history of AIDS and 75 (70.8%) were receiving an INSTI-based ART. The study population was divided into two groups: PSQI < 5 (62, 58.5%) and PSQI ≥ 5 (44, 41.5%). Using a PSQI cut-off score of 5, no significant differences were found among the two groups in terms of epidemiological and clinical features. At logistic regression female sex and higher body mass index (BMI) were associated with severe sleep disturbances (PSQI > 10).

Conclusion: Severe sleep disturbances are quite frequent in this real-life population of PLWH, occurring predominantly in women and subjects with higher BMI.

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Clinical HIV

P 48 IMPACT OF SARS-COV2 PANDEMIC ON IMMUNE, VIRAL AND METABOLIC STATUS IN AN UMBRIAN PLWH COHORT

D. Altobelli, C. Papalini, D. Francisci

Infectious Diseases Clinic, Santa Maria della Misericordia Hospital, University of Perugia, Perugia, Italy

Introduction: Sars-CoV2 pandemic has made more difficult the access to treatment for all patients given the public hospitals' effort exerted against the virus. In Umbria Region, the pandemic has forced Perugia Hospital's Infectious Diseases Day Hospital to stop the activity from March to June 2020. Among people living with HIV (PLWH), is known that transgender women (TGW) often live discrimination and social isolation that may decrease engagement in care and worsen the adherence to HIV treatment.
The aim of the study was to assess the impact of this temporary decreased access to care on viral, immune and metabolic status of PLWH visited in our Clinic.
Materials and Methods: We conducted a retrospective observational study involving TGW, Men who have Sex with Men (MSM) and heterosexual PLWH visited in the Infectious Diseases Clinic of Perugia Hospital with at least a 6-month follow-up. We collected clinical (CD4+ T cell count, HIV-RNA, antiretroviral therapy (ART), CDC classification) and laboratory data (triglycerides; total, LDL and HDL cholesterol; glycaemia) belonging to the period before (that we considered as study's baseline) and after the temporary interruption of Infectious Diseases Day Hospital activity. Viral suppression was defined according to EACS guidelines as HIV-RNA < 50 copies/ml.
Results: We enrolled a total of 319 patients: 36 TGW, 148 MSM, 73 heterosexual males and 62 heterosexual females. Their characteristics are summarized in Table 1.
Concerning immune status, CD4+ T cell count in heterosexual males resulted lower at baseline while no statistically relevant difference resulted in the following period. On the other hand, at baseline, mean value of HIV RNA did not differ among our groups while at re-opening of Infectious Diseases Day Hospital we noticed detectable viremia in 66% TGW compared to about 90% of the other 3 groups (92,5 in MSM; 91% in heterosexual males; 87% in heterosexual females).
Regarding the metabolic profile, we found a statistically relevant increase in total cholesterol after stop activity: LDL raised in TGW, MSM and heterosexual females; HDL increased in MSM while in the heterosexual male group no differences occurred. We did not find any statistically relevant differences between mean values of triglycerides and glycaemia, in the two temporal checkpoints analysed.
Conclusions: In our PLWH cohort, we observed post-pandemic viremic blip occurring mainly in TGW. On the other hand, with the exception of the heterosexual male group, there was a statistically significant increase in cholesterol blood level in all groups in post-pandemic period analysed.

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Clinical HIV

P 49 CEREBROSPINAL FLUID DRAIN INFECTION CAUSED BY PANDRUG-RESISTANT STAPHYLOCOCCUS EPIDERMIDIS TREATED WITH CEFTAROLINE IN COMBINATION WITH FOSFOMYCIN AND VANCOMYCIN IN A PLWHIV WITH AIDS-DEFINING ILLNESS

E. Rando[1], P. Del Giacomo[2], G. Maiuro[2], A. Dusina[2], E. Matteini[1], E. Magrini[1], F. Sanmartin[1], A. Carbone[1], A. Cingolani[2]

[1]Dipartimento di Sicurezza e Bioetica - Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Rome, Italy, [2]Dipartimento di Scienze di Laboratorio e Infettivologiche, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background: People living with HIV/AIDS are at higher risk of infectious complications. External ventricular drain-related cerebrospinal fluid (CSF) infection represents a fearsome event of neurosurgical interventions. Although vancomycin represents the standard of care for methicillin-resistant CoNS healthcare-associated ventriculitis, resistance phenomena have been described. Ceftaroline use for central nervous system infections is not fully explored. We reported a case of a persistent external ventricular fluid drain (EVFD) infection after device removal by pandrug-resistant Staphylococcus epidermidis successfully treated with intravenous ceftaroline in combination with fosfomycin and vancomycin in a PLWHIV with AIDS-defining condition.

Case Description: A 44-year-old person was admitted for P. jirovecii pneumonia and CMV-encephalitis, for whom an EVFD device was placed. For fever persistence, after CSF analysis with multiple CSF cultures yielding methicillin-resistant S. epidermidis an EVFD infection was confirmed. Linezolid was initially started, and the device was replaced. Vancomycin was then used due to the evidence of linezolid resistance and vancomycin susceptibility in CSF cultures. The device was eventually removed for hydrocephalus stability, despite not achieving resolution of the febrile status. A lumbar puncture (LP) was then performed for fever persistence, and in this case, bacterial cultures yielded pandrug-resistant S. epidermidis (Table 1). Due to a lack of alternative therapies, ceftaroline 600 mg TID was started, with prompt resolution of fever, mental status improvement, and C-reactive protein reduction the day after. After 14 days of antibiotic therapy, a new LP revealed normal CSF chemical analysis, and a sterile culture, for which antibiotics were discontinued due to clinical and microbiological cures. Unfortunately, the patient deceased one week later due to a carbapenem-resistant K. pneumoniae bloodstream infection from a pulmonary source.

Conclusions: No evidence regarding pandrug-resistant S. epidermidis therapy currently exists to our knowledge. In this case, the S. epidermidis phenotype emerged during the therapy course, possibly due to initial device retention, biofilm formation and the host immune impaired response. Despite being poorly studied in vivo, ceftaroline may be considered an option when other alternatives are unavailable, thanks to its described activity against CoNS in vitro. This case extends the experience with ceftaroline for CNS infections suggesting this drug could also be used in high antimicrobial resistance settings for severely immunocompromised people.

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Clinical HIV

P 50 A CASE OF CENTRAL NERVOUS SYSTEM INFECTION DIAGNOSED AS FRONTOTEMPORAL DEMENTIA

E. Staffilano, L. Carani, F. Vischia, D. Vai, D. Imperiale, G. Orofino, A. Calcagno, G. Calleri

Dipartimento di Scienze Mediche, Università degli Studi di Torino, Torino

Introduction: From the beginning of the AIDS epidemic, HIV has been shown to affect the central nervous system (CNS) and having the potential to cause dementia. HIV associated neurocognitive disorder (HAND) may show clinical and radiological features similar to other neurodegenerative disorders (NDD) and it needs to be excluded, especially in young patients with rapid progression. We will discuss several useful tools that could help physicians in this challenging diagnosis.

Case Report: a 60 year old male presented with rapidly progressive impairment in memory (learning), executive function, apathy and some episode of wandering. The magnetic resonance (MRI) showed areas of parenchymal gliosis and enlargement of subarachnoid spaces in frontotemporal areas. Neurocognitive tests as Mini Mental State Examination (MMSE) resulted in 17/30 at the first medical assessment; Instrumental Activities of Daily Living (I-ADL) of 1/5 revealed a completely lost in autonomy and need of supervision on the daily living activities; the visuo-spatial learning tests showed alterations of the working memory and short-term memory mainly. The disorder was attributed to frontal cortex domain, and he was firstly diagnosed with frontotemporal dementia.

After one year, he was admitted to the Emergency Department for an episode of unexplained loss of consciousness: clinical examination revealed multiple lymphadenopathies and blood tests showed pancytopenia. Consequently, HIV serology was performed and tested positive and he was admitted to the Infectious Disease ward. CD4+ T lymphocytes were 92 cells/mm3 and HIV RNA was 3,130,000 cp/ml on peripheral blood. Cerebrospinal fluid (CSF) analysis showed HIV-RNA 206,000 cp/ml; protein 14.3.3 negative; total TAU 346 pg/ml; p-TAU (181P) 19,8 pg/ml; 1-42Beta amyloid 309 pg/ml; 1-40Beta amyloid 4457 pg/ml. Moreover, CSF results indicated an intrathecal synthesis of oligoclonal bands of IgG antibodies (profile 4 at immunoblotting).

Diagnosis of HIV associated dementia was made on the basis of imaging, CSF analysis and neurocognitive tests. Antiretroviral treatment was started with bictegravir/emtricitabine/tenofovir alafenamide and he was discharged to a nursing home. One year later, neurocognitive tests show an improvement of the cognitive performance (MMSE 28/30) whereas functional activities remain compromised (ADL 3/6 and I-ADL 1/5).

Discussion/conclusion: With the increasing age of PLWH, HIV infection should be considered in the differential diagnosis of neurodegenerative disorders.

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Clinical HIV

P 51 CARDIOVASCULAR SAFETY OF DORAVIRINE/LAMIVUDINE/TENOFOVIR DISOPROXIL FUMARATE IN A COHORT OF VIROLOGICALLY SUPPRESSED PLWHIV

A. Ciccullo[1], V. Iannone[2], D. Farinacci[3], R.J. Steiner[2], F. Lombardi[2], V. Massaroni[2], V. Delle Donne[2], G. Baldin[4], A. Borghetti[4], S. Di Giambenedetto[2,4]

[1]UOC Malattie Infettive, Ospedale S. Salvatore, L'Aquila, Italia, [2]Università Cattolica del Sacro Cuore, [3]UOC Medicina Protetta - Malattie Infettive, ASL Viterbo, Italia, [4]UOC Malattie Infettive, Fondazione Policlinico A. Gemelli IRCCS, Roma, Italia

Introduction: Cardiovascular disease has become one of the leading causes of mortality in PLWHIV and the metabolic impact of ARV molecules is a topic of interest for Clinicians. Doravirine has shown a favorable metabolic profile in both clinical trials and real-life cohorts. Aim of this study is to assess the cardiovascular safety of the STR of doravirine/ lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF).

Methods: We analyzed data from a cohort of treatment-experienced, virologically-suppressed PLWHIV starting DOR/3TC/TDF. We collected viro-immunological and metabolic parameters at time of DOR initiation and during follow-up; moreover, we also calculated 10-year risk of cardiovascular disease (10Y-CD) using both Framingham risk score and DAD score. We compared variables using non-parametric tests and searched for predictors via regression analyses.

Results: We analyzed 37 PLWHIV: 23 (62.2%) were males, with a median age of 52 years (IQR 45-58) and a median time from HIV diagnosis of 13.8 years (IQR 5.7-21.8). As to cardiovascular risk factors, 24 patients (64.9%) were active smokers, 2 patients (5.4%) had diabetes and 8 patients (21.6%) had hypertension. Full patients' characteristics are shown in Table 1.

At baseline, median predicted 10Y-CD estimated via Framingham risk score was 8.0% (IQR 4.0-11.5); meanwhile, using DAD score, estimated 10Y-CD at baseline was 6.4% (IQR 4.7-12.8). After 48 weeks, we observed a significant reduction in 10Y-CD both via the Framingham score (median -0.7, p=0.021) and the DAD score (-0.41, p=0.012). Week-48 changes in 10Y-CD were predicted by baseline 10Y-CD (B -0.25, p=0.037). After 96 weeks, we registered a significant reduction in 10Y-CD calculated via the DAD score (-0.98, p=0.009). Changes in 10Y-CD at 96 weeks were not predicted by baseline 10Y-CD or by the use of lipid-lowering drugs, at a multivariate analysis.

Regarding serum lipid markers, after 48 weeks we observed a significant reduction in total cholesterol (median -17 mg/dL, p<0.001), triglycerides (-21 mg/dL, p=0.015) and LDL cholesterol (-8 mg/dL, p=0.022). Week-48 change in total cholesterol was predicted by baseline cholesterol (B-31, p=0.027). No predictors were found for changes in LDL cholesterol and triglycerides.

After 96 weeks, we registered a significant reduction in total cholesterol (-19 mg/dL, p<0.001) and a reduction, although non-significant, in triglycerides (-17 mg/dL, p=0.073). Week-96 decrease in total cholesterol was solely predicted by baseline cholesterol (B-0.28, p=0.028) after adjusting for age, sex, years of HIV, smoking habit and use of statins. Regarding BMI, we observed a significant reduction after 96 weeks (median -0.6, p<0.001).

Conclusions: The single-tablet regimen of DOR/3TC/TDF has shown a favorable metabolic profile as a switch strategy in our cohort, with a significant reduction in 10Y-CD, independently from the use of lipid-lowering drugs.

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Clinical HIV

P 52 AGING AND HIV: BETWEEN GAPS AND PERSPECTIVES

G. Guaraldi[1,2,3], G. Rizzardini[4], G. Marchetti[5], A. Gori[6,7], L. Brogonzoli[8], J. Milic[1,2], C. Falcinella[5], P. Saltini[9,7], R. Iardino[8]

[1]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy, [2]Modena HIV Metabolic Clinic (MHMC), University of Modena and Reggio Emilia, Modena, Italy, [3]Department of Infectious Diseases, Azienda Ospedaliero-Universitaria, Policlinico of Modena, Modena, Italy, [4]I Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [5]Clinic of Infectious Diseases and Tropical Medicine, San Paolo Hospital ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [6]II Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [7]Department of Pathophysiology and Transplantation, University of Milano, Milano, Italy, [8]The Bridge Foundation (Fondazione The Bridge), Milano, Italy, [9]Infectious Diseases Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

Background: EACS (2021) and SIMIT (2017) guidelines on HIV treatment provide specific statements regarding models of care for older people living with HIV (OPLWH). The objective of the study was to explore unmet needs of OPLWH regarding the compliance of Italian HIV clinics to the national and international recommendations on HIV aging care.

Methods: Part 1: EACS and SIMIT guidelines were compared regarding specific statements addressing OPLWH care needs. These included items such as co-morbidities, multimorbidity, polypharmacy, frailty and falls. A synoptic table was built to summarize key statements and agreements between guidelines. These statements were used to build a survey exploring aging model of care and unmet clinical needs.

Part 2: This was a cross sectional country wide survey, offered to all HIV clinics and their attendees aged>50 years in Italy, composed of two parts: the first referred to health care workers, with questions related to model of care for OPLWH, while the second referred to OPLWH and addressed health domains including: frailty through Frailty scale, resilience through CD-RISC-2, functional capacity by self-reported Duke Activity Status Instrument (DASI), health-related quality of life through EQ-5D-5L questionnaire. Other geriatric syndromes included falls and polypharmacy. Questions regarding stigma, isolation, loneliness, sex life, social support, and relationships were also included.

Results: EACS and SIMIT guidelines result concordant on OPLWH health needs. Both quote HRQoL as the ultimate goal of clinical care but neither of the two specify how to integrate it in a person-centered approach. Of the 35 HIV clinics that answered, 27 (77%) declared that there were no dedicated care models for OPLWH and 28 (80%) reported that geriatric consultation was not available at the clinic. Nevertheless, 29 (82.2%) HIV clinics provided health information on aging to their patients, and 23 (66.6%) facilitated access to treatment and care for OPLWH through telemedicine. A total of 66 OPLWH were interviewed, mean age was 61 years, 51 (77%) were males, median time since HIV diagnosis was 21 years, median nadir CD4 cell count was 208 c/microL and 64 (96.4%) had undetectable HIV RNA. Screening for frailty assessed by FS showed that 27 (41%) required geriatric evaluation, 12 (18.1%) reported falls in the last year and 14 (21.1%) polypharmacy. Functional capacity assessed by DASI questionnaire was impaired in 71% of OPLWH, while 58% presented both poor resilience and suboptimal HRQoL.

Conclusions: Our findings show relevant gaps between guidelines recommendations and clinical practice. This calls for the need for a multidisciplinary person-centered approach, coupled with comprehensive geriatric assessment and screening tools to assess comorbidities, frailty and geriatric syndromes, using HRQoL as a key outcome measure in OPLWH. In order to fulfill these strategies for the emerging needs of OPLWH, Integrated Care Pathways (PDTA) are the most apt tool to ensure implementation of the guidelines proposed.

Clinical HIV

P 53 STUDY OF A NOVEL COMBINATION OF IMMUNOVIROLOGIC AND GENETIC PARAMETERS IN EARLY--TREATED HIV--1 PATIENTS UNDERGONE TO ANTIRETROVIRAL THERAPY INTERRUPTION (ATI) AIMED AT DEFINING AN ALGORITHM PREDICTIVE OF POST-−TREATMENT CONTROL (PCT)

F. Sironi[1], S. Dispinseri[1], R. Chimienti[1], R. Dell'Acqua[2], S. Nozza[2], A. Castagna[2], G. Scarlatti[1], M. Malnati[1]

[1]Viral Evolution and Transmission Unit, DIBIT, IRCCS San Raffaele, Milan, Italy, [2]Clinic of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy; Vita-Salute San Raffaele University, Milan, Italy

Background: Some HIV-1 infected individuals control infection naturally [Elite controllers (EC), viral controllers (VC) and long-−term non progressors (LTNP)] or after treatment interruption [post treatment controllers (PTCs)], constituting ideal models to identify predictive biomarkers of disease progression, fostering therapeutic interventions aimed to reproduce them in a larger population. PTCs represent up to 15% of HIV positive individual maintaining a viral load <400 copies/ml after suspension of ART. This condition is more frequent amongst early than late treated patients (13 vs 4%) raising the idea that the introduction of ART during primary infection might curtail the establishment of a latent HIV reservoir facilitating viral control after ATI. Moreover, the failure to obtain PTC upon ATI in chronic patients (APACHE cohort) selected by a long period of suppressive ART (≥10ys) and low viral reservoir (HIV-−1 DNA< 100cp/106PBMCs), suggests that the biological bases of PTC are still unknown, underlining the lack of reliable predictors of PTC

Material and Methods: We will enroll HIV-−infected participants, treated early (Fiebig II-−V) post infection showing a different behavior in reconstituting T lymphocytes subpopulations (see fig.1)

The subjects will be male and female subjects aged 18 – 70 years, with CD4 >350 cells/mm3 and pVL <50 copies/ml for at least two year. All clinical tests results (HIV-−1 RNA load, CD4+, CD4%, CD8+, CD8%, CD4/CD8)) will be copied to an electronic patient record ad-− hoc developed for the study. Blood will be processed for genetic and FACS analysis. Serum will be analyzed for the assessment of HIV-−1 antibody specificities and for the presence of HIV-−specific antibodies mediating ADCC by NK-−cells; dried pelleted PBMC will be used for nucleic acid extraction and testing for KIR genotyping, HLA typing and SNPs rs67384697 G/-− and SNP rs2395471 A/G affecting HLA-−C expression, as well as SNP rs7935564A/G and rs1063303C/G affecting TRIM22 anti-−HIV-−1 functions on customized cards containing 48 different TaqMan assays in a QuantStudio 12K apparatus. Purified DNA will be also used for quantification of total HIV-−1 proviral DNA and intact and defective proviral DNA genome; cryo-−preserved PBMCs will be stained to assess KIRs exhaustion markers expressions (PD-−1, LAG-−3, TIM-−3) on NK and CD4 and CD8 T-−cells as well as the B-−cell phenotype

Results and conclusions: The primary objective of the study is to investigate a set of immune-−genetic and viro-− immunologic biomarkers that might be useful to individuate PTC whereas the secondary objective is to validate the immune-−genetics platform for the genotyping of KIRs/TRIM22/SNPs regulating HLA-−C expression in a clinical setting. All the data will be integrated with the different profile of immune reconstitution to generate a Predictive Algorithms of PTC that will be subsequently validated by an ad hoc designed Monitored ART Pause (MAP) protocol.

Clinical HIV

P 54 VIRO-IMMUNOLOGIC PRE-TREATMENT PREDICTORS OF SUBOPTIMAL VIRAL SUPPRESSION AT 48 WEEKS OF ANTIRETROVIRAL THERAPY

G. Bozzi[1], P. Saltini[1,3], M. Centazzo[2], G.M. Butta[2], A. Liparoti[1,3], C. Bobbio[1], A. Muscatello[1], A. Gori[1,3], L. Manganaro[2,3], A. Bandera[1,3]

[1]Infection Diseases Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico - Milan, Italy, [2]Virology Unit, INGM-Istituto Nazionale di Genetica Molecolare - Milan, Italy, [3]University of Milan - Milan, Italy

Background: In the current era of high-efficacy antiretroviral treatment (ART), detectable viremia below the threshold of 200 cps/ml remains a not fully understood, yet common finding in a proportion of drug-adherent patients. Low-level viremia (LLV) between 50 and 200 cps/mL has been weakly associated with virologic failure, and shown to be predicted by both pre-treatment HIV RNA and HIV DNA levels. Much less is known about the significance and correlates of viremia levels slightly above the detection limit of high sensitivity quantitation kits (i.e. 20-50 cps/mL). We aimed at investigating pre-treatment correlates of suboptimal virologic response to 48 weeks of ART in a prospective cohort of persons living with HIV (PLWH).

Materials and Methods: Sub-analysis of the GR-2018-12365699 study ongoing at IRCCS Policlinico, Milan. Pre-ART clinical parameters, HIV-RNA, total HIV DNA quantification (through ddPCR, Bio-Rad QX200 System) and CD4+ T cell subsets (determined through cell-surface staining) were collected. Drug-adherent patients with optimal virologic response (OVR, HIV RNA undetectable or ≤20 cps/mL) and suboptimal virologic response (SubVR, HIV RNA 20-200 cp/mL) at week 48 were compared.

Results: We analysed 31 naïve PLWH diagnosed and started on ART between 2019 and 2022. While 23/31 (74.2%) had OVR, 8/31 (25.8%) had SubVR. SubVR had median HIV RNA at 48 weeks of ART of 48 cps/mL [IQR 36.5 - 50]). Age, gender, route of transmission, stage of infection (acute vs. chronic), CD4 count at diagnosis and CD4/CD8 ratio at diagnosis were similar between groups. Median pre-ART HIV RNA was markedly higher in SubVR than OVR (165000 cp/mL [79150-242000] vs 46300 cp/mL [9400-58150], respectively). Pre-treatment HIV DNA quantification did not show differences between subgroups. Median HIV DNA was 71800 cp/million cells [66900-295000] for SubVR, and 308000 cp/million cells [112500-997250] for OVR. Pre-ART CD4+ subset differentiation was similar in the naïve, effector memory, central memory and stem cell memory T cells; a higher proportion of terminally differentiated effector memory cells (TEMRA) in OVR was observed compared to SubVR.

Conclusions: Our cohort shows the association to high pre-ART HIV RNA levels to suboptimal viral suppression, confirming it as a predictor even for the detection of low-level HIV RNA (20 - 50 cps/mL) at 48 weeks in patients with high ART adherence. On the other hand, our study does not confirm the role of HIV DNA as a predictor to SubVR, either due to a driver different than reservoir size for very low-level viremias, or possibly to sampling issues given the limited sample size. Further studies are needed to explore the correlation between pre-treatment proportion of the Temra subset and optimal viral suppression. A cohort expansion with quantitation of HIV DNA and CD4+ subsets at 48 weeks of ART are underway.

Clinical HIV

P 55 CRYPTOCOCCAL MENINGITIS AS THE FIRST CLINICAL PRESENTATION OF HIV INFECTION

C. Frisenda, C. Febo, A. Zarroli, G. Castrignanò, E. D'Arcangelo, S. Di Giovine, C. Ucciferri, K. Falasca, J. Vecchiet

Clinica Malattie Infettive, Università "G. d'Annunzio" Chieti

Background: Disseminated Cryptococcus neoformans infection is a serious opportunistic infection that occurs in patients with untreated AIDS. HIV-associated cryptococcal meningitis usually presents as a subacute meningo-encephalitis in profoundly immunosuppressed patients (CD4 cell counts < 100 cells/ml), with malaise, headache, fever and, later, visual disturbance and altered mental status.

Case Report: In february 2022, a 52-year-old man, SARS-CoV-2 positive, presented to the emergency department of our hospital with a two weeks hystory of asthenia, cough and headache, unresponsive to anti-inflammatory therapy. His medical history was silent. Epidemiological history: bird breeder. The computer tomography (CT) scan of the chest showed bilateral ground-glass opacities and pulmonary nodules, this radiological findings was referred to interstitial pneumonia, secondary to SARS-CoV-2 infection. The patient was, therefore, hospitalized for the continuation of treatment and investigations. On admission, the patient was alert, oriented and cooperative, he complained of severe headache, blood tests showed mild lymphocytopenia 0.50 x 10^3/uL, with CRP 1.31 mg/L. In the following days, there was a rapid worsening of the patient's clinical conditions with an episode of absence and was transferred to the ICU. The CT scan of the brain with intravenous contrast did not show expansive lesions or impregnations of pathological significance. The patient then underwent lumbar puncture. The CSF examination was initially not significant for pathologies of infectious etiology. The CSF appeared clear, with normal glycorrachia, normal protidorrachia, WBC 34 cells/uL, lymphocytes 68%, monocytes 6%, polymorphonuclear cells 26%; PCR for Herpes 1, Herpes 2, Herpes zoster 3, Epstein-Barr, Cytomegalovirus resulted negative. Then, the Microbiology isolated from CSF Cryptococcus neoformans and the blood cultures collected resulted positive for Cryptococcus neoformans. Therefore, in view of the diagnostic result obtained, the patient started therapy with amphotericin B and flucytosine and HIV serology was sought, which resulted positive. Lymphocyte phenotyping was performed, showing CD4 cell counts= 7 cells/ml. A diagnosis was then made: AIDS related cryptococcal meningitis. The patient died a few days later of cardiac arrest.

Conclusions: Cryptococcal meningitis is one of the most common opportunistic infections in the course of AIDS; it presents in a severe form and requires immediate, careful and prolonged therapeutic intervention. In AIDS patients, the disease often manifests itself acutely, as opposed to the chronic course it presents in immunocompetent subjects. The appearance of cryptococcal meningitis, combined with the concomitant finding of positive serology for HIV infection, is a prognostic sign of the transition to conclamated AIDS disease. The diagnostic delay, therefore, the delay in starting antifungal treatment correlates with a worse prognosis (as happened in our patient).

Clinical HIV

P 56 PROGNOSTIC FACTORS OF CD4 RECOVERY AFTER 12 MONTHS OF TREATMENT IN A COHORT OF HIV-1 POSITIVE PATIENTS

M.A. Carleo[1], S. Martini[2], A. Russo[2,3], A. Cascone[2], V. Rizzo[1], A. Guida[1], P. Rosario[1], V. Zollo[3], M. Di Lorenzo[1], M. Pisaturo[2,3], V. Esposito[1], N. Coppola[2,3]

[1]Infectious Diseases and Gender Medicine Unit, PO Cotugno, AO dei Colli, Naples, [2]AOU Vanvitelli, Naples, [3]Department of Mental Health and Public Medicine, Section of Infectious Diseases, Second University of Naples

Aims: Our aim is to evaluate the prognostic factors of worst CD4 recovery in our cohort of HIV-1 positive patients followed for at least 12 months from antiretroviral treatment start.

Methods: We conducted a multicenter observational cohort study including HIV-positive naïve patients followed at two third-level centers in Naples from January 2018 to February 2023. All included individuals are adults (>18 years), with the first diagnosis of HIV infection, with a documented follow up of at least 12 months from treatment initiation.

Results: 160 patients were admitted to our Units for first diagnosis of HIV-1 infection from January 2018. 98 patients considering inclusion criteria were included in our study. Enrolled patients were mostly male (70.7%), with median age of 43 years (34-50 years). 68.4% were Italian, and 55.2% were heterosexual. Considering viro-immunological parameters at admission, 30.3% of patients were stage C (CDC '93 Atlanta), the median of CD4+ were 192.5 (69-469) and the median of HIV RNA was 139000 (42300-416506). Mostly started treatment with INI +2NRTI (73.7%) [Table 1]. Considering the median and first and third quartile of Delta CD4+ (CD4 at 12 months – CD4 at diagnosis) we divided patients in four groups [Table 2]. Considering demographic data and viro-immunological parameters there were no statistical difference between group. Higher incidence of Kaposi's sarcoma was observed in group with Delta CD4 from 247 to 353 (p =0.036), and arterial hypertension prevalence was higher in the first group (Delta CD4 <137) (p=0.008). Considering antiretroviral treatment, switch to another treatment and HIV RNA after 12 months there were no statistical difference between groups.

Conclusion: In our cohort of 98 naïve patients followed for at least 1 year from the start of antiretroviral treatment, we have not found predictors of a lower recovery of CD4+, neither in demographic nor viroimmunological variables, nor clinical variable, except for the presence of arterial hypertension that appears more frequent in patients that recover less than 137 CD4+ after one year of treatment.

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Clinical HIV

P 57 SURVIVAL OF HIV/HCV CO-INFECTED INDIVIDUALS RECEIVED LIVER TRANSPLANTATION IN THE POST-DAA ERA IN MODENA

A. Cervo[1], G. Dolci[1], E. Franceschini[1], J. Milic[2], F. Casari[1], E. Ghidoni[1], G.P. Guerrini[3], N. De Maria[4], B. Catellani[3], P. Magistri[3], F. Di Benedetto[3], C. Mussini[1,2], G. Guaraldi[1,2]

[1]Infectious Diseases Clinic, University Hospital of Modena, Modena, [2]University of Modena and Reggio Emilia, Modena, [3]Hepato-Pancreato-Biliary Surgery and Liver Transplantation Unit, University Hospital of Modena, Modena, [4]Gastroenterology Unit, University Hospital of Modena, Modena

Background: Antiretroviral therapy (ART) allowed to expand the panorama of solid organ transplantation to people with HIV (PLH). HCV co-infection led to increased risk of hepatocellular carcinoma (HCC) and end-stage liver disease compared to HCV mono-infection, and also to higher risk of complications and negative outcomes after ortothopic liver transplantation (OLT). The advent of anti-HCV direct antiviral agents (DAAs) changed radically recipients' survival. We aimed to evaluate overall mortality in OLT recipients (OLTr) with HIV/HCV co-infection from 2003 to 2022 in Modena.

Methods: In this retrospective study we included all PWH with HIV/HCV co-infection who underwent OLT in Modena from January 2003 to June 2022. The date of 1 Jan 2014 was arbitrary chosen as an approximate date of DAAs start in our centre. Patients were compared according with year of OLT (pre vs post-2014). Kaplan-Meier curves were compared using log rank. Risk factors for death were estimated by logistic regression.

Results: 64 PWH with HIV/HCV co-infection received OLT from 2003 to 2022. At hospital admission for transplant, 51 (79.7%) were males, median age 50 yrs (IQR 32-68), 96.9% had undetectable HIV RNA, with CD4+ cells count 307 (IQR 53-1154). The main indication for OLT was HCC (N=34, 53.1%). OLTr in pre-DAA era were younger (47 vs 55 years, p<0.001), with more compromised liver function (MELD score 22 vs 11, p<0.001). They also had more often detectable HCV RNA at OLT (75.6% vs 1.6%, p<0.001) and shorter HIV duration (21 vs 30 years, p<0.001). PIs (84% vs 19%, p>0.001) and 2nd generation INSTIs (0% vs 49%, p>0.001) were the most used anchor drug before and after 2014, respectively. In pre-DAA period, OLTr experienced more adverse outcomes depicted by a higher rate of: post-OLT complications (97% vs 55%, p=0.015), graft rejection (14% vs 3%, p=0.007) and longer hospitalisation (21 vs 11 days, p<0.001). Stratifying by quadrennials, number of OLTr with detectable HCV RNA decreased over time, as well as the fatal outcome (Figure 1a-b). During 381-person-year follow-up (PYFU) period, 19 OLTr deceased. The unadjusted incidence rate of death in recipients with active HCV infection (99.8 per 1000PYFU, 95% CI 55.6-148.2) was higher than that in recipients with negative HCV RNA at OLT (14.6 per 1000PYFU, 95 CI% 4.7-45.2)(p<0.001). No differences were observed in the median time to death (months) between pre and post-DAA group [3.2(IQR 1.5-9.0) vs. 5.3(IQR 2.7-27), p=0.424]. Overall survival improved significantly over time, from 54% in pre-DAA to 87% in post DAA (p=0.01), in particular in PWH who had undetectable HCV RNA at OLT (Figure 2). In the logistic regression, the main predictor of death was presence of active HCV RNA replication (aOR 19.4, 95% CI 2.23-168.2, p=0.007), while HIV-related factors were not associated to the outcome.

Conclusion: Anti-HCV DAAs changed radically the outcome of HIV/HCV co-infected patients, in particular in those undergoing liver transplantation.

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Clinical HIV

P 58 EFFICACY, CONVENIENCE, SAFETY AND DURABILITY OF DTG-BASED ANTIRETROVIRAL THERAPIES: EVIDENCE FROM A PROSPECTIVE STUDY BY THE ITALIAN MASTER COHORT

P. Fusco[1], P. Nasta[2], E. Quiros-Roldan[2], A. Tondinelli[3], C. Costa[4], C. Fornabaio[5], N. Mazzini[6], M. Prosperi[7], C. Torti[1], G. Carosi[6]

[1]Infectious Diseases Unit, Department of Medical and Surgical Sciences, "Magna Graecia" University, Catanzaro, Italy, [2]University Division of Infectious and Tropical Diseases, University of Brescia and Brescia ASST Spedali Civili Hospital, Brescia, Italy, [3]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [4]Infectious Diseases Unit, S. Maria Annunziata Hospital, Florence, Italy, [5]Infectious Diseases Unit, Cremona ASST Hospital, Cremona, Italy, [6]M.I.S.I. Foundation, Brescia, Italy, [7]Department of Epidemiology, College of Public Health and Health Professions and College of Medicine, University of Florida, Gainesville, FL, USA

Background: Dolutegravir is recommended by international guidelines as a main component of an optimal initial regimen of cART in people living with HIV and in case of switching for failure or optimization strategies. However, studies on the performance of DTG containing regimens are sparse. The purpose of this study was to evaluate prospectively the performance of DTG based regimens, using a multi-dimensional evaluation of the metrics of efficacy, safety, convenience and durability, among a nationally representative cohort of PLWH in Italy.

Methods: We selected all PLWH who initiated a DTG based regimen either when naïve or following a regimen switch between July 11th, 2018 and July 2nd, 2021. Participants were followed until the study outcomes or until the end of the study on August 4, 2022, whichever occurred first. Survival regression models were fitted to evaluate associations between therapy performance and age, sex, nationality, risk of HIV transmission, HIV RNA, CD4+ T-cell count, year of HIV diagnosis, cART status (naïve or experienced), cART backbone and viral hepatitis coinfection. Results: Participants included in the study were 371. They were prevalently male (75.2%) and experienced for cART (80.9%). Median age was 53 years (IQR: 45-58). Prior cART regimen was based mostly on a combination of NRTI drugs plus a PI-boosted drug (34.2%) while backbone was composed mostly of 3TC plus ABC (34.5%). The most reported transmission risk factor was heterosexual intercourses (44.2%). Total interruptions of the first DTG based regimen were registered in 58 (15.6%) participants. The most frequent reason for interruption was due to cART simplification strategies, which accounted for 52%, followed by only 1.1 % of interruptions due to virological failure. Only 1 death was reported. Risk factors associated with the study metrics were found to be: a backbone regimen containing tenofovir, being cART naïve, having detectable HIV RNA at baseline and FIB-4 score >3.25 (with all metrics); HBsAg positive carriers (with the metric of convenience); eGFR < 60 ml/min (with the metric of convenience and safety); having cancer diagnosis (with the metric of durability). By contrast, protective factors were found to be: prior cART not containing an INSTI, higher CD4+ T-cell counts and higher CD4/CD8 ratio at baseline (with all metrics); increased value of Framingham score at baseline (with the metric of safety and durability) [Table1].

Conclusion: Durability of DTG based regimens was maintained in 84.4% of participants with a modest incidence of interruptions mostly due to cART simplification strategies. Although the results of this prospective real-life study confirm the apparent low risk of changing DTG containing regimens due to virological failure, they highlight the possible association between certain factors and the occurrence of an unfavorable event. Such multi-dimensional evaluation could help physicians to identify people with increased risk of interruption, suggesting targeted medical interventions.

The data analysis included in this study was funded with the support of ViiV Healthcare

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Clinical HIV

P 59 TOXOPLASMOSIS MIMICKING CMV CHORIORETINITIS IN NEWLY DIAGNOSED PLWH: A CASE REPORT

F. Lamanna[1], R.A. Passerotto[1], A. Carbone[1], R.J. Steiner[1], V. Iannone[1], P.F. Salvo[1], A. Ciccullo[2], G. Baldin[3], A. Borghetti[3]

[1]Dipartimento di Sicurezza e Bioetica - Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Rome, Italy, [2]Dipartimento di Scienze di Laboratorio e Infettivologiche, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [3]Infectious Diseases Unit, San Salvatore Hospital, L'Aquila, Italy

Background: cytomegalovirus (CMV) retinitis, cerebral toxoplasmosis and ocular toxoplasmosis are common infections in patients with acquired immunodeficiency syndrome (AIDS).
Material and Methods: this is a case of a 46-year-old female with previous Kaposi's sarcoma and Pneumocystis jirovecii pneumonia (PJP), diagnosed with an HIV infection two weeks prior to hospitalization. Blood test at diagnosis showed a CD4+ count of 77 cell/μL and HIV-RNA 3.758.745 copies/mL. Therapy with bictegravir/emtricitabine/tenofovir alafenamide fumarate was then started and clinical, viroimmunological and microbiological investigations were performed.
Results: the patient went to our hospital for the onset of left occipito-parietal headache and blurred vision. Brain CT and brain MRI were performed which did not show focal lesions or vascular alterations. Syphilis serology was negative, while Toxoplasma gondii serology showed positive IgG and negative IgM. Following an ophthalmological examination of the eye fundus showing evidence of intraretinal hemorrhages, fluorescein angiography and computed optical tomography (OCT) documenting cottony exudates, retinal hemorrhages and vitreous involvement and serum CMV-DNA 31184 IU/mL, therapy with valganciclovir was initiated for suspicion of CMV retinitis. About a month later, the patient reported blurred vision for which she was re-admitted. An ophthalmological examination of the ocular fundus was performed which highlighted a cottony lesion near the macula. A vitrectomy was performed with samples sent for microbiological testing: the molecular test was positive for Toxoplasma gondii. A lumbar puncture was performed with a negative molecular test for Toxoplasma gondii. In addition, an MRI of the brain with contrast medium was performed which showed an area of altered hyperintense signal in the right anterior perforated white matter on T2-weighted/FLAIR sequences, with marginal enhancement after administration of contrast agent, with a minimal perilesional vasogenic edema. A diagnosis of Toxoplasma gondii uveitis and neurotoxoplasmosis was made. Therapy with pyrimethamine and clindamycin (allergy for sulfonamide reported by the patient) was started. Allergy counseling was performed with the execution of allergy tests (patch test) with negative result; therefore the administration of clindamycin was replaced with sulfadiazine. A month following the start of anti-toxoplasma therapy, there was an clinical and radiological improvement.
Conclusions: important advances have been made in the management of antiretroviral therapy and living with HIV infection is possible. Despite these developments, there are still cases of AIDS, so it is important to evaluate the possibility of the presence of one or more opportunistic infections, recognize them, diagnose them and treat them promptly given the high mortality. Especially in the case of ocular and central nervous system infections, extra vigilance must be exercised for Toxoplasma, especially in the presence of symptoms such as headache and reduced visual acuity.

Clinical HIV

P 60 TUBERCULAR RHOMBENCEPHALITIS AND OCULAR SYPHILIS, WITH POSSIBLE CENTRAL NERVOUS SYSTEM COMPARTIMENTALIZATION, IN A NEWLY DIAGNOSED AIDS PATIENT

M. Moccione, V. Barchi, D. Kontogiannis, G. Muratore, D. Zace, D. Benvenuto, A. Cekrezi, A. Imeneo, M.L. Giacalone, T. Mulas, L. Coppola, M. Iannetta, L. Campogiani, L. Sarmati

Department of System Medicine, Infectious Diseases Unit, Tor Vergata University, Rome, Italy

Rhombencephalitis (RE) is an inflammatory disease that can be caused by autoimmune and paraneoplastic diseases or infections such as Lysteria monocytogenes, enterovirus, herpes viruses and Mycobacterium tuberculosis (MTB), mostly in AIDS-patients. Here we report a complex case of RE in a newly diagnosed AIDS-patient.

Case Report: A 45-year-old Caucasian man with a history of illicit drug abuse and a recent latero-cervical lymphadenopathy and uveitis, was admitted to the emergency room due to agitation, delirium and anisocoria. Brain CT-scan did not showed any pathological findings. A lumbar punctur (LP) revealed a clear and colourless cerebrospinal fluid (CSF),with hypoglicorrachia (16 mg/dl), increased proteins (272 mg/dl) and white blood cells (708/mmc, mainly lymphocytes). Viral tests showed the presence of HIV-RNA (749000 copies/mL) in the CSF. Therefore, a fourth generation HIV-test followed by the confirmation immunoblotting were positive for HIV-1 infection. Plasma HIV-1 viral load was 227000 copies/ml; baseline CD3+CD4+ absolute count was 213 cells/µl; CD4+/CD8+ratio was 0.28. An initial empiric treatment with acyclovir, ceftriaxone, ampicillin and vancomycin was started, together with dexamethasone, and switched to ceftriaxone, ampicillin and co-trimoxazole after the evidence of negative results of CSF cultures and multiplex PCR for bacterial, viral and fungal pathogens (FilmArray). A brain magnetic resonance imaging (MRI) showed the presence of RE. The QuantiFERON-TB Gold Plus and Treponema Pallidum Haemagglutination Assay(TPHA) resulted positive, with a negative Veneral Disease Research Laboratory(VDRL). A second LP was then performed: CSF was clear and colourless, with confirmed hypoglycorrhachia (14 mg/dL), increased proteins (200 mg/dL) and white blood cells (707/mmc). Molecular tests for MTB were positive on a CSF sample, as well as CSF-TPHA and CSF-VDRL (titer:1:16), leading to the diagnosis of tubercular RE and neurosyphilis. Active pulmonary tuberculosis was ruled out. The fundus oculi examination confirmed a luetic uveitis. Intravenous treatment for tubercular RE was started with isoniazid, rifampicin, ethambutol, levofloxacin and steroid, later switched to oral antitubercular four-drug regimen (HRZE). Intravenous treatment for neurosyphilis with benzylpenicillin was also administered for 14 days, and then switched to ceftriaxone for further 7 days, due to penicillin allergy. Administration of the listed therapies led to the progressive resolution of neurological and ocular signs and symptoms.

Conclusions: Central nervous system compartmentalization may be the likely explanation of the initial CSF/plasma VDRL discordance. In this patient, the RE was mainly attributed to MTB, although a role of Treponema pallidum cannot be completely ruled out. The simultaneity of several opportunistic diseases is a hallmark of the severe immune impairment which characterizes AIDS, and must always be thoroughly investigated in these patients.

Clinical HIV

P 61 IDENTIKIT OF THE HIV PATIENT WITH ACUTE PATHOLOGY: EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF HIV PATIENTS HOSPITALIZED IN THE LAST YEAR IN AN ITALIAN UNIVERSITY HOSPITAL

P. Mantini[1], S. Mazzanti[1,2], V. Barocci[1], B. Candelaresi[1,2], S. Olivieri[1,2], F. Pallotta[1,2], I. Luchetti[1,2], G. Cesaretti[1,2], F. Ginevri[1,2], A. Ianovitz[1,2], V. Perticaroli[1,2], A. Di Fortunato[1,2], A. Ficola[1,2], A. Iannacone[1,2], G. Gelo Signorino[1,2], L. Brescini[1,2], A. Giacometti[1,2]

[1]Azienda Ospedaliero Universitaria delle Marche Ospedali Riuniti Ancona, Ancona, [2]Università politecnica delle Marche Facoltà di Medicina e Chirurgia, Ancona

For several years, literature and clinical practice have shown that patients with HIV have a very long life expectancy. The phenomenon is due to the introduction of increasingly effective and well-tolerated antiretroviral therapies and to the greater awareness of the disease by the patients themselves. This leads to an increase in this population of patients with chronic and senility-related diseases that are evident in daily outpatient activity.
One might expect that the same would also occur in hospital wards, i.e. that the majority of hospitalizations could be related to the management of cardiovascular, neoplastic or infectious diseases related to ageing.
The purpose of this study is to characterize the population of HIV+ patients who were hospitalized in the department “Clinica Malattie Infettive” of Ancona in the period March 2022-April 2023 (reference ward for an outpatient population of about 600 patients).
During that period, 19 HIV+ patients required hospitalization: 79% were male and with an average age of 45 years. In seven cases (36%), it was a new diagnoses of HIV late-presenters and in 3 cases (15%) of patients with infectious complications caused by a prolonged suspension of HAART. These last two categories make the cases of hospitalization for AIDS-related pathologies rise to 51%. In one case (5%), it was a mild form of COVID 19 pneumonia, 6 cases (31%) of non-AIDS-related infectious diseases in patients with a good number of CD4s (erysipelas, cholangitis, spondylodiscitis, influenza, community pneumonia, uveitis) and in one case (5%) it was a neoplastic disease.
So the profile of the HIV+ patient with acute pathology therefore shows a more frequently male, young patient with AIDS who is often hospitalized due to complications related to a late diagnosis or poor compliance with therapy. This should make us reflect on the fact that in addition to the complex management of the elderly HIV patient (on which a lot is focused, also obtaining excellent results in terms of prevention), the problem of raising awareness of the disease among younger people is still too frequent. Finally the large number of new AIDS diagnoses demonstrates how much awareness campaigns are still needed, including on public health, towards the early diagnosis of HIV.

Clinical HIV

P 62 A CASE OF PCP IN A PATIENT WITH UNDIAGNOSED HIV INFECTION

A. Zarroli, C. Febo, C. Frisenda, S. Di Giovine, E. D'Arcangelo, G. Castrignanò, K. Falasca, C. Ucciferri, J. Vecchiet

Ospedale SS. Annunziata, Chieti

Background: Pneumocystis pneumonia (PCP) is a form of pneumonia that is caused by the yeast-like fungus Pneumocystis jirovecii. It is a source of opportunistic infections and can cause lung infections in people with a weak immune system or other predisposing health conditions, such as people with HIV/AIDS (who account for 30 -40% of PCP cases). The incidence of PCP is now rising rapidly and represents a significant burden to the healthcare system.

Case Report: We present a case of a 55 years old patient with undiagnosed HIV infection.

On October 2022 a male patient came to our Emergency Room with generalized malaise, confusion, fever and sore throat for 1 month.

The initial laboratory results were: c-reactive protein (CRP) 79 mg/L, procalcitonin 0,2 ng/mL, neutrophils (5220/uL), lymphopenia (890/uL) and WBC (6540/uL), arterial blood gas analysis with pO2 69,4 mmHg with supportive Oxygen (Venturi Mask FiO2 50%). Chest computed tomography (CT) revealed ground-glass opacity and consolidations. Brain CT showed chronic vascular leukoencephalopathy and was negative for ischemic or hemorrhagic damages.

Given his radiographic findings along with his clinical picture and his respiratory failure (and the negativity of SARS-CoV-2 swab), we performed on 13th October a fibrobronchoscopy with a Bronchoalveolar Lavage (BAL), that showed up a B-d-Glucan (BDG) positivity, confirmed in blood serum too. This led us to confirm the suspicion of Pneumocystis Pneumonia, treated with trimethoprim-sulfamethoxazole (Bactrim). Then he recovered from PCP and O2-support was suspended.

Several blood tests, like the lymphocyte subpopulation, showed up a severe immunodeficiency, with CD4+ count: 67 cells/uL (nadir). On October 17th we performed an HIV-test, resulted positive for HIV infection. Thus HIV-RNA test showed an elevated number of viral copies (226.000 cps).

Due to a clinical worsening of neurological conditions of the patient, a MR brain, EEG and rachicentesis were performed with the evidence of HIV detected in CSF and of the neurological manifestations HIV-related. ART involving FTC/TDF+DRV/r was introduced immediately on 24th October.

On 11st November, after clinical, laboratory (CRP 9,99 mg/L and procalcitonin 0,030 ng/mL) and clinical improvement, the patient was dismissed and at the moment the patient is followed at our Day Hospital of Infectious Disease in Chieti, obtaining HIV virosuppression.

Conclusions: PCP is a frequent AIDS-defining diagnosis and is a more and more frequent opportunistic pneumonia in the United States and in Europe.

The incidence of PCP increased from 2,2/100.000 population between 2012 and 2020 to 2,7/100.000 in 2020, turning to 3,9/100.000 in 2021/2022. The proportion of PCP patients aged 75+ increased from 14% to 26%. These data are probably related to the SARS-CoV-2 pandemic and the lack of check-up and follow up by naive and not-patients during that two-year period.

Clinical HIV

P 63 AN UNUSUAL INCREASE IN KAPOSI SARCOMA DIAGNOSIS IN NAÏVE PLWH IN THE LAST YEAR IN OUR AREA. DID THE DOCTORS FORGET THIS CANCER OR IS IT JUST ANOTHER LATE GIFT OF THE PANDEMIC?

B. Bellocchi[1,2], L. Todaro[1,2], E. Pistarà[1,2], A. Guarneri[1,2], M.S. Paternò Raddusa[1,2], V. Boscia[1], A. Onorante[1], B. Santi Cacopardo[3], M. Ceccarelli[3], G. Nunnari[3], B.M. Celesia[1]

[1]ARNAS Garibaldi, Unit of Infectious Diseases, Catania, Italy, [2]University of Messina, Department of Clinical and Experimental Medicine, Messina, Italy, [3]University of Catania, Department of Clinical and Experimental Medicine, Catania, Italy

Background: Kaposi's sarcoma (KS) is a human herpesvirus 8 (HHV-8) associated cancer that occurs in people with weakened immune systems, such as those living with HIV (PLWH). Antiretroviral therapy (ART) has been shown to improve immune function and reduce the risk of developing KS in PLWH. Some studies have suggested that ART interruption, leading to a rebound in HIV viral load (VL) and a decline in immune function, makes the patient more susceptible to the HHV-8 virus reactivation and KS onset.

Material and Methods: Retrospective study. We analyzed the Kaposi's Sarcoma cases diagnosed at the Infectious Diseases Unit of the Garibaldi Nesima in Catania during the last ten years. We collected data about demographic characteristics (age, sex, sex orientation), comorbidities, year of diagnosis, prescribed therapy, and HIV-RNA at the time of diagnosis and at the time of diagnosis of KS. All data has been collected in a worksheet before analysis.

Results: From 2013 to 2021, 408 new diagnoses of HIV were performed; out of them, 44 were AIDS presenters 5 with KS (graphic 1). During 2022 we identified globally 37 new HIV diagnosis, 8 AIDS cases, and 6 with KS (N). Moreover, in the last year, we diagnosed two cases of KS in patients voluntarily stopping ART (E). Globally five had both cutaneous and visceral KS, 2 only visceral. All were male, the median age 36.5 years (IQR 31.5 – 46.5). In the N group, 5 had oral candidiasis and 1 non-Hodgkin's lymphoma. HIV-RNA viremia (VL) was > 500000 copies/mL in 4 cases and a median CD4 cells count < 100 cells/µl (tab. 1). Four received anthracycline chemotherapy, 1 of whom died after the first administration. The two patients in group E discontinued ART respectively for 6 and 12 months after having obtained an undetectable viremia before the appearance of cutaneous manifestations of KS; at the time of KS diagnosis VL was > 50000 copies/mL and CD4 cells count > 200 cells/µl (tab. 1). One showed visceral KS and required anthracycline chemotherapy.

Conclusions: Despite effective ART, KS remains the leading cancer among HIV/AIDS patients worldwide. While in recent years we have observed a progressive decrease in the number of AIDS and KS cases, in 2022 there was a considerable increase in KS diagnosis among AIDS presenters and among experienced patients who stopped treatment. A possible explanation of this phenomenon could be the late presentation with very low CD4 cells and high HIV-RNA viremia of naive patients because of the disruption of HIV service associated with SARS-CoV-2 pandemic. Moreover, in some cases, the late diagnosis of KS was associated with the non-recognition of typical skin lesions by other specialists or general practitioners. Finally, we cannot exclude an outbreak of HHV8 associated with unsafe sex in the last years after the end of the lockdown restriction.

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Clinical HIV

P 64 REASONS FOR LONG-ACTING TREATMENT REFUSAL DESPITE ELIGIBILITY IN A COHORT OF PEOPLE LIVING WITH HIV

S. Gardin, M. Mazzitelli, L. Sasset, D. Leoni, E. Agostini, A.M. Cattelan

Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, Italy

Background: Recently the introduction of long-acting treatment (LAT) strategies for HIV-1 further revolutionized the therapeutic approaches and gave more options for stigma reduction in people living with HIV (PLWH). However, even if many patients showed enthusiasm for this option, many remain doubtful, insecure, or unwilling about a possible switch to LAT. We therefore investigated reasons for long-acting refusal in our cohort.

Methods: LAT is available in our center (Padua, Veneto region, Northern Italy) from August 2022. Since then, we proposed this treatment option to all eligible PLWH who sequentially were admitted to our Infectious disease outpatient department, by informing them about this new strategy. We therefore recorded and analyzed reasons for refusal in PLWH who were fully eligible. Moreover, we considered whether distance from our center could have had an impact on refusal of treatment.

Results: From August 26th 2022 to February 28th 2023, 94 PLWH refused to receive LA, despite eligibility. Median age was 52 years (IQR: 43-59), 76% were males, 87% were Italian. Main population characteristics are depicted in Table 1.

The most common reasons for refusal were doubts/fear of treatment failure (85%), fear of adverse effects (87%), fear of injections (63%), increase of visit number/access to center (67%) regardless of the distance from the HIV center, aversion to therapeutic change (81%). Fourteen PLWH (15%) presented more than one reason for refusal. Moreover, 67 PLWH (71%) who refused LA live in Padua City and province, meanwhile 27 PLWH (29%) live in other Veneto's provinces.

Conclusions: This experience showed how fears and doubts among PLWH are quite common. Fears and doubt involved mostly the possible efficacy of the treatment. By contrast distance from the HIV clinic seemed to be not a real issue. Therefore, we believe that health care providers should properly counsel PLWH about efficacy and tolerability of this treatment and that communication should be targeted to address patient's fears and doubts.

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Clinical HIV

P 65 PROGRESSIVE DISSEMINATED HISTOPLASMOSIS IN PATIENTS LIVING WITH HIV: CASE SERIES AND REVIEW OF LITERATURE IN NON-ENDEMIC AREAS

D. Kontogiannis[1], D. Zaçe[1], D. Benvenuto[1], M. Moccione[1], G. Muratore[1], M.L. Giacalone[1], V. Barchi[1], L. Carnevale[1], G. Montagnari[1], A. Di Lorenzo[1], T. Mulas[1], L. Coppola[1], L. Campogiani[1], R. Petruccelli[2], C. Seghetti[3], M. Sebastiani[4], K. Casinelli[4], A. Ferlosio[3], C. D'Agostini[5], L. Sarmati[1,6], M. Iannetta[1,6]

[1]Department of Systems Medicine, Infectious Disease Clinic, Tor Vergata University, Rome, Italy, [2]Laboratory of Clinical Microbiology, Policlinico Tor Vergata, Rome, Italy, [3]Anatomic Pathology, Department of Biomedicine and Prevention, Tor Vergata University, Rome, Italy, [4]Infectious Disease Clinic, F. Spaziani Hospital, Frosinone FR, [5]Department of Experimental Medicine, Tor Vergata University, Rome, Italy, [6]Infectious Disease Clinic, Policlinico Tor Vergata, Rome, Italy

Histoplasma capsulatum (var. capsulatum (Hcc) and duboisii (Hcd)), is a dimorphic fungus endemic in America, Asia, Africa that causes histoplasmosis. In Europe it usually affects people coming from endemic areas, causing progressive disseminated diseases especially among people living with HIV (PLWH). In a recent WHO report on fungal pathogens, Histoplasma was listed in the "high priority group" and Italy was identified as an area likely to be hyperendemic.

We report two cases of histoplasmosis in patients hospitalized in the Infectious Diseases (ID) Unit of Policlinico Tor Vergata, Rome with a review of literature published from 2004 to 2023 in the PubMed database (key words ''histoplasmosis,'' ''Europe'', ''AIDS''). Further cases were included by examining the reference lists of the original articles.

Case 1: A 53-year-old Colombian woman, was admitted to the ID ward because of fever, cough, asthenia and weight loss. She underwent a hystero-annexectomy for a high-risk HPV infection.

During the hospitalization, pancytopenia was found, and the patient was diagnosed with HIV infection (HIV-RNA: 512.000 cp/ml, CD4: 17/mm3). Hcc was isolated in bone marrow samples and disseminated histoplasmosis was diagnosed. Lung CT scan also revealed a lung histoplasmoma (Figure 1). Isavuconazole and antiretroviral treatment were promptly started. After isavuconazole discontinuation, the patient developed skin granulomas, which regressed after reintroduction of the antifungal therapy. Follow-up is still ongoing.

Case 2: A 46-year-old Venezuelan man was transferred to our ID ward from a peripheral hospital due to fever, nausea, vomiting and respiratory failure. Four months before, the patient was diagnosed with advanced HIV infection (HIV-RNA 598000 cp/ml, CD4+ 12/mm3) with visceral leishmaniasis and CMV reactivation. Total body CT scan showed multiple lymphadenopathies in cervical, mediastinal and abdominal districts, multiple bilateral lung nodules and hepatosplenomegaly (Figure 2). Bronchoalveolar lavage and lymph node biopsy were performed with microbiological and histological evidence of Hcc (Figure 3,4). Treatment with liposomial amphotericin B was started and switched to isavuconazole after 5 weeks. Follow-up is still ongoing.

From 2004 to 2023, 78 cases of histoplasmosis in HIV patients have been described in Europe, including our case reports. 27 were women (34.6%), median age was 36 (29-43) years. 1 man had HIV-2. 67 (85.9%) Hcc and 7 (9%) Hcd were identified, in 4 cases it was not specified. 74 (94.9%) cases were imported, mainly from Latin America (41, 52.6%), and the infections were reported mainly in Spain (46, 59%). A total of 4 autochthonous cases were registered, 2 in Italy and 2 in Spain.

Histoplasmosis should be considered amongst opportunistic infection in PLWH, even in Europe, especially if the patients originate from or have travelled to endemic areas.

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Clinical HIV

P 66 A CASE OF HIV-2 INFECTION IN AN AFRICAN MAN RESIDENT IN ITALY FOR A LONG TIME

D. Benvenuto[1], F. De Maria[1], G. Muratore[1], A. Imeneo[1], D. Kontogiannis[1], D. Zaçe[1], M. Moccione[1], M.L. Giacalone[1], A. Cavasio[1], V. Barchi[1], R. Iannazzo[1], B. Massa[1], L. Carnevale[1], G. Montagnari[1], A. Cekrezi[1], F. Nina[1], L. Minardi[1], V. D'Aquila[1], A. Lodi[1], T. Mulas[1], L. Coppola[1], L. Campogiani[1], V. Malagnino[1], E. Teti[1], L. Sarmati[1,2], M. Iannetta[1,2]

[1]Department of Systems Medicine, Infectious Disease Clinic, Tor Vergata University, Rome, Italy, [2]Infectious Disease Clinic, Policlinico Tor Vergata, Rome, Italy

Background: HIV-2 infects 1-2 million people worldwide, with a higher prevalence in West African countries, where it is endemic. Due to migration phenomena the number of cases worldwide is increasing, although frequently undiagnosed.

Case Presentation: A 76-year-old man from Burkina Faso, permanently living in Italy since 1981, was admitted to the emergency room due to fever and cognitive impairment. Chest CT-scan showed ground-glass areas in the lungs. A lumbar puncture was performed and cerebrospinal fluid (CSF) analysis showed the presence of hypoglicorrachia (3 mg/dl), increased proteins (372 mg/dl) and white blood cells (2645/mmc, mainly neutrophils) while culture exam were positive to Streptococcus pneumoniae. Moreover, brain MRI showed cerebral abscesses and blood cultures were positive for Streptococcus pneumoniae. On admission to our ward, lymphopenia was noted (830/uL) and the serum protein electrophoresis showed a hypergamma peak. When the patient's cognitive status improved, during antibiotic treatment with ceftriaxone, informed consent to perform a fourth generation HIV1/2-test was obtained and the test resulted positive, with immunoblotting positivity confirmation. However, viral tests were negative for HIV-1 RNA on both CSF and plasma. Baseline CD3+ CD4+ absolute count was 292 cells/µl; CD4+/CD8+ ratio was 0.67. To rule out a false positive immunoassay, the test was repeated, confirming positive immunoblotting with positive gp 36. Therefore, alsoconsidering the origin of the patient from a highly endemic area, a diagnosis of HIV-2 infection was made. Unfortunately, no tests for the detection of HIV-2 RNA were available in our laboratory at that time, nor in other hospitals. Anti-retroviral therapy (ART) with TAF/FTC/BIC was started. One month after ART initiation, the CD3+ CD4+ absolute count increased to 413/uL; after three months a test for detection of HIV-2 RNA was performed, resulting negative.

Discussion: HIV-2 infection tends to present with a less aggressive course than HIV-1, with attenuated infection and lower pathogenicity. Unlike HIV-1, there are no commercial HIV-2 RNA assays and variability exists between in-house assays, therefore HIV-2 can be misdiagnosed, especially in non-endemic countries. The presence of opportunistic infections, the origin from endemic areas and a suggestive lymphocyte subpopulation assay should lead the clinician to suspect an HIV-2 infection/co-infection.

Clinical HIV

P 67 EBV-RELATED SMOOTH MUSCLE LEIOMYOSARCOMA, DISSEMINATED NON TUBERCULOUS MYCOBACTERIAL INFECTION AND KAPOSI'S SARCOMA IN AIDS: A CASE REPORT

M.C. Chionsini[1], D. Santoro[1], N. Dentale[2], A. Cascavilla[2], L. Marconi[2], M. Tadolini[1,2]

[1]Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy, [2]Infectious Disease Unit, IRCCS Azienda Ospedaliera-Universitaria di Bologna, Bologna, Italy

Introduction: EBV-related smooth muscle cell tumor is a rare disease that can be observed in immunocompromised patients, typically subjects with AIDS. Despite an increasing number of published case reports, there is no well-defined therapy for this disease yet.
Case presentation: At December 2022 a 38-year-old man presented to the ER due to pitting edema at lower limbs, dry cough since a month and weight loss in the last 6 months. He reported HIV infection known since 2014, not on HAART due to patient's refusal. On admission, the patient was febrile, had some bluish-colored lesions on the right tight and foot and palpable cervical lymph nodes. Blood tests showed leukopenia, lymphopenia and anemia. Renal and hepatic function were in range. CRP was 21 mg/dL and PCT was 1.1 ng/mL. CD4 cell count was equal to 26/mmc, HIV-RNA 319.024 copies/mL. At chest high resolution CT scan, there were bilateral parenchymal consolidations with cavities at left lower lobe, right upper lobe and right lower lobe, and pericardial effusion. A fibrobronchoscopy was then performed: smear microscopy of the broncholavage fluid was positive for acid-fast bacilli (2+), while Xpert MTB/RIF Ultra was negative. Culture test confirmed the presence of Mycobacterium avium. Blood and pericardial effusion cultures resulted positive for M. avium too. Biopsy of lower limbs skin lesion was performed, posing the diagnosis of Kaposi's Sarcoma. Therapy with daily rifampin, ethambutol, azithromycin and amikacin for disseminated M. Avium infection was then started along with steroid therapy. After 14 days of antimycobacterial therapy, antiretroviral therapy with TDF/FTC+DTG was also started. The 18 FDG PET/CT scan revealed intense uptake at mediastinal, inguinal, popliteal, retroclavicular and laterocervical lymph nodes (SUV max 21). Excisional biopsy of the cervical lymph node was performed: during surgery, at cervical site, a whitish nodule with no uptake at the PET scan was also found, collected and sent for pathology. Histologic examination on lymph node showed Kaposi's sarcoma, while examination of the nodule showed low-grade leiomyosarcoma with the PCR positive for EBV (EBV-LMS).
Discussion: In our case, the EBV-LMS was an incidental finding. According to published data, EBV-LMS has a better prognosis than conventional LMS, as it tends to grow slower and does not have the aggressive hematogenous dissemination typical of conventional LMS. In the most of cases, surgical excision is the treatment of choice, when the disease is not multifocal. However, in our case, it was not possible to complete the EBV-LMS stadiation, given the concomitant diagnosis of Kaposi's sarcoma and the need to timely start doxorubicin. At the end of chemotherapy, a new PET-CT scan will inform about residual disease and need of further eradication.
Conclusions: Although not included among AIDS-defining diseases, EBV-LMS might occur in severely immunocompromised HIV-positive subjects, with unclear impact on prognosis.

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Clinical HIV

P 68 THE TWO SIDES OF DORAVIRINE-BASED REGIMENS: A DESCRIPTIVE STUDY FOCUSING ON KIDNEY FUNCTION AND LIPIDIC PROFILE

M. Menozzi[1], M. Mazzitelli[2], B. Fontana[1], M. Albertini[1], M.D. Di Trapani[1], A.M. Cattelan[2], C. Mussini[1]

[1]Infectious Disease Department, University Hospital of Modena, Italy, [2]Infectious Disease Unit, Padova University Hospital, Italy

Background: Doravirine (DOR) is a recently approved NNRTI, often used in combination with Tenofovir Disoproxil Fumarate (TDF) or Tenofovir Alafenamide Fumarate (TAF) backbone. We investigated the differences in lipid profile and serum creatinine in a cohort of people living with HIV who switched to DOR-based regimens containing TDF or TAF.

Materials/Methods: A retrospective study was conducted collecting data of patients (pts) from Modena and Padova HIV Clinics who initiated a DOR based regimen, in particular DOR+TAF/FTC (TAF-group) or DOR/TDF/3TC (TDF-group). Data on lipid profile (total cholesterol – TC, LDL, HDL, triglycerides – TG) and serum creatinine were collected at DOR initiation (baseline), then at 6 and 12 months. Total hypercholesterolemia (H-COL), LDL H-COL and hypertriglyceridemia (H-TG) were defined if TC >200mg/dl, LDL >120mg/dl and TG >150mg/dl, respectively. Kidney impairment (KI) was defined as serum creatinine >1.2 mg/dl. The reasons for DOR initiation and discontinuation, side effects and previous antiretroviral (ARV) regimens were recorded. A descriptive statistical analysis was performed stratifying pts according to DOR regimen (TDF-group and TAF-group). A p-per-trend analysis was used to investigate serum lipid profile and creatinine trend during the follow up.

Results: 80 pts were included: 57 (71.3%) males, median age 57 years (IQR 50-60), 54 (67.5%) and 26 (32.5%) were on TDF and TAF group, respectively. Table 1 describes cohort characteristics, reasons for DOR initiation and interruption and side effects. Previous and post ARV regimens are shown in table 2. We recorded 13 (16.3%) DOR interruptions, mainly due to side effects, in particular gastroenteric and neurologic; one patient in TDF backbone experienced acute kidney injury. As shown in Table 3, during follow-up, pts in TDF-group showed a higher TC decline Vs TAF-group (-37 Vs -16 mg/dl, p 0.056 for pts with baseline H-COL, -15 Vs -2 mg/dl p 0.017 for baseline normal TC levels). No change was observed for TG. TAF-based regimens were more common (20 pts, 55.6%) before the switch in pts with H-COL: 12 (40%) in TDF-group and 7 (63%) in TAF-group. These pts were predominantly switching from NNRTI-based triple ARV: 12 (40%) and 3 (37%) in pts included in TDF or TAF-group respectively.Regarding creatinine levels, a significant improvement was detected in people with KI in TAF Vs TDF group (- 0,29 Vs -0,13 ml/min, p 0.036). None of pts with KI at baseline was previously treated with TDF: the principal backbone used was TAF in both switch groups. Main previous ARV strategies included NNRTI-based-triple therapy 4(66%) in TDF group and INSTI-based triple regimen 1(50%) in TAF group.

Conclusions: DOR-based regimen confirmed a favourable lipid profile, especially when combined with TDF/FTC. The association with TAF/FTC seemed to be safer in pts with baseline KI. However, the side effects prevalence was not negligible and it deserves to be better investigated on larger cohort.

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Clinical HIV

P 69 SERODISCORDANT TWINS: A CASE REPORT OF VERTICAL HIV TRASMISSION AND A MINIREVIEW OF THE LITERATURE

M. Alfonzo[1], M. Trizzino[1], G. Boncori[1], G. Valenti[1], L. Pipitò[1], C. Colomba[1,2], A. Cascio[1]

[1]Infectious and Tropical Diseases Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy, [2]Division of Pediatric Infectious Diseases, "G. Di Cristina" Hospital, ARNAS Civico Di Cristina Benfratelli, Palermo, Italy

Background: Mother-to-infant transmission of human immunodeficit virus-1 (HIV-1) can occur during gestation, labor, delivery, or during breast feeding. Woman infected with HIV-1 trasmits the infection to some, but not all, of their offspring. Increased risk of transmission have been noted with prematurity, vaginal delivery, and advanced immunodeficiency in the mother, but most of these associations have been found in some studies and not confirmed in others. Twins and second born children of HIV-infected mothers are not an increased risk of vertical transmission of the infection. Here we describe a case of HIV siero-discordant twins and compare our case with others described in the litterature.

Case Report: We describe a case of twenty-three years old woman who gave birth two male twins. She cames from Ivory Coast and landed in Lampedusa with her family on September 2022. One of the twins was urgently trasported to the Childrens Hospital "Di Cristina" in Palermo for respiratory failure and fever caused by Haemophilus influenzae and Human Parainfluenza virus pneumonia. He was twenty months old, and was the first born of bichorial and diamniotic twins pregnancy, with spontaneus, in term, and vaginally delivery. HIV infection was diagnosed in Africa when he was two weeks old, and never treated. The HIV test was performed also to his brother, which results seronegative, and to his parents: father negative and mother positive.

Baseline mother viro-immunological status was as follows: HIV viral load 70,900 cp/mL e CD4 T cell count 346/mmc (22%); genotypic resistance test (GRT) showed sensitivity to all drug classes; she started therapy with RAL + TDF/FTC.

Child baseline HIV viral load and CD4 T cell count were 31,400 cp/mL and 58/mmc (14,5 %), respectively. The GRT showed sensitivity to all drugs classes. He started therapy with zidovudine 80 mg, lamivudine 50 mg and lopinavir/ritonavir 160 mg, than zidovudine was switched to abacavir because of HLA-B57 negative. HIV RNA was 1820 cp/mL at one month of therapy. Lopinavir/ritonavir was switched to dolutegravir. On the last visit on March 2023, HIV RNA was 67 cp/mL, and patient was in good clinical features.

Material and Methods: We identified 26 articles from Pubmed with the search string HIV[TITLE] AND twins [TITLE]. 19 papers were excluded for non-fullfilling inclusion criteria according to article type, study designed or outcome of interest; so 7 full-lenght articles were reviewed.

Conclusions: HIV infection is more common in first-born than second-born twins, and HIV infection status tended to be concordant more in monozygotic than dizygotic sets. Three factors were strongly associated with HIV- 1 infection of twins: mother HIV-1 status, birth order and vaginal delivery. The first delivered infant of the twins is more exposed to contaminated blood and mucus in the cervix and has a highest risk to HIV transmission. The use of zidovudine peri- and post-partum can reduce mother-to-infant transmission.

Clinical HIV

P 70 EXTRACEREBRAL TOXOPLASMOSIS IN AIDS: A RARE CASE OF T. GONDII MYOSITIS

G. Lingua[1], A. Crocetta[1], A. Bernardi[1], C. Bobba[1], R. Balbiano[2], V. Pirriatore[2], A.M. Caputo[2], M. Chiriotto[2], S. Bonora[3], G. Calleri[2]

[1]Dipartimento Scienze Mediche, Malattie Infettive e Tropicali, Università degli Studi di Torino, Torino, [2]S.C. Malattie Infettive Divisione A, A.O Ospedale Amedeo di Savoia, A.S.L. Città di Torino, Torino, [3]Dipartimento Scienze Mediche, Malattie Infettive e Tropicali, Università degli Studi di Torino, Clinica Universitaria A.O Ospedale Amedeo di Savoia, Torino

Toxoplasmosis represents the most common infection involving the central nervous system (CNS) in patients with HIV not on antiretroviral treatment, most frequently related to a reactivation of previous infection than an acute infection. Extracerebral disease is an uncommon manifestation, mainly involving lungs, eyes and more rarely other sites like the musculoskeletal system, whose incidence is difficult to establish because of frequent miss-diagnosis.
We describe the case of a 58-years-old Caucasian man, admitted to the hospital with fever, asthenia, and unsteadiness of gait. Brain CT was negative; examinations on spinal fluid (CSF) showed: proteins 55 mg/dl, leukocytes 4/mm3, glycorrhachia within range, filmArray and culture negative for neurotrophic pathogens. Electromyography was compatible with Guillain-Barré syndrome: a treatment with intravenous immunoglobulins (IV IG) was administered. Concurrently, HIV was detected in blood [HIV-1 RNA > 10^7 cp/ml, CD4 2%, 11 cells, ratio <0.1] in addition to a low title of CMV and EBV DNA. Therapy with BIC/FTC/TAF + MRV, TMP/SMX and ganciclovir was started.
Due to a sudden worsening of the neurological state, encephalic MRI was performed, with no evidence of lesions. In parallel, findings of Toxoplasmosis IgG 69, IgM 46, Avidity 12%, and Toxoplasma DNA on CSF led to the diagnosis of acute Toxoplasma encephalitis (TE), treated with sulfadiazine/pyrimethamine and corticosteroids for eight weeks. A clinical improvement correlated with Toxoplasma DNA negativization on CSF enabled the beginning of secondary prophylaxis with TMP/SMX.
One month later, the patient displayed neurological deterioration along with multiple lesions at brain MRI and Toxoplasma DNA positivity on CSF, compatible with TE reactivation. Therefore, a new cycle of sulfadiazine/pyrimethamine and corticosteroid was administered. Because of the poor motor response with persistent myasthenia and elevated creatine kinase levels, an inflammatory myopathy was suspected. The muscle biopsy revealed pseudo-cystic inclusions of T. gondii at different stages of maturation with immunohistochemistry positive for anti-toxoplasma antibodies and perivascular and interstitial inflammatory infiltrate with focal atrophy and myocyte distress.
Because of the worsening of axonal sensorimotor polyneuropathy, a new cycle of IV IG was given, with a gradual clinical response and recovery of walking. After twelve weeks of TE treatment, secondary prophylaxis with sulfadiazine/pyrimethamine was prescribed. We finally report a fair immuno-virological response at nine months after HAART initiation [HIV RNA 94 cp/ml, CD4+ 99/µL (8.7%) ratio 0.12].
The aim of this Case report is to underline how clinical myositis due to T. gondii may be an overlooked condition in AIDS patients. Muscular involvement can include weakness and myalgia with elevated serum creatine kinase levels. In case of these symptoms, muscle biopsy is necessary to confirm the presence of T. gondii.

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Clinical HIV

P 71 VARICELLA-ZOSTER VIRUS IS AN IMPORTANT BUT OFTEN FORGOTTEN PATHOGEN IN PEOPLE LIVING WITH HIV

R.A. Cavasio[1], C. Sorace[1], L. Alborghetti[1], T. Mulas[2], L. Ferrari[2], G. De Simone[2], A. Crea[2], M. Compagno[2], E. Teti[2], A.M. Geretti[1,2,3], and the Tor Vergata Hospital group

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Infectiuos Diseases Clinic Policlinico Tor Vergata University Hospital, Rome, Italy, [3]School of Immunity and Microbial Sciences, King's College London, London, United Kingdom

Background: VZV can cause significant disease in people with HIV. A primary VZV infection can become life-threatening and despite effective ART there remains an increased risk of herpes zoster and its complications. Guidelines recommend people with HIV are screened for VZV IgG and if negative are offered the live varicella vaccine, provided their CD4 count is >200 cells/mm3. Those who are VZV IgG positive should be offered zoster vaccination, preferably with the subunit vaccine; the live zoster vaccine may be used as an alternative in those >50 years with CD4 count >200 cells/mm3. Our aim was to audit our clinical practice in relation to ZVZ disease prevention at the HIV Clinic of Policlinco Tor Vergata, and use the findings to develop an action plan.

Material and methods: Based on a population size of ~750 patients in active follow-up, we calculated that a retrospective analysis of 100 randomly selected patients would provide reliable audit estimates. The sample was identified in Aug-Sept 2021 among all patients with a medical record. Data were retrieved from the medical files. We assessed the availability of VZV IgG screening results, any indication for vaccination, and the availability of evidence of vaccination where indicated. Data about measles IgG screening and vaccination were retrieved as a comparator.

Results: Among 100 patients, 68% were men and 75% were of white ethnicity. The mean age was 50 years and 28% were aged >50 years. All were receiving ART; the median CD4 count was 657 cells/uL and 56% had a suppressed HIV RNA (<50 copies/mL). Overall, 47% had received their HIV diagnosis at Policlinico Tor Vergata whereas 53% had transferred care from other centres. A VZV IgG record was available in 44%. Of these, 6/44 (%) were VZV IgG seronegative and 38/44 (%) were VZV IgG seropositive. Based on the medical files, of those without VZV IgG, 4 were eligible for varicella vaccination (CD4 >200 cells/uL), 1 had vaccination prescribed and received it. Of the 13 with detectable VZV IgG who were eligible for zoster vaccination using the available live vaccine (age >50 years and CD4 >200 cells/uL), 4 were prescribed vaccination and none received it.
Data for measles were similar: 14% had a measles IgG record and of all of these were measles IgG seropositive, data were not available for 86 % of the patients.

Conclusions: There are unrealised opportunities to strengthen control of vaccine preventable infections in people with HIV. In response to the audit findings, we decided to build a recorded vaccination schedule and to create a baseline test package that includes serology for VZV and measles.

Clinical HIV

P 72 SHOULD ECHO-DOPPLER OF THE SUPRA AORTIC VESSELS BE CONSIDERED AS A SCREENING TEST IN ALL PATIENTS OR ONLY IN THOSE WITH A SIGNIFICANT CARDIOVASCULAR RISK PREDICTION BY FRAMINGHAM SCORE?

G. Bruno, M.T. Tassone, H. Morrone, P. Fusco, S. Rotundo, C. Costa, C. Torti

Department of Medical and Surgical Sciences, Chair of Infectious and Tropical Diseases, University "Magna Graecia", Catanzaro, Italy

Background: The evolution of combination antiretroviral therapy (cART) has significantly improved the quality of life and average survival of people living with HIV (PLWH). Due to ageing and to the side effects of the available cART drugs, cardio-metabolic comorbidities such as dyslipidemia, cardiovascular diseases and diabetes are emerging as new challenges in the clinical management of PLWH. According to Italian guidelines, all PLWH should be periodically assessed for cardiovascular risk. Non expensive and non-invasive indexes such as Framingham Score (FS) are used in routine clinical practice for this purpose. The aim of this study is to evaluate whether a correlation exists between FS and an increase in the intima-media vascular thickness (MIT) in PLWH in the modern cART era.

Materials and methods: This cross-sectional retrospective study was conducted in a third-level Hospital in Catanzaro. All HIV patients on regular cART treatment for at least one year with an Echo-Doppler of the supra aortic vessels (ECO-TSA) available were included. Demographic features, CD4+ T-cell count, serum HIV RNA and FS were collected on the same date of the ECO-TSA. Patients were divided into two groups based on presence/absence of significant MIT. The two groups were compared using a non parametric Student's t-test.

Results: 36 PLWH were enrolled. Of those, significant MIT was found in 23 (63.9%), while 13 subjects had normal MIT. Among the two groups, no significant differences were found with regard to CD4+ T-cell count and serum HIV RNA. Patients with increased MIT showed a FS significantly higher than those in the normal MIT group (p=0.0002). Considering patients with a FS≥10% (medium/high risk of a cardiovascular events up to 10 years), the analysis showed that 10/10 (100%) patients had a significant MIT, while amongthe 26 patients with FS<10%, 13/26 (50%) had a significant MIT.

Conclusions: In a cohort of PLWH on cART treatment under regular follow-up, high Framingham score is associated with increased intima media tickness measured by ECO-TSA. However, among patients with FS<10%, half of them had significant MIT, meaning that ECO-TSA could be useful even in this category. While waiting for further data, we therefore propose that ECO-TSA should be prescribed a screening test in all patients.

Clinical HIV

P 73 NEXT GENERATION SEQUENCING IN THE HIV-INFECTED NAIVE PATIENT: A SINGLE CENTRE PERFORMANCE EVALUATION

M. Cerchiaro[1,2], M. Bavastro[1,2], C. Russo Artimagnella[1,2], L. Labate[1,2], F. Stefanelli[3], V. Ricucci[3], M. Lucente[3], B. Bruzzone[3], S. Cardaci[1], L. Taramasso[1], M. Bassetti[1,2], A. Di Biagio[1,2]

[1]Infectious Diseases Unit, Policlinico San Martino Hospital-IRCCS, Genoa, Italy, [2]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [3]Hygiene Laboratory Unit, Policlinico San Martino Hospital-IRCCS, Genoa, Italy

Background: At HIV diagnosis, guidelines recommended to perform genotypic resistance test (GRT) in order to establish both viral sub-type and resistance associated mutations (RAMs). Up to now, GRT was traditionally performed by the Sanger sequencing (SS) method, but in the last years, Next Generation Sequencing (NGS) has been rapidly taking over. From 2021, in our hospital the routine usage of NGS was started. The aim of this prospective, observational study was to evaluate NGS performance in the HIV-infected naive patients and to estimate virological success (VS).

Material and methods: Clinical and laboratory data were collected and analysed with electronic data capture system (www.medinfo.it). Viral RNA was extracted using the EZ1&2 Virus Mini Kit v2.0 on automated platform. Library preparation for NGS was performed using the commercial kit AD4SEQ HIV-1 Solution v2 (Arrow Diagnostics) and sequenced on iSeq100 platform (illumina). FastQ files were analysed on SmartVir (SmartSeq S.r.l.) software for RAMs inference. The primary objective was to describe virological success at 24 weeks in relation to RAMs detected by NGS. A secondary objective was to describe RAMs.

Results: From February 2021 to February 2023, 69 treatment naïve HIV infected patients were enrolled. Baseline median age was 43.9 years, 54 were male. The main risk factor for HIV infection were sexual intercourse (93%). At diagnosis, the mean baseline plasma HIV RNA load was 4.7 log10 cp/ml (2 to 7), the mean nadir CD4 was 272 cells/mm3 (2 to 948).

The subtype B was detected in 37/69 (54%) samples. One patient had PI's mutations, 4 NNRTI's, 8 NRTI's and 7 INI's. Sixty-eight initiated INI based regimen, 1 died before starting ART. Sixteen were then excluded (6 because lost to follow-up and 10 because diagnosed with recent HIV infection and did not reach the 24-week time endpoint).

Therefore, we analysed 52 patients, 39 without RAMs, 6 with RAMs between 5-20% and 7 with RAMs >20%. The median time to virological success for subjects without RAMs was 48 days (IQR [31-109]), for the subjects with only RAMS >20% was 42 (IQR [28-88]), while for the subjects with RAMs between 5-20% was longer: 82.5 (IQR [64-97]). Figure 1 shows all the identified RAMs.

Conclusions: With the limit of the small sample size, we observed a longer time to virological success in patients with RAMs harboring virus. Using a method such as NGS that increases the of detection of RAMS to as low as 5% threshold could improve clinical outcome. Further studies with a larger sample size are needed to test this hypothesis.

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Clinical HIV

P 74 DEMOGRAPHICAL, CLINICAL, AND IMMUNOLOGICAL CHARACTERISTICS OF C-ART NAIVE PATIENTS AND RISK FACTORS OF ADVANCED DISEASE ACROSS THE YEARS: PRELIMINARY RESULTS FROM A TERTIARY UNIVERSITY HOSPITAL IN ITALY

E. Zappulo, A. Truono, A. d'Agostino, M. Faiella, M.E. Forte, F. Licciardi, E. Trucillo, A. Tanzillo, I. Vecchietti, N. Esposito, S. Mercinelli, G. Di Filippo, M. Cotugno, I. Gentile

Department of Clinical Medicine and Surgery- Section of Infectious Diseases, University of Naples "Federico II", Naples, Italy

Background: Optimal management of c-ART naïve PLWH with AHD(Advanced HIV Disease, presenting with a CD4 cell count <200 cells/μL or with an AIDS-defining event) represents a research priority due to poorest outcomes associate with this condition, including increased risk of clinical progression, morbidity and mortality. We reviewed main clinical features of PLWH diagnosed with HIV infection during the last five years and compared predictive factors of AHD.

Methods: We retrospectively recruited 209 patients among those followed at the Infectious Diseases Unit of the "Federico II" Hospital in Naples, Italy. Data were collected from electronic health records and charts review.

Results: A total of 209 patients (63% male) were enrolled with a median age of 33 years [IQR:24-40]. A comparison of baseline characteristics of c-ART negative PLWH diagnosed in the last five years compared to historical cohort is presented in Fig.1. Significant differences were observed in advanced age(>50 years), CDC '93 A category, immunological status (cd4>500 cells/mm3), which were significantly more frequent in patients starting treatment in the last 5 years (23% vs 4%,71 vs 45%,27% vs 11%, p<0.001,p=0.002,p=0.005, respectively). Patients diagnosed before 2017 had more often other comorbidities, were classified in CDC '93 B category and showed lower CD4 counts (88%vs 67%, 32%vs 15%, 46%vs 25%, p<0.001,p=0.017, p=0.009,respectively). Overall, people initiating c-ART with advanced HIV infection were 89 (43%). When comparing patients according to AHD(Fig.2), sex, age, ethnicity, and comorbidities did not come out as significant factors associated with this condition. However, prior to 1996, 40% patients showed AHD (vs 14%,p<0.001); on the other hand, patients in homosexual relationships or diagnosed from 2017 were significantly less likely to present advanced disease(26% vs 43%, p=0.021; 15% vs 30%, p=0.010). Predictably, opportunistic infection rate and prevalence of HIV related malignancy were significantly higher in AHD group (40%vs 3%, 14%vs 3%, p<0.001, p=0.002). We recognize that missing data may constitute a possible limitation of our study and our rate of AHD might have been overestimated.

Conclusions: Among people diagnosed with HIV infection followed at our centre, those who initiated c-ART after 2017 had higher baseline CD4 cell counts and lower rate of AHD.

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Clinical HIV

P 75 CHARACTERIZATION AND ROLE OF HIV-DNA MINORITY MUTATIONS IN A LONG-TERM TREATED PAEDIATRIC PATIENTS COHORT

L. Colagrossi[1], S. Bernardi[2], R. Scutari[3,4], K. Yu La Rosa[1], A. Granaglia[1], V. Fini[1], L. Forqué Rodriguez[1], L. Coltella[1], S. Ranno[1], G. Linardos[1], V.C. Di Maio[1], L. Gentile[1], M. Di Giuseppe[2], F. Leone[2], C. Russo[1], C.F. Perno[1]

[1]Microbiology and Diagnostic Immunology Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy, [2]Unit of Immune and Infectious Disease, University Department of Pediatrics DPUO, Bambino Gesù Children's Hospital, Rome, Italy, [3]Multimodal Research Area, Microbiology and Diagnostics of Immunology Unit, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [4]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy

Background: Next Generation Sequencing (NGS) has changed the paradigm of HIV-1 drug resistance monitoring mostly in individuals with a long history of treatment, such as paediatric patients (pts). The aim of the study was to better understand the impact of HIV-1 minority mutations to guide the best personalize antiretroviral treatment (ART).

Materials and methods: An observational study was carried out during the period from August 2022 to March 2023 at IRCCS Bambino Gesù Children's Hospital among 18 paediatric/young adults pts with HIV-1 diagnosis, of them three received a first HIV diagnosis within this period. The HIV-RNA and total HIV-DNA were determined by Xpert HIV-1 (Cepheid) and droplet digital PCR (ddPCR) technique, respectively. NGS was performed on HIV-1 positive samples using DeepChek Assay (ABL diagnostics). The presence of minority resistance mutations (mRMs) (frequency of 5-20%) and signature APOBEC-related mutations (APO-Ms) was evaluated through the DeepChek and HIVdb Stanford tools.

Results: The enrolled pts were mainly female (10,55.6%) with a median(IQR) age of 18(11-24) years. All pts were followed in our hospital since the first diagnosis, three of them received a HIV-1 diagnosis during the analysis period and thus were naïve-treated at the enrolment. Fourteen (77.8%) pts had an undetectable or <200 cp/mL of HIV-RNA, the remaining 4 pts, had a median(IQR) HIV-RNA of 43272(16373-488497) cp/mL. The HIV-DNA load was detectable for all tested pts with a median(IQR) of 1435(553-3503) copies/106 CD4+T-cells.

Nine pts (50%) received an early ART with a median duration of 10 years (IQR 6-18). The majority of pts (16,88.9%) had received Nucleoside Reverse Transcriptase inhibitors (NRTi) and Integrase inhibitor (INI) regimen, 16.7% (N=3) Protease Inhibitors (PI) regimen and 11.1% (N=2) Non-Nucleoside Reverse Transcriptase inhibitors (NNRTi) regimen.

The strains obtained were B (6, 33.3%), A (4, 22.2%), CRF02_AG (4, 22.2%), C (3, 16.7%) and CRF02_AE (1, 5.6%).

Looking at drug resistance mutation in HIV-DNA, 10 (55.6%) pts had at least one HIV-1 major RMs, in particular the NRTI, NNRTI and PI resistance were present in 27.8%, 22.2% and 5.6% of cases, respectively. Eleven (61.1%) pts were detected to harbour at least one HIV-1 mRMs, mainly localized in RT region followed by Integrase and Protease regions. Half of patients showed at least one APO-Mutation and only one APO-related stop codon.

Conclusions: This study demonstrated that despite the prolonged and in some cases early treatment the HIV-1 reservoir results in minority and APOBEC-related mutations. However, the role of minority variants in the context of personalized therapy remains unclear, also considering the historical HIV-RNA resistance test. Further analysis is needed to understand whether these mutations are the evolutionary adaptation of the virus under pharmacological pressure that could affect viral fitness.

Clinical HIV

P 76 EVALUATION OF THE CLINICAL PRESENTATION OF NAÏVE HIV PATIENTS IN THE PRE-COVID ERA VS THOSE ENROLLED IN THE COVID ERA: DATA FROM A NEAPOLITAN MULTICENTER COHORT

S. Martini[1], A. Russo[1,2], M.A. Carleo[3], A. Cascone[1], M. Pisaturo[1,2], V. Esposito[3], N. Coppola[1,2]

[1]UOC Infectious Diseases, University of Campania, Luigi Vanvitelli, Napoli, [2]Department of Mental Health and Public Medicine, Section of Infectious Diseases, University of Campania, Luigi Vanvitelli, Napoli, [3]Infectious Diseases and Gender Medicine Unit, AO dei Colli, PO Cotugno, Napoli

Background: The COVID-19 pandemic has impeded the diagnosis and treatment of HIV around the world. Literature data show that late diagnosis has increased during the COVID-19 pandemic1, resulting in more opportunistic infections and higher hospitalization rates, possibly due to reduced testing and conversion of infectious disease specialist facilities in Covid wards. This reduced the prevention of increased AIDS-related morbidity and mortality.

Materials and Methods: We therefore evaluated the characteristics of the HIV-naïve patients enrolled in a multicenter Neapolitan cohort from 2018 to 2022. Our aim was to evaluate any differences between the patients enrolled from 2018 to 2019 in the pre-Covid era (Group PC) and those from 2020 to 2022 (Group C) during the pandemic. We enrolled 45 patients in group PC and 54 in group C, enrolled at the University of Campania Luigi Vanvitelli and at the X Division of the Cotugno Hospital in Naples. In Table 1 we show the baseline data, evaluating many aspects in a univariate analysis.

Results: Our data show substantially few differences between the 2 groups. In the group hospitalized during the Covid pandemic there are more males (81.5%), less heterosexuals, more patients with HBs Ag positivity, less evidence of dyslipidemia and osteoporosis. These patients were also treated with TAF/FTC/INI to a greater extent than patients admitted to the PC group, being a newer regimen. There were essentially no statistical differences in clinical presentation and CD4 count at diagnosis between the 2 groups.

Conclusions: In conclusion, our data, unlike those in the literature, show no differences in clinical presentation and CD4 count at diagnosis between patients hospitalized in the pre-Covid era compared to those hospitalized during the Covid pandemic. We observed some differences, notably a reduced rate of dyslipidemia and osteoporosis in patients enrolled during the Covid pandemic. It is necessary however to enrol more patients to better analyze any differences between the clinical presentation of HIV-naïve patients in the 2 periods considered.

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Clinical HIV

P 77 MANAGEMENT AND OUTCOME OF PREGNANCY IN HIV-INFECTED WOMEN IN A NORTHERN ITALIAN HOSPITAL

C. Russo[1,2], G. Cattardico[1,2], A. Allodi[3], C. Arioni[3], C. Gustavino[4], A. Ferraiolo[4], L. Taramasso[1], M. Bassetti[1,2], A. Di Biagio[1,2]

[1]DISSAL - University of Genova – Genoa, Italy, [2]IRCCS Ospedale Policlinico San Martino, Infectious Disease Unit – Genova, Italy, [3]IRCCS Ospedale Policlinico San Martino, Neonatal Department – Genova, Italy, [4]IRCCS Ospedale Policlinico San Martino, Gynecology Department – Genova, Italy

Background: In the last decades, recommendations for antiretroviral therapy (ART) in pregnant HIV-infected women changed considerably. Indeed, since ART was recommended for all pregnant women, risk of mother-to-child transmission (MTCT) reduced consistently.
The aim of this study is to describe epidemiological, clinical and laboratory characteristics of pregnant HIV-infected women in a tertiary care Hospital.
Material and Methods: Clinical, demographic and laboratory data from pregnant HIV-infected women from 2015 to March 2023 were collected. Clinical and laboratory data were collected with electronic data capture system.
Special emphasis has been placed on mother and child outcomes depending on timing from HIV diagnosis (and therefore ART initiation) and date of delivery.
Results: In the study period, 41 pregnancies from 25 HIV-infected women were collected. Twelve women were from Italy, 5 from North Africa, 5 from South America, 1 from Albania and 1 from Bangladesh. We registered 8 abortions (median age 28 years; min-max: 22-37), in 2 cases for voluntary decision. In one patient HIV was diagnosed at time of abortion.
In the remaining 33 pregnancies with childbirth, median age was 30 years (min-max: 22-44). Among them, 27/33 patients had known HIV infection and continued ART (regimen was modified based on current guidelines) during pregnancy, with a HIV-RNA load always < 50 copies/mL. In 5/33 HIV was diagnosed during pregnancy and ART was started at least 3 months before delivery, allowing to reach undetectable HIV-RNA load at time of delivery. In all these 32/33 deliveries, zidovudine prophylaxis was administered to newborn, in only 2 women was also administered to the mother during labor. In only one case HIV diagnosis was made peripartum; intrapartum zidovudine was administered to the mother and ART was started in the newborn.
Overall, we registered 5 preterm delivery (< 37 weeks) and 1 case of newborn small for gestational age, all in known HIV-infected women in ART with median age of 31 (min-max: 28-44).
None mother to child transmission (MTCT) occurred.
Conclusions: In our cohort we collected a substantial number of abortions considering the total number of pregnancies, it could be interesting to further investigate if HIV-infection can predispose this condition.
Also, our results confirm how adequately administration of ART during pregnancy can reduce down to zero the risk of MCTC, without, however, increasing the side effects due to ART. We also abolished in women with undetectable HIV RNA the use of peripartum zidovudine except in critical conditions. This aspect is very important in reducing stigma in HIV-infected women. A further step could be the abolition of zidovudine to the newborn, which currently the new guidelines have reduced to only 14 days of administration.

Comorbidities

P 78 INCIDENCE AND OUTCOME OF TB/HIV CO-INFECTION IN A RURAL AREA OF SENEGAL: A 13-YEAR RETROSPECTIVE STUDY

M. Giglia[1,2,3], G. Menotti[1,2,3], T. Matucci[1,4], N. Riccardi[1,4], B. Granozzi[1,2,3], M.D. Yacine[5], M. Ndiaye[6], G. Besozzi[1], M. Tadolini[1,2,3]

[1]Stop TB Italia, Milan, Italy, [2]Infectious Diseases Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, [3]Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy, [4]Clinic of Infectious Diseases and Tropical Medicine, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy, [5]Ministry of Health, Dakar, Senegal, [6]Health Care Centre of Diofior, Diofior, Senegal

Background: Tuberculosis (TB)/Human Immunodeficiency Virus (HIV) co-infection remains a major public health problem, especially in resource-limited settings. The aim of our study, performed in a rural area of Senegal, was to investigate the incidence of TB among people living with HIV (PLWH), the burden of TB/HIV co-infection, the impact of HIV infection on TB treatment outcomes, and to outline possible strategies to reduce the co-infection burden.

Material and Methods: A retrospective observational study was conducted at the integrated TB-HIV outpatient clinic of the Health Care Centre of Diofior (HCD) (Fimela District, Fatick Region of Senegal) from the 1st of January 2009 to the 31st of December 2022.

Results: Of the 268 PLWH attending the HCD (66.0% female, median age at HIV diagnosis 40.2 years), 42 (15.7%) were diagnosed with TB for a total of 43 TB episodes. 23/42 (54.8%) were male, with a median age at TB diagnosis of 44.0 years. 38/42 (90.5%) had pulmonary localization, of which 47.4% were diagnosed by sputum smear microscopy, 18.4% by Xpert MTB/RIF, 10.5% by chest X-ray and 23.7% only by clinical evaluation. 24/42 (61.5%) subjects achieved TB treatment success, 15/42 (35.7%) died due to TB and 1/42 (2.4%) was lost to follow-up.

Regarding HIV infection, 70.7% of patients received HIV diagnosis at TB onset, with a median CD4+ cell count of 268 cells/mm3. The World Health Organization (WHO) clinical stage at HIV diagnosis was mostly 3 (36.6%) and 4 (43.9%) and 72.4% started antiretroviral treatment (ART) within one month after HIV diagnosis. 26/42 (61.9%) individuals have never had an HIV viral load determination and, out of the remaining 16, undetectability of HIV-RNA (<50 copies/mL) was reached only in 62.5% of subjects. At the end of the study, 24/42 (57.1%) individuals were dead (of which 15/24 due to TB), 15/42 (35.7%) alive and 3/42 (7.1%) were lost to follow-up.

In the study period, a total of 644 TB cases were registered in the Fimela district, out of which 6.7% were in co-infected subjects. Overall treatment success rate in TB monoinfected individuals was 85.9% vs. 62.8% in TB/HIV co-infected patients, while mortality was 5% vs. 34.9% in TB only and TB/HIV co-infected individuals, respectively (table 1).

Conclusions: TB/HIV co-infection is responsible for increased morbidity and mortality compared to TB alone in the rural area of Fimela in Senegal. The unfavourable outcome may be due to HIV late diagnosis, often made at the onset of TB, or to inadequate HIV retention in care, despite the presence of an integrated TB/HIV outpatient service. Therefore, investing in early diagnosis and strategies to optimize retention in care could massively contribute to reduce the significant mortality related to TB/HIV co-infection.

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Comorbidities

P 79 PREVALENCE AND TYPE OF SLEEP DISTURBANCES IN A MODERN COHORT OF PEOPLE LIVING WITH HIV

M. Mazzitelli[1], M. Trunfio[2,3], A. Milinkovic[4], E. Castelli[1], L. Sasset[1], D. Leoni[1], V. Scaglione[1], A.M. Cattelan[1]

[1]Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, Italy, [2]Infectious Diseases Unit, Department of Medical Sciences, University of Turin at Amedeo di Savoia Hospital, Turin, Italy, [3]HIV Neurobehavioral Research Program and Departments of Neurosciences and Psychiatry, School of Medicine, University of California, San Diego, CA, [4]Chelsea and Westminster Foundation Trust, SW10 9NH, London, United Kingdom

Background: Data on sleep disturbance (SD) type and prevalence in modern cohort of people living with HIV (PLWH) are scarce. Hence, we aimed at describing them by using a multidimensional assessment in our outpatient HIV clinic.

Methods: We prospectively recruited all adult PLWH during clinical checks at Padua Hospital from November 2021 to March 2022. All patients completed Epworth Sleepiness scale (ESS), Insomnia severity Index (ISI), Berlin Questionnaire for sleep apnea (SA), and Pittsburg Sleep Quality Index (PSQI).

The presence of MD (anxiety and depression) was assessed by General Anxiety Disorder-7 (GAD7), Patient Health Questionnaire-9 (PHQ9), and psychiatric consultation. We recorded clinical information and comedications, including drugs for SD or affecting sleep. Specific multivariate models (MM) were run per each SD scale, adjusting for relevant variables.

Results: We included 721 PLWH (median age 53 years, 71.8% males), more than 95% with an undetectable HIV RNA. Among these, 77% reported SD. Sleep metrics and alterations are reported in table 1. PSQI was the scale whose alterations were more common (60.3%), and 40.8% PWH had alterations in two or more scales. SA was reported by 31.3% PWH, while insomnia by 31.1%. In 7.9% and 1.8% PWH we detected high daily sleepiness and other SD (such as somnambulism, restless leg syndrome, pavor, etc.), respectively.

20.4% PWH took hypno-inducing drugs. Anxiety and depression were found in 204 (28.3%) and 116 (16.1%) PLWH, respectively. Poor sleep quality and insomnia were both significantly associated with depression (aOR 8.8, p< 0.01 and aOR 7.15, p< 0.001) and anxiety (aOR 2.3, p< 0.01 and aOR 2.41, p< 0.001), and the former also with CD4 count (aOR:1.01, p=0.03) and to IVDU among routes of HIV acquisition (aOR 0.217, p=0.04).

Conclusions: SD were highly frequent and strongly correlated with depression and anxiety in our cohort. We did not detect substantial correlations with HIV-related factors, but CD4+ count and route of HIV acquisition (intravenous drug use). We believe that sleep quality assessment should be routinely performed in our HIV clinics.

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Comorbidities

P 80 IMPROVEMENT IN INSULIN SENSITIVITY AFTER THE SWITCH FROM DOLUTEGRAVIR/LAMIVUDINE OR BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE TO DORAVIRINE/TENOFOVIR DISOPROXIL FUMARATE/LAMIVUDINE IN HIV-INFECTED PATIENTS WITH WEIGHT GAIN

L. Calza[1], V. Colangeli[1], M. Giglia[1], S. Cretella[1], I. Bon[2], P. Viale[1]

[1]Unit of Infectious Diseases, [2]Unit of Microbiology, IRCCS S.Orsola Hospital, University of Bologna, Bologna, Italy

Objectives: An observational, retrospective, cohort study was performed to assess changes in insulin sensitivity after a switch from dolutegravir/lamivudine (DOL/3TC) or bictegravir/emtricitabine/tenofovir alafenamide (BIC/F/TAF) to doravirine/tenofovir disoproxil fumarate/lamivudine (DOR/TDF/3TC) in virologically suppressed people living with HIV (PLWHIV) with recent significant weight gain.
Methods: All non-diabetic HIV-infected patients treated with DOL/3TC or BIC/F/TAF for >12 months, with HIV RNA <50 copies/mL, and with a weight increase >3 Kg in the last year, who underwent a switch to DOR/TDF/3TC were enrolled into the study. Serum levels of glucose, insulin and homeostasis model assessment of insulin resistance (HOMA-IR) index were evaluated every 6 months during a 12-month follow-up.
Results: Overall, 75 patients were enrolled: 41 treated with DOL/3TC and 34 with BIC/F/TAF. The mean age was 48.3 years, and 68 (91%) were males. At baseline, mean concentrations (+SD) of glucose and insulin were 86.2 (+23.2) mg/dL and 15.3 (+7.3) mcrUI/mL; mean HOMA-IR index (+SD) was 3.19 (+0.88); insulin resistance (HOMA-IR index >2.5) was present in 48 subjects (64%). Twelve months after the switch to DOR/TDF/3TC, change in mean serum glucose concentration was not significant, but a significant reduction in mean concentration of insulin (+SD) was reported (-3.66 mcrUi/L; +1.73; p=0.019), associated with a significant reduction in mean HOMA-IR index (+SD) (-0.52; +0.23; p=0.026). At the end of follow-up, insulin resistance was present in 27 patients (36%). A significant reduction in total and LDL cholesterol was also reported (-26.2 mg/dL, p=0.034, and -14.9 mg/dL, p=0.023, respectively), while decrease in mean body weight (-1.17 Kg) and mean BMI (-0.38 Kg/m2) were not significant. At the end of follow-up, 70 patients (93.3%) maintained HIV RNA <50 copies/mL: one subject had virological failure (with no resistance mutations for DOR/TDF/3TC), two discontinued for adverse events (gastrointestinal symptoms), and two had missing data. During the follow-up, adverse events were reported in 23 patients (30.6%), but there were no serious adverse events. Most commonly reported grade 1-2 adverse events were gastrointestinal symptoms (21%), and headache (14%).
Conclusion: In suppressed PLWHIV treated with DOL/3TC or BIC/F/TAF and with recent weight gain, the switch to DOR/TDF/3TC led to a significant improvement in insulin sensitivity and plasma lipids, with a trend to decrease in body weight.

Comorbidities

P 81 COMPLETE REMISSION OF POLYARTERITIS NODOSA USING ETANERCEPT IN A HIV POSITIVE PATIENT: A CASE REPORT

M. Gilio[1], G. Tramontano[2], M. Frontuto[1], D. Palazzo[1], N. Bertolini[3], C. Acierno[1], F. Picaro[1], A. Erezanu[1], S. Morella[1], M. Purgatorio[1], G. De Stefano[1]

[1]San Carlo Regional Hospital, Division of Infectious Diseases, Potenza, Italy, [2]Asl3 Genovese, Rheumatology, Genova, Italy, [3]Federico II University Hospital, Rheumatology, Napoli, Italy

Vasculitis continue to be a rare disease in patients with HIV. There are no well defined therapeutic guidelines for HIV-associated vasculitis. Herein we report a case of polyarteritis nodosa identified by American College of Rheumatology (ACR) criteria in HIV-OBI coinfected patient. A 54-old Nigerian woman, followed in our outpatient clinic and treated with Bictegravir/emtricitabine/tenofovir alafenamide, was hospitalized in the Potenza Infectious Disease Unit in November 2021 for weight loss, lower leg myalgias, arthralgias, paresthesia, oscillating fever of two weeks duration and poorly controlled arterial hypertension. On physical examination she showed tender subcutaneous nodules localized on the lower legs (particularly on the calf), skin ulceration and eschar (figure1 a-b-c), necrosis of the distal phalanx of the first toe of the right foot and tibiotarsal edema. Routine laboratory test revealed increased CRP (185 <5mg/L) HIV RNA undetectable, CD4 (684 cells/mcL). Additionally, ANA and ANCA titers and HCV antibodies were absent. Routine screening results for common opportunistic infections, such as tuberculosis, was negative. Histological examination of a skin biopsy showed a medium-sized dermal artery wall prevalently infiltrated by neutrophils. HIV in situ hybridization could not be performed. Based on electromyographic examination of lower legs multiple mononeuritis was diagnosed. Angiography supported the diagnosis of PAN, demonstrating segmental bilateral occlusion of femoral and popliteal arteries. Intravenous corticosteroids were initiated at 1 mg/kg/day, associated with intravenous infusion of iloprost 1,5 ng/kg/min for 6 h from 8 days. However, disease was still not controlled and cutaneous necrosis required amputation of the 1st finger of the right foot. Despite of treatment escalation and low-dose aspirin, new ischemic signs appeared on the 4th finger of the same foot. Given the no clinical and biologic response, iatrogenic diabetes and potential drug-drug interaction between ART and cDMARDs, based on a case-based review, Etanercept 50 mg weekly was added with clinical and biological improvement within few weeks. Prednisone was discontinued after 2 months. 14 months after treatment initiation, complete clinical (figure1 d) remission persists on weekly ETN administration and low-dose aspirin. Recognizing vasculitis in HIV-positive patients is important because sometimes it require immunosuppressive treatment. We propose that anti-TNF therapy is a viable alternative for the treatment of PAN in patients with HIV infection who DMARDs are not effective or contraindicated, as long as the underlying HIV infection status is stable. Close monitoring of clinical parameters of HIV infection status, with judicious use of antiretroviral agents, should be considered. Further clinical studies are needed to provide definitive evidence regarding the effectiveness and safety of anti-TNF agents for vasculitis in patients with HIV.

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Comorbidities

P 82 LIVER FIBROSIS ASSESMENT BY FIBROSIS4 INDEX AND CORRELATION WITH CARDIOVASCULAR RISK IN PEOPLE LIVING WITH HIV

C. Bertoni[1,2], D. Ceccarelli[2], L. Galli[2], H. Hasson[2], A. Siribelli[1,2], R. Lolatto[2], A. Castagna[1,2], C. Uberti-Foppa[1,2], G. Morsica[2]

[1]Vita-Salute University, Milan, Italy, [2]Dept. of Infectious Diseases, San Raffaele Hospital, Milan, Italy

Background: We investigated the diagnostic performance of fibrosis4 (Fib4) index as non-invasive marker of liver fibrosis (LF)and the association between Fib4 and cardiovascular risk (CVR) in people living with HIV (PLWH).
Methods: CVR and Fib4 were calculated in 5235 PLWH using the atherosclerotic cardiovascular disease (ASCVD) score. ASCVD was categorized as< 7.5=low risk, 7.5-20=intermediate risk, >20=high risk. The diagnostic performance of Fib4 was assessed in 855 PLWH with paired fibroscan as gold standard for LF categorized according to manufacturer's cutoff: F0-F1=< 7KpA;F2=7-9KpA;F3-F4 >9KpA). The area-under-the-curve (AUC) and the cut-off values of Fib4, compared to LF classification (F0-F1vsF2 and F2vsF3-F4), were determined by the logistic regression and the receiver operating characteristics (ROC) curves.
Results: The AUC-ROC identified a Fib4 threshold of 1.30 for F2 vs F0-F1 and 2.35 for F3-F4 vs F2 (Fig.1). Of 5235 PLWH, 3167 had Fib4< 1.30 (group1)1551 had Fib4 >1.30< 2.35(group2) and 517 had Fib4 >2.35(group3). PLWH in group1 were younger, median age 47 years (yr) compared with group2 and 3(median age 57 and 57 yr, respectively) P< 0.0001. PLWH in group2 and 3 had a longer duration of ART, median 17.9 and 18.5 yr, respectively, vs 10 yr in group1 with higher rate of detectable HIV-RNA (>50 copies/mL in 10% of group2 and 13% of group3) compared to group1 (7%); lower CD4, median 547 and 662 cells/mmc, respectively, vs 733 cells/mmc in group1. HBV and HCV were present in 5.0% and 16% of group1, in 7% and 31% of group2 and 10% and 50% of group3, respectively, P<0.001; PLWH with a Fib4 >1.30-2.35 (corresponding to fibrosis degree F2) compared to those with a Fib4<=1.30 had a risk of intermediate ASCVD of 2.89 (95%CI: 2.52-3.32) and a risk of high ASCVD of 6.26 (95%CI: 4.91-7.99). PLWH with a Fib4 >2.35 compared to those with a Fib4 >1.30-2.35 had a risk of intermediate ASCVD of 1.44 (95%CI: 1.26-1.66) and a risk of a high ASCVD of 2.72(95%CI: 2.98-3.23).
Conclusions: We identified a Fib4 thresholds distinguishing F0-F1 vs F2 vs F3-F4 stiffness categories in PLWH. We found a correlation of Fib4 as noninvasive marker of liver fibrosis with CVR in a large sample size of PLWH.

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Comorbidities

P 83 METABOLIC, HORMONAL, VASCULAR AND PSYCHOLOGICAL CHARACTERIZATION OF ERECTILE DYSFUNCTION IN YOUNG MAN LIVING WITH HIV: PRELIMINARY RESULTS OF A CROSS-SECTIONAL ONGOING STUDY

G. Tiecco[1], M. Di Gregorio[1], C. Colangelo[1], P. Facondo[2], A. Delbarba[3], S. Storti[1], E. Focà[1], F. Castelli[1], E. Quiros-Roldan[1]

[1]Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia, Italy, [2]Department of Clinical and Experimental Sciences, Unit of Endocrinology and Metabolism, University of Brescia and ASST Spedali Civili di Brescia, Brescia, Italy, [3]Unit of Endocrinology and Metabolism, ASST Spedali Civili di Brescia, Brescia, Italy

Background: Erectile dysfunction (ED) is a common issue in young men living with HIV (yMLWH) with a higher prevalence in comparison to age-matched general population. We designed a cross-sectional study to better characterize ED in yMLWH from a metabolic, hormonal, vascular and psychological point of view.
Methods: This is a monocentric cross-sectional ongoing study in which we enrolled yMLWH attending our Unit of Infectious Diseases in Brescia. Inclusion criteria were a HIV-infection and age between 18 and 50 years old. All yMLWH included were asked for symptoms of ED during the routinary HIV follow up visits. In case of referred ED, the severity and its psychological aspects were assessed respectively through 2 validated questionnaires: the International Index of Erectile Function-5 (IIEF-5) and the Structured Interview on Erectile Dysfunction (SIEDY). Metabolic and hormonal assays were performed using the Score2 to assess the cardiovascular risk. A dynamic penile color-doppler echography (dpCDE) was performed by an Endocrinology and Andrology Specialist to assess functional and structural vascular issues causing ED.
Results: Up to date, 10 yMLWH were enrolled with a median age of 43.5 (range 37-47) years old, a median Body Mass Index of 26.1 (range 22.6-28.4) and a median Score2 of 2.50% (range 1%-5%). All yMLWH were virologically suppressed and 4 (40%) assumed a dolutegravir/lamivudine regimen. The median CD4, CD8 and CD4/CD8 was respectively 616.5 cells/mcL (range 230-1633), 1001.5 cells/mcL (range 470-1929) and 0.8 (range 0.2-1.2). The IIEF-5 questionnaire revealed a severe ED in 6 yMLWH (60%), while, according to SIEDY scale 3, 8 (80%) presented psychologic factors causing sexual dysfunction. Overall, 2 (20%) subclinical hypogonadisms were diagnosed. As regards dpCDE, 4 yMLWH (40%) presented a suboptimal or delayed R-ICI (response to intracavernous injection). PSV (peak systolic velocity) was pathological (<35 cm/sec) in 2 (20%) yMLWH, while a suboptimal age-matched PSV was found only in 1 (10%) yMLWH. A decreased EDV (end diastolic velocity) was found in 4 (40%) yMLWH. As regards structural vascular abnormalities, 6 (60%) yMLWH presented an elevated IMT (intima-media thickness) and 1 Peyronie's diseases was diagnosed. In total, 7 (70%) yMLWH presented a cavernous artery tortuosity and 8 (80%) at least 1 significant arterial anastomosis.
Conclusions: Our preliminary findings point out that psychological and vascular factors might play a central role in yMLWH. No ED was explained based on hormonal levels, while significant functional or structural vascular alteration were found almost in every yMLWH enrolled. As IMT is a predictor for major cardiovascular events, a treadmill stress test and a supra-aortic trunks color Doppler were recommended in patients with impaired IMT. A tailored clinical approach focusing the multidimensional domains of sexual dysfunction may improve sexual health and quality of life in yMLWH.

Comorbidities

P 84 SLEEP DISORDERS AND ANTIRETROVIRAL THERAPY: A REAL-LIFE STUDY

L. Pipitò[1,2], M. Trizzino[2], G. Valenti1[,2], G. Bongiorno[1], M. Piccione[1,2], A. Cascio[1,2]

[1]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties "G D'Alessandro," University of Palermo, Palermo, Italy, [2]Infectious and Tropical Disease Unit and Sicilian Regional Reference Center for the fight against AIDS, AOU Policlinico "P. Giaccone", Palermo, Italy

Background: Sleep disorders can affect life quality and physical and social functioning. People living with HIV (PLWH) have a high incidence of sleep disturbances; insomnia and nightmares are reported as antiretroviral therapy (ART) collateral effects, especially for integrase inhibitors. This real-life study aims to evaluate the sleep disorders present in a population of PLWH.

Material and Methods: The Pittsburgh sleep quality index (PSQI) questionnaire was administered to PLWH in our Hospital. Demographic and ART data were collected. A PSQI >5 (sensitivity of 89.6% and specificity of 86.5%) is a surrogate marker of "poor sleepers". Mann Whitney U Test was applied to evaluate the association with PSQI score and age, sex, sleeping pills assumption and type of ART. PLWH were subdivided into “good sleepers” (PSQI score ≤5) and “poor sleepers” (PSQI score >5), and the $\chi 2$ test was applied to verify the association with the type of ART.

Results: Four-hundred-twenty-five completed questionnaires were collected, mainly from male patients (74.0%). The median age was 50 years old (IQR 42-58). Most of the patients were on integrase inhibitor-based ART (INI, 74%), whose 62% assumed dolutegravir (DTG) and 27% assumed bictegravir (BIC). Non-nucleoside reverse transcriptase inhibitors (NNRTI) and protease inhibitors (PI) were taken by 20% and 14%, respectively. Among patients with NNRTI, 41 also took INI; among patients in therapy with PI, 8 assumed INI. 14% of patients assumed sleeping pills, and 40% were poor sleepers (PSQI>5).

Statistical analysis showed no association between PSQI score or “poor sleepers” with antiretroviral drugs (see table 1). Adjusted analysis for co-administration of INI in patients in therapy with NNRTI and PI didn’t demonstrate an association with “poor sleeper”. Younger age was associated with a PSQI score more elevated (p=0.000), such as the sleeping pills assumption. However, studying the percentage of patients with sleep disturbances for each class of antiretroviral medicines, we observed that the PLWH that assumed INI (especially DTG) and PI had the highest percentage of sleep disorders (41% and 44%, respectively).

Conclusions: Our study showed a high incidence of sleep disorders in the PLWH of our centre, although a specific antiretroviral drug was not significatively associated with them. More studies are needed to understand the pathogenesis of sleep disturbances in PLWH and the presence of association with ART.

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Comorbidities

P 85 ERECTILE DYSFUNCTION IN YOUNG MEN WITH VERTICALLY ACQUIRED HIV INFECTION: A RETROSPECTIVE STUDY

G. Tiecco[1], C. Colangelo[1], M. Di Gregorio[1], P. Facondo[2], A. Delbarba[3], E. Focà[1], F. Castelli[1], E. Quiros-Roldan[1]

[1]Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia, Italy, [2]Department of Clinical and Experimental Sciences, Unit of Endocrinology and Metabolism, University of Brescia and ASST Spedali Civili di Brescia, Brescia, Italy, [3]Unit of Endocrinology and Metabolism, ASST Spedali Civili di Brescia, Brescia, Italy

Background: Erectile dysfunction (ED) is a common issue in young men living with HIV (yMLWH). Several studies proved that the prevalence of ED in yMLWH is higher than age-matched general population. Moreover, an earlier ED onset in yMLWH compared to uninfected HIV men has been noticed. To our knowledge, no studies have already assessed the extent of this problem in men with vertically acquired HIV infection (VA-yMLWH). The aim of the study is to investigate the prevalence of ED in VA-yMLWH of our cohort.
Methods: This is a monocentric retrospective study in which we enrolled VA-yMLWH attending our Unit of Infectious Diseases in Brescia. Inclusion criteria were a documented vertically acquired HIV-infection and age between 18 and 50 years old. Sexual function was assessed in all patients through 2 validated questionnaires: the International Index of Erectile Function-5 (IIEF-5) and the Structured Interview on Erectile Dysfunction (SIEDY). To assess cardiovascular risk factors, we used the Framingham Risk Score (FRS).
Results: Our Unit follows 33 young adults with vertically acquired HIV infection: 13 (39.4%) males and 20 (60.6%) females. Among the 13 VA-yMLWH only 1 patient was impossible to contact. The 12 VA-yMLWH included had a median age of 29 (range 21-39) years old and a median FRS of 1.05% (range 0.1%-11.0%). A median Body Mass Index of 23.1 (range 18.7-37.2) was reported with 2 class 1 (16.7%) and 1 class 2 obesity (8.3%). No significant comorbidities were reported in the study group except for 2 patients (16.7%) in treatment for hypertension and 1 patient (8.3%) for Systemic Lupus Erythematosus. All patients were virologically suppressed and 3 (25%) of them assumed a dolutegravir/lamivudine dual regimen. The median CD4, CD8 and CD4/CD8 were respectively 879.5 cells/mcL (range 448-1465), 962.5 cells/mcL (range 351-2162) and 0.8 (range 0.7-2.0). Although only 1 (8.3%) patient reported ED, the IIEF-5 questionnaire revealed a mild ED in 5 patients (41.7%): 1 (20%) reported a previous use of phosphodiesterase type 5 inhibitors. According to SIEDY scale 1 and 3, 1 (8.3%) VA-yMLWH might present an organic component for ED, while 8 (66.7%) VA-yMLWH might have psychogenetic factors causing a sexual dysfunction. All patients enrolled have shown interest in deepening the potential presence of an organic component for ED by performing a dynamic penile color doppler echography (dpCDE) in the future.
Conclusions: Our findings suggest that ED in VA-yMLWH might be underreported enlightening the essential role of administering the IIEF-5 questionnaire during the routinary outpatient activity. Moreover, a relevant psychological component seems to be predominant in the onset of ED in VA-yMLWH. Further analysis including hormonal levels and dpCDE will be performed in this group to better understand and treat the ED in VA-yMLWH. A tailored clinical approach focusing the multidimensional domains of sexual dysfunction may improve sexual health in VA-yMLWH.

Comorbidities

P 86 POLYPHARMACY AND AGING IN PEOPLE LIVING WITH HIV: 6 YEARS OF EXPERIENCE IN A MULTIDISCIPLINARY OUTPATIENT CLINIC

D. Cattaneo[1,2], L. Oreni[2], P. Meraviglia[2], D. Minisci[3], N. Astuti[2], S. Antinori[2], A. Gori[2], C. Gervasoni[1,2]

[1]Gestione Ambulatoriale Politerapie (GAP) Outpatient Clinic, ASST Fatebenefratelli-Sacco University Hospital, Milan, Italy, [2]Department of Infectious Diseases, ASST Fatebenefratelli-Sacco University Hospital, Milan, Italy, [3]Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

Background: Despite the availability of potent antiretroviral drugs, the management of HIV infection still present some important challenges such in older patients who often experience age-related comorbidities and complex polypharmacy. The higher number of comorbidities with ageing is correlated with a higher use of co-medications and consequently a higher risk of polypharmacy. For these reasons, in 2016 we set up an outpatient clinic for the management of polypharmacy in PWH (Gestione Ambulatoriale Politerapie [GAP]).
Objective: To describe the results of our 6-year experience with the GAP clinic for the management of polypharmacy in PWH.
Methods: Demographic characteristics, antiretroviral regimens, number and type of co-medications were collected in all PLWH included in the database of GAP. Therapies were stratified based on the number of anti-HIV drugs (dual vs. triple) and on the presence of pharmacokinetic boosters (ritonavir or cobicistat). The burden of medications with anticholinergic effects was also assessed using the Anticholinergic Cognitive Burden (ACB) scale. The frequency distribution data are expressed as absolute numbers and percentages, and all of the other measures as mean values ± standard deviation. Differences between groups were tested using the Student t test for continuous variables and Pearson's chi-squared test for dichotomous and unordered categorical data.
Results: 556 PLWH were included in the GAP database. Overall, the enrolled patients were given 4.2±2.7 drugs (range 1-17) in addition to their antiretroviral therapies. The number of co-medications greatly increased with age (3.0±2.2 vs. 4.1±2.5 vs. 6.3±3.2 comparing < 50 vs. 50-64 vs. >65 years; p<0.001 for all comparisons). 2672 prescriptions of non-antiretrovirals (drugs, n= 1972; dietary supplements, n=700) were documented: the most commonly prescribed co-medications were statins (12%), antiplatelet drugs (8%) and proton pump inhibitors (6%). With regard to the single molecules, the most frequently prescribed drugs were rosuvastatin, acetylsalicylic acid (as antiplatelet), enalapril and metformin. Twenty-six percent of non-antiretroviral medications were represented by dietary supplements.
PLWH on dual antiretroviral therapies were significantly older (58±9 vs. 54±11 years; p<0.001) and were concomitantly treated with more drugs (5.1±3.2 vs. 3.8±2.5; p<0.001) compared with those on triple therapies. A significant reduction of boosted antiretroviral regimens was observed in the subgroup of patients (n=188) with 2 GAP visits (53% vs. 23%; p<0.0001).
Overall, 4.8% of PLWH showed an ACB score ≥3; 2.6% of patients aged 65 years or older and 5.1% of those younger than 65 years.
Conclusions: The high prevalence of polypharmacy in PLWH, especially in the elderly, pose these patients at high risk for clinically relevant drug-drug interactions. A multidisciplinary approach involving physicians and clinical pharmacologists could help to identify the best antiretroviral and non-antiretroviral medications associated with reduced risk.

Comorbidities

P 87 EVALUATION OF LIPID PROFILE AND INTIMA MEDIA THICKNESS IN HIV EXPERIENCED PATIENTS TREATED WITH PI-BASED REGIMENS VS PI-SPARING REGIMENS

M.G. Palamone, S. Martini, M. Pisaturo, A. Russo, V. Zollo, M.T. Russo, P. Maggi, N. Coppola

Infectious Diseases, Departement of Mental Health and Public Medicine, University of Campania "Luigi Vanvitelli" Naples, Italy

Background: Antiretroviral therapy has increasingly improved management of HIV infection, ensuring long-term efficacy and tolerability. Each class of antiretrovirals has however different characteristics and different tolerability profiles. Literature data show that protease inhibitors (PIs) are associated with higher incidence of dyslipidemia. The aim of our study is to evaluate whether patients treated with PIs have both greater dyslipidemia and increased intima media thickness (IMT) and atheromatous plaques compared to patients treated without PIs.

Materials and Methods: To evaluate the association between PIs and dyslipidemia associated with increased IMT, we enrolled 110 HIV-experienced patients in a retrospective observational study. We enrolled all patients who were screened with Doppler ultrasonography of the supra-aortic trunks in 2019. Patients were divided into 2 groups, 59 in the PI-based group, treated with PIs and 51 in PI-sparing group. In the 2 groups we evaluated lipids, cardiovascular risk factors (smoking, BMI, age, hypertension), increased IMT and eventual atheromatous plaques, assessed by Doppler ultrasonography. We also performed a binary logistic regression analysis to assess the association of several patient factors (age, sex, BMI, smoke, lipids, PI regimen), to plaque.

Results: Analysis of the data showed a clear association between the Cases group and dyslipidemia, in particular statistical significance was achieved for the patients with level of cholesterol > 200 mg/dl (p= 0,036). Similarly, we observed in the PI-based group the evidence of increased IMT and plaques. In particular, in the evaluation of left sections of carotid artery, PI-based group showed higher percentage of increased IMT than PI-sparing group (p= 0,036).

Conclusions: In conclusion, our real-life data, although partial, show that patients treated with PIs have a trend to develop both greater dyslipidemia, in accordance with the literature, and increased IMT and atheromatous plaques compared to patients treated without PIs. Our data reach statistical significance only for evidence of increased IMT in the left sections of carotid artery in Cases group. These findings however could be useful to optimize the therapy of patients with cardiovascular risk factors.

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Comorbidities

P 88 VERTEBRAL OSTEOMYELITIS FROM MYCOBACTERIUM AVIUM COMPLEX IN ID ACQUIRED, SIX YEARS AFTER IMMUNOLOGICAL RECOVERY

V. Gennaro[1], C. Montrucchio[2], T. De Blasi[2], M. Chiriotto[2], G. Orofino[2], G. Calleri[2]

[1]Dipartimento Scienze Mediche, Malattie Infettive e Tropicali, Università degli Studi di Torino, Torino, [2]S.C. Malattie Infettive div.A, Ospedale Amedeo di Savoia, A. S.L. Città di Torino, Torino

Introduction: MAC is a category of non-tuberculous mycobacteria. MAC can cause disease in both immunocompetent and HIV-infected patients. However, the risk of developing an infection is closely related to the CD4 count, with a high risk in the case of CD4 <50 cells/microL. Other risk factors include a high viral load, >1 000 copies/mL, persistence of viral replication despite ART, and a history of opportunistic infections.
Clinical Case: Our clinical case is about R.C. , who came to our attention in June 2017 for low back pain, fever, weight loss, and diarrhea. MRI found L5-S1 spondylodiscitis. After investigations, HIV infection was diagnosed with CD4 3 cells/uL, ratio 0.1, HIV RNA 281 794 cp/mL. At the biopsy of the lumbar lesion, at the BAL, at the blood cultures and at the coproculture we isolated Mycobacterium avium. Therefore, therapy with azithromycin, rifabutin, ethambutol, levofloxacin and cycles of linezolid was started, which continued until June 2019. At the same time, our patient started ART with DTG+ABC+3TC, with negative viral load since November 2017 and CD >300 since December 2020. At the MRI check in October 2021 worsening of the lesion appeared. In December 2021, therefore, we performed another biopsy, the culture showed: S. aureus Oxa S, S. agalactiae R tetracycline, Mycobatrium avium with genotypic test of susceptibility to macrolides and aminoglocosides. We performed 15 day amikacin, ceftriaxone, azithromycin, clarithromycin and levofloxacin, followed by oral therapy with rifabutin, levofloxacin, azithromycin, ethambutol and linezolid. At that time the patient was in treatment with TDF/FTC + DTG, and the immunovirological status was stable. In the level II antibiogram, received in January 2022, we isolated resistance to linezolid. The patient discontinued all therapy shortly after, due to poor tolerance. He returned for MRI control in October 2022, with evidence of further extension of the abscess. Parenteral therapy was started in a Day Hospital regimen with rifampicin, azithromycin, ethambutol and 100 mg tigecycline. Contextually we doubled DTG dosage.He did another MRI in January 2023 for re-evaluation: further extension of the affected area. Tigecycline was discontinued for repeated episodes of nausea. From the culture, we got positivity exclusively for the same M.avium, with negative blood cultures. At the moment we decided to continue therapy with rifampicin, monitored with TDM, levofloxacin and azithromycin.
Conclusions: In summary, there are few cases in the literature of MAC bone infections in HIV patients. In the few reported cases, the clinical manifestation occurs despite the initiation of ARV therapy, and often the infection is diagnosed after immune recovery. Generally, a good response to antibiotic therapy is reported, for this reason the case presented may be of interest, especially considering the presence of a pathogen resistent to linezolid, not mentioned in previously published cases.

Comorbidities

P 89 LIVER ENZYME VARIATION AFTER SWITCHING TO EMTRICITABINE/TENOFOVIR ALAFENAMIDE/BICTEGRAVIR IS ASSOCIATED WITH GLUCOSE INCREASE IN A REAL-LIFE COHORT

N. Squillace[1], E. Ricci[2], P. Maggi[3], B. Menzaghi[4], G.V. De Socio[5], G. Orofino[6], B.M. Celesia[7], A. Bandera[8], F. Vichi[9], A. Di Biagio[10], L. Taramasso[10], S. Piconi[11], E. Sarchi[12], L. Valsecchi[13], G.F. Pellicanò[14], G. Cenderello[15], P. Bonfanti[1], for the CISAI Study Group

[1]Infectious Diseases Unit, Fondazione IRCCS San Gerardo Hospital-University of Milano-Bicocca, Monza, [2]Fondazione ASIA Onlus, Buccinasco (MI), Italy, [3]Infectious Diseases Unit, AORN Sant'Anna e San Sebastiano, Caserta, Italy, [4]Unit of Infectious Diseases, ASST della Valle Olona – Busto Arsizio (VA), [5]Unit of Infectious Diseases, Santa Maria Hospital, Perugia, [6]Division I of Infectious and Tropical Diseases, ASL Città di Torino, [7]Unit of Infectious Diseases, Garibaldi Hospital, Catania, [8]Infectious Disease Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [9]Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Florence, [10]Infectious Diseases, San Martino Hospital Genoa, University of Genoa, Genoa, [11]Unit of Infectious Diseases, A. Manzoni Hospital, Lecco, [12]Infectious Diseases Unit, S.Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy, [13]1st Department of Infectious Diseases, ASST Fatebenefratelli Sacco, Milan, Italy, [14]Infectious Diseases, G. Martino Hospital -University of Messina, Messina, [15]Infectious Diseases Department, Sanremo Hospital, Sanremo, Italy

Background: Our aim was to investigate the role of emtricitabine/tenofovir alafenamide/bictegravir (FTC/TAF/BIC) regimen on metabolic and hepatic safety in a real-life setting.

Material and Methods: Consecutive patients living with HIV infection (PLWH) enrolled in SCOLTA project switching to or initiating their first antiretroviral treatment (ART) with FTC/TAF/BIC were included. T0 and T1 were defined as results at baseline and 6-month follow-up respectively. PLWH with HBV co-infection were excluded. AST/creatinine (ac)NASH score was calculated.

Results: Out of 861 enrolled PLWH, 650 had at least one follow-up visit and were included in the analysis. Mean age was 48.3 y (±12.2), 74.8% were male, mean BMI was 25.4 Kg/m2 (±4.7), 18.9% were naïve (N) to antiretrovirals at T0. The median CD4+ was 597 cells/mm3 (interquartile range (IQR) 422-830) in experienced (Ex)-PLWH and 318 cells/mm3 (IQR 89-500) in N-PLWH. Ex-PLWH had mostly HIV-RNA <40 copies/mL (83.1%). Previous regimens (before switching to FTC/TAF/BIC) were predominantly: FTC/TAF/ELV/COBI [174 PLWH (37.1%)] , FTC/TAF/DTG [78 (16.6%)], FTC/TAF/DRV/COBI [32 (6.8%)] , 3TC/ABC/DTG [30 (6.4%)], FTC/TAF/RAL [24 (5.1%)], FTC/TAF/RPV [20 (4.3%] , FTC/TAF/ATV/COBI/ [10 (2%], Other PI-based regimens [25 (5.3%)], Other INSTI-based regimens [24 (5.1%)], Other NNRTI-Based regimens [14 (3.0%].

At T1 (see table 1), in N-PLWH, total cholesterol (TC), LDL-Cholesterol (LDL-c), HDL-cholesterol (HDL-c) and triglycerides (TGL) showed a significant increase, while ALT and acNASH decreased significantly. Weight increased by more than 2 Kg on average.

Ex-PLWH showed a significant reduction of TC, LDL-c and TGL and an increase in blood glucose (BG) in Ex-PLWH without diabetes. ALT increased significantly but the proportion of altered level did not vary. Weight did not change: Ex-PLWH with or without TAF in the previous regimen did not differ.

In Ex-PLWH, at T0, a correlation was found between BG and TGL (Spearman rho=0.13, p=0.003), TGL/HDL-c (rho=0.11, p=0.01), ALT (rho=0.13, p=0.009) and acNASH (rho=0.10, p=0.049). At T1, the correlation was confirmed between BG and TGL (Spearman rho=0.16, p=0.0004), TGL/HDL-c (rho=0.15, p=0.0009), ALT (rho=0.11, p=0.02).

eGFR reduced significantly both in experienced and naïve subjects.

Conclusions: ART initiation with FTC/TAF/BIC determined ALT decrease associated with acNASH reduction.

In experienced PLWH, switching to FTC/TAF/BIC is associated with a significant amelioration of lipid profile (TC and TGL reduction), but with a mild but significant increase of ALT and glucose.

The correlation between glucose increase and ALT and TGL/HDL ratio increase, observed in Ex-PLWH without diabetes, suggests a potential role of insulin resistance in the development of ALT increase.

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Comorbidities

P 90 WEIGHT GAIN IN PLWH: ROLE OF MULTIDISCIPLINARY APPROACH

M.A. Carleo[1], F.M. Fusco[2], M. Di Lorenzo[1], M. Vitale[1], L. Santoro[1], S. Mascolo[1], V. Rizzo[1], A. Guida[1], O. Tambaro[2], F. Borrelli[2], P. Rosario1, R. Viglietti[2], V. Esposito[1]

[1]Infectious Diseases and Gender Medicine Unit, AO dei Colli, PO Cotugno, Napoli, [2]Infectious Diseases and Immunodeficiencies Unit, AO dei Colli, PO Cotugno, Napoli

Background: People living with HIV (PLWH), although stably virus-suppressed,have a high risk of developing non-HIV-related metabolic diseases. Latest generation of antiretroviral therapy (ART) can contribute to weight and body mass index (BMI) gain, worsening metabolic disorders. In addition, incorrect dietary habits, sedentary life and latent depressive states can also contribute to weight gain.The project aims to evaluate the impact of a multidisciplinary approach to patients, including infectious disease specialist, nutritionist, psychologist and personal trainer in developing customized courses to improve well-being (Quality of Life,QoL) conditions and perception in PLWH.

Materials and Methods: Clinical evaluations (anthropometric measures and bioimpedancemetry, dietary habits, lifestyle, and psychological conditions) were performed at baseline and in periodic follow-ups. In addition, a diet plan and a physical activity program were offered together with a psychological assessment. QoL was estimated through validated questionnaires (SF-36, HADS, VAS). Variations in clinical parameters and questionnaire scores were analysed to evaluate the impact on QoL. A database and a specific web-app have been developed for activities monitoring.

Results: 96 patients have been enrolled (median age 46; males 78%; Italians 91%; all in ART). Demographical, bio-metrical and clinical data are reported in table 1. 74 patients (77%) had weight loss as their objective, the remaining 22 weight maintenance or gain. 45 PLWH (46%) were lost-to-follow-up (LTFU) during the project. LTFU occurred significantly more frequently after the first visit (82% vs 18%, p 0.000) and more frequently among those with target “maintenance/increase of weight” (66% vs 51%, p 0.315).

A 3-month follow-up is available for 25 patients, including 22 with a weight loss objective: among these, there is a significant reduction in BMI (29.1 vs 27.1;p 0.001), with a significant increase in physical activity (23% vs 59%, p 0.014). Changes in parameters of interest in patients with a "weight loss" goal at the 3-month follow-up are reported in table 2.

For QoL, follow-up data are available for 14 patients, showing an improvement inparameters measured through the SF-36 questionnaires, HADS for anxiety and depression, and VAS.

Conclusions: The obtained results, even if with a reduced sample size and follow-up time, suggest an improvement in the well-being of the enrolled subjects. The high dropout rate is compatible with other experiences in the nutritional field. A multidisciplinary approach can, then, represent an important tool for increasing QoL and applying a correct lifestyle in PLWH.

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Comorbidities

P 91 CORRELATING QUALITATIVE/QUANTITATIVE QUANTIFERON- TB GOLD PLUS RESULTS AND CD4+/CD8+ COUNT: A RETROSPECTIVE STUDY IN A HIV COHORT

A. Tavano, E. Asperges, P. Cambieri, M. Corbella, P. Guidicini, E. Bono, R. Gulminetti, L. Maiocchi, B. Mariani, S. Novati, L. Pagnucco, P. Sacchi, V. Zuccaro, R. Bruno

Department of Infectious Diseases, Fondazione IRCCS Policlinico San Matteo - Pavia (Italy), Department of Microbiology and Virology, Fondazione IRCCS Policlinico San Matteo – Pavia (Italy), Department of Clinical, Surgical, Diagnostics and Pediatric Sciences. University of Pavia - Pavia (Italy), Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico - Milano (Italy)

Background: Tuberculosis is the worldwide leading cause of morbidity and mortality in HIV+ people. Current CDC guidelines for the detection of Mycobacterium tuberculosis infection state that QuantiFERON tests should be used to screen for TB infection in all HIV+ individuals. QuantiFERON-TB Gold in Tube (QFT-GIT) was the most widely used test in high resources settings until the approval of QuantiFERON-TB Gold Plus (QFT-Plus) by the Food and Drug Administration (2016). The QFT-Plus differs for the presence of an additional test tube (TB2), which is designed to elicit and quantify the response of CD8+ T cells in addition to that of CD4+ T cells, while TB1 only assesses the CD4+ T cells response. The implementation of TB2 should provide a more precise assessment of the individual's immune response to tubercular antigens compared to QFT-GIT, since it would not be affected by CD4 depletion, but this theory has not been proven. We aimed at proving that the CD4 count does not impact on the QFT-Plus results in a HIV+ population.

Material and Methods: We retrospectively collected a large sample of HIV+ patients that had at least 1 QFT-Plus test done in our hospital (Italy) between 1 March 2017 and 31 December 2021. Logistic regression was used to explore the relationship between CD4+ and CD8+ and QFT-Plus results, while Kruskal-Wallis test was used to compare TB1 and TB2 values in different categories of positive test (false positive, treated TB, latent TB).

Results: We collected 701 patients, the median nadir CD4+ value was 199 cell/ul. Only 1,2% of QFT-Plus were indeterminate, and 7,4% (51) were positive. We found no correlation between CD4+ and CD8+ count (both the nadir and the present value) and the quantitative and qualitative results of the QFT-Plus. The Kruskal-Wallis test test found a correlation between categories of positive QFT- Plus and TB1, but not TB2.

Conclusions: QFT-Plus is reliable, with few indeterminate results, even in patients with a low CD4+ count. The quantitative TB1 results, which relies on CD4+ response, may vary depending on clinical status, but TB2 does not, confirming the role of CD8+ in compensating this variability.

Comorbidities

P 92 IS CAP (CONTROLLED ATTENUATION PARAMETER) A USEFUL TEST IN THE MANAGEMENT OF OLDER HIV POSITIVE PATIENTS?

E.P. Drago, M. Poliseno, A. Narducci, C. Grillo, F. De Gregorio, S. Ferrara, T.A. Santantonio, S. Lo Caputo

Infectious Diseases Unit, Department of Clinical and Experimental Medicine, University of Foggia

Introduction: Liver steatosis is common among PLWH (People Living With HIV) who have the traditional risk factors for NAFLD (non-alcoholic fatty liver disease) such as male sex, increased waist circumference and elevation in serum alanine level. The liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) determined by FibroScan are evidence-based non-invasive measures of liver fibrosis and steatosis respectively. We evaluate the proportion of liver steatosis and fibrosis among HIV-infected patients older than 50 years.

Materials and Methods: LSM and CAP and was obtained by FibroScan. In a dedicate database we collected the following data of patients older than 50 years: AIDS status, CD4/mmc count, HIV-RNA value, antiretroviral regimens, comorbidities, medications, last values of total Cholesterol, LDL, HDL, Triglycerides, Glycemia, blood pressure measurement, BMI and waist circumference. The calculation of the D:A:D score was also performed for each patient. Chi-square test and Mann-Whitney U test were performed to highlight differences between HIV-related variables, comorbidities, and laboratory data in the two groups. Spearman's correlation test was performed to highlight whether there was proportionality between the CAP values and the metabolic parameters. Finally, the multivariate regression with calculation of the odds ratio was performed to evaluate the risk factors of fibrosis and steatosis.

Results: We enrolled consecutive 95 over 50yy HIV infected patients to whom LSM and CAP exams were performed as screening for the evaluation of liver steatosis and liver stiffness in outpatient follow-up. Table 1 describes the characteristics PLWH without and with liver steatosis. A significant difference was highlighted for the percentage of those diagnosed with AIDS, higher in the group with steatosis. Among the comorbidities, obesity, waist circumference, and BMI all correlated with an increased likelihood of having fatty liver disease. Higher values of CAP correlate significantly with higher values of BMI, abdominal circumference and GPT (glutamic-pyruvic transaminase). This is in turn strictly attributable to the accuracy, precision and high specificity and significance of the FibroScan exam in identifying the accumulation of fat inside the hepatocytes. At the multivariate analysis previous AIDS diagnosis, BMI > 30 and having an abdominal circumference >100 cm correlate with a greater risk of steatosis; on the other hand, a diagnosis of AIDS and being anti-HCV positive correlate with a higher risk of fibrosis.

Conclusions: Our observation suggests that CAP calculation by ultrasounds is a minimally invasive and useful test for identifying patients with liver steatosis. They should be offered a second level screening for cardiometabolic diseases, and it should absolutely be suggested that they correct their lifestyle.

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Comorbidities

P 93 PSYCHOLOGICAL WELL-BEING IN A COHORT OF PEOPLE LIVING WITH HIV: A SINGLE CENTER STUDY

D. D'Elia[1], A. Londero[1], M. Garzitto[2], M. Colizzi[2], C. Tascini[1]

[1]Infectious Diseases Division, Department of Medicine, University of Udine and Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy, [2]Unit of Psychiatry, Department of Medicine (DAME), University of Udine, Udine, Italy

Background: Mental health conditions (MHC) are frequent in people living with HIV (PLWH) because of stigma, social status and drug addiction1. PLWH suffering from MHC may be less compliant to medication and follow-up assessments, leading to a major risk of opportunistic infections and hospitalization2. Here, we aimed to evaluate the psychological well-being of PLWH and its association with viro-immunological profile.

Material and Methods: From November 2022 to March 2023, we enrolled 72 patients at the Infectious Disease outpatient clinic of the University Hospital of Udine. The Hospital Anxiety and Depression Scale (HADS) was used to assess current Anxiety (A) and Depression (D) symptoms. Fatigue was measured with the Fatigue Severity Scale (FSS) and sleep problems with the Insomnia Severity Index (ISI). The Cognitive Failures Questionnaire (CFQ) was used to measure subjective neurocognitive difficulties (sub-scales: Distractibility, Di; Forgetfulness, Fo; False Triggering, FT). General sociodemographic and clinical information, including viro-immunological profile and current Highly Active Anti-Retroviral Therapy (HAART) were also collected. We then tested for statistically significant between-group differences and correlations.

Results: Over the study period, we recruited 72 patients, mostly male (83.3%), with a mean age of 51.1 ±11.37 years, and an HIV history of 14.53 ±8.85 years. Of them, 15.3% showed clinically relevant symptoms of anxiety and 12.5% of depression. Sleep problems (32.0%), fatigue (20.8%), and cognitive problems (8.3%), were also reported. At assessment, 20.8% of the participants were receiving psychopharmacological treatment, and 13.9% were on treatment from before HIV infection diagnosis. Participants with previous MHC (22.2%) had higher current scores at the HADS-A/D, ISI, and FSS (all with $t<-2.5$, $p<0.032$). Similarly, those with recent stressful life-events (46.5%) scored higher on HADS-A/D and ISI ($t<-2.1$, $p<0.040$). Participants with a detectable viral load at the last examination (from 20/µL to 218,000/µL) showed positive moderate correlations with the CFQ ($r=+0.569$; Figure 2) and its Di ($r=+0.587$) and FT ($r=+0.670$) sub-scales (Figure 2). Some associations were also observed between HAART and psychological well-being. As shown in Figure 1, patients assuming bictegravir (26.4%) showed lower scores at the CFQ-Fo and CFQ-FT, while those assuming rilpivirine (12.5%) had higher scores at the CFQ, CFQ-Fo, and CFQ-Di. Finally, the assumption of doravirine (5.6%) was associated with lower HADS-D scores and FSS.

Conclusions: Although preliminary and limited in terms of sample size, our data provides evidence for psychological distress among PLWH at our center. Further investigations are needed to profile PLWH from a mental health perspective, to support quality of life and overall outcome.

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Comorbidities

P 94 NAFLD IN PEOPLE LIVING WITH HIV (PLHIV): RISK FACTORS ASSOCIATED WITH STEATOSIS CONFIRMED BY FIBROSCAN

N.B. Bana[1], N. Squillace[1], E. Ricci[2], P. Vitiello[3], P. Maggi[4], F. Colucci[4], A. Di Biagio[5,6], L.A. Nicolini[5], K. Falasca[7], E. Salomoni[8], P. Bonfanti[1]

[1]Infectious Disease Unit, Fondazione IRCCS San Gerardo dei Tintori, Università Milano-Bicocca, Monza, [2]Fondazione ASIA Onlus, Buccinasco (MI), [3]Unit of Infectious Diseases, ASST della Valle Olona, Busto Arsizio (VA), [4]Infectious Diseases Unit, AORN Sant'Anna e San Sebastiano, Caserta, [5]Infectious Diseases, IRCCS Ospedale Policlinico San Martino, Genoa, Italy, [6]Department of Health Science (Dissal), University of Genoa, Genoa, Italy, [7]Department of Medicine and Science of Aging, Clinic of Infectious Diseases, University "G. D'Annunzio", Chieti, Pescara, [8]Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Florence

Background: Non-Alcoholic-Fatty-Liver-Disease (NAFLD) is now considered an emerging cause of cirrhosis and HCC, especially in High-Income Countries where it often overcame chronic viral hepatitis and alcoholic liver disease as main liver failure trigger. Our aim is to define the main risk factors for NAFLD in a group of PLHIV diagnosed with steatosis by ultrasound sonography (US) and classified by CAP (Control Attenuated Parameter).
Materials and Methods: This is a multicentric prospective cohort study including PLHIV >18 years old diagnosed with hepatic steatosis by US. We excluded patients with an excessive alcohol intake, BMI>40 and HBV or HCV co-infection. A fibroscan with CAP was prescribed, stratifying patients in groups as follow: S0 (CAP <248 dB/m), S1 (248<CAP <268 dB/m), S2 (269<CAP<280 dB/m), S3 (CAP> 280 dB/m). Categorical variables were compared using the chi-square test, and continuous variables by anova or Mann-Whitney test as appropriate.
Results: We enrolled 105 PLHIV diagnosed with steatosis by US. Among them, we managed to obtain fibroscan results for 75 patients (71.4%). Patients' main characteristics are described in Table 1 and Table 2.
At univariate analysis the following factors were associated with steatosis considering CAP (S1-S3 vs S0): concomitant diabetes (36 vs 10%, p=0.03), higher BMI (mean 29.2 vs 26.1, p<0.01) and waist circumference (mean 103.4 vs 97.7 cm, p=0.03), higher triglycerides (TGL, mean 168.3 vs 108.7 mg/dl, p=0.01). Considering antiretroviral therapy (ART), we found that TAF exposition seems to be a protective factor against steatosis (57.4 vs 84.2%, p=0.04), while the exposition to dolutegravir (DTG) does not reach statistical significance (69.1 vs 47.4%, p= 0,09). No effect was seen for other ART drugs and co-medications.
Stratifying patients by the specific steatosis class (S3 vs S1-S2 vs S0), only two factors were associated with higher grades of steatosis: higher BMI (29.2 vs 29.1 vs 26.1, p=0.01) and TGL (175.6 mg/dl vs 139,1 mg/dl vs 108.7 mg/dl, p=0.02). Also here we could see how TAF seems to have a mild protective activity on steatosis (53.5% vs 72.7% vs 84.2%, p=0.05).
In both cases, no effect was seen considering sleep quality, physical activity, nadir CD4+ count and concomitant medications.
Considering only data from US (moderate/severe vs mild steatosis), a lower nadir CD4+ count, as well as bad sleep quality, low physical activity and previous exposition to lopinavir/ritonavir were significantly associated with a higher risk for steatosis.
Conclusion: Considering fibroscan, steatosis was confirmed only in 55 among 75 PLHIV. BMI and higher TGL levels were the only two factors strongly associated with steatosis considering both S1-S3 vs S0 and S3 vs S1-S2 vs S0 analysis. TAF exposition seems to be a protective factor. US based-classification of steatosis was associated with low physical activity, previous exposure to LPV/r and lower nadir CD4+ count.

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Comorbidities

P 95 CORRELATION BETWEEN BONE AND MIOINTIMAL DAMAGE IN PATIENTS WITH HIV

A. Masiello[1], A. Boccia[2], A. Limone[2], F. Simeone[1], A. Iodice[1], P. Maggi[1]

[1]UOC Malattie Infettive, AORN "S. Anna e S. Sebastiano" Caserta, [2]UOC Malattie Infettive, Università della Campania "L. Vanvitelli" Napoli

Background: Patients with HIV infection (PLWH) are at increased risk of non-AIDS-related comorbidities such as osteoporosis and atherosclerosis. These two comorbidities are generally associated with aging but there are currently few studies on their correlation. Recent analyzes on the general population have shown that patients with osteoporosis have a greater risk of developing cardiovascular disease than those with normal bone mass density. The aim of our study is to evaluate the possible correlation between bone and endothelial damage in PLWHs receiving antiretroviral therapy

Patients and Methods: We enrolled 146 patients, 42 females and 104 males. All the patients underwent measurement of carotid myo-intimal thickness (cIMT) with carotids doppler Ultrasonography and bone density with bioimpedance analysis. We divided the patients into 2 groups according to cIMT: A) (#86) without plaque (cIMT=/<1.3 mm) and B) (#60) with plaque (cIMT> 1.3 mm). For both groups we evaluated the T/Z score values. For each group we also assessed CD4, CD4 nadir, CD4/CD8 ratio, years of ART, type of ART, serum cholesterol (total, LDL and HDL), triglycerides and Vitamin D values. For statistical analysis we used the student t-test and Chi square.

Results: Data are reported in the Table 1. No statistically significant differences emerged between the two groups for CD4, CD4 nadir, CD4/CD8 ratio and years of ART. A statistical significance was highlighted for the type of ART, showing that in group A there is a prevalence of two drugs regimens (2DR) and a lower percentage of PI-based therapies compared to group B (respectively p 0.008 and p 0.003). Furthermore, statistical significance was found in the values of total cholesterol and LDL and in the values of triglycerides with a prevalence of dyslipidemia in group B (respectively p 0.003, p 0.01 and p 0.003). Vitamin D also showed lower values in the group with IMT >1.3. Finally, a significant difference in the values of T and Z scores between the two groups showed pathological values of bone density in group B (p<0.0006).

Conclusions: These data highlight a correlation between bone and miointimal damage in ART-treated PLWH: patients with increased cIMT (>1.3 mm) more often show bone density alterations with osteopenia or osteoporosis. Furthermore, it is confirmed that the type of ART can play a decisive role in the development of comorbidities based on the alteration of lipid metabolism. The main limitation of our analysis is the still small number of enrolled patients. However, these data underscore the need for more extensive diagnostic evaluation in PLWHs.

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Comorbidities

P 96 A NOCARDIA FROM NOWHERE

A.L. Croci, A. Cascavilla, M. Giglia, G. Beci, L. Calza

Infectious Diseases Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy

Case Presentation: We report the case of a 65 year old man, who was diagnosed with HIV in 2004, on treatment with TAF/FTC/DRV/c + MVC (INSTI resistant virus), with suboptimal adherence. The immuno-virological status was CD4 + 427/mmc (26%), CD4/CD8 0.47, HIV-VL 78 cp/ml.

On 04/06/2022 the patient was admitted to the emergency department for a subacute right lower limb pain, unresponsive to steroid therapy. The lower-limb CT scan showed a large pluriconcameral infected hematoma not dissociable from the proximal metaphysis of the right femur (figure 1).

An echo-driven FNA was performed, with the isolation of Nocardia farcinica, thus TMP/SMX was started.

Unfortunately, after 5 days we observed an allergic rash that forced us to discontinue TMP/SMX, switching to linezolid and meropenem.

On the same day, the patient underwent a surgical toilette of the lower limb, but the post-surgery was complicated by septic/hypovolemic shock that required ICU admission for 3 days.

Returning to our Unit, he presented a severe allergic reaction with cutaneous and mucosal involvement, leading us to discontinue the whole antibiotic therapy and to start ciprofloxacin.

Ten days later, we assisted an acute sensory deterioration with the development of seizure.

We performed an urgent brain CT scan that showed two lesions compatible with abscesses in the right frontal and occipital lobe, therefore we promptly stopped ciprofloxacin and started antiedemigenic therapy with steroids.

The following MRI confirmed the presence of the cerebral lesions (figure 2), while the chest CT, the echocardiography and the fundoscopy were negative for septic localization.

A few days later, we reintroduced linezolid with no adverse reactions and progressive clinical improvement.

Finally, the patient was discharged to our DH unit, where he's still on treatment. Follow-up MRI showed a volume reduction of brain lesions.

Discussion: Nocardia spp. infection is disseminated in 20-50% of immunocompromised patients at diagnosis (in particular with brain involvement) and the main site of entry is the respiratory tract. Thus, the lung represents 80% [1] of the primary localization of infection, but skin penetration through contaminated objects has also been described.

The case is interesting because of its unusual presentation: the infection was diagnosed by echo-guided FNA on a lower-limb hematoma, whereas the chest-CT scan was negative for lung involvement. The patient didn't report any traumatic lesion in the infection site, suggesting an hematogenous spread, but with an unknown site of origin. Moreover, the case highlights how the treatment of Nocardia can be challenging, due to the limited drugs available, their side effects and the considerable duration of therapy.

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Comorbidities

P 97 SALMONELLA ENTERIDITIS SPONDYLODISCITIS IN A LIVER TRANSPLANTED HIV-HBV-HCV-HDV PATIENT: A CASE REPORT

A. Iannacone, M. Cimatti, A. Ficola, S. Mazzanti, M. Tavio, A. Giacometti

UNIVPM - Azienda Ospedaliera Universitaria delle Marche, Ancona

Background: We are presenting the case of BG, male, 55 years old. His medical history presents HIV, HCV (1c genotype – SVR 2015) and HBV/HDV infections, liver transplant, type 2 diabetes, SCA-STEMI, nephrolithiasis. Three days after a traumatic fall in November 2022, he presented to the emergency room of another hospital for fever and a left renal colic pain. The diagnosis was L1 spinal fracture, with no surgical indications, left pyelonephritis with placement of a JJ stent and urinary tract infection from Enterococcus faecalis, treated with piperacillin-tazobactam, meropenem and eventually tygeciclin. He was transferred to our hospital for the reappearance of fever, back pain and urinary symptoms. A new urine culture resulted positive for Klebsiella pneumoniae and a computed tomography (TC) was performed and showed D12-L1 spondylodiscitis. Keeping in mind the previous positive culture for Enterococcus faecalis, it was administered an antibiotic therapy with ceftazidime and teicoplanin for ten days, switched to ceftidoren and dalbavancin, with a second dose one week apart, in order to discharge the patient, who manifested the will to continue the therapy at home. During the hospitalization, due to the persistence of fever and liver enzymes elevation, the eating habits of the patient were analyzed and he admitted to eat raw seafood. A Widal-Wright analysis was performed and it showed a positivity for Salmonella typhi O antigen. A post hospitalization MRI showed a worsening of the spondylodiscitis, involving the vertebrae from D9 to L3. The patients entered again our hospital ward and a biopsy was performed at the level of L1. The culture showed a positivity for Salmonella enteriditis and the patient underwent an antibiotic therapy with ceftriaxone for one week. Again, the patient showed intolerance to the hospitalization and was discharged with oral ciprofloxacin 500 mg bid.

Results: It was performed a new vertebral column TC after one month of therapy, which showed unchanged radiological finds. The neurosurgeon evaluated the images and suggested a strict follow up with RMI. He has followed this therapeutic scheme for more than 6 weeks and showed liver enzymes elevation, so it was decided to interrupt the therapy, in accord to an appropriate length of the antibiotic therapy. Now he is apyretic, doesn't suffer an invalid back pain and is waiting the new valuation with RMI.

Conclusions: The eating habits and the immunocompromised status may have facilitated the localization of the infection at the vertebral column, in particular in the presence of a fracture. In literature there are few cases of Salmonella enteriditis spondylodiscitis, most of all treated with antibiotic therapies, rarely with surgical debridement. The patient doesn't show a radiological improvement, but a clinical one. At the moment, the surgical debridement is not indicated for the multiples comorbidities of the patient.

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Comorbidities

P 98 NOT ALL THAT'S INDOLENT CAN'T HURT: AN AGGRESSIVE CASE OF EBV-POSITIVE MUCOCUTANEOUS ULCER (EBVMCU) IN AN HIV NAIVE PATIENT

P. Valsecchi[1], E. Asperges[1], M. Sambo[2], V. Zuccaro[1], P. Sacchi[1], R. Bruno[1,3]

[1]Division of Infectious Diseases I, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [2]Infectious and Tropical Diseases Unit, Siena University Hospital, Siena, Italy, [3]Department of Clinical Surgical Diagnostic & Pediatric Sciences, University of Pavia, Italy

Background: EBV-positive mucocutaneous ulcer (EBVMCU) is a newly recognized clinicopathologic entity included in the WHO's 2016 classification of lymphoid neoplasms. It presents as a mucosal or cutaneous ulcer in an immunocompromised patient. EBVMCU is considered an indolent disease, as most cases show spontaneous resolution or after reduction of immunosuppression.
Case description: a previously healthy male of 46 years was referred to our Infectious Disease Unit from HEENT Unit after testing positive for HIV. He presented a large necrotic ulcer in the left oropharynx. CT-scan of the neck and the head showed an ulcerated lesion (26x23 mm) located in the poster-lateral wall of the left oropharynx and another one in the right palatine tonsil and measured 12x8 mm. Bilateral cervical lymphadenopathies were described. A previous biopsy of the ulcer resulted non-conclusive. HIV-RNA was 199156 copies/ml, CD4+ count 45/µL, and he had high levels of serum CMV-DNA (36990 copies/ml) and EBV-DNA (2520 copies/ml). He started antiretroviral therapy with BIC/FTC/TAF and ganciclovir. A new biopsy showed intense lymphoid infiltration of large, atypical cells CD 20+/-, CD 79-, CD 30+, EBER 1-2+. These pathological findings were diagnosed as EBVMCU. Total body PET-CT scan didn't show other organ involvement. Since EBVMCU is considered as an indolent disease responsive to the reduction of immunosuppression, it was decided not to start chemotherapy and to reevaluate the patient on effective HAART. One month later he complained worsening dysphagia, pain, fever, and weight loss. He presented with diffuse oral candidiasis, for whom antifungal treatment with fluconazole was started, and painful left cervical lymphadenopathy. His blood test showed HIV-RNA 30 copies/ml, CD4+ 168/µL, EBV-DNA 103500 copies/ml, CMV-DNA 158400 copies/ml. A new CT scan showed local progression of the lesion (maximum diameter 80 mm) wrapping and compressing both the internal and the external left carotid arteries (Figure), which later had to undergo arterial embolization. The diagnosis was confirmed by another lymph nodal biopsy and then he was treated with two cycles of Rituximab 375 mg/mq. Since after ten days his conditions weren't improving cyclophosphamide, adriamycin, and vincristine were added. Despite developing febrile neutropenia, the patient resigned against medical advice and was unfortunately lost at follow-up.
Conclusion: EBVMCU has been poorly described in HIV patients. Since the disease can be locally aggressive, HAART may not be sufficient to control disease progression and treatment with rituximab and chemotherapy should therefore be considered.

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Comorbidities

P 99 A MULTIDISCIPLINARY APPROACH FOR AN UNCOMMUN CASE OF INFECTIVE ENDOCARDITIS

A. Cornelli[1], C. Monari[2], L. Alessio[2], S. De Pascalis[2], G. Cimmino[3], M. Torella[3], N. Coppola[1,2]

[1]Department of Mental Health and Public Medicine, Section of Infectious Diseases, University of Studies of Campania Luigi Vanvitelli, [2]AOU Vanvitelli, Naples, [3]Department of Translational Medical Sciences, University of Studies of Campania Luigi Vanvitelli

Introduction: Infective endocarditis (IE) is a severe infection of the endocardium and heart valves. Despite remarkable improvements in diagnostics, therapeutic and microbiological tools, IE is still associated with a significant morbidity and mortality. Multivalvular endocarditis (MVE) is uncommon, it mostly involves mitral and aortic valves, and is related to a higher risk of congestive heart failure and a higher mortality.

Clinical Case: We report the clinical case of a 68-year-old male who was transferred to our Infectious Disease Unit with the diagnosis of a right-sided infective endocarditis on native tricuspid valve due to MRSA complicated by pulmonary embolization. The patient was previously admitted in another Hospital because of a 1-month history of low-grade fever (maximum temperature 37.8 °C), lumbar back pain, and a suspected intestinal occlusion, for which he underwent an exploratory laparotomy. In the postoperative period, three blood cultures (BC) were performed because of the appearance of high-grade fever (above 38°C) and all resulted positive for a methicillin-resistant Staphylococcus aures (MRSA). An antibiotic therapy with vancomycin 1 g bid (bis in die) was started and a transthoracic echocardiogram was performed, revealing a 12 x 13 millimeters vegetation on the posterior leaflet of the tricuspid valve, and a moderate tricuspid regurgitation. A thorax CT scan described multiple septic emboli at the superior right and left lobes.

Given the diagnosis, we decided to optimize the antibiotic therapy starting a combination therapy with daptomycin 10 mg/kg once daily and ceftaroline 600 mg tid (ter in die). A trans-esophageal echocardiogram (TEE) confirmed a moderate regurgitation of the tricuspid valve, with an 18x10 mm vegetation attached to the posterior cusp, and described a new finding, i.e., a 12x16 mm vegetation attached to the atrial slope of the mitral, with a mild regurgitation. During the hospital stay, a cerebral MRI revealed numerous cardio-embolic ischemic foci in acute/subacute phase, a lumbar spine MRI with contrast showed an inflammatory process affecting the L2-L5 tract, and an abdomen CT scan with contrast described multiple splenic infarcts. Lastly, a total body PET-CT scan showed focal uptake of the tracer at the tricuspid and mitral valve planes, and at L2-L3 vertebral bodies.

The case was repeatedly discussed by the “Endocarditis team”, which agreed to give indication for surgery. The patient underwent a mitral and tricuspid valve replacement with bio-prosthesis). During surgery, cardiac surgeons detected and closed a previously unknown atrial septal defect, which probably caused the multiple septic right- and left-sided embolisms.

Conclusions: This peculiar clinical case underlines how important are the past clinical history (1-month of fever at home), a detailed clinical examination (mitral murmur, low back in a right-sided IE) and diagnostic process (TEE, 2nd level imaging), and a multidisciplinary approach.

Comorbidities

P 100 THE IMPACT ON BODY WEIGHT AND BODY MASS INDEX OF GLUCAGON-LIKE PEPTIDE 1 RECEPTOR AGONISTS IN DIABETIC PEOPLE LIVING WITH HIV

M. Bottanelli[1,2], L. Galli[2], R. Lolatto[2], M. Guffanti[2], A. Danise[2], G. Mori[1,2], C. Maci[1,2], C. Bertoni[1,2], F. Badalucco Ciotta[1,2], V. Spagnuolo[2], A. Castagna[1,2], C. Muccini[2]

[1]Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases Unit, San Raffaele Scientific Institute, Milan, Italy

Background: The use of glucagon-like peptide 1 receptor agonists (GLP-1RAs) in patients with type 2 diabetes (T2D) is known to be associated with significant body weight (BW) lowering induction, up to 10% within 56 weeks. To date, no data about GLP-1RA treatment in people living with HIV (PLWH) are available in literature.
The aim of our study is to evaluate the changes of BW and body mass index (BMI) related to the use of GLP-1RAs in a cohort of diabetic PLWH on antiretroviral therapy (ART).
Material and methods: We conducted a retrospective study on PLWH on ART treated with GLP-1RAs (liraglutide, dulaglutide or oral semaglutide) for T2D, who had a BW detection within 6 months before the initiation of GLP-1RA treatment. Patients' characteristics were reported as median (interquartile range, IQR) or frequency (%). We defined as baseline (BL) the start of GLP-1RA treatment. Homeostasis Model Assessment–Insulin Resistance (HOMA-IR) was considered normal if ≤2.5, according to literature data.
Results: We evaluated 15 PLWH on ART treated with GLP-1RAs for a median duration of 20.2 (10.8; 38.1) months. Overall, median age was 57.3 (52.5; 65.1) years and 13/15 (86.7%) were male; median years from HIV diagnosis were 22.5 (15.46; 24.1), median years of ART were 16.3 (13.4; 23.5) and median CD4+T-cells nadir was 250 (182; 323) cells/μL.
At BL, 3/15 (20%) PLWH were treated with a protease inhibitor (PI)-based ART, 4/15 (26.7%) with an integrase inhibitor (INSTI)-based regimen, 6/15 (40%) with a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART and 2/15 (13.3%) with a NNRTI + INSTI combined ART. Moreover, HIV-1 RNA was undetectable in 7/15 (46.7%) and between 0.9 and 50 cps/mL in 8/15 (53.3%) PLWH; median blood glucose was 137 (97; 163) mg/dL, median HOMA-IR was 5.5 (3.2; 5.9), median BW was 82 (80; 107) kg and median BMI 30.2 (26.9; 33.6) kg/m2.
Twelve months after BL, patients had a median blood glucose change of 0 (-23; 13) mg/dL, a median HOMA-IR change of -0.4 (-1.3; 0.5), a median BW loss of -1.3 (-2; 1.5) kg and a median BMI change of -0.4 (-0.9; 0.6) kg/m2 [changes at other timepoints (6, 24 and 36 months after BL) are reported in Figure].
Conclusions: In our cohort, GLP-1RA treatment seemed to lead only to a slight BW loss and a limited BMI reduction in diabetic PLWH. Further studies are needed to understand the mechanisms underlying the limited BW and BMI outcomes of GLP-1RA treatment in diabetic PLWH as compared to the general population.

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Comorbidities

P 101 CANCER IN PEOPLE LIVING WITH HIV: STUDY OF THE OUTPATIENT POPULATION AT TOR VERGATA HOSPITAL

V. D'Aquila[1], C. Sorace[1], N. Braccialarghe[1], A. Di Lorenzo[1], T. Mulas[1], M. Compagno[1], E. Teti[1], V. Malagnino[2], L. Sarmati[2]

[1]Clinical Infectious Diseases, Tor Vergata Hospital, Rome, Italy, [2]Clinical Infectious Diseases, Department of System Medicine, Tor Vergata University, Rome, Italy

The possibility of administering highly active antiretroviral therapies (HAART) has allowed longer survival of people living with HIV (PLWH). Consequently, an increasing number of patients can develop non-AIDS-related cancers. Our study describes of the prevalence of AIDS-defining and/or HIV-related and/or non-HIV-related cancer and it investigates the association between cancer development, viroimmunologic status, co-infections, comorbidities and duration of HIV infection.

We enrolled 55 patients with a diagnosis of cancer out of 800 patients attending the Infectious Diseases Clinic of Tor Vergata Hospital. Patients were recruited on the basis of clinical information gathered from outpatient records. All patients examined had an AIDS-defining and/or HIV-related and/or non-HIV-associated tumors. All patients were on HAART. We collected data on age, sex, origin, viro-immunological status, comorbidities, co-infections and year of HIV diagnosis.

55 patients with a history of current or previous oncological disease were enrolled, 3 patients were excluded due to lack of data. The median age of the population was 55 years, 73% (38/52) were male and 88% (46/52) from Italy. According to the CDC classification: 4 patients were in A1, 4 in A2 and 2 in A3, 10 in B2 and 2 in B3 and 1 patient was in C1, 4 in C2 and 23 in C3.

Among our patients 72% had undetectable viremia at last follow-up (36/50 - two patients were excluded because data were not available). 16/52 (30.7%) patients had an AIDS-defining cancer (6 high-grade non-Hodgkin lymphomas, 9 Kaposi's sarcomas and 1 Burkitt lymphoma), 24/52 (46.1%) an HIV-related cancer (4 HPV-related anal carcinoma, 8 Hodgkin lymphomas, 2 skin cancers , 3 laryngeal carcinomas, 3 lung cancers, 1 testicular cancer, 1 cervical not invasive cancer, 1 follicolar lymphoma and 1 lymphoproliferative syndrome) and 12/52 (23.1%) a non-HIV-related cancer (6 breast cancer, 1 urothelial and 2 kidney and 3 others cancers). 28.8% of the enrolled patients died. The median time distance between the diagnosis of HIV infection and the onset of oncological disease was 3.5 years. The median baseline CD8 cell count was 631 cells/mcL and CD4 count was 169 cells/mcL. The median zenith viraemia was 1119000 cp/ml. The median CD8 cell count at the time of oncological diagnosis was 627 cells/mcL and CD4 cell count was 272 cells/mcL, while the median viraemia was 21 cp/mL. There were no statistically significant correlations between CD4 cell count, CD8 cell count or viraemia at the baseline and HIV-related cancer. Time between HIV diagnosis and oncological diagnosis did not show a statistical significant correlation to HIV-related tumor (p=0.9) as well.

The present study didn't show statistically significant correlation between cancer development, viroimmunologic status and duration of infection of HIV because of small sample size. This population remains high risk to developing cancer therefore adequate screening is recommended.

Comorbidities

P 102 CANCERS OF THE SKIN AND MUCOUS MEMBRANES IN HIV-INFECTED PATIENTS COMPARED TO THE GENERAL POPULATION

G. Ciccarese[1], S. Ferrara[2], E. Drago[2], C. Grillo[2], F. Sanguedolce[3], C. Pizzulli[3], M. Mastrolonardo[1], T. Santantonio[2], S. Lo Caputo[2]

[1]Unit of Dermatology, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy, [2]Clinic of Infectious Diseases, Department of Clinical and Surgical Sciences, University of Foggia, Foggia, Italy, [3]Department of Pathology, University of Foggia, Foggia, Italy

Background: In spite of the recent improvements in clinical management of human immunodeficiency virus (HIV)-infected patients, cancers still represent a serious issue. While it is already known that HIV-infected patients are at increased risk of squamous cell carcinoma of the anus, vulva, penis, and of head-neck region, data about the risk of cutaneous and mucosal cancers in sites different from the anogenital/oropharyngeal ones are conflicting. This study aimed to assess the prevalence and type of skin and visible mucosae cancers in a population of HIV-infected patients compared to the general population.

Materials and methods: A cross-sectional analysis of consecutive HIV-infected patients referred to the Infectious Disease Unit at Policlinico Riuniti (Foggia, Italy) between November 2022 and March 2023 was conducted. The presence of cancers through a full-body skin and visible mucosae examination was assessed by a board-certified dermatologist. All suspicious skin/mucosal lesions were surgically resected and evaluated by a pathologist for histological diagnosis.

Results: Thirthy-nine HIV-infected patients on antiretroviral therapy, of which 31 male (79%) with a mean age of 48.4 (+/-11.9) years, were collected. Phototype II was the most common (21 patients, 54%) and 23 patients (59%) reported sunburn in childhood/adolescence. Two patients (5%) had family history for cutaneous melanoma and 7 (18%) had used photosensitizing drugs beyond 5 years. More than half of HIV-infected patients (51%) had nevus count between 10 and 50 units whereas 9 patients (23%) had more than 50 units. These patients were compared to a matched series of 88 control HIV-negative patients, of which 4 (7%) were on immunosuppressive therapy. Fourty-six (52%) control patients had nevus count between 10 and 50 units and 16 patients (17%) had more than 50 units.

Only one HIV-infected patient (2%) presented a skin cancer, namely basal cell carcinoma, compared to 7 control patients (8%), of which 4 (4.5%) had basal cell carcinoma, 1 (1%) basosquamous carcinoma, 2 (2%) melanoma (p=0.24). Actinic keratosis was detected in 3 HIV-infected patients (8%) as compared to 10 (11%) controls (p=0.52).

Conclusions: The incidence of skin cancer in HIV-infected patients on antiretroviral therapy is not significantly different as compared to the general population. Skin cancer screening in HIV-infected patients should not be different from that of the general population.

Comorbidities

P 103 PREVALENCE OF METABOLIC SYNDROME IN A COHORT OF PEOPLE LIVING WITH HIV: LIFESTYLE AND RISK FACTORS ANALYSIS

A. Narducci, M. Poliseno, C. Grillo, M. Caggese, E. Colletti, M. Calabrese, S. Ferrara, T.A. Santantonio, S. Lo Caputo

Infectious Disease Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy

Background: efficacy of the antiretroviral therapy has increased life expectancy of people living with HIV (PLWH) whose are at increased risk for metabolic syndrome because of ageing, comorbidity and frailty. The metabolic syndrome (MS) is a group of clinical conditions (hypertension, high waist circumference, high glucose and tryglicerides and low HDL-Cholesterol fasting levels) leading to higher risk for cardiovascular disease. Aim of the study is to describe a cohort of PLWH over 50 matched to under 50 ones in terms of immune-virological features, metabolic assessment and lifestyle habits. Prevalence of MS and possible associated risk factors will be investigated.

Material and methods: Demographic, viro-immunological, therapeutical and metabolic parameters (total-, HLD- and LDL- cholesterol, BMI, waist circumference, fasting glucose and triglycerides levels) of PLWH followed in the HIV outpatient service were retrospectively collected. Dietary habits and adherence to cART were investigated using validated questionnaires (CREA, MMAS-8). The 5-years risk of cardiovascular diseases was calculated using D:A:D score. All data were compared using the Chi-square test and the Mann-Whitney U test for categorical and continuous, non parametric variables, respectively. The multivariate Cox regression analysis corrected for age, male sex, duration of HIV infection, type and duration of ART, HCV co-infection, smoking and dietary habits and level of physical activity was performed to calculate the Odds Ratio (OR), with 95% Confidence Interval (C.I.) for MS in our cohort.

Results: 254 patients were enrolled, 177 (70%) were male and 184 (72,4%) were over 50. Higher prevalence of co-morbidities (specifically Hypertension and Type II Diabetes) and co-medications (anti hypertensive, anti platelets, statins) were observed among older PLWH, in addition to longer, more complex history of HIV infection (Table 1). Overall, 28 subjects had MS, 26 of whom were over 50 years (14% vs 3% among PLWH <50years, p= 0.01). Nevertheless, PLWH > 50 years had better dietary habits (68% vs 58%, p=0.02). No statistical significant difference between the 2 groups has been highlighted for the adherence to antiretroviral therapy and level of physical activity (Table 2). At multivariate analysis, only being >50 years related to a significantly higher risk of MS (aOR 7.56, 95% C.I.1.66-58.15, p=0.02).

Conclusion: In our cohort, low prevalence, but strong association with ageing was reported for MS. A close, dedicated to PLWH> 50 years follow-up is needed. Moreover, data about lifestyle habits are difficult to be collected and therefore to be investigated.

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Comorbidities

P 104 EFFICACY AND SAFETY OF DOLUTEGRAVIR + LAMIVUDINE IN PATIENTS IN ONCO-HAEMATOLOGICAL TREATMENT

L. Pagnucco, A. Tavano, R. Gulminetti, P. Sacchi, S. Novati, R. Bruno

Infectious Diseases Unit, Department of Medical Science and Infectious Diseases Fondazione IRCCS Policlinico San Matteo - University of Pavia

Introduction: Since the introduction of combined antiretroviral therapies(cART), the epidemiology of AIDS-defining neoplasms has changed. In most developed countries, the incidence AIDS-associated malignancies have decreased, while other non-AIDS defining neoplasms have increased. Diagnosis of neoplasms can occur in pts with unrecognized HIV infection or in pts HIV+ on cART. Co-administration of anticancer therapies and antiviral therapies without drug interactions can be a challenge. Drug interactions are in oncology of particular importance due to the narrow therapeutic index and intrinsic toxicity of anticancer agents;interactions with antiretroviral drugs can cause changes in the pharmacokinetics or pharmacodynamics of an antiretroviral or chemotherapy agent that could significantly alter its efficacy or toxicity. Italian and international guidelines for the Use of Antiretroviral Agents in PLWH, recommend the use of two-drug regimens(2DR) both in naïve patients and, in switch,in experienced pts. It is therefore relevant, in the era of 2DR, to evaluate the efficacy and safety of these therapeutic regimens in onco-haematological pts receiving an antineoplastic agent.

Material and methods: We conducted a retrospective cohort study, from December 2015 to March 2023, in pts on 2DR with dolutegravir+lamivudine (DTG+3TC) treated for solid or hematological neoplasms. The primary endpoint was to assess the efficacy of DTG+3TC in these pts. Variables collected were sex, age,VL,type of neoplasm, scheme of neoplastic treatment and adverse effects. Follow-up accrued from the start of antineoplastic treatment to one year to the end of oncologic treatment.

Results: 29 HIV+pts with solid or hematological malignancies on DTG+3TC were enrolled. All pts hadn't documented resistance for studied drugs and were HBsAg negative. Some pts were already on DTG+3TC while others were switched due to potential interactions between cancer treatment and previous cART. The types of tumors and antineoplastic drugs used are summarized in Figures1. During follow-up no virologic failure occurred. 2pts presented a viral blip(39cp/mL and 55cp/mL)that returned negative at the following control without modifying the antiretroviral treatment.1 pt discontinued the treatment because of death due to the neoplastic disease.CD4 count,as influenced by immunosuppressive treatment,was not considered. Adverse effects reported were those expected related to antineoplastic drugs.

Conclusions: Cancer pts often need to be subjected to antineoplastic treatments with very complex schemes and, at the same time, they need to receive effective, safe antiretroviral therapy that has no interactions with neoplastic drugs. According to our results,DTG+3TC appears to be safe, effective and well tolerated alternative cART in pts in onco-haematological treatments.Maintenance of virologic suppression was kept in all pts,although 2 temporary viral blips emerged that returned negative at the following control.

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Comorbidities

P 105 STATINS AND ASPIRIN USE IN PEOPLE LIVING WITH HIV (PLWH): GAP BETWEEN EUROPEAN AIDS CLINICAL SOCIETY GUIDELINES AND CLINICAL PRACTICE

C. Giarratana[1,2], A. Bandiera[1,2], S. Pulvirenti[1,2], C. Gullotta[1,2], R. Ippolito[1,2], A.E. Campanella[1,2], B. Bellocchi[1,2], R. Bruno[1,3], A. Onorante[1], B.S. Cacopardo[1,3], G. Nunnari[1,3], M. Ceccarelli[1,3], B.M. Celesia[1]

[1]ARNAS Garibaldi, U.O. di Malattie Infettive, Catania, [2]Università degli Studi di Messina, Dipartimento di Medicina Clinica e Sperimentale, Messina, [3]Università di Catania, Dipartimento di Medicina Clinica e Sperimentale, Catania

Background: Comorbidities, such as coronary heart disease, raised an increasing concern in people chronically treated with modern combination an¬tiretroviral therapy (cART). The control of traditional risk factors such as dyslipidemia, smoking and the metabolic syndrome remain key objectives for prevention strategies.
Material and methods: With the aim to evaluate the concordance between any indication to statins or acetylsalicylic acid (ASA) prescription and the real use of these drugs, we analyzed, from January to March 2023, three hundred consecutive HIV positive patients related to our outpatient unit. Sex, age, smoking habits, arterial blood pressure, history of diabetes, use of lipid-lowering drugs and ASA, antiretroviral therapy were recorded. Laboratory tests included absolute and percentage CD4+ and CD8+ T-lymphocyte count, fasting total cholesterol, low-density (LDL) and high-density lipoprotein (HDL) cholesterol, triglycerides, blood glucose and creatinine levels. Patients receiving anti-diabetic or BP-lowering medications were classified as having diabetes and hypertension respectively. Statin and ASA prescription were evaluated according to EACS guidelines 11.1. The 10-year coronary heart disease (CHD) risk was evaluated with ACC-AHA score. According with CHD risk stratification, CV risk was categorized as low for CHD<5%, borderline for 5-7,4%, intermediate for 7,5-19,9%, high for ≥20%. EACS recommended the use of statin in patients with CVD >7,5, in patients with total cholesterol>200 mg/dl or LDL-c >190 mg/dl, chronic kidney disease, diabetes with organ damage. Similarly, ASA was recommended in patient aged ≥ 50 years and at high (≥20%) 10-year CVD risk.
Results: Patients were mostly males (81,7%) with a median age of 54,5 years (IQR 46-61). 8,7% were eradicated HCV coinfected. 115 (38%) patients have fasting total cholesterol ≥ 200mg/dl. 10,3% LDL cholesterol ≥ 160 mg/dl, 20% triglycerides ≥150 mg/dl. 22% of patients have hypertension, 9% diabetes, 46% were smokers. According to the LDL value and ASCVD score, statins were recommended in 173 (57,7%) patients. Out of candidates for any lipid-lowering drugs treatment, only 64 (37%) take it. Moreover, 18 patients take statins without any indications. Among the 185 subjects with indication for treatment with ASA, only 56 (30,3%) take it regularly.
Conclusions: Clinical management of lipid-lowering therapy was inadequate in many HIV-infected patients, as more than half of the patients in need were untreated. The use of lipid-lowering therapy in people with HIV remains suboptimal in the prevention of CVD. The effects of the Sars-CoV2 pandemic associated with a significant increase in TAF-based regimens in recent years may have played a decisive role in the discrepancy between prescription and indication of lipid-lowering therapy. Finally, many patients starting lipid-lowering therapy could not continue the treatment due to non-renewal of the prescription by the general practitioners.

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Comorbidities

P 106 EVALUATION OF INTIMAL MEDIA THICKNESS IN HIV-EXPERIENCED PATIENTS TREATED WITH TRIPLE THERAPY VS PATIENTS TREATED WITH DUAL THERAPY: MULTICENTER COHORT DATA

M.T. Russo[1], S. Martini[1], A. Masiello[2], N. Coppola[1], P. Maggi[1,2]

[1]Università della Campania Luigi Vanvitelli, Naples, Italy, [2]AORN Sant'Anna e San Sebastiano, Caserta, Italy

Background: Antiretroviral therapy has allowed HIV patients to improve prognosis and quality of life, but metabolic problems, especially dyslipidemias, still sometimes occur. Over time, this can lead to a progressive myointimal thickening of the supra-aortic trunks up to the formation of atheromatous plaques, which determine a greater cardiovascular risk for affected patients1. Our aim is to evaluate whether the type of antiretroviral regimen can influence the occurrence of high myintimal thickness (IMT) in HIV-experienced patients.

Materials and Methods: To evaluate the association between the type of antiretroviral regimen and vascular pathology, we performed a cross-sectional study, retrospectively observing 116 HIV-experienced patients who had a Doppler scan of the supra-aortic trunks performed. Patients were enrolled in a multicenter cohort at the University of Campania Luigi Vanvitelli and at the AORN Sant'Anna and San Sebastiano, Caserta. 78 patients were treated with 3 drugs and 38 with dual therapy. Table 1 summarizes the data for these 2 groups of patients. We adopted a univariate analysis evaluating the age, gender, CD4 count and the different sections of the supra-aortic trunks studied by Doppler scanning.

Results: Evaluating the data of 2 groups of patients, there are no statistical differences between the patients treated with 3 drugs vs 2 drugs. The baseline characteristics are not different in the 2 groups and at the same time the Doppler scan data are superimposable in terms of median IMT in all the different sections analysed.

Conclusions: Our real-life study shows that the type of antiviral regimen adopted for the treatment of HIV-infected patients has no impact in the evolution of IMT. Of course it will be useful to try to enroll more patients to better analyze whether there is a safer regimen to reduce the development of IMT in HIV-infected patients.

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Comorbidities

P 107 PERITONEAL-PLEURAL TUBERCULOSIS IN A HIV POSITIVE AND CIRRHOTIC PATIENT

A. Cilli, F. Malerba, M. Tadolini, L. Calza, P. Viale

Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy

Case presentation: Here we report the case of a 46-years-old patient, with HIV-infection on antiretroviral therapy (ART) and multifactorial liver cirrhosis (eradicated HCV and alcohol-related), who developed a decompensated cirrhosis (Child-Pugh score B9, MELD score 16) in December 2022.
His last immunovirological evaluation was performed in November 2022 and it revealed CD4 cell count equal to 270 cells/mm3, CD4 percentage 36, CD4/CD8 0.95, HIV-RNA 23 copies/mL.
The last negative QuantiFERON-TB Gold Plus was performed in November 2021. The next one performed in December 2022 had a positive result (TB1 0.79 UI/mL, TB2 0.96 UI/mL).
Despite the start of supportive therapy, the ascites increased, requiring a peritoneal drainage. In the following weeks we observed a clinical deterioration towards sepsis. Thus, on 20th January 2023 an empiric antibiotic therapy was started. A chest CT scan performed on 30th January 2023 revealed the presence of abundant left pleural effusion. Meanwhile the result of ascites culture for mycobacteria became available, showing positivity for drug susceptible M. tuberculosis complex. Therefore, on 30th January 2023 the empiric antibiotic therapy was stopped and ART was switched from bictegravir/tenofovir alafenamide/emtricitabine (BIC/TAF/FTC) to tenofovir disoproxil/emtricitabine+dolutegravir (TDF/FTC+DTG) in order to allow the gradual introduction of anti-tuberculosis treatment based on rifabutin (300 mg orally daily), ethambutol (17 mg/kg daily), isoniazid (4.7 mg/kg daily). A thoracentesis was performed on 10th February 2023: Xpert MTB/RIF Ultra gave a trace result and the culture for Mycobacteria was negative.
Two months after the beginning of the anti-TB treatment both ascites and pleural effusion resolved and continuation phase with rifabutin and isoniazid was started.
Discussion: This case is interesting because liver cirrhosis and low CD4 cell count represented the back-bone of the immunocompromised status of the patient, and this could facilitate the onset of a peritoneal-pleural active TB after a likely recent exposure to the mycobacterium. Moreover, this case is useful to remind how clinical presentation could be confounding in such patients with multiple comorbidities. The onset of a septic scenario led to suspicion of spontaneous bacterial peritonitis as first hypothesis considering the underlying liver cirrhosis, despite a recent QuantiFERON-TB Gold Plus positive result. Although there are inconclusive data about the utilization of steroid therapy in peritoneal TB, in our case a low-dose steroid treatment (prednisone 25 mg with subsequent 6 weeks tapering) was used in order to reduce the risk of peritoneal adhesions, symptomatic stricture or possible intestinal obstruction.

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Comorbidities

P 108 DEPRESSIVE DISORDER AND VITAMIN D IN A GROUP OF HIV PATIENTS IN CART: DUAL THERAPY VERSUS TRIPLE THERAPY

L. Moffa[1], F. Mucedola[1], S. Moffa[2], C. Ucciferri[1], J. Vecchiet[1], K. Falasca[1]

[1]Clinic of Infectious Diseases - Department of Medicine and Science of Aging, University "G. d'Annunzio" Chieti-Pescara- Italy, [2]Department of Pharmacy, University "G. D'Annunzio", Chieti, Pescara, Italy

Introduction: HIV patients are at higher risk of psychiatric diseases. In particular, depressive disorder, anxiety disorder and substance abuse are more prevalent among HIV infected individuals than among the general population. The aim of this study was to evaluate the presence of depression in 37 patients with HIV infection followed at the Infectious Disease Center in Chieti, Italy and to study any correlation with vitamin D levels, CD4 levels and type of cART drugs taken: dual therapy versus triple therapy.

Methods: A sample of 37 patients (7 women (18,9%) and 30 men (81,1%)) followed at the Infectious Disease Center in Chieti between 1 and 15 February 2023 were enrolled. For each patient, the presence or absence of a depressive disorder, diagnosed by a psychiatric test, blood levels of vitamin D, CD4 count and the number of cART drugs taken were evaluated.

Results: 23/37 were affected by major depressive disorder (4 were women). The mean age of the sample was 47.8 yrs (31-72 yrs). 10 were in dual cART therapy; 27 in triple standard therapy. Data analysis revealed that 18 patients had <30 ng/ml 25-OHvitamin D levels despite supplementation. Of these, 14 suffered from major depressive disorder (significance between depression and low vitamin D levels p value < 0.03); 6 patients had CD4 levels below 400 c/mmc, of these 5 had major depressive disorder (p value < 0.0004). Finally, 4/10 (40%) in dual therapy (DTG based) and 19/27 (70%) in triple therapy had a diagnosis of major depressive disorder (p value < 0,005).

Conclusions: The present study revealed a correlation between major depressive disorder and low levels of vitamin D, reduced levels of CD4 and the number of cART drugs taken. It has been clear for years that vitamin D can play a key role in regulating the immune system, which is particularly impaired in patients with HIV infection. However, the role of vitamin D in these patients on the nervous system and how it may be implicated in the development of psychiatric events such as depression remains to be clarified.

The limitation of the study was the small patients sample size, but the analysis of further data could better establish the possible correlation between levels of vitamin D, CD4 and the patients therapy in order to identify any risk of psychiatric disorders and to act promptly for the correct management of this frequent HIV comorbidity.

Comorbidities

P 109 MALE BREAST CANCER IN A PATIENT WITH HIV-HCV COINFECTION: A CASE REPORT

N. Amarasinghe, L. Pagnucco, R. Gulminetti, R. Pesare, R. Bruno

Infectious Diseases Unit, Department of Medical Science and Infectious Diseases Fondazione IRCCS Policlinico San Matteo - University of Pavia, Italy

Introduction: The incidence of AIDS-defining malignancies decreased, but there has been a relative increase in non-AIDS-defining cancers compared with the general population that now are a major factor contributing to mortality in people living with HIV. Male breast cancer (MBC) is rare, it appears to share some of the risk factors of women breast cancer and may be related to hepatic diseases that lead to liver disfunction and hyperestrogenism.
Case description: A 56-yrs man with history HIV/HCV. In 2012 was treated for HCV GT3 infection, fibrosis F3, with pegylated Interferon/Ribavirin obtaining sustained virological response (SVR).After several HIV therapeutic lines he was virological suppressed when, in 2014, was enrolled in"2PM trial-AIFA"and remain virologically suppressed on cART treatment with darunavir/ritonavir monotherapy. In 2015 he was diagnosed with infiltrating carcinoma of the left breast nonspecial histotype G2 for which he underwent mastectomy and left axillary lymphadenectomy, endocrine therapy with tamoxifen and locoregional radiotherapy. Because of the cancer comorbidity and potential interaction with tamoxifen, the observational study with DRV/r was discontinued for SAE and cART was replaced with TAF/FTC/DRV/COBI that, despite it may potentially reduce the efficacy of tamoxifen as inhibition of CYPs 3A4 and 2D6 by DRV/COBI may reduce the amount of drug converted to endoxifen (a pharmacologically active metabolite), at that time seemed the only therapeutic way to follow. At subsequent follow-up apparent resolution of the oncologic disease has been observed. In December 2021 due to dyspnea patient underwent a CT Chest that showed multiple lung and mediastinal nodules with bilateral hilar adenopathies. A needle biopsy of a lung nodule was performed and metastatic localization of mammaryan carcinoma had been confirmed. FDG PET showed lymphnode, lung, pleural, and bone metastases. In March 2022, he started chemotherapy for breast cancer, with letrozole+leuprorelin+palbociclib, that was associated with important drug interactions with DAT/FTC/TAF/COBI, so he was switched to DTG/3TC and DOR.With an exception of an HIV viral blip, with this cART the patient has always remained virologically suppressed with good CD4+ count. The patient is currently on the same cancer therapy
Discussion: PLWHs have an increased risk of developing malignancies and need continuous and careful follow-up also for the potential occurrence of clinical conditions, such as MBC, which are otherwise very rare even in the general population. In particular in the presence of co-infection with other directly or indirectly oncogenic viruses.
MBC remains a rare condition, but this case demonstrates how it still needs to be considered if there are signs and symptoms compatible with this condition.
Choosing antiretroviral therapy in the context of an oncological condition can be challenging considering the many interactions between chemotherapy and antiretroviral drugs.

COVID-19

P 110 SCALING UP COVID 19 RESPONSE AMONG ADOLESCENTS AND YOUNG PEOPLE IN LIMBE HEALTH DISTRICT OF CAMEROON

A. Fontu, J. Esame, I.B. Beloli, T. Evet Adeola, N. Eucharla

Alliance for Community Initiative, Reach-out Cameroon

Background: Since the beginning of 2020, COVID 19 has seriously affected the sexual and reproductive health and rights of adolescents and young people in many ways. The pandemic has disrupted access to care, diverted funding, hampered supply chains, and diverted the attention of policymakers and the media away from sexual and reproductive health priorities. In the North-West and South-West regions already devastated by the ongoing crisis, the battered and vulnerable populations in some localities have almost no support framework. In this light, this program sought to educate and address this gap in the South-West region of Cameroon.

Method: Build the capacities of Peer educators on the key messages to pass on COVID 19 and vaccination, SRHR, psychosocial support. Raise awareness among young people through a peer approach on the attendance of SRHR health services, psychosocial support and prevention and vaccination on COVID-19 Contracting with community radio and television stations for the broadcasting of audio and video spots produced for young people on COVID 19 and psychosocial support Instruments used were both open and close ended surveys, focus group dissuasions testing participants for COVID 19.

Results: From January to March 2022. 8 Focus group discussions were held across areas of intervention. A total of 570 and 69 participants were tested for COVID 19. 673 participants were referred for psychosocial counselling. During the program, a total of 6 participants were referred for and received sexual reproductive health services. 10 Educational Talks (120 Young Girls; 80 Young Boys).30 face to face meetings (16 Young Girls; 14 Young Boys). 04 speaking groups (24 Young Girls; 18 Young Boys) Organize during the implementation period 02 mass awareness campaigns organized (160 Young Girls; 140 Young Boys) on the themes of Coved -19, Psychosocial support; 376 people are referred to a COVID-19 vaccination center (75%) (200 Young Girls; 176 Boys). 376 people are referred to health facilities for a COVID 19 test (75%); (200 Girls; 176 Boys)

Conclusion and recommendation: This program entailed addressing challenges associated with COVID 19 such as limited knowledge and it also fostered COVID 19 testing. In a time when there was so much uncertainty in the air, this intervention equipped peer educators with the knowledge they needed to further educate the community and reduce the burden of the COVID 19 pandemic in the southwest while taking into consideration the mental health of the participants.The systematic wearing of masks by beneficiaries and community actors during field activities was an asset.

COVID-19

P 111 RISK OF HOSPITALIZATION AND SEQUELAE IN PATIENTS WITH COVID-19 TREATED WITH 3-DAY EARLY REMDESIVIR VS. CONTROLS IN THE VACCINE AND OMICRON ERA: A REAL-LIFE COHORT STUDY

M. Mazzitelli[1], M. Trunfio[2], L. Sasset[1], V. Scaglione[1], A. Ferrari[1], D. Mengato[3], S. Gardin[1], N. Bonadiman[1], L. Calandrino[1], E. Agostini[1], A.M. Cattelan[1,4]

[1]Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, Italy, [2]Infectious Disease Unit, Department of Medical Sciences at Amedeo di Savoia Hospital, University of Torino, Torino, Italy, [3]Hospital Pharmacy Department, Padua University Hospital, Padua, Italy, [4]University of Padua, Padua, Italy

Background: Recently, a benefit from administration of a 3-day course of early remdesivir (ER) in the outpatients' setting was reported. However, real-life data on its use is scarce. Therefore, we explored the ER clinical outcome in our outpatients' s cohort, compared to untreated controls.
Methods: We included all patients who were prescribed ER from February to May 2022 and followed them up for three months and compared patients who received treatment with untreated controls. In the two groups the following outcomes were investigated: hospitalization and mortality rate, time of negativization and symptom's resolution, and post-acute COVID-19 syndrome prevalence.
Results: Overall, 681 patients were analyzed, mostly females (53.6%), and with a median age of 66 years (IQR: 54-77), 316 (46.4%) patients received ER, and 365 (53.6%) did not receive antiviral treatment (control group). Table 1 depicts characteristics of the overall population and of each treatment group. Overall, 8.5% patients eventually required oxygen support, 8.7% were hospitalized for COVID-19, and 1.5% died. SARS-CoV-2 immunization and ER (aOR 0.049 [0.015; 0.16], p<0.001) independently reduced hospitalization risk. ER was significantly associated with a shorter duration of SARS-CoV-2 positivity at nasopharyngeal swabs (aβ -8.15 [-9.21; -7.09], p<0.001) and of symptoms (aβ -5.11 [-5.82; -4.39], p<0.001), and with lower rate of COVID-19 sequelae compared to control group (aOR 0.18 [0.10;0.31], p<0.001).
Conclusions: This is to date one of the biggest real-life studies confirming efficacy of ER compared to untreated controls. Even in the SARS-CoV-2 vaccination and Omicron era, in patients at high risk of developing severe disease, ER demonstrated to have a good safety profile and to significantly reduce the risk of disease progression and COVID-19 sequelae.

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COVID-19

P 112 PROGNOSTIC VALUE OF CREATININE LEVELS AT ADMISSION ON DISEASE PROGRESSION AND MORTALITY IN PATIENTS WITH COVID-19. AN OBSERVATIONAL RETROSPECTIVE STUDY

A. Russo[1], M. Pisaturo[1], C. Monari[1], F. Ciminelli[1], P. Maggi[2], F.G. Numis[3], I.Gentile[4], V. Sangiovanni[5], V. Esposito[6], R. Punzi[7], G. Calabria[8], R. Pisapia[9], A.S. Megna[10], A. Masullo[11], E. Manzillo[12], G. Russo[13], R. Parrella[14], G. Dell'Aquila[15], M. Gambardella[16], A. Ponticiello[17], N. Coppola[1]

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania L. Vanvitelli, Napoli, Italy, [2]Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, Italy, [3]Emergency unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, [4]Infectious disease unit; University Federico II, Naples, Italy, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [6]IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [8]IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [9]First Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [10]Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, [12]VIII Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [13]Infectious Disease Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, [14]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [15]Infectious Diseases Unit, AO Avellino, Italy, [16]Infectious Diseease Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, [17]Pneumology Unit, AORN Caserta, Italy

Introduction: The aim of this was to assess the impact of creatinine levels at admission in hospital on COVID-19 disease progression and mortality.

Methods: We performed a multicenter, observational, retrospective study involving seventeen COVID-19 Units in eight cities in the Campania region in southern Italy. All adult (≥18 years) patients, hospitalized with a diagnosis of SARS-CoV-2 infection confirmed by a positive reverse transcriptase-polymerase chain reaction on a naso-oropharyngeal swab, from February 28 th 2020 to May 31 st 2021, were enrolled in the CoviCamp cohort. Exclusion criteria included minority age and lack of clinical data and/or of informed consent.

Results: Evaluating inclusion exclusion criteria, 1357 patients were included (Figure 1). Considering in-hospital mortality and creatinine value at admission (Figure 2), the best cut-off point to discriminate a death during hospitalization was 1.115 mg/dl. The logistic regression demonstrated that factors independently associated with mortality were age (OR 1.082, CI: 1.054-1.110), Charlson Comorbidity Index (OR 1.341, CI: 1.178-1.526), and abnormal creatinine value at admission defined as equal or above 1.12
mg/dL (OR 2.233, CI: 1.373-3.634) (Figure 3).

Discussion: In conclusion our study is in line with previous study confirming that creatinine serum level can predict mortality in COVID-19 patients and defining that the best cut off of creatinine serum levels at admission to predict mortality was 1.12 mg/dl.

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COVID-19

P 113 LONG-COVID CHARACTERIZATION IN A COHORT OF PATIENTS FROM CAMPANIA: PROSPECTIVE COHORT STUDY RESULTS

F. Caruso, C. Monari, A. Russo, L. Onorato, P. Grimaldi, C. Curatolo, R. Palladino, M. Pisaturo, N. Coppola

UOC Malattie Infettive; Università degli Studi della Campania "Luigi Vanvitelli"

Background: Long-COVID is a clinical syndrome characterized by persistence or new onset of symptoms beyond 12 weeks after SARS-CoV-2 infection.
Our goal (the aim of our study) is to estimate prevalence of long-COVID in a cohort of patients hospitalized in our unit.
Materials and Methods: Prospective cohort study which hospitalized patients for COVID-19 from the Infectious Disease unit of L. Vanvitelli AOU of Naples from March 2020 to July 2022 were enrolled.
We collect demographic, clinical and radiological data at the time of admission and at 1,3 and 6 months post-admission. We considered long-COVID the persistence or new onset of symptoms at 12 weeks after infection.
Results: Were enrolled 427 patients [table 1]: 264(61.8%) male, mean age of 61 years ±14; 357 (83.6%) had comorbidities (arterial hypertension in 52% of cases).
368 (86.2%) subjects had at least one initial symptom such as fever, dyspnoea, cough or asthenia. Pneumonia was present in 390 (91.3%) individuals. During the follow-up we evaluated 289 (67.7%) patients at 1 month after admission, 151/427 (35.4%) at 3 months and 88/427 (20.6%) at 6 months. Dyspnea was the most frequently reported symptom at 1, 3 and 6 months (33.2%, 17.2% and 19.3%, respectively). The walking test was positive in 9.7%, 9% and 5.3% at 1, 3 and 6 months respectively. Persistence of GGO was described in 50.2%, 27.9% and 18.2% of patients at 1, 3 and 6 months, respectively. [Table 2]
We compared 83 (19.4%) patients with long-COVID symptoms and 87 patients without long-COVID [Table 3]: patients with long-COVID reported more frequently persistence of dyspnea and asthenia 1 month after discharge (41.0% vs 17.2%, p ≤ 0.001; 19.3% vs 6.9%, p00.2). There were no other differences in clinical and radiological characteristics between groups.
Conclusions: Our study described a long-COVID prevalence of 19.4% in a cohort of patients from Campania. We reported a higher rate of dyspnoea and asthenia at the one-month visit, especially in patients with long covid
Our study characterizes subjects with long-COVID in a cohort of patients from Campania. Our results show that dyspnoea and asthenia are the most frequently reported symptoms in the follow up. The study has limitations: a high drop-out rate of follow-up after the first month and the lack of data 12 months after hospitalization. Further prospective multicenter studies are needed to describe long-covid in more detail and to be able to define a better therapeutic approach.

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P 114 RISK FACTORS FOR ACUTE KIDNEY INJURY (AKI) IN PATIENTS HOSPITALIZED WITH COVID-19: RESULTS OF A RETROSPECTIVE COHORT STUDY

F. Ambrisi[1], F. Spatola[1], R. Nevola[2], A. Russo[1], S. Imbriani[2], C. Aprea[2], D. Beccia[2], C. Brin[2], G. Cirigliano[2], M. Del Core[2], K. Gjeloshi[2], L. Agnese Meo[2], A. Padula[2], R. Ranieri[2], C. Ricozzi[2], L. Rinaldi[2], R. Ruocco[2], C. Ruosi[2], P. Sommese[2], A. Villani[2], M. Pisaturo[1], N. Coppola[1], L.E. Adinolfi[2]

[1]Infectious Diseases Unit, COVID Center, Department of Mental Health and Public Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy, [2]Internal Medicine Unit, COVID Center, Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy

Background: The aim of this study is to identify risk factors for AKI in patients hospitalized for COVID-19.
Materials and Methods: We performed a multicenter, observational, retrospective study involving seventeen COVID-19 Units in eight cities in the Campania region in southern Italy. Included patients were extrapolated from the CoviCamp cohort. Exclusion criteria included minority age and lack of clinical data and/or of informed consent.
Results: 379 participants hospitalized for Covid-19 were included in the study, and 92 developed AKI during hospitalization. Patients with AKI were older (mean age 72 vs 61, p=0.001) and showed significant differences in laboratory diagnostics: higher creatinine at admission, CRP, PCT, D-Dimer (p<0.001) but lower platelets count (p<0,006). They had a mean of 3 comorbidities, mainly arterial hypertension (73%, p=0.001). Considering Covid -19 outcome: they presented higher rate of IOT/IMV (6.7% vs 2.1%, p=0.029) and presented a higher in-hospital mortality (11% vs 2.4%, P=0.001). Among the various characteristics studied that could be potential predictors of AKI in patients hospitalized for Covid-19, the multivariable analysis showed that the CKD (OR: 7.959; 95%CI: 3.192-19.845), age (OR: 1.039; 95% CI: 1.015-1.064), and severe ARDS (OR: 2.121; 95% CI 1.014-4.437) are independent predictors of AKI.
Conclusions: Patients hospitalized for Covid-19 with advanced age, CKD and severe ARDS have a higher risk of developing AKI.

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COVID-19

P 115 THE IMPACT OF CO-INFECTIONS AND ANTIBIOTIC USE IN SARS-COV-2 HOSPITALIZED PATIENTS AT POLICLINICO TOR VERGATA HOSPITAL, ROME, ITALY

A. Di Lorenzo, R. Iannazzo, L. Campogiani, A. Imeneo, G. Alessio, V. D'Aquila, B. Massa, I. Fato, V. Malagnigno, E. Teti, M. Andreoni, M. Iannetta, L. Sarmati

Infectious Disease Unit, Department of System Medicine, Tor Vergata University and Hospital, Rome, Italy

Co-infections (bacterial, fungal and viral) during COVID-19 have been described to worsen patient outcomes and be present in 50% of deceased patients. In the early phases of the pandemic, antibiotics were often prescribed to reduce secondary infection occurrence, with a possible impact on the selection of multiresistant germs. In our ward during the pandemic, all hospitalized patients underwent an infectious disease screening aimed at assessing the possible presence of co-infections. The purpose of this study is to report the results of the retrospective analysis.
This is a retrospective observational study, including patients hospitalized because of SARS-CoV-2 infection in the Infectious Diseases (ID) Ward of Policlinico Tor Vergata Hospital, Rome, Italy, from January 1st 2021 to December 31st 2021. Patients were routinely screened at ward admission for Hepatitis C, Hepatitis B, urinary antigens for Legionella pneumophila and Streptococcus pneumoniae, pharyngeal swab for respiratory viruses, QuantiFERON®-TB Gold Plus assay (QFT-P). These data, together with pre-hospitalization antibiotic prescription, blood cultures drawn within 48 hours from ID ward admission, and clinical data were recorded in an ad hoc database. Mortality was considered as death within 30 days from hospitalization.
Overall, 482 patients were included, with 294 (61%) males, median age of 65 years (IQR 52-77) and median Charlson Comorbidity Index of 4 (IQR 2-5). Cardiovascular, cerebrovascular, renal, hematologic comorbidity and solid tumor were significally associated with higher mortality rate. One hundred and fifty (31.3%) patients received home antibiotic treatment without any association with the outcome.
The mortality rate was 12.4%; 366 (75.9%) patients needed oxygen supply. 472 (97.9%) patients were screened for viral hepatitis, without any statistically significant association between mortality and positivity of viral hepatitis markers. QFT-P was performed in 442 (91.7%) patients and was indeterminate in 125 (25.9%) patients with a significant association with increased mortality (p=0.002). As for respiratory co-infections, 389 (80.7%) pharyngeal swabs were performed, and SARS-CoV-2 was the only respiratory virus detected; urinary antigens for L. pneumophila and S. pneumoniae were searched in 428 patients (88.8%): 15 (3.1%) were positive for S. pneumoniae, none for L. pneumophila. 237 (49.2%) blood cultures were drawn within 48 hours from ID ward admission: 28 (11.8%) were positive and associated with increased mortality (p=0.021), although only 7 (25%) were considered clinically relevant and treated (table 1).
In our cohort, bacterial and viral co-infections in COVID-19 hospitalized patients were rare. Indeterminate results of QFT-P and positive blood cultures were associated with higher mortality rate. HBV and HCV viral marker positivity was not associated to increased mortality. Viral respiratory infection incidence was lower compared to the COVID -19 pre-pandemic era.

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P 116 PREDICTORS OF SARS-COV-2 INFECTION IN TREATMENT-EXPERIENCED PLWHIV: CASE-CONTROL STUDY

V. Iannone[1], P.F. Salvo[1], F. Lombardi[2], A. Ciccullo[3], F. Lamanna[1], R.A. Passerotto[1], G. Placidi[2], V. Massaroni[4], S. Di Giambenedetto[1,2], A. Borghetti[2]

[1]Dipartimento di Sicurezza e Bioetica, Università Cattolica del Sacro Cuore, Malattie Infettive, Roma, [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Malattie Infettive, Roma, [3]Ospedale San Salvatore, L'Aquila, [4]Università Cattolica del Sacro Cuore, Roma

Background: Incidence and risk factors for acquiring SARS-CoV-2 infection and developing severe disease in PLWHIV, are still not fully understood.

Methods: From January 2022 to June 2022,220 PLWHIV, afferent to a third-level University Hospital in Rome, Italy, accepted to undergo a questionnaire to investigate known history of SARS CoV-2 infection, related symptoms, vaccine status and therapies.For each participant reporting a history of SARS-CoV-2 (cases), at least two PLWH were selected (controls),with a similar potential exposure time to SARS-CoV- 2. Demographics features, vaccination status, clinical and immune-virological characteristics potentially associated with SARS-CoV2, were collected.A multivariable logistic regression model was used to estimate independent risk factors for SARS-CoV-2 acquisition. Due to low number of events, no risk factors for severe diseases could be evaluated.

Results: Seventy-two participants reported an history of SARS CoV-2 infection (32.7%) between March 2020 and June 2022. Mean age of our population was 55y (± 11.5),with 18y (± 8.9) of mean duration of HIV infection. Fifty-one participants (23%) reported symptoms:36 fever (16.4%),13 cough (5.9%),14 sore throat (6.4%),10 arthralgia (4.6%),8 headache (3.6%),9 coriza (4.0%),3 anosmia (1.4%),2 ageusia (0.9%). No one developed severe Covid -19 disease and only one participant required hospitalization for administration of early antiviral therapy. Characteristics of cases and controls were similar, except for antiretroviral regimen and last HIV-RNA before enrolment date. All the characteristics of study population are shown in table 1.After adjusting for age, sex, antiretroviral therapy and zenith HIV-RNA, the risk of reporting a previous SARS- CoV-2 infection was higher in more recent years (2022 versus 2020 aOR 20.74, 95% CI 5.26-81.8, p< 0.001) and in patients with last HIV-RNA >50 cp/mL (versus < 50, aOR 4.56, 95% CI 1.01-20.46, p 0.047). A reduced risk of infection was evidenced for patients with 3 vaccine doses (versus less than 3 or not vaccinated, aOR 0.08, 95% CI 0.02-0.24, p< 0.001).

Conclusions: In this cohort of treatment-experienced PLWH, severe COVID-19 was not reported. Risk of SARS-CoV-2 acquisition increased over time, probably due to change in lock-down measures and in SARS-CoV-2 circulating variants. Three vaccine doses were highly protective towards infection, whereas detectable viral load was associated with increased risk of infection, further highlighting the importance of HIV-RNA monitoring during pandemics.

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P 117 DELTA VARIANT AS A STRONG PREDICTOR OF LONG COVID INCIDENCE AND NEUROPSYCHIATRIC SYMPTOMATOLOGY: DATA FROM A LARGE, MULTICENTER, PROSPECTIVE COHORT STUDY

L. Frallonardo[1], N. Veronese[2], F.V. Segala[1], M. Cormio[1], G. Romita[1], A. Parisi[2], E. Marrone[2], M.E. Ciuppa[2], A. La Carrubba[2], L. Carruba[2], A. Licata[2], G. Cavallaro[3], V.Pagliuso[3], T. Maino[3], S. Lollo[3], L. Latino[4], L.T. Solimeo[4], A. Ianniello[4], D. Montalbò[4], D.F. Bavaro[1], M.L. Fiorella[3], M. Barbagallo[1], F. Di Gennaro[1], A. Saracino[1]

[1]Department of Precision and Regenerative Medicine and Ionian Area - (DiMePRe-J), University of Bari "Aldo Moro", Bari - Italy, [2]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties "G. D'Alessandro", University of Palermo, Palermo, Italy, [3]Otolaryngology Unit, Department of Translational Biomedicine and Neuroscience (DiBraiN), University of Bari "Aldo Moro", Italy, [4]Department of Basic Medical Sciences, Neuroscience and Sense Organs, University of Bari "Aldo Moro", Bari, Italy

Background: Long-COVID is emerging as an urgent public health threat, but data on the predictors of specific clinical manifestations are limited. Aim of this study is to investigate the role of viral variants and other predictors in long-COVID incidence and symptomatology.

Methods: All COVID-19 patients aged >18 years hospitalized up to April 2022 in two Italian University Hospitals were enrolled. Incidence of long-COVID was assessed through structured questionnaires delivered by phone calls. The association between possible risk factors and long-COVID were assessed by adjusted logistic regression and reported as odds ratios (ORs).

Results: Among 1012 patients recruited over a median follow-up of 19 (IQR: 15-24) months, cumulative incidence of long-COVID was 91.7%, with clinical manifestations involving most commonly the respiratory (80.5%) and neurological systems (77.3%). Multivariate analysis suggested that being vaccinated against SARS-CoV2 was associated with reduced odds of reporting any long-COVID symptomatology (OR:0.34; 95%CI 0.21-0.58), while infection from Delta variant was a strong predictor (OR 9.61, p<0.0001) for reporting neuro-psychiatric symptomatology.

Conclusions: In this study, long-COVID symptoms were still highly prevalent after 18-24 months of follow-up, and, when compared to wild-type virus, infection with Delta variant was associated with a higher risk of developing a neurological post-COVID condition.

Keywords: long COVID, post-acute sequelae of COVID 19, COVID vaccination, Delta variant, Omicron variant.

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P 118 IMPACT OF COVID-19 ON THE LONG-TERM OUTCOME AMONG PLWH: A REAL-LIFE STUDY

M. Degli Antoni[1], G. Maifredi[2], S. Storti[1], F. Viola[1], M. Di Gregorio[1], G. Tiecco[1], I. Izzo[1], E. Focà[1], F. Castelli[1], E. Quiros-Roldan[1]

[1]University Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia, [2]ATS Brescia (Brescia Health Protection Agency), Brescia

Introduction: Our Hospital in Northern Italy assists 3817 people living with HIV (PLWH) and has faced the impact of COVID-19 and its clinical outcome among PLWH. We aimed to assess the possible relation between the viro-immunological and vaccinal status in PLWH and the clinical outcome of those affected by COVID-19. Furthermore, we aimed at evaluating the impact of long-COVID.

Methods: We conducted a retrospective observational cohort study involving all PLWH connected to the Brescia Health Protection Agency (HPA), assessing SARS-CoV-2 burden, viro-immunological parameters, and vaccinations from February 2020 until May 2022. All data from HPA administrative database has been matched with our clinical database. Outcome was assessed in terms of hospitalization, death and long-COVID. We interviewed patients regarding persistence of symptoms (fever, dysgeusia/anosmia, respiratory, gastroenteric or neurobehavioral symptoms) after 3 months.

Results: During the study period, 748 (19.6%) PLWH followed at our clinic were diagnosed with SARS-CoV-2 infection. Only 19 (2.9%) had a SARS-CoV-2 reinfection.

Preliminary data from 653 subjects (70.4% males, 89.7 % Italian, mean age 52.6 years, mean CD4+ T-cell count nadir 254.5 cell/mm3) showed the highest incidence of infection during the Omicron era (61.4%).

Seventy-five patients (11.5%) were unvaccinated, while 343 patients (52.5%) received three doses before SARS-COV infection. There was no difference in SARS-CoV 2 incidence among percentiles of CD4+ T-cell nadir (p=0.404) or after comparing fully vaccinated PLWH and those who did not complete vaccination (p=0.151).

Seventy-one subjects (10.8%) were hospitalized for COVID-19 and 3 (0.5%) died. Hospitalization rate was higher among the unvaccinated population (17.5% vs 4.3%) and among PLWH with CD4+ T-Cell nadir in the lowest percentile.

We managed to interview 510 PLWH: persistent symptoms were observed in 178 PLWH (34.9%), with no significant difference between unvaccinated (37.7%) and vaccinated before the infection with two or three doses (28.7%, 35.9%), or after comparing CD4+ T-cell count nadir percentiles.

Conclusion: We observed no significant association between SARS-CoV-2 infection and the viro-immunological and vaccinal status of PLWH. A higher incidence of hospitalizations was observed among unvaccinated patients. Our results showed that a significant proportion of PLWH reported long-COVID symptoms. The strength of this study is the presence of robust results through the pairing of an administrative and clinical database. A comprehensive analysis of our population is still ongoing to better understand the long-term impact of SARS-CoV -2 in PLWH.

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P 119 COVID-19 IN IMMUNOCOMPROMISED PATIENTS: WHAT IS THE ROLE OF PASSIVE AND ACTIVE IMMUNISATION?

L. Coppola[1], M. Iannetta[1,2], L. Campogiani[1], M. Compagno[1], V. Malagnino[1,2], E. Teti[1], D. Zaçe[2], L. Alborghetti[1], A. Cekrezi[2], L. Sarmati[1,2]

[1]Infectious Diseases Clinic, Policlinico Tor Vergata, Rome Italy, [2]Department of System Medicine, Tor Vergata University, Rome, Italy

Background: Immunocompromised patients have a reduced vaccine response and an increased risk of severe forms of coronavirus disease 2019 (COVID-19). Tixagevimab/cilgavimab (EVS) is the only monoclonal antibody (mAb) combination authorized for pre-exposure prophylaxis of COVID-19.
We aimed to describe the incidence and outcomes of COVID-19 immunocompromised patients receiving EVS as preexposure prophylaxis, during the Omicron variant wave.
Material and Methods: A retrospective single centre cohort study was carried out in Policlinico Tor Vergata of Rome between March 2022 and March 2023. Immunocompromised patients receiving EVS as preexposure prophylaxis were enrolled in the study. Italian Medicine Agency (AIFA) eligibility criteria for prophylactic EVS 150/150 mg intramuscular administration were an impaired vaccine response and/or a high risk of severe form of COVID-19. Data are represented as median with ranges and absolute frequency with percentages, as appropriate.
Results: EVS was administered to 328 immunocompromised patients. The median age was 64 years (20-92), 54,6% were male, the median BMI was 25 Kg/m2. We performed the serum dosage of antibodies against Anti-Spike glycoprotein in 25/328 patients (10,5%), in all these patients the value of antibodies was non-protective.
197/328 (83%) of patients had an haematological malignancy, 26/328 (11%) were kidney or liver transplant recipients, 10/328 (4%) had autoimmune diseases on active treatment. 6/328 (2%) had other conditions.
188/328 (80%) patients had received at least 3 doses of SARS-CoV-2 vaccine, with at least two doses an mRNA vaccine.
Follow-up was performed after 6 months in 215/328 (66%) patients, and a SARS-CoV-2 infection was self-reported in 50 (23%) individuals, after a median period of 88 days from EVS administration.
Among infected, most reported symptoms were fever (64%), cough (42%) and asthenia (32%). 20/50 (40%) patients received early-treatments: 16 oral antivirals, 3 mAb, and 1 both treatments. Healing occurred after 10 days, as demonstrated by the negativization of the SARS-CoV-2 antigenic nasopharyngeal swab (TNF).
Among the infected patients, 43/50 (86%) had a mild-to-moderate form and 3 (6%) had a moderate-to-severe form of COVID-19. One patient, with severe haematological malignancy, had three SARS-CoV-2 infections and died from COVID-19.
Conclusions: Our study reported a low rate of infections and severe illnesses associated with a rapid switching from positive to negative TNF among immunocompromised patients treated with EVS as preexposure prophylaxis. A global preventive strategy including vaccines, preexposure prophylaxis with mAbs, and early therapies might be effective to prevent severe forms of COVID-19 among fragile immunocompromised patients.

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P 120 FACTORS ASSOCIATED WITH ANTI-SPIKE SARS-COV2 ANTIBODY TITER AMONG PATIENTS HOSPITALIZED WITH COVID-19-RELATED PNEUMONIA

G. Lo Cascio[1], G. Lapadula[1,2], L. Mezzadri[1], L. Antolini[1], M. Rossi[2], E. Colella[2], E. Pollastri[2], A. Ranzani[2], S. Malandrin[2], A. Cavallero[2], P. Bonfanti[1,2]

[1]School of Medicine, University of Milano-Bicocca, Milan, Italy, [2]IRCCS Fondazione "San Gerardo dei Tintori", Monza, Italy

Background: Humoral response is a correlate of protection from severe COVID-19. Identifying conditions that hinder antibody production against SARS-CoV2, whether during natural infection or after vaccination, can help to understand risk stratification, guide treatment decisions and inform on the need for vaccination boosters.
Methods: In a cross-sectional study, we included adults admitted between July 2021 and July 2022 for COVID-19 pneumonia (defined by presence of respiratory failure or radiological evidence of lung involvement), provided that anti-spike SARS-CoV2 antibody titer (AT) had been measured within 72h from hospital admission, using LIAISON SARS-CoV2 TrimericS IgG assay. Uni- and multivariable quantile regressions, conducted separately for vaccinated and unvaccinated individuals, were used to identify predictors of AT. The following covariates were explored: age, gender, days of symptoms, oxygen requirement and presence of immunosuppressive conditions (hematological malignancy, solid tumor, serum creatinine >3 mg/dl or end-stage renal disease, diabetes, cirrhosis, HIV infection, organ transplant or use of immunosuppressive drugs).
Results: 534 patients were included. Most were male (63%), with a mean age of 71.5 years (SD 14.4); 61% were vaccinated with at least 1 dose and 42% had ≥1 immunosuppressive condition. Overall, median AT was 216 BAU/ml (IQR 11-2080). Antibody titer was undetectable in 9% and 35% of vaccinated and unvaccinated, respectively. Vaccinated subjects were, on average, older (75.1 vs 65.6 years, p<0.001) and more likely to have immunosuppressive conditions (53% vs 26%, p<0.001). As expected, median AT was significantly higher among vaccinated than unvaccinated people (1166 vs 158 BAU/ml; p <0.001). Table 1 shows results for the uni- and multivariable regression analysis assessing factors associated with median AT, grouped by vaccination status. Among vaccinated individuals, haematological malignancies and use of immunosuppressive drugs were significantly associated with a lower median AT. No significant association was found with age, gender and other immunosuppressive conditions. Among unvaccinated individuals, neither demographics nor presence of immunosuppressive conditions significantly influenced AT. Using multivariable analysis, having symptoms for >10 days was associated with higher AT, independently of age, advanced renal disease or immunosuppressive drugs.
Conclusions: Haematological malignancies and use of immunosuppressive drugs hampered humoral response among patients who developed severe COVID-19 despite vaccination. This suggests that AT monitoring in immunocompromised may help to determine the timing of additional booster doses. Conversely, early antibody response among unvaccinated people developing pneumonia was independent of patient conditions and only influenced by time since infection. Whether the extent of AT in these patients is associated with survival merits to be evaluated further.

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P 121 EPIDEMIOLOGICAL AND CLINICAL FACTORS RELATED TO LATE NEGATIVIZATION OF SARS-COV 2 SWAB

P. Grimaldi[1], M. Pisaturo[1], A. Russo[1], P. Maggi[2], R. Astorri[1], F.G. Numis[3], I. Gentile[4], V. Sangiovanni[5], A. Russomando[6], R. Punzi[7], G. Calabria[8], C. Rescigno[9], A.Salomone Megna[10], A. Masullo[11], E. Manzillo[12], G. Russo[13], R. Parrella[14], G. Dell'Aquila[15], M. Gambardella[16], A. Ponticiello[17], N. Coppola[1] on behalf of CoviCam group

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [2]Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, Italy, [3]Emergency unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, [4]Infectious disease unit; University Federico II, Naples, Italy, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [6]IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [8]IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [9]First Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [10]Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, [12]VIII Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [13]Infectious Disease Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, [14]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [15]Infectious Diseases Unit, AO Avellino, Italy, [16]Infectious Diseease Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, [17]Pneumology Unit, AORN Caserta, Italy

Background: RT-PCR for SARS-CoV 2 on nasopharyngeal swab is considered a standard for COVID-19 etiological diagnosis. Beside their use for clinical diagnosis, RT-PCR swabs are often routinely performed in out- and inpatients to reduce the viral spread. Our aim is to determine which elements influence the time span to get a negative swab.

Materials and Methods: We enrolled, in a multicenter, observational, retrospective study, coordinated by Simit Campania and involving nine COVID-19 Units in seven cities of the Campania region in Italy, all patients hospitalized from 3/2020 to 6/2021 diagnosed with SARS CoV-2 infection. At the admission the demographic, clinical, hematobiochemical, virological data of the subjects hospitalized for COVID-19 were collected in a shared electronic database.

Results: 963 patients were enrolled, with their characteristics showed in table 1. The median time from the first positive to the first negative swab was 19d (IQR 13-26). To distinguish groups with an abnormally longer positivity time span, we made a first group including patients that had the first negative swab before the 26th day (the 75th percentile), a second group with patients with a time span from 26 to 39 days (the 95th percentile), and a third group with a span >39 days. Each group included respectively 721, 194 and 52 patients. Swabs frequency was on physician independent decision, so we analyzed how long before the first negative swab the patient had the previous swab, to investigate how the clinician decision would influence the time span: the median time was one day longer in the second group compared to the first and in the third compared to the second; albeit this was statistically significant, the median time in groups differed of much more than one day so we didn't consider this impactive.

Results of the Statistical analyses are represented in detail in table 2. Belonging to group 2 and 3 seemed to be influenced by age, arterial hypertension, cardiovascular disease, chronic kidney disease (CKD) and the need of ICU. The time in between the last positive swab and the first negative was longer in groups 2 and 3 compared to the previous.

The multivariable analysis, showed in table 3, confers a leading role to age and especially CKD as factors influencing the belonging to the groups showing a longer positivity time span.

Conclusions: Our analysis seems to demonstrate that CKD and age are factors related with longer positivity time spans, probably according to the immunosuppression related with these conditions. A longer positivity time span, even when no signs and symptoms are present, can represent an issue in the correct management of the patient for what concerns the infection control. A patient with recent COVID history that needs outpatient services (e.g.: hemodialysis) can mimic a new infection if a routine swab is performed.

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COVID-19

P 122 EARLY TREATMENT OF COVID-19 IN OUT-PATIENT SETTING: A SINGLE-CENTER RETROSPECTIVE STUDY

E. Binetti, F. Ciccone, A. Falletta, S. Trapani, S. Lobello, C. Leanza, M.A. Albanese, I. De Angelis, C. Ajassa, C.M. Mastroianni

Sapienza Università di Roma, Rome

Background: Since the beginning of the SARS-CoV2 pandemic a large number of drugs were used to decrease the severity and mortality of this infection. The oral antivirals (OA) Ritonavir-boosted-Nirmatrelvir (RN) and Molnupiravir (Mo) and the monoclonal antibodies Tixagevimab/cilgavimab (Tc) were among the newest weapon at the time of the study. Our aim is to evaluate the efficacy of such therapies in a real-life setting.

Material and Methods: We conducted a real-life retrospective, single-center study at Policlinico Umberto I of Rome from October 2022 to February 2023. The patients involved had a diagnosis of SARS-CoV2 infection, mild to moderate symptoms, and were treated with RbN, Mo or Tc.

The patients had at least one risk factor that made them eligible for treatment, according to AIFA indications. The risk factors taken into consideration were cardiometabolic disease, chronic lung disease, chronic kidney disease, solid or haematological malignancy, immunodepression, age >65.

The best treatment was chosen in consideration of the number of days from the first positive nasopharyngeal swab, the pharmacological interactions with home therapy, the renal function and the weight of the patient. The patients were then followed up until negativization.

Data relative to the patients and the evolution of the infection were then collected and analysed through descriptive statistics. The time of negativization was compared among groups who received different treatments using ANOVA analysis.

Results: The study included 252 patients (126 males, 126 females) with a mean age of 69. 173 patients were >65 y.o.; the most common comorbidities were cardiometabolic diseases (150), immunodepression (77) and haematological malignancies (58); 38% had two, and 32% had three risk factors for severe infection. 60 patients received RN, 135 Mo and 57 Tc.

The mean age of those treated with RN, Mo and Tc was 62.4, 72.4 and 71.6 y.o., respectively. 11 patients were hospitalized (4.4%): 5 had received Mo and 6 Tc; all of them had at least 2 risk factors; none of them died.

The average time to negativization was 10.7 days. A significant difference was found when considering the different treatments: 8.2 days for RN, 10.9 for Mo and 13.0 for Tc ($p<0.05$).

The patients with a higher number of risk factors had significantly longer time to negativization, although the type of risk factor was not significant. To eliminate this confounding factor, the negativization time was stratified according to the number of comorbidities. In those with two or three risk factors a significant difference was confirmed. Significance in the other groups was limited by the small sample size.

Conclusions: RN, Mo and Tc seem to be safe and effective in the early treatment of SARS-CoV2. RN showed a faster negativization time, which could be relevant in patients with haematological or solid malignancies who need to clear the virus as soon as possible to start treatment for their underlying disease.

Attach: https://www.icar2023.it/public/abstract/Attach_ABS_117.png

COVID-19

P 123 GLUCOCORTICOIDS IN DIABETIC COVID-19 PATIENTS: EFFICACY AND SAFETY OF DEFLAZACORT

A. Di Gasbarro[1], C. Ucciferri[1], G. Taraschi[1], K. Falasca[1], J. Vecchiet[2]

[1]Università G. D'Annunzio, Chieti, [2]Clinica di Malattie Infettive, P.O. S.S. Annunziata, Chieti

Background: During Sars-Cov-2 pandemic, corticosteroids proved to be a valid therapeutic option during the inflammatory phase of disease, even in outpatients. One of the known adverse effects of this drug class is hyperglycemia which can complicate home management, especially in diabetic patients. We have investigated the efficacy and safety of Delfazacort in this category of patients when affected by Sars-Cov-2.
Methods: In collaboration with U.S.C.A., a total of 231 diabetic patients, positive for Sars-Cov-2, between January and June 2021, have been screened. 63 non-vaccinated, diabetic patients, in treatment with diet or oral therapies, with moderate COVID-19 (persistent fever, initial desaturation) in second week of illness were enrolled and divided into 2 groups: group-A (15) have undergone therapy with Deflazacort 45mg/die and group-B (48) have been treated with other corticosteroids at equivalent dosage, until clinical improvement. We excluded who have undergone complete vaccination course or Monoclonal anti-spike/Antivirals. The primary outcome chosen was hospitalization or death for Covid-related causes; the secondary outcome chosen was the duration of COVID-19 illness (number of days between first positive and first negative nasal swab for Sars-Cov-2). Among hospitalized patients we evaluated those who presented glycemic decompensation on admission (glycemia >300).
Results: 19 patients (30.2%) required hospitalization, 5 in group-A and 14 in group-B (33,3% vs 29.2%, p=0.76). No patients in group A showed glycemic decompensation at admission vs 4 patients in group B (0% vs 28.57%, p=0.019). The average disease duration in group-A was 28.4 days (17-42) vs 27.40 (11-70) in group-B (p=0.40).
Conclusions: Corticosteroids have demonstrated their effectiveness in COVID-19 illness, particularly in patients with systemic inflammation and desaturation; they have also been used extensively in non-hospital settings. Deflazacort has been shown, in previous literature, to have a lower metabolic impact than other steroids, particularly on lipidic and glucose metabolisms. Our study shows how this drug can represent an equally effective, but safer, alternative in diabetic patients affected by COVID-19: it could ensure safer home management, particularly in those patients with glycemic alterations who are not on insulin treatment.

COVID-19

P 124 POST-COVID-19 SYNDROME: A RETROSPECTIVE STUDY OF OUR CENTER'S PATIENTS

G. Taraschi[1], A. Di Gasbarro[1], C. Ucciferri[1], K. Falasca[1], J. Vecchiet[2]

[1]Università degli Studi G.D'Annunzio, Chieti, [2]Clinica di Malattie Infettive e Tropicali, P.O. S.S. Annunziata, Chieti

Background: WHO defines Post COVID-19 as “a condition that occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis”. The incidence of this condition account for 10 -20% of Covid-19 patients particularly in women and over 20 years of age. Post-COVID-19 symptoms typically include fatigue, dyspnea, chest pain, cough, psychological disorders and cognitive impairment. We performed a retrospective descriptive analysis on Post-Covid-19 patients referring to our dedicated clinic.

Materials and Methods: A total of 76 patients related to our Post-COVID-19 clinic between October 2021 and December 2022 have been screened through a validated survey: we obtained a comprehensive history of the patient’s Covid-19 illness, including illness timeline, management strategies, and we also investigated the presence and severity of the main manifestations of Post-COVID-19 condition. 52% were females, mean age was 50.25 years, 69% had at least one comorbidity (among which heart disease was the most common). All were vaccinated for Sars-Cov-2, the mean duration of COVID-19 illness was 17 days, 69% did at least one treatment for acute disease.

Results: The most common symptom found in our sample was asthenia (72.3%), followed by musculoskeletal (67.1%), respiratory (65.8%), sleep (59.2%), cognitive functions (56.6%) and mood disorders (55.2%). Less frequent were taste/olfactory (36.8%), ocular (22.4%), acoustic (19.7%), and skin disturbances (14.5%). We found an association between duration of COVID-19 illness, frequency and severity of main post-COVID-19 symptoms (Asthenia $p<0.046$; Myalgia $p<0.01$; Dyspnea $p<0.02$; Concentration disorders $p<0.01$). Furthermore, we did not find a correlation between age and incidence of post-COVID-19 symptoms.

Conclusions: The Covid-19 pandemic has resulted in a growing population of individuals with a wide range of persistent symptoms after acute infection. We need to unveil the mechanism at base of post-COVID-19 syndrome and the factors that can promote it’s development in order to prevent or treat this disabling condition and improve millions people’s quality of life.

COVID-19

P 125 IMPACT OF SARS-COV2 INFECTION IN PLWH IN THE VACCINE ERA

L. Comi[1], S. Venturelli[1], E. Di Filippo[1], D. Valenti[1,2], F. Maggiolo[1]

[1]UOC Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, [2]FROM Foundation, ASST Papa Giovanni XXIII, Bergamo

Background: At the begining of the SARS-CoV2 pandemic, people living with HIV (PLWH) were supposed to be at higher risk for having a severe disease. Furthermore, aging PLWH have a higher prevalence of noninfectious comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease, and the Centers for Disease Control and Prevention (CDC) has identified these as risk factors for severe disease among patients with SARS-CoV-2 infection. Actually, existing evidence about HIV and SARS-CoV-2 co-infection has yield conflicting results.
Material and Methods: This is a cohort, single center, retrospective study which aim was to identify possible characteristics of PLWH that acquired SARS-CoV2 infection during 2022 in 3 different calendar periods.
We also performed an analysis comparing demographic characteristics of patients depending on the grade of SARS-CoV2 infection. Comparison were assessed by Chi-square and Fisher's exact tests.
Results: We identified 125 cases of SARS-CoV2 infection in our cohort of PLWH during 2022.
Thirty-two percent were female, mean age was 52 years (95%CI 50-54); 94.4% had HIVRNA < 50 copies/ml and the mean last CD4 cells count was 888 (95%CI 816-960). Sixty-one (48.5%) cases were observed in the first quarter of the year, 45 (36%) in the second and 19 (15.5%) in the last quarter. Even if not statistically significant, PLWH that became infected with SARS-CoV2 during the third quarter seemed to had a worse immuno-virologic profile, with lower CD4 at baseline, higher prevalence of AIDS defining events and a lower percentage of undetectable HIV viral load.at the time of SARS-CoV2 infection.
Comparing patients characteristics in the three calendar periods we observed differences in the type of SARS-CoV2 infection (mild vs asymptomatic, P = 0.05), mostly because of the presence of fever (P = 0.003) and, as expected, based on the vaccination status (one versus more doses).
Counterintuitive, patients with asymptomatic SARS-CoV2 infection presented a higher proportion of co-morbidities (cardiovascular disease, P = 0.005; hypertension, P = 0.021 and renal disease, P = 0.001).
Conclusions: All the cases of SARS-CoV2 infection we observed in our HIV cohort were either asymptomatic or, at the most, presented with a few and mild symptoms lasting a few days. Patients infected in the last quarter of the year did not present significant differences of the immune-virologic profile although their CD4 counts were slightly lower and their CD4/CD8 ratio indicated a less effective immune-reconstitution. The significant differences highlighted from our study concern the COVID 19 clinical presentation and, as expected, the patient's vaccination status.
These data are probably due to the effect of SARS-CoV2 vaccination strategy (PLWH were within priority groups) and the prevalence in Italy during the year 2022 of the Omicron variant, that seems to cause a higher prevalence of asymptomatic/mild infection.

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COVID-19

P 126 INCIDENCE AND BURDEN OF LONG COVID IN AFRICA: A SYSTEMATIC REVIEW AND META-ANALYSIS

R. Novara[1], F.V. Segala[1], F. Di Gennaro[1], S. Cotugno[1], G. Guido[1], R. Papagni[1], A. Colpani[2], A. De Vito[2], M. Barbagallo[3], G. Madeddu[2], S. Babudieri[2], G. Putoto[4], N. Veronese[3], A. Saracino[1]

[1]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy, [2]Unit of Infectious and Tropical diseases, Department of Medicine, Surgery and Pharmacy - University of Sassari, Sassari, Italy, [3]Geriatrics Section, Department of Internal Medicine, University of Palermo, Palermo, Italy, [4]Operational Research Unit, Doctors with Africa CUAMM, Italy

Background: Long COVID, also referred as "post-acute sequelae of COVID-19", is an emerging global health problem affecting at least 65 million people worldwide, who experience a wide range of symptoms that may last weeks or months and, in some cases, may be permanent. Despite the increasing amount of evidence being produced on this matter, little is known about epidemiology and burden of this condition in Africa. The aim of this meta-analysis is to explore the burden of the long-term effects of COVID-19 in the WHO African Region.
Methods: A systematic search in several databases was carried out up to 12 February 2023 for observational studies reporting the cumulative incidence of long COVID signs and symptoms divided according to affected body organs and systems. Only studies conducted in African countries were included. Data are reported as incidence and 95% confidence intervals (CIs). Several sensitivity and meta-regression analyses were performed.
Results: Among 1,147 papers initially screened, 25 were included, consisting of 29,213 participants who were followed-up for a median of four months. As shown in Table 1, the incidence of any long COVID symptomatology was 48.6% (95% CI 37.4-59.8). Psychiatric conditions were the most frequent, with post-traumatic stress disorder reaching a cumulative incidence of 25% (95% CI 21.1 – 30.4). Higher mean age and higher percentage of hospitalized people were associated with a higher frequency of long COVID symptomatology with beta values, respectively, of 0.1 (p = 0.027) and 0.003 (p=0.05) (Table 2). The incidence of long COVID symptomatology was significantly higher in Southern countries of Africa.
Conclusions: Despite the overall lack of evidence produced in sub-Saharan countries, long COVID poses a substantial burden in Africa, with psychiatric conditions being of special concern. The study calls for identifying individuals at risk, and for developing clinical pathways and guidelines for the care of long-COVID patients living in Africa. Prospective, high-quality studies addressing this condition in African low-resource settings are urgently needed.

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COVID-19

P 127 VACCINATION AGAINST SARS-COV2: ARE ANTIBODIES PREDICTIVE OF PROTECTION?

S. Dispinseri[1], I. Marzinotto[2], M. Tolazzi[1], A. Cara[3], D. Negri[4], P. Cinque[5], R. Vercesi[5], V. Lampasona[2], G. Scarlatti[1]

[1]Viral Evolution and Transmission Unit, IRCCS San Raffaele, Milan, Italy, [2]Diabetes Research Institute, IRCCS Ospedale San Raffaele, Milan, Italy, [3]National Center for Global Health, Istituto Superiore Di Sanità, Rome, Italy, [4]Department of Infectious Diseases, Istituto Superiore Di Sanità, Rome, Italy, [5]Unit of Infectious Diseases, IRCCS Ospedale San Raffaele, Milan, Italy

Background: Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) is responsible for the Coronavirus Disease 2019 pandemic declared in March 2020. Several vaccines were developed that induce antibodies capable to bind both the original SARS-CoV-2 Wuhan-Hu-1 strain and also its variants of concerns (VoCs). While these vaccines were extremely effective in protecting from severe disease, vaccine induced antibodies had a reduced capacity to neutralize VoCs and waned over time. The continued emergence of VoCs has raised questions about the need for vaccine booster administration and the overall ability of SARS-CoV-2 vaccines to protect from infection. In this study, we evaluated whether the level of binding and/or neutralizing antibodies developed after the third dose of vaccination could be considered a biomarker predictive of prevention from subsequent infection.

Material and Methods: A cohort of 30 health care workers of the IRCCS Ospedale San Raffaele was followed post-vaccination with BNT162b2-Comirnaty (Pfizer-BioNTech) for up to 486 days. Sequential serum samples were tested for neutralizing and binding antibodies against the Spike protein of the Wuhan-Hu-1 virus and the Omicron VoC using a Lentiviral Vector pseudotype (LV-luc) based neutralization assays and a Luciferase Immunoprecipitation System (LIPS) assay, respectively.

Results: Binding and neutralizing antibodies peaked at 10 days post the third booster vaccination and declined thereafter. Neither binding nor neutralizing peak ab levels correlated with protection from subsequent infection. However, at 40 days from the third dose, neutralization abs titers against the Wuhan-Hu-1 virus (p=0.047) modestly correlated with reduced SARS-CoV2 infection in the follow-up. Interestingly, the best correlate with protection during follow-up consisted of binding ab levels at day 90 post the third dose, either against the Wuhan-Hu-1 RBD (p=0.046) or cross-reactive with the omicron RBD (p=0.0034).

Conclusion: The persistence and cross reactivity of RBD binding antibodies are predictive of protection from SARS-CoV2 infection.

COVID-19

P 128 SURVIVAL STRATIFICATION ACCORDING TO SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR (SUPAR) LEVELS OF COVID-19 HOSPITALISED PATIENTS

M. Maggi[1], G. Gazzaniga[1], M. Senatore[2], A. Pani[3], F. Scaglione[2,3]

[1]Postgraduate School of Clinical Pharmacology and Toxicology-Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, [2]Department of Oncology and Hemato-Oncology, University of Milan, Milan, [3]Chemical-Clinical Analysis Department, Niguarda Hospital, Milan

Background: SARS-CoV-2 infections have a wide variety of clinical presentations in patients, ranging from asymptomatic to severe multi-organ failure.
Early identification of patients who will have a more severe COVID-19 course has always been a challenge for clinicians. Soluble urokinase plasminogen activator receptor (suPAR) lab test has been proposed as a marker associated with development of severe forms of COVID-19, given that this receptor cleaves into soluble form during the course of inflammation. However, few data are available in this setting, and mostly concerning septic patients.
The aim of our study was to investigate if high suPAR levels may be associated with a poorer survival of COVID -19 patients.
Material and Methods: COVID-19 patients admitted to Niguarda Hospital from December 2021 to April 2022 who underwent suPAR lab test at admission were continuously enrolled. Data concerning demographics, comorbidities, vaccination status and outcome were collected from medical records.
Patients were stratified in two groups according to suPAR values: low suPAR level (< 6.0 ng/ml) vs high suPAR level (≥ 6.0 ng/ml). This cut-off was chosen according to data available in literature. Survival rates according to suPAR level were estimated using the Kaplan-Meier method and log-rank test was used to analyse differences in survival curves. Statistical analyses were performed with R software.
Results: 177 patients were included: 123 with high suPAR level and 54 with low.
High suPAR and low suPAR groups were comparable for sex (41.5 % vs 38.9% respectively) and cancer prevalence (35% vs 33.3 %), while high-suPAR patients were older (mean age 73.7 vs 65.5 years respectively), more vaccinated (73.2% vs 64.8% completed 2-doses SARS-CoV-2 vaccination course respectively) and had a higher comorbidity burden measured by Charlson Comorbidity Index (mean 5.4 vs 3.6 respectively).
Comparison of survival using Kaplan Meier curves is reported in Figure 1. Median follow-up time was 15 days (IQR 10 - 24). 2 deaths (4%) were observed in low suPAR group vs 34 (28%) in high suPAR one.
Survival was significantly longer for patients with low suPAR at admission compared to high suPAR group (log-rank p =0.0042).
Conclusion: High suPAR levels seem to be associated with a poorer prognosis in patients admitted for COVID -19. suPAR lab test might be useful in early risk stratification of SARS-CoV-2 infections. However, given the small sample size and the unbalanced distribution of patients' characteristics in our work, further studies are required to confirm these results.

Attach: https://www.icar2023.it/public/abstract/Attach_ABS_172.png

COVID-19

P 129 DOES REMDESIVIR AFFECT RENAL FUNCTION IN SARS-COV2 INFECTED PATIENTS? REAL LIFE DATA IN A SINGLE CENTER IN PERUGIA

E. Svizzeretto, D. Altobelli, E. Baranello, L. Curci, G. Gonnelli, D. Francisci

Clinica delle Malattie Infettive, Azienda Ospedaliera di Perugia, Università degli Studi di Perugia

Background: Remdesivir is approved as antiviral therapy for SARS-CoV2 infected patients who are hospitalized; a decrease of the creatinine clearance associated with remdesivir has been reported, but there are many studies in scientific literature that ensure the safety of this therapy for renal function.

This study was a retrospective observational single-center study. We evaluated renal function (Glomerular Filtration Rate, GFR) before and after remdesivir; we also studied the correlation between renal injury and other variables: age, sex, comorbidities and presence of pneumonia.

Inclusion criteria: SARS-CoV2 infected patients admitted to S. Maria della Misericordia Hospital in Perugia who received remdesivir from October 2022 to February 2023.

Materials and Methods: For each patient we described age, sex, comorbidities (hypertension, diabetes, cardiovascular disease), concomitant therapy with Ace-inhibitors or angiotensin II receptor blockers (ACE-i or ARBs), presence or absence of Covid-related pneumonia, duration of remdesivir therapy (3, 5 or 10 days), GFR before and after remdesivir therapy and outcome.

Results: A total of 156 patients were enrolled. Mean age was 78.5 years. The population characteristics are described in Table 1.

We analyzed GFR before and after remdesivir therapy (maximum 2 days before/later); We compared GFR before and after remdesivir and calculated the difference (a negative number in case of reduction of GFR and a positive number in case of improvement).

Compared to the start of remdesivir, we observed unchanged or increased GFR at the end therapy in 121 patients, while 35 patients had renal injury (reduced GFR); the renal impairment was confirmed at subsequent blood tests in only 11 of them. Among them we found another cause of renal failure (septic shock and MOF) in 9 patients, while 2 patients had no other cause of renal injury.

Lastly, we evaluated a possible correlation between reduced GFR and others variables examined (age, hypertension, diabetes, ACE-i/ARBs, cardiovascular disease, presence of pneumonia) using t-test and Chi square test. No association was found. Results are attached in Tables 2-7.

Conclusions: We enrolled SARS-CoV2 infected patients over a short period of time, so we may assume that they became infected with the same SARS-CoV2 variant. It was an elderly population with many comorbidities, who were often hospitalized for reasons unrelated to Covid-19.

Only 1.3% of patients had a reduction of GFR during remdesivir therapy without other apparent cause of renal injury, and none of them had severe renal failure.

We studied a possible correlation between age and comorbidities with worsened GFR: we found no correlation between older age or renal-involving diseases and renal injury.

We can conclude that using remdesivir in elderly or pluricomorbid patients doesn't increase the risk of renal impairment.

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COVID-19

P 130 WHICH IS THE EFFICACY OF SOTROVIMAB IN REDUCING DISEASE PROGRESSION AND DEATH DURING THE OMICRON ERA? ANSWER FROM A REAL-LIFE STUDY

A. De Vito[1], F.R.P. Ieva[2], L. Diella[3], A. Colpani[1], R. Papale[2], A. Belati[3], S. Babudieri[1], L. De Santis[3], T. Santantonio[2], A. Saracino[3], S. Lo Caputo[2], G. Madeddu[1]

[1]Unit of Infectious Diseases, Department of Medicine, Surgery, and Pharmacy, University of Sassari, Italy, [2]S.C. Malattie Infettive, Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Foggia, Foggia, Italy, [3]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area - (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy

Introduction: Since May 2021, sotrovimab has been available in Italy to treat SARS-CoV-2 infections to prevent disease progression. However, some in vitro studies have questioned its efficacy on omicron variants. Therefore, we aim to evaluate the efficacy of sotrovimab in real-life settings.

Methods: We conducted a retrospective study collecting medical records of people with SARS-CoV-2 infection evaluated in the Infectious Diseases Unit of Sassari, Foggia, and Bari. We included both people with SARS-CoV-2 infection treated with sotrovimab in 2022 and those people who did not receive any treatment. The reason for not prescribing a treatment could be: i) no symptoms at the moment of evaluation; ii) more than five days since the onset of the symptoms; iii) patient's choice.

The study outcome was to evaluate the efficacy of sotrovimab in reducing disease progression (necessity of starting oxygen supplementation) and COVID-19-related death. The secondary outcome was to evaluate the safety of sotrovimab.

Results: We included 689 people; of them, 341 were treated with sotrovimab, while 348 had not received any treatment. Characteristics of the two groups are summarized in Table 1.

Overall, we registered 161 (23.4%) disease progressions and 65 (9.4%) deaths, with a significant difference between treated and not-treated people (p <0.001).

At the multivariate logistic regression, increasing age [OR for ten years increased age 1.23 (95%CI 1.04-1.45)] was associated with a higher risk of disease progression. In addition, cardiovascular diseases [OR 1.69 (1.01 -2.80)), fever (OR 3.88 (2.35-6.38)], and dyspnea [OR 7.24 (95%CI 4.17-12.58)] were associated with an increased risk of disease progression. On the contrary, vaccination [OR 0.21 (95%CI 0.12-0.37)] and sotrovimab administration [OR 0.05 (95%CI 0.02-0.11)] were associated with a lower risk of having severe disease.

Regarding mortality, people with older age [OR for ten years increased age 1.36 (95%CI 1.09-1.69)] had a higher risk of death. In addition, in the multivariate analysis, cardiovascular disease lost statistical significance. At the same time, people on chemotherapy for haematological cancer [OR 4.07 (95%CI 1.45-11.4)], and those with dyspnea [OR 3.63 (95%CI 2.02-6.50)] had an increased risk of death. On the contrary, vaccination [OR 0.37 (95% CI0.20-0.68)] and sotrovimab treatment [OR 0.16 (95%CI 0.06-0.42)] were associated with lower risk.

Only two adverse events have been reported; one person complained of diarrhoea a few hours after sotrovimab administration, and one had an allergic reaction with cutaneous rash and itching.

Conclusion: In our study, sotrovimab is shown to minimize the risk of disease progression and death in a cohort with 70% of people over 65 years and a high vaccination rate, with excellent safety. Therefore, we reinforce the evidence about the efficacy and safety of sotrovimab during the omicron era in a real-world setting.

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COVID-19

P 131 TREATMENT WITH NIRMATRELVIR/RITONAVIR PREVENTED HOSPITALIZATIONS AND DEATHS IN PATIENTS DIAGNOSED WITH COVID-19 AT A RESIDENTIAL CARE FACILITY IN MILAN, ITALY

M. Franzetti[1], L. Pezzati[1,2], A. Gatti[3], F. Salmoiraghi[3], E. Magni[3], N. Antoniotti[3], S. Baruffi[3], G. Esposti[3], C. Balotta[3], B. Caimi[3], S. Rusconi[1,2]

[1]Infectious Diseases Unit, ASST Ovest Milanese, Legnano, Milan, [2]Department of Biomedical and Clinical Sciences L. Sacco, University of Milan, [3]Azienda Servizi alla Persona, Istituti Milanesi Martinitt e Stelline e Pio Albergo Trivulzio, Milan

Background: Nirmatrelvir/ritonavir was approved to prevent severe COVID-19 in symptomatic patients with at least 1 risk factor of progression. This indication was based on registration studies evaluating subjects with a median age of less than 50 years. Thus, we aimed to evaluate the treatment outcome of nirmatrelvir/ritonavir in the geriatric population in a real-life setting of care allowing full access to reliable clinical data and follow-up.
Materials and Methods: From July 12th 2022 to January 12th 2023, we evaluated nirmatrelvir/ritonavir treatment in the long-term care facility “Pio Albergo Trivulzio” (Milan, Italy). Treatment was proposed to subjects with less than 5 days onset of mild/moderate symptoms, confirmed COVID-19 diagnosis and at least one risk factor for progression, including age of 65 years or more. Potential drug-drug interactions were evaluated through the University of Liverpool Interaction Checker.
Results: During the study period, 264 patients tested positive for SARS-CoV-2: 73.2% were female, median age was 85 years (interquartile range, IQR 80-90 years). All had received full course vaccination and a booster dose and 22 (8.3%) had a history of previous COVID-19. Nirmatrelvir/ritonavir was administered to 92 subjects (34.8%). Contraindications to treatment included: drug-drug interactions (43.1%), glomerular filtration rate (GFR) < 30 mL/min (16.9%), dysphagia (20.9%), refusal of patient or next-of-kin (7.0%). Adjustment of dose was warranted in 76 subjects (82.6%) and it was due to renal function (GFR between 30 and 60 mL/min) in 25 patients (27.2%) and to potential interactions in 51 (55.4%). Median time to negativity of nasal swab test in the treated vs untreated group was 8 days (IQR 7-12) vs 9 days (IQR 7-14), respectively. In the treatment group, we did not observe any significant difference in median time to negativity between those receiving full and adjusted dose (7 vs 8 days, respectively). We observed 1 hospitalization in the treated group vs 9 in the non-treated group (0.6% vs 5.2%, p=0.09). No death was observed in the treatment group, while five patients who did not meet criteria for treatment died of respiratory failure (0.0% vs. 2.9%, p=0.09). The most reported side effect was diarrhea (2.2%).
Conclusions: We observed no deaths and less hospitalizations compared to those who could not be treated, in a group of residents of a long-term care facility at high risk for COVID-19 progression treated with nirmatrelvir/ritonavir. This therapy was proposed to a minority of patients with SARS-CoV-2 infection, due to frequent contraindications, mainly represented by concomitant interacting medications; nonetheless, it was extremely well tolerated, despite the frequent need for dose adjustment. Considering the high burden of hospitalization in this fragile population and the associated direct and indirect costs, real life use of nirmatrelvir/ritonavir in the elderly should be implemented when possible.

COVID-19

P 132 OLDEST OLD OUTPATIENTS WITH MILD-MODERATE SARS-COV-2 INFECTION TREATED WITH MONOCLONAL ANTIBODIES: A REAL LIFE SINGLE CENTER STUDY

N. Bonadiman[1], M. Basso[1,2], V. Scaglione[1], S. Gardin[1], M. Canova[1], E. Agostini[1], A.M. Cattelan[1]

[1]Infectious Diseases Unit, Department of Medicine, Azienda Ospedale Università Padova, Padova, Italy, [2]Department of Molecular Medicine, University of Padova, Padova, Italy

Background: Elderly population is at high risk of SARS-CoV-2 infection morbidity and mortality. However, most available data on clinical outcomes in this population came from hospitalized patients (pts) in whom the older age was an independent risk factor of mortality. This real-life study aimed to evaluate clinical outcomes of a cohort of oldest old patients who received monoclonal antibodies (MoAb) for mild-moderate COVID-19.
Material and Methods: We included all patients aged ≥85yrs, with mild/moderate COVID-19 (according to the WHO criteria), evaluated in outpatient setting at the Infectious Diseases Unit of Padua University Hospital from April 2021 to December 2022 and who received (according to the Italian Drug Agency criteria) an early treatment with MoAb. Type of MoAb administered was based on clinical decision and drug availability. SARS-CoV-2 anti-spike protein RBD IgG levels were measured at baseline (T0) and at week 1(T1). SARS-CoV-2 variant identification was performed using Sanger sequencing. Mann-Whitney test, Wilcoxon test, chi-squared test and Fisher's exact test were applied. Significance was set up<0.05. Statistical analyses were performed with MedCalc® Statistical Software.
Results: 152 pts (M/F 87/65), median age 88yrs (IQR 86-91) were included in the study:103 (67.8%) were treated with sotrovimab 500mg iv, 25 (16.4%) with bamlanivimab 700mg-etesevimab 1400mg iv, 20 (13.2%) with casirivimab 600mg–imdevimab 600mg iv, and 4 (2.6%) with tixagevimab 300mg-cilgavimab 300mg im. Overall, 45-day all-cause mortality was 7.2% (11/152 pts) and 30-day all cause hospitalization rate was 5.7% (8/141 pts), with no difference between 2021 and 2022 for the two outcomes (8.3% vs 6.9% and 9.1% vs 4.6% respectively). Deceased pts were older (90,IQR 86-93 vs 88,IQR 86-91): 4 had a diagnosis of COVID pneumonia, 5 had a diagnosis of SARS-CoV-2 infection, no diagnosis was available for 2 pts. Sequencing and serology were performed in more restricted groups of pts. Variant sequencing was available for 82 pts, B.1.617.2 was predominant in 2021 (p<0.0001), BA.2 and BA.4/BA.5 in 2022 (p=0.003 and p=0.034 respectively)(Table 1). IgG levels at T0 were available for 118 subjects, 19 (16.1%) were negative: median value of the 99 positive pts was 87.5 kAU/L (IQR 27.3-287.4), comparable in pts with unfavourable and favourable outcome (104.5,IQR 18.1-655.1 vs 82.4,IQR 28.5-225.9). In 42 pts paired data available: IgGs were significantly higher at T1 (87.9, 21.4-374.3 vs 1144.5,IQR 608.8-9108, p <0.0001). Pts with negative serology at T0 had significantly lower IgG levels at T1 respect to pts with positive serology (183.5,IQR 173.6- 294.6 vs 1390,IQR 772.4-10450.2, p=0.0006)(Figure1).
Conclusions: Oldest old people with mild/moderate disease are still at risk of early unfavourable outcomes. Selected oldest pts with insufficient antibody response despite treatment may necessitate closer monitoring and, with further data support, a different treatment schedule.

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COVID-19

P 133 RELATIONSHIP BETWEEN ULTRASENSITIVE SARS-COV-2 VIRAEMIA, INFLAMMATORY PARAMETERS AND LYMPHOCYTE STIMULATION TEST

A. Imeneo[1], G. Alessio[1], A. Di Lorenzo[1], L. Benedetti[1], L. Piermatteo[2], F. Ceccherini-Silberstein[2], M. Andreoni[1], L. Sarmati[1], M. Iannetta[1]

[1]Department of Systems Medicine, Tor Vergata University, Rome, Italy, [2]Department of Experimental Medicine, Tor Vergata University, Rome, Italy

Introduction: Several studies reported an increased rate of indeterminate QuantiFERON-TB Gold Plus (QFT-P) assay results in patients hospitalized for severe SARS-CoV-2 infection, due to peripheral blood T-lymphocyte depletion and dysfunction. Our study aims to evaluate the possible relationship between QFT-P results, disease severity and viraemia for SARS-CoV-2.

Methods: An observational retrospective case-control study (1:1) was conducted on patients hospitalized for SARS-CoV-2 infection at Tor Vergata Hospital from November 2020 to December 2021, including patients with indeterminate (cases) and determined (controls) QFT-P assay results. Blood tests, SARS-CoV-2 RNA assessment through Digital Droplet Polymerase Chain Reaction (ddPCR) on plasma and Real-Time PCR (RT-PCR) on nasopharyngeal swabs were performed. Patients were stratified in non-severe (ambient air [AA] and Venturi Oxygen Mask [VMK]) and severe (Non-Rebreather Mask [NRM], Non-Invasive Ventilation [NIV], or Orotracheal Intubation [OTI] for mechanical ventilation) according to oxygen needed during the hospitalization. Demographic, clinical, and laboratory data were collected in an ad hoc database. All statistical analyses were performed with JASP v.0.17.1. The level of statistical significance was <0.005.

Results: 42 cases and 37 controls were analyzed. The median age was 61 (interquartile range [IQR] 51-71) in cases and 60 (IQR 50-71) in controls, with a prevalence of male (66,7% in cases and 62,2% in controls) and a median Charlson Comorbidity Index (CCI) of 2 (IQR 1-4) in both groups. Cases and controls were comparable in the rate of SARS-CoV-2 vaccination (7% vs 16%, p value 0,205), mortality (19,0% vs 10,8%, p value 0,309) and Intensive Care Unit (ICU) admission (16,7% vs 8,1%, p value 0,254). The time between the ddPCR test on blood and the RT-PCR examination on nasopharyngeal swab was 1 day (IQR 1-2). The median value of SARS-CoV-2-RNA (RdRP gene) on plasma was 4 copies/ml (IQR 0-8,3) and 3.6 copies/ml (IQR 0-11,2) in cases and controls respectively (p=0,814). 27 patients had undetectable SARS-CoV-2 viraemia (14 cases and 13 controls). There was no statistically significant association between SARS-CoV-2-RNA and disease severity, outcome, ICU admission, SARS-CoV-2 vaccination, C-reactive protein (CRP), CD3, CD4, CD19 absolute counts, interferon-gamma production after Mitogen stimulation (table 1). Interestingly, we observed a 82-year-old unvaccinated man, with a CCI=8 and an indeterminate QFT-P assay, who had a SARS-CoV-2 plasma viral load of 67.320 copies/ml and died shortly after hospitalization.

Conclusions: From our preliminary study, an ultrasensitive SARS-CoV-2 viral load was not associated with poorer outcomes, increased disease severity or immune dysfunction. In one patient, a high viral load was associated with a fatal outcome. Further studies on wider cohorts are needed.

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COVID-19

P 134 SARS COV 2 INFECTION IN A PATIENT AFFECTED BY CEREBRAL AMYLOID ANGIOPATHY: CASE REPORT AND LITERATURE COMMENTARY

A.M. Spera, A. Campagna, C. D'Amore, V. Fortunato, S. Madonia, A. Masullo, M. Onofrio, G. Parrella, R. Verrioli

Infectious Disease Unit, AOU OO RR San Giovanni di Dio e Ruggi d'Aragona, Salerno

Introduction: The COVID 19 pandemic still represent an unresolved challenge for the international scientific community placing the clinician in front of complex scenarios where the viral infection can complicate the development, reactivation and progression of other pathologies.
Aim of the study:Overview of a clinical case involving a patient with a recent diagnosis of cerebral amyloid angiopathy (CAA) admitted at our Infectious Disease Unit because of viral infection due to SARS CoV 2.
Clinical case: We report the clinical case of a patients of 80 years old with CAA, cognitive impairment, arterial hypertension, dyslipidemia and chronic renal failure. Three cerebral hemorrhage of the right parieto-occipital region along with left lateral hemianopia were described in her medical history. A magnetic resonance performed in September 2022 revealed findings compatible with CAA. The research of tau, phospho-tau, beta-amyloid and 14 -3-3 protein on cerebrospinal fluid sample and progranulin dosing on plasma performed at IRCCS "Besta" of Milan, confirmed the diagnosis of CAA. The patient was admitted in October 2022 to the Neurologic Unit with altered mental status secondary to non-convulsive status epilepticus. In ten days she was relocated to our Infectious Disease Unit because of SARS CoV 2 infection at high risk of progression to severe form of COVID 19. After the clinical assessment and the evaluation of drug-drug interactions, she was considered eligible to Remdesivir. The antiviral treatment licensed by the European Medical Agency (EMA) was properly administered at single loading dose of 200 mg on day 1 followed by daily maintenance dose of 100 mg for the next three days with no observed adverse events. A gradual clinical improvement was obtained until the virologic recovery, occurred ten days later. Then, the patient was transferred again to the Neurologic Unit for the follow up.
Discussion: CAA is a degenerative neurological disease characterized by deposits of β-amyloid within small/medium cerebral blood vessels and leptomeninges. The incidence of the disease is related to the patient's age. The most common clinical manifestations of CAA are cognitive impairment and acute intracerebral hemorrhage. The diagnostic gold standard of CAA is brain biopsy. In clinical practice, MRI of the brain, CSF analysis, and clinical evaluation are adequate. Treatment options currently available are supportive only.
There are several studies in the literature regarding any correlations between COVID 19 and CAA. Goncalves et al hypothesize that SARS CoV 2 may be able to contribute to CAA inducing amyloidogenesis, leading to long-COVID. Yamakawa et al. describe a case of inflammatory variant of CAA secondary to a SARS-CoV-2 vaccine. Liang et al in 2021 assume that the secondary immune response to COVID-19 may have further compromised the cerebral vascular system, already weakened by the pre-existing CAA, in a 74-year-old patient leading to multiple micro-hemorrhages.

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COVID-19

P 135 REMDESIVIR-NIRMATRELVIR COMBINATION: IN VITRO ACTIVITY AND A CASE REPORT

A. Gidari[1,2], S. Sabbatini[3], E. Schiaroli[1], S. Bastianelli[1], S. Pierucci[1], C. Busti[1], L.M. Saraca[2], L. Capogrossi[1], M.B. Pasticci[1,2], D. Francisci[1]

[1]Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy, [2]Clinic of Infectious Diseases, "Santa Maria " Hospital, Terni, Italy, [3]Department of Medicine and Surgery, Medical Microbiology Section, University of Perugia, Perugia, Italy

Background: This study aims to investigate the activity of remdesivir and nirmatrelvir combination on Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) to verify the synergistic effect. Here, we also reported a case of a Coronavirus Disease 2019 (COVID-19) patient treated with this combination.

Methods: A Vero E6 cell-based infection assay was used to investigate the in vitro activity of the remdesivir-nirmatrelvir combination. All experiments were performed using a 20A.EU1 SARS-CoV-2 strain. After 48 and 72 h post-infection, a viability assay was performed. The supernatants of cell viability experiments were used for viral titration (plaque assay).

To test whether the drug combinations act synergistically, the Highest Single Agent (HSA) reference model was calculated. An HSA score > 10 is considered synergic.

Results: Remdesivir and nirmatrelvir showed synergistic activity at 48 and 72 h with an HSA score of 52.8 and 28.6, respectively ($p<0.0001$, Figure 1A-B). This data has been confirmed performing supernatant titration: the combination significantly reduced the viral titer better than the more active compound alone (Figure 1C).

Case Report: A 50-year-old woman was readmitted to the Clinic of Infectious Diseases of “Santa Maria” hospital of Terni for COVID-19 on September 21st, 2022. She has a history of non-Hodgkin follicular lymphoma treated with anti-CD20 therapy (rituximab). She was SARS-CoV-2 positive from 18th February 2022 and was treated with early antiviral therapy (remdesivir for three days course and sotrovimab). Multiple nasopharyngeal swabs were collected and always resulted positive. On April 19th, May 4th, and September 5th, SARS-CoV-2 was isolated from nasopharyngeal swabs and the viruses were identified as BA.1 variant.

At the hospital readmission, the clinical conditions immediately appeared serious with acute progressive respiratory failure due to extensive COVID-19 interstitial pneumonia. A bronchoalveolar lavage was performed and other infections have been excluded.

She required high-flow nasal cannula oxygen support and inotropic support. The resuscitator specialist judged the prognosis poor and defined the patient as not eligible for intensive care.

The medical therapy was set as follows: antibiotic therapy, off-label antiviral therapy with remdesivir (10 days course) plus nirmatrelvir/ritonavir (5 days course), tixagevimab/cilgavimab, and dexamethasone (6 mg/die for 10 days). The patient presented an excellent clinical-radiological response with progressive reduction of oxygen requirement up to the suspension and improvement on control CT after 2 weeks. However, she required further off-label prolonged therapy with nirmatrelvir/ritonavir up to the negativization obtained on 2nd November 2022.

Conclusion: Remdesivir-nirmatrelvir combination showed good synergic activity in vitro. This combination may have a global impact on difficult-to-treat and severe COVID-19, especially in immunocompromised patients.

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COVID-19

P 136 CORRELATION BETWEEN IGM AND IGG ANTI-SARS-COV-2 AND CLINICAL COVID STADIATION

A. Di Fraia, M. Pisaturo, M. Starace, C. Minichini, L. Occhiello, A. Russo, N. Coppola

Infectious Diseases Unit, Department of Mental Health and Public Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy

Aim: to correlate the clinical staging with the quantification of Sars-Cov-2 IgG and IgM.

Patients and Methods: 62 patients were enrolled from October 2020 to November 2021, hospitalized for covid -19, of which we had a serum sample and a nasopharyngeal swab at the time of admission. The real time-PCR was performed to detect viral RNA from nasopharyngeal swab with Bosphore Novel Coronavirus 2019-nCoV Detection Kit V3 CE-IVD and the Elisa test for the quantization of IgG and IgM anti-Sars-Cov-2 was performed on serum sample with Human Anti-Sars-Vov2 (N) IgM and IgG Elisa kit - FineTest

Results: table 1 shows the Epidemiological, clinical and serological characteristics of the enrolled subjects and the covid staging of the patients. Patients had a median age of 62 (range 23-91), 43 (69.4%) were male, 4 (6.45%) were asymptomatic (0), 18 (29.03) moderate (1), 20 (32.26%) severe (2), 19 (30.65%) critics (3) and 1 (1.61%) exitus (4). Subjects had a median anti-Sars Cov-2 IgM and IgG value of 8.603 (IQR 6.980) and 56.948 (IQR 21.715) respectively.

Table 2 shows the epidemioloical and serological characteristics according to covid stadiation, without statistical significance.

Conclusions: there is no data correlating the staging of covid with the quantification of IgG and IgM anti-Sars-Cov2, with the increase in cases we can better study this phenomenon and identify if there is a correlation.

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COVID-19

P 137 IMMUNOGENICITY OF PRIMARY TWO DOSE CYCLE AND THREE DOSE OF MRNA VACCINE IN TREATED SOLID CANCER PATIENTS

A. Gabrieli[1], A. Riva[1], N. La Verde[2], D. Dalu[2], C. Della Ventura[1], S. Cona[2], M. Tarkowski[1], L. Ruggieri[2], C. Fasola[2], M. De Monte[2], A. Bergna[1], C. Buonomo[2], A. Lai[1], D. Chizzonti[2]

[1]Luigi Sacco Department of Biomedical and Clinical Sciences DIBIC, University of Milan, Milan, Italy, [2]Department of Oncology, Sacco Hospital, ASST Fatebenefratelli Sacco, Milan, Italy

Background: Cancer patients are susceptible to SARS-COV-2 infection and COVID-19 complications, therefore the vaccination is the most effective method to prevent of severe COVID-19. In this study we evaluated the serological immune response to the primary two-dose and third dose of mRNA- vaccines (mRNA-1273, tozinameran).

Material and Methods: This is prospective, observational, cohort study conducted between March 2021 and April 2022 at the Luigi Sacco Hospital. Quantitative serological testing for antibodies against RBD and S1 and N was performed before the first dose (T0) and 30 days after the second dose of vaccine (T1) in 195 patients on anticancer treatment and in 99 patients, who previously received primary vaccine cycle, 30 days after 3rd dose (T2). IgG levels anti N, S1 and RBD of SARS-COV-2 were simultaneously measured in human plasma samples using Luminex xMAP SARS-COV-2 Multi- Antigen IgG kit (Luminex Corp, Austrin), setting threshold values for all 3 antigens to 700 median fluorescence intensity (MFI).

Results: Demografic and clinical charactersitics of cancer patients are presented in table 1.The seroconversion rate of 195 cancer patients with previous expore to SARS-COV-2 (93.3%) was similar to 28 healthy individuals (95.0%, P= 1.000). The rate of seroconversion in patients without previous SARS-CoV-2 infection (66.7%) was significantly lower than that observed in healthy controls (p=0.0085) and in patients with a previous SARS-CoV-2 infection (p=0.0020). MFI values for anti-RBD and anti-S1 IgG levels in the three groups are described in Figure 1. Univariate and multivariate analyses proved that antibody levels were independent from age, gender, timing of vaccination and use of steroids. Seroconversion after the 3rd dose was reached in 99% of individuals: anti-RBD IgG mean level 18419 MFI; anti-S1 IgG mean level 10289 MFI (Figure 2A). After the primary vaccination, 22 patients failed to seroconvert. Among them, 21 seroconverted after the 3rd dose (mean level 8200 MFI at post-V3). (Figure 2B). A homologous vaccination scheme reduces anti-S1 IgG levels (p .04). Regarding this, at the multivariate analysis, primary cycle with mRNA-1273 and tozinameran as third dose was associated with increased anti-S1 levels (vs homologous, p .01; vs primary tozinameran/booster mRNA-1273, p .001). A further analysis showed that primary-vaccination non-responders increased their relative amount of anti-S1 and anti-RBD IgG after the 3rd dose if compared to the responder group.

Conclusion: Vaccine immunogenicity in patients receiving anti-cancer treatments, who received primary cycle, with a previous exposure to SARS-CoV-2 seems comparable to the healthy controls. The third dose of mRNA-vaccines proved to be immunogenic in most of the patients, including subjects who failed to seroconvert after the two-dose primary cycle The heterologous mRNA-vaccination regimen is able to enhance the humoral immune response in patients treated for solid tumors.

COVID-19

P 138 CLINICAL EFFICACY OF TWO DOSES OF MRNA-BASED VACCINES COVID-19 FOR SOLID CANCER PATIENTS ON TREATMENT

A. Gabrieli[1], A. Riva[1], N. La Verde[2], D. Dalu[2], C. Della Ventura[1], S. Cona[2], M. Tarkowski[1], L. Ruggieri[2], C. Fasola[2], M. De Monte[2], A. Bergna[1], C. Buonomo[2], A. Lai[1], D.Chizzonti[2]

[1]Luigi Sacco Department of Biomedical and Clinical Sciences DIBIC, University of Milan, Milan, Italy, [2]Department of Oncology, Sacco Hospital, ASST Fatebenefratelli Sacco, Milan, Italy

Background: Prevention of severe COVID-19 is crucial for cancer patients and vaccination is the most effective method to achieve this goal. There are few data in cancer population regarding the clinical efficacy of the vaccine, which is a more realistic measure of the real degree of protection from infection and severe disease. The aim of the present study is to evaluate the clinical efficacy of mRNA-based vaccines against SARS-CoV-2 after two doses in a population of cancer patients on active treatment and in follow-up.

Material and Methods: This is a single institution, prospective, non-randomized study conducted from January to December 2021 at the Luigi Sacco Hospital in Milan. Clinical data were collected through a pre-defined questionnaire performed by phone in the period between the 2nd and the 3rd dose. The primary end point was to assess clinical efficacy of vaccine, defined as the percentage of vaccinated subjects who did not develop COVID -19 within six months after the second dose. The secondary end point was to describe the clinical features of patients who developed COVID-19.

Results: From January to June 2021, 195 cancer patients, who had received two doses of mRNA-based vaccine anti SARS-CoV-2, were enrolled. The median age at first vaccine dose was 64.1 years (Q1-Q3: 53.8-72.0) and 70.8% of patients were females. Breast was the most common tumor site (51.3%) and the largest part of patients had metastatic cancer (67.2%). After the completion of primary vaccination, 7 (3.59%) patients tested positive for SARS-CoV-2; 5 cases developed symptomatic disease. Based on the results obtained, the clinical efficacy of two doses of mRNA-based vaccine against COVID-19 was of 97.4 %. The main features of these 7 patients are described in Table 1. Among the 5 infected patients, 3 patients had not reached seroconversion after two doses of vaccine; the 2 seroconverted patients who developed symptomatic disease, contracted the infection at least five months after administration of the 2nd dose of vaccine. The maximum duration of COVID-19 was 10 days in 6 patients; only in one patient the symptoms lasted for 30 days, causing delay over 7 days of the administration of oncological treatment. Only one symptomatic patient required hospitalization due to severity of disease. No patient needed invasive ventilation or hospitalization in ICU. The other patients had mild illness and were managed at home and treated with ancillary and supportive therapy. Conversely, the patient admitted at the hospital received oxygen therapy, broad-spectrum antibiotic, dexamethasone, remdesivir and tocilizumab.

Conclusion: Our data underline the relevance of vaccination also in frail patient as a tool to prevent infection and severe manifestations of COVID-19. Increasing vaccination coverage and extended mitigation measures could be a successful strategy to protect cancer patients in the fight against the virus.

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COVID-19

P 139 INCIDENCE OF POST-COVID CONDITIONS IN PEOPLE TREATED WITH MONLUPIRAVIR: A SINGLE-CENTER EXPERIENCE

A. De Vito, P. Filigheddu, A. Colpani, G. Moi, B. Zauli, M. Fois, A. Bitti, M.C. Meloni, C.M. Panu Napodano, A. Muredda, I. Maida, V. Fiore, S. Babudieri, G. Madeddu

Unit of Infectious Diseases, Department of Medicine, Surgery, Pharmacy, University of Sassari, Italy

Background: The long-term consequences of the coronavirus disease 19 (COVID-19) are likely to be frequent after SARS-CoV-2 infection. Different studies reported a prevalence of around 30%. However, few data are available on people who received early antiviral treatment. Therefore, we aimed to define the incidence of long-term COVID signs and symptoms one year after SARS-CoV-2 infection in people treated with monlupiravir.
Methods: We conducted a cross-sectional study, including people who received monlupiravir for SARS-CoV-2 between January 1 and April 5 2022. We collected demographical data, clinical history, and data on SARS-CoV-2 infections. In addition, we contacted all people to assess the presence of Post COVID-19 conditions after one year from the infection. We investigated the presence of symptoms and signs according to the WHO definition. We excluded those people who reported SARS-CoV-2 re-infection since then.
Results: Between January 2022 and April 5 2022, we prescribed monlupiravir to 278 people; of them, 18 (6.4%) died during the hospitalization, while 260 survived. After one year, 43 (16.5%) additional deaths were reported, six (2.3%) underwent a SARS-CoV-2 re-infection, and 23 (8.8%) were not reachable. Overall, we included 188 people, of which 34 (18.1%) reported at least one Post COVID-19 condition. In particular, 28 (14.9%) complained of asthenia, 13 (6.9%) shortness of breath, 9 (4.8%) dyspnea, 8 (4.2%) cough, 6 (3.2%) sore throat, 14 (7.4%) arthralgia, 12 (6.4%) myalgia, 10 (5.3%) insomnia, 10 (5.3%) brain fog, 3 (1.65) anxiety, 4 (2.1%) paresthesia, 2 (1.1%) vertigo, 2 (1.1%) tinnitus, and 2 (1.1%) anosmia.
In Table 1, we reported the characteristics and differences between those with Post COVID-19 conditions and those without.
At the logistic regression, obesity [OR 2.29 (95%CI 1.07-4.91)] and having a Charlson comorbidity index less than 5 [(OR 2.71 (95CI% 1.24-5.96)] were associated with an increased risk of having Post COVID-19 condition. Also, having had dyspnea during the infection [OR 2.85 (95%CI 1.10-7.41)] and having had a severe disease [3.97 (95% CI 1.01-15.68)] were associated with an increased risk. Finally, people with congestive heart failure had a lower risk of having Post COVID-19 condition [OR 0.40 (95%CI 0.17-0.94)].
Conclusions: Our study shows a lower prevalence of Post COVID-19 conditions in people treated with monlupiravir than what is reported in the general population by the available literature. Also, particular attention shall be given to those with a low comorbidity burden and to those who have had a severe SARS-CoV-2 disease. Further studies with a larger sample size are needed to better assess the incidence of each Post COVID-19 condition and to explore the role of early antiviral treatment.

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COVID-19

P 140 SARS-COV-2 INFECTION AND SOLID ORGAN TRANSPLANT RECIPIENTS: A SINGLE CENTER EXPERIENCE

F. Peracchi[1,2], M. Merli[2], R. Rossotti[2], M. Puoti[1,2], G.Travi[2]

[1]University of Milano-Bicocca, School of Medicine and Surgery, Monza, Italy, [2]Division of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda Milan, Italy

Background: Pandemic has significantly impacted on solid organ transplant (SOT) recipients, who are at high risk of infection and worse outcome, moreover therapeutical management in this population is not clear yet. The aims of this study are to evaluate the overall survival of SOT recipients and predictive factors for mortality. We also aimed to evaluate the impact of antiviral treatments and immunosuppressant changes on overall mortality and to evaluate length of in hospital stay (LoS) of SOT compared to general population.
Methods: This is a retrospective monocenter study. We included all SOT recipients with laboratory confirmed SARS-CoV2 infection admitted at Niguarda Hospital in Milan, from February 2020 through January 2022.
Results: We enrolled 74 solid organ transplant recipients; median age 59 years old. Overall mortality rate was 19%. Older age, male sex, diabetes and high LDH values were associated with an increase of fatality rate. Median LoS was 17 days. Low levels of white blood count and lymphocytes were associated to 19 days LoS. No impact of COVID-19 therapies and change of immunosuppression were related to mortality and LoS.
Conclusions: In our study, we confirm previous described risk factors for worse outcome. More studies are needed to assess best therapeutical options, including, immunosuppressant modulation, in SOTs.

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COVID-19

P 141 KEYSTONE BACTERIAL SPECIES OF ALTERED BLOOD AND ORAL MICROBIOTA PROFILE DURING SARS-COV-2 INFECTION

L. Santinelli[1], L. Sorrentino[2], M. Fracella2, L. Maddaloni[1], F. Frasca[2], A. Dauria[2], G. Radocchia[1], V. Iebba[3], G. Bugani[1], C. Lofaro[1], E. Binetti[1], A. Pierangeli[2], G. Antonelli[2], C.M. Mastroianni[1], S. Schippa[1], G. d'Ettorre[1], C. Scagnolari[2]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, [2]Laboratory of Virology, Department of Molecular Medicine, affiliated to Istituto Pasteur Italia, Sapienza University, Rome, [3]Department of Medical Sciences, University of Trieste, Trieste, Italy

Background: Although SARS-CoV-2 infection was associated with relevant disturbance of resident bacterial community within the gut of COVID-19 patients, the role of oral and blood microbiota in response to SARS-CoV-2 infection represents a highly interesting but incompletely understood aspect of COVID-19. To the best of our knowledge, this first study focused on the characterization of oral and blood microbiota profile in COVID-19 patients, aimed to provide an overview of the dominant bacterial species typifying these two compartments during SARS-CoV-2 infection.

Methods: 16rRNA gene sequencing was applied to blood and oral swabs from SARS-CoV-2 infected patients (n=44) and healthy volunteers (HV). α-diversity (within sample diversity) measurements, the Shannon and Simpson indexes and observed operational taxonomic units (OTUs) were calculated at species level. β-diversity (between-sample diversity) analysis was calculated using the Bray–Curtis measure of dissimilarity and represented in Principal Coordinate Analysis (PCoA), along with methods to compare groups of multivariate sample units (ANOSIM and PERMANOVA). Partial Least Square Discriminant Analysis (PLS-DA) and the subsequent Variable Importance Plot (VIP) were used to identify the most discriminant bacterial species. This research was supported by EU funding within the NextGenerationEU-MUR PNRR Extended Partnership initiative on Emerging Infectious Diseases (Project no PE00000007, INF-ACT).

Results: An increased alpha-diversity was observed in peripheral blood (p=2.63*10-14) and oral swab (p=2.03*10 -2) of SARS-CoV-2 infected patients as compared to HV. The same trend was observed for Shannon biodiversity index both in blood and oral samples (p=1.14*10-14 and p= 9.761*10-3, respectively). A significant separation of COVID-19 microbial community from those of HV was also assessed with two different measures of beta-diversity both in blood (p=9.0*10-4) and oral (p=9.0*10-4) samples. Highly discriminant bacterial species of blood of COVID -19 patients were Sphingomonas paucimobilis and Cutibacterium acnes, while five keystone bacterial species, namely Streptococcus peridonticum, Velonella dispar, Streptococcus sinensis, Staphylococcus epidermidis, and Flavobacterium succinicans were distinctive for oral swabs. However, 12 species characterized the microbiota of COVID-19 patients both at peripheral and oral cavity levels, while no species were shared between the two compartments among HV.

Conclusions: A definite but synergistic structure of blood and oral microbiota composition in COVID-19 subjects might help to identify specific bacterial consortia as disease biomarkers and improve management and treatment of COVID-19.

COVID-19

P 142 LATINA SCORE FOR DISCRIMINATION BETWEEN PROGRESSOR AND NON PROGRESSOR SARS-COV-2 INFECTED PATIENTS

P. Zuccalà[1], D. Alunni Fegatelli[2], C. Del Borgo[1], R. Marocco[1], B. Kertusha[1], T. Tieghi[1], A. Gasperin[2], A. Parente[2], P. Fabietti[1], G. Mancarella[2], S. Garattini[2], A. Spagnolo[2], M. Lichtner[2]

[1]Infectious Diseases Unit, SM Goretti Hospital, Sapienza University of Rome, Latina, Italy, [2]Department of Public Healt, microbiology and Infectious Diseases, Sapienza University of Rome, Polo Pontino , Latina, Italy

Background: COVID 19 could presents with mild flu manifestations but even can progress towards severe cases with major complications such as ARDS, MOF and death. Early identification of patients that are likely to evolve into severe ARDS will help to identify those who need hospitalization among those requiring home treatment and choose correct antiviral and immunological therapy. The aim of the study is to identify determinants in the severe progression of COVID-19 disease in a cohort of patients with a mild initial clinical features at the time of hospitalization. We propose a score that including the main determinants is able to discriminate progressor from non progressor subjects.

Material and Methods: in the observational retrospective cohort study performed in “S. Maria Goretti Hospital” we stratify patients (pts) according to their P/F at the admission and enrolled only those who have P/F >300. Patients were stratified into progressor subjects who presented at baseline pneumonia and develope in the subsequent days ARDS, and non progressor.

Data are expressed as mean and standard deviation (SD) or median and interquartile range (IQR) Comparison between groups was performed by Chi square test or Mann Whitney test.

We developed a score based on the prognostic value of predictor variables in multivariable analysis. The model selection was performed by stepwise procedure based on the Akaike Information Criterion. Analyses were performed using R version 4.0.1 (The R Project for Statistical Computing).

Results: population enrolled in the study included 689 subjects with P/F>300 on admission in Hospital: 346 pts developed pneumonia without ARDS, while the other half progressed to ARDS (347 pts). Lower levels of lymphocyte and elevated blood glucose, neutrophils and C-reactive protein (CRP) were associated with COVID-19 pneumonia combined with ARDS rather than those without ARDS ($p<0.001$, each). Hypertension, diabetes, cardiovascular disease and dementia were highly associated with the severity and prognosis of COVID-19: ($p=0.037$, $p=0.031$, $p=0.015$, $p<0.001$ respectively). Fever, dyspnea and pharyngitis were symptoms more present in the population that will develop ARDS ($p=0.029$, $p<0.0001$ and $p=0.039$ respectively).

A multivariable logistic regression model based on neutrophils value, Age, PCR (mg/dl), Fever, Glycemia (mg/dl) and adjusted for variant was estimated. Latina score was defined as the linear combination of Neutrophils (cell/µl, %) value, Age (years), PCR (mg/dl), Fever, Glycemia (mg/dl) values where the weights were proportional to the rounded logistic regression coefficients.

The Latina score showed good discrimination with the AUC of 0.790.

Conclusions: Latina score could permit an early detection of pts with SARS-CoV-2 with an high risk of progression to severe disease: identification of this pts is important in order to improve their outcome and identify subjects who should be hospitalized and treated with specific treatments.

COVID-19

P 143 A RETROSPECTIVE COHORT STUDY TO UNDERSTAND THE IMPACT OF THE DRUGS INDICATED IN THE EARLY TREATMENT OF SARS-COV-2 DISEASE AND THE RISK OF HOSPITALIZATION

D. Cicetti[1,2], G. Pierfelice[1,2], G. Pensalfine[1,2], R. Caprara[1,2], S. Vitale[1,2], S. Cavara[3], L. Appolloni[1,2], A. Stancari[1]

[1]IRCCS University Hospital Company - S.Orsola-Malpighi Polyclinic - Clinical Pharmacy, Bologna, [2]IRCCS University Hospital Company - S.Orsola-Malpighi Polyclinic - Department of Infectious Disease, Bologna, [3]Alma Mater Studiorum University of Bologna – Course of study in Pharmacy

Background: According to the guidelines published by AIFA in March 2023, the currently available drugs for the treatment of the COVID-19 infection are divided into symptomatic, including paracetamol and FANS, and drugs for specific stages of infection including two antiviral drugs, remdesivir (Veklury®) and the nirmatrelvir/ritonavir combination (Paxlovid®), monoclonal antibodies, corticosteroids, and low molecular weight heparins.
Aim: This study aims to analyze how early treatment using specific COVID-19 drugs allows to reduce or avoid hospitalization for associated COVID-19 complications in patients treated at our center from Jan 2022 to Mar 2023. For the early treatment of the coronavirus disease, three different drugs were available in Italy, of which, Veklury (administered by injection) within 7 days of the onset of symptoms with a three-day treatment, and two (administered orally) within 5 days, such as Paxlovid and molnupiravir (Lagevrio®). Following studies demonstrating lack of real clinical benefit, Lagevrio was discontinued form use in February 2023.
Methods and Materials: This retrospective study was performed examining patients who received the prescription of early Covid therapies in the Emergency room and in the Covid outpatient Department from Jan 2022 to early Mar 2023. An Excel database was subsequently created containing patients' comorbidities and then cross-reference tax codes with the hospital discharge form database.
Results: The study involved 2100 patients (1153 males and 947 females) with an average age of 71 years. 13% (n.272) were treated with Veklury, 26% (n.549) with Paxlovid, and 61% (n.1279) with Lagevrio. Only for 74 it is possible to hypothesize a correlation of hospitalization due to lack of efficacy of the drugs being within 10 days of the request date, of these 82% (n.61) were within 3 days. Of the hospitalized patients, 49 (66%) had one comorbidity, n.19 (26%) two and n.6 (8%) more than two. Specifically, the most frequently comorbidities encountered were: age ≥65 years (40%), cardio-cerebrovascular disease (14%) and chronic obstructive pulmonary disease (COPD) and/or other chronic respiratory disease (13%). Of the 12 patients who died, the most common risk factor was age>65 years (n.7). 64% (N.47) of hospitalized patients had a successful outcome.
Conclusions: The study shows how the use of early anti-COVID-19 treatments carried out from January 2022 to early March resulted in a limited number of hospitalizations. Of the 74 hospitalized patients, n.62 had a positive outcome, confirming how the use of these drugs has effectively led to an improvement in the disease even within the population considered "frail". Although the data obtained are positive, advanced age, the presence of concomitant pathologies that reduce the response capacity of the immune system, and the presence of one or more risk factors still today represent the main responsible for the progression of the disease towards a severe form.

COVID-19

P 144 IMPACT OF COVID PANDEMIC AND COVID DISEASE ON AGING TRAJECTORIES IN OLDER NURSING HOMES RESIDENTS IN ITALY

B. Manni[1], F. Romani[2], J. Milic[2], S. Renzetti[3], G. Dolci[4], S. Braglia[1], C. Mussi[5], C. Mussini[2,4], S. Calza[6], A. Fabbo[1], G. Guaraldi[2,4]

[1]Geriatric Service - Cognitive Disorders and Dementia Unit, Health Authority and Services of Modena, Italy, [2]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, Italy, [3]Department of Medical-Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Italy, [4]Infectious Diseases Clinic, Azienda Ospedaliero-Universitaria, Policlinico of Modena, Modena, Italy, [5]Geriatric Clinic, Biomedical Science, Metabolism and Neuroscience, University of Modena and Reggio Emilia, Modena, Italy, [6]Department of Molecular and Translational Medicine, University of Brescia, Italy

Background: The objective of this study was to describe changes in multimorbidity, polypharmacy, frailty, physical and cognitive function, and disability, in older nursing homes (NH) residents who had or did not have COVID between March 2019 and October 2020.

Methods: This was a retrospective, multicentric observational cohort study including residents of four NH, divided into two groups (COVID and non-COVID). Comprehensive geriatric assessment was performed at four time points: before (March 2019-T0 and October 2019-T1), during (May 2020-T2) and after (October 2020-T3) the first pandemic wave. Study outcomes comprised multimorbidity, polypharmacy, frailty, cognitive function, physical function, and disability. The effect of COVID-19 infection on changes in aging trajectories over time was tested through a mixed effect models.

Results: Out of 107 residents included in the study, 93 survived over all four time periods and 14 died, all in COVID group. At T0, median age was 83 years, 65 (69.9%) were females and 48 (51.6%) had COVID between T1 and T2. Isolation measures were applied on most residents (58, 62.4%). Figure 1 depicts trends over time derived from linear mixed models of clinical frailty scale (CFS) (1A), polypharmacy (1B), mini-mental state examination (1C), neuropsychiatric Inventory (1D), Tinetti scale (1E) and disability (ADL) scale (1F). Frailty was higher in the COVID group (vs. no COVID) at T3 (beta=0.498, p=0.05). Polypharmacy was significantly higher in the COVID group at T1 (beta=0.373, p=0.04), T2 (beta=0.654, p<0.001), T3 (beta=0.483, p=0.006). The Pearson correlation coefficient was used to explore correlations among different domains of comprehensive geriatric assessment. The association between Tinetti scale and CFS (r= 0.43) and Tinetti scale and MMSE (r=0.50) were moderate. Other associations were either very weak or weak. Global score is depicted in Figure 2A-D as polygon areas in which vertices are the normalized mean values of each health domain. Lower values are near the center, while higher values are towards periphery. It shows separately in COVID (Figure 2A-B) and no-COVID (Figure 2C-D) the areas at T0 and T3. It can be observed that the area of the polygon 2B is smaller than polygon 3A and describes that the global score is reduced comparing T3 to T0 in the COVID group. No change is observed in the polygon areas which describe the no-COVID group. Figure 2E depicts trends of global score over time. It shows a significant decline of global score in the COVID group from T3 to T0 (beta= -0.353, p=0.004). At T3, a significant trend difference was observed comparing COVID and no-COVID (beta= -0.450, p=0.05) (Figure 2).

Conclusion: We depicted an accelerating aging trajectory mainly in NH residents who survived COVID. However, physical function assessed by Tinetti scale worsened in both groups presumably as the results of confinement measures.

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COVID-19

P 145 USE OF A RAPID MOLECULAR MULTIPLEX REAL TIME PCR TEST FOR THE DETECTION OF SARS-COV-2, INFLUENZA A/B AND RESPIRATORY SYNCYTIAL VIRUS

C. Orlandi, M. Magnani, A. Casabianca

Department of Biomolecular Sciences, University of Urbino Carlo Bo, Italy

Background: The development of molecular syndromic panels that allow the simultaneous search for pathogens in the context of clinical infections represents an important opportunity for rapid virological diagnosis of respiratory infections.

Saliva has more recently entered the shortlist of clinical samples to which the current laboratory SARS-CoV-2 tests can be applied because the increasing evidence of comparable sensitivity and specificity to nasopharyngeal swabs.

In this retrospective study, starting from a single sample, we investigate the effectiveness of a multiplex PCR method by swab-based and saliva-based approaches.

Material and Methods: One hundred swab-samples (50 SARS-CoV-2 RNA positive and 50 SARS-CoV-2 RNA negative samples) collected between Nov-Dec 2021 and already tested by COVID-19 PCR DIATHEVA Detection kit (C-PCR), based on the WHO guideline [Corman et al. 2020] and 10 saliva-samples collected on March 2023 were analyzed by COVID-FLU-RSV All-in-One RT PCR (CFR-multiplexPCR) following manufacturer instructions. Starting from the extracted RNA, a single reaction of reverse transcription and specific amplification for SARS-CoV -2, Flu A/B, RSV A/B and the endogenous control RNaseP is carried out. The endogenous control is used to monitor the adequacy of the sample, the RNA extraction process and the presence of PCR inhibitors. The target regions and the fluorophores used for every specific pathogen are in Table 1.

Results: All samples had a valid result with a mean (SD) RNAseP ct value of 24.63 (2.15). All SARS CoV-2 positive samples had a confirmed positive test with a mean (SD) ORF1b/N ct value of 24.83 (6.87) [range 15.90 -37.39] higher than the RdRp ct value from the first analysis (mean 26.80 (7.26) range 16.48-42.51). None of SARS-CoV-2 positive samples had co-infection with the other respiratory viruses. Among the 50 negative SARS CoV-2 samples, two had a positive result although with a high ct value (33.25 and 34.02). Among the 10 saliva samples, two resulted SARS-CoV-2 positive with a ct value of 38,6 and 23.54, with the latter presenting severe infection symptoms.

Conclusions: The results obtained showed the detection of the SARS-CoV-2 RNA in 4% of samples previously tested negative demonstrating increasing sensitivity of the CFR-multiplexPCR compared to C-PCR. The detection of SARS-CoV-2 RNA in 20% of saliva samples showed that the SARS-CoV-2 virus circulation is still present at the end of the flu seasonal 2022-2023.These preliminary experiments are part of a study for the monitoring of respiratory viruses started in March 2023 and prolonged to the flu season 2023-2024 which involves a voluntarily cohort of University workers.

The implementation of molecular methods with syndromic panels has the potential to be a powerful decision-making tool for the rapid differential diagnosis of SARS-CoV-2, Flu A/B and RSV A/B in nasopharingeal and saliva samples in combination with other clinical and epidemiological data of patients.

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COVID-19

P 146 ACTIVE METABOLITE OF ERDOSTEINE (MET-1) INHIBITS SARS-COV-2 INFECTION AND MODULATES INFLAMMATORY STATE IN A549 CELLS

S. Strizzi[1], F. Danzo[2], C. Vanetti[1], M. Biasin[1], D. Radovanovic[2], P. Santus[2], D. Trabattoni[1]

[1]Department of Biomedical and Clinical Sciences, Università degli Studi di Milano, Milan, Italy, [2]Department of Biomedical and Clinical Sciences, Università degli Studi di Milano, Division of Respiratory Diseses, University Hospital "L. Sacco", Milan, Italy

Background: The decrease in the antioxidant Glutathione (GSH) content characterizes several viral infections, suggesting that maintenance or restoration of GSH levels may be a novel potential therapeutic approach for these diseases. Unfortunately, a limit to GSH use as a therapeutic agent is given by its biochemical and pharmacokinetic properties. Thus, other molecules have been proposed to restore or increase GSH levels. Among these, Erdosteine and its active metabolite MET-1 seem to have a rationale in the treatment of patients affected by respiratory viruses as SARS-CoV-2.

Aims: The main objective of this study was to evaluate effects of Erdosteine and its active metabolite (MET-1) in SARS-CoV-2 infection.

Methods: Viral infection assay on A549 cell line has been set up adding Erdosteine or MET-1 at different doses (100mg/mL and 1000mg/mL) before and after infection with SARS-CoV-2 (EU, lineage B.1) at a concentration of 1,26 TCID50/µL. Viral replication in culture supernatant was assessed by qPCR method at 48h post-infection (hpi) and Reverse Transcription-PCR was performed on cell lysates at 72h post-infection (hpi) focusing on different target in order to evaluate immune state modulation. Finally, inflammatory and anti-inflammatory cytokine/chemokine production was analysed in cell culture supernatants by a Multiplex Immunoassay.

Results: Post-treatment with 1000µg/mL of MET-1 showed a statistically significant antiviral effect (p= 0.006) against SARS-CoV-2. Furthermore, it has been reported a statistically significant reduction in IL-6 (E1000: p= 0.02), IL-8 (E1000: p= 0.03), IFN-gamma (E1000 and M1000: p>0.001), MCP-1 (E1000: p>0.001), and MIP-1beta (E1000: p<0.001 and M1000: p=0.01) production. No significant effects were observed in pre-treatment condition with both Erdosteine or MET-1. Results from the analysis of intracellular transcripts confirmed a reduction in IL-8 (M1000: p= 0.04) expression and reported a reduction of BCL-2 level (E1000: p= 0.04, M100: p= 0.03, M1000: p= 0.02).

Conclusions: Erdosteine active metabolite (MET-1) has proven to have an antiviral effect, thus confirming the possibility to use this compound as an adjuvant agent against SARS-CoV-2. Further analysis is planned in order to understand the transcriptomic response of cells to the drugs and to evaluate the antiviral effect on other viruses, such as H1N1.

COVID-19

P 147 SARS-COV-2 INFECTION IN CHIMERIC ANTIGEN RECEPTOR T CELL PATIENTS

E. Metafuni[1], I. Pansini[2], F. Sorà[1,2], E. Galli[1], A. Cingolani[3,4], M. Fantoni[3,4], F. Frondizi[4], S. Giammarco[1], R. Santangelo[1,5], N. Piccirillo[1,2], L. Teofili[1,2], E. Maiolo[1], S. Hohaus[1,2], P. Chiusolo[1,2], S. Sica[1,2]

[1]Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome (IT), [2]Sezione di Ematologia, Dipartimento di Scienze Radiologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Rome (IT), [3]Dipartimento di Sicurezza e Bioetica, Università Cattolica del Sacro Cuore, Rome (IT), [4]Dipartimento di Scienze di Laboratorio e Infettivologiche, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome (IT), [5]Dipartimento di Scienze di Laboratorio e Infettivologiche, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome (IT)

Background: Chimeric Antigen receptor T cell (CAR-T) therapy emerged as potentially curative for around 45% of patients with some relapsed/refractory B-cell malignancies and has spread worldwide in the same years of Sars-CoV-2 pandemic. CAR-T cell therapy increases the risk of poor outcome for Sars-CoV-2, due to long-lasting immune impairment. Few studies reported infection outcomes for these patients, what emerged is a high hospitalization and mortality rate.

Material and Methods: CAR-T cell infusion has been performed on 46 patients from September 2019 to December 2022.

At the follow-up time fixed on February 2023, 74% of them were alive. Sars-CoV-2 diagnosis was made with RT-PCR on nasal swab using AllplexTM SARS-Cov-2 Assay kit (Seegene Inc).

Results: Eighteen Sars-Cov-2 infection cases were recorded in 15 patients. There was no difference in the infection rate according to sex, instead it resulted lower among older patients (58 vs. 47 years, p=0.04). A reduced infection rate was registered among patients who had received pre-exposure tixagevimab/cilgavimab (21% vs. 45%, p=0.07). Median age at infection was 47 years. Three patients experienced Sars-Cov-2 twice after CAR-T cell infusion. Disease status was complete remission in 66.7% cases, partial response in 20% and progressive disease in 13.3%.

Median number of previous therapy lines was 3.5 at the Sars-Cov-2 positivity. Median time from last therapy to infection was 5.5 months. The 86.7% of patients had received at least the primary two-doses schedule of vaccine against Sars-Cov-2. The most frequent symptom at diagnosis was fever 55.6%. Asymptomatic infection occurred in 27.7% cases.

In 3 cases (16.7%) a lower respiratory tract infection was documented. Two of them required hospitalization due to Sars-Cov-2 pneumonia requiring moderate oxygen support in one case. Two of them survived while the last died due to underlying disease progression.

Thirteen Sars-Cov-2 infection cases received ad hoc treatment: Molnupiravir 15%, Casirivimab-Imdevimab 15%, Nirmatrelvir plus Ritonavir 39%, Sotrovimab 15%, Remdesivir 8%, Remdesivir pus Nirmatrelvir and Ritonavir 8%.

The 20% of patients died, at the follow up time fixed on February 2023 (80% alive).

After CAR-T cells infusion, the median time of first Sars-Cov-2 positivity was of 5 months from the last treatment.

Three patients of our cohort contracted Sars-Cov-2 infection before CAR-T cells infusion, and again after 3, 1 and 9 months from infusion, respectively.

Conclusions: Although patients submitted to CAR-T cell therapy represent a high-risk population for infectious complications and mortality, our experience showed a less catastrophic picture than previous reported. None of the patients died because of Sars-Cov-2 infection. Given the lack of laboratory data, we cannot assess if our results depended on previous vaccination, pre-exposure tixagevimab/cilgavimab prophylaxis or on prevalence of mild Sars-Cov-2 infection.

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COVID-19

P 148 ALPHA-SYNUCLEIN MULTIMER/MONOMER RATIO IS AN IMPORTANT DETERMINANT OF TYPE-I INTERFERON RESPONSE AGAINST SARS-COV-2 INFECTION

F. Limanaqi[1,2], S. Zecchini[2], I. Saulle[1,2], S. Strizzi[2], C. Vanetti[2], M. Garziano[1,2], G. Cappelletti[2], D. Parolin[2], S. Caccia[2], D. Trabattoni[2], C. Fenizia[1,2], M. Clerici[1,3], M. Biasin[2]

[1]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [2]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [3]IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy

Background: Recent evidence in West Nile and Venezuelan equine virus infections indicates that alpha-synuclein (a-syn), a hallmark of synucleinopathies, induces anti-viral innate immunity by acting as an Interferon-Stimulated Gene (ISG). However, its role in SARS-CoV-2 infection remains unclear. Beyond the brain, a-syn is expressed in a variety of human tissues that are potentially susceptible to SARS-CoV-2 infection and/or related sequelae. Here, we investigate the role of a-syn and its dynamic conformations in relation with Type-I Interferon (IFN) response in the frame of SARS-CoV-2 infection in peripheral cells.

Methods: Human epithelial lung cells (A549, CaLu-3), and umbilical vein endothelial cells (HUVECs) were treated with IFN-b (500 IU/ml) and/or a-syn monomers (1uM) for 24h. Cells were Mock- or SARS-CoV-2-infected and cultured for 48h. In another set, A549 cells were treated with Non-Targeting (NT) or synuclein-alpha(SNCA)-siRNA for 24h, and infected as above. Supernatants and/or cells were processed for i)Quantification of viral titers through RT-qPCR; ii)mRNA expression of ISGs by qPCR; ii)WB for a-syn quantification; iii)Immunofluorescence for a-syn and SARS-CoV-2 proteins detection. Cells were differently fixed and permeabilized for the detection of monomeric (4% PFA 15 min, 0.1% Triton 100X 10 min) vs multimeric a-syn species (4% Formaldehyde solution 15 min, 0.3% Triton 100X 15 min). MTT and Trypan Blue were employed to assess cell viability.

Results: SNCA-siRNA promoted viral replication, while the antiviral effect of IFN-b was associated with increased a-syn levels in epithelial lung cells. The beneficial role of a-syn was limited to multimeric a-syn species, and multimer/monomer ratio. In fact, SARS-CoV-2 reduced multimeric but not monomeric a-syn, which was instead prevented by IFN-b. Again, in SARS-CoV-2-infected cells treated with a-syn monomers, a dramatic reduction in multimer/monomer a-syn ratio was associated with increased SARS-CoV-2 replication and reduced ISG expression. These effects were once again prevented by IFN-b rescuing multimer/monomer a-syn ratio. Cell viability assays ruled out a toxic nature of IFN-b-induced a-syn multimers. Finally, in endothelial cells displaying abortive SARS-CoV-2 replication, a-syn multimers and multimer/monomer ratio were not reduced following either exposure to the virus or exogenous a-syn, suggesting that only productive infection alters a-syn multimer/monomer equilibrium.

Conclusions: a-Syn multimers and the multimer/monomer equilibrium modulate the innate immune response against SARS-CoV-2 infection, with the promotion of non-toxic a-syn multimers likely sustaining the beneficial effects of Type-I IFNs. Our study provides novel insights into the immunobiology of a-syn, and its potential suitability as a peripheral biomarker in infectious diseases. Further studies are needed to replicate our findings in neuronal cells and to ascertain the nature of such a-syn conformations.

COVID-19

P 149 EARLY SARS-COV-2 TREATMENT IN SOLID ORGAN TRANSPLANT RECIPIENTS: A SINGLE-CENTRE RETROSPECTIVE COHORT STUDY DURING THE OMICRON ERA

E. Milozzi[1], V. Mazzotta[1], A. Caioli[1], E. Biliotti[1], L. Loiacono[1], A. Rianda[1], R. Libertone[1], A. Mariano[1], D.R. Donno[1], P. De Paolis[2], A. Antinori[1], G. D'Offizi[1]

[1]INMI L. Spallanzani, Rome, [2]A.O.S. Camillo-Forlanini, Rome

Solid organ transplant recipients (SOTRs) had a risk of COVID-19-related hospitalization or death four-time greater than the immunocompetent population. Data on early treatment for mild-to-moderate COVID-19 in SOTRs is limited. The aim of the study was to evaluate clinical outcomes (hospitalization and death) and safety of early SARS-CoV-2 treatment in SOTRs.

Single-center, retrospective study including consecutive SOTRs with a laboratory-confirmed diagnosis of symptomatic SARS-Cov-2 infection, enrolled within the early treatment access program of Lazzaro Spallanzani Institute, between January and November 2022. All patients were followed for 30 days after treatment. Primary outcome was COVID-19-related hospitalization/death; secondary outcome was to assess median time from treatment start to first negative nasopharyngeal (NF) swab. Adverse events were recorded. Continuous variables were compared between the two groups by the t-test or the Mann-Whitney U-test. Predictors of viral clearance were evaluated by fitting univariate and multivariate linear regression.

A total of 91 SOTRs were included (58 kidney; 20 liver; 10 heart; 2 liver/kidney; 1 kidney/heart), 62.6% (57/91) were males, mean age was 54.9 ± 13.5 years, mean BMI was 24.5 ± 3.6 Kg/m2, mean e-GFR was 52 [38.9-72.1] mL/min/1.73m2, median ALT levels were 18 [12-33] U/L. The median time from onset of symptoms to treatment starting was 3 [2-4] days. All patients except three were vaccinated. Early treatment consisted of sotrovimab 65.9%, tixagevimab/cilgavimib 3.3%, casirivimab/imdevimab 2.2%, bamlanivimab/etesemivab 5.5%, remdesivir 4.4%, molnupiravir in 17.6% and nirmaltrelvir/ritonavir 1.1%. All patient except one completed treatment, 1 case treatment with molnupinavir was discontinued due to gastrointestinal intolerance. Rate of hospitalization within 30 days of initiating treatment was 2.2%. Two patients were hospitalized due to pneumonia, one in the sotrovimab and one in the molnupinavir group, no oxygen supplementation was needed. No death for all causes occurred. The median time from treatment starting to first negative swab was 13 [9-17.7] days. On univariate and multivariate linear regression, age, sex, number of comorbities, type of transplant or immunosuppressive therapy and SARS-Cov-2 treatment were not found to be significantly associated with viral clearance. No significant increase in ALT levels (18 [12-33] vs 17 [12-26] U/L, p=0.19) and e-GFR 52 [38.9-72.1] vs 57.6 [44.3-71.3] mL/min/1.73m2, p=0.14) occurred from baseline to day 7 after starting treatment.

Our single-center study demonstrates the good efficacy profile of early SARS-CoV-2 treatment in vaccinated SOTRs in the Omicron era, a fragile population generally excluded from randomized clinical trials. The study also demonstrates the optimal kidney and liver safety profile of early treatment in SOTRs. The limitations of the study are the lack of a control group, the retrospective design and the short follow-up.

COVID-19

P 150 CHARACTERIZATION OF THE SECOND, THIRD AND FOURTH WAVE OF COVID 19 OCCURRING IN CAMPANIA: RESULTS OF A COHORT STUDY

R. Palladino[1], A. Russo[1], M. Pisaturo[1], P. Maggi[2], F.G. Numis[3], I. Gentile[4], C. Sagnelli[1], V. Sangiovanni[5], V. Esposito[6], R. Punzi[7], G. Calabria[8], R. Pisapia[9], A. Salomone Megna[10], A. Masullo[11], E. Manzillo[12], R. Parrella[13], G. Dell'Aquila[14], A. Ponticiello[15], C. Camaioni[5], N. Coppola[1] Covicamp group

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [2]Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, Italy, [3]Emergency unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, [4]Infectious disease unit; University Federico II, Naples, Italy, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [6]IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [8]IX Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [9]First Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [10]Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, [12]VIII Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [13]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [14]Infectious Diseases Unit, AO Avellino, Italy, [15]Pneumology Unit, AORN Caserta, Italy

Aims: The aim of this study is to analyze the demographic and clinical characteristics of patients hospitalized for COVID-19 in the four waves in Campania, a region of southern Italy

Methods: We conducted a multicenter observational cohort study involving patients hospitalized during the four waves until November 2022 in different COVID-19 Units of Campania. All adult (≥18 years) patients, hospitalized with a diagnosis of SARS-CoV-2 infection confirmed by a positive RT-PCR on a naso-oropharyngeal swab were enrolled.

Results: 1623 COVID-19- hospitalized patients were enrolled during the second and third waves and 264 were enrolled in the fourth wave of the SARS CoV2 epidemic in Campania.

Patients of 4th wave had a greater severe clinical presentation (84,5% P=0.000), the lenght of hospitalization expressed in days was greater during the 2ndand 3rd waves [Median (Q1-Q3): 14 (11) vs 11 (11) respectively, P=0.000)] and also mortality during hospitalizzation was similiar among the different waves: 9,7% vs 9,2% respectively (p= 0,796). Deaths were more frequently male in the second and third waves (54% vs 40% p = 0.161).

Charlson comorbidity index was worse in the fourth wave than in second and in third wave [median, (IQR): 5(3) and 3(4), respectively, P = 0.000].

Comparing death patients from the different waves: hypertension, cardiovascular disease and diabetes were more frequent. Dementia was more frequent in dead patients in fourth [46,7% p=0,03] wave while chronic kidney failure [23,5% p=0,413] and obesity [17,4 p=0,014] were more frequent among patients in 2ndand 3rd.

Conclusions: Our multicenter study showed a cross-sectional view of what the covid 19 pandemic represented in Campania, a densely populated region in southern Italy. It is a large cohort of patients hospitalized for COVID-19 in Covid centers and therefore we believe that it is representative of the cases of our Region.

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COVID-19

P 151 ANTI-SARS-COV-2 HUMORAL AND CELLULAR IMMUNE RESPONSES IN HEALTH CARE WORKERS 4 MONTHS AFTER A 4TH VACCINATION WITH THE PFIZER-BIONTECH BIVALENT VACCINE

C. Stefani[1], M. Iannetta[2], L. Benedetti[2], A. Matucci[3], L. Ferrari[2], L. Sarmati[2], D. Zipeto[1], C. Piubelli[3], A.M. Geretti[1,4,5], A. Ruggiero[1], EVAN-COV Study Group

[1]Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy, [2]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, [3]Department of Infectious, Tropical Diseases and Microbiology, IRCCS Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy, [4]Infectious Diseases Unit, Fondazione PTV, University of Rome Tor Vergata, Rome, Italy, [5]School of Immunity and Microbial Sciences, King's College London, London, United Kingdom

Background: In 2022, healthcare workers (HCWs) in Italy were advised to receive a 4th SARS-CoV-2 vaccine dose using a Wuhan/Omicron bivalent formulation. We studied SARS-CoV-2 specific humoral and cellular immune responses in a prospective HCW cohort that received the Pfizer-BioNTech bivalent booster vaccine, exploring the use of a SARS-CoV-2 interferon-g (IFN-g) release assay (IGRA) to measure cellular immunity.
Methods: HCWs were recruited at the Ospedale Don Calabria (Negrar, Verona). We quantified anti-spike IgM (IgM-S) and anti-spike receptor binding domain IgG (IgG-S-RBD) using the Abbott chemiluminescence immune assays. For the IGRA, whole blood was incubated overnight with the Miltenyi Biotec SARS-CoV-2 N (nucleocapsid) and S1+S2 (spike, S) overlapping peptides; a positive (PHA-stimulated) and a negative (non-stimulated, NS) control was included for each patient. IFN-g (pg/ml) was quantified on the ELLA platform; levels for stimulated conditions were calculated after subtraction of NS values.
Results: To date, we recruited 16 HCWs (10/16 male, median age 48 years [IQR 38-55]), including 10/16 (63%) that had received a COVID-19 diagnosis at some time before the 4th vaccine dose (pC19 group). None of the participants received a COVID-19 diagnosis in the 18 weeks following the 4th vaccine dose. At 18 weeks (IQR 17 -18), all participants had detectable IgG-S-RBD with a median value of 3.6 log10 BAU/mL (IQR 3.5-3.7). In addition, 2/16 (13%) had measurable IgM-S (IgG-S-RBD titres 3.6 log10 BAU/mL for both of them). All also showed IFN-g responses after stimulation with N peptides (median 1.5 log10 pg/ml [IQR 0.9-1.6]) and S1+S2 peptides (median 2.5 log10 pg/ml [IQR 2.3-2.7]), with higher median IFN-g levels induced by S1+S2 than N ($p<0.0001$, Wilcoxon matched-pairs signed rank test; Fig.1A). Participants with a previous COVID-19 diagnosis showed a trend for higher IFN-g responses to N but not to S1+S2 peptides compared with those without a diagnosis (Fig.1B, Mann Withey test); there was no difference in IgG-S-RBD levels. It was no correlation between IgG-S-RBD titres and S-specific IFN-g levels (rho 0.15; $p=0.6$).
Interpretation: In this ongoing prospective cohort, all participants had detectable SARS-CoV-2 specific humoral and cellular immune responses 4 months after the 4th vaccination. It was possible to detect anti-spike IgM in two participants and significance is being evaluated in follow-up. Further studies are needed to establish the utility of the SARS-CoV-2 IGRA test to inform management of infection and vaccination in healthy populations.

Figure 1 caption. IFN-g release after stimulation with nucleocapsid (N) or spike (S1+S2) overlapping peptides, overall (A, n=16) and according to a history of COVID-19 diagnosis prior to the 4th vaccination (B, n=10 with a diagnosis [pC19] and n=6 without [No pC19]).

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COVID-19

P 152 ANALYSIS OF T CELL RECEPTOR REPERTOIRE IN VACCINATED AND UNVACCINATED COVID-19 PATIENTS

E. Vecchio[1], S. Rotundo[2], C. Veneziano[1], L. Berardelli[2], S. Palma Gulli[2], S. Mongiardi[2], A. Abatino[3], I. Aversa[3], R. Gallo[3], C. Giordano[3], A. Russo[2], E.M. Trecarichi[2], C. Torti[2], C. Palmieri[3]

[1]Interdepartmental Centre of Services, "Magna Graecia" University of Catanzaro, Italy, [2]Department of Medical and Surgical Sciences, Chair of Infectious and Tropical Diseases, University "Magna Graecia", Catanzaro, Italy, [3]Department of Experimental and Clinical Medicine, University "Magna Graecia", Catanzaro, Italy

Background: The emergence of SARS-CoV-2 variants of concern (VoCs) is a significant public health challenge due to increased transmissibility and potential immunity evasion.
Previous studies demonstrated the capability of T-cell receptor (TCR) repertoire analysis to identify conserved and immunodominant peptides with cross-reactive potential among VoCs, predicting disease severity to inform treatment strategies and guiding vaccine development. However, there is a need to extend the analysis of the TCR repertoire to different clinical scenarios.
The aim of this study was to uncover the differences in TCR specificity between natural and breakthrough infections.
Materials and Methods: This study was carried out at "Mater Domini" University Hospital of Catanzaro. 14 patients with mild to severe COVID-19 from January 24th, 2022 to July 7th, 2022 were enrolled (during the Omicron wave).
We conducted high-throughput TCRβ chain sequencing on peripheral blood samples from both vaccinated (V) and unvaccinated (NV) COVID-19 patients. TCR repertoires clonal expansion in COVID-19 patients was compared to that of 14 individuals from the TCRB-V4b Control Database matched for age, gender and ethnicity.
Results: Patients (V) with breakthrough infections had less diversity and homogeneity, and greater clonality in their TCR repertoires than NV COVID-19 patients confirming the role of vaccination in shaping the repertoire towards greater clonality and less diversity (Figure A).
In breakthrough infections the TCR repertoires showed a higher degree of convergence, indicating a more focused and specific immune response. Moreover, we observed an enrichment of public TCR sequences, which may contribute to the protection afforded by vaccination (Figure B).
The analysis of epitope specificity showed that distinct S protein regions were preferentially associated with TCRβ from V or NV groups (Figure C). The more relevant was the S672-687 region, distinctly associated with TCRβ clusters of the NV group. Some authors suggested that the S672-687 region is endowed with superantigen properties contributing to severe immune responses. Finally, an in-silico analysis of TCRβ binding probability showed that Omicron variants in the S365-378 and S975-987 regions increased the peptide binding probability score of the associated TCRβ clonotypes, while variant in the S673-696 region did not affect the peptide binding probability (Figure D).
Conclusions: These results reinforce the hypothesis that viral variants have a minor impact on the efficacy of T cell responses. Overall, our findings reveal significant differences in TCR specificity between natural and breakthrough infections and identified unique TCR signatures associated with disease severity, providing insights into the potential factors influencing clinical outcomes.

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COVID-19

P 153 RISK FACTORS OF PROLONGED SARS-COV-2 INFECTION IN PATIENTS WITH MILD SYMPTHOMS, A RETROSPECTIVE ANALYSIS

F. Milite, A. Russo, M. Pisaturo, S. De Pascalis, C. Sagnelli, N. Coppola

Department of Mental and Physical Health and Preventive Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy

Objectives: The aim of this study is to conduct a monocentric retrospective observational analysis from 01/30/2021 to 01/27/2023, to evaluate the effectiveness of early therapies such as Molnupiravir, mAbs, Nirmatrelvir/Ritonavir, and Remdesivir in clinical and virological terms for patients affected by high-risk COVID-19.
Methods: We performed a monocentric retrospective study involving the Infectious Disease Unit of University of Campania. All adults (>18 years old) patients who performed an early antiretroviral treatment for COVID-19, and presented the date of first positive test and first negative test to SARS-CoV-2 were included in the study.
Results: At our Unit 429 patients performed early treatment 332 presented data on first positive test and first negative test. Patients were divided in three groups: the first included all patients with a time to negativization <10 days, the second group included patients with a time to negativization included from 10 to 17 days, the third included patients with time to negativization more than 17 days. Considering the analysis patients in the third group were less vaccinated (81.2% vs 89% vs 97.8%), and were more frequently affected by immune-deficency (42% vs 19.2% vs 22%) and were more frequently affected by moderate chronic kidney disease (23.8% vs 5.9% vs 2.6%). The ordered regression performed considering age >65 years, vaccination, case of immune-deficency, and treatment with monoclonal antibody highlighted that immune-deficency (OR 3.226 95%CI 1.646-6.324) was a risk factor for the increase of time to negativization, and patients vaccinated (OR 0.39 95%CI 0.17-0.88) showed less time to negativization.
Conclusions: In our observational retrospective study included 332 patients underwent to an early treatment drug for COVID-19 showed that vaccination was able to reduce time to negativization (OR 0.39, p=0.024), and immune deficiency was a risk factor able to increase time to negativization (OR 3.226, p=0.001).

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COVID-19

P 154 IMPAIRED NEUTRALIZING ANTIBODY EFFICACY OF TIXAGEVIMAB-CILGAVIMAB 150+150 MG AS PRE-EXPOSURE PROPHYLAXIS AGAINST OMICRON BA.5 IN BOOSTER VACCINATED IMMUNOCOMPROMISED PATIENTS AT THE INFECTIOUS DISEASES CLINIC OF PERUGIA

E. Schiaroli[1], A. Gidari[1], G. Brachelente[2], G. Bicchieraro[3], R. Spaccapelo[4], S. Bastianelli[1], S. Pierucci[1], C. Busti[1], C. Pallotto[1], L. Malincarne[1], B. Camilloni[5], G.V. De Socio[1], A. Villa[2], A. Mencacci[5], D. Francisci[1]

[1]Clinic of Infectious Diseases, Department of Medicine and Surgery, University of Perugia, Perugia, Italy, [2]Clinical Pathology and Ematology, Santa Maria della Misericordia Hospital, Perugia, Italy, [3]Genomics and Genetics Section, Department of Medicine and Surgery, University of Perugia, Perugia, Italy, [4]Functional Genomic Center (C.U.R.Ge.F), Department of Medicine and Surgery, Genomics and Genetics section Department of Medicine and Surgery, University of Perugia, [5]Microbiology and Clinical Microbiology, Department of Medicine and Surgery, University of Perugia, Perugia, Italy

Background: Vulnerable individuals are prone to more severe SARS-CoV-2 infections, an increased risk of hospitalization, complications and associated mortality regardless of the underlying pathologies as well as of long lasting infections with a longer viral shedding and possible intra host mutations.
Tixagevimab-cilgavimab as primary pre-exposure prophylaxis in immune-compromised subjects as support of or replacement for vaccination was approved by FDA on December 2021 and by EMA on March 2022, even though Omicron Variants of Concern (VOCs) were prevailing at that time.
Aim of our study was to evaluate the post injection neutralizing activity (NT90-Abs titer) against the Omicron BA.5 which was at that moment the prevailing one in fully vaccinated immunocompromised subjects who had undergone tixagevimab-cilgavimab 300 mg as pre-exposure prophylaxis .
Methods: Between July and August 2022 fifty four frail patients, negative for an incoming infection, underwent a pre-exposure anti-SARS-CoV-2 prophylaxis with tixagevimab-cilgavimab 300 mg i.m. at the Day Hospital of the Infectious Diseases Clinic of Perugia.
All had already been vaccinated but were suffering from diseases that, according to Italian Medicine Agency (AIFA) criteria eligibility, could compromise vaccination efficacy.
We took serial venous blood samples after the injection, in order to measure their neutralizing activity against the currently prevailing viral variants.
NT90-Abs titers against BA.5 and 20A.EU1 as well as anti-Spike and anti-receptor-binding domain IgG were evaluated at 0, 14 and 30 days. The primary end point was NT90-Abs titers ≥ 80 against BA.5 in ≥ 25% of individuals and the secondary was NT90-Abs titers ≥ 1280 against 20A.EU1 in over 50% of the subjects at day 14.
Results: At baseline 35·2%, 37,02%, 32,5% of boosted vaccinated patients had undetectable anti-S and anti-RBD IgG antibodies such as NT90-Abs titers against A20.EU1, respectively. Moreover, 61,5% had undetectable NT90-Abs titers against BA.5. Afterwards, at day 14 IgG anti-S and anti-RBD were 3880 BAU/ml and 776·6 AU/ml, respectively (Fig.1). Only 12·5% of the patients met a NT90-Abs titer ≥ 80 against BA.5, whereas the median NT90-Abs titer against 20A.EU1 was 1280. NT90-Abs titers against BA.5 were 64 times lower than against A20. EU1 (Fig.2). Four patients (7,5%) had a SARS-CoV-2 infection in the following three months, all with a long gap between the booster vaccination and injection.
Conclusions: To date, tixagevimab-cilgavimab can't be considered a substitute for vaccination but might be a useful support if the recommended dose for pre-exposure prophylaxis is doubled and if the next variants will be at least partially susceptible.

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COVID-19

P 155 A REFINE ANALYSIS ON SARS-COV-2 OMICRON VARIABILITY IN INFECTED IMMUNOCOMPROMISED INDIVIDUALS

M.C. Bellocchi[1], L. Carioti[1], G. Marchegiani[1], L. Coppola[2], M. Iannetta[2], L. Duca[1], A. Di Lorenzo[2], L. Alborghetti[2], L. Piermatteo[1], V. Malagnino[2], L. Benedetti[1], M.M. Santoro[1], M. Andreoni[2], L. Sarmati[2], F. Ceccherini-Silberstein[1]

[1]University of Rome Tor Vergata, Rome, Italy, [2]University Hospital of Rome Tor Vergata, Rome, Italy

Background: We aim to characterize SARS-CoV-2 omicron variability with a focus in immunocompromised patients (IPs).
Methods: This retrospective study includes SARS-CoV-2 infected hospitalized and non-hospitalized IPs (HIP/NHIP) and non-IPs (HP/NHP). Nasopharyngeal swabs (NS) were collected over Jan-Dec 2022 and SARS-CoV-2 genome sequences were obtained by Miseq-platform. Additional mutations (AMs) (intra-host prevalence>20%) not present in sublineage consensus, were analyzed in spike, nucleocapsid and nonstructural proteins (RNA-dependent RNA polymerase, main-protease, papain-like-protease, helicase, Orf6 and Orf9b).
Results: 211 SARS-CoV-2 omicron infected individuals (126 NHIP, 12 HIP, 57 NHP, 16 HP) were characterized: 49.8% were female, with a median [IQR] age of 61[50-72] yrs and 10.0% reporting no SARS-CoV-2 vaccination (Tab.1). IPs were younger (median[IQR]yrs: 58[48-69] in HIP+NHIP vs 67[53-77] in HP+NHP, p= 0.0015). Different rate of pneumonia was observed, particularly higher in HP (0%, 0%, 58.0%, 93.8% in NHIP, NHP, HIP, HP, respectively p<0.001) and higher frequency of no-vaccination was observed in hospitalized patients (37.5% HP, 25% HIP, vs 8.8% NHP and 5.6% NHIP, p<0.001).
Overall, 34 different Omicron sublineages were identified: BA.1.1(21.3%) the most prevalent, followed by BA.1/BA.2(17.5%), BA.2.9(7.6%) and BA.5.1(3.8%), without any significant different prevalence among the groups (Fig.1). About AMs analysis, 60.7% of individuals showed ≥ 1 AM, in ≥1 of the analyzed genes. A different prevalence of AMs in NHIP,HIP,NHP,HP groups was found only in spike (17.5%, 33.3%, 7%, 25%, p=0.041) and in the receptor binding domain (RBD, 3.9%, 16.7%, 0%, 12.5% p=0.015), respectively. Higher prevalence of AMs was observed in hospitalized (HIP+HP) vs non-hospitalized individuals (NHIP+NHP) in both spike (28.5% vs 14.2%, p=0.054) and RBD (14.3% vs 2.7%, p=0.019). These results correlate with the Δ days from first COVID-19 symptoms to NS sampling, that were significantly longer in hospitalized patients (median [IQR] days: 9[7-12] in HP vs 5[3-8] in HIP vs 4[3-5] in NHIP vs 4[3-5] in NHP p<0.001).
About innate response genes, in Orf6, the D61L mutation (typical of BA.2 or BA.4) was found with an overall prevalence of 36.5%. Its presence (as BA.2 and BA.4 infection) was higher in IPs (41.3% in HIP+NHIP vs 23.4% in HP+NHP,p=0.046) and less in hospitalized patients (17.8% in HIP+HP vs 39.3% in NHIP+NHP,p=0.028). In IPs, a higher prevalence of AMs in Orf9b was found in hospitalized patients (16.7% in HIP vs 2.4% NHIP,p=0.06).
AMs associated with resistance to mAbs (346K/446D/452R/445L/460KS) were found only in HIP and/or NHIP, while none of AMs associated with resistance to molnupiravir and nirmatrelvir was observed in the cohort.
Conclusion: We confirmed a higher variability in IPs, particularly when hospitalized. These results deserve further investigation in a larger population, specifically for Orf6 and Orf9b genes related to the innate antiviral response.

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COVID-19

P 156 A DATA-DRIVEN IDENTIFICATION OF PASC CLUSTERS TO PREDICT RECOVERY

F. Motta[1], V. Guidetti[1], J. Milic[1], A. Cattelan[2], S. Cavinato[2], M. Belli[3], V. Menozzi[1], M.D. Di Trapani[1], S. Esperti[1], G. Mancini[3], C. Mussini[1,3], F. Mandreoli[1], G. Guaraldi[1,3]

[1]Università degli Studi di Modena e Reggio Emilia, Modena, Italy, [2]Azienda Ospedale Università Padova, Padua, Italy, [3]Azienda Ospedaliero Universitaria di Modena, Modena, Italy

Background: This study aims to characterize post-acute sequelae COVID-19 (PASC) clusters obtained using machine learning techniques, such as topic modelling and clustering, and to predict PASC recovery at 1-year follow-up.

Methods: This is a prospective multi-center study collecting incident symptoms, clinical variables including: demographics, anthropometric, physical performance measures, frailty, lifestyle and patient reported outcomes data collected at 90-270 days after COVID-19 and at 1-year follow-up. We stratified patients into 3 periods by infection time: period A (02/20-02/21), period B (03/21-12/21), period C (01/22-11/22). Inclusion criteria was PASC diagnosis, defined as ≥1 of a list of 31 symptoms. We performed topic modelling to condensate, in a data-driven way, symptoms into a parsimonious set of domains. Patients can belong to multiple domains with different probabilities. This makes it possible to synthesize different symptom scenarios without enforcing a strict partitioning of the symptoms into the clusters. Clinical variables and symptoms were clustered using KNN method. Logistic regression was used to identify PASC recovery predictors. Multiple PASC recovery definitions were explored using follow-up data available for only period A and B, using a composite of: symptoms' resolution, quality of life improvement, and return to health status prior to COVID-19 using clinical frailty scale.

Results: A total of 995 patients (707, 231 and 57 in periods A, B and C respectively), 59% males, mean age 60 years, 50% previously hospitalized, were analyzed. 4 major data driven symptoms' domains were identified: (1) Respiratory: dyspnea, anosmia, fatigue; (2) Gastrointestinal: diarrhea, appetite loss, abdominal pain; (3) Neurological: brain fog, fatigue, sleep disorder; (4) Miscellaneous symptoms. Table 1 depicts for each period the most prevalent symptoms of each domain and clinical variables significant to describe the data-driven clusters. Risk factors for PASC recovery in period A were: domains 1 (OR=0.002, 95%CI: 5e-6-0.69), 3 (OR=0.06 95%CI: 0.005-0.72), 4 (OR=0.37 95%CI: 0.16-0.88), and cluster 1 (OR=0.52 95%CI: 0.28-0.97); while in period B, domains 3 (OR=0.03, 95%CI: 0.001-0.97), and 4 (OR=0.12, 95%CI: 0.01-0.99).

Conclusions: PASC clusters increase across time periods depicting a higher heterogeneity in clinical presentation. Recovery depends on both PASC domains and clinical variables, suggesting the need for a multidimensional evaluation.

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COVID-19

P 157 COMBINATION THERAPY TO ERADICATE SARSCOV2 INFECTION IN A PATIENT TREATED WITH CAR-T

M. Pisaturo[1,2,3], A. Russo[1,2,3], A. dell'Aquila[3], I. Palma[3], N. Carro[3], P. Medusa[3], C. Ricozzi[3], S. Imbriani[3], C. Sagnelli[1,2,3], K. Gjeloshi[3], N. Coppola[1,2,3]

[1]Department of Mental Health and Public Medicine, Section of Infectious Diseases, Università degli studi della Campania Luigi Vanvitelli, [2]AOU Vanvitelli, Naples, [3]Covid 19 UNIT, Vanvitelli

Introduction: The term CAR-T, Chimeric Antigen Receptor (T cells with chimeric antigen receptor), defines a type of treatment in which the T lymphocytes taken from a patient are reinfused into his body after being genetically modified in the laboratory to enhance action against cancer.
Possible side effects observed are: cytokine release syndrome with associated impairment of immune system function and neurological adverse effects (neurotoxicity). There are few data on outcome of sarscov2 infection in patient in CAR-t
Aims: to the describe sarscov2 infection in subjects in CAR-t.
Case report: 63-year-old patient with non-Hodgkin's lymphoma of lymphocytic derivation type DLBCL/FL grade 3b, onset in stage IIa bulky peri-pancreatic abdomen. In October 2021, primary refractory and underwent yescarta cell therapy on 12/21/22 (III line). COVID vaccinated with 2 doses, and COVID infection in March 2022 delaying 2nd cycle of GCHOP
On 24 January 2023, the molecular swab for sarscov2 was positive, this swab had been performed for a PET response of bilateral Ground glass in a symptomatic patient with cough and colds and was treated in the hospital where he was hospitalized with remdesevir for three days as early therapy.
Due to the long positivity of the nasopharyngeal swab for sarscov2 which did not allow him to carry out the haematological checks required for his onco-haematological condition, the patient was hospitalized in Day hospital at our infectious disease unit from 3 to 6 March 2023 to perform antiviral therapy with Remdesivir (day 1: loading dose of 200 mg, days 2-3: 100 mg) and March 6, 2023 to perform intravenous infusion of Sotrovimab.
Nasopharyngeal swabs for sarscov2 were performed every day after hospitalization with a progressive increase in CT until the virus was negative on 6 March 2023.
The patient thus had the opportunity to continue the diagnostic and therapeutic procedure for his underlying pathology.
Conclusions: in the literature there are not many data on sarcov2 retreatment for a persistent infection of sarscov2 in patients undergoing CAR-T. In these subjects it is probably necessary to identify personalized treatments for the duration of the antiviral therapy and for the combination of anti sarscov2 drugs to be used.

COVID-19

P 158 THE HYPOTHESIS OF DYSERGIC DIATHESIS IN LONG-COVID SYNDROME AND IN SARS-COV2 POST-VACCINATION REACTIONS: PRELIMINARY DATA FROM A PROSPECTIVE COHORT STUDY

D. Recinelli, E. Mazzotta, G. Rapacchiale, S. Coladonato, M. Bondanese, G. Ferrandu, S. Ianniruberto, F. Trave, D. Silletta, C. De Flaviis, E. Polilli, G. Parruti

Infectious Disease Unit, Pescara's General Hospital

Background: Patients with persistent cardio-vascular, respiratory and neurologic symptoms after SARS-CoV2 infection have been referred to COVID clinical centers since the first pandemic waves in 2020. Similar symptoms were recorded after exposure to SARS-CoV2 vaccination. A retrospective study was conducted to investigate risk factors and features of patients with Post-COVID syndrome and persistent post-vaccination adverse event at our site.

Methods: We prospectively enrolled patients referred to our COVID-19 clinical Regional Center of Pescara General Hospital, due to the persistence of mild or severe symptomatology after the clearance of COVID-19 infection or SARS-CoV2 vaccination, between June 2020 and February 2023. Length and clinical presentation of acute SARS-CoV2i infection; dermatological, neurological, cardiovascular, respiratory and systemic persistent symptoms were evaluated. Laboratory data such as Eosinophil Cationic Protein (ECP); total IgE;immune system values;inflammatory indexes and liver-kidney tests were recorded. Statistical analysis were performed by STATA (17.0).

Results: 350 patients were enrolled with 55.9 (16.9) mean age; 41% male; 294(84%) were enrolled for post-COVID symptoms, 56(16%) after post-vaccine persistent symptoms. IgE and ECP were evaluated in 286 and 98 patients in post-COVID group and 50 and 44 in the other, respectively. Patients were divided in two groups according to the presence of alteration of ECP and/or IgE (group 1) vs normal values (group 2). Among relevant parameters, univariate analyses revealed a 3-fold increased risk of dermatological signs (OR=3.41,1.68-6.95, <0.001); neuropathic (OR=3.04, 1.40-6.62, p<0.01) or cardiovascular (OR=3.24 1.96-5.35,p<0.01) manifestations. An increased risk between 2 and 3-fold was found for respiratory (OR=2.26,1.46-3.50,p<0.001), asthenia (OR=2.74,1.68-4.49,p<0.001), arthralgias (OR=2.34,1.45-3.76, p<0.001), fever (OR=2.72,1.49-4.98,p<0.001) and myalgia (OR=2.22,1.44-3.43,p<0.001). At multivariate analysis, after adjustment, neither age (unit increase, OR = 0.99,0.98-1.01, p=0.4) or gender (OR=1.46,0.86-2.49,p=0.1) were associated with the risk to being positive for IgE and/or ECP. The risk was over 16-fold higher among patients suffering from reaction to vaccine (OR=16.30,5.98 -54.38,p<0.001) and 3-fold for patients who presented cardiovascular symptoms (OR=4.61,2.55-8.57,p<0.001), fever (OR=3.01,1.49-6.22,p=0.002), dermatitis (OR=3.99,1.69-10.02,p=0.002) and percentage of eosinophils >4.4 at blood counts (OR=3.59,1.59-8.68,p=0.003).

Conclusions: Our study revealed for the first time that cardiovascular, dermatological and systemic symptoms were associated to dysergic diathesis, while respiratory, arthromialgic and neuropathic signs were not. Pathogenic mechanisms may be different: dysergic signs may be indeed related to Th1/Th2 disregulation. Further analyses will be necessary to confirm the above reported correlations and explore possible therapeutic interventions.

COVID-19

P 159 ACTIVE ROLE OF TELEFONO VERDE AIDS AND IST IN THE COMMUNICATION ON COVID-19 PANDEMIC IN ITALY

E. Fanales Belasio, P. Gallo, R. Valli, R. dalla Torre, M. Schwarz, A. D'Agostini, A, Colucci

Unità Operativa Ricerca psico-socio-comportamentale, Comunicazione, Formazione del Dipartimento Malattie Infettive – Istituto Superiore di Sanità, Rome, Italy

Background: Since March 2020 the COVID-19 pandemic has deeply affected life of individuals all over the world, due to an invisible health threat causing heavy social limitations. Particularly during the period March-May 2020, Italians suffered uncertainty and fear of contracting the disease through social interactions. In this context, the Italian Ministry of Health promoted institutional websites and Phone Helplines to provide information and recommendations about the prevention of COVID-19. The Telefono Verde AIDS e Infezioni Sessualmente Trasmesse – TV AIDS and IST- National AIDS and STI Helpline, provided by the Istituto Superiore di Sanità since 1987, was asked to answer also questions about COVID-19 from the general public.

Material and methods: In the period since March 2020 to December 2022 TV AIDS and IST answered calls from 418 users seeking for information on COVID-19. During the same period TV AIDS and IST also informed other 886 users, calling for STI issues, on the COVID-19 risk linked to referred behaviour. Phone intervention by trained researchers was anonymous and free of charge, based on a counselling approach to reinforce awareness and choices relating to healthy behaviors. Non-identifiable data (age, gender, place of call) and questions on COVID -19 (disease course, prevention, therapy, vaccination, legal issues, access to health services) were included in a specific database and stored in a protected archive for a proper analysis.

Results: TV AIDS and IST users calling for specific information on COVID-19 were prevalently males (77.7%) and in an age range between 25 and 40 years (43.3 %). About 50% of users also referred sexual behaviors potentially associated with a COVID-19 risk. Users' questions about COVID-19 included general issues (15%), transmission ways (29.2%), disease course (10.5%), vaccination (22.7%), prevention (5.7%) and impact on IST diagnosis or treatment (5.7%). The type of questions markedly changed over the 3 year period with a prevalence of COVID-19 transmission (41.9%) in the 2020, vaccination (61.8%) in 2021 and disease course (28.8%) in 2022. TV AIDS andIST users sensitized for potential risk of COVID-19 infection were mainly males (86%) and in age range between 25 and 39 years (53.2%). In 74.1% of cases a sexual behavior was referred and questions by users focused mainly on information on STI transmission (29.6%) and diagnostic procedures (18.1%).

Conclusions: In the context of COVID-19 pandemic, TV AIDS and IST was an institutional Service providing updated and scientifically correct information about COVID-19 to users, including disease course, transmission risk, prevention and vaccination. Besides, researchers raised the awareness of infection risk in users calling only for information on STI transmission risk or diagnosis. TV AIDS and IST may have played an useful role in the institutional information and control of the COVID-19 pandemic in Italy.

COVID-19

P 160 SARS-COV-2 SEROPREVALENCE AND ASSOCIATED FACTORS IN YOUNG PEOPLE LIVING WITH HIV ATTENDING YOUTH-FRIENDLY HEALTH SERVICES IN THE SOFALA PROVINCE, MOZAMBIQUE

V. Casigliani[1,2], R. Benoni[1,3], A. Zin[3], K. Chhaganlal[4], H. Guambe Dos Anjos[5], A. Merolle[1], N. Ronzoni[1], D. Giannini[1], D. Donà[3], C. Di Chiara[3], G. Putoto[6], C. Giaquinto[3]

[1]Doctors with Africa CUAMM, Beira, Mozambique, [2]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, [3]Department of Women's and Children's Health, University of Padua, Padua, [4]Faculty of Medical Health Sciences, Universidade Católica de Moçambique, Beira, Mozambique, [5]UNICEF Mozambique, Maputo, Mozambique, [6]Operational Research Unit, Doctors with Africa CUAMM, Padua, Italy

Background: Among adolescents and young people, HIV is a crucial health challenge, and its prevalence is estimated at 7% among this age group in Sofala province, in Mozambique. Even though the COVID-19 pandemic threatened the positive trend of reducing HIV infections, data on the impact of COVID-19 on people living with HIV (PLWHIV) are lacking. This study aims to explore the prevalence of SARS-CoV-2 and associated factors among youth attending youth-friendly health facilities in Sofala province, based on their HIV status.
Materials and Methods: A cross-sectional study was conducted including people aged 18-24 years old attending a visit to youth-friendly health services in the Sofala province (8 in Beira, 1 in Nhamatanda), between October and November 2022. People vaccinated against SARS-COV-2 or PLWHIV with WHO stage III-IV were excluded. A SARS-CoV-2 antibodies qualitative test and a questionnaire, investigating socio-demographic characteristics, HIV status, COVID-19 preventive measures and symptoms, were proposed. SARS-CoV-2 seroprevalence with a 95% confidential interval (CI) was calculated with the Clopper-Pearson method. Multivariable binomial logistic regression was used to estimate the positive SARS-CoV-2 antibodies test odds ratio (OR).
Results: Of the 540 people included, 355 (65.8%) were females. The mean age was 20.2 years (SD 2.0). PLWHIV were 90 (16.7%) more frequently workers than students (p=0.002). Almost all the sample (96.1%) reported adopting at least one preventive measure for COVID-19. The adjusted seroprevalence of SARS-CoV-2 in the whole sample was 46.8% (95%CI 42.6-51.2). It was 35.9% (95%CI 25.3-47.5) and 49.1% (95%CI 44.1-54.1) in the HIV+ and HIV- groups, respectively. The OR of testing positive at the SARS-CoV-2 antibodies test was higher in students compared to workers (AOR:2.02 [95%CI 1.01-4.21], p=0.051) and in those with symptoms (AOR:1.52 [95%CI 1.01-2.30], p=0.043). There were no differences based on HIV status (p=0.095). COVID-19 symptoms were reported by 68 (28.2%) people with a positive SARS-CoV-2 test, lasting in most cases (76.6%) 3-7 days, with no differences based on HV status (p=0.527, p=0.204). None of the symptomatic patients required hospitalization.
Conclusions: Young people complied well with COVID-19 preventive measures and no differences were found in seroprevalence or clinical presentation based on HIV status. The higher risk among students seems to confirm the role of schools in the spread of the virus.

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COVID-19

P 161 ARE THERE ANY DIFFERENCES IN EFFECTIVENESS BETWEEN AVAILABLE ANTIVIRALS AND MONOCLONAL ANTIBODIES TREATMENTS IN PAUCISYMPTOMATIC SARS-COV-2 INFECTED PATIENTS? A REAL LIFE EXPERIENCE

L. Galli[2], A. Lai[1], A. Bergna[1], C. della Ventura[1], A. Riva[1,2], L. Cordier[2], G. Scaglione[2], V. Colombo[2], D. Bernasconi[2], S. Landonio[2], S. Sollima[2], M. Corbellino[2], G. Dedivitiis[2], G. Casalini[2], S. Passerini[2], M. Matone[2], G. Rizzardini[2], A. Gori[2], S. Antinori[1,2], D. Visigalli[3], G. Zehender[1], M. Schiavini[2]

[1]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [2]Infectious Diseases Department, L Sacco Hospital, Milan, Italy, [3]Pharmacy Unit, L Sacco Hospital, Milan, Italy

Background: the availability of several antiviral drugs and monoclonal antibodies (mAbs) for the treatment of symptomatic adults, with mild to moderate SARS-CoV-2 infection and increased risk for progression to severe disease, have changed the natural history of COVID-19. The study aims to assess whether there are differences in effectiveness between these treatments.

Materials and Methods: in this retrospective observational study, we enrolled 292 COVID-19 outpatients (pts) who received early treatment with antivirals and/or mAbs at our Outpatient service from December 2021 to January 2023. Differences between treatment groups were valued by t test/chi-square test for parametric data and by Wilcoxon Mann-Whitney/Kruskal-Wallis for no parametric data. Lineage assignment was performed by real time PCR and/or whole genome sequencing. Viral load variation was indirectly assessed through PCR cycle threshold (Ct) values in the nasopharyngeal swab obtained in 108 pts at day treatment (T0) and on average 6 days after the start of treatment (T6).

Results: of 292 pts, 154 (52.7%) were males and median age was 62 years [IQR:52-75]. Among the pts, 32.9% received mAbs, 15.1% molnupiravir, 37.7% nirmatrelvir/r, 12.0% remdesivir and 2.40% mAbs and antiviral therapy. The characteristics of pts enrolled in the study are described in Table 1. The mean age was resulted significantly higher in subjects treated with molnupiravir (73.3 y, p<.001). Among patients >65 y, a large proportion was treated with mAbs (34.1%) and nirmatrelvir/r (31.9%) compared to molnupiravir (21.7%) or remdesivir (12.3%) (p=.002). In addition, a large part of pts affected by cardiovascular disease (31.7%), COPD (34.9%) and immunodeficiency (49.5%) mainly received nirmatrelvir/r than other treatments (p<.0001, p<.02 and p<.0001, respectively). Lineages and their descendents were distributed as follows: Delta 13%, BA.1 26.1%, BA.2 33.8%, BA.4 3.2% and BA.5 23.9%. No differences were observed among lineages distribution and patients age or vaccination status. Median Ct values at baseline was not significantly different on either T0 and T6 swabs among different treatments; ΔCt values mean between T0-T6 was 0.59 (SD: 0.29) and was higher in pts treated with nirmatrelvir/r and mAbs vs. remdesivir and monlupiravir, however differences are not statistically significant (0.64 and 0.62 vs. 0.44 and 0.54, respectively; p=0-009). The median time to first negative swab was longer in males than in females (9 vs. 7 days; p=.002). (9 vs. 7 days; p=.002). No differences were observed between negativization time and different treatment, lineages, period from last vaccine dose and infection.

Conclusion: the several treatments were administered according to pts' characteristics and drugs interactions, which justified the baseline differences between the various groups. In this study we did not observe any differences regarding effectiveness between available antivirals and monoclonal antibodies treatments.

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COVID-19

P 162 MONOCLONAL ANTIBODIES (MABS) AND ANTIVIRAL DRUGS FOR SARS-COV2 TREATMENT IN PATIENTS WITH ONCOHEMATOLOGICAL DISEASE

S.G. De Maria, S. Corazza, A. Grimaldi, A. Gasperin, D. Di Trento, S. Garattini, A. Carraro, V. Belvisi, B. Kertusha, A. Parente, P. Zuccalà, P. Fabietti, R. Marocco, C. Del Borgo, N. Cenfra, A. Romeo, M. Lichtner

Università di Roma La Sapienza, Ospedale S.M. Goretti Latina

Background: The immune system of those who are undergoing cancer chemotherapies could be weakened and, consequently, more exposed to diseases such as COVID-19. To date, there are limited studies related to early treatment for SARS-CoV-2 infections in these fragile patients and it would be desiderable that timely treatment could be available in order to reduce the risk of progression to severe forms, shorter timing to negativization and decrease long-term consequences.

Material and Methods: In this single center observational and real world study, we enrolled 173 oncohematological patients resulted positive to a nasopharyngeral swab for SARS-CoV2. Data were collected from March 2021 to March 2023. Participants were divided in two groups (no progression/progression of disease) and for each group we evaluated age, vaccination cycle, pre-exposure prophylaxis, class of drug used for early treatment, median time lenght of negativization and death. Thus, final endpoints were negativization time and progression to pneumonia documented at thorax CT scan.

Statistical significance of the collected data was calculated through chi-square and Mann Whitney T-test using the Prism software, v9.5.1.

Results: A total of 173 patients were recruited, 56% (98) of which were males. 162 patients had no progression of SARS-CoV2 infection, while 11 participants belonged to the progression group. There was a difference between the median age (64,5 years old for no progression group versus 77 years old for the progression group), and this result was statistically significant (p value 0,0014). Furthermore, 58% of patients were treated with antivirals and 35% with mAbs, resulting in a not- statistically significant difference in terms of disease progression between the two groups. Moreover, between the 5 patients treated with the monoclonal antibody Evusheld (tixagevimab, cilgavimab), 3 had a progression of disease, with a statistically significant correlation (p value <0,00001).

Finally, 126 patients from the no progression group had a negative nasopharyngeal swab into 30 days, whilst only 4 participants from the progression group had a median length of negativization of less than 30 days (p value <0,00066).

Conclusions: SARS-CoV2 infection has a great impact on oncohematological patients because of their insulted immune system; thus their treatment is always challenging for clinicians. Our study has demonstrated that older patients have increased risk of disease progression, thus being more to susceptible to develop pneumonia. Furthermore, this class of patients are more prone to persistence of SARS-COV2 nasal swab positivity, even after 30 days. Therefore, it's crucial that further studies are conducted in order to ease early diagnosis, careful and personalized home management of this class of clinically extremely vulnerable patients.

COVID-19

P 163 TISSUE INHIBITOR OF MATRIX METALLOPROTEINASE-1 (TIMP-1) AND LUNG INVOLVEMENT IN ACUTE AND POST-ACUTE SARS-COV-2 INFECTION

M.A Zingaropoli[1], T. Latronico[2], P. Pasculli[1], G.G. Masci[3], R. Merz[1], F. Ciccone[1], F. Dominelli[1], C. Del Borgo[4], M. Lichtner[4,5], F. Iafrate[3], G. Galardo[6], F. Pugliese[7], V. Panebianco[3], P. Ricci[3,8], C. Catalano[9], M.R. Ciardi[1], G.M. Liuzzi[2], C.M. Mastroianni[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, Rome, Italy, [2]Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari "Aldo Moro", Bari, Italy, [3]Department of Radiological, Oncological and Pathological Sciences, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy, [4]Infectious Diseases Unit, Santa Maria Goretti Hospital, Sapienza, University of Rome, Latina, Italy, [5]Department of Neurosciences Mental Health and Sensory Organs, Sapienza University of Rome, Italy, [6]Medical Emergency Unit, Sapienza University of Rome, Policlinico Umberto I, Rome, Italy, [7]Department of Specialist Surgery and Organ Transplantation "Paride Stefanini", Policlinico Umberto I, Sapienza University of Rome, Rome, Italy, [8]Unit of Emergency Radiology, Policlinico Umberto I, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy, [9]Department of Radiological, Oncological and Pathological Sciences, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy

Background: The upregulation of matrix metalloproteinases (MMPs) contributes to chronic inflammation, by contrast the increase of tissue inhibitor of matrix metalloproteinase-1 (TIMP-1) causes lung fibrosis. The aim of the study was to longitudinally evaluate the association between MMP-2, MMP-9 and TIMP-1 and chest radiological findings in COVID-19 patients.

Methods: On hospitalized COVID-19 patients, plasma levels of MMP-9 and TIMP-1 and plasma activity of MMP-2 and MMP-9 were evaluated. As control group, healthy donors (HD) matched for gender and age were included in the study. For COVID-19 subjects, blood samples were taken at two time-points: baseline and after three months from hospital discharge (T post). According to outcome, COVID-19 subjects were stratified into two group: ARDS and non-ARDS and the differences were evaluated.

Results: At baseline, compared to HD (n=53), COVID-19 patients (n=129) showed higher plasma levels of MMP-9 ($p<0.0001$) and TIMP-1 ($p<0.0001$) and higher plasma activity of MMP-2 ($p<0.0001$) and MMP-9 ($p<0.0001$). Stratifying COVID-19 patients according to ARDS development, in ARDS group higher plasma levels of MMP-9 ($p=0.0339$) and TIMP-1 ($p=0.0044$) as well as plasma activity of MMP-2 ($p=0.0258$) and MMP-9 ($p=0.0021$) compared to non-ARDS group were observed. At baseline, negative correlations between plasma levels of MMP-9 and TIMP-1 with P/F ratio ($\rho=-0.1917$, $p=0.0352$ and $\rho=-0.2796$, $p=0.0060$, respectively) were observed. Conversely, a positive correlation between plasma levels of TIMP-1 and chest computed tomography (CT) score ($\rho=0.2302$, $p=0.0160$) was observed. At T post, a reduction in plasma levels of TIMP-1 ($p<0.0001$) whereas an increase in plasma levels of MMP-9 was observed ($p=0.0088$).

Conclusions: The increase in plasma levels of MMP-9 and TIMP-1 and plasma activity of MMP-2 and MMP-9 observed on hospital admission in COVID-19 patients, especially in those who developed ARDS, underline a potential use as prognostic markers and potential therapeutic targets. Moreover, the positive correlation between plasma levels of TIMP-1 and chest CT score highlights the potential use of TIMP-1 as marker of fibrotic burden and disease prognosis. At T post, the increase in MMP-9 plasmatic levels and the reduction in TIMP-1 plasmatic levels suggest that the inflammation and the fibrosis resolution are still ongoing.

COVID-19

P 164 RISK-FACTORS FOR MORTALITY OF COVID-19 IN HEMATOLOGIC PATIENTS: A MULTIVARIATE ANALYSIS IN GALLIERA HOSPITAL COVID-19 COHORT

S. Boni, A. Parisini, F. Del Puente, E. Blasi Vacca, R. Prinapori, M. Feasi, N. Bobbio, E. Pontali

S.C. Malattie Infettive Ente Ospedaliero Galliera Genova

Introduction: published studies on COVID-19 in hematologic patients reported mortality rates ranging from 30% to 40%. Identified risk-factors for such poor prognosis were: age >65 years, male gender, lymphopenia and thrombocytopenia. We performed a retrospective analysis consulting our database to identify risk factors for mortality in these patients in clinical practice.

Materials and methods: The main outcome variable was all-cause mortality. The considered independent variables were: demographic data, time between symptom onset and hospitalization, radiological score, respiratory parameters (particularly the P/F at admission), CRP and PCT levels, and lymphocytes at hospital admission, comorbidities, vaccination status, previous oral antiviral therapy. Principal component analysis (PCA) was carried out using R to obtain coefficients for variables associated with the greatest variance and to reduce the dimensionality of the database due to the large number of analyzed variables and the relatively small number of cases and then a multivariate analysis and a ROC curve was performed to assess model's predictive capacity.

Results: A total of 36 cases (18 males) were evaluated. All patients presented to the emergency room with COVID pneumonia and respiratory failure, with a mean age of 75±11 years. The P/F values at admission were 274±104. The primary hematologic disorders were non-Hodgkin lymphoma and chronic lymphocytic leukemia (28 out of 36 cases). 16 patients had received an Anti-CD20 drug in previous 3 months; 6 had received other chemotherapy, and only one a bone marrow transplantation. 25 patients had completed the anti-SARS-COV-2 vaccination cycle. 14 deaths were recorded. In 12 cases SARS-COV-2 swab became negative during hospitalization. PCA revealed that age, radiological score, anti-CD20 drug use, peripheral vascular disease, Charlson Comorbidity Index, and vaccination status were the variables associated with the greatest variance (Figure 1). Multivariate analysis revealed a significant correlation between death and previous anti-CD20 drug use (p=.014) and age (p=.04) (Figure 2). The model was further analyzed using a ROC curve, with a result of 0.87 (Figure 3).

Conclusion: In our study death-associated variables were age and comorbidity as expected. Not described in other published studies, in this subgroup, severity of radiological score was linked to poor outcome. Anti-CD-20 drug use was statistically correlated to mortality, even at multivariate analysis; this has not yet been previously described. The great vaccination variance was probably due to poor response in these patients.

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COVID-19

P 165 REMDESIVIR 3-DAY COURSE REDUCES THE RISK OF DISEASE PROGRESSION IN A REAL-LIFE MATCHED COHORT

A. De Vito[1], A. Bitti[1], L. Saderi[2], M. Puci[2], A. Colpani[1], B. Zauli[1], V. Fiore[1], M. Fois[1], M.C. Meloni[1], G. Moi[1], I. Maida[1], S. Babudieri[1], G. Sotgiu[2], G. Madeddu[1]

[1]Unit of Infectious Diseases, Department of Medicine, Surgery, and Pharmacy, University of Sassari, Italy, [2]Clinical Epidemiology and Medical Statistics Unit, Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy

Introduction: Remdesivir was initially approved for COVID-19 patients with pneumonia and respiratory failure. In 2022 it was approved for non-hospitalized patients to reduce the risk of disease progression. Aim of the study was to assess its efficacy in a real-life scenario.

Methods: A case-control study of COVID-19 patients recruited between January and November 2022 in an Italian hospital was performed. Data on demographics, medical history, CT signs, and therapy were collected. Those with missing data, respiratory failure at evaluation, and treated with monlupiravir, nirmatrelvir/ritonavir, and monoclonal antibodies were excluded. Selected patients who received a 3-day course of remdesivir were matched 1:1 forage, gender, Charlson Comorbidity Index (CCI), and vaccination status with not treated patients. The primary outcome was disease progression (i.e., oxygen administration or increase ofoxygen in those chronically exposed).

Result: 286 patients were enrolled, with 143 exposed toremdesivir. The edian(IQR) age was 78.0 (70.1-85) years; the prevalenceof vaccination with at least two doses was high (89.9%). Chronic liver disease and CT signs were more prevalent in not treated patients, whereas the presence of at least one symptom was 100% in the remdesivir group. In addition, over half of the patients treated with remdesivir acquired SARS-CoV-2 infection during hospitalization for non-COVID-19 reasons. Characteristics of the patients are summarized in Table 1.

Ninety (31.5%) developed severe COVID-19 and required oxygen supplementation. Having been treated with remdesivir and a complete vaccination schedule resulted in a reduced risk of disease progression, whereashaving fever, dyspnea at baseline, and CT signs were associated with an increased risk of disease progression (Table 2).

Conclusions: Remdesivir, administered for three days, can reduce the risk of disease progression by 86%. However, further studies are needed to assess the more effective time of administration.

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COVID-19

P 166 SARS-COV2 INFECTION IN DIALYSIS PATIENTS: EARLY TREATMENT IMPACT ON CLINICAL OUTCOME

S. Corazza, S.G. De Maria, A. Grimaldi, S. Garattini, A. Carraro, D. Di Trento, A. Gasperin, V. Belvisi, T. Tieghi, P. Cirillo, B. Kertusha, A. Parente, P. Zuccalà, R. Marocco, Del Borgo, P. Fabietti, M. De Masi, M. Lichtner

Sapienza, U.O.C. Malattie Infettive Santa Maria Goretti, Latina

Background: The COVID-19 pandemic represents one of the most difficult challenge for clinicians especially in high risk patients, like the ones undergoing maintenance hemodialysis. It has been demonstrated that new anti-viral drugs and monoclonal antibodies have a great impact on disease progression on vulnerable groups but limited evidence is available about this category.

Particularly, patients with COVID-19 disease and under dialysis treatment seem to have a poor prognosis due to repeated access to hospital, prolonged treatment and common presence of comorbidities and limited treatment option.

The COVID-19 pandemic has had a major impact around the world, with dialysis patients being among the patient groups with the highest mortality [1, 2]. If infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), these patients often develop a serious course of COVID-19,

Methods: A retrospective analysis was conducted on 67 dialysis outpatients from Infectious Diseases Operative Unit from March 2021 to March 2023. The diagnosis of SARS-CoV-2 infection was based on nasopharyngeal swab positivity. On this population we evaluated vaccination status, time length of negativization, therapeutic approach and disease progression.

Statistical significance of the collected data was calculated through chi-square and Mann Whitney T-test using the Prism software, v9.5.1.

Results: The overall median age of the cohort was 74 years old [30;96],62% of the enrolled patients were men. We evaluated vaccination adherence in this population, with a total of 6 not vaccinated patients, and 61 vaccinated participants; among these, 49 were fully covered with a booster dose, 11 had a complete primary cycle and 1 had incomplete vaccination. 39 patients resulted negative to a nasopharyngeal swab in less than 30 days, while 7 were positive for more than 30 days and, finally, 21 participants were lost during follow-up. With the regard to pharmacological treatment, due to limited therapeutic possibilities, the most of patients are treated whith monoclonal antibodies: 3 patients were treated with antiviral drugs and 64 with monoclonal antibodies. Moreover, 4 patients out of 67(5%) experienced disease progression; 13 patients (21%) were treated with tixagevimab/cilgavimab: no patient progressed.

The end point of our study was the evaluation of clinical progression and death.

Conclusions: In conclusion, the tailored early treatment with antiviral drugs/monoclonal antibodies in dialysis patients with COVID-19 infection, represent a useful therapeutic option to prevent disease progression, an attractive option during the early course of infection. One of the strenghts of our work was the tracking of the infection and the observational window carried out for a long period of time. However, since our real case scenario was conducted on a small population, studies with a larger cohort of patients are needed in order to assess the real impact of COVID-19 treatment strategies.

COVID-19

P 167 SOTROVIMAB VS TIXAGEVIMAB/CILGAVIMAB IN OUTPATIENTS WITH COVID-19: CLINICAL PRACTICE

F.R.P. Ieva, R. Papale, M.C. Poliseno, F. De Gregorio, C. Muscatiello, G.A. Minafra, T.A. Santantonio, S. Lo Caputo

Infectious Disease Unit, Department of Medical and Surgical Science, University of Foggia, Foggia, Italy

Neutralizing monoclonal antibodies (mAbs) significantly reduce the risk of COVID-19 progression in patients with underlying risk factors. However, recent in vitro studies showed no efficacy of Sotrovimab against the omicron variants of SARS-CoV-2.

Here we report our experience with Sotrovimab and Tixagevimab/Cilgavimab (Tix/Cig) as treatment of non-hospitalized adult patients at high risk of clinical evolution of COVID-19 during Omicron waves.

From January 2022 to February 2023, 209 non-hospitalized adult patients with SARS-CoV-2 infection and a high risk of severe outcomes were treated with Sotrovimab or Tix/Cig, within 14 days (median: 3 days) after the onset of symptoms. All patients were followed and evaluated approximately 7 days after the administration of mAbs. Chi squared-test and Mann-Withney U-test were used for statistical analysis.

The median age of treated patients was 71 years, 168 received Sotrovimab and 41 were treated with Tix/Cig. In the Sotrovimab group, 12% of patients had hematologic malignancies vs 27% in the Tix/Cig group. Most patients had at least two comorbidities, 99% and 93% in the Sotrovimab and Tix/Cig groups respectively. Three comorbidities or more were present in 66% of patients treated with Sotrovimab and in 32% of patients in the Tix/Cig group. Overall, 12% of the patients were unvaccinated for SARS-CoV-2, respectively 13% in the Sotrovimab group, and 10% in the Tix/Cig group.

Two patients (1%) reported serious adverse events, 1 (0.6%) in the Sotrovimab cohort and 1 (2.4) in the Tix/Cig cohort, both patients presented allergy-like reactions.

The nasal swab test was negative within 7 days from mAbs administration in 50 patients (30%) treated with Sotrovimab and in 14 (34%) patients in the Tix/Cig cohort.

At the follow-up visit, 45 patients (27%) treated with Sotrovimab, and 19 patients (46%) of the Tix/Cig cohort showed remission of COVID-19 symptoms.

Hospitalization due to COVID-19 occurred in 5 patients (3%) in the Sotrovimab cohort on the same day of administration, none of them died. Two patients (5%) treated with Tix/Cig were hospitalized due to COVID-19, respectively one day and four days after the administration of mAbs, but none of them died.

Only one patient died of causes unrelated to COVID-19 during the follow-up period.

Our real-life experience demonstrated that mAbs are effective “in vivo” in preventing COVID-19 clinical evolution in non-hospitalized patients at high risk even during Omicron waves, with a good tolerability profile.

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COVID-19

P 168 A COMPARATIVE FOCUS BETWEEN IMMUNOCOMPROMISED AND IMMUNOCOMPETENT PATIENTS WITH COVID19 INFECTION RECEIVING EARLY ANTIVIRAL THERAPY IN A REAL-WORLD SCENARIO

S. Garattini[1,2], C. Bortignon[1], A. Carraro[1,2], D. Di Trento[1,2], A. Gasperin[1,2], A. Grimaldi[1,2], S.G. De Maria[1,2], S. Corazza[1,2], V. Belvisi[2], B. Kertusha[2], A. Parente[1,2], P. Zuccalà[2], P. Fabietti[2], E. Tortellini[1,3], M.S. Guardiani[1,3], A. Spagnoli[1,3], R. Marocco[2], C. Del Borgo[2], D. Alunni Fegatelli[1,3], M. Lichtner[1,2,3]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy, [2]Infectious Diseases Unit, Santa Maria (SM) Goretti Hospital, Sapienza University of Rome, Latina, Italy, [3]Department of Neurosciences, Mental Health, and Sense Organs, NESMOS, Sapienza University of Rome, Rome, Italy

Background: the COVID19 pandemic placed us in front of continuous and abrupt challenges. The latest and rising one is the management of immunocompromised patients with SARS-CoV2 infection. In fact, this special category of individuals, particularly those with hematologic malignancies, are at increased risk for SARS-CoV-2-associated morbidity and mortality. Moreover, little is known about targeted COVID19 treatment in this population.

Material and Methods: in this single-center observational real-world study (RWS) that took place at Santa Maria Goretti Hospital, in Latina - Central Italy from the 5th of January to the 3rd of October 2022, we recruited patients with a positive nasopharyngeal swab (NPS) for SARS-CoV2 and one or more risk factors for progression to severe illness that could make them eligible for early COVID treatment. The available therapeutical choices were a 3-days-scheme remdesivir (RDV), nirmatrelvir/ritonavir (NMV/r) and molnupiravir (MP). A focus on the effectiveness, tolerability and prescribing choice for immunocompromised patients was conducted and compared to the immunocompetent ones. We considered a composite endpoint (pneumonia, ARDS, COVID-19 and non-COVID-19 related death), the persistence of symptoms at 30 days and NPS negativization.

Results: we recruited a total of 1118 patients, 320 of them were immunocompromised and 798 were immunocompetent. Among patients with altered immunological status, 94 were treated with RDV, 97 with MP and 129 with NMV/r. They were further subdivided based on the pre-existing disease.

From the composite endpoint analysis about the overall outcome, no statistically significative difference was found between the three groups of treatment in the immunocompromised group and neither from the comparison with the immunocompetent ones. Patients treated with MP and NMV/r showed a lower persistence of symptoms at 30 days in both groups and finally, NMV/r seems to be related to an early NPS negativization in both groups.

Conclusions: our study underlined the importance of an antiviral early-treatment for COVID19 acute infection, both in immunocompetent and immunocompromised patients and its similar effectiveness and tolerability in the two groups of study. From our results we can also intrinsically deduced that a more tailored and standardized therapeutic approach in case of immunocompromised subjects is fundamental.

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COVID-19

P 169 THE IMPACT OF COGNITIVE RESERVE ON NEUROCOGNITIVE IMPAIRMENT DURING LONG-COVID-19

G. Del Duca[1], A.C. Brita[1], A. Lonigro[2], M. Camici[1], I. Mastrorosa[1], A. Vergori[1], A. Mondi[1], C. Pinnetti[1], A. Antinori[1]

[1]Lazzaro Spallanzani National Institute for Infectious Diseases, Rome, Italy, [2]Department of Education, University of Roma Tre, Italy

Background: Cognitive reserve (CR) refers to a set of mentally stimulating factors and activities that may serve a protective role in a variety of clinical conditions. The purpose of the present study is to investigate the relationship between CR levels and cognitive performance during post-acute COVID-19 syndrome.

Material and Methods: All patients (pts) included of the "Neurocovid" Study attended the post-COVID outpatient service of INMI L. Spallanzani from September 2020 to July 2022, regardless of neurocognitive symptoms. All pts signed informed consent. A standardized battery of 20 tests evaluating different cognitive areas (episodic verbal memory, visual memory, working/short-term/visuo-spatial memory, constructive praxis, attention, verbal fluency, speed of information processing and mental flexibility) and the Cognitive Reserve Questionnaire (CRIq) were administered. In addition, pts were classified into Low CR (CRIq range score 0-114) and High CR (CRIq range score 115-130). To assess neurocognitive performance, tests were compared with the reference cut-off and scores were classified into equivalent points (PE). A series of ANCOVA, controlling for gender, age and hospitalization condition, were run to verify differences in cognitive domains by CR groups.

Results: We included N=461 participants (F = 53.1%; Mean age = 53.77 years; SD = 11.91; age range = 18-85 years) 44.5% previously hospitalized. Results revealed significant differences between CR groups for RAVLT-ST [$F(1,460) = 22.671$, $p < .001$, $\eta2 = .047$], RAVLT-LT [$F(1,460) = 8.111$, $p < .01$, $\eta2 = .017$], RAVLT-REC [$F(1,452) = 8.051$, $p < .01$, $\eta2 = .018$], DSB [$F(1,457) = 4.213$, $p < .05$, $\eta2 = .009$], CSB [$F(1,460) = 9.464$, $p < .01$, $\eta2 = .020$], PVF [$F(1,460) = 7.713$, $p < .01$, $\eta2 = .017$], CVF [$F(1,460) = 9.281$, $p < .01$, $\eta2 = .020$], TMTA [$F(1,458) = 10.221$, $p < .01$, $\eta2 = .022$] and DST [$F(1,459) = 19.631$, $p < .001$, $\eta2 = .041$]. Specifically, High CR group obtained higher mean scores compared to Low CR group, controlling for gender, age and hospitalization condition. In order to verify the relation between CR and COVID-19-NCI (C19NCI, <cutoff-PE = 0) and CR and COVID-19 SUBJECTIVE-NCI (C19SNCI, >cutoff-PE = 1,2,3,4), chi-square test showed no significant relation between CR and C19NCI [$\chi2(1, N = 461) = 2.983$, $p = .084$] and conversely, a significant one between CR and C19SNCI [$\chi2(1, N = 461) = 5.757$, $p < .05$]; additionally, 85% pts with Low CR vs 75% pts with High CR showed no C19SNCI, whereas 15.6% pts with Low CR vs 25% pts with High CR showed C19SNCI (Figure 1).

Conclusions: Our findings suggest that CR index might have an impact on cognitive performance during post-acute COVID-19 syndrome; High CR could represent a protective factor for reporting pathological scores in cognitive tests. Interestingly, pts with High CR more often complain C19SNCI. Further data are needed to confirm these preliminary findings and to introduce CR in neuropsychological evaluation.

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COVID-19

P 170 RECURRENT COVID-19 INFECTION IN A PATIENT WITH POST-REMISSION ONCO-HAEMATOLOGICAL DISEASES

A. Fulgione[1], M. Pisaturo[1,3], A. Russo[1,3], A. dell'Aquila[3], I. Palma[3], N. Carro[3], P. Medusa[3], S. de Pascalis[2], L. Alessio[2], N. Coppola[1]

[1]Department of Mental Health and Public Medicine, Section of Infectious Diseases, University of Campania "Luigi Vanvitelli", [2]AOU Vanvitelli, Naples, [3]Covid 19 UNIT, Vanvitelli

Introduction: We report the clinical case of a 74-year-old-male with a history of a non Hodgkin follicular lymphoma G2, diagnosticated in may 2019 and treated with chemotherapy (last cycle on December 2020) and immunotherapy (last cycle on April 2022) with recurrent sarscov2 infections.
Clinical Case: A 74-year-old male who was transferred to our Covid Unit in January 2023. On 4 December 2022, due to the onset of fever, he performed a molecular nasopharyngeal swab (TNF) for sarscov2 with a positive result and was treated with ritonavir/nirmatrelvir.
The patient no longer had a fever but the positivity of the TNF persisted.
On 27 December 2022 fever reappears with peaks of 38, he performed a chest CT scan and was hospitalized on 13 Jan 2023 in our division and was treated with remdesivir for (from 21 to 31 January) for 10 days. HRCT scan described multiple GGO areas and some consolidated peripheral areas, especially at the right middle and lower regions (Severity Score 10/25). The patient developed fever (maximum T 38,5° C) and blood exams remained stationary with low WBC levels and high C-reactive protein (CRP) level, that decreased after antiviral therapy (28 times the upper level of normal). All the blood cultures taken during the stay resulted negative; similarly QTF Tb test, cmv-dna test, β-d-glucan test (BG), aspergillus galactomannan antigen were negative. Also, the phenotypic identification and count of lymphocyte subpopulation in peripheral blood revealed an immunodepressed state (total CD4 lymphocytes T count of 148 cells/uL; CD4/CD8 ratio of 0,60). After 10 days of apirexia he was discharged on 02 feb 23 with a negative TNF for sarscov2.
On February 15th, the patient was admitted to our unit because of a new positivity to Sars-Cov-2 PCR test. The new thorax CT scan described Severity Score of 6/25. A therapy with Sotrovimab was started. No other infections were found. The patient was discharged from hospital on February 25th apiretic and in stable conditions with a negative nasopharyngeal swab for sarscov2.
On March 14th, the patient accessed to our Infectious Diseases department, because of reappearance of fever after having performed a thorax CT scan which highlighted a Severity Score of 6/25. We performed a total body PET-CT scan that ruled out the recurrence of the onco-haematologic disease; tumor markers were negative and bronchoalveolar lavage procedure was negative for sarscov2 and for bacterial pneumonias, tuberculous lesions, fungal infections, and malignancies. Despite a negative nasopharyngeal swab for sarscov2 he was treated with Remdesivir, Paxlovid and Sotrovimab off label therapy and the fever resolved within two days of treatment.
Conclusions: covid 19 in subjects with oncohaematological disease is a new entity that has interesting challenges, in this case we used only clinical and radiological criteria to treat the patient even in the absence of the virus in the nasopharynx swab and in bronchoalveolar lavage.

COVID-19

P 171 IS IT POSSIBLE TO IDENTIFY PREDICTIVE FACTORS FOR COVID-19 SEVERE DISEASE AND MORTALITY IN THE POST-VACCINE ERA? A REAL-LIFE SINGLE COHORT ITALIAN EXPERIENCE

C. Fusetti[1,2], A. Foschi[1], M. Colaneri[1], L. Cordier[1], F. Borgonovo[1,2], F. Petri[1,2], M. Matone[1,2], M. Gerbi[1,2], M. Piscaglia[1,2], D. Bernasconi[1], I. Faggion[1], G. Gubertini[1], A. Gori[1,2], G. Rizzardini[1], M. Schiavini[1]

[1]Department of Infectious Diseases, ASST Fatebenefratelli Sacco – Milan (Italy), [2]University of Milan – Milan (Italy)

Background: Several studies in literature have shown that large-scale administration of approved SARS-CoV-2 vaccines have reduced both hospitalization and mortality for COVID-19. However, a certain proportion of vaccinated subjects could develop severe disease as well. The aim of our study was to identify potential risk factors for severe COVID-19 and mortality in vaccinated patients.

Materials and methods: We retrospectively collected the data of 299 patients (pts) hospitalised for symptomatic SARS-CoV-2 infection in our wards from September 2021 to February 2022. All the pts have received at least one dose of COVID-19 vaccines.

Data for continuous variables are presented as means and standard deviations and categorical variables as frequencies and percentages. Comparisons between the COVID-19 severe and not severe groups of pts were performed using chi-square tests for categorical variables and Mann–Whitney tests for non-normal continuous data. A generalized linear model for the binomial family was carried out to estimate the risk of severe COVID-19, mortality, and admission to Intensive Care Unit (ICU), adjusting for demographic and clinical features [age, Charlson Comorbidity Index (CCI) immunodepression, anti-S antibodies titre].

The results are reported as odds ratios (OR) and 95% confidence intervals (CIs). Statistical analyses were conducted using R (version 4.1.2).

Results: Sixty-five per cent of pts were males, with a mean age of 76.2 years (SD 15). 21% of pts had <65 years. Mean CCI was 4.9 (SD 2.8). Overall mortality was 16.7%. Fifty-seven per cent pts developed severe pneumoniae with hypoxemic respiratory failure requiring high flow (HF) oxygen therapy; among them, the 12.3% was admitted to the ICU and the 24.6% died.

There were more males and pts affected by diabetes treated with hypoglycemic therapy in the group of pts with HF compared with pts requiring lower oxygen flow only (Table 1). No difference was found in terms of anti-S titer. With regard to our primary objective, only CCI was found as significant risk factor for in-hospital mortality, while no other variable was found to be significantly related to the ICU admission and HF requirement.

Conclusions: We found that the underlying comorbidities of pts are a significant risk factor for death in vaccinated pts hospitalized for COVID-19. On the other side, no risk factor for disease severity and ICU admission was found. We consider that it is useful to mention this finding, as it is a study carried out in the post-vaccine era, but before early antiviral and antibody treatments came into use. In fact, given the same vaccine status, this study might show what have worsened the disease to the extent of requiring admission to the ICU, as well as death. The lack of other statistically significant predictive factors requires further studies with comparisons between pre-vaccine, post-vaccine, and early antivirals treatment era.

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COVID-19

P 172 THE IMPACT AND OUTCOME OF EARLY TREATMENT FOR COVID-19 IN TRANSPLANTED PATIENTS: A REAL LIFE STUDY

A. Grimaldi, S.G. De Maria, S. Corazza, S. Garattini, A. Carraro, D. Di Trento, A. Gasperin, V. Belvisi, T. Tieghi, B. Kertusha, A. Parente, P. Zuccalà, R. Marocco, Del Borgo, P. Fabietti, M. De Masi, M. Lichtner

Università Roma "La Sapienza"

Background: Coronavirus disease is a global pandemic characterized by a diverse spectrum of clinical manifestations, going from asymptomatic to acute respiratory distress syndrome (ARDS) with septic shock and multiorgan failure. The availability of vaccination and the advent of the early therapy with monoclonal antibodies/antiviral drugs has changed the management of the disease, reducing hospitalization and improving survival rates.

Solid organ transplant (SOT) patients are generally at increased risk of bacterial, viral and fungal infections and the continue spread of SARS-CoV2 infection has a potential impact on SOT recipients across the globe. Since immunosuppressive agents modulate several features of the immune response, these patients have been associated with a more severe SARS-CoV2 infection and a higher risk of mortality.

This study examines how early therapy with monoclonal antibodies and antivirals have impacted on clinical outcome in SOT recipients preventing disease progression and deaths.

Material and methods: We conducted a retrospective observational study on solid organ transplant recipients with SARS-CoV2 infection attending the Infectious Diseases Operative Unit (UOC) from March 2021 to March 2023. We distinguished patients upon vaccination status, type of treatment for COVID-19, and outcome.

Results: We enrolled 101 SOTs, 63 of which were males (62%) and median age was 57 years old [25;90]). Among them, 4 patients were not vaccinated, 10 received a primary complete vaccination cycle, and 85 got booster doses. At the time of writing, we have a complete information about negativization on 87 patients out of 101; among these 83 had a time lenght of negativization of less than 30 days, while 4 patients were persistently positive to a nasopharyngeal swab for more than 30 days. Moreover, all the patients from our cohort received SARS-CoV2 infection early therapy: 47 were treated with antiviral drugs, 50 with monoclonal antibodies and only 2 with a combination therapy. In the end, 2 patients had infection progression, with evidence COVID-related pneumonia at CT thorax scan.

Conclusions: Solid organ transplant patients are a heterogeneous group with long-lasting immunosoppression as a common element, with an increased risk of SARS-CoV2 infection progression. In our real-life study we showed a lower development of severe course of SARS-CoV2 infection in patients treated with early therapy, highlighting the favorable impact of early therapy with antivirals and monoclonal antibodies. However, more studies are needed to assess further evidence and therefore allowing a better management of disease and a possible reduction in hospitalization rates and deaths.

COVID-19

P 173 RISK FACTORS ASSOCIATED WITH LONG COVID: A RETROSPECTIVE STUDY

P. Pasculli[1], M.A. Zingaropoli[1], F. Ciccone[1], F. Paribeni[1], G. Masci[3], R. Merz[1], F. Dominelli[1], G. Siccardi[1], S. Pellegrini[1], M. Pasculli[3], G. Galardo[2], C.M. Mastroianni[1], M.R. Ciardi[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy, [2]Medical Emergency Unit, Sapienza, University of Rome, Policlinico Umberto I, Rome, Italy, [3]Department of Radiological, Oncological and Pathological Sciences, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy

Background: An increasing number of observational studies have reported the persistence of symptoms following recovery from acute COVID-19 disease. The purpose of this study is to describe the persistent symptoms of COVID-19 patients evaluating the most appropriate interdisciplinary approach for COVID-19 patients worldwide. Furthermore, an assessment of risk factors for the development of long-COVID symptoms and residual radiological damage was performed .

Methods: A retrospective study of unvaccinated COVID-19 patients was performed at post-COVID-19 clinic of Policlinico Umberto I hospital, Sapienza, Rome, Italy. For each patient, population characteristics, frequency of symptoms, and long-term sequelae were evaluated. Long-COVID symptoms were identified as symptoms persisting for an average of 90 days after discharge. Odds ratios (OR) were calculated using logistic regression models to assess the association of risk factors and sequelae.

Results: Overall, 364 patients, (152 females/212 males) with a median age [interquartile range] of 58 [49-86] were enrolled.

291 (79.9%) patients reported at least one post-COVID-19 symptom and 202 (56%) two or more symptoms. Asthenia was the most reported symptom. Over two thirds (84%) were admitted to hospital for treatment of COVID -19, others managed at home (16%). During acute stage of the disease, they received heparin (53%), corticosteroid (49%), remdesivir (36.5%), anti-IL-6 (22%), hydroxychloroquine (40%). The risk of presenting at least only one symptom at follow-up visit was lower in men (OR= 0.42, 95%IC 0.23, 0.73) and higher in patients treated with corticosteroid (OR = 1.76 , 95%IC 1.05, 3.00) In the multivariable model, only sex was significative (OR = 0.34, 95%IC 0.18, 0.62).

The risk of presenting computed tomography (CT) residual lesion at follow-up visit was higher in hospitalized patients (OR= 2.17, 95% IC 1.11,4.23, p=0.023) and in hydroxychloroquine-treated patients (OR=1.92, 95% IC1.12,3.36, p=0.020). The risk of impaired pulmonary function was higher in older patients (OR=1.03, 95%IC 1.01,1.04, p=0.001), patients with one or more comorbidities (OR=1.39, 95% IC1.07,1.80, p=0.014), particularly with pulmonary comorbidities (OR=2.31, 95% IC 1.24,4.40, p=0.009) and in patient with high levels of CRP (OR=2.09, 95% IC 1.23,4.00, p=0.015) and D-Dimer (OR=1.00, 95% IC1.00,1.00, p=0.046) at follow-up. These data were confirmed in the multivariable analysis.

Conclusion: Long-COVID symptoms are present in a significant number of COVID-19 patients and represent a new challenge for the healthcare system. Female gender and corticosteroids appear to be risk factors for the development of long-COVID symptoms. CT residual lesions seem to be correlated to hospitalization. Pulmonary function alteration is correlated to old age and comorbidities.

Multidisciplinary teams are essential to develop preventive measures and clinical and therapeutic management strategies.

COVID-19

P 174 REAL-WORLD USE OF SOTROVIMAB IN OUTPATIENTS AND HOSPITALIZED COVID-19 DURING OMICRON PANDEMIC WAVE

C. Muscatiello[1,3], F. Cuccaro[2], S. Bruno[3], L. Montemurro[3], A. Calamo[3], A. Giannelli[3], M. Mazzola[3], S. Carbonara[3]

[1]Infectious Disease Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy, [2]Epidemiology and Statistics Unit, Barletta, Local Health Unit BT, Italy, [3]Infectious Diseases Unit, V. Emanuele II Hospital, Bisceglie, Local Health Unit BT, Italy

Background: Sotrovimab (STR) is approved for early treatment of mild/moderate COVID-19. Herein we report our experience on STR administration in either outpatients or inpatients (COVID-19 related hospitalization) during the current pandemic wave sustained by SARS-CoV-2 (SC-2) Omicron subvariants.

Methods: We retrospectively collected data of consecutive patients treated with STR (January 1, 2022 – January 31, 2023) at the Infectious Diseases Unit, Bisceglie (BT). Investigated outcomes were the time to negative SC-2 antigenic test on nasal-pharyngeal swab (NFS), all-cause 30-day mortality and the adverse events rate; in addition, we assessed the 30-day hospitalization rate among outpatients as well as the intensive care admission rate among inpatients. Correlations between the above-mentioned outcomes and features of patients were also investigated by univariate analysis adjusted, when necessary, for age. We analyzed different proportions between categorical variables by chi-square test. We used Wilcoxon rank sum test to compare continuous variables in independent samples (inpatients vs. outpatients), and logistic regression to measure the association between explanatory variables and outcome variables producing odds-ratios.

Results: Overall, 105 patients were included in the analysis. Table 1 illustrates presenting characteristics, treatment and outcomes of the study population, divided by the setting of STR administration (500 mg i.v., single dose). Patients presented with an old age and a high Charlson comorbidity index, which were significantly greater among inpatients vs. outpatients (p<.005).

Only a minority of subjects had received >3 vaccine doses against SC-2. Remarkably, 41.4% of inpatients showed a severe COVID-19 when received STR. As compared to outpatients, more inpatients received STR >7 days after the symptoms onset (p<.005). STR was mainly combined to molnupiravir among outpatients (p= 0.029) and to remdesivir among inpatients (p=0.005). In comparison to outpatients, inpatients showed a lower rate of negative SC-2 antigenic test on NFS seven days after STR (p=0.041) but a similar rate at 14 days. The 30-day mortality was higher among inpatients (p<.005). At the univariate analysis, outpatients with chronic obstructive lung disease showed a higher 30-day mortality (p=0.032; OR= 15.78; 90% C.I. 1.26-197.31). No other chronic condition nor the Charlson comorbidity index correlated with either the time to negative SC-2 test on NFS or the 30-day mortality. One outpatient only was hospitalized at 30 days. No STR-treated inpatient was admitted to intensive care. We observed no STR-related adverse events.

Conclusions: STR may represent a valuable and well-tolerated tool for treatment of very fragile subjects infected by SARS-CoV-2 Omicron subvariants, in both outpatient setting and COVID-19-related hospitalization.

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COVID-19

P 175 SOTROVIMAB TREATMENT IN SEVERE COVID-19

C. Muscatiello[1,3], F. Cuccaro[2], S. Bruno[3], L. Montemurro[3], M. Altamura[3], G. Infante[3], R. Losappio[3], S. Carbonara[3]

[1]Infectious Disease Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy, [2]Epidemiology and Statistics Unit, Barletta, Local Health Unit BT, Italy, [3]Infectious Diseases Unit, V. Emanuele II Hospital, Bisceglie, Local Health Unit BT, Italy

Background: Sotrovimab (STR) is approved for early treatment of patients with mild-moderate SARS-CoV-2 infection. However, a prolonged viral activity and direct organ damage may be occurring in immune-compromised subjects when presenting with a severe COVID-19. Moreover, remdesivir, the only approved direct antiviral drug for severe COVID-19, is often contraindicated or possibly ineffective in these patients, in whom, therefore, anti-SARS-CoV-2 monoclonal antibodies might have a therapeutic usefulness.

Methods: We retrospectively recorded data from all consecutive patients hospitalized because of severe COVID -19 (NIH, 2020-2023) and treated with STR (500 mg i.v. single dose), between January 1, 2022 and January 31, 2023 at the Infectious Diseases Unit, V. Emanuele II Hospital, Bisceglie (BT). Starting January 2022, only Omicron variants of SARS-CoV-2 were assessed circulating in Apulia Region.

Results: Twelve patients, described in Table 1, responded to the enrollment criteria. In particular, we observed an elevated age (median 82,5 years) and a high Charlson comorbidity index (median 6,5). The majority of subjects (66,7%) suffered of chronic kidney disease. All patients had received three vaccine doses against SARS-CoV-2, but only 33% 4 doses. Total number of subjects presented an interstitial pneumonia with a variable need for oxygen supplement. Remdesivir was co-administered to STR in three patients, whereas it was contraindicated in those remaining. The median time from symptoms onset to STR infusion was 2 days (IQR 2 – 1.5).

No STR-related adverse event was observed. SARS-CoV-2 antigenic test on nasopharyngeal swab turned negative in one patient at day 7 and in seven at day 14 after STR infusion. No patient was transferred to intensive care. Intra-hospital death was recorded in one patient and 30-day death in three.

Conclusions: Further, controlled studies are warranted to assess Sotrovimab safety and efficacy in treating severe COVID-19 in immunocompromised subjects, who pose relevant therapeutic unmet needs when direct antiviral drugs are contraindicated or at increased risk of failure.

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COVID-19

P 176 A SARS-COV-2 CLUSTER IN PATIENTS WITH ONCO-HEMATOLOGICAL DISEASE

A. Gasperin[1], D. Di Trento[1], S.G. De Maria[1], M.Lichtner[1,3], S. Perrone[2], E. Ortu La Barbera[2], C. Del Borgo[1], A. Carraro[1], T. Tieghi[1], B. Kertusha[1], P. Fabietti[1], V. Belvisi[1], R. Marocco[1], M. De Masi[1], A.Grimaldi[1], S. Corazza[1], S. Garattini[1]

[1]Infectious Diseases Unit, SM Goretti Hospital, Latina, [2]Hematology Operative Unit, SM Goretti Hospital, Latina, [3]Department of Public Health and Infectious Diseases, "La Sapienza" University, Rome

Background: Hematological patients, due to their weakened immune systems, have an increased risk of COVID -19 infection and a greater chance of progression. For this reason, the healthcare professionals working in the Hematological wards need to be even more careful to standard infection-control precautions. Unfortunately, in December 2022 we reported a cluster in the Hematological ward from SM Goretti Hospital in Latina, due to the asymptomatic positivity of two nurses working in the same ward.

It is well known that the SARS-CoV-2 infection in hematological or immunocompromised patients causes more frequently a clinical progression and a prolonged viral phase, with longer times length of negativization (TLN). Therefore, it is of extreme importance to control the viral replication.

Methods: This retrospective observational study interested six inpatients from Heamatology Operative Unit, resulted positive to a SARS-CoV-2 nasopharyngeal swab in December 2022 and monitored until February 2023. We evaluated sex, age, hematologic disease, vaccination status, pre-exposure prophylaxis therapy, therapeutic approach, disease progression, TLN, chemotherapy phase and final outcome.

Results: Among six patients, 66.7% were males, the median age was 64.5 years old [IQR 58-82] and all had a complete vaccination cycle. Most patients (83%) were affected by acute leukemia, whilst one was affected by lymphoma. Five patients were undergoing chemiotherapy while one was in a recovery phase. Two patients did a CT-scan, that showed a non COVID-related pneumoniae.

Due to the extreme fragility of this type of patients it has been decided to use maximum therapeutic regimens, characterized by a combination between Mabs and antiviral drugs, in most cases used as an off-label 10 days course.

Four patients (66.7%) received a combination therapy with 10 days regimen of remdesivir and a sotrovimab infusion since they previously received prophylactic therapy with tixagevimab/cilgavimab (tixa/cilga) with an average TLN of 34 days (IQR 15-72). One patient, affected by a Retinoic-Acid Syndrome (RAS), underwent a double 10-days regimen of remdesivir and a tixa/cilga administration (TLN 33 days). Only one patient, treated with tixa/cilga and oral antiviral therapy (ritonavir/nirmatrelvir), died for non COVID-related cause.

Conclusions: In case of intrahospital clusters it is always important to remark the importance in paying attention to the fragile patients. In this case, despite the higher risk of progression, none of them developed a COVID syndrome.

There are very few studies and general guidelines regarding the correct regimens for hematological and immunocompromised patients with concomitant SARS-CoV-2 infection. Our cluster scenario could represent a picture of current state of science on hematological patients. However, the benefits of all these prophylactic and therapeutic treatments deserve larger sample sizes in order to understand the effects of COVID-19 outcome.

COVID-19

P 177 SARS-COV-2 INFECTION IN ONCOHEMATOLOGICAL PATIENTS: A REAL-WORLD EXPERIENCE

F. Izzo[1], S. Garattini[1], S. Di Bari[2], L. Bresciani[2], A. Carraro[1], A. Gasperin[1], D. Di Trento[1], G. Mancarella[1], A. Parente[1], A. Grimaldi[1], S. Corazza[1], S.G. De Maria[1], A. Destro[1], B. Kertusha[1], T. Tieghi[1], C. Del Borgo[1], P. Cirillo[1], C. Pasquazzi[2], A. Teggi[2], M. Lichtner[1]

[1]Dept of Public Health and Infectious Disease, "Santa Maria Goretti" Hospital, Sapienza University of Rome, Latina, Latium, Italy, [2]Dept of Pubic Health and Infectious Disease, "Sant'Andrea" Hospital, Sapienza University of Rome, Rome, Latium, Italy

Background: At present, patients with acute SARS-CoV-2 infection and a pre-existing oncohematological disease still represent a real “challenge” both in terms of therapeutic choices and success of the therapy itself. In fact, these patients present an increased risk of developing a more severe form of COVID-19 disease, including a higher risk of hospitalization, a lower response to pharmacological therapies and a higher risk of developing complications (e.g ARDS, multi-organ failure and nosocomial infections). Since the start of the pandemic, numerous drugs have been put forward either to prevent disease progression in patients without pneumonia, the so called “early therapy”, or to treat more advanced COVID-19 manifestations. Currently, clinical evidence on the effectiveness and appropriateness of these therapies is lacking for oncohematological patients.

Methods: In this retrospective study we recruited 88 patients (65.9% M, median age 71.3 y.o [25-92]) with the diagnosis of SARS-CoV-2 infection from March 2020 to March 2023 who presented to the Units of Infectious Diseases of two hospital in Latium, Italy: the “Santa Maria Goretti” Hospital in Latina, and the “Sant’Andrea” Hospital in Rome. These patients were divided into two groups according to the final outcome: discharge or death (by any cause during the hospitalization). We also considered different factors such as age, hematological disease, vaccination status at the time of hospitalization, severity of infection (absence or presence of pneumonia at admission) and type of therapy administered, if administered.

Results: Of the patients recruited, more than half (66.2%) did not receive early therapy. These untreated patients developed a more severe form of COVID-19 disease, with an overall higher rate of pneumonia (73.8% of the untreated patients) and a higher mortality rate (12 deaths, 85.7%) as compared to patients treated with early therapy (2 deaths, 14,3%). For inpatient therapy, patients treated with a combination of drugs had a lower mortality during hospitalization: in particular, the combination of both intravenous and oral antiviral (with a 10-days course of remdesivir and a 5 or 10-days course of nirmatrelvir/ritonavir) associated with monoclonal antibodies (sotrovimab or tixagevimab/cilgavimab) is related to a lower mortality rate during the hospitalization (0 out of 7 patients treated).

Conclusions: In immunocompromised patients with COVID-19 infection, early therapy and, or, targeted treatment during hospitalization with a combination of antiviral drugs, monoclonal antibodies and immunosuppressive drugs can reduce mortality. Anyway, further studies (possibly multicentric) with a larger population are needed to evaluate the impact of different anti-SARS-CoV-2 therapies and their combinations in onchohematologic patients.

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COVID-19

P 178 CHARACTERIZATION AND MONITORING OF POST-ACUTE SEQUELAE OF SARS-COV-2 INFECTION (PASC) THROUGH A VOICE ASSISTANT PLATFORM: AN ECOLOGICAL PROSPECTIVE STUDY

A. Caselgrandi[1], J. Milic[2], L. Gozzi[2], S. Renzetti[3], F. Motta[4], M. Pacchioni[5], M. Orsini[5], E. Mescoli[5], L. Sighinolfi[2], M. Belli[2], V. Menozzi[6], M.D. Di Trapani[6], S. Esperti[6], F. Medioli[6], G. Mancini[6], A. Verduri, B. Beghé[7,8], E. Clini[7,8], S. Calza[9], C. Mussini[2,6], G. Guaraldi[2,6]

[1]School of Medicine and Surgery, University of Modena and Reggio Emilia, Modena, Italy, [2]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, Italy, [3]Department of Medical-Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Italy, [4]Department of Physics, Informatics and Mathematics, University of Modena and Reggio Emilia, Modena, Italy, [5]DataRiver Srl, Modena, Italy, [6]Department of Infectious Diseases, Azienda Ospedaliero-Universitaria, Policlinico of Modena, Modena, Italy, [7]Respiratory Unit, Azienda Ospedaliero-Universitaria, Policlinico of Modena, Modena, Italy, [8]Department of Medical and Surgical Sciences for Children and Adults, University of Modena, and Reggio Emilia, Modena, Italy, [9]Department of Molecular and Translational Medicine, University of Brescia, Italy

Background: Voice assistance (VA) tools may be used to characterize and monitor post-acute sequelae of SARS-CoV-2 (PASC) in older people previously hospitalized for COVID and empower individuals' education-based program. The objective of the study was to prospectively characterize 6 months changes in symptoms, frailty and health-related quality of life (HRQoL) in people with (PASC) who used or did not use, a voice assistant telemedicine software platform (MyHealh VA) properly engineered to empower people with PASC.

Methods: This was a longitudinal prospective study of consecutive patients evaluated for PASC after hospital admission. MyHealh VA allows to use a voice interface, exploiting the commercially available Google Nest Mini with education-based program advice. Population was divided into two groups: Voice Assistant Group (VAG) who were asked to install at home and daily use VA device and Control Group (CG) who were asked to comply lifestyle intervention in diet and physical exercise only.

Results: A total of 93 individuals, 50 in the VAG and 43 in CG were enrolled. At baseline, no difference was observed between groups in demographic and anthropometric variables. An unadjusted regression model was built to explore the interaction between VAG and follow-up time in the CG. Greater BMI reduction over time was more likely in the VAG per -1.03 kg/m2 (p=0.002) vs. control group. In a multivariable logistic regression model for frailty, patients in VAG had significantly lower probability of frailty at follow-up (OR= 0.02, 95% CI: 0.0 – 0.53; p=0.03). Table 1 shows multivariable logistic regression models for frailty and HRQoL. Lower odds of frailty were also associated with longer time from hospitalization (OR= 0.75, 95% CI: 0.59 – 0.91; p=0.007). Older age (OR= 1.17, 95% CI: 1.05 – 1.37; p=0.02), BMI change (OR= 1.27, 95% CI: 1.02 – 1.69; p=0.005) and frailty at baseline (OR= 162.7, 95% CI: 13.2 – 8108.3; p=0.001) were associated with higher risk of frailty at follow-up. SF-36 total score at follow-up was predicted by baseline SF-36 total score only as well as EQ-5D-5L score was predicted by baseline EQ-5D-5L (OR= 87.7, 95% CI: 22.3 – 344.4; p<0.001) and male sex
(OR=1.54, 95% CI: 1.04 – 2.3, p=0.03) All patients appreciated the VA platform use.
Patients' empowerment in VAG use were estimated by a 48% reduction in sedentary life and a 42-46% increase in mild or moderate physical activity.

Conclusion: Frailty was reduced in people with PASC who used the VA platform, improving users' lifestyle. This pilot study well depicts a participatory and action research which took advantage of an innovative technological device. MyHealth VA may overcome digital divide limitations and be perceived as a promoter of continuity of care strengthening the relationship between health care providers and people with PASC.

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COVID-19

P 179 IMPORTANCE OF USE OF ANTIVIRAL AND MONOCLONAL THERAPIES IN PATIENTS AT RISK OF DEVELOPING SEVERE DISEASE AND COMPLICATIONS FROM SARS-COV2 INFECTION: EXPERIENCE OF COVID-DH OF PESCARA CIVIL HOSPITAL

D.A. Silletta, G. Rapacchiale, D. Recinelli, E. Mazzotta, M. Bondanese, S. Coladonato, S. Ianniruberto, G. Ferrandu, F. Trave, C. De Flavis, M. Giulianelli, D. Pietrantonio, G. Aventaggiato, G. Parruti

Infectious Disease Unit, Pescara's General Hospital

Introduction: During the Sars-cov2 pandemic new molecules, become standard therapies for patients suffering from Sars-cov2 disease, were discovered. The rationale for the therapeutic success is the temporal correlation between the onset of the Covid-related symptoms and the administration of therapy. We conducted an observational study with all patients evaluated in 2022 at the Covid Infectious Diseases DH of Pescara's General Hospital for mild forms of Sars-Cov2 with and without vaccination coverage.
The purpose of the study was to describe the use of new drugs and their impact on the evolution of disease to severe forms and hospitalizations.
Methods: Patients evaluated at Covid DH, from January 2022 to 31 December 2022, came from the territory with presentation of a medical record drawn up by the general practioner or by the emergency services. Risk factors, period of symptom onset, vaccination schedule and risk of disease progression were rated. At admission, vital parameters were assessed, EGA and laboratory tests were performed. Clinical evaluations were also performed by chest ultrasound or CT-chest, with follow-ups at 28 days. Oral and/or intravenous antivirals (Paxlovid; Lagevrio; Veklury) and/or MoAbs (Sotrovimab;Evusheld) were administred as appropriate. Statistical analyses were performed by STATA (17.0).
Results: A total of 2352 patients aged between 13 and 102 years (mean age 76±5) were treated with oral or systemic antivirals or MoAbs, considering the onset period of the covid-related symptoms. The different outcomes among patients who arrived within 5 days from the onset of symptoms and those who arrived later were considered. There were 188 patients treated with Paxlovid, with a hospitalization rate of 0.53%(n 1 pt); patients treated with Molnupiravir were 521, with a hospitalization rate of 1.15%(n 6 pts) and a mortality rate of 0.384%(n 2 pts); patients treated with Remdesevir were 315, with a hospitalization rate of 2.54% (n 8 pts); finally patients treated with Evusheld were 72, with a hospitalization rate of 2.79%(n 2 pts) and a mortality rate of 1.39%; patients treated with Sotrovimab were 291, with a hospitalization rate of 2.4% (n 7 pts) among patient treated within the first 5 days and with a hospitalization rate of 3.78%(n 11 pts) and mortality rate of 0.344%(n 1 pt) among patients treated later. Comorbidities present in the enrolled patients, mostly elderly (>80 years, 79%) and with immunopathies, were evaluated whit the Charlson comorbidity index.
Conclusions: The study highlights the importance of starting Covid-specific therapy within the first days of the onset of symptoms and underlines their impact of reduction of mortality and hospitalizations and decrising. Crucial is an adequate urban structural organization through the strenghtening of trainings and relations with local medicine, which is responsible for intercepting potentially at-risk patients, so as to optimize the timely patient care.

COVID-19

P 180 THE CLINICAL MANAGEMENT OF FULLY VACCINATED PATIENTS AT HIGH RISK OF DISEASE PROGRESSION WITH SYMPTOMATIC COVID-19 INFECTION AT ASST LECCO: REAL-LIFE EXPERIENCE

L. Bradanini[1], S. Pontiggia[1], M. Bottanelli[2], R. Monardo[2], F. Badalucco Ciotta[2], D. Turoli[1], V. Morena[1], F. Conti[1], C. Molteni[1], A. Pandolfo[1], A. Castagna[2], S. Piconi[1]

[1]Infectious Diseases Unit, Alessandro Manzoni Hospital, Lecco, Italy, [2]Università Vita-Salute San Raffaele, Milan, Italy

Background: The extensive vaccination campaign against SARS CoV-2 had markedly decreased incidence of severe COVID-19, although it was not completely effective in preventing new infections. Early antiviral treatments were developed to prevent severe form of COVID-19 in patients with high risk of disease progression. The aim of this study was to describe the "real-life" experience of COVID-19 outpatient clinic at Alessandro Manzoni Hospital in fully vaccinated symptomatic COVID-19 patients treated with molnupiravir, nirmatrelvir/ritonavir or remdesivir and in who did not receive any antiviral therapy.

Methods: This retrospective analysis was conducted on patients with mild-to-moderate SARS-CoV-2 infection referred to our outpatient clinic between January 2022 and August 2022. Therapeutic choice depended on patients' clinical condition and co-drugs medications according to Italian Agency of Drug (AIFA) indications.

Clinical outcomes were time of symptoms resolution, time of negativization of nasopharyngeal swab and any causes of hospitalization; these data were collected contacting all enrolled patients, treated or not treated with antiviral therapy, by phone calls. Categorical variables were analyzed with chi-square test or Fisher's exact test, while continuous variables were analyzed with U Mann Whitney and Kruskal Wallis test.

Results: 317 patients were included in this study. Among them 32/317 refused any antiviral therapies. 188, 66 and 32 patients were treated with molnupiravir, nirmatrelvir/ritonavir and remdesivir, respectively. Demographics, comorbidities and co-medications in the four groups of patients are described in Table 1. No differences were found on baseline demographic and clinical conditions between the groups. Polipharmacy (more than 5 drugs a day) was more significantly reported in molnupiravir group (p=0.002). Regarding clinical outcomes, time of negativization of nasopharyngeal swab was statistically longer in patients that refused any treatment for COVID-19 (p=0,01) compared to treated-patients groups as reported in Table 2. Between patients treated with early antiviral drugs, 53 (22,4%) patients reported adverse events: 21/66 (36,8%) with nirmatrelvir/ritonavir, 22/188 (12,7%) with molnupiravir and 10/22 (33,3%) with remdesivir (p=0.000). Gastrointestinal symptoms were the most reported (Table 3).

Conclusion: Our data support the positive impact of early treatment in fully vaccinated mild-to-moderate COVID19 symptomatic patients in term of time to negativization of SARS-CoV2 swab. No difference were found for the other clinical outcomes evaluated. Molnupiravir seems to be more well tolerated compared to the other two treatments.

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COVID-19

P 181 EVALUATION OF THE IMMUNE RESPONSE TO SARS-COV-2 VACCINATION ONE YEAR AFTER THE BOOSTER DOSE IN ONCOLOGY PATIENTS

R. Campagna[1], F. Dominelli[2], M.A. Zingaropoli[2], F. Ciurluini[3], V. Picone[4], E. Cortesi[4], G. Antonelli[1], O. Turriziani[1]

[1]Department of Molecular Medicine, Laboratory of Virology, Sapienza University of Rome, [2]Department of Public Health and Infectious diseases, Sapienza University of Rome, [3]Department of Radiological, Oncological and Pathological Science, Sapienza University of Rome, [4]Medical Oncology Department, Policlinico Umberto I, Sapienza University of Rome

Background: Aim of this work was to evaluate both the humoral and the T-cell mediated response in patients with solid tumors undergoing chemotherapy and/or immunotherapy in comparison with a group of healthy donors (HDs).

Material and methods: The specimen collection was carried out one year after receiving the booster dose of anti-SARS-CoV-2 vaccine. Whole blood samples were collected to assess the humoral response and the T-cell mediated response. IgG titers were quantified and expressed in Binding Antibody Units/ml (BAU/ml).

T-cell specific response was assessed on isolated PBMC using multiparametric flow cytometry after overnight stimulation with SARS-CoV-2 peptide libraries. All possible combinations of intracellular IFNγ, IL2 and TNFα T-cell production were evaluated, and T-cells were labelled “responding T-cells”, those cells that produced at least one of the three cytokines of interest, and “triple positive T-cells”, those cells that produced simultaneously all three cytokines.

Results: Sixty-seven oncology patients (OPs, 29 females/28 males, median age [interquartile range, IQR] of 60 [53-68] years) and 33 HDs (27 females/6 males, median age [IQR] of 54 [39-59] years) were included in the study. Among OPs, the most frequent primary tumor was lung cancer (33%) followed by breast cancer (28%) and colon cancer (7%). Overall, 26 patients (39%) were in treatment with immunotherapy. Forty-one OPs and 14 HDs experienced COVID-19 before specimen collection.

OPs group showed a lower IgG production (median 1640 [823-4820] BAU/ml) compared to HDs (median=2810 [1880-6650] BAU/ml) (p=0.026). No significant difference was found between patients receiving immunotherapy and those receiving chemotherapy. A higher level of antibodies was found in patients who experienced SARS-CoV -2 infection (OPs+, 2440 [1247-6510]) in comparison with those without referred infection (OPs-, 1043 [314-1781]) (p<0.001).

Furthermore, comparing HDs who didn’t experience COVID-19 (HDs-; 2470 [661-6650]) and OPs, a higher titer of IgG was observed in HDs- (p=0.031) while no significant difference was found between HDs and OPs with previous infection.

In OPs, lower percentages of responding T-cells (CD4: p=0.0078; CD8: p=0.0022) and triple positive T-cells compared to HDs were observed (CD4: p=0.0067 and CD8: p=0.0003).

Conclusions: One year after the third dose of anti-SARS-CoV-2 vaccination we found that IgG titers were lower in OPs than in HDs. In our study population the treatment received does not seem to influence the antibody production after vaccination. Since the IgG titer is still not considered a reliable correlate of protection, to improve our results we intend to evaluate the neutralizing capacity of the detected antibodies. Moreover, in OPs, a lower T-cell response compared to HDs was observed. Further studies are needed to complement our results and determine the implication of low T-cell response on clinical protection of OPs against SARS-CoV-2 infection.

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COVID-19

P 182 SARS-COV-2 INFECTION IN PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES: IN SEARCH OF LOST TIMING?

R. Astorri[1,2], N. Carro[2], A. Dell'Aquila[2], P. Medusa[2], I. Palma[2], S. Imbriani[2], K. Gjeloshi[2], C. Ricozzi[2], Russo[1,2], C. Sagnelli[1,2], M. Pisaturo[1,2], N. Coppola[1,2]

[1]Department of Mental Health and Public Medicine, Section of Infectious Diseases, University of Campania L. Vanvitelli, Naples, Italy, [2]Vanvitelli COVID-19 Unit, University of Campania L.Vanvitelli, Naples, Italy

Background: immunocompromised patients, particularly those with haematological malignancies, may have an impaired response to COVID-19 vaccines, with a baseline systemic inflammation that may result in a slow progression of COVID-19, also with a typical lung injury. The management of these patients is one of the major challenges of this new phase of the COVID-19 era, as their clinical evolution can be inesorable and even imprevedible.

Case presentation and discussion: we present the case of a 64-year-old man, vaccinated with three doses of COVID-19 vaccines, affected by chronic lymphatic leukemia (receiving monthly cycles of Rituximab), ankylosing spondylitis, arterial hypertension, obstructive sleep apnea syndrome, recent myocardial infarction (2022). On 17 February 2023, the patient was febrile and received azithromycin for 3 days without benefit. On 26 February, he presented to the emergency room (ER) with dyspnea and a first positive nasopharyngeal (NP) swab for SARS-CoV-2. His chest CT was typical, with a CT severity score of 12/25. On 1 March, he was admitted to our COVID Unit, where he maintained satisfactory clinical conditions, room-air blood gas analyses, laboratory exams. He received a cycle of 5 days of Remdesivir, in addition to his usual therapy. On 7 March, the patient was discharged in good general conditions. The following days, the patient had low-grade fever and increased inflammatory markers, but refused to be admitted to hospital again. Due to clinical worsening, with fever (Tmax 38°C), dyspnea and desaturation (SpO2 80%), on 20 March, he went to the ER and was placed in oxygen supplementation with Venturi Mask (FiO2 60%) due to a PaO2/FiO2 (P/F) ratio of 162, his nadir. His CT score severity was now 20/25. He received tocilizumab and sotrovimab, and started a new 5-days cycle of Remdesivir therapy. On 22 March, he was transferred to our Unit, with a satisfactory (95-96%) oxygen saturation with nasal cannules at 4 L/min. A CPAP therapy was added, with a setting of 8 cmH20 and 21% FiO2, with a constant improvement (P/F >400), until he was placed again in room air, continuing his CPAP cycles for some days. The patient remained positive SARS-CoV-2 NP swabs.

Results: our patient had a marked improvement of his conditions following a multi-approach therapy, although he remained persistently positive at SARS-CoV-2 NP swabs. A new 10-days therapy with Remdesivir was proposed, aiming at viral clearance and clinical stability.

Conclusions: even when vaccinated, COVID-19 patients with hematological malignancies can represent a major challenge for clinicians. Immune modulators, monoclonal antibodies and antivirals constitute important tools, but their use is sometimes strictly or blurrily regulated and off-label schemes appeared beneficial in selected patients. Perhaps, we should rethink timing, therapy duration and multilevel approaches to improve clinical outcomes in these peculiar patients.

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Epidemiology and Prevention

P 183 CONVENIENT&QUICK - LET'S DO IT IN PHARMACIES

R. Galipò[1], R. Bellagamba[1,2], E. Farinola[1], P. Ferri[1], A. Palummieri[1]

[1]Anlaids Lazio, Rome, [2]INMI Spallanzani, Rome

Introduction: The latest COA data from the Istituto Superiore di Sanità confirm that HIV cases detected in Italy have continued to decline, as they have since 2012. At the same time, late diagnoses have increased in 2020 and 2021. In fact, as the latest ISS Newsletter reports, "In 2021, more than one-third of newly diagnosed HIV-positive people find out that they are HIV-positive due to the presence of HIV-related symptoms or pathologies."
Anlaids Lazio in order to intensify testing access services, which are already active in its own premises with the Let's Make It Fast Project, and to enable an even more effective and comprehensive program, has decided to activate a pilot program in some pharmacies, creating on site a free reserved space for HIV testing.
Method: Three Pharmacies located in 3 different Municipalities of the Municipality of Rome were identified. The administration of the HIV test on oral fluid (OraQuick ADVANCE® HIV-1/2 Test) was performed by Anlaids Lazio operators (psychologist and peer operator) on 1/2 days in January/February/March 2023. Access was free and free of charge. Pharmacies provided the space generally used for performing the Covid19 swab and supported the Association in promotion. Each user was asked to complete informed consent and an anonymous data collection form, which was followed by pre- and post-test HIV counseling. Information on HIV/AIDS/STI was provided and information materials and condoms were handed out.
Results: A total of 87 HIV tests were performed over the course of the 5 days. People tested were predominantly male (55 males vs. 32 females), Italian (7 foreigners in total), median age of 26 years (range 17-46) for females, and 34 years (range 21-71) for males. One third of the users had never taken the test before. Almost all reported unprotected sexual intercourse or condom breakage episode as the reason for requesting HIV test. 27/55 males and 7/32 females report having same-sex relationships. All tests yielded NON-reactive results.
Conclusion: HIV testing and periodic repetition have proven to be effective tools for early diagnosis, enabling people to access treatment early (linkage to care).
Given the considerable demand for rapid testing outside of traditional settings and in the wake of the Covid-19 pandemic that has seen pharmacies at the forefront of activating the Covid 19 swab, we assessed that this experience may be useful for the widespread dissemination of rapid HIV testing in the territory. Pharmacies are now a point of reference and particularly with respect to prevention issues. In this regard, the Fifth Annual Pharmacy Report shows that 34 percent of pharmacists have carried out screening campaigns in the past year to identify individuals at risk for chronic diseases.

Epidemiology and Prevention

P 184 SEXUALLY TRANSMITTED INFECTIONS' (STIS) SCREENING OFFERED BY NOT-FOR-PROFIT SECTOR ENTITIES DURING THE COVID-19 PANDEMIC: A DESCRIPTIVE OBSERVATIONAL STUDY OF THE POPULATION ACCESSING A LGBT+ DEDICATED SERVICE

R. Piccirillo, B. Allegretti, G. Aulicino, S. Carotenuto, A. Cioffi, G. Cioffi, V. Coluccino, G. D'Ambrosio, B. Diana, F. Merolle, N. Piazza

Rain Arcigay Caserta ODV, Caserta, Università degli studi di Palermo dipartimento di Igiene e medicina Preventiva, Palermo

Background: During the COVID-19 pandemic, Italian National Health Service(NHS) has focused all its efforts to manage the emergency. As a result screening tests for some diseases have been neglected. In this context, the main Italian LGBT+ non-for-profit organization (Arcigay) of Caserta has set up a Checkpoint to provide counseling and screening services for STIs. This study investigated sexual health of people accessing the service and the outcome of regional regional funded project " QTCcheckpoint" .

Material and Methods: A questionnaire was administered to people accessing the screening service to collect information on their sexual health. All participants completed an informed consent for the screening test as well as for the questionnaire. Volunteer trained staff members were present to help participants understand the questionnaire. The tests were performed by medical personnel or experienced professionals. After the questionnaires were collected, data were entered into a Microsoft Excel database All statistical analyses were conducted using STATA.

Results: In the two-year period 2021-2022, 458 questionnaires and 1374 tests were administered. In 2021, there were 390 accesses(85.15%), while in 2022 68(14.85%). Users were mainly Italian(96.72%), male(60.39%) and heterosexual(61.1%), while 38.4% belonged to the LGBT+ community. 70% of the participants were tested for HIV for the first time, 5.9% had had an STD. Most of the people screened(64.85%) reported that they preferred the service offered by Arcigay, rather than the service offered by NHS. With regard to sexual behaviors,88% of the people interviewed reported having had penetrative sex in the past 12 months, but 83%of them did not use a condom; 39.86% reported to use psychotropic substances during sex. There were 3 Syphilis and 1 HIV diagnoses, including 1 Syphilis in a heterosexual person and 2 Syphilis and 1 HIV in LGBT+ people, respectively.

Conclusions: The service, designed for the LGBT+ population, had mainly heterosexual users. From the available data, the prevalence of STIs in the heterosexual population is estimated at 359 cases per 100,000, while in the LGBT+ community it is 1704 cases per 100,000, indicating a higher risk for LGBT+ community. Nevertheless, STIs in this group are often subjected to low notification. The results suggests that the offer of the NHS STIs services should be expanded with community-based services also targeting vulnerable populations. Staff providing these services should be trained to appropriately communicate with the target population, to reduce fear of judgement which is one of the factor influencing health-seeking behaviors. Despite the successful outcomes of this project, in 2022 the lack of funds made available by Campania Region, which was the main donor of the project has led to a lower service offer. It is desirable that economic investments are put in place which include the non-profit sector entities to support the NHS.

Epidemiology and Prevention

P 185 THE FUTURE IMPACT OF SARS-COV-2 ON SEXUALLY TRASMITTED DISEASES SPREAD

I. Uccella[1], E. Anzalone[1], S. Viri[1], C. Gargiulo[2], R. Pulselli[2], C. Sias[2]

[1]UOSD AIDS, F. Spaziani Hospital, Frosinone, Italy, [2]Clinical Pathology, F. Spaziani Hospital, Frosinone, Italy

Background: The scientific community's efforts have been focused on solving the back-breaking challenge of the COVID-19 pandemic, but sexually transmitted infections (STIs) are still one of the most common global health problems. During pandemic era, the STI prevention programs and cure, that could be monitored both clinically and with laboratory testing to ensure an appropriate response to therapy, were stopped. Material and methods. We compared HIV and Syphilis testing pre and during the outbreak, in Frosinone Province-450.000 inhabitants,4 hospitals, 4 districts, 16 Territorial Health Facilities- to understanding what happened on screening programs of STIs.

Results: Comparing testing and incidence of both infection, we observed during Covid restrictions a significant decrease of people tested for Syphilis, only(p=0.046) and testing number for both (p=0.05). No significant reduction of tested people for both (p=0.06). In 2019, HIV testing was 9504 with reduction during the epidemic:7717 in 2020, 8199 in 2021 e 7141 in 2022 (p=0.25). In general, we lost 1500 tests/year, but only inside the bigger hospitals and health care surveillance (from 681 to 446). About Syphilis, people tested were 4391 vs 11937 during pandemic era. Of them 3 Syphilis +/ HIV+, 3314 Syphilis -/HIV-,18 Syphilis +/ HIV-,4 Syphilis -/ HIV+. The remaining 534, only tested for Syphilis, 4 +and 492-. In 2020-2022 period, regarding 7309 people, 4 Syphilis +/HIV+,7239 Syphilis -/HIV-,36 Syphilis +/ HIV-, 31 Syphilis -/+HIV. The remaining 536, tested only for Syphilis, resulted 41+ and 495-. The naïve HIV population is characterized by young Italian homosexual men, with Syphilis. But during the pandemic >50% new diagnosis were young heterosexual migrants, on advanced stage, tested because concomitantCovid-19 infection, without Syphilis. An increase of post-exposure prophylaxis for HIV and bacterial sexual infections on MSM and gender violence and HIV hospitalized advanced stage was observed . The late diagnosis caused an increase of HIV death, particularly on Intensive Units. HIV+/SARS-Cov2+ were 60. Of them 10 with pneumonia and bacterial superinfection,13 treated with Mbs/antivirals. The remaining, thanks to vaccination, manifested infection, only. Telehealth was a strategy to connect people to HIV and STIs care and prevention services who were not reached through conventional methods in order to support viral suppression and retention in care for others.

Conclusions: The negative impact of Covid on screening and diagnostic and therapeutic delay will impact the morbidity and mortality of the major STIs. All new HIV+ were in advanced diseases, most of them died. The incidence of Syphilis increased, particularly latent phase-difficult to treat and eradicate- indirect sign of barrier to access to healthcare. Vaccination against the most important bacteria and viruses, long acting as prevention and Telehealth could be used inside the strategy to reduce the negative healthcare outcomes.

Epidemiology and Prevention

P 186 HUMAN PAPILLOMAVIRUS VACCINE UPTAKE BEFORE AND AFTER THE IMPLEMENTATION OF AN ON-SITE VACCINATION SERVICE AT AN HIV CLINIC IN MILAN, ITALY: A RETROSPECTIVE OBSERVATIONAL STUDY

A. Giacomelli[1], M.L. Colombo[1,2], M.V. Cossu[3], D. Moschese[3], G. Carrozzo[1,2], A. Poloni[1,2], G. Casalini[1,2], G. Pozza[1,2], L. Oreni[1], S. Antinori[1,2], A. L. Ridolfo[1]

[1]III Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [2]Università degli Studi di Milano, DIBIC Luigi Sacco, Milan, Italy, [3]I Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy

Background: Vaccination against HPV is an effective and safe intervention to prevent and reduce the risk of HPV-related disease and it is therefore recommended for all PLWH up to 45 years of age. However, there is little evidence on the uptake and barriers to HPV vaccination in PLWH. Aim of this study was to assess the rate of HPV vaccination uptake before and after the implementation of an on-site vaccination service.

Materials and Methods: This was a retrospective observational study conducted at the out-patient clinic of the III Infectious Disease Unit, Luigi Sacco Hospital (Milan, Italy) between 28th October 2017 and 31th December 2022. From 28th October 2018 an on-site vaccination service dedicated to all PLWH in care at the center was implemented: it runs three days a week offering a complete vaccination anamnesis and the administration of appropriated vaccines in accordance with the national guidelines. All PLWH aged <45 years who had at least one visit in the 12 months before the start of our vaccination service were enrolled in the study and followed up until 31th December 2022. Their demographic and epidemiological characteristics and date of uptake of HPV vaccine doses were collected. The main outcome of interest was the completion of HPV vaccination 3-dose schedule. A descriptive statistical analysis of the rate of vaccination uptake was performed.

Results: A total of 586 subjects were enrolled in the study. They had a median age of 38 years (IQR: 32-42), were prevalently males (74.1%), men who have sex with men (53.9%), of Italian origin (65.4%), and employed (78.7%) (Table 1). Overall, 157 (27%) subjects received at least one dose of HPV vaccine and 122 (77.7%) of them completed the 3-dose vaccination schedule. Almost all of subjects who received the HPV vaccine did so at the on-site service, with only 5 subjects vaccinated before the implementation of the service (Figure 1). There was a trend in increasing in the absolute number of subjects who started the HPV vaccination programme during the period 2019-2021, although this trend seemed to reverse in 2022. At the end of the study period the overall HPV vaccination completion rate was of 20.8%. Males when compared to females had higher odds of being fully vaccinated for HPV (OR 3.40 95%CI 1.76-6.55), as were the Italians when compared to non-Italians (OR 3.10 95% CI 1.87-5.14). None of the enrolled irregular migrants completed the vaccination schedule during the study period. Occupation was not associated with HPV vaccine completion (p=0.553).

Conclusions: HPV vaccine uptake increased after the implementation of an on-site vaccination service at our HIV Clinic, with males and Italian subjects presenting higher odds of being fully vaccinated. However, the overall HPV vaccine uptake remains worrisomely low. It is therefore important continuing to promote HPV vaccination targeting high-risk population, and to identify barriers limiting the access to vaccines.

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Epidemiology and Prevention

P 187 INCIDENCE OF HCV AND HIV IN THE FEMALE PRISON POPULATION: ANALYSIS OF TWO ITALIAN CENTERS

V. Manca[1], V. Fiore[1], N. Geremia[2], I. Maida[1], S. Babudieri[1]

[1]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [2]Unit of Infectious Diseases, Department of Clinical Medicine, 'Ospedale dell'Angelo', Venezia, Italy

Background: The female prison population represents a minority of the entire prison population in Italy, out of 54134 prisoners only 2237 (4.1%) are women, for this reason it is considered an underserved population.
Material and Metod: Our study aims to analyze the incidence of HCV and HIV in the female prison population by taking an accurate anamnesis (from the two centers it is clear that the population is of heterogeneous nationality, Africa, Italy, Romania, Eastern Europe) and by testing the female population where possible with blood chemistry analyses, alternatively with rapid tests each time they return to prison, especially if they present risk factors.
Results: The analyzed population is based on two prisons, the prison of Sassari and that of Venice, for a total of 101 inmates, of which 2 girls are daughters of prisoners, 18 of these belong to the Sassari penitentiary and 84 to that of Venice. The median age was 42 (0-66) years, of these screening was offered to all and out of 101 they accepted in 87 (86%) and refused in 14 (14%). They tested positive for HIV in 2 (1.98%) and for HCV in 15 (14.85%) out of 3 it was not possible to carry out HIV screening. The medical history shows that most of the inmates have had or are using drugs or have tattoos as risk factors for HCV and HIV.
Conclusion: The female prison population has a high risk of contracting HCV, the refusal to screen is often due to poor counseling, cultural and religious beliefs for which more targeted interventions aimed at eradication from the female prison population would be needed.

Epidemiology and Prevention

P 188 DETECTION OF ASYMPTOMATIC MPOX VIRUS INFECTION IN HIGH-RISK MEN WHO HAVE SEX WITH MEN: A PROSPECTIVE ANALYSIS

R. Rossotti[1,2], D. Calzavara[2], M. Cernuschi[2,3], F. D'Amico[1], D. Moschese[2,4], A. De Bona[2,5], S. Bossolasco[2,3], D. Tesoro[2,5], C. Muccini[2,3], A. d'Arminio Monforte[6]

[1]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [2]Milano Checkpoint, Milan, Italy, [3]San Raffaele Scientific Institute, Milan, Italy, [4]ASST Fatebenefratelli Sacco, Milan, Italy, [5]ASST Santi Paolo e Carlo, Milan, Italy, [6]University of Milan, Milan, Italy

Background: A recent study evaluated anal swabs belonging to 200 asymptomatic men who have sex with men (MSM) that were retrospectively tested for mpox virus (previously known as monkeypox) finding the infection in 13 samples (6.5%). This observation has important consequences in terms of contact management and epidemic control. We aimed to prospectively assess the presence of mpox in asymptomatic high-risk individuals.
Methods: PrEP users and people living with HIV MSM attending a community-based service that provides sexual health assistance in the Milan metropolitan area were consecutively evaluated. Inclusion criteria were: (i) no prior diagnosis of mpox infection; (ii) no suggestive complaints in the previous 21 days. If no mpox-related symptoms were detected, oral and anal swabs were collected to undergo testing for mpox through the rapid Standard M10 platform with MPX/OPX test (SD Biosensor, South Korea). This point-of-care test recognizes different target genes allowing to identify the presence of Orthopoxvirus, to diagnose the presence of mpox, and then to distinguish between I and II clades. Individuals received phone calls every 5 days to complete 21 days of follow up. Given the prevalence described, the calculated sample size was 67 individuals.
Results: We evaluated 92 subjects, but 25 (25.8%) were excluded for previous mpox diagnosis. The enrolled 72 individuals were mainly PrEP users (87.5%) and with a median age of 37 (IQR 32-46) years. Table 1 shows the features of study population, characterized by high prevalence of recent STI diagnosis (13.9%), common use of recreative drugs (26.4%) and large number of sexual intercourses in the previous 3 months. One third received at least one injection of MVA-BN vaccination. None of the enrolled subjects tested positive for mpox infection nor developed suggestive symptoms during the follow up.
Discussion: We selected a high-risk population with a significant history of sexual exposure, but we failed to detect any infection in the absence of consistent symptoms. Although the sample size was small, our data suggest that the prevalence of asymptomatic mpox infections could be lower than what previously reported. Thus, sexual contacts might continue to undergo only self-monitoring with no need of quarantine nor additional testing.

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P 189 LIFE EXPECTANCY AND DETERMINANTS OF INCREASED RISK OF DEATH IN PLWH

F. Maggiolo[1], L. Comi[1], D. Valenti[1,2], R. Teocchi[3], E. Di Filippo[1], S. Venturelli[1]

[1]UOC Infectious Diseases, [2]FROM foundation, [3]Informatics department, ASST Papa Giovanni XXII, Bergamo Italy

Background: The life expectancy for successfully treated patients who achieve viral suppression and attain a CD4 + cell count of at least 350 cells/mcL is considered similar to that of uninfected people and they are estimated to live to about 80 years on average. We explored if these affirmations are true and studied determinants increasing the risk of death.

Methods: In this retrospective study 2780 ART treated subjects active in our cohort were compared to 187 PLWH who died in the last 5 years (2018-2022). WE used a probit model to verify the impact of baseline and other variables on the event of death.

Results: The distribution curve of ages of the 2780 active subjects appears skewed to the left with a peak at about 60 years and a rapid decline afterwards (figure panel A). In the last five years the median age of patients at death ranged from 59 to 63 years with the lower quartile ranging from 51 to 57 years and the upper quartile in the range 63-70 years (figure panel B). As a whole, the median age of deceased subjects was 60 years with an interquartile range from 53 to 69 years. The median age of the control cohort was significantly ($P < 0.0001$) lower with a value of 53 years (IQR 45-49). Gender and ethnicity were not significantly different between the 2 groups, while an excess of subjects who acquired HIV through needle exchange was present among deceased 46.5%) compared to survivals (24.4%) ($P < 0.0001$). The most relevant differences were:

1. last CD4+ count that had a median of 524 cells/mcL (IQR 340-698) for deceased subjects and 843 cells/mcL (IQR 607-1124) for the control group
2. last HIV RNA measure that was > 200 copies/ml in 4.3% of deceased and only in 0.8% of controls ($P < 0.0001$)
3. presence of cirrhosis that was 14.4% for deceased and 3.8% for controls ($P < 0.0001$).
4. presence of active neoplastic disease that was 24.1% for deceased and 8.2% for controls ($P < 0.0001$).

The nature of neoplastic diseases was different between the two groups, too. Among deceased subjects the most common cancer was HCC followed by lung, gastro-enteric, prostate cancers and leukemia; among controls the most common neoplastic disease was breast cancer followed by lymphoma, HCC, KS and anal cancer.

When entered in the multivariate probit model, however only age, last CD4+ count, years of diagnosis (a proxy of infection length) and the presence of a neoplastic disease (in active phase) retained a statistical significance (figure panel C).

Conclusions: Previous calculations of life expectancy for PLWH could have been a little too optimistic. In our cohort the median age at death remained constant at 60 years in the last five years. A reduced immune restoration remains a significant driver of death risk. We found a concomitant neoplastic disease in a significantly higher proportion of deceased patients, therefore screening plans to allow early diagnosis and healthy life habits should be reinforced to improve life expectancy in all PLWH.

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Epidemiology and Prevention

P 190 USE OF MVA-BN VACCINE IN THE CONTEXT OF THE CURRENT MPOX OUTBREAK: EARLY EXPERIENCE OF AN INFECTIOUS AND TROPICAL DISEASES UNIT IN FLORENCE, ITALY

F. Lagi[1], G. Formica[2], S. Gaggioli[2], V. Petrini[2], P. Corsi[1], A. Di Felice[2], C. Fiorelli[1], C. Malcontenti[1], E. Francalanci[2], G. Modi[2], M. Trotta[1], S.T. Kiros[2], E. Gazzarri[3], I. Macrì[3], N. Zocco[3], A. Bartoloni[1,2]

[1]Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, Italy, [2]Department of Experimental and Clinical Medicine, University of Florence, Florence Italy, [3]Cooperativa Sociale C.A.T. Street unit Vivian Love, project S.A.T.I.S., Florence, Italy

Background: Around 86500 Monkeypox (Mpox) cases have been registered worldwide since the beginning of the current outbreak. FDA approved a live attenuated, non-replicating vaccine (MVA-BN) for groups at risk like men who have sex with men (MSM), people living with HIV (PLWH), sex workers, laboratory, and healthcare workers. Following the Italian Ministry of Health indications, MVA-BN was intradermally administered (0.1mL) in two doses 28 days apart; one dose was administered in people previously immunized for smallpox.

Materials and Methods: We retrospectively collected routine data of people vaccinated for Mpox in a tertiary-level hospital in Florence, Italy, from September 15 to December 31, 2022. Data were collected from standard pre-vaccination screening questionnaires. Patients were recruited either from the doctor at the HIV and sexually transmitted infections (STD)/PrEP clinic or from the general population by a self-application through a dedicated email/phone number contact. Moreover, a walk-in session was organized with CAT – Cooperativa Sociale. CAT is a local association supporting victims of trafficking/exploitation and sex workers. Patients could report any adverse events anytime through phone or email contact.

Results: A total of 200 subjects were vaccinated: 45.5% (n=91) were recruited in the HIV outpatient clinic, 12.5% (n=25) in the STD/PrEP clinic, 6.5% (n=13) in the laboratory, and 35.5% (n=71) were people from the general population, not previously known to the center who applied through the dedicated email/phone number. HIV screening was performed in 47.9% of people not previously known to the center: no cases of HIV infection were detected. During the walk-in session, 19 undocumented migrants self-defining as sex workers have vaccinated thanks to the CAT awareness campaign. The incidence of local and systemic adverse events after the first shot was 28.0% and 1.3%., respectively. All events were mild, with a median duration of 7 days [7-21]. Eleven patients (5.5%) have voluntarily decided not to complete the recommended vaccination course. Demographic and clinical data are summarized in Table 1.

Conclusions: In our experience, collaboration with local associations could be essential for promoting screening and awareness campaigns in marginalized communities. MVA-BN appeared to be a safe vaccine.

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Epidemiology and Prevention

P 191 OUTBREAK OF HIV AMONG PEOPLE WHO INJECT DRUGS DISCOVERED THROUGH PHYLOGENETIC ANALYSIS: ARE WE SEEING JUST THE TOP OF THE ICEBERG?

A. Soria[1], M. Carbotti[1,2], B. Monti[1,3], G. Paparatto[4], M. Tallarita[1], M. Sciabica[1], S. Malandrin[1], E. Chiesa[1], P. Fortuna[1], N. Squillace[1], E. Colella[1], P. Columpsi[1], G. Bozzi[5], C. Alteri[6], L. Tavoschi[4], G. Lapadula[1,3], P. Bonfanti[1,3]

[1]Fondazione IRCCS San Gerardo dei Tintori, Monza, [2]University of Pavia, Pavia, [3]University of Milano-Bicocca, Monza, [4]University of Pisa, Pisa, [5]Fondazione IRCCS Ca' Granda Policlinico, Milan, [6]University of Milan, Milan

Background: In high income countries, HIV transmission through needle sharing in people who inject drugs (PWID) has been reduced by harm reduction (HR) interventions. Though, isolated new HIV infections in PWID still occur, and outbreaks have been reported over time. Identification of transmission clusters could foster public health measures to stop the chain of contagion.

Methods: Available sequences from PLWH attending an outpatient clinic in Lombardy since 2015 were included in a phylogenetic analysis based on Maximum Likelihood (ML) method to confirm subtype and define transmission clusters (ref. HIV-1 subtype B HXB2, bootstrap >90%). Epidemiological investigation was carried out through interview with available cases and retrospective consultation of medical records.

Results: Among 794 PLWH followed up between 01/01/2015 and 31/12/2022, with at least one pol sequence available while viraemic, ML tree based on 161 individual B-subtype sequences identified a single cluster of 14 subjects (Fig. 1, bootstrap 98%). Of interest, 13 out of 14 (93%) had the presence of V106I mutation, normally found in 2% of untreated individuals; in our cohort 2/161 (1.2%) had a V106I mutation and were unlinked to the above-mentioned cluster. There were other 6 sequences with subtype B and V106I mutation which are not showed in the ML tree, because they were unavailable at the time of current phylogenetic analysis, but are belonging to epidemiologically linked individuals.

Of these 20 "outbreak members", 4 (20%) were women, the median (range) age was 32 (21-57) years. Four (20%) were diagnosed in prison, 3 (15%) in addiction centres, 6 (30%) in outpatient HCV clinic, 6 (30%) in different inpatient settings, 1 (5%) in street mobile unit. All cases were HCVAb positive. All patients had a known history of injecting drug use and most had common drug use network. The first case was diagnosed in 2006, while the second, in 2015, had a documented symptomatic primary HIV infection (Figure 2).

We hypothesize a founder effect of the first case during a period of low adherence to antiretroviral therapy which included efavirenz, possibly selecting for V106I mutation. The subsequent spread of the HIV outbreak over the following 7 years is likely due to sharing of injecting equipment in a close group of epidemiologically linked individuals. Further epidemiological and phylodynamic analyses are under way.

Conclusions: HIV transmission through injecting drug use is not over and should be continuously monitored as potentially re-emerging route, including the associated risk of transmitted drug resistance. Phylogenetic analysis is a powerful tool to identify transmission clusters. Innovative strategies like web platform for real-time monitoring of HIV sequences could help identifying existing clusters in a timely manner and subsequently implement outbreak response interventions (i.e., enhanced case findings, tailored linkage to care, scale up of HR measures) to rapidly halt transmission.

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P 192 EVALUATION OF THE ACCEPTANCE OF SALIVARY RAPID HIV TESTS IN THE IDU POPULATION AFFERENT TO THE SER.D. OF TREVISO

M.C. Rossi[1], F. Farina[1], G. Berto[2], S. Pavanello[2], E. Marzola[2], G.M. Mauro[2], M. Piccinini[2], V. Pagnotta[2], E. Favero[2], A. Bertocco[2], L. Sutto[2], R. Manera[2]

[1]ANLAIDS Treviso, Treviso, [2]Unità Dipartimento per le Dipendenze, Azienda ULSS 2 "Marca Trevigiana", Treviso

Background: In 2021, 1770 new HIV infections were diagnosed in Italy, out of which 4.2% concerned Intravenous Drug Users (IDU). The use of drugs increases the risk of infection also because it alters the perception of risk, which may lead to unsafe behaviors. For these reasons the IDU population needs to be tested more often: ideally every 6 months. 30% of IDU patients followed in the last 10 years at the Treviso Ser.D. (Servizio per le Dipendenze) have never been tested for HIV. Testing such patients presents several challenges: the difficulty of finding venous access (implying the need to resort to jugular vein, temporal vein, arterial sampling); the unavailability of specialized personnel, the frequent lack of a sampling point at Ser.D., large amount of time needed to perform blood tests under these conditions. The objective of this study is to evaluate the degree of acceptance of the rapid saliva test for HIV among patients in substitution therapy followed by the Treviso Ser.D. (Treviso + Oderzo); to detect HIV infection early and treat the patient; to reduce the virus transmission.
Materials and Methods: Patients in substitution therapy attending the Ser.D. of Treviso (Treviso + Oderzo) from March 2022 to March 2023 were tested. Rapid saliva HIV tests were offered every 6 months for one year. The OraQuick Advance HIV 1/2 Meridian BIOSCIENCE antibody test was used.
Results: Between March 2022 and September 2022, 342 patients (235 in Treviso, 107 in Oderzo) underwent rapid salivary HIV testing. 6/342 patients tested positive, but their HIV-positivity was already known (prevalence 1.75%). After 6 months 277 patients were retested (185 in Treviso, 92 in Oderzo; 6 positive patients were excluded); none of them was positive. 59 patients (17.5%) were not retested for various reasons: 10 refused, 1 died in an accident, 48 were lost in the follow-up. Only 3% of patients refused the second test.
Conclusions: The rapid saliva test for HIV is well accepted by the IDU population, so it can be adopted in this population as a frequent screening method. There is, however, a proportion of patients who refused the second test, due to a poor risk perception. It will have to be assessed whether acceptance of the test will persist over time even in those patients who have have accepted the testing every 6 months for a year. A limitation to the use of rapid salivary tests for HIV is the cost (approximately 12 euros), compared to the lower cost of serological tests.

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P 193 LACK OF ANTIBODY PROTECTION FOR HBV IN YOUNG PEOPLE UNDERGOING NON-OCCUPATIONAL POST-EXPOSURE PROPHYLAXIS (PEP) FOR HIV IN A LARGE TERTIARY HOSPITAL IN MILAN, ITALY

G. Bozzi[1], A. Liparoti[1,2], M. Fava[1,2], G. Ancona[1], C. Bobbio[1], N. Iannotti[1], B. Mariani[1], A. Muscatello[1], A. Bandera[1,2]

[1]Infectious Diseases Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy, [2]Department of Pathophysiology and Transplantation, University of Milano, Milano, Italy

Background: Post-exposure prophylaxis (PEP) is an important measure to reduce the risk of HIV transmission to people with occupational and non-occupational risk exposures. Updated data describing the population undergoing PEP in our geographic and social context are needed to design risk reduction interventions. To investigate possible unmet needs of this population, we analysed data from consecutive infectious diseases (ID) consultations for PEP within 60 days in the real-life setting of our tertiary hospital in northern Italy, which includes an STI center, a general ER and an ob-gyn ER.

Materials and Methods: Subanalysis of the monocentric observational cohort study APE, aimed at assessing PEP adherence. Study population is people who received an ID consultation for PEP from February 1 to March 31, 2023 at IRCCS Policlinico, Milan. Demographic, epidemiologic and serologic data at ID consultation (at both ER and outpatient settings) were collected and analyzed. Frequencies for categorical variables and medians with [inter-quartile range, IQR] for continuous variables were used; Fisher's exact test was used for associations of categorical variables.

Results: A total of 51 patients received ID evaluation for PEP within 60 days, 8 reporting occupational exposure (OE) and 43 reporting non-occupational exposure (NE). Evaluations were within 48 hours from exposure in 7/8 OE and 33/43 NE.

Overall, PEP was started in 38/51 cases (74.5%) according to guidelines and specialist's opinion.

OE median age was 38 years [IQR 32-44], 5/8 were female, country of origin was Italy in all cases. NE median age was 28 years [IQR 22-33], 18/43 were female, 12/43 were foreigners (2 Europeans, 10 extra-UE); they had a known history of STI in 7/43, 13/43 were previously tested for HIV, and 3/43 cases had received previous PEP.

While all occupational cases had a protective hepatitis B antibody titer (anti-HBs ≥10 mIU/mL),17/43 patients (39.5%) did not show protective titers at baseline, despite 16/17 reporting vaccination. Age, gender, Italian citizenship did not show significant correlations with protection for HBV. Lack of protection was more common in patients reporting sexual violence than other forms of non-occupational exposure (10/14 and 7/22, respectively, p=.006). A vaccine booster was offered to unprotected patients as per guidelines.

Conclusion: More than a third (39.5%) of people evaluated for non-occupational risk exposure for HIV in our real-life metropolitan setting in Northern Italy had non-protective antibody titers for hepatitis B, mostly being vaccine non-responders. This is in line with literature estimating the non-responder prevalence in Italy (i.e. 37.7% in medical students) and higher than proportions reported in other cohorts for non-occupational PEP (22 – 23%). This result highlights an unmet need for public health interventions. A cohort expansion is underway.

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P 194 HIGH PREVALENCE OF HIV INFECTION AND LATE DIAGNOSES BY HIV INDICATOR CONDITIONS GUIDED SCREENING IN THE EMERGENCY DEPARTMENT: PRELIMINARY RESULTS FROM THE INDI STUDY

D. Barbanotti[1], A. Santoro[1], C. Tincati[1], A. Tavelli[1], L. Colombo[2], A. d'Arminio Monforte[1], G. Marchetti[1]

[1]Unit of Infectious Diseases, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Italy, [2]Emergency Departiment, ASST Santi Paolo e Carlo, San Paolo Hospital, Department of Health Sciences, University of Milan, Italy

Background: Despite remarkable advancements in understanding and fighting HIV pandemic, high prevalence of late presenters, i.e. people with CD4+ T-cell counts <350/mmc at the time of diagnosis, and advanced disease are still a major concern. Late presenters not only have higher rates of HIV-related complications, but also pose a public health issue, as they may transmit infection. In Europe, around 50% of people who are diagnosed with HIV belong to this category, and numbers are actually slightly higher in Italy (58.7%). European guidelines suggest offering HIV test to people presenting with medical conditions associated with HIV prevalence > 0.1% (HIV Indicator Conditions, HIV-ICs) to achieve early diagnosis. The objective of this study is to assess the benefit of offering HIV testing to subjects affected by at least one HIV-IC in a the Emergency Department (ED).

Methods: A HIV screening campaign involving patients admitted to the ED suffering from one or more HIV-IC was organized in San Paolo Hospital, Milan, Italy, from September 2022 and is currently ongoing. Here we present data up to February 2023. Clinical and demographic information (age, sex, nationality, ethnicity) was collected into an anonymous database. Enrolled subjects provided informed consent for HIV test and data collection. For HIV positive subjects, CD4+ lymphocyte count and presumed transmission mode were also registered.

Results: A total of 97 subjects were tested, with 120 HIV-ICs (Table 1). Most patients presented with one HIV-IC (71%, 69/97), 24 presented with two (25%) and only a minority presented with three (4/97, 4%). More than 60% of the total were males, median age was 48(IQR 35-64) years. Most patients were Caucasian (60/97, 62%), the majority of which were Italian (56/97, 57%). The most common HIV-IC was tuberculosis (29/120), followed by HBV infection (21/120) and mononucleosis-like syndrome (15/120, Table 1).

To date, 8/97 participants were diagnosed with HIV, overall HIV prevalence of 8% (Table 2): 6 were males, 5 Italian, median age was 47 (IQR 33-63) years. Most HIV positive patients identified as heterosexual males (50%), one as homosexual and one reported IV drug abuse; two patients did not disclose infection modality. Median CD4 T-cell count and percentage were 33 (20- 157)/mmc, and 6(3-9)% respectively. All but one patient (87%) had with advanced disease, with CD4+ T-cell counts < 200/mm3 and 5/8 (62%) suffered from an AIDS-defining condition.

Conclusions: The overall prevalence of HIV infection in our hospital setting turned out to be relatively high. Despite the selection bias intrinsic with the study design of patients recruitment in ED, our results strongly support the need to implement HIV-ICs screening. Furthermore, most patients were diagnosed at a late stage, presenting with low CD4+ counts. These findings suggest that HIV-ICs, though useful to identify missed cases, may not actually be the most appropriate tool to capture early HIV diagnosis.

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Epidemiology and Prevention

P 195 HIGHLIGHTS FROM AN ONGOING ANAL CANCER PREVENTION PROTOCOL FOR PEOPLE LIVING WITH HIV AT THE INFECTIOUS AND TROPICAL DISEASES UNIT OF PADUA UNIVERSITY HOSPITAL

D. Leoni[1], C. Ruffolo[2], M. Mazzitelli[1], L. Sasset[1], M. Scarpa[2], A. Masin[2], S. Gardin[1], S. Pucciarelli[2], A.M. Cattelan[1]

[1]Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, Italy, [2]General Surgery 3 Unit, Padua University Hospital, Padua, Italy

Background: Despite HIV undetectability and immunological recovery, people living with HIV (PLWH) remain at higher risk of chronic anal HPV infections and HPV-related cancers when compared to the general population. Therefore, early identification and treatment of anal lesions are emerging as effective measures for reduction of anal cancer rates. Herein, we aim at retrospectively describing the outcome from an ongoing anal cancer prevention protocol for people living with HIV implemented since March 2022 at the Infectious and Tropical Diseases Unit of Padua University Hospital.

Methods: We included PLWH who were screened for anal HPV infection and genotyping from March 2022 to March 2023. Inclusion criteria were: high-risk sexual behaviour, history of anal HPV-related disease, HPV cervical infection in women, previous positive HPV tests, and reported anal complaints. HPV positive PLWH were referred for anal Pap test at our service and for anoscopy at the Proctology Unit. Histology was performed on suspected lesions identified at the anoscopy.

Results: Overall, 144 PLWH were tested for anal HPV-DNA, 135 (93.8%) were men (demographic and clinical characteristics are reported in Tab.1).

125 patients (86.8%) tested positive, of whom 38 (30.4%) resulted HPV mono-infected; 87 (69.6%) resulted coinfected with more than 1 HPV genotype: 24 coinfected with 2 (19.2%), 25 (20%) with 3, 38 (30.4%) with 4 or more genotypes.

Seven women (78%) tested positive.

87/125 (69.6%) PLWH resulted positive for proven or probable high-risk HPV genotypes, 38 (30.4%) for low-risk genotypes.

75 HPV positive patients (60%) underwent anal PAP test. 64 (85.3%) specimens were adequate for cytologic examination: 45/64 (70.3%) yielded a negative result, L-SIL was detected in 13 patients (20.3%), ASCUS in 4 (6.2%), H-SIL in 2 (3.2%).

89 patients (71.2%) underwent anoscopy. By biopsies (n=25), we detected: 4 H-SIL/AIN3 (1/4 in a woman), 2 H-SIL/AIN2, 3 L-SIL/AIN1. Moreover, we found 9 HPV-related epithelial modifications without dysplasia and 7 benign non-HPV related conditions. PLWH with AIN underwent surgical removal to reduce the risk of progression.

Conclusions: High rates of high-risk HPV anal infection and HPV co-infections were identified; women with cervical infection showed a high rate of consensual anal HPV localization. Around 4% of patients in our cohort resulted positive for high-grade AIN. Limitations were restrictions in anoscopies accessibility and patient protocol adherence. Our results show the importance of pursuing a strategy for the early recognition of anal precancerous lesions in PLWH, including women, and a closer cooperation with the proctology services to increase diagnostic rates.

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Epidemiology and Prevention

P 196 STRATEGIES TO REDUCE VACCINE HESITANCY. FIRST STEP: KNOW YOUR POPULATION. A SINGLE CENTER IN-DEPHT ANALYSIS OF PLWHA ADHERENCE TO VACCINATION SCHEDULE

G. Orofino[1], M. Guastavigna[1], M.C. Ottino[2], A. Ianniello[1], E. Remani[3], G. Lo Moro[4], F. Bert[4], G.D. Greco[5], G. Calleri[1]

[1]Divisione A Mal Inf e Trop, Ospedale Amedeo di Savoia, Torino, [2]Dipartimento di Scienze Mediche, Università di Torino, [3]Farmacia Ospedaliera, Ospedale Amedeo di Savoia, Torino, [4]Dipartimento di Salute Pubblica, Università di Torino, [5]SSD SISP Emergenze infettive e Prevenzione, ASL Città di Torino

Background: In our center many efforts have been made to implement vaccinations in PLWHA, as recommended by guidelines, especially after COVID19 outbreak. Our practice involves sending the patient to the competent vaccination centre, but we managed to create a close link with the public health and hygiene service and we are able to carry out anti-Pneumococcus (PCV/PPV), anti-Papilloma Virus (HPV9), anti-HerpesZoster (HZric) vaccines in our clinics and we have access to the SIRVA, the Piemonte Regional Informative System of Vaccination, to monitor adherence to vaccinations. Our work aims to thoroughly analyze our patients adherence to the vaccination schedule to address cases of vaccine hesitancy.

Materials and Methods: We included 1385 PLWHA. Mean age (years) 52.88; 1185 (85.6%) individuals were Italian while 200 (14.4%) were foreigners (we included in our study only foreigners permanently in care); 1079 (78%) male and 306 (22.1%) female subjects; risk of HIV transmission: MSM 832 (61%), ETX 403 (29.1%), TD 97 (7%), vertical 3 (0.22%) and parenteral 3 (0.22%) (missing data 47 – 3.4%). We analized adherence to anti-SARS-CoV2, PCV/PPV, anti-Meningococcus ACWY (MenACWY) and B (MenB), anti-Haemophilus Influenzae (HIB), HPV9, HZric and anti-Tetanus and Diphtheria (DT) vaccines.

Results: Data analysis: we focused our attention on carrying out the complete vaccination course. PCV/PPV: 676 (48.8%) yes, 709 (51.2%) no; MenACWY: 666 (48.1%) yes, 719 (51.9%) no; MenB: 664 (47.9%) yes, 721 (52%) no; HIB: 417 (30.1%) yes, 968 (70%) no; HPV: 413 (30%) yes; 972 (70%) no; HZric 375 (27,1%) yes, 1010 (72,9%) no; DT booster 452 (32.6%) yes, 972 (70.2%) no. Anti-SARS-CoV2: primary cycle 1280 (92.4%) yes, 105 (7.58%) no; 3rd dose 1145 (82.7%) yes, 240 (17.3%) no; 4th dose 458 (33.1%) yes, 927 (66.7%) no; 5th dose 154 (11.1%) yes, 1231 (88.9%) no. We found statistically significant associations ($p<0.05$) between adherence to vaccinations and risk, nationality and gender and we are studying how to implement strategies to remove barriers to vaccination access.

Conclusions: Except for Covid, the adherence rate to complete cycle of recommended vaccination is still low. Although the long time-lapse between the doses my be a recollecting bias, we have to strengthen the strategies to remove barriers (convenience) and support complacency.

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Epidemiology and Prevention

P 197 RETROSPECTIVE ANALYSIS OF ACCIDENTAL AND OCCUPATIONAL EXPOSURES, POST-EXPOSURE PROPHYLAXIS (PEP) PRESCRIPTION AND SURVEILLANCE PROGRAM IN A LARGE HOSPITAL, NORTHERN ITALY

S. Arsuffi, D. Minisci, B. Fioretti, F. Pennati, I. Izzo, S. Di Iuglio, I. Polesini, D. Bonetta, I. El Hamad, E. Quiros-Roldan, F. Castelli, E. Focà

Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy

Background: Occupational and accidental exposure at risk for HIV transmission can be reduced but not eliminated completely. Correct administration of post-exposure prophylaxis (PEP) following percutaneous or mucocutaneus blood exposure is fundamental for the prevention of HIV transmission. Nevertheless, PEP has been associated with insufficient compliance and difficulties to balance quick and proper prescription. The aim of our study is to analyze accidental and occupational exposures, post-exposure prophylaxis (PEP) prescription and surveillance program.

Methods: This is a retrospective monocentric study, conducted at the ASST Spedali Civili General Hospital. We performed the study relying on data gathered from the post-exposure surveillance program at the Infectious Diseases Unit between 01/01/2018 and 31/12/2021. Data collected included demographic characteristics, prophylaxis and surveillance prescribed and adherence to surveillance programs.

Results: The study population included 599 subjects who were evaluated in our clinic because of an accidental (n=74, 12.4%) or occupational (n=525, 87.6%) exposure from 2018 to 2021. Overall, 378 (63.1%) were females, with a mean age of 42 years old. Considering occupational exposure, 59 11%) subjects were physicians, 232 (43.4%) nurses, 91 (17%) clinical assistants, and 152 (28.4%) other professional roles. We evaluated 218 (36.4%) needle injury, 100 (16.7%) sharp instrument or suture needle injury, 121 (20.2%) abandoned needle injury, 75 (12.5%) exposures on mucocutaneous/non-intact skin and 81 (13.5%) on intact skin or to not-at-risk biological fluids. In the total of the record examined, in 459 (76.6%) cases the source had unknown serostatus, in 25 4.2%) it was HIV+, in 48 (8.0%) it was HCV+, in 3 (0.5%) it was HIV+/HCV+. Surveillance was activated in 529 (88.3%) cases. PEP was prescribed to 104 (17.4%) patients: in 76 (73%) cases the selected regimen was TDF/FTC+RAL bid, in 3 (2.9%) TAF/FTC/BIC, while in the other cases the regimen prescribed was derived from the source's antiretroviral therapy or was unknown. We also evaluated adherence to surveillance: 149 (24.9%) patients did not complete the surveillance program, in 68 (11.4%) cases it was not indicated, in 355 (59.3%) it was completed, 15 (2.5%) patients continued it in other hospitals.

Analyzing surveillances activated, we found 54 (9%) cases in which surveillance was began for not-at-risk exposure and 115 (19.2%) cases for abandoned needles.

Conclusions: Our study highlights a high rate of accidental and occupational risk exposures. It also clarifies the necessity to standardize the PEP prescription and the surveillance programs, mainly to avoid inappropriate and excessive treatment and follow up. Moreover, even in a selected population such as health care personnel, there's a strong need to implement strategies to improve the adherence to surveillance program after the first evaluation.

Epidemiology and Prevention

P 198 HPV VACCINATION COVERAGE IN MSM LIVING WITH HIV: A RETROSPECTIVE MONOCENTRIC STUDY IN NORTHERN ITALY

D. Laurenda, D. Castelli, I. Izzo, I. Polesini, F. Gaffurini, E. Focà, P. Zanotti, S. Arsuffi, M. Migliorati, E. Quiros-Roldan, F. Castelli

Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy

Background: Human papillomavirus (HPV) is a sexually transmitted infection that can lead to anogenital and oropharyngeal cancers.

Men who have sex with men (MSM) are at increased risk for HPV infection. Additionally, the prevalence of HPV infection is even higher among people living with HIV (PLWH). The majority of HPV attributable cancers in men are due to serotypes targeted by vaccination. Globally, uptake of HPV vaccination has been suboptimal, especially in the MSM population independently of HIV status. Free of charge HPV vaccination for MSM PLWH is authorized up to age 45 and three doses are recommended to complete the schedule. In our study, we aimed to estimate the HPV vaccination coverage among MSM PLWH followed at our Clinic in Brescia and to actively offer vaccination to eligible patients.

Materials and Methods: This is a retrospective study of PLWH conducted in the department of infectious diseases of Spedali Civili in Brescia.

We included in our analysis all participants that verbally declared to be homosexual or bisexual. Reviewing our medical charts, we collected data on demographic characteristics and current HPV vaccination status.

Results: 899 MSM living with HIV were included in our study, with a mean age of 52,1 (±11,6; 20-86). Of them 25 (2,8%) were IV drug users (IVDU). 222 (24,7%) were younger than 45 years old. 211 patients received at least one dose (23,5%) and 148 of them (70,1%) completed the schedule. 28 men (13,3%) received 1 out of 3 doses and 35 (16,6%) 2 of out 3 doses. No data regarding coverage were available only for 3 patients (0,3%). 685 patients (76,2%) were unvaccinated, of them 85 (12,4%) were still eligible with a mean age of 38,2. 37 of 63 patients (58,7%) who didn't complete the schedule were eligible to conclude it with a mean of age of 36,2. 600 patients unvaccinated were not eligible (87,6%).

Conclusions: Accordingly to literature, unsatisfactory level of HPV vaccination was found in our cohort of MSM PLWH. Lower uptake was associated with older age. This raises concerns about the odds of decreasing the burden of HPV related conditions in the immediate future. Recently, in our hospital a dedicated vaccination service exclusively for PLWH has been implemented. Still, further resources need to be invested in order to increase HPV vaccination uptake. Notably, widening the eligibility period for free of charge HPV vaccination should be evaluated. As the literature suggests, though vaccinating before HPV exposure is more beneficial, unvaccinated at risk individuals still benefit from it even at older age.

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Epidemiology and Prevention

P 199 DO WE THINK ENOUGH ABOUT STRONGYLOIDIASIS, SCHISTOSOMIASIS AND CHAGAS DISEASE AMONG HIV-POSITIVE MIGRANT PATIENTS? SCREENING RATIO AND SEROPREVALENCE IN A TERTIARY HEALTH-CARE CENTER IN ITALY

A. Barbiero[1], R. Paggi[1], C. Malcontenti[2], M. Pozzi[2], F. Lagi[2], A. Mantella[1,3], S. Tekle Kiros[1], A. Bartoloni[1,2,3], L. Zammarchi[1,2,3]

[1]Dipartimento di Medicina Sperimentale e Clinica, Università degli Studi di Firenze, Firenze, [2]SOD Malattie Infettive e Tropicali, Azienda Ospedaliero Universitaria Careggi, Firenze, [3]Centro di Riferimento Regionale per le Malattie Tropicali, Azienda Ospedaliero Universitaria Careggi, Firenze

Introduction: Due to migration phenomena, Chagas disease (CD), strongyloidiasis and schistosomiasis (CSS) are increasing in Europe and national and international guidelines have recommended their screening in migrants. Given their insidious clinical manifestations and frequent underdiagnosis, CSS can lead to lethal complications in immunocompromised patients. We describe the CSS screening ratio and seroprevalence among HIV-positive migrants in a tertiary health-care center in Italy.

Materials and Methods: We examined clinical records, demographical characteristics, screening ratios and seroprevalence data in HIV-positive migrant patients from countries at risk for CSS (according to updated literature), taken in care at Careggi University Hospital outpatients' clinic (Florence, Italy). CD screening data were examined from 2001 to August 2022; strongyloidiasis and schistosomiasis screening data were available from 2010 to August 2022.

Results: During the study period, 312 PLHIV migrants at risk for CSS were taken in care. Most patients were from Latin America (46.47%) and Africa (28.21%). Strongyloidiasis screening ratios were significantly higher in migrants from Africa (42.86%) and Latin America (46.85%), while schistosomiasis screening was significantly more performed in African migrants (40.82%), if compared with other areas of origin; schistosomiasis and strongyloidiasis seroprevalence did not significantly differ depending on area of origin (Figure1). The screening ratio in PLHIV migrants at risk for schistosomiasis, strongyloidiasis and CD, accounted for 24.25%, 38.64%, and 68.75% and seroprevalence was 8.00%, 5.88% and 1.01%, respectively (Table1).

Conclusion: In our population, higher strongyloidiasis (5.88%) and schistosomiasis (8.00%) seroprevalences were observed if compared with those reported for non-HIV migrants (4.5% and 6%, respectively), while published seroprevalence data in HIV-positive migrants are heterogeneous, suggesting the need for further investigation; CD seroprevalence was coherent with reported data about HIV and non-HIV patients. Overall, seroprevalence studies of CSS among HIV-positive migrants are scant. The screening ratio exceeded 60% only for CD, while screening ratios for strongyloidiasis and schistosomiasis in patients at risk need to be improved and clinical suspicion should be higher towards those areas of origin that tended to have lower screening coverage. These results underline the burden of CSS and the need for better sensibilization towards these pathologies in this fragile group of migrant population.

Epidemiology and Prevention

P 200 MONKEYPOX VACCINATION IN A COHORT OF PEOPLE ON PRE-EXPOSURE PROPHILAXIS (PREP) OR LIVING WITH HIV INFECTION (PLWH): A RETROSPECTIVE OBSERVATIONAL STUDY FROM THE UMBRIA REGION, ITALY

G. Quartini[1], G. Genga[2], C. Vernelli[1], B. Tiri[1], C. Pallotto[2], M.B. Pasticci[1], D. Francisci[2]

[1]Infectious Disease Clinic, Ospedale Santa Maria Terni, Università degli Studi di Perugia, Terni, [2]Infectious Disease Clinic, Ospedale Santa Maria della Misericordia, Università degli Studi di Perugia, Perugia

Background and aim: Human monkeypox (MPXV) is a zoonotic Orthopoxvirus with a presentation similar to smallpox. Due to antigenic similarity, smallpox vaccine cross-protect against MPXV; however, over 70% of people living today never received this vaccination.
The World Health Organization declared monkeypox a global health emergency on 23 July 2022. MPVX vaccine, along with other reccomandations were implented to control the spread of the infection.
Priority groups for MPXV vaccine included healthcare workers at high risk for occupational exposure, immunocompromised patients like people living with HIV (PLWH) and individuals with multiple partners.
Methods: From September 2022 an active vaccination campain was applied in Umbria and vaccine was offered to individuals on PrEP and PLWH in follow up at Infectious Disease Clinic in Perugia and PLWH in follow-up at Infectious Disease Clinic in Terni. All of them who agreed to get vaccinated from September to March 2023 were included in this retrospective observational study.
For each patient demographic data were collected, along with laboratory parameters, CD4 cell count and HIV viral load. We recorded also side effect of vaccine. All the persons included are in follow-up.
Results: Overall, 137 individuals were enrolled: 115 from the center of Perugia and 22 from that of Terni. A double dose of MPVX of vaccine was injected in all of them eccept in people born before 1975 who received only one dose because had smallpox vaccination. One person refused to receive the second dose, 29/137 (21%) received only one dose being born before 1975, 112/137 (81.7%) were italian. 119/137 (86.9%) man, two female, 17/137 (12.4%) were transgender. Their mean age was 45 years, 75/137 (54.7%) were PLWH. All of them resulted to have HIV-RNA <20 copies/mL and all had CD4+ >500 cell/mmc. In regard to side effect, one person reported itching and one fever resolving spontaneously.
Conclusion: Overall, the vaccine strategy allowed to vaccinate 137 persons among those at high risk for monkeypox infection. No vaccine serious adverse effects were detected. No one of the vaccinated individuals was subsequently diagnosed with monkeypox.
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Epidemiology and Prevention

P 201 HIV TESTING IN THE EMERGENCY DEPARTMENT: AN EFFECTIVE STRATEGY TO INCREASE NEW DIAGNOSES

F. Romano[1], A. Lazzaro[1], A. Falletta[1], L. Santinelli[1], F. Cancelli[1], F. Biamonte[2], L. Zinnamosca[2], G. Della Grotta[2], C. Marinelli[2], G. Ceccarelli[1], C.M. Mastroianni[1], G. Galardo[2], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Policlinico Umberto I of Rome, Rome, Italy, [2]Medical Emergency Unit, Sapienza University of Rome, Rome, Italy

Background: Despite the great advances in the continuum of care of HIV infection, it is still a pandemic with an estimated prevalence of 38.4 million in 2021, whose about 15% (25-3%) does not know their serologic status [1]. HIV testing is one of the most important strategies in reducing the burden of HIV worldwide. Nonetheless, barriers to the access to HIV testing do exists, even in those hospital settings characterized by a high burden of people with known risk factors for HIV acquisition, such as the emergencies departments.
We aimed to assess the prevalence of newly diagnosed HIV infection among the people referring to the Emergency Department (ED), with the goal to increase new diagnoses thanks to a opt-out, risk-based screening approach.
Material and Methods: This is an interim analysis of a single center, longitudinal, interventional study including participants referring to the Emergency Department of Policlinico Umberto I, University Hospital of Sapienza University (Rome, Italy). People presenting with clinical features suggestive of (opt-in strategy), or with risk factors associated to HIV infection (risk-based strategy), were asked to be enrolled into the study. Participants underwent a rapid immunochromatographic point of care HIV testing assay (Bio-Rad GeneTM Fast HIV ½ Assay), which utilizes antigens specific to HIV-1/2 to detect antibodies against the virus, and provides a result in up to 30 minutes. Positive results were confirmed by fourth generation ELISA blood test and western blot. Demographic and clinical data were collected. Data collected from October 2022 to March 2023 were used for a descriptive statistical analysis.
Result: Over the study period considered, a total of 288 participants were enrolled into the study and accepted to undergo rapid HIV testing. Demographics, reasons to refer to the ED and risk factors for HIV acquisition are shown in Figure 1.
Out of the 288 rapid HIV tests performed, 3 provided a positive result, which was confirmed in 2 cases, allowing a new diagnosis of HIV infection among 2 participants (prevalence: 0.69%); both were presenting with pneumonia and no other known risk factor for HIV. The third participant was offered the test because of fever at the access to the ED; after a positive result at the rapid screening test for HIV, the downstream tests resulted negative, thus it was considered a false positive.
Conclusion: Our results alarmingly showed a high prevalence of new diagnosis of HIV infection among people referring to the ED, considered the small sample size of the interim analysis of this ongoing study. This highlights the added value of the use of rapid HIV testing strategies within the context of the ED. Moreover, screening approaches aiming to address directly those people at higher risk for HIV infection, such as the opt-in and risk-based strategies adopted, showed effectiveness in high prevalence settings, such as the ED.

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Epidemiology and Prevention

P 202 HPV VACCINATION DAYS IN HIV AND STI OUTPATIENT CLINIC

A. Carraro[1,2], E. Tortellini[2], S. Guardiani[2], S. Garattini[2], S. Corazza[2], A. Destro[2], R. Marocco[1], V. Belvisi[1], F. Dominelli[1], C. Falvino[1], C. Giambi[3], A. Zerbetto[3], M. Lichtner[1,2]

[1]Infectious Diseases Unit, SM Goretti Hospital, Sapienza University of Rome, Latina, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, [3]Prevention Unit, ASL Latina, Latina

Background: The Gardasil nonavalent vaccine is a vaccine against nine HPV genotypes (6, 11, 16, 18, 31, 33, 45, 52, 58), effective in preventing the development of cervical vaginal and vulvar intraepithelial, oral and anal papillomavirus-related cervical intraepithelial neoplasms. Once the vaccine cycle is completed, seroconversion occurs in 99.99% of cases.

HPV vaccination is recommended through age 26 years, in Men who have Sex with Men (MSM) and in immunocompromised persons; among them, people living with HIV have an increased risk of developing HPV-related lesions, due to B-, T- and NK-lineage cell dysfunction, and due to persistent systemic and mucosal inflammation.

Methods: In order to increase HPV vaccination adherence of our patients with HIV, and, in general, of the people to whom the free vaccination is intended (as stated by Regione Lazio), vaccination open days have been organized at the Infectious Diseases Outpatient Clinic of the S.M. Goretti Hospital in Latina.

For patients living with HIV, active enrollment was performed by the Center's physicians through telephone contact. For the rest of the targeted population, vaccination open days were publicized through posts on the social pages (Instagram and Facebook) of the Infectious Diseases Outpatient Clinic and Latina Checkpoint.

At the time of HPV vaccine administration, counselling was conducted to assess the need for other vaccines.

Results: Overall, in 5 vaccination open days, 71 people (46 men (64%), median age 33 years(22-51)) were vaccinated, including 30 people living with HIV (42%), 20 men who have sex with men (28%), 7 women diagnosed with a precancerous lesion for which they had already had surgical treatment. 31 people had never been to our outpatient clinic before. Among people with HIV, HPV related lesions had already been diagnosed in 5 patients (16%).

Our patients appreciated the opportunity to get vaccinated directly in the outpatient clinic, so we will continue with more open days.

Conclusions: The initiative allowed HIV patients to access the vaccine program more quickly and conveniently by performing it at them outpatient clinic they are already familiar with. At the same time, the initiative made MSM aware of our outpatient clinic where it is possible to screen for STIs and access HIV-PrEP.

In addition, the initiative reached many young people who were not aware that they were eligible for free vaccination.

Epidemiology and Prevention

P 203 MISSED OPPORTUNITIES IN HIV DIAGNOSIS: TO RECOGNIZE SENTINEL CONDITIONS FOR HIV TO REDUCE LATE PRESENTATION IN AN URBAN SETTING IN NORTHERN ITALY

M. Bavastro[1,2], M. Cerchiaro[1,2], L. Labate[1,2], C. Russo Artimagnella[1,2], S. Cardaci[1], L. Crupi[1,2], G. Brucci[1,2], L. Taramasso[1], M. Bassetti[1,2], A. Di Biagio[1,2]

[1]Infectious Diseases Unit, Policlinico San Martino Hospital-IRCCS, Genoa, Italy, [2]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy

Background: People diagnosed with HIV (PWH), when they are already symptomatic and/or immunosuppressed, represent missed opportunities to delay progression of diseases by timely initiation of ART, also allowing rapid HIV-RNA load reduction and faster immunereconstitution. Lowering viral load minimizes the risk of viral transmission and the circulation of HIV. In this study we investigate the elapsed time between the first access at a health care facility, for symptomatology compatible with HIV, and the real date of HIV testing, in people recently been diagnosed with HIV, attended by our hospital.

Material and methods: A prospective, observational study was conducted from February 2021 to February 2023 in a tertiary care Italian hospital.

The study considered people diagnosed with HIV who accessed the healthcare system for a sentinel clinical condition for HIV, which was not recognized and they were not offered HIV testing at that time. These patients represent missed opportunities.

Clinical and laboratory data regarding the onset of HIV infection and sentinel conditions for HIV were collected with electronic data capture system. (HIV Ligurian Network, Ethics Committee approved August 2013).

Missing data were supplemented through phone calls with our patients.

Results: Globally we included 69 naïve PWH, baseline median age was 43.9 years, 54 were male, 45 were Caucasian, 27 were MSM, 37 heterosexual, and 4 drug addicts. At diagnosis, the mean baseline plasma viral load was 4.7 log10 cp/ml (2 to 7), the mean nadir CD4 was 272/mm^3 (2 to 948). Of the 69 patients in our study, 27 (39%) were late presenter and were admitted at our study. Of the 27 patients 20 were male, baseline median age was 39.5 years, 14 were Caucasian, 9 were Hispanic and 4 were Africans. 8 were MSM, 17 were heterosexual, and 1 was drug addicts. About education they had 2 elementary school license, 5 middle school license, 6 high school diploma, 3 college degree.

Of the 27 patients, 12 presented with mononucleosic-like syndrome, 1 for pneumonia, 2 for seborrheic dermatitis interpreted as dermatologic pathology, 3 with herpes Zoster infection (age <60 years), 1 for oral candidiasis, 5 were referred for hematologic examination for lymphopenia (2), pancytopenia (1) and suspected lymphoproliferative syndrome (2), 1 case of luetic iridocyclitis , 1 Salmonella spp infection with associated proctitis.

The median time from first admission to the NHS to diagnosis of HIV in these 27 patients was 210 days (IQR 60 -390).

This time can be considered as the delay on making HIV diagnosis in these patients, which may affect their future management.

At diagnosis, 19 of the 27 patients (70%) had HIV RNA > 10^5 cp/ml; 18 patients (66%) had CD4< 200 at diagnosis.

Conclusions: The best strategy we have to reduce the time to diagnosis, is to implement HIV testing provision and to know how to recognize sentinel conditions of HIV in patients who come to our attention, so that we don't miss diagnosis.

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Hepatitis and other viral infections

P 204 AN OCCULT HEPATITIS B VIRUS INFECTION REACTIVATION IN AN HIV/HCV COINFECTED PATIENT DURING AN IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME

S. Zaltron, A. Cambianica, M. Di Gregorio, C. Colangelo, S. Storti, G. Tiecco, E. Quiros-Roldan

Unit of Infectious and Tropical Diseases, ASST Spedali Civili di Brescia, Brescia, Italy, Unit of Infectious and Tropical Diseases, Department of Clinical and Experimental Sciences, ASST Spedali Civili di Brescia and University of Brescia, Brescia, Italy

Background: Occult HBV infection (OBI) is defined as the presence of replication-competent HBV DNA in the liver and/or HBV DNA in the blood of people who test negative for hepatitis B surface antigen (HBsAg) by currently available assays. HBV reactivation might occur as consequence of the presence of replication-competent HBV DNA in liver hepatocytes during long-term immunosuppression. It is characterized by sudden increase in serum HBV DNA levels and HBsAg reappearance, often associated with a hepatitis flare. Here we present the case of OBI reactivation in an HIV/HCV co-infected patient with severe immunodeficiency after self-suspension of ART and HCV eradication.

Case Report: A 64-year-old patient with HIV/HCV/OBI and cirrhosis was lost to follow-up about 19 months after DAAs treatment. Previous blood tests showed an optimal immunological status with suppressed HIV viral load, isolated anti-HBc seropositivity and a sustained viral response for HCV. In June 2021, he resumed the follow-up showing high levels of HIV-RNA and a CD4 < 200 cells/mm3. An integrase inhibitor (INI)-based regimen containing tenofovir (emtricitabine/tenofovir-alafenamide/bictegravir) was started. At that time, no signs of hepatitis flare were detected. Few months later after reintroduction of ART, together with an improvement of the immunological profile and a significant increase of CD8 cells, HBsAg turned positive with high-levels of HBV DNA. This was suggestive of ongoing immune reconstitution inflammatory syndrome (IRIS). Eventually, at the end of 2022, hepatic markers normalized, and HBV-DNA was stably undetectable. HBsAg was newly lost (Table 1).

Discussion: Several predisposing immunological factors could have contributing to OBI reactivation in our patient, although reinfection cannot be excluded although rather unlikely. Failure of immune surveillance and the following immune reconstitution-induced inflammatory syndrome after ART reintroduction, impaired HBV-specific CD4 cell response, which has been associated in previous studies with HBV persistence, even in presence of HBV-specific CD8 cells in HBV/HCV co-infected patients, might offer another explanation: CD4 cells play an important role in the immune response against HBV by activating innate immune cells, priming and maintaining the effector function of CD8 cells, which have a pivotal role in the viral clearance and pathogenesis during acute and chronic HBV infection.

Conclusions: Host immune response can suppress viral replication to minimal levels, achieving control of the infection and OBI status. However, when multiple factors associated with a low chance of OBI reactivation are concomitantly present, the risk of this complication may exponentially increase. Therefore, especially in patients with an impaired immune system and on a tenofovir or lamivudine-sparing regimen, HBV serological and virological markers should always be strictly monitored, even in the absence of a hepatitis flare.

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Hepatitis and other viral infections

P 205 HUMAN ORF: AN UNDER-RECOGNIZED AND UNDER-REPORTED VIRAL INFECTION

L. Rossi[1], G. Tiecco[1], M. Salvi[1], M. Venturini[2], F. Castelli[1], E. Quiros-Roldan[1]

[1]Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia, Italy, [2]Department of Clinical and Experimental Sciences, Section of Dermatology, University of Brescia, Brescia, Italy

Introduction: Orf is a zoonotic skin infection caused by Orf virus, a DNA virus belonging to the Parapoxvirus genus. The infection is endemic in sheep and goats, while in humans, at risk populations, include mostly shepherds, wool shearers, butchers, farmers, and veterinarians. Although Orf infection usually causes as a single self-limiting papule or nodule, the lesion can resemble other localized poxvirus infections as well as more serious conditions. Moreover, potential immune-mediated complications may occur making the diagnosis an issue for clinicians. Here we describe a case report of Orf complicated infection to rise concern about this commonly underrecognized viral disease.

Case Report: A 51-year-old woman presented with a 1-week history of a single asymptomatic swelling nodule with grey necrotic center and red outer halo on her index finger (Figure A, B). At physical examination, a pruritic papulovesicular eruption was also assessed on her hands and feet (Figure C-D). Laboratory tests were within normal ranges and no past medical history was reported. Both the finger nodule and one of the papulovesicular lesions were biopsied. Although the patient

denied any occupational exposure, she reported a recent contact with a goat which had a similar nodule in her mouth (Figure E). Orf virus infection with an autoimmune widespread erythema multiforme was diagnosed. The lesions spontaneously resolved within the next 2 weeks (Figure F).

Discussion: Orf is considered an occupational disease, but infection may also occur in individuals with non-occupational contact with sheep or goats. Transmission to humans can occur through inoculation of broken or abraded skin by direct contact with infected animals. About 3 to 7 days after inoculation, infection in humans usually presents as a single papule or nodule, evolving through 6 different stages until spontaneous resolution in approximately 6-8 weeks.

The primary lesion might be associated with a wide spectrum of hypersensitivity reactions; erythema multiforme is the most frequently reported immunological complication. However, mechanisms of Orf-induced autoimmune diseases are still unknown. Despite in literature, several drugs are reported in Orf virus infection management, this is a self-limiting disease.

Conclusions: Orf is still underrecognized. To make a proper diagnosis and avoid unnecessary investigations and overtreatment, clinicians should be aware of the primary presentation and the potential complications that may occur. Erythema multiforme is the most frequently reported Orf-induced immunological diseases and, although the diagnosis is usually based on clinical and epidemiological features, histopathological examination may help achieving a prompt diagnosis.

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Hepatitis and other viral infections

P 206 EVALUATION OF THE EFFECTIVENESS OF A POPULATION-BASED HEALTH POLICY TO INCREASE HCV TREATMENT COVERAGE: AN INTERRUPTED TIME SERIES ANALYSIS

L. Ceccarelli[1,2], C. Seghieri[2], C. Tortù[2], L. Tavoschi[3]

[1]Università di Bologna, Bologna, [2]Scuola Superiore Sant'Anna, Pisa, [3]Università di Pisa, Pisa

Introduction: An estimated 3.9 million people in the European Union are living with chronic HCV infection. The advent of direct-acting antivirals (DAAs) has made it possible to set elimination targets by 2030, in terms of reducing the fraction of undiagnosed population and extending treatment coverage. In Tuscany, a three-year action plan to increase treatment coverage with DAAs was launched in 2018. This study aims to evaluate the effectiveness of the Tuscany Region action plan to extend access to DAAs treatment for people living with chronic HCV infection.

Material and Methods: Data included monthly observations from administrative healthcare records - collected between January 2015 and December 2019 - on i) the number of serological tests to detect anti-HCV antibodies ii) the number of PCR tests to detect viral load (HCV-RNA) and iii) the number of DAAs prescriptions. The analysis was conducted by implementing an interrupted time series (ITS) model, in which the number of monthly DAAs prescriptions was considered the primary outcome, while the number of tests to detect anti-HCV antibodies and viral load (HCV-RNA) were included as control variables. The analysis was conducted (i) in the general population and (ii) in subgroups including people living in prisons (PLP) or people who use drugs (PWUD), identified by specific exemption codes active during the study period.

Results: The results showed that the policy issued by Tuscany Region in 2018, which followed the extension of criteria for access to treatment enacted at a national level, was effective ($p<0.05$) in increasing treatment coverage with DAAs (+71% compared to the pre-intervention period) within the general population, even disaggregating data by sex (males +78%) and by the age group considered to have the highest prevalence (33-53 years, +75%); on the other hand, it had no significant impact on PLP and PWUD ($p>0.05$).

Conclusions: The marked increase in treatment coverage rates with DAAs against HCV infection is probably related to the impact of the action plan issued by Tuscany Region, designed with the aim of pursuing elimination targets by 2030. The policy has proved to be significantly effective in increasing access to treatment within the general population, thanks to the implementation of simplified healthcare pathways for access to testing and treatment. In the case of PLPs and PWUDs, on the other hand, there was no significant increase in treatment coverage: this may be related to the inherent limitations arising from the use of administrative healthcare records, which identify subgroups with a high degree of approximation. However, the possibility cannot be ruled out that treatment coverage of persons belonging to these groups was sufficiently effective even before the intervention.

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P 207 EVALUATION OF ANTI-MPOX IGG DEVELOPMENT IN INFECTED PATIENTS

D. Farinacci[1], F. Lombardi[2], A. Ciccullo[3], G. Baldin[4], E. Visconti[4], A. Borghetti[4], S. Di Giambenedetto[2,4]

[1]UOC Medicina Protetta – Malattie Infettive, ASL Viterbo, [2]Università Cattolica Del Sacro Cuore, Roma, [3]Ospedale San Salvatore, L'Aquila, [4]Fondazione Policlinico Universitario "A. Gemelli", Roma

Background: Monkeypox is a zoonosis due to infection with the mpox virus (MPXV), already endemic in some African countries and currently present for the first time since May 2022 as an outbreak in non-African countries. [1]

Both IgM and IgG antibodies are known to occur as a result of infection or vaccination. Isolated IgG allows diagnosis after the resolution of the disease, while IgM indicates the presence of a more recent infection. [2] Although both antibodies are measurable and allow an etiological diagnosis, their protective role against infection itself or their correlation with the severity of the disease is not yet very clear, although some studies we have carried out seem to confirm that, in subjects undergoing smallpox vaccination, the development of mpox disease is more moderate. [3]

Methods: In this work, we aimed to describe the production of anti-mpox IgG in patients who have clinically developed the disease and who are followed at our center. We collected a blood sample at the time of diagnosis and 2 months after recovery and performed an ELISA test for the quantification of anti-mpox IgGs.

Results: We recruited a total of 9 patients with Monkeypox infection, whose general characteristics are summarized in Table 1.

At the diagnosis of Monkeypox infection, a median amount of antibodies of 998 ng/mL was found, while approximately two months after recovery the median was 1079 ng/mL, with no significant changes (p=0.953).

Persons living with HIV seemed to have a little lower median baseline IgG compared to HIV-negative patients (755 ng/mL vs 1024 ng/mL) with a median increase of +124 ng/mL and +161 ng/mL after 2 months respectively. People who developed skin rash without systemic symptoms seemed to have a greater amount of antibodies (2377 ng/mL vs 755 ng/mL) but without an increase after two months (-37 ng/mL). Even people who received vaccination against smallpox seem to have a higher antibody level (175 ng/mL vs not vaccinated 511 ng/mL), with an increase of +220 ng/mL after 2 months. Patients who developed a greater amount of skin lesions had a higher baseline concentration compared to patients with a milder manifestation (1124 ng/mL vs 850 ng/mL), the first one also had a decrease in median IgG after recovery (-589 ng/mL vs +352 ng/mL).

These findings are detailed in table 2.

Conclusions: The following study has several important limits: firstly the scarce sample size of enrolled subjects, for whom it was possible to collect the blood sample for antibodies measurement. Another important limitation is the lack of a protective cut-off that makes it difficult to draw conclusions about the clinical implication of these results.

Based on that, our study has set itself the purely descriptive purpose of analyzing some clinical or epidemiological features that may influence the antibody response against this virus, however, further studies are needed to understand the role of these antibodies and to learn more about the disease.

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P 208 PERFORMANCE EVALUATION OF HIV-2 RNA PLASMA QUANTIFICATION USING A COMMERCIAL RUO RT-PCR ASSAY

F. Salari, A. Rizzo, F. Bracchitta, L. Morelli, A. Tamoni, F. De Poli, M. Cuomo, M. R. Gismondo, V. Micheli

Laboratory of Clinical Microbiology, Virology and Bioemergencies. ASST Fatebenefratelli Sacco, "L. Sacco" University Hospital, Milan, Italy

Background: HIV-2 infection is characterized by a low viral titers, slow disease progression, and poor response to standard antiretroviral therapies. The availability of a sensitive and consistent assay for the quantification of HIV-2 RNA is crucial for supporting laboratory HIV-2 infection diagnosis, as well as for managing antiretroviral decisions and for monitoring infected patients over time.

The aim of this study was to assess the performance of a commercial RUO RT-PCR based assay for the quantification of HIV-2 RNA using plasma from suspected HIV-2 positive patients and an HIV-2 external quantification standard.

Material and Methods: RealStar® HIV-2 RT-PCR kit 1.0 (RUO) on AltoStar® AM16 platform (altona Diagnostics, Germany) was used on 13 plasma samples from 11 HIV-2 suspected patients and on dilution series of the external International Standard (IS) P0318 ViraQ HIV-2 Check 125 (genotype A). The IS (concentration: 161.25 UI/mL) was diluted using a 65 mL human plasma pool from HIV-1/2 negative patients to prepare ten replicates of IS at different concentrations (30, 20, 15 and 10 UI/mL). HIV-2 RNA was extracted from 1 mL of plasma and eluted in 80 µL using the AltoStar® purification kit 1.5 (altona Diagnostics, Germany). The 96-well plate was automatically set up as follows: 4 RT-PCR standards (1x10^4, 1x10^3, 1x10^2, 1x10^1 UI/µL) and the negative control of the assay, 15 plasma samples for diagnostic purposes, 10 replicates of each IS concentration, 2 replicates of IS at 40 UI/mL (1 in plasma and 1 in PBS), 1 undiluted IS (161.25 UI/mL) and a negative sample (plasma pool).

Results: The standard curve showed the following parameters: E=99.1%; R2=1.000; slope=-3.344; y int=32.752. All the ten IS replicates of each concentration were detected and showed a mean (SD; CV) Cycle threshold (Ct) value of 33.87 (0.70; 0.02), 34.44 (0.48; 0.01), 34.83 (0.75; 0.02), 35.96 (0.67; 0.02), corresponding to 40.98 (19.75; 0.48), 26.28 (8.75; 0.33), 21.61 (11.13; 0.52) and 9.61 (4.14; 0.43) UI/mL, respectively. The undiluted IS sample resulted 126.8 UI/mL, while there were no differences comparing plasma vs PBS diluted IS sample at 40 UI/mL.

All but one of the routine plasma samples resulted undetectable: the only positive sample showed a viral load corresponding to 126.800 UI/mL, consistently with the untreated status of the patient.

Conclusion: the assay showed a good performance, especially at the concentrations of 20 and 10 UI/mL (lower CVs compared to the others). The sensitivity of the assay coupled with the detection of HIV-2 RNA in plasma sample from an untreated patient confirm its usefulness in the clinical practice. Further analysis are needed to better investigate the sensitivity below 10 UI/mL.

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P 209 INHERITEHD CHROMOSOMALLY INTEGRATED HHV6: A CASE REPORT

G. D'Aguanno[1], F. Savalli[1], G. Consuelo[1], P.Miraglia[1], M.C. Morsellino[1], S. Cianchino[1], G. Colomba[2], G. Di Quattro[2], P. Colletti[1]

[1]Department of Infection Diseases, Paolo Borsellino Hospital (Marsala), [2]Microbiology Department, Villa Sofia-Cervello Hospital (Palermo)

Case presentation: 34-year-old woman goes to hospital of the city with fever, sudden blurred vision, and headache. She performs negative brain CT scan, LP with clear CSF, 27 leukocytes /mcl, PMN 22%, glycorrhachia 0.63 g /l, protidorrachia 42 mg/dl, film-array positive for HHV6. Brain MRI, blood cultures, serology HIV, CMV, EBV, Syphilis, West Nile, R.conorii are normal but HHV-6 viraemia is 1165372 c/ml. She practices therapy with gancyclovir i.v and after one week she performs control viraemia equal to 2072143 c/ml. She continues gancyclovir for a total of 17 days and will be discharged with a diagnosis of "HHV6 meningoencephalitis", asymptomatic and with valacyclovir until next control viraemia. The patient discontinues therapy and asks for a new specialist consultation at our Centre. She performs HHV-6 viraemia control: 11.000.000 c/ml and after noticing that DNAemia persisted, despite treatment for HHV-6, we ordered testing for chromosomally integrated virus (iciHHV-6). Test result confirms the presence of iciHHV-6, explaining its consistently elevated serum viral load.

Discussion: HHV6 transmission may occur prenatally trough germline transmission of iciHHV6 from either parent. Confirmation of HHV-6 as a causative pathogen is complicated by the high seroprevalence of HHV- 6 in individuals older than three years, the persistence of HHV-6 DNA after primary infection and the possibility of integration of HHV-6 DNA into chromosomes (in approximately 1 % of the population). iciHHV-6 is characterized by persistent detection of the HHV-6 genome at high copy number in whole blood and in other samples including hair follicles and nail clippings. Primary HHV-6 infection in adults causes a transient increase in viral load with resolution and clearance after a few weeks, while iciHHV-6 is characterized by persistent detection of viral DNA at a high copy number. Therefore, clinical improvement after therapy without decrease in viral load may indicate that HHV-6 isn't the causative agent of encephalitis.

Conclusions: In case of suspected encephalitis, a positive CSF HHV-6 result isn't a diagnostic test for active infection, instead high levels of viraemia are suggestive of iciHHV6. Diagnosing HHV-6 infection based on detection from CSF can be challenging since individuals with iciHHV-6 have the virus in every cell. When deciding to treat for HHV-6 encephalitis, it's important to consider the possibility of chromosomally integrated virus rather than drug-resistant virus in order to reduce exposure to ineffective and potentially toxic antiviral therapy.

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P 210 EARLY HCV TREATMENT DURING RCHOP THERAPY IN SUBJECTS WITH NON HODGKIN LYMPHOMA

R. Palladino[1], G. Stornaiuolo[2], M. Stanzione[2], C. Liagkoua[1], M. Pisaturo[1], N. Coppola[1]

[1]Dipartimento di salute mentale, fisica e medicina preventiva, Università degli studi della Campania L. Vanvitelli, Napoli, [2]AOU Vanvitelli, Napoli

Background: direct-acting antivirals (DAA) are the current standard of care for chronic hepatitis C. Oncologic patients are the most difficult-to-treat subgroups of hepatitis C virus (HCV)-infected patients due to clinical frailty and complex therapeutic protocols received.

Case Report: We would like to present a case involving a 61-year-old woman who was diagnosed with stage IIIA diffuse large B-cell non-Hodgkin's lymphoma with subdiaphragmatic bulky in January 2022. Her only significant medical history was hypertension. Following screening for HBV, HCV, and HIV, all tests came back negative, and the patient was started on RCHOP therapy (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone).

During the course of her chemotherapy cycles, the patient developed hypertransaminasemia, with AST levels reaching 390 (eight times higher than normal) and ALT levels at 94 (three times higher than normal). As a result, the patient was referred to our hepatitis outpatient clinic for further diagnostic evaluation. Upon conducting a thorough investigation, we determined that the patient had acute Hepatitis C, as her HCVab was positive, and her HCV RNA was 4.5 x 105. Notably, the patient had no family history or risk factors for hepatitis C, but had previously undergone a transfusion during a hospitalization.

We initiated off-label therapy with Sofosbuvir/Velpatasvir (one capsule daily) for 86 days to treat the patient's acute hepatitis C. The treatment successfully normalized her transaminase levels, making her a suitable candidate for Glofitamab treatment, given the high risk of relapse associated with her cancer pathology.

In May 2022, the patient contracted a Sars-CoV-2 infection, but did not experience severe respiratory symptoms. Despite the infection, we did not discontinue DAA therapy and suspended chemotherapy until she tested negative for nasopharyngeal swab.

At the end of her treatment, the patient had normal transaminase levels, negative HCV RNA, and achieved sustained virologic response (SVR), indicating a successful outcome.

Conclusions: This case underscores the importance of promptly diagnosing and managing hepatitis C in patients with lymphoma, especially during chemotherapy cycles, to minimize treatment interruptions and ensure optimal cancer care.

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P 211 HEPATIC FLARE AND IMMUNE RECONSTITUTION IN HEPATITIS B VIRUS-HUMAN IMMUNODEFICIENCY VIRUS COINFECTED PATIENTS

A.M.A. Crea[1], L. Campogiani[1], T. Mulas[1], M. Compagno[1], A. Di Lorenzo[1], E. Teti[1], V. Malagnino[1,2], M. Andreoni[2], L. Sarmati[1,2], M. Iannetta[1,2]

[1]Infectious Diseases Unit-Policlinico Tor Vergata, Rome, Italy, [2]Department of System medicine-Tor Vergata University, Rome, Italy

Background: After starting highly active antiretroviral therapy (HAART), HIV-HBV coinfected patients can experience a hepatic flare (HF) that can represent an immune reconstitution inflammatory syndrome (IRIS). In addition, HBV-IRIS may affect the increased levels of functional cure seen in HIV-HBV coinfection. Therefore, we investigated the relationship between HF, immune reconstitution, and functional cure.
Methods: We retrospectively examined a cohort of HAART-naïve HIV-HBV coinfected patients initiating HAART from the Infectious Diseases Unit of Policlinico Tor Vergata (Italy). We collected medical records before HAART initiation and recorded HF and immunovirological profile within the first six months from HAART initiation.
Results: From 2011 to 2021, 16 HIV-HBV coinfected patients were enrolled. Male sex (81,25%), Caucasian (43,75%), and African (43,75%) origin were predominant in our cohort, with a median age of 33,5 years. Five patients (31,25%) had AIDS at baseline, and seven (43,75%) were HBeAg-positive at the first recorded lab result. Integrase inhibitor (INI)-based regimens were the most frequent (56,25%). Nine patients received treatments containing tenofovir alafenamide (TAF) (56,25%), with the remaining 7 receiving tenofovir disoproxil (TDF). Complete virological suppression of HIV (<50 c/ml) and HBV (<20 c/ml) was observed in 100% and 93,7% of subjects, respectively. Ten patients (62,5%) developed HF at a median of 43,5 days after starting HAART. The HF was 3,75-fold greater than baseline ALT. Patients with HF had lower CD4+ nadir and higher HIV and HBV viral loads at baseline than patients without HF. An increase in lymphocyte count (CD4+ and CD8+) and a reduction in the HIV-RNA and HBV-DNA levels were observed concomitantly with the HF. In addition, 80% of patients with HF were on INI, and the association was statistically significant (p=0,036). HBsAg clearance was observed in two patients (12,5%), both with HF and a more significant increase in CD4+ T lymphocytes than in HBsAg-positive patients with HF. The clinical details are summarized in figures 1, 2 and 3.
Conclusion: This study suggests that HBV-IRIS may cause the HF in HIV-HBV coinfected patients after starting HAART. Integrase inhibitors may be a risk factor for HBV-IRIS, and immune reconstitution can play a critical role in the clearance of HBV.

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P 212 TUSCANY REGION: EPIDEMIOLOGY OF HEPATITIS C

M.P. Tramonti Fantozzi[1], L. Ceccarelli[1,2], D. Petri[1], A. Agostini[1], R. Berni[3], C. Bianco[4], S. Chigiotti[5], P. Colombatto[6], S. Iacopini[7], E. Mariabelli[8], S. Modica[7], S. Moneta[7], G. Ottaviano[5], F. Panza[9], P. Pierotti[8], A. Porretta[1], D. Redi[4], B. Rossetti[5], C. Stasi[10], P. Blanc[8], M.R. Brunetto[6], M. Fabbiani[9], S. Luchi[7], C. Nencioni[5], C. Silvestri[3], D. Tacconi[4], A.L. Zignego[10], L. Tavoschi[1]

[1]Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa, Pisa, Italy, [2]Infectious Diseases Unit, Department of Medical and Surgical Sciences, Policlinico Sant'Orsola Malpighi, University of Bologna, Bologna, Italy, [3]Epidemiology Unit, Tuscany Regional Health Agency, Florence, Italy, [4]Division of Infectious Diseases, Arezzo Hospital, Arezzo, Italy, [5]Division of Infectious Diseases, AUSL Toscana Sud Est, Grosseto Hospital, Grosseto, Italy, [6]Hepatology Unit, University Hospital of Pisa, Pisa, Italy, [7]Division of Infectious Diseases and Hepatology, San Luca Hospital, AUSL Toscana Nord Ovest, Lucca, [8]Division of Infectious Diseases 1-2 AUSL Toscana Centro, Firenze, Italy, [9]Infectious and Tropical Diseases Unit, Azienda Ospedaliero-Universitaria Senese, Siena, Italy, [10]Careggi University Hospital, Florence, Italy

Background: Chronic hepatitis C virus (HCV) infection is a major global public health problem. In 2015, Italian Medicines Agency approved the use of highly effective and well-tolerated direct-acting antiviral (DAA) therapy against HCV infection providing its universal access in 2017. In line with the World Health Organization's strategy to eliminate HCV infection by 2030, Italy has launched a free national screening for early HCV diagnosis and treatment to avoid disease complications. Tuscany region, in order to pursue this objective, has therefore launched an action plan to increase treatment coverage and contribute to HCV elimination in the region.

Material and Methods: Characterization of people living with HCV belonging to the prescribing centres of Arezzo, Bagno a Ripoli, Careggi, Grosseto, Lucca, Pisa and Siena - Regional Health Services, with starting treatment time between 01/01/2015-31/12/2022. To study the impact of the universal availability of DAA and COVID-19 pandemic on HCV diagnosis and treatment efficacy, we analysed the liver fibrosis and SVR12 data in 3 periods: before (01/01/2015-30/06/2017) and after (01/07/2017-31/12/2019) DAA universal availability, and during COVID-19 pandemic (2020-2022). One-way ANOVA analysis was used to detect significant differences in liver fibrosis and SRV12 between these temporal eras.

Results: In 2015-2022, the people with chronic HCV infection treated by the Regional Health Services participating at the study were 6858 (age: 58.93±14.17). In this population, there were more males (57%, age: 56.60±13.24) than females (43%, age: 61.86±14.75), high proportion lied in the 51–60 age band (31.46%) and 90.55% of the individuals were Italian. Genotype 1 (57.19%), followed by genotype 3 (19.25%) and genotype 2 (16.41%), was found to be the most common one. Liver fibrosis was mild (F1) in 25.06%; moderate (F2) in 15.91%, severe (F3) in 17.24% and cirrhosis (F4) was found in 27.44%. Significant F3-F4 predominance was observed before (79.91%) than after (22.72%, $p<0.0005$) DAA universal availability and COVID-19 (35.44%, $p<0.0005$) period. Moreover, significant difference was observed between these latter periods ($p<0.0005$). The main treatment used was Sofosbuvir/Vepatasvir (30.92%), followed by Glecaprevir/Pibrentasvir (27.69%). 12 weeks after the end of treatment, HCV RNA was undetectable in 99.01% of the population and no significant differences were observed between the 3 periods analysed (I: 98.90%; II: 99.09%; III: 99.16%).

Conclusions: Regional data availability allowed a first characterization of HCV patients who had access to DAA treatment over time. F3-F4 was predominant and increased again before DAA universal availability and COVID-19 periods, respectively. The study is still ongoing and future investigations will be carried out on anthropometric and clinical data (i.e. pre-existing pathologies). This study will be useful to evaluate the outcome of the screening campaign which will start in 2023.

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P 213 PATIENT WITH HCV/HBV-RELATED CIRRHOSIS AND COLON CANCER: A DIFFICULT PATIENT TO TREAT

C. Liagkoua[1], G. Stornaiuolo[2], M. Stanzione[2], R. Palladino[1], M. Pisaturo[1], N. Coppola[1]

[1]Dipartimento di salute mentale, fisica e medicina preventiva, Università degli studi della Campania L. Vanvitelli, Napoli, [2]AOU Vanvitelli, Napoli

Background: oncologic patients with coinfection HCV/HBV are difficult to treat due to reducted tollerability to chemiotherapics

Case Report: The 75-year-old patient was diagnosed in August 2017 with adenocarcinoma of the right colon, stage pT4N2(4/7)M0G1,on 04/08/2017 she undergone right hemicolectomy.She began adjuvant treatment according to the schedule XELOXq21(oxaliplatin and capecitabine) for a total of 6 months (8 cycles), of which the patient practiced only IV cycles due to reduced tolerability. In December 2017, the patient carried out an outpatient check-up, including blood test which evidenced: negative tumor markers, hypertransaminasemia and persistent neutropenia 4 weeks after last course of XELOX. In February 2018 she repeated the outpatient check-up where she performed blood test which evidenced coinfection by HBV+ and HCV+ (HBsAg-, HBsAb+, HBcAb+, HBeAb+, qualitative HCV RNA+).In March of the same year she returned for an outpatient check-up, awaiting hepatological evaluation to start the anti-viral treatment, where she performed a Total Body CT scan with contrast medium which evidenced: “millimeter nonspecific parenchymal micronodules less than 3mm on the right lung, cyst on the VI hepatic segment and calcification on the VIII; porcelain gallbladder”.In April she repeated blood tests which showed: HCV RNA 4.1x10^5 UI/mL, with 2a2c genotype and HBV DNA 165 UI/mL and in August she followed hepatological outpatient checkup, where she practiced: abdominal ultrasonography which showed: “enlarged liver with irregular margins and spleen 137mm in size”, EGDS showing no esophageal varices and blood tests which evidenced hypertransaminasemia and she began therapy with ENTECAVIR 0.5mg per day. Furthermore, in October, she began therapy with EPCLUSA 1 tablet/day (from 23/10-16/01). In November she repeated the tests for HCV RNA and HBV DNA which were negative.In January 2019, due to liver recurrence, she practiced IVs metastasectomy and thermo-ablation of IIs, Vs and VIs. In March due to further recurrence of liver and peritoneal disease, in consideration of the patient's refusal to place a venous access, the clinical conditions, the previous toxicities reported with chemotherapy treatment and the mutational status (RAS WT), the patient started chemotherapy first line treatment according to CETUXIMAB single agent g1 q14 scheme.Meanwhile in follow-up, he maintained SVR1 for up to one year.

Conclusions: although the treatment with direct-acting antivirals (DAA) was successful, it was difficult to treat the cancer.

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P 214 PATHWAYS UNDERLYING HDV PERSISTENCE ACT INDEPENDENTLY FROM THE EXTENT OF HBV RESEVOIR AND ARE SUSTAINED BY AN ABUNDANT PRODUCTION OF HBSAG DERIVED FROM INTEGRATED HBV-DNA

R. Salpini[1], S. D'Anna[1], L. Piermatteo[1,2], E. Teti[3], A. Di Lorenzo[3], G. Brancaccio[4], G. Torre[1], V. Malagnino[3], M. Iannetta[3], F. Ceccherini-Silberstein[1], C. Pasquazzi[5], U. Cillo[6], A. Vitale[6], E. Gringeri[6], M. Magrofuoco[6], M. Pacenti[7], L. Baiocchi[8], S. Francioso[8], I. Lenci[8], A.M. Geretti[3], M.L. Abate[9], M. Milella[10], A. Saracino[10], A. Olivero[9], G.B. Gaeta[11], L. Sarmati[3], M. Rizzetto[9], G.P. Caviglia[9], V. Svicher[1,2]

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Department of Biology, University of Rome Tor Vergata, Rome, Italy, [3]Department of Systems Medicine, Infectious Disease Clinic, University of Rome Tor Vergata, Rome, Italy, [4]Infectious Diseases Unit, Department of Molecular Medicine, University of Padova, Padova, Italy, [5]Sant'Andrea Hospital, Rome, Italy, [6]Hepatobiliary Surgery and Liver Transplantation Unit, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy, [7]Microbiology and Virology Unit, Padova University Hospital, Padova, Italy, [8]Hepatology Unit, Policlinico Tor Vergata, Rome, Italy, [9]Department of Medical Sciences, University of Turin, Turin, Italy, [10]Clinic of Infectious Diseases, University of Bari, Bari, Italy, [11]Infectious Disease Unit, University L. Vanvitelli, Naples, Italy

Background: HDV exploits HBV surface proteins (HBsAg) for viral morphogenesis and de novo entry into hepatocytes. The interplay between the two viruses is poorly understood and has been mainly evaluated in peripheral blood. Here, we investigate HBV and HDV replicative activity and their interplay by analysing a well-defined set of liver biopsies from patients (pts) with chronic HBV/HDV infection.

Method: Liver tissue was analysed from 25 pts (71% NUC-treated; 96% HBeAg-neg, all infected with HDV genotype 1 and 84% with HBV genotype D). Intrahepatic levels of covalently closed circular DNA (cccDNA), pregenomic HBV-RNA (pgRNA) and HDV-RNA were quantified by high-sensitive droplet digital PCR (ddPCR). ddPCR assays were set up to quantify total HBs transcripts and to distinguish HBs transcripts deriving from cccDNA and from integrated HBV-DNA according to Grudda, 2022.

Results: Pts were characterized by high serum levels of HDV-RNA and HBsAg (median[IQR]: 6.3[3.8-7.7] logIU/mL and 14,460[5,207-21,118] IU/mL, respectively) and low HBV viremia (serum HBV-DNA detectable in only 48% of pts with median[IQR] of 50[34-214] IU/ml). Median(IQR) ALT was 72(52-102) U/L and half of pts had a fibrosis score >F5.

Intrahepatic HDV-RNA was median(IQR) 787(1-2913) copies/1000cells and positively correlated with serum HDV-RNA (Rho=0.63, P=0.05).

Regarding HBV intrahepatic reservoir, median(IQR) cccDNA was 3(0.1-24) copies/1000cells and pgRNA was 8(1-147) copies/1000cells. Despite a limited HBV reservoir, we observed an abundant production of total HBs transcripts (median[IQR] total HBs RNAs: 6,028[409-19,137] copies/1000 cells), positively correlated with serum HBsAg (Rho=0.54; P=0.04).

Notably, by analyzing the source of HBs transcripts, we found that >90% of HBs transcripts derived from integrated HBV-DNA, with a limited contribution of cccDNA transcriptional activity, supporting that HDV persistence is mainly sustained by HBsAg produced from integrated HBV-DNA in HBeAg-neg HDV chronic infection.

Finally, no difference in intrahepatic HDV-RNA levels was observed according to the size of HBV reservoir (median[IQR]: 787[1-5,495] and 880[1-3,338] copies/1000cells in pts with cccDNA<5 and >5 copies/1000cells, p=0.9), while markers of HBV activity were significantly lower in pts with a more restricted HBV reservoir (median [IQR]: 1[1-10] vs 147[9-406] copies/1000cells for pgRNA and 0.3[0.2-1] vs 73[7-243] copies/1000cells for cccDNA-derived HBs transcripts in cccDNA<5 vs >5 copies/1000cells, p<0.01 for both). Overall data suggest the existence of independent paths underlying the replication of the two viruses.

Conclusion: Pathways sustaining HDV replication act independently from the extent of intrahepatic HBV reservoir and are fueled by an abundant production of HBs transcripts, mainly derived from integrated HBV-DNA. These issues are crucial for deciphering mechanisms underlying HDV persistence, that could jeopardise the success of anti-HDV therapeutic strategies.

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P 215 KINETICS OF THE THREE HBSAG ISOFORMS ALONG WITH HDV-RNA PREDICT VIROLOGICAL RESPONSE IN CHD PATIENTS TREATED WITH BULEVIRTIDE UP TO 96 WEEKS

S. D'Anna[1], R. Salpini[1], E. Degasperi[2], L. Duca[1], M.P. Anolli[2], L. Piermatteo[1,3], D. Sambarino[2], M. Borghi[2], F. Facchetti[2], F. Ceccherini-Silberstein[1], R. Perbellini[2], P. Lampertico[2,4], V. Svicher[1,3]

[1]University of Rome Tor Vergata, Department of Experimental Medicine, Rome, Italy, [2]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy, [3]University of Rome Tor Vergata, Department of Biology, Rome, Italy, [4]CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Background: HDV exploits the HBV surface protein (HBsAg) for the release of its progeny and entry into hepatocytes. HBsAg consists of three different proteins: Large (L-HBs), including preS-1, preS-2 and S regions; Middle (M-HBs), including pre-2 and S regions, and small HBsAg (S-HBs), containing only the S region. Among them, L-HBs is mainly present in virions and is crucial for the binding to the NTCP receptor and thus for entry into the hepatocytes. Here, we investigate the still unknown kinetics of HBs forms in patients (pts) receiving the entry inhibitor bulevirtide (BLV).

Method: Twenty consecutive pts with HDV-related compensated cirrhosis starting BLV monotherapy 2mg/day were enrolled in this single-center retrospective/longitudinal study. All pts were under effective NUC treatment at entry. L-HBs, M-HBs and S-HBs were quantified by ad hoc ELISAs (Beacle Inc.) at baseline and week 48 (W48) for all pts and at week 96 (W96) for a subset of 16 pts. HDV-RNA was quantified by Robogene 2.0 (LoD:6IU/mL). Virological response (VR) was defined as HDV-RNA<6IU/mL or >2log decline compared to baseline.

Results: At baseline, median (IQR) serum HDV-RNA and HBsAg were 4.9 (4.4-5.7) logIU/mL and 3.7 (3.4-3.9) logIU/mL, respectively, while ALT was 110 (83-147) U/L. Pre-treatment median (IQR) levels of S-HBs, M-HBs and L-HBs were 3421 (1240-6209), 791 (260-1930) and 7 (2-15) ng/mL, respectively.

Following BLV treatment, VR was achieved in 70% (14/20) and 81.2% (13/16) of pts at W48 and W96, while HDV-RNA undetectability in 35% (7/20) and 43.8% (7/16) at W48 and W96. In pts with undetectable HDV-RNA, ALT<40U/L was observed in 5/7 and 6/7 pts at these time-points. In particular, HDV-RNA<5logIU/mL at baseline was predictive of HDV-RNA undetectability at W48 and W96 (endpoint achieved in 60% with vs 10% without HDV-RNA<5logIU/mL at W48 and in 80% vs 27.3% at W96, p<0.05 for both).

After 96 weeks of BLV treatment, S-HBs, M-HBs and L-HBs decreased in 68.8%, 43.8% and 62.5% of pts with a median (IQR) decline of 994 (248-4686), 518 (393-715), 4 (1-12) ng/mL, respectively. A level of L-HBs<9ng/mL at baseline significantly correlated with the achievement of HDV-RNA undetectability at W48 (endpoint achieved in 54.5% with vs 11.1% without L-HBs<9ng/ml, p=0.04). Superimposable result was observed in relation to the achievement of HDV-RNA undetectability plus ALT<40U/L at W48 (endpoint achieved in 50% with vs 0% without L-HBs<9ng/mL, p=0.03). Even more, the combination of L-HBs<9ng/mL+HDV-RNA<5logIU/mL was the best predictor for achieving HDV-RNA undetectability plus ALT<40U/L at W48 (endpoint achieved in 66.7% with vs 7.1% without this combination, p=0.01). Notably, this datum was further confirmed at W96 (80.0% with vs 18.2% without, p=0.03).

Conclusion: Quantification of L-HBs along with serum HDV-RNA can reflect the burden of circulating infectious virions, providing a new promising tool to identify pts more likely to respond to BLV monotherapy.

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P 216 IDENTIFICATION OF NOVEL MOLECULAR TARGETS FOR THERAPEUTIC RECONSTITUTION OF HBV-SPECIFIC CD8 T CELL REACTIVITY IN CHRONIC HEPATITIS B VIRUS INFECTION

I. Montali[1], C. Ceccatelli Berti[1], M. Morselli[2], C. Boni[3], A. Penna[3], D. Laccabue[1,3], A. Vecchi[3], M. Rossi[1], C. Tiezzi[1,3], V. Reverberi[3], A. Montali[1], S. Doselli[3], A. Alfieri[3], D. Sambarino[4], P. Lampertico[4,5], M. Massari[6], G. Missale[1,3], C. Ferrari[1,3], P. Fisicaro[3]

[1]Department of Medicine and Surgery, University of Parma, Parma, Italy, [2]Laboratory of Biochemistry and Molecular Biology, Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy, [3]Laboratory of Viral Immunopathology, Unit of Infectious Diseases and Hepatology, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy, [4]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy, [5]CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [6]Unit of Infectious Diseases, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy

Background and Aims: Correction of HBV-specific T cell dysfunction can represent a strategy to cure chronic hepatitis B (CHB) and this may be achieved by targeting impaired intracellular pathways of key functional relevance for antiviral T cell effector activity. In chronic HBV infection elevated ROS levels caused by dysfunctional mitochondria can induce increased protein oxidation, proteostasis engulfment and DNA damage in exhausted virus-specific CD8 T cells. Thus, our objective was to provide novel mechanistic insights into CD8 T cell exhaustion with the final goal of identifying specific cellular defects to be targeted for functional T cell reconstitution.

Methods: DNA damage and DNA repair mechanisms, including parylation, CD38 expression, histone acetylation and methylation as well as telomere length were studied by flow cytometry in dextramer-stained HBV-specific CD8 T cells from chronic HBV patients. FLU-specific CD8 cells from the same patients and from healthy subjects served as controls. Correction of intracellular signaling alterations and improvement of anti-viral T cell functions by epigenetic interventions was assessed by fluorescent probes and antibodies in flow cytometry.

Results: Elevated DNA damage in association with defective DNA repair processes, as well as a diminished histone acetylation has been observed in HBV-specific CD8 cells from chronic HBV patients. Inhibition of histone deacetylases in these patients, induced a significant improvement of DNA repair mechanisms, mitochondrial and proteostasis functions and epigenetic regulation. These interventions improved the HBV-specific antiviral CD8 T cell function.

Conclusions: Our study delineates a model of CD8 T cell exhaustion whereby multiple functionally interconnected intracellular defects, including telomere shortening and histone acetylation, are causally related to NAD depletion suggesting similarities between T cell exhaustion and cell senescence. Correction of these deregulated intracellular functions by epigenetic targeting can also restore anti-viral CD8 T cell activity and thus represent promising potential therapeutic strategies for chronic HBV infection.

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P 217 ECTHYMA GANGRENOSUM WITH FACIAL AND ORAL LOCALIZATION IN A YOUNG NEUTROPENIC WOMAN WITH RECENT DENGUE INFECTION

F. Catania[1], F. Damiano[1,2], I.M. Izzi[1,2], F. Raffaelli[2], F. Frondizi[1], E. Matteini[1], F. Sangiorgi[1], G. Scoppettuolo[2]

[1]Dipartimento di Sicurezza e Bioetica - Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore - Rome (Italy), [2]Dipartimento di Scienze di Laboratorio e Infettivologiche, Fondazione Policlinico Universitario Agostino Gemelli IRCCS - Rome (Italy)

Introduction: Dengue is a viral infection caused by one of the four Dengue viruses (DENV) transmitted by Aedes aegypti or Aedes albopictus. Although Dengue is not a major concern in our latitudes, its global burden is large, with estimated 100–400 million new infections each year. Tropical Asia and America show the highest density, while most cases reported in Europe are acquired during travels to endemic areas. Clinical manifestations include a febrile phase, a critical phase and a recovery phase. Trombocitopenia is often described, but some reports also depict the occurrence of occasional leukopenia with neutropenia. Hence, management of such complications can be challenging also in our settings, especially when linked to immunosuppression.

Case Description: Our case depicts the story of a 30-years-old woman with a recent diagnosis of hyperthyroidism, treated with methimazole, with reported penicillin allergy, conducted to our hospital for the development of fever, oral and skin lesions, after a vacation in Nepal. There, she received several insect bites and discontinued methimazole. After her return, she developed fever, three bullous lesions on her face and three hemorrhagic lesions on gingival surface. Laboratory tests showed severe neutropenia, CRP 465.1 mg/dl and procalcitonin 6.79 ng/mL. All malaria's blood smear and molecular tests, serology for HIV, Chikungunya and Zika viruses resulted negative. Serology for Dengue viruses was inconclusive. As blood cultures were performed, an empiric antibiotic therapy, with endovenous daptomycin and ciprofloxacin was started. Therapy with methimazole was confirmed. Blood cultures resulted positive for Pseudomonas aeruginosa and ecthyma gangrenosum (EG) was diagnosed. Hence, daptomycin was interrupted, while ciprofloxacin was prosecuted. The patient's clinical conditions improved, with a complete defervescence, a crusty evolution of the skin lesions and a gradual resolution of the gingival ones. Laboratory tests showed a resolution of leukopenia. New Dengue serology showed seroconversion of IgM, with negative IgG. At discharge, ciprofloxacin was prosecuted orally for 14 days. An almost complete resolution of both oral and skin lesions was documented at follow-up.

Discussion: Several case reports describe how often EG uncovers primary subclinical immunodeficiencies. Parallelly, literature shows how neutropenia results as one of the principal laboratory findings in Dengue disease. Here, it is reasonable to assume that virosis could have caused a transient immunosuppression, leading in turn to the onset of EG. Even if it is reasonable to consider methimazole a cause of immunosuppression, the fact that it was discontinued before the symptoms onset, without any worsening of neutropenia once restarted, confirms our hypothesis that neutropenia itself could be ascribed to Dengue disease and consequently immunosuppression brought to the development of EG, in a context of P.aeruginosa BSI.

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P 218 HCV RELAPSE AFTER SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA: SPECULATIONS ON A POTENTIAL CAUSE

C. Fusetti[1,2], C. Magni[1], D. Moschese[1], R. Giorgi[1], S. Merli[1], F. Petri[1,2], M.V. Cossu[1], G. Gubertini[1], G. Rizzardini[1], A. Gori[1,2]

[1]Department of Infectious Diseases, Luigi Sacco Hospital, ASST Fatebenefratelli Sacco – Milan, Italy, [2]University of Milan, Milan – Italy

Background: Direct antiviral agents (DAAs) have completely changed the scenario of HCV infection achieving cure rates close to 100%. HCV therapy involves a first-line treatment, consisting of two different DAAs, and, in case of virological relapse, a second-line with three DAAs.
We present the case of a patient affected by chronic lymphocytic leukemia (CLL) who experienced both first and second-line treatment failure.
Report: A 71-year-old male with HCV infection detected in 2005 (genotype 3a, no HIV/HBV coinfection), who always refused eradication therapy with both interferon or DAAs, received a diagnosis of CLL in July 2021. No oncological therapy was needed at the beginning, but after the diagnosis, the patient granted his consent for HCV treatment (table 1).
An 8-week treatment with glecaprevir/pibrentasvir was started in October 2021 and undetectability of HCV-RNA was achieved during treatment. However, a relapse was detected after the end of treatment (EOT).
The same genotype was confirmed in the absence of risk factors for reinfection. He was thus prescribed with sofosbuvir/velpatasvir/voxilaprevir for 12 weeks in March 2022; once again, after an initial response during treatment, a viral relapse after the EOT was detected.
Adherence was reported as optimal and concomitant DDIs were excluded. Resistance test was performed confirming genotype 3a and showing no mutations in NS3, NS5A and NS5B regions.
Due to the concomitant worsening of CLL, acalabrutinib was started in June 2022 and is still ongoing.
Discussion: In the literature, cases of failure after second-line HCV therapy are extremely rare and even more scarce are the data on failure in patients with lymphoma.
It is known that the risk of failure is higher in patients with genotype 3, advanced liver disease and those with viral mutations conferring resistance to DAAs.
Although our patient actually had a genotype 3 virus, liver disease was mild and no resistance mutations were identified, and this is consistent with the virological response obtained during treatment.
We believe that immune system dysregulation in CLL may have played a role in this case of treatment failure. In particular, peripheral blood mononuclear cells (PBMCs) and bone marrow cells (BMCs) represent a reservoir of HCV; their aberrant production in CLL could have led to the persistence of HCV reservoir with consequent relapse of viral replication at the EOT.
Conclusions: Although we failed to identify a certain reason for second-line treatment failure, we speculate that a role could be played by the enormous lymphocyte expansion featured during CLL who potentially led to a greater HCV reservoir in PBMCs and BMCs. Still, limitation to such hypothesis is that quantitative viral load is not a clear risk factor of virologic relapse. Further studies are needed in order to clarify if this could be a possible explanation for treatment failure and whether or not a different treatment schedule could be useful in such patients.

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P 219 PRELIMINARY RESULTS OF A CASE FINDING AND LINKAGE TO CARE PROGRAM FOR HIGH-RISK HCV INFECTED INDIVIDUALS

F.G. Spatola[1], M. Pisaturo[1], P. Grimaldi[1], S. Capuano[1], A. Russo[1], F. Ambrisi[1], F. Milite[1], B. Morello[1], F. Sautariello[1], C. Sagnelli[1], M. Stanzione[2], G. Stornaiuolo[2], P. Caruso[3], K. Esposito[3], M.R. Rizzo[3], F. Simonelli[4], P. Bucci[1], S. Galderisi[1], N. Coppola[1]

[1]Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli" - Napoli (Italy), [2]AOU Luigi Vanvitelli - Napoli (Italy), [3]Department of Advanced Medical and Surgical Sciences (DAMSS) University of Campania "L. Vanvitelli" - Napoli (Italy), [4]Multidisciplinary Department of Medical-Surgical and Dental Specialties, University of Campania "L. Vanvitelli"- Napoli (Italy)

Background: Hepatitis C is now a curable disease: screening is fundamental.

Material and Methods: This is a multicentric, prospective case study run from October 2021 to February 2023, including 4 wards from Vanvitelli University Hospital, diabetology, psychiatry, ophthalmology, geriatrics, and an NGO ambulatory, coordinated by Vanvitelli's Infectious Diseases unit. The project started from the wards diabetology and geriatrics. Subsequently in 2022 the project was expanded, including a cooperation with the NGO "Emergency", and the psychiatry and ophthalmology units. Information on demographics, schooling, comorbidities, risk factors for HCV were collected. A rapid capillary HCV test was performed, and positive patients were "linked to care". Our group joined the European Testing Week 21-28 November 2022 and we rented the GeneXpert 4-4 instrument (CEPHEID Test user Agreement) to practice HCV RNA.

Results: 627 subjects (median age 55 years, Q1-Q3 37-68) were enrolled. 55.8% were male, 61.7% reported schooling (>8 years). 224 (35.73%), 138 (22.01%), 54 (8.61%), 55 (8.77%) and 156 (24.88%) patients were enrolled respectively in diabetology, psychiatry, ophthalmology, geriatrics wards and in the NGO outpatients' clinics. (Fig 1).

Enrollees from the NGO ambulatory and the psychiatric center were younger, and most patients in each setting were educated (a parameter not evaluated in ophthalmology population). As expected, the diabetology center had a higher percentage of diabetes and the ophhtalmology center had a higher percentage of ophthalmological pathologies, while the geriatric service had a higher percentage of cardiovascular comorbidities, as the ophthalmology ward (as in figure 2).

Diabetology and ophthalmology ward's outpatients had more frequently surgery history, the NGO outpatient's unit compared to the other settings enrolled had a higher percentage of prison history and the patients of the psychiatric setting had higher percentage of drug addiction (Fig. 2).

Nine subjects out of the 627 enrolled (1.44%) resulted positive at the HCV test, 2 from the diabetology ward (both had already undergone therapy to eradicate HCV in a different center), 4 from ophthalmology ward (a patient refused to undergo treatment, 2 patients have been contacted in order to mediate the linkage-to-care at our center and another is already undergoing treatment) and 3 from the NGO ambulatory (one patient had already practiced eradication therapy, another after confirmation by HCV-RNA became untraceable and another was negative for HCV-RNA) (Fig. 3).

In the NGO outpatient service setting we performed HCV RNA Rt-PCR on 10 patients, 4 male and 6 females, 8 with history of recent migration. All of then resulted negative.

Conclusions: Tracking down and treating HCV patients will allow to eradicate this pathology.

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P 220 LONG-TERM MORTALITY AFTER HCV ERADICATION AMONG PLWH

A. Siribelli[2], S. Diotallevi[2], L. Galli[2], G. Morsica[2], R. Lolatto[2], C. Bertoni[2], E. Messina[2], C. Tassan Din[2], M. Ripa[1,2], C. Uberti-Foppa[1,2], A. Castagna[1,2], H. Hasson[2]

[1]Vita-Salute University, Milan, Italy, [2]Unit of Infectious Diseases, San Raffaele Hospital, Milan, Italy

Background: People coinfected with HCV-HIV, even with suppressed HIV viremia, are at high risk of developing cirrhosis and hepatocellular carcinoma (HCC) and there are no studies providing long-term mortality after HCV eradication in this setting. This study aimed to assess the long-term incidence and risk factors of mortality in HIV-HCV coinfected people treated with direct acting antivirals (DAAs).

Methods: Retrospective observational study including HIV-HCV coinfected people, followed at San Raffaele Hospital, who achieved week 12 of suppressed virological response (SVR) after treatment with DAAs. All individuals were assessed for biochemical and virological data at baseline (BL), defined as the end of treatment; follow-up accrued since BL until death, lost-to follow-up or last visit. Cirrhosis was defined as stiffness value ≥ 13 kPa obtained by transient elastography (FibroScan). Mann-Whitney rank-sum test or chi-square/Fisher's exact test were applied. Kaplan-Meier analysis and the log-rank test were used to analyze cumulative probability of mortality for any cause since the BL. Cox proportional hazards regression was used to estimate adjusted hazard ratio (aHR) of mortality, with the corresponding 95% confidence interval (95%CI); BL variables included in the model were: age, cirrhosis, diabetes, HCC and BMI.

Results: Overall, 649 people were analyzed; BL characteristics are reported in Table 1. During a median follow-up of 4.41 years (IQR=3.5-5.5), 42 people died: 64% of non-liver related causes,mainly cardiovascular events; 36% of deaths were liver-related and 50% were malignancies, of those 29% liver and 71% non-liver cancers. The overall 3-, 5- and 7-year cumulative probability of all causes-mortality were 4.1% (95%CI=2.5%-5.6%), 7.1% (95% CI=4.8%-9.5%) and 11.5% (95%CI=7.1%-15.8%), respectively. The mortality probability was higher among individuals with vs without cirrhosis (figure 1) and in older compared to younger individuals (figure 2). In the multivariate analysis, mortality was more likely in older people [aHR(5-year increment)=1.41, 95%CI=1.10-1.79, p=0.005], in people with cirrhosis [aHR=3.46, 95%CI=1.84-6.50, p=0.0001], diabetes [aHR=2.74, 95%CI=1.34 -5.59, p=0.005], HCC [aHR=3.50, 95%CI=1.19-10.28, p=0.02]; the risk of mortality was lower in people with normal BMI compared with obese [aHR=0.37, 95%CI=0.14-0.97, p=0.04].

Conclusions: We observed a favorable impact on mortality after HCV eradication in PLWH, confirming literature data from studies with shorter follow up. Albeit to a lesser extent compared to studies on untreated individuals, liver-related events influenced mortality even after SVR. People with cirrhosis, HCC, diabetes and obesity prior to treatment with DAAs had a higher risk of mortality and the main cause of death was cancer related. According to our results, surveillance of liver and non-liver events after SVR, particularly malignancies, may be recommended.

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P 221 A PILOT INTERVENTION FOR HCV ELIMINATION AMONG MSM IN ROME: RESULTS FROM A PROGRAM OF MICRO-ELIMINATION OF HCV

P. Piselli[1], M. Giuliani[2], M. Farinella[3], F. Leserri[4], F. Angeli[5], R. Galipò[6], C. Cimaglia[1], A. Nappo[1], N. Orchi[1], A. Latini[2], F. Carduccelli[3], O. Bruzzi[1], S. Foracappa[2], E. Piscitelli[1], D. Tonnini[1], E. Gennaro[1], S. Pittalis[1], R. Esvan[1], A. Faticoni[1], G. De Carli[1], F. Gili[1], A. Genovese[3], S. Meschi[1], A.R. Garbuglia[1], A. Amendola[1], S. Cicalini[1], M. De Palo[1], E. Grilli[1], E. Biliotti[1], M. Marra[3], G.M. Corbelli[4], P. Ferri[6], A. Cristaudo[2], F. Maggi[1], G. D'Offizi[1], A. Antinori[1], V. Puro[1], E. Girardi[1]

[1]INMI "L. Spallanzani" IRCCS, Rome, [2]Istituto Dermatologico San Gallicano, IRCCS, Rome, [3]Circolo di Cultura Omosessuale "Mario Mieli", Rome, [4]Plus Roma - Checkpoint, Rome, [5]ARCIGAY Roma, Rome, [6]ANLAIDS Lazio APS, Rome

Background: HCV prevalence among men who have sex with men (MSM) is not negligible, but information in Italy is scarce, particularly for HIV-uninfected MSM. An HCV screening program in MSM in Rome began in summer 2019 in two hospital settings and in four urban community settings run by a NGOs, offering rapid testing for HCV aimed to identify, linking to care and treating with DAA, MSM with a previously undiagnosed HCV infection.

Methods: Adult (>18 years old) MSM attending two clinical centers dealing with HIV and other STI in Rome and four NGOs, were invited to undergo a free-of-charge rapid HCV Antibody test (OraQuick HCV®). For all participants, demographic, clinical and behavioural data using an anonymous questionnaire were collected. Free confirmatory standard serology tests were offered for those found as HCV antibodies reactive, referring individuals with a confirmed chronic HCV-infection through a dedicated "fast track" pathway for further clinical assessment and DAA-treatment according to the national treatment guidelines.

Results: From Jul 2019 to Apr 2023, 2633 MSM agreed to be screened for HCV infection (89.8% Italians, median age 36 years, interquartile range: 28-46), mostly (1536, 58.3%) tested in the two clinical centers. HIV-infection was reported by 295 (11.2%) MSM and 48.4% of all participants of being previously tested for HCV (84.1% in HIV-pos and 43.9% in HIV-neg participants). Overall, 8 MSM were found to be reactive at rapid test (0.3%): 3 of them were HIV-pos (all confirmed) while among 5 found in HIV-neg, 4 were retested and 3 confirmed (Fig.1). Five out of six confirmed cases have never been tested for HCV before (two HIV-pos and all three HIV-neg). Overall HCV-pos confirmed prevalence was 0.23% (95% CI: 0.09-0.47), higher in HIV-pos subjects than HIV-neg (1.02% vs 0.13%, see Fig.2). All confirmed cases were viraemic (range 8x103-23x106 UI/mL) harboring HCV genotype 1a (4 cases) or 4 (2 case). All of them were linked to care, clinically assessed and started DAA treatment (8 weeks protocol with Glecaprevir/Pibrentasvir), already completed reaching sustained viral response in five of them (one case still on treatment).

Conclusions: Our data suggest the feasibility and potential effectiveness of a program aimed at MSM living in Rome, which combines HCV screening and linkage to care with prevention strategies. Overall, HCV-prevalence in this population is quite low, although it is higher (more than 8 times) in those HIV co-infected. The high proportion of HCV-positive participants never tested for HCV before especially in HIV-positive participants highlight the necessity to periodically screen this population.

Supported by: Grant Gilead IN-IT- 987-5359, part of the LEGA-C™ program "Local Elimination Programs leading to Global Action in HCV".

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P 222 INTEGRATION OF HEPATITIS C AND ADDICTION TREATMENT IN PEOPLE WHO INJECTS DRUGS. THE SAN PATRIGNANO HCV-FREE AND DRUG-FREE EXPERIENCE

P. Piselli[1], A. Boschini[2], S. Duehren[2], A. Nappo[1], C. Smacchia[2], G. Scarfò[1], C. Pagliardini[2], C. Cimaglia[1], E. Girardi[1]

[1]Clinical Epidemiology Unit, National Institute for Infectious Diseases "L. Spallanzani" IRCCS, Rome - Italy, [2]Medical Center, Comunità di S. Patrignano, Coriano (RN), Italy

Background: Persons who inject drugs (PWIDs) are considered as a key population for HCV infection and therapeutic communities (TCs) are promising points of care in order to reach such population, although scarce information on HCV Cascade of Care (CoC) is available about this setting. Our aim was to evaluate CoC in the San Patrignano therapeutic community (SPTC) during a 5 years period (2018-2022).
Methods: We evaluated the effectiveness and efficacy of HCV micro-elimination program targeting PWIDs in the context of a drug-free TC. Progression through Coc was monitored by calculating frequencies of infection diagnosis, confirmation, treatment and achievement of sustained virological response (SVR). All PWIDs already resident at the beginning of observation period (Jan 2018–Mar 2022) or admitted thereafter at SPTC aged 18+ years at last entry were included. Baseline information were recorded at admission, including socio-demographic data, history of previous HCV testing and treatment. At admission, participants were assessed for HCV and HIV serology and viral load by standard laboratory procedures. Ongoing HCV infections were treated with direct acting antivirals, according to national guidelines.
Results: A total of 811 participants were included, 77.1% were males, median age at last entry of 32 years (IQR: 26-39), mostly Italians (92.6%). Median age at starting intravenous drug use was 20 years (IQR: 18-24) with a median period of drug abuse of 7 years (IQR: 3-16). Regarding history of a previous HCV-testing, 79.2% referred to have been already tested for HCV before SPTC-entry and 58.7% referred a previous HCV-positive test with or without previous HCV-treatment. Overall, 792/811 (97.7%) were screened for HCV antibodies at admission, and among these 503 (63.5%) were found to be HCV-seropositive. HCV-positive subjects were more likely to be older (median age 35 vs 29, p<0.001), have an history of incarceration (32.4% vs 17.0%, p<0.001) and being HIV-positive (9.9% vs 1.7%, p<0.001). Most of those found to be HCV-ab positive underwent subsequent HCV-RNA testing (n=481, 95.6%), and 331/481 (68.8%) were found to be HCV-RNA positive and eligible for treatment. One-hundred-six subjects HCV-RNA positive (32.0%) missed DAA therapy mainly because either dropped-out (n=42, 39.6%) or were discharged from SPTC before DAA start. Overall, 225 out of 331 HCV-RNA positive participants (68.0%), were prescribed DAA treatment and 221 (98.2%) were completely assessed and considered cured (SVR12) (summarized in Figure 1).
Conclusions: According to the CoC monitoring, TCs is an optimal point of care for the treatment of HCV infection in PWIDs. The risk of losing patient for HCV treatment could be greatly reduced by speeding up bureaucracy by promoting retention in care of individuals, closely associated to addiction treatment purpose.
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P 223 ACUTE VIRAL HEPATITIS FROM HBV DUE TO IMMUNE-RECONSTITUTION IN A PATIENT WITH PLEURAL TUBERCULOSIS RECEIVING TREATMENT

L. Ansaldo[1], C. Sorace[1], M.L. Minardi[1], A. Lodi[1], F. Barreca[1], M. Compagno[1], E. Teti[1], L. Sarmati[1,2], A.M. Geretti[1,2]

[1]Infectious Diseases Unit, Policlinico Tor Vergata, Roma, Italia, [2]Clinical Infectious Diseases, Department of System Medicine, Tor Vergata University, Rome, Italy

Background: Tuberculosis(TB)-HBV coinfection is estimated to have a high prevalence and in 40% of cases can cause hepatitis with even fatal evolution[1].

Summary: A 37-year-old Somali patient with no medical history accessed the Emergency Department of Policlinico Tor Vergata in January 2022 for chest pain, weight loss and night sweats for about 2 months; Chest CT was performed and showed pleural effusion and lymphadenomegaly. On suspicion of TB and positive nasal swab for SARS-CoV-2, the patient was admitted to Infectious Diseases ward. Mantoux test was performed and resulted positive, IGRA test indeterminate, serologies for HCV, HDV, HIV negative, HBV infection was diagnosed (viral genotype A, subtype A1, wild-type strain) with HBcAb and HBeAb positive, HBsAb negative and HBeAg negative, quantitative HbsAg 17698.51 IU/ml and HBV viremia 7950 IU/ml. The CD4 count was 244cell/uL. Thoracocentesis and fibrobronchoscopy were performed with bronchoalveolar lavage, resulting negative for culture, molecular and microscopic research of mycobacteria. Anti-TB therapy was started with rifampicin, isoniazid, pyrazinamide and ethambutol without signs of hepatotoxicity. The patient was discharged after two weeks, with negative nasal swab for SARS-CoV–2. At the outpatient follow-up 9 weeks after the start of the anti-TB therapy, pain in the right hypochondrium, nausea, an increase in AST/ALT 1948/1146 IU/L and HBV-DNA 5,9x107 IU/ml appeared. Simplified anti-TB therapy was stopped and oral entecavir 1 mg/day was started. The patient was admitted to perform liver ultrasound which showed thickened echostructure without focal alterations and liver biopsy which documented signs of acute hepatitis with also immunohistochemistry that tested positive for HbsAg. IGRA test was positive and CD4 count 436cell/uL. The patient was discharged after 4 weeks with reduction of AST/ALT 304/292 IU/L and HBV viremia 6300 IU/L. At the one-month follow-up, improvement was observed with normalization of transaminases and reduction of viraemia (274 IU/L).

Conclusions: TB-HBV coinfection increases the risk of HBV reactivation and liver damage with a mechanism that is not exclusively drug-induced, but could be linked to immunoreconstitution during TB therapy and/or excessive immune responses against HBV; in this case, a role could also be played by SARS-CoV–2-related immunosuppression. Although there aren't definitive guidelines on the exact timing of initiation of therapy, nor on the HBV antiviral regimen in this specific patient population, assessing these two key points should be considered as it may reduce the risk of subsequent liver injury [1,2].

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Hepatitis and other viral infections

P 224 A CASE OF CONGENITAL CMV INFECTION DUE TO PRE-CONCEPTIONAL MATERNAL PRIMARY INFECTION: SEROLOGIC PITFALLS IN VALACYCLOVIR ERA

M. Maffezzoni[1], I. Gallazzi[1], M. Furione[2], A. Sarasini[2], C. Fornara[2], F. Brillo[3], A. Ricciardi[1]

[1]Infectious Diseases Unit, Department of Medical Science and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo - University of Pavia - Italy, [2]Molecular Virology Unit, Microbiology and Virology Department, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [3]Unit of Infectious Diseases and Hepatology, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy

Introduction: Human Cytomegalovirus (HCMV) is the leading cause of congenital infection with a global seroprevalence of 0.5-2% and the main non-genetic cause of congenital sensorineural hearing loss and neurological damage. The risk of placental transmission after maternal primary infection is around 30-40% increasing from I to III trimester; in pre-conceptional infection, the risk is around 5%. The morbidity is highest in case of primary CMV infections acquired early in pregnancy and in those patients treatment with high doses of valacyclovir is now available which led to the reduction of maternal-fetal transmission and neurological sequelae

Case: An 18-year-old primigravid woman with no past clinical history accessed our outpatient clinic at 12 gestational weeks with suspected HCMV gestational infection.

Serologic examinations performed at 11 gestational weeks showed HCMV-specific positive IgM and IgG with high CMV avidity (0.441, PV>0.25).

A new virologic control resulted in IgG 104 UI/ml (positive value >14), negative IgM (CLIA and ELISA), high avidity of CMV IgG (0.809, PV>0.25) and a serum HCMV-DNA polymerase chain-reaction (PCR) of 300 copies/ml.

Suspecting a pre-conceptional infection, we performed immune T-cell adaptive test compatible with not recent infection (>3 months). A monthly ultrasound follow-up and the possibility to perform amniocentesis at 20 weeks of pregnancy, was recommended. The patient denied amniocentesis and was lost to follow up.

In another centre, at 20 gestational weeks ultrasound, neonatal hyper-echogenic bowel was demonstrated (typical ecographic sign of congenital infection). Clinicians decides to perform an amniocentesis that showed in amniotic liquid a CMV-DNA of 9.605.720 copies/ml. With the diagnosis of congenital CMV infection the patient decided to undergo to a voluntary termination of pregnancy at 21 gestational weeks. The autopsy concludes in an immature fetus free of viscero-somatic malformations.

Discussion: As showed in previous works, IgG serology in recent HCMV primary infection might show high avidity and, in addition, the risk of pre-conceptional transmission, despite low is potentially serious in terms of morbidity.

Additional tests as CMV-DNA but also invasive diagnostic tools (as diagnostic amniocentesis) or non invasive (as ultrasounds) might help in addressing the correct diagnosis.

Currently in Italy, based on AIFA criteria, treatment with high doses of valacyclovir is only approved in the case of low or intermediate avidity with CMV-DNA in other samples (blood, urine, saliva), losing the possibility of treatment in the case of atypical primary infection

Conclusion: Our case reports a CMV serology pitfalls in early screening of pregnancy infection. In Valacyclovir era, amplifying diagnostic capability and widening AIFA criteria can help clinicians on the choice of which patient can benefit from early treatment and reduces the burden of CMV congenital infections.

Hepatitis and other viral infections

P 225 ANTI-HBV THERAPY IN HEMODIALYTIC PATIENT: A NOT EASY APPROACHES

R. Pesare, L. Pagnucco, R. Gulminetti, N. Amarasinghe, R. Bruno

Infectious Diseases Unit, Department of Medical Science and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo - University of Pavia - Italy

Introduction: People with end-stage renal disease (ESRD) who undergo hemodialysis represent a small share of patients in whom optimal anti-HBV treatment is still under investigation; even further, a rescue therapy in failed patients represents an exceptional clinical entity.

Case report: A 55-years-old woman with a history of HBV-HCV co-infection (HDV seronegative) and a chronic kidney disease (CKD) received from 2009 entecavir (ETV) and in 2015 undergone HCV antiviral DAAs therapy obtaining SVR. In January 2020 she started hemodialysis treatment and ETV was remodulated from renal dosage to ESRD-dosage. In August 2020 she self-suspended the treatment for intolerance and, considering that HBV-DNA after some weeks was still not detectable and quantitative HBsAg was at low level, treatment suspension was maintained and a close monitoring of HBV-DNA was conducted. After 4 months, HBV-DNA began to rebound so ETV was reintroduced at 0.5 mg every 7 days. At the start a virological decline was detected but afterwards, in November 2022, a virological breakthrough was encountered with a transient flare of liver enzymes documented. The patient reported a closely therapy adherence, but we discovered that she had started performing dialysis 3 times a week and she took ETV before hemodialytic session. HBV genotyping resistance test revealed 204I and 80I RT mutations that identify lamivudine resistance and partial ETV resistance. HBV therapy, initially empowered by adding TAF 25 mg/day, was again changed based on the resistance test and ETV was dismissed. The patient was then strongly recommended to assume the daily TAF after the end of the hemodialytic session. A slow but continuous reduction in HBV-DNA serum levels was observed and the patient currently continues 3 months follow-up.

Discussion: NAs have high safety profile and are well-tolerated but lacking real-life experience in patients with CKD. Moreover, in clinical trials concerning HBV treatment, patients with ESRD were regularly excluded. ETV is usually preferred in CKD patients, because of its high efficacy and favorable renal safety profile even if requires dose adjustment when GFR<50 ml/min. On the contrary, TAF is the NA of choice for patients with resistance to ETV and do not necessitate changes since GFR>15 ml/min or in hemodialysis. In treatment naïve patients, ETV resistance pattern is rare but more commonly 3 or more mutations are selected during long-term therapy. In our case, two substitutions are identified as YMDD mutation, which is linked to LAM resistance and it is widely recognized as the basis for further ETV resistance.

Conclusion: Our case report should contribute to amplifying real-life experience in utilization of HBV-therapy in hemodialysis patients enlightening the relevance of patient's education on the correct intake of therapy during hemodialysis, explicitly clarifying the necessity of taking anti HBV therapy after the session itself to avoid HBV virological failure.

Hepatitis and other viral infections

P 226 PREVALENCE OF HDV INFECTION IN HBV POSITIVE PATIENTS FROM UNIVERSITY HOSPITAL IN NORTH SARDINIA. UPDATED DATA

L. Denti[1], C. Marcia[1], E. Bozzi[1], G. Alagna[2], A. Muredda[1], C. Panu Napodano[1], M.A. Seazzu[1], S. Uzzau[3], S. Babudieri[1], I. Maida[1]

[1]S.C. Malattie Infettive e Tropicali, Sassari, [2]U.O.C. Medicina Interna, Sassari, [3]S.C. Microbiologia e Virologia, Sassari

Background: In Italy, the introduction of the mandatory hepatitis B vaccination for all newborns starting from 1979, has led to a progressive decrease in the predominance of HDV infection from 24% in the 1990s to the current 8.8%. There as been lack of regional data in this regard in the last years. Therefore, the aim of this study is to estimate the prevalence of Delta hepatitis in a group of HBsAg positive patients from North Sardinia.

Material and methods: Screening of anti-HDV antibodies was performed in all consecutive HBsAg positive patients followed in two hepatology units of the University Hospital in Sassari from May 2022 to 4 April 2023. The test was performed regardless of the degree of severity of the liver disease.

Results: We included in the study and currently tested for anti-HDV antibodies 136 of the 245 HbsAg positive patients followed in our hepatology units: ten of them (7,35%) were positive for HDV screening (seven males and three females). Six patients are Italian, one is a Romanian woman and two men come from Africa. In the positive ones, we proceeded to search for HDV-RNA and found out evidence of a viral load >500 copies/ml in three Italian males and <150 copies/ml in a Romanian woman (2,96% of the total number). Examination is still in progress in an Italian man. An undetectable load has been found in the remaining ones. The four patients with confirmed Delta hepatitis are an of average age of 57 and have evidence of moderate- severe chronic liver disease.

Conclusion: Chronic hepatitis D is considered the most severe of chronic viral hepatitis due to more rapid progression to hepatocellular carcinoma and liver- related death. Taking into consideration the new therapeutic approaches, this study, although conduced on a small sample of population, shows the importance of universal HDV screening in all HBsAg positive patients, especially in those with moderate to severe liver disease.

Hepatitis and other viral infections

P 227 ACUTE HBV HEPATITIS LEADING TO LIVER FAILURE: WHEN TO TREAT?

A. Gizzi, F. Guida Marascia, M. Abbott, S. Agrenzano, G. Pipitone, G. Ciusa, F. Onorato, A. Ficalora, C. Iaria

UOC Malattie Infettive e Tropicali, ARNAS Civico, Palermo

Background: Chronic HBV infection is a global burden for its increased risk of progression and significative morbidity and mortality. More than 95% of adults with acute HBV hepatitis do not require treatment and recover spontaneously, in the majority of cases (90%) within 6 months the surface antigen is cleared. Indications for chronic HBV treatment is well acknowledged by International Associations, first of all the EASL 2017 guidelines and WHO 2015, but there is a lack of knowledge for the indication for severe to fulminant acute HBV infection treatments. We present a report of a young woman with acute HBV hepatitis.

Case report: A 48-year-old Caucasian woman working as a dental assistant presented with acholic stool, dark urine, joint pain, fatigue and scleral icterus. Blood exams showed biochemical alterations: total bilirubin 7 mg/dl – direct bilirubin 6.17 mg/dl; AST/ALT 1379/2466 U/L, INR 1.44. HBsAg and HBcAb IgM tested positive and she was admitted to our Unit. She reported several needlestick injuries with no following medical consult and high-risk sexual activity, so we ran a full STD screening, including HIV test with negative results. Basal HBV-DNA was 27080248 U/ml and we ruled out HDV and HCV co-infection. During the hospital stay we monitored liver function blood exams and administered 5% glucose solution infusions. In one week of observation hepatic function tests dramatically worsened: AST/ALT 4290/4309 U/L, total bilirubin 15.87 mg/dl – direct bilirubin 13.69 mg/dl, INR 1.82, without hepatic encephalopathy onset. This severe acute hepatitis lead us to start antiviral therapy with NA (TDF).

Discussion and conclusion: while most of acute HBV hepatitis does not need treatment, all guidelines we consulted agreed that patients with acute prolonged or severe hepatitis should be treated for preventing the risk of acute or fulminant liver failure. The indications are coagulopathy (INR > 1.5), protracted course (> 4 weeks) and signs of acute liver failure. Early antiviral therapy with potent NAs is used to prevent progression, liver transplantation and mortality but literature lacks of randomized controlled trials.

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Immunopathogenesis and Vaccines

P 228 HIGH FREQUENCY OF TYPE I INTERFERON AUTOANTIBODIES IN A COHORT OF MIDDLE-AGED PEOPLE WITH HIV: A RETROSPECTIVE PILOT STUDY

L. Imberti[1], G. Tiecco2, A. Sottini[3], V. Quaresima[3], F. Castelli[2], E. Quiros-Roldan[2]

[1]Section of Microbiology, University of Brescia and ASST Spedali Civili di Brescia, Brescia, Italy, [2]Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia, Italy, [3]Clinical Chemistry Laboratory, ASST Spedali Civili di Brescia, Brescia, Italy

Background: Several compelling studies have recently confirmed the link between type 1 interferon (IFN1) auto-antibodies (IFN1-aAb) and COVID-19 severity. However, it is known that IFN1 plays a detrimental function in the outcomes of tuberculosis (TB), by delaying the Th1 cell specific response in the lungs and in lifelong control of cytomegalovirus (CMV) infection. Moreover, in people living with HIV (PLWH), IFN1 pathway exerts a dichotomous role: initially, it blocks HIV replication delaying the disease progression, but chronically it is associated with altered immune activation exacerbating clinical conditions. Few studies have investigated whether other pathogens may take advantage of the presence of IFN1-Ab. The aim of this study is to assess the prevalence of IFN1-aAb in a cohort of PLWH with TB, non-tuberculosis mycobacterium (NTB) disease or active CMV infections.

Methods: This is a retrospective pilot study (NP4000 and NP3061) in which we included PLWH enrolled in the MASTER cohort. The analysis of IFN1-aAb against two types of IFN1 (IFN-α2 and IFN-ω) was performed using the ELISA test in PLWH with concomitant TB, NTB or CMV infections. Results were compared with those of SARS-CoV-2 swab positive patients showing mild to severe pneumonia. A chi-square ($\chi 2$) test and the Wilcoxon–Mann–Whitney test were used to compare the PLWH categorical or continuous variables, respectively.

Results: IFN1-aAb against IFN-α and IFN-ω were tested in 60 PLWH patients with a mean age of 47 years (±10.29). Specifically, we included 50 (83%) patients with positive plasma CMV DNA, 9 (15%) with TB disease and 10 (16.7%) with NTB disease. As comparison group, we used samples from 283 patients with COVID-19. IFN1-aAb were detected in 7 (11.6%) PLWH and in 15 (5.3%) subjects with mild to severe COVID-19 ($p<0.05$). IFN1-aAb against both IFN-α and IFN-ω subtypes were found in 6 (85.7%) PLWH and 9 (60%) patients with COVID-19. No statistically difference was found in viro-immunological markers (CD4, CD8 cell counts and viral load) among PLWH with and without IFN1-aAb. Notwithstanding the lack of statistically differences, we observed that PLWH with IFN1-aAb had higher HIV viral load at HIV diagnosis.

Conclusions: This study demonstrates that a higher prevalence of IFN1-aAb might be found in PLWH with several opportunistic infections. This implies that these autoantibodies are non-specifically increased in critical SARS-CoV-2 infection. The significance of IFN1-aAb in PLWH is hard to be interpreted: the role of IFN1-aAb in the control of HIV spread and the initiation of immunologic damage still remains controversial despite over 30 years of researches.

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P 229 VIRAL BLIPS AND VIROLOGIC FAILURES FOLLOWING MPOX MVA-BN VACCINATION AMONG PEOPLE LIVING WITH HIV

A.R. Raccagni[1], S. Diotallevi[2], R. Lolatto[2], M.F. Lucente[1], C. Candela[1], N. Gianotti[2], B. Trentacapilli[1], D. Canetti[2], A. Castagna[1,2], S. Nozza[1,2]

[1]Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases Unit, San Raffaele Scientific Institute, Milan, Italy

Background: Aim of this study was to assess whether mpox vaccination with modified vaccina Ankara-Bavarian Nordic (MVA-BN) may determine viral blips or virologic failures in people living with HIV (PLWH).

Material and Methods: PLWH in care at San Raffaele Scientific Institute who received MVA-BN vaccination (baseline, BL), with HIV-RNA<50copies/mL and CD4+ lymphocytes ≥200cells/μL in the 6 months prior to vaccination and ≥1 HIV-RNA determination within 3 months from BL were included. PLWH already vaccinated against smallpox received single-dose MVA-BN. Follow-up of each individual accrued from BL until last visit. The primary outcome was the occurrence of viral blip (VB) and confirmed virologic failure (CVF). Changes in CD4+ cell count and CD4+/CD8+ ratio were considered as secondary outcomes. A VB was defined as a single determination of HIV-RNA≥50 copies/mL and a CVF as a single determination of HIV-RNA≥1000 copies/mL or ≥2 consecutive determinations of HIV-RNA≥50 copies/mL following MVA-BN. Residual viremia was defined as detectable HIV-RNA below 50 copies/mL. Mann-Whitney rank-sum test or chi-square/Fisher's exact test applied.

Results: Overall, 187 PLWH were included: 147 received 2 doses of MVA-BN, 40 a single-dose. After a median follow-up of 3.91 months (interquartile (IQR) 2.96-4.11), we observed 6 VBs [incidence rate (IR)=0.87/100-person months of follow-up (PMFU), 95% confidence interval (95%CI) 0.32-1.90] and 3 CVFs [IR=0.44/100-PMFU (95% CI=0.09-1.28)] [Table 1]. Characteristics of included individuals according to presence of VBs or CVFs are presented in Table 2. Among those who received single-dose MVA-BN, VBs were between 50-100copies/mL; among those with two doses, between 100-200copies/mL. Two CVFs occurred at second MVA-BN vaccination with presence of a VB following first dose. Compliance to antiretroviral therapy (ART) was high in these two individuals but not in a third case of CVF (HIV-RNA≥1000 copies/mL following single-dose MVA-BN). In 8/9 cases no VBs or CVFs were identified in the two years prior to MVA-BN vaccination. PLWH with VBs or CVFs had, prior to first vaccination, a lower CD4+/CD8+ ratio [0.67 (IQR=0.34-0.87) vs 0.94 (IQR=0.70-1.27), p=0.015], more had a AIDS-related event [44% (n=4) vs 6% (n=11), p=0.003] and more had residual viremia [77% (n=7) vs 35% (n=62), p=0.013]. No differences in type of ART (p=0.170) and number of MBA-BN doses (p=0.405) was found. In two cases of CVFs, ART was changed; all VBs resolved within 1 month. Virologic details on VBs and CVFs are presented in Figure 1. Median changes at last visit of CD4+ count and CD4+/CD8+ ratio since MVA-BN were +26 cells/μL (IQR=-69.5/+134.2) and +0.02 (IQR=-0.11/+0.11).

Conclusions: We identified VBs and CVFs following MVA-BN vaccination among PLWH. Caution might be required when administering a second dose of MVA-BN in presence of a VBs following the first dose, given the evidence of CVFs and the strong community implications on transmission.

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P 230 HOW COVID-19 ASYMPTOMATIC INFECTION INFLUENCE RESPONSE TO BNT162B2 VACCINE AMONG PERSONS LIVING WITH HIV (PLWH): DATA FROM PATIENTS IN CHARGE AT COTUGNO HOSPITAL, NAPLES, ITALY

F.M. Fusco, M.A. Carleo, N. Sangiovanni, M. D'Abbraccio, R. Viglietti, O. Tambaro, F. Borrelli, R. Pisapia, V. Rizzo, A. Guida, P. Rosario, M. Di Lorenzo, N. Cuomo, V. Esposito, V. Sangiovanni

"D. Cotugno" hospital, AOS dei Colli, Naples, Italy

Background: According to several data from the general population, hybrid immunity against COVID-19 (natural infection AND one or more doses of vaccination) provides better protection against clinical COVID-19, hospital admission and death, compared to vaccination or natural infection only (Larkin at al, JAMA, 2023). We have poor knowledge about these immunological dynamics among Persons Living with HIV PLWH).
We assessed the variation of anti-spike levels according to the occurrence or not of asymptomatic/pauci-symptomatic COVID-19 infections, determined by positive anti-nucleocapsid Ab, in a population of PLWH in charge at Cotugno hospital, Naples, after 2 or 3 doses of BNT162b2 vaccine.
Methods: The study was conducted in the period January 2021-June 2022. We included in the study: (i) PLWH who get vaccinated at Cotugno Vaccination facility, (ii) for which immunological and virological data, collected during periodical follow-up per HIV infection, were available in the 12 months prior to and in the 6 months following the second and third dose of vaccine (iii) for which no previous COVID-19 infection was known and (iv) for which total anti-nucleocapsid antibodies were available. The level of anti-spike Ab for COVID-19 after the second and the third dose of BNT162b2 was carried out with chemiluminescence (SARS-Cov-2 antispike IgG S1 / S2 / RBD Diasorin; positive value> 33.8 BAU/mL; range of linearity 0-2080 BAU/mL). Total anti-nucleocapsid antibodies were measured by electrochemioluminescence with the Roche qualitative test.
Results: Among a larger number of PLWH (about 500) who get vaccinated at Cotugno vaccination facility, 148 fulfilled inclusion criteria. Table 1 describe the demographical and clinical characteristic of the study population. Table 2 summarizes the effect of asymptomatic/pauci-symptomatic infection, determined by occurrence of anti-nucleocapsid Ab, on SARS-CoV-2 anti-spike Ab level. Data are available for 148 patients after the second dose of BNT162b2 vaccine (mean 51 days after) and for 55 patients after the third dose (mean 64 days after). Anti-spike Ab are significantly higher among those with asymptomatic/pauci-symptomatic natural infection after the second dose ($p<0.000$), while this difference disappears after the third dose.
Discussion: As reported in the general population also, among PLWH anti-spike Ab are significantly higher among those with natural infection, even if asymptomatic/pauci-symptomatic. This effect is evident, and statistically significant, after the second dose, while this difference is not more significant after the third dose. We can argue that the third dose is essential to reach an adequate level of immunity response for those who did not experienced natural infection, in PLWH as well as in the general population.

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Immunopathogenesis and Vaccines

P 231 GUT MICROBIOME INFLUENCES THE RESERVOIR IN ACUTE, CART-TREATED HIV

C. Tincati[1], V. Bono[1], M. Augello[1], R. Rovito[1], S. Rusconi[2], A. Gabrieli[2], A. Giacomelli[3], A. Muscatello[4], S. Dispinseri[5], A. d'Arminio Monforte[1], A. Calcagno[6], S. Nozza[5], A. Gori[4], G. Marchetti[1] for the Inaction (Italian Network of Acute HIV Infection) Study Group

[1]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, [2]UOC Malattie Infettive, Ospedale Civile di Legnano, DIBIC, University of Milan, ASST Ovest Milanese, Legnano, [3]Clinic of Infectious Diseases, Department of Biomedical and Clinical Sciences, L. Sacco Hospital, University of Milan, Milan, [4]Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, [5]Viral Evolution and Transmission Unit, IRCCS Ospedale San Raffaele, Milan, [6]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin

Background: Acute HIV infection (AHI) features mucosal damage and rapid establishment of the reservoir as well as microbiome imbalances which may drive inflammation/immune activation thus fuelling HIV pathogenesis. Whether early cART introduction in AHI may reverse such alterations is currently unknown.

Methods: AHI subjects were studied prior to (T0) and after 12 weeks (T12) of cART. At both time-points we analyzed: i) plasma markers of gut integrity (E-cadherin) and peripheral inflammation (sCD14, IL-6) (ELISA) ii) peripheral HIV-1 DNA by Droplet Digital PCR (Biorad QX100), normalized to RPP30 reference gene; iii) mucosal microbiome by MiSeq Illumina on ileum and colon biopsies. Wilcoxon matched-pairs test and Spearman's correlation were used as appropriate.

Results: 11 PHI were enrolled. cART was introduced at 12 (IQR 9-24) days from diagnosis and lead to significant viral decay and CD4+ gain (Figure 1A). Despite a trend in decreased peripheral HIV DNA (Figure 1A) and IL-6 (T0: 2.33 pg/mL, 1.35-3.38; T12: 1.49 pg/mL, 0.97-1.95; p=0.07), this did not reach statistical significance; likewise, no significant changes were observed in markers of gut damage (E-cadherin; T0: 180 ng/mL, 111-241; T12: 166 ng/mL, 118-229; p=0.9) and peripheral inflammation (sCD14; T0: 4.78 ug/mL, 3.16-5.50; T12: 3.56 ug/mL, 3.38 -4.05; p=0.3) as well as ileum/colon microbiota alpha- and beta-diversity.

Prior to cART, a positive correlation was found between plasma E-cadherin and sCD14 (p=0.03, r=0.7; Figure 1B). HIV DNA was inversely linked, at T0, with ileum Bacteroides (p=0.02, r=-0.7; Figure 1C) and at T12, with ileum Ruminococcus gnavus (p=0.03, r=-0.6; Figure 1D). Of note, also IL-6 was negatively correlated with the latter (p=0.01, r=-0.8; Figure 1E) following cART. Similarly, ileum Prevotella was inversely correlated with sCD14 (p=0.03, r=-0.7; Figure 1F).

No significant correlations were found between HIV DNA, plasma biomarkers and microbial composition in the colon.

Conclusions: We show a strict correlation between markers of gut damage and peripheral inflammation in AHI, which are largely unmodified by short-term cART. Similarly, cART introduced in AHI has a limited impact on the peripheral HIV reservoir as well as mucosal microbial composition. Enduring microbial imbalances which occur in AHI may be linked to peripheral inflammation and HIV persistence.

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Immunopathogenesis and Vaccines

P 232 ASSOCIATION BETWEEN SARS-COV-2 RNAEMIA AND SYSTEMIC INFLAMMATION IN PEOPLE WITH HIV HOSPITALIZED FOR ACUTE COVID-19 PNEUMONIA

M. Augello[1], V. Bono[1], R. Rovito[1], C. Tincati[1], S. Bianchi[2], L. Taramasso[3], A. Di Biagio[3,4], A. Callegaro[5], F. Maggiolo[6], E. Borghi[2], A. d'Arminio Monforte[1], G. Marchetti[1]

[1]Clinic of Infectious Diseases and Tropical Medicine, San Paolo Hospital, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [2]Microbiology and Clinical Microbiology, Department of Health Sciences, University of Milan, Milan, Italy, [3]Infectious Diseases Unit, San Martino Policlinico Hospital, [4]Department of Health Sciences, University of Genoa, Genoa, Italy, [5]Biobank Unit and Microbiology and Virology Laboratory, ASST Papa Giovanni XXIII, Bergamo, Italy, [6]Division of Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy

Introduction: People with HIV (PWH) may experience worse COVID-19 outcomes. Both SARS-CoV-2 RNAemia and cytokine storm have been reported to associate with severe disease, yet their reciprocal interaction in driving the pathogenesis of COVID-19 in PWH is currently unknown. We hereby measured SARS-CoV-2 RNAemia and explored its association with markers of systemic inflammation and disease severity in PWH compared to people without HIV (PWoH).

Methods: Unvaccinated PWH and age/sex-matched PWoH hospitalized for radiologically-confirmed COVID-19 pneumonia were consecutively enrolled between March 2020 and January 2021. We measured SARS-CoV-2 RNAemia (N gene; RT-qPCR) and plasma cytokines (IFN-α, IFN-γ, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12p70, IL -17A, TNF-α, GM-CSF; cytometric bead array). Principal Component Analysis (PCA), Mann-Whitney test and Spearman's correlation were used for statistical analyses.

Results: 18 PWH (16/18 on cART; median CD4 T-cell count 361.5/μL; HIV-RNA<50 cp/mL in 15/18) and 18 PWoH were included at a median of 10 days from symptoms onset (Fig.1A). PWH had lower PaO2/FiO2 nadir [140 (122–151.5) vs 207 (156.3–309.3); P=0.0005] and higher SARS-CoV-2 RNAemia (Fig.1B). The visual evaluation of all plasma cytokines simultaneously by PCA showed a clear separation between PWH and PWoH based on the PC scores, while the loading values assessment displayed distinct cytokines clusters, suggesting that some of them had a prominent effect in determining the differences between the two groups (Fig.1C). Indeed, plasma concentrations of GM-CSF, TNF-α, IL-4, IL-5 and IL-17A were higher in PWH, whilst plasma levels of IL-2 and IL-9 were greater in PWoH (Fig.1D). Accordingly, SARS-CoV-2 RNAemia was positively correlated with plasma GM-CSF, TNF-α and IL-4, yet negatively with IL-2 and IL-9 (Fig.1E). Lastly, PaO2/FiO2 nadir correlated negatively with SARS-CoV-2 RNAemia, GM-CSF and TNF-α, but negatively with IL-9 (Fig.1E).

Conclusions: Compared to PWoH, PWH feature a higher SARS-CoV-2 RNAemia, which is in turn associated with greater plasma levels of inflammatory cytokines and worse respiratory insufficiency. By contrast, PWoH display higher plasma concentrations of IL-2 and IL-9, which are associated with lower SARS-CoV-2 RNAemia and higher PaO2/FiO2 nadir. Our data suggest a link between poor control over SARS-CoV-2 replication/dissemination and higher systemic inflammation, which may influence COVID-19 severity in PWH. Furthermore, plasma IL-2 and IL-9, that are depleted in PWH, might exert a protective effect in COVID-19, which, however, requires further research.

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Immunopathogenesis and Vaccines

P 233 HEAVILY TREATMENT-EXPERIENCED (HTE) PEOPLE LIVING WITH HIV (PLWH) WITH VERTICAL TRANSMISSION AND DETECTABLE VIREMIA DO NOT DISPLAY INCREASED PERIPHERAL INFLAMMATION MARKERS: DATA FROM THE PRESTIGIO REGISTRY

C. Tincati[1], V. Bono[1], V. Spagnuolo[2], L. Galli[2], A. di Biagio[3], M. Augello[1], R. Rovito[1], E. Garlassi[4], M.C. Moioli[5], E. Focà[6], A. Castagna[2], G. Marchetti[1]

[1]Clinica di Malattie Infettive, San Paolo Hospital, University of Milan, Milan, Italy, [2]Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [3]Department of Infectious Disease, IRCCS AOU San Martino IST, (DISSAL), University of Genoa, Italy, [4]Malattie Infettive Arcispedale S. Maria Nuova-IRCSS, Reggio Emilia, Italy, [5]Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [6]Division of Infectious and Tropical Diseases, ASST Spedali Civili Hospital, University of Brescia, Brescia, Italy

Introduction: Ineffective viral control in Heavily Treatment-Experienced (HTE) contributes to inflammation which may be increased in HTE with vertical transmission (VT), given that HIV infection at birth may alter immune homeostasis. Therefore, we investigated inflammation in HTE with and without VT, according to viral load (VL) status.

Methods: The study cohort included individuals with vertical transmission (VT) matched to individuals not infected by vertical transmission (no-VT) from the Prestigio Registry with resistance to NRTIs, NNRTIs, PIs, and INSTIs. Each group was divided according to undetectable (VL <50 copies/mL) or detectable viremia (VL >200 copies/mL). A broad range of cytokines and chemokines, GM-CSF, IFN-α, IFN-γ, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12p70, IL -17A, TNF-α (Cytometric Bead Array) and sCD14 (ELISA) was assessed on plasma samples. Propensity score was used to match VT and no-VT for sex, HIV duration, CD4 nadir and VL at plasma sampling. Mann-Whitney test and Spearman's correlation were used for statistical analyses.

Results: We evaluated 16 VT and 16 no-VT HIV individuals (Table1); in each group, 8/16 had undetectable viremia (VL<50 copies/mL) and 8/16 had detectable viremia VL>200 copies/mL. Both groups were comparable to each other although VT were younger than no-VT individuals (p<0.0001). VT and no-VT individuals showed similar cytokines levels, with the exception of IL-6 which was significantly lower among VT (median=0.526 pg/ml, IQR=0 -2.85 vs 2.198 pg/ml, IQR=0.94-6.17; p=0.04; Fig. 1A) as well as a non-significant trend towards lower IL-10 was noted in VT than no-VT individuals (p=0.08). Of note, IL-6 did not differ between VT and no-VT, within viremia strata (Fig. 1B-C), while a tendency to lower IL-10 was retained in viremic VT (p=0.06; Fig. 1D). Lastly, IL-6 positively correlated with age (r=0.362, p=0.04; Fig. 1E), whereas no other correlations between cytokines and demographic/viro-immunologic parameters were found.

Conclusions: HTE with VT feature comparable inflammation levels to those of HTE without VT and significantly older, regardless of viral load detectability. The positive correlation between IL-6 and age suggests that age, rather than mode of transmission and viremia, might drive inflammation in treated HIV infection.

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Immunopathogenesis and Vaccines

P 234 IMPLEMENTATION OF RECOMBINANT ANTI-HERPES ZOSTER VACCINATION IN PEOPLE LIVING WITH HIV: A SINGLE-CENTER EXPERIENCE

B. Trentacapilli[1], G. Catalano[1], L. Galli[2], R. Lolatto[2], A.R. Raccagni[1], S. Nozza[1,2], A.C. D'Amelio[3], G. Ponta[1], V. Spagnuolo[1,2], M. Cernuschi[2], N. Gianotti[2], A. Castagna[1,2], D. Canetti[2]

[1]Infectious Diseases Unit, Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases Unit, San Raffaele Scientific Institute, Milano, Italy, [3]Public Health School, San Raffaele Scientific Institute, Milano, Italy

Background: People living with HIV (PLWH) are at increased risk of herpes zoster (HZ). For long, they were excluded from vaccination with anti-HZ live attenuated vaccine. Newly, the recombinant anti-HZ vaccine (RZV) has proved to be effective and safe even in PLWH. Aim of the study is to describe our single-centre experience with the implementation of RZV.

Materials and Methods: Prospective, cohort-study on PLWH, in care at San Raffaele Infectious Diseases Unit, eligible for RZV. It was administered between February 2022 and March 2023, initially during dedicated consultations and then, since January 2023, during routine HIV clinical visits. PLWH ≥50-year-old or with >=1 previous HZ episode or with a previous AIDS episode had priority. First dose of RZV was considered baseline (BL). Characteristics of included individuals were reported with median [interquartile range (IQR)] or frequency (%). The characteristics of those who received or not >=1 dose of RZV were compared by means of Mann Whitney test or chi-square/Fishers' exact test, as appropriate.

Results: Out of 5122 PLWH in care, 280 received 357 RZV doses over 13 months; 203 PLWH received the first RZV dose and 77 the complete schedule. Second doses were administered after a median time of 2.2 months (IQR=1.88-3.68). Characteristics of individuals according to administration of RZV are presented in Table. Among vaccinated PLWH, 234 (83.6%) were men, median age was 60.2 years (IQR=56.1-65.1) and 95 (33.9%) had >=1 previous episode of HZ. No serious adverse events were reported by the cohort.

Out of all people in care, vaccinated PLWH were more frequently older [age>=50 years: 92.1% (n=258) vs 64.5% (n=3124), p<0.001], with a median time of 11.9 months with HIV-RNA<50 copies/mL [(IQR=7.6-15.7) vs 9.9 (IQR=5.7-14.8), p<0.0001]. They had a longer history of HIV [24.2 years (IQR=16.6-30.3) vs 19.2 years (IQR=11.2 -28.2), p<0.001], more frequently CD4+cells count nadir ≤200 cells/μL [41.1% (n=115) vs 31.9% (n=1544), p<0.0001], a higher prevalence of past AIDS events [25.7% (n=72) vs 17.3% (n=838), p=0.0007] and previous HZ episodes [33.9% (n=95) vs 9.5% (n=458), p<0.0001]. Priority for RZV was assigned to age>=50 or previous AIDS or HZ [96.1% (n=269) vs 68.6% (n=3320) among vaccinated vs not vaccinated people; p<0.001].

In our centre, RZV administration raised expecially in the second part of 2022, due to recovery of regular outpatient activities after SARS-CoV-2 pandemic (Figure). So far, only one subject (1.3%) received the second dose beyond the recommended 6 months, confirming a high adherence to the vaccination.

Conclusion: Onsite vaccination during routine medical HIV visits is a powerful strategy to boost vaccine delivery and take advantage of linkage to care to optimize adherence. During implementation of a new vaccine, this strategy seems useful to ensure effective prevention.

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Immunopathogenesis and Vaccines

P 235 DETERMINANTS OF RECORDED SARS-COV-2 VACCINE UPTAKE AMONG ART-COMPLIANT PEOPLE LIVING WITH HIV

G. Alessio, A. Imeneo, A. Di Lorenzo, L. Ferrari, T. Mulas, M. Compagno, V. Malagnino, M. Iannetta, E. Teti, L. Sarmati, A.M. Geretti

Fondazione PTV, University of Rome Tor Vergata, Rome, Italy

Background: People with HIV are at increased risk of severe COVID-19 and must be prioritised for vaccination. There are limited data on vaccine uptake in this potentially vulnerable population, but surveys (largely from North America) indicate that a substantial fraction holds vaccine hesitancy believes and that vaccine uptake varies by demographic factors and HIV health-related behaviours. Our aim was to audit COVID-19 vaccine uptake in a cohort of people who were actively engaged with HIV care.

Methods: The main outcome was a record of receiving a complete COVID-19 vaccination series including a 3rd dose, which was recommended in Italy in 2022 allowing for ≥120 days since a last vaccine dose or a SARS-CoV-2 infection. Based on our out-patient population size (n=~750), reliable audit estimates required a random sample of 100 people. To focus the analysis on those actively engaged with care, we retrospectively identified the sample among patients who had booked their 3-monthly appointment for retrieval of ART prescriptions as of 15th March 2023. We searched the Lazio Vaccination Registry to evaluate COVID-19 and influenza vaccination records and any recorded SARS-CoV-2 infection. Demographic, clinical, and laboratory data were retrieved from medical files. Statistical analyses were performed in STATA v14.2.

Results: Table 1 shows the characteristics of the cohort (n=100). Most were assigned male at birth (71%) and of white ethnicity (82%), and the median age was 48 years; 99% had collected their ART prescription in the previous 3 months, 78% were virologically suppressed (<50 copies/mL) and the median CD4 count was 670 cells/uL. A total of 35% had a recorded diagnosis of SARS-CoV-2 infection. Overall, 18% had no record of any COVID-19 vaccination. Of the 82 participants that had received primary vaccination (typically 2 doses 3-4 weeks apart), 69 (84%) had also received a 3rd dose. A record of receiving a complete COVID-19 vaccination series (3 doses) was most common among MSM and least common among people reporting IDU and was also more common among those with a recorded diagnosis of SARS-CoV-2 infection and with a longer interval since primary vaccination (Table 1). Among the 29 (29%) participants with an influenza vaccine record, 24 (83%) had also received a complete COVID-19 vaccination series.

Conclusions: In this randomly sampled cohort, 18% had no record of COVID-19 vaccination (vs. 12% for the eligible population of Lazio overall) and a further 13% had not received a 3rd vaccine dose, with evidence of uneven uptake based on characteristics such as sex/sexual orientation. There was a low recorded uptake of influenza vaccination. Considering these worrisome findings, the audit is being extended and patients are being recalled for a review of their vaccine needs. Ongoing efforts are required to tailor health messaging to the highly diverse population of people living with HIV.

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Immunopathogenesis and Vaccines

P 236 TARGETING NEF AS THE PRIMARY DRIVER OF HIV PERSISTENCE AND IMMUNE ESCAPE

C. Brosgart, M. Curlin, R. Ogden

Immgenuity, Inc., Dover Delaware

Background: HIV persistence in reservoirs and increases in drug resistance demand that new targets be sought against HIV-1 accessory proteins essential for viral proliferation and immune escape. Because life spans of patient populations have substantially increased, studies have shown that chronic antiretroviral therapy is unable to address HIV persistence and resulting comorbidities such as HAND. Several studies have shown a high incidence and prevalence of comorbidities in patients well-controlled on cART. HIV persistence, causing elevated inflammatory cytokines from the innate immune system is the primary driver of comorbidities. An urgent need exists for the discovery and development of new immunologic approaches that can address persistence.

Methods: We reviewed the literature focusing on HIV-1 Nef, a protein essential for HIV pathogenesis and responsible for disrupting immune signaling. We also reviewed corresponding relationships of Nef to literature on HAND, Long Term Non-progressors (LTNP) and Elite controllers (EC),

Findings: A review of studies demonstrates immune escape, immune disruption and increased viral pathogenicity attributed to Nef. Nef is shown to be responsible for downregulating MHC-I, downregulating CD4, disrupting SH3, Lck, HLA-B7 signals, disrupting NF-κ signaling, interfering with Leucine Zipper, downregulating SERINC3 & SERINC5, disrupting host cell restrictive factors and upregulating CTLA-4. This makes Nef the primary determinant of viral pathogenesis and immune escape. Addressing this role of Nef in blocking immune signaling creates a target for therapeutic intervention which has the potential to re-enable immune detection and clearance of reservoirs. Evidence has established that most HIV non-progressors and elite controllers of HIV are infected with a nef deleted HIV.

Conclusions: The findings above create a strong case for a trial of a therapeutic vaccine that would eliminate the functions of the nef gene. This is likely to restore immune signaling and establish control by activated ∂ßcytotoxic T cells. This subsequent modulation is very likely to decrease levels of circulating inflammatory cytokines by favoring the establishment of a viable immune response to HIV infection and be an emerging therapeutic model to address persistence and achieve remission.

Immunopathogenesis and Vaccines

P 237 TOLERABILITY OF SHINGRIX IN PATIENTS WITH MULTIPLE SCLEROSIS AND OTHER NEUROLOGICAL DISEASES ON IMMUNE MODULATING TREATMENTS

I. Fato, G. Alessio, D. Landi, F. Napoli, A. Imeneo, L. Benedetti, B. Massa, V. Barchi, C. Picarelli, F. Angelone, A.C. Epifani, A. Di Lorenzo, G. Mataluni, C. Gabri Nicoletti, G.A. Marfia, L. Sarmati, M. Iannetta

Fondazione PTV, University of Rome Tor Vergata, Rome, Italy

Background: Up to 33% of people develop herpes zoster (HZ) in their lifetime, due to impaired cell-mediated immunity, in older age or under immunosuppressive treatments A new adjuvanted recombinant subunit vaccine (HZ/su) has been approved for the prevention of HZ in adults > 50 years or >18 years with immunodeficiency or immunosuppression. No data are currently available on HZ/su reactogenicity in patients with multiple sclerosis (MS) and other neurological conditions on immunosuppressive treatments. Our study aimed to provide insights into the reactogenicity of HZ/su in this subset of patients.

Methods: Patients in active follow-up in the MS Unit of Policlinico Tor Vergata were enrolled in the study. Two doses of HZ/su were administered 2 months apart (T0 and T1 respectively), with a follow-up visit 1 month after the second dose (T2). All adverse events were collected in a structured questionnaire 1 week after each HZ/su dose. All statistical analysis were performed with JASP v.0.17.1.

Results: 24 patients with SM and 1 with ocular myasthenia (75% females) were enrolled in the study. Median age was 58 (interquartile range, IQR 43-60), median Expanded Disability Status Scale (EDSS) was 3,5. Most of them had varicella in pediatric age (20/25, 80%) and 15/25 (60%) had a reactivation of VZV. Only 3 (12%) had been vaccinated for varicella, while 24 had been vaccinated with 3 doses of a mRNA vaccine for SARS-CoV-2 (and 11 with 4 doses). One patient refused SARS-CoV-2 vaccination, although was prone to HZ/su vaccination because of previous HZ. All patients were receiving immunosuppressive drugs at the time of vaccination, except for the patient with ocular myasthenia. The most represented treatments were fingolimod (8/25, 32%), dimethyl fumarate (7/25, 28%) and natalizumab (4/25, 16%). 11 patients completed the vaccination cycle, so far. Swelling and reddening in the injection site, fever, chills, asthenia, headache, gastrointestinal symptoms and arthromyalgia were actively investigated 1 week after T0 and T1, as reported in table 1. Arthromyalgia seems to be more frequent after the second dose (p=0.06), while no statistically significant differences in the rate of the other adverse events were observed comparing the two timepoints. Most of the reported adverse effects were mild or moderate and resolved within 1-3 days. One patient experienced sever dizziness which lasted for >5 days after the first vaccine dose needing medical assistance (this case has been reported to AIFA).

Conclusions: According to our preliminary data, HZ/su was well tolerated in patients with neurological diseases under immune modulating treatments, as the reported adverse events were generally mild to moderate and resolved within 3 days. However, 1 patient experienced severe adverse effects, needing medical assistance. Patients who had previously experienced HZ were more prone to HZ/su vaccination. Further analyses are ongoing, with the competition of the vaccination schedule.

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Immunopathogenesis and Vaccines

P 238 ANTIBODY RESPONSE TO THE THIRD DOSE OF SARS-COV-2 MRNA VACCINE IN PLWH ON ART AT 12 MONTHS AFTER ITS ADMINISTRATION

E. Tortellini[1], M.A. Zingaropoli[1], G. Mancarella[1,2], R. Marocco[2], A. Carraro[1,2], S. Garattini[1,2], M. Jhamour[2], M. Guardiani[1], F. Dominelli[1], V. Perri[1], P. Pasculli[1], A. Napoli[4], A. Gaeta[1], F. Mengoni[1], P. Zuccalà[2], V. Belvisi[2], B. Kertusha[1,2], A. Parente[1,2], C. Del Borgo[2], V. Vullo[1], M.R. Ciardi[1], C. M. Mastroianni[1], M. Lichtner[2,3]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy, [2]Infectious Diseases Unit, SM Goretti Hospital, Sapienza University of Rome, Latina, Italy, [3]Department of NESMOS, Sapienza University of Rome, Rome, Italy, [4]Department of Molecular Medicine, Sapienza University of Rome, Rome, Italy

Background: The duration of protection conferred by vaccination against SARS-CoV-2 remains to clarify, particularly in immunosuppressed populations. Therefore, we investigated specific antibody response to the third dose of mRNA vaccine over-time in a cohort of people living with HIV (PLWH).

Materials and Methods: PLWH on ART under routine follow-up at the Infectious Diseases Unit of S.M Goretti Hospital of Latina, Italy, were enrolled between September 2021 and February 2022. Specific humoral response was evaluated before (T0), after 45 days (T1), after 6 months (T2) and after 12 months (T3) from the administration of the third dose. LIAISON SARS-CoV-2 S1/S2 IgG chemiluminescent assay against recombinant Spike (S) protein (S1/S2) was used to assess serum anti-S antibody levels. PLWH were stratified according to CD4 cell count. Furthermore, at T3, the difference in anti-S antibody levels between PLWH who had received the fourth dose and those who had not was evaluated. As control group, healthy donors (HD) were enrolled.

Results: Thirty-seven PLWH (median current CD4 cell count [IQR] 547 [308–714] cells/μl) all on antiretroviral therapy (ART) and 18 HD were enrolled.

Overall, 86% (32/37) and 94% (29/31) of PLWH showed detectable levels of anti-S antibody levels at T0 and T1 versus 100% (18/18) of HD, reaching the 100% of seroconversion at all consecutive time-points.

The cross-sectional evaluation of anti-S antibody levels showed no significant differences between PLWH and HD at all time-points and a significant increase in anti-S antibody levels was observed at T3 compared to T0 in PLWH ($p<0.0001$).

Stratifying PLWH according to CD4 cell count, no differences were found in anti-S antibody levels comparing <200 cells/μl and >200 cells/μl subgroups.

Furthermore, at T3, no differences were found in anti-S antibody levels between PLWH who had received the fourth dose and those who had not.

Conclusions: In ART treated PLWH a specific antibody response was present in most of the participants already after the second dose, but the booster dose increased the rate and magnitude of it. The response seems to last over-time, independently of CD4 cell count, supporting the idea that PLWH are able to develop a better immune response to SARS-CoV-2 vaccination with respect to other immunosuppressed populations.

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P 239 IMMUNOLOGICAL AND INFLAMMATORY PROFILE OF CEREBROSPINAL FLUID (CSF) AND PLASMA OF PEOPLE LIVING WITH HIV (PLWH) WITH OR WITHOUT CENTRAL NERVOUS SYSTEM (CNS) INVOLVEMENT

C. Pinnetti[1], V. Bordoni[2,3], A. Vergori[1], A. Mondi[1], V. Mazzotta[1], I. Mastrorosa[1], S. Notari[3], E. Cimini[3], O. Forini[3], S. Grisetti[1], R. Gagliardini[1], M. Camici[1], A. Antinori[1], C. Agrati[2,3]

[1]Clinical and Research Infectious Diseases Department, National Institute for Infectious Diseases, Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Oncoematologia e Officina Farmaceutica, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy, [3]Cellular Immunology and Pharmacology Laboratory, National Institute for Infectious Diseases, Lazzaro Spallanzani IRCCS, Rome, Italy

Background: Aim of the study was to define the immune signature and inflammatory profile in CSF of PLWH with or without documented CNS diseases.
Material and Methods: Single-center, retrospective study on CSF/plasma paired samples from PLWH undergoing lumbar puncture (LP) for CNS staging of lymphoma (sCNS) or neurological CNS diseases assessment (dCNS). NK, B and T immune phenotype in plasma and in CSF was performed by flow cytometry. IL-1β, IL-6, TNF-α, kappa (K) and Lambda (L) free light chains, sCD14 and MCP-1 were quantified in plasma and CSF by ELISA assays. Principal Component Analysis (PCA) was also performed to discriminate between sCNS and dCNS.
Results: 94 CSF/plasma pairs from 70 PLWH included: 83.6% male, median age 48y (IQR: 41-55), MSM 40%, IDU 16%. 48% had CD4 cells/mm3 <200, 78% in CDC stage C. At LP, 80% patients (pts) were on cART. Median HIV-RNA in plasma was 39 cp/mL (IQR 29-466) and in CSF HIV-RNA 39 cp/mL (IQR 26-498); at LP, 67% had a neurological disease. The immune profile of CSF was characterized by a lower frequency of NK, NKT, and B-lymphocytes and a higher frequency of T cells compared to the peripheral blood ($p<0.01$) both in sCNS and in dCNS. PCA showed no significant differences in immune cells profile of CSF from sCNS and dCNS. In contrast, PCA of soluble mediators in CSF was able to segregate the two groups (Figure 1A). The factors mainly responsible for this segregation were IL-1β, IL-6, TNF-a and K+L, that were significantly higher in CSF from dCNS than in sCNS pts ($p<0.01$), suggesting a deep inflammatory environment in dCNS. The inflammatory cytokines in CSF correlated each other ($p<0.01$) only in d-CNS group (Figure 1B), and CD38+CD4 and CD38+CD8 T cells in CSF were significantly associated to the pleocytosis ($p<0.01$). Moreover, in dCNS, HIV-RNA in CSF correlated directly with the frequency of CSF-CD8 T cells ($p<0.0001$) and negatively with CSF-CD4 T cells ($p<0.0001$). Pts with HIV viral escape (with a higher CSF HIV-RNA, $p=0.007$), presented a higher frequency of CD8 and lower CD4 T cells in CSF than subjects without CSF viral escape ($p<0.05$).
The immune phenotype in plasma can mirror the signature in the CSF in both groups (Figure 1C): i) the frequency of circulating CD4 and CD8 were associated with CSF-HIV-RNA; ii) the frequency of activated CD4 and CD8 T cells (CD38+) in the blood correlated with the same subsets in the CSF ($p<0.0001$). In contrast, the correlation of circulating CD38+T cells with the pleocytosis and the CSF inflammation was observed only in d-CNS group.
Conclusions: In 94 CSF/plasma paired samples obtained from PLWH, the inflammatory profile characterizes d-CNS patients, as well as the correlation between activated CD4 and CD8 T cells in CSF and pleocytosis. The CSF-recruitment of CD8 was associated with a higher CSF-HIV-RNA. Of note, the immune phenotype in the blood can mirror the immune profile in CSF in both groups and the brain inflammation in d-CNS.

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P 240 HERPES ZOSTER PREVENTION THROUGH ADMINISTRATION OF RECOMBINANT ZOSTER VACCINE (RZV) IN A COHORT OF PLWH IN ROME

P.F. Salvo[1], E. Tamburrini[1,2], A.Dusina[2], S. Martinelli[3], R.A. Passerotto[1], F. Lamanna[1], V. Iannone[1], E. Visconti[2], P. Laurenti[3,4], F. Lombardi[2]

[1]Dipartimento di Sicurezza e Bioetica, Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, [2]UOC Malattie Infettive, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, [3]Sezione di Igiene, Dipartimento Universitario di Scienze della Vita e Sanità Pubblica, Università Cattolica del Sacro Cuore, Roma, [4]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma

Background: Recombinant zoster vaccine (RZV) is a two-dose intramuscular vaccine labeled for the prevention of herpes zoster (HZ) in adults 50 years of age and older and in adults 18 years of age and older considered at increased risk of HZ due to immunodeficiency or immunosuppression for diseases or treatments. People living with HIV (PLWH) are considered to be at increased risk of HZ, even in the ART era. A subunit vaccine may be an appropriate alternative, considering the concerns about the use of live-attenuated vaccines in this immunocompromised population. Aim of the study was to evaluate efficacy and safety of RZV in a population of PLWH.

Materials and Methods: We collected clinical, serological and viro-immunological data of PLWH who received RZV during regular clinical practice at baseline (BL) and at the time of the second intramuscular administration.

Results: In our outpatient clinic, RZV has been offered and administered to 59 PLWH from April 2022 to march 2023; 23 participants completed the vaccination schedule at the time of this study. The second dose was administered after a median time of 2.27 months after the first dose. The majority of the fully vaccinated population were men (14; 60.9%) with a median age of 58 years (IQR 52–68). The 69.6% of the PLWH enrolled in this study acquired HIV-1 infection through sexual intercourses (43.5% heterosexuals; 26.1% MSM). The median duration of HIV-1 infection of our population was 24 (IQR 6–30) years with a median time of exposure to antiretroviral agents of 23 (IQR 6–26) years. A previous AIDS diagnosis was present in the clinical history of 12 participants (52.2%). The median zenith of plasmatic HIV-RNA was 5.16 (IQR 4.66–5.87) log10 cp/mL and the median nadir of CD4 cell count was 68 (IQR 23–205) cells/mmc.

Our findings showed no statistically significant differences in viro-immunological data after the administration of the first dose of RZV.

Side effect in our population were infrequent. We observed 3 (13.0%) side effects events in 3 different patients: 2 episodes of reported pain at the injection site and 1 episode of transient low-grade fever.

All the vaccinated PLWH developed immunization, as evidenced by the increase of the IgG anti RZV after the administration of the first vaccine dose. No episodes of HZ were reported at the time this study was written.

Conclusions: RZV is an important instrument for the prevention of episodes of HZ in a population of fragile patients such as PLWH, with a great clinical and serological efficacy and minor side effects.

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Immunopathogenesis and Vaccines

P 241 SERUM AND PLASMA BIOMARKERS OF CENTRAL NERVOUS SYSTEM INVOLVEMENT MEASURED THROUGH SINGLE MOLECULE ARRAY IN PLWH AND CONTROLS

J. Cusato[1], M. Antonucci[2], M. Trunfio[3], D. Imperiale[4], E. Vuaran[3], A. Palermiti[1], G. Di Perri[3], A. D'Avolio[1], S. Bonora[3], A. Calcagno[3]

[1]Laboratory of Clinical Pharmacology and Pharmacogenetics, Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, Italy, [2]SCDU Infectious Diseases, Amedeo di Savoia Hospital, ASL Città di Torino, Turin, Italy, [3]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, Italy, [4]Unit of Neurology, Maria Vittoria Hospital, ASL Città Di Torino, Turin, Italy

Background: Despite the efficacy of combination antiretroviral therapy, central nervous system (CNS) involvement is prevalent in people living with HIV (PLWH). There is an unmet need of non-invasive biomarkers of CNS Involvement for addressing the causes and potential treatment in patients with neurological or neurocognitive complains. Aim of this study is to compare serum (s), plasma (p) and cerebrospinal fluid (CSF) biomarkers of CNS involvement in PLWH and controls.

Material and Methods: PLWH and HIV-negative controls were enrolled in two prospective studies (PRODIN and SOLFAMU): besides clinically meaningful exams, serum, plasma and CSF were collected and stored at -80°C. Available samples were analysed through Single Molecule Array (Simoa SR-X, Quanterix®) for markers of neuronal damage (NFL, TAU), amyloidosis (β-42 and β-40), signalling and plasticity (BNDF), astrocyte activation (GFAP) and ubiquitin-proteasome involvement (UCHL-1). Data are described as medians (interquartile ranges) and compared through non-parametric tests. CSF cut-offs are available for NFL (500 pg/mL for multiple sclerosis prediction), TAU (272 pg/mL for neurodegeneration prediction) and β-42/β-40 ratio (0.068 for amyloidosis).

Results: 287 samples were analysed. Patients were either living with HIV (95.8%) or negative controls (4.2%). PLWH were diagnosed with neurocognitive disorders, primary HIV infection or CNS opportunistic diseases; controls were mostly patients with Alzheimer's dementia or CNS infections. S, p and CSF biomarkers and s/CSF, p/CSF correlations are shown in Table 1. Statistically significant correlations between peripheral and CNS biomarkers were reported for TAU, NFL, GFAP and UCH-L1 (p values <0.05), but not for sUCHL-1 and CSF (rho= -0.0236, p=0.802). Controls showed higher levels of CSF TAU (p<0.001, 281.9 vs. 76.3), CSF NFL (p<0.001, 1844.2 vs. 604.2), sGFAP (p<0.001, 204.9 vs. 72.0), CSF GFAP (p=0.012, 9857.6 vs. 6236.3) and CSF UCH-L1 (p<0.001, 2691.6 vs. 1435.0).

Using CSF published cut-offs, we used ROC curves for defining potential s/p concentrations: s/p TAU >1.54 pg/mL (predicting CSF Tau>272 pg/mL, 89% sensitivity, 75% specificity, p<0.001, AUROC 0.839) and s/p NFL>10.7 pg/mL (predicting CSF NFL > 500 pg/mL, 80% sensitivity, 66% specificity, p<0.001, AUROC=0.835).

No correlations or predicting cut-offs were suggested for β-42 and β-40, also considering the ratio.

Conclusions: In a large sample of heterogeneous patients, we were able to show robust correlations between serum/plasma and CSF biomarkers and to, tentatively, propose cut-offs for predicting abnormal levels in the cerebrospinal fluid. Prospective studies are needed to assess the diagnostic and predictive role of blood biomarkers in PLWH.

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Immunopathogenesis and Vaccines

P 242 IMMUNIZATION COVERAGE IN OLDER PEOPLE LIVING WITH HIV IN A LARGE HOSPITAL, NORTHERN ITALY

S. Arsuffi, A. Cambianica, I. Izzo, I. Polesini, F. Gaffurini, D. Castelli, P. Zanotti, F. Pennati, D. Laurenda, E. Quiros-Roldan, F. Castelli, E. Focà

Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy

Background: Both people living with HIV (PLWH) and people aged over 65 years old are considered populations with an increased risk of severe illness manifestations and poorer outcome in case of several preventable diseases.

For this reason, specific vaccination schedules are granted for PLWH over 65 years old. The aim of this study is to evaluate the immunization coverage in older PLWH.

Material and methods: This is a retrospective monocentric study, conducted at the ASST Spedali Civili General Hospital. We performed the study relying on data gathered from the vaccination schedules and the clinical records of PLWH aged older than 65 years in care at the Infectious Diseases Outpatients Clinic. Data collected included demographic characteristics and vaccination doses administered.

Results: Overall, we included 337 subjects: 270 (80.1%) males, mean age 78.6 years. Evaluating vaccination schedules, 40 (11.9%) received at least one dose of herpes zoster vaccine and only 22 (6.5%) completed it; 97 (28.8%) received at least one dose of pneumococcal conjugate vaccine (PCV13) and only 45 (13.4%) completed it with pneumococcal polysaccharide vaccine (PPSV23). Considering influenza vaccine, 101 (30%) were not ever immunized; 133 (39.5%) were vaccinated in all the three last years (2020-2022), while only 14 (4.2%) received it in the previous three years (2017-2019). Evaluating COVID-19 vaccine, 136 (40.4%) individuals received at least four doses, 142 (42.1%) three doses, 24 (7.1%) two doses, 34 (10.1%) no dose. Quadrivalent meningococcal conjugated vaccine was administered to 14 (4.2%) patients and only 4 (1.2%) of them completed the cycle. Finally, 234 (69.4%) appeared to have never received a tetanus vaccine dose and only 57 (16.9%) have received a dose of vaccines containing diphtheria and tetanus toxoids, and acellular pertussis in the last ten years.

Conclusions: Our study evidenced a very low vaccination coverage in the PLWH aged over 65 years old. COVID -19 vaccine had the highest vaccination rate, with a contemporary increase also of influenza vaccine coverage in the three years subsequent to the pandemics and the COVID-19 vaccination campaigns.

Our data suggests the need to implement strategy aimed to improve the patients' awareness and adherence regarding the recommended immunizations schedule.

Immunopathogenesis and Vaccines

P 243 IMMUNE RESPONSES TO VACCINATION IN HIV VERTICALLY-INFECTED PATIENTS: A LONG TERM EVALUATION

A. Zin[1], D. Mengato[2], A. Francavilla[3], L. Chiusaroli[1], C. Giaquinto[1], D. Donà[1], O. Rampon[1]

[1]Division of Pediatric Infectious Diseases, Department of Women's and Children's Health, University of Padua, Padua, Italy, [2]Hospital Pharmacy Department, University Hospital of Padua, Padua, Italy, [3]Unit of Biostatistics, Epidemiology and Public Health, Department of Cardiac Thoracic Vascular Sciences and Public Health, University of Padua, Padua, Italy

Background: Despite successful antiretroviral therapy (ART), people living with HIV are at risk of suboptimal vaccine response, exposing this vulnerable population to common vaccine-preventable diseases.
Methods: This was a cross-sectional observational study investigating humoral responses to vaccination in HIV-vertically infected patients. We analyzed the seroprotection rate at specific time points since primary immunization for diphtheria, tetanus, measles, mumps, rubella, varicella and hepatitis B, reviewing the serological analysis and medical records available for each patient from 2004 to 2022. Only vaccinated patients were included in the study, and booster doses were excluded. Associations between vaccine outcome and predictive factors were analyzed.
Results: 82 vertically-infected patients were included; all were on ART with a median age of 24 years (IQR 16-29) at enrollment. Two years after the last vaccine dose, the seroprotection rate was 71% for diphtheria, 79% for tetanus and measles, 67% for mumps, 87% for rubella and 54% for varicella. After five years, 50-70% of patients maintain protective antibodies, dropping to 50-58% after ten years. After 20 years, protection is < 30% for all vaccines, except for rubella (47%). Seroprotection for hepatitis B is the lowest: only 60%, 37%, 24% and 7.5% maintained protective IgG titre after, respectively, 2-5-10 and 20 years since vaccination. Patients who maintained protective antibody levels over time were younger, started ART by 12 months, and were fully vaccinated after being started on ART ($p<0.05$).
Conclusions: in this small-size population of HIV vertically-infected patients, seroprotection to vaccination was lower and less durable than expected in the general population. Therefore, periodic seroprotection monitoring and revaccination are crucial in managing these patients. Early initiation of ART seems to create the most favorable conditions for optimizing vaccination outcomes.

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Immunopathogenesis and Vaccines

P 244 COMPLIANCE WITH IMMUNISATION AMONGST HIV-INFECTED PATIENTS AND CLINICIANS VACCINES OFFER RATES IN THE HIV OUTPATIENT CLINIC OF THE VALLE D'AOSTA REGION

M. Colafigli[1], N. Pagani[1], J. Ledakowicz[1], G. Doveri[2], S. Magnani[1]

[1]SS Malattie Infettive, Ospedale Regionale U. Parini, Aosta, [2]Dipartimento Scienze Mediche, Ospedale Regionale U. Parini, Aosta

Background: Vaccination against encapsulated bacteria (S. pneumoniae, SP, N. meningitidis ACYW135 and B strains, NM ACYW135 and NM B, H. influenzae, HiB) and hepatitis B (HBV) for people living with HIV (PLWH) are recommended by National and International Guidelines. At least three doses of COVID19 Vaccine (C19Vax) were mandatory in Italy for PLWH as well as the General Population.
Aim of this study was to assess the rates of patients compliance and vaccine offer from clinicians for recommended and mandatory vaccines in our HIV Outpatient Clinic.
Methods: Data on C19Vax rates as well as active clinician recommendation for mandatory and recommended vaccines for PLWH were collected from the Electronic Clinical Record of the Azienda USL Valle d'Aosta.
A descriptive analysis was performed.
Results: A total of 142 HIV-infected patients (pts) were actively followed in the Outpatient Clinic of the Parini Regional hospital at the data Collection on Feb 11th 2023. Among those, n=124 (87.3%) received C19Vax, n=76 (54%) with 3, n=19 (13%) with 2 or 4 and 4 with 5 doses, n=13 (9%) refused. The data was missing (patients declared vaccination elsewhere/abroad but showed no documentation) for n=5 (3.5%).
Up to june 2020 only 2 pts had been proposed vaccination against encapsulated bacteria in the HIV Clinic. The proposal was then made to 80 (56%) pts, mainly (n=67, 47%) between june and december 2020. The reason for missed proposal (n=62, 44%) was recent diagnosis (n=11, 18%, including 5 advanced naive patients), other Clinical priorities (treatment failure or switch, comorbidities, n=11, 13%), irregular follow-up (FU) (n=8, 13%, including 1 inmate, 5 non compliant to visits, 2 recently regained after loss to FU), patients recently acquired from other Regions (n=7, 11%), social or logistic issues (n=6, 10%, including 4 travelling workers, 1 immigrant, 1 living abroad 6 months per year), no vax (n=3, 6%) and unknown reasons (n=15, 24%). Among the 80 pts who were referred to the Vaccination service mean adherence was 41% (SP n=35, 43.8%, NM ACYW135 n=33, 41.3%, NM B n=32, 40%, HiB n=31, 38.8%), mean nonadherence 52% (SP n=39, 48.8%, NM ACYW135 n=41, 51.2%, NM B n=42, 52.5%, HiB n=44, 55%), 2 pts (2.5%) refused, 2 more started or scheduled it and 3 declared to have received it elsewhere but showed no documentation.
N=50 (35,2%)pt received complete and n=4 (2,8%) incomplete HBV vaccination, while n=27 (19%) had protective antibodies from a previous infection, n=6 (4,2%) have an occult and n=6 (4,2%) a chronic infection. N=49 (34,5%) are still susceptible to HBV infection, only n=5 (3,5%) have been offered a vaccination.
Conclusions: Despite the recent efforts to comply with guidelines recommendations, vaccine uptake amongst PLWH in our Clinic can be significantly improved. We need to implement better vaccine proposal and counseling strategies in order to promote adherence to the recommended vaccine schedule and ensure a better protection to our patients.

Immunopathogenesis and Vaccines

P 245 THE IMPACT OF HIV-1 INFECTION AND SEXUAL ORIENTATION ON THE INTESTINAL MICROBIOTA COMPOSITION IN HIV-1 SERODISCORDANT COUPLES

G. Bugani[1], V. Iebba[2], L. Santinelli[1], L. Maddaloni[1], A. Lazzaro[1], C.M. Lofaro[1], M. Fracella[3], L. Sorrentino[3], G. Coia[1], G. Ceccarelli[1], G. Antonelli[3], C.M. Mastroianni[1], C. Scagnolari[3], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome - Rome (Italy), [2]Department of Medical Sciences, University of Trieste, Trieste (Italy), [3]Department of Molecular Medicine, Sapienza University of Rome, Rome (Italy)

Background: Up to date, the scientifically established principle U=U asserts that virological suppressed People living with HIV-1 (PLWH) do not transmit the infection to their HIV - partner after unprotected intercourses: the so-called serodiscordant couples. Considering that both HIV status and sexual behavior can affect human gut microbiota, providing insights on the effect of these factors on the intestinal microbiota composition in serodiscordant couples was the main purpose of this study.

Material and methods: 22 HIV serodiscordant couples (SD), 9 HIV+ seroconcordant couples (SCH+) and 8 HIV - seroconcordant couples (SCH-), as control groups, were enrolled, also considering their sexual orientation. Analysis of gut microbiota composition was performed by 16S rRNA gene sequencing on fecal samples. α-diversity measurements, the Shannon and the Simpson indexes and observed operational taxonomic units (OTUs) were calculated at species level. β-diversity analysis was calculated using the Bray–Curtis measure of dissimilarity and represented in Principal Coordinate Analysis (PCoA), along with analysis of similarities—ANOSIM to compare groups of multivariate sample units and assess significance in data points clustering. Partial Least Square Discriminant Analysis (PLS-DA) and the subsequent Variable Importance Plot (VIP) were used to identify the most discriminant bacterial species between all study participants.

Results: No differences were observed in the overall α-diversity in SD compared to SCH+ and SCH-, both considering HIV status and sexual orientation ($p>0.05$) (Figure 1, Panel A,B,C). PCoA analysis for β-diversity, calculated on relative abundances, highlighted a trend toward a separation among SD and control groups ($p=0.05$), with F.Prausnitzii as the most discriminant bacterial species for SD ($p<0.01$). Nevertheless, 14 species characterized the microbiota of SD and SCH+ (e.g. M.massiliensis), while 16 species were detected in SD and SCH- (e.g. B.catenulatum) (Figure 1, Panel D,E,F). β-diversity divergences were reported among heterosexual PLWH in SD, heterosexual PLWH in SCH+ and heterosexual SCH- ($p=0.01$). Moreover, E.muris ($p<0.001$) mostly distinguished heterosexual PLWH in SD, while A.muciniphila ($p<0.05$) and A.macyae ($p<0.01$) mostly typified heterosexual PLWH in SCH+ and heterosexual SCH-, respectively (Figure 1, Panel L,M,N). No β-diversity dissimilarities were observed between homosexual PLWH in SD and homosexual controls ($p>0.05$). Also, gut microbiota of homosexual PLWH in SD shared 15 species with homosexual PLWH in SCH+ (e.g. G. urolithinfaciens), and 16 species with SCH- (e.g. A. chartisolvens) (Figure 1, Panel G,H,I).

Conclusions: Both sexual behaviour and HIV status contribute to define a gut bacterial profile in serodiscordant and seroconcordant couples. Further analysis will allow to set up strategies aimed to identify specific therapeutic targets to restore intestinal microbial health in PLWH and/or their HIV- partners.

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Immunopathogenesis and Vaccines

P 246 IDIOPATHIC CD4 LYMPHOCYTOPENIA: NOVEL INSIGHTS INTO THE IMMUNOLOGICAL FUNCTIONS OF CD4 T CELLS

A. Lisco, A.M. Ortega-Villa, M.V. Anderson, A. Mateja, A.F. Freeman, V. Sheikh, I. Sereti

Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), Bethesda, MD, USA

Background: Idiopathic CD4 lymphocytopenia (ICL) is a clinical syndrome defined by CD4 lymphopenia <300 cells/μL in the absence of any primary or acquired cause of immunodeficiency. We present a prospective analysis of ICL patients 30 years after the original identification of this condition.

Methods: The clinical, genetic, immunological, and prognostic characteristics of 108 participants enrolled over 11 years are presented. Whole-exome and targeted-gene panel sequencing was performed to identify genetic causes for lymphopenia. Longitudinal linear mixed-model of T-cell count trajectories, predictors of clinical events, evaluation of response to SARS-CoV2 immunization, and mortality analysis were performed.

Results: After diagnosis of genetic and acquired causes of CD4 lymphopenia were excluded, a population of 91 ICL patients with median CD4 count of 80 cells/ L was identified and had a total follow-up of 374 person-years. The most prevalent opportunistic infections were HPV-related diseases (29%), cryptococcosis (24%), molluscum contagiosum (9%) and non-tuberculous mycobacterial diseases (5.5%). Lower CD4-T-cell counts (<100 cells/μL) were associated with higher odds of opportunistic infections and invasive cancers [Odds-Ratio (OR) =5.3, Confidence-Interval (CI):2.8-10.7; OR=2.1, CI:1.1-4.3, respectively], poor response to SARS-CoV2 immunizations and lower odds of autoimmunity (OR=0.5 CI:0.2-0.9). There was no impact on mortality, but the prevalence of cancer was higher than the age- and sex-adjusted general population.

Conclusions: ICL is distinct from other primary or acquired immunodeficiencies. CD4 lymphopenia continues to be associated with increased susceptibility to viral, encapsulated fungal, and mycobacterial diseases, break of tolerance with autoimmunity, as well as impaired cancer immunosurveillance and response to novel antigens.

PrEP

P 247 CHEMSEX IN PREP USERS OF A COMMUNITY-BASED CENTER PREP POINT PLUS (PPP)

S. Mattioli[1], L. Badia[2], M. Pedone[1], S. Cecere[1], R. Masina[1], A. Leo[1], F. Pavone[1], L. Cinti[1], S. Lo Bianco[1]

[1]Plus Rete Persone LGBT+ Sieropositive aps, [2]Azienda Unità Sanitaria Locale di Imola

Background: Chemsex, a phenomenon that concerns MSM in particular, is on the rise in Bologna, too. Based on the current narrative, there could be a correlation between the use of PrEP, the increase in chemsex and the increase in STIs.

Method: The analysis was performed on risk exposure, substance use and frequency, on the basis of online questionnaires completed by PPP users every 3 months, and from the results of the screening/molecular tests performed at the PPP . All users were enrolled in the observational study "Sexcheck" in 2021-2022.

Population characteristics 99% of the sample are MSM in PrEP, some are chem users. Users live in central-northern Italy mostly Italians, the median age is 39 years.

Results: In 2021, we had 46 chem users out of 150 prep users (30.7%). In 2022, PrEP users rose to 165 and chem users to 63 (38%). In 2022, the no. of sexual partners among chem users increased from 38.5% to 47.5% (>10), while it remains stable or even declining in the other segments analyzed.

Risky sexual practices such as group sex (41.8% in 2022, 37.4% in 2021), fisting (19% in 2022, 8.2% in 2021), UAI (53 7% in 2022, 49.8% in 2021), non-use of condoms (34.7% in 2022, 30.7% in 2021). The most used substances are mephedrone – used in various ways (see table 1) and GHB. On STIs in the chem user group (see table 2), in 2022 we observe 38.6% of NG and 36.4% of CT both stationaries compared to 2021; syphilis at 25% in 2022, was at 22.2% in 2021. The median age of users who received at least 1 of this diagnosis is between 35 and 38 years in 2022, between 38 and 45 years in 2021. In the group of PrEP users who do not use chem, in 2022 we observe 31% of NG (it was 40% in 2021), 50.8% of CT (it was 40% in 2021), 18% of syphilis (it was 19.2% in 2021).

Conclusion: In the two-year reference period, we observe a decline in the use of mephedrone and GHB traditionally associated with chemsex in PrEP users. However, this does not seem to follow a decline in STIs that are stable. Moreover, in those who don't do chemsex we see an increase in chlamydia of over 10% despite a slight decline in the other STIs. Exposure to risk remains high: number of sexual partners, anal sex without condoms and group sex is growing. It should be remembered that the PPP only enrolls people deemed to be at high risk of contagion. We also see an increase in demand for PrEP. A follow-up is planned for the two-year period 2023 -2024. The data confirms the importance of these users being tested for STIs on an ongoing basis.

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PrEP

P 248 THE ANLAIDS FORUM MAY IDENTIFY NEW SUBJECTS TO BE ADDRESSED FOR PREP

A. Venturelli, C. Balotta, R. Galipò, G.V. Calvino, B. Marchini

Anlaids Onlus, Rome, Italy

Background: The ANLAIDS Forum is an online platform where users can post questions about HIV. In this study, we aimed to understand whether Forum users could be targeted for PrEP protocol, according to Italian Guidelines (LG).

Material and Methods: We re-read and categorized discussions posted on the Forum in the biennium 2021-2022. Only discussions with an actual HIV risk were considered, profiling subjects by sex and type of exposure.

We checked if risk factors were among those suggested by the LG for PrEP initiation.

We analysed whether Forum people meeting the eligibility criteria for PrEP are a population with similar characteristics of subjects newly diagnosed with HIV in Italy in 2021 as reported by CoA – ISS in "Notiziario dell'ISS vol. 35 – n. 11, 2022" (referred as ND data).

Furthermore, the characteristics of Forum subjects were compared with those of people reported to be taking PrEP in Italy in 2021 (PrEP in Italy: how many people access it and what kind of services are offered? - M. Stizioli, G.M. Corbelli, M. Falaguasta, E. Nittolo; abs. OP19, ICAR, Bergamo, 2022).

Results: Of 101 PrEP-eligible persons (83 men, 82.2%; 17 women, 16.8%; 1 transgender woman, 1.0%) identified in the Forum, 61 (60.4%) declared themselves as heterosexuals (HEs) and 40 (39.6%) as homosexuals (all men, MSM). Thirty-two subjects (31.7%) were eligible for PrEP they had previously being on PEP, while the remaining reported frequent occasional sexual encounters with inconsistent condom use or condom improper use. In addition to these people, 9 others were already following the PrEP protocol (all men: 3 HEs, 6 MSM).

By looking at the characteristics of individuals in the Forum who could initiate PrEP and ND data, we verified that men were 84.4% vs 79.5%, and women were 15.6% vs 20.5%, respectively. Analogously, in the two case files, monitored unprotected sexual intercourses were 91.8% vs 83.5%, of which those among MSM were 38.4% vs 39.5%. Considering the same risk, HEs men were 39.2% vs 27.2%, and HEs woman were 14.2% vs 16.8%.

Performing a linear regression to compare this proportions, a significant correlation was found between the two data sets ($p<0.05$; $R2=0,95$).

Then comparing the characteristics of individuals on PrEP in Italy in 2021 with those of Forum users eligible to take prophylaxis, several differences could be observed. Although HEs men taking PrEP in 2021 were 2.2%, Forum individuals eligible for PrEP were 43.5%. Accordingly, women on PrEP were 0.6% compared to as high as 16.8% in the Forum.

Conclusions: The data analysed show that the Forum study population reflects the traits of people diagnosed in 2021, as reported by CoA – ISS. Despite previous real world data highlighted that very little proportion of HEs were on PrEP, our data suggest that prophylaxis should also be offered to a greater extent to heterosexuals who have high-risk behaviours.

PrEP

P 249 PRE-EXPOSURE PROPHILAXIS (PREP) USAGE IN A MSM ADULT POPULATION: ORGANIZATIONAL PROCEDURES, ISSUES AND OBSERVATIONS

A. Franco[1], P. Bellopede[1], R.M. Franco[1], A. Gallicchio[1], A. Giaccone[1], A. Maddaloni[1], S. Parente[1], S. Susini[1], M. Talamo[1], A. Bianchi[2], V. Iodice[2], A. Lanzardo[2], A. Marocco[2], M. Sardo[2], I. Vecchietti[2], E. Manzillo[2]

[1]UOC di Malattie Infettive dell'età Geriatrica AORN "Ospedali dei Colli", Napoli, [2]UOC di Immunodeficienze e Malattie dell'Emigrazione AORN "Ospedali dei Colli", Napoli

Introduction: Pre-Exposure Prophilaxis (PrEP), as an association of Tenofovir Disoproxil (TDF)/ Emtricitabine (FTC) is an efficient way of preventing HIV infection. PrEP is mainly aimed at high risk populations (MSM, transgender and non binary people, sex workers, partners of non-compliant Hiv patients, sero-discordant couples who want a child etc.). Patients can take the drug continuously (daily) or occasionally (on demand).
Materials and Method: From September 2020 to February 2023, despite the pandemic taking a toll on public health structures, our hospital held a PrEP clinic, initially only using organizational procedures provided by the "Italian Guidelines for antiretroviral therapy".
Afterwards, from September 2021 on, we followed the guidelines mentioned on the "Action Protocol for PrEP in Campania".
Overall 78 patients came to our clinic in 30 months of activity (Tab).
The visits were done for free, with no needed prescription from the general practicioner and online reservations.
After undergoing tests propaedeutic to PrEP enrollment, a counseling on motivations was done and the patients were informed of the risks and benefits of this practice, with the help of specific modules.
Prophylaxis with TDF/FTC (group C drug, not reimbursed by the State) was prescribed during the second visit, after recieving adequate results on the aforementioned tests. First prescription lasted a month.
From the third visit onwards, prescriptions were given every three months, requiring a renal function test and a IV generation HIV antibodies test each time.
Enrolled users were closely followed by the clinic for every emergency, especially those regarding sexually transmitted diseases.
Results: Over the course of our observation (30 months) a total of 258 visits were carried out by our clinic (circa 3,3 visits for each patient).
Average age of patients was 38,9 yo (22 -57 yo).
Of the 77 male PrEP users, 100% was MSM. The only enrolled female was the partner of an HIV-positive man and took pericoital prophylaxis.
Of the 78 patients, 17 (22%) requested continuous prophylaxis (day by day) while 61 (78%) only used PrEP on demand. 30/78 (38%) have not come back to the clinic for 12 months (lost at follow up). There was no case of HIV seroconversion among the users. In 2 out of 78 cases (2,5%) there was a worsening of a syphilitic infection (reactivation or primary infection), treated with antibiotics.
Conclusions: PrEP, when administered under the guide of an expert physician, is a highly efficient strategy to reduce risk of infection. According to the analyzised data, it has mostly been requested by MSM adults, rather than adolescents or young adults. Cost of the drug is probably the reason why.
Patients mostly prefer discontinuous therapy (on demand) while a particular increase in sexually transmitted diseases was not registered.
Furthermore, the usage of PrEP seems to very often represent a momentary choice among MSM adults (high number of lost to follow up).

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PrEP

P 250 HIGH PROPENSITY TO SWITCH TO LONG-ACTING INJECTABLE PREP WITH CABOTEGRAVIR IN A COHORT OF ORAL PREP EXPERIENCED MEN WHO HAVE SEX WITH MEN

A.R. Raccagni[1], M.F. Lucente[1], C. Candela[1], R. Lolatto[2], L. Galli[2], B. Trentacapilli[1], G. Ponta[1], E. Messina[2], N. Gianotti[2], A. Castagna[1,2], S. Nozza[1,2]

[1]Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases Unit, San Raffaele Scientific Institute, Milan, Italy

Background: Long-acting injectable pre-exposure prophylaxis (LAI-PrEP) with cabotegravir (CAB) has demonstrated to be superior to daily oral TDF/FTC in preventing HIV infection among men who have sex with men (MSM). The aims of this study were to investigate the propensity to switch LAI-PrEP with CAB among MSM receiving oral PrEP (O-PrEP) and evaluate the associated factors.

Methods: MSM receiving out-of-pocket O-PrEP with FTC/TDF from at least 6 months at the Infectious Diseases Unit of San Raffaele Scientific Institute, Milan, eligible to LAI-PrEP with CAB, were included. Individuals were asked by the referring physician in January 2023 (freezing date), during routine PrEP visits, to complete a survey on their propensity (interested: would switch and considering: might switch) to switch to LAI-PrEP with CAB every 2 months (q2M). Date of O-PrEP prescription was considered as baseline (BL); O-PrEP non-adherence was defined according to international guidelines and based on self-reported data. Mann-Whitney rank-sum test and Chi-square test applied.

Results: Overall, 377 cis-gender MSM receiving O-PrEP completed the survey. Median age was 35 years (interquartile, IQR 31-41), 367 (97%) were Caucasian and 370 (98%) attended upper school/university, 137 (36%) were chemsex users and 274 (72%) had >10 partners in the previous 3 months; 224 (59%) were event-based O-PrEP users. Median follow-up from BL was 18 months (IQR 10-35). Individuals interested or considering to switch to LAI-PrEP with CAB were 326/377 (86%); 0/326 (0%) perceived receiving q2M injections in-hospital as problematic and 307/326 (94%) were willing to pay out-of-pocket for LAI-PrEP. Individuals' characteristics according to the propensity or not to switch to LAI-PrEP are presented in Table 1. People propense to switch to LAI-PrEP were significantly younger (35 years, IQR 30-40 versus 37, IQR 33-43, p=0.051) and had more partners (>10 partners in previous 3 months: 243, 74% versus 31, 60%, p=0.044) than those not propense. Event-based or daily-based O-PrEP (194/224, 87% versus 132/153, 86%) and chemsex users (users: 119/137, 87%, non-users: 207/240, 86%) showed similar propensity. Among MSM self-reporting non-adherence to O-PrEP, propensity to switch to LAI-PrEP was significantly higher (non-adherent: 79/84, 94%, adherent: 247/293, 84%; p=0.028).

Conclusions: We observed very high propensity to switch to q2M LAI-PrEP with CAB in this cohort of cis-gender MSM receiving O-PrEP. Among individuals self-reporting non-adherence to O-PrEP, the propensity to switch was significantly higher. Rapid availability of LAI-PrEP with CAB might address unmet needs of O-PrEP users in Italy.

Attach: https://www.icar2023.it/public/abstract/Attach_ABS_162.PNG

PrEP

P 251 IS HYPOPHOSPHATEMIA A REAL CONTRAINDICATION FOR PREP? LET'S ASK THE RENAL TUBULE

G. Guglielmetti[1], O. Bargiacchi[2], S. Prenna[1], F. Rinaldi[2], A. Barco[2], V. Cantaluppi[1]

[1]Nephrology and Kidney Transplantation Unit, Department of Translational Medicine, University of Eastern Piedmont , "Maggiore della Carità" University Hospital, Novara, ITALY, [2]Infectious Diseases Unit, "Maggiore della Carità" University Hospital, Novara, Italy

Background: Oral Pre-exposure prophylaxis (PrEP) with antiretroviral drugs has been recommended for HIV infection prevention among individuals at high risk of acquiring HIV. In Italy, the use of a fixed dose combination of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) is the only drug authorized for non-reimbursed PrEP since 2017. Renal function impairment with eGFR < 60 ml/min, proteinuria and mild-severe hypophosphatemia (P<2 mg/dL) are considered contraindications to PrEP due to its potential nephrotoxicity.

Material and Methods: We present a case of a healthy 36 year-old man interested in PrEP with a mild-severe hypophosphatemia (P 1,4 mg/dL). We performed a metabolic and tubular study to assess the underlying condition and consequently if it would represent a real contraindication for PrEP. After PrEP start, we closely monitored renal function every 4 weeks in the first 2 months, then every 3 months.

Results: A 36-year old man, MSM, with a past history of kidney stones and an actual stone free status came to our Infectious Diseases Outpatient Clinic to start PrEP. Before PrEP start, he underwent laboratory test that showed a previous unacknowledged hypophosphatemia (1,4 mg/dL) with a normal renal function with serum creatinine 0,90 mg/dL, eGFR (CKD-EPI) 110 ml/min and normal urinalyisis. After a nephrology consultation, a second level laboratory analysis with 24-hour urine collection was performed showing an increased fractional excretion of phosphate (FeP) 23,2 % (normal values 10-20%), no other signs of proximal tubulopathy, glomerular hyperfiltration with increased creatinine clearance (140 ml/min); moreover we found neither proteinuria nor albuminuria, normal values of parathyroid hormone, vitamin D, magnesium, slight hyperuricemia (7,6 mg/dL) with normal fractional excretion. Since no signs of tubulopathy was found except for the increase of FeP that was slight, no nephrological contraindication was present. The patient also underwent a diet consulting: a normocaloric, normoproteic diet was started with higher phosphorus intake. PrEP was finally started: on demand for the first month and then daily. During follow-up period (9 months), the patient underwent 4 testing, which showed an unexpected increase in P levels (2,4 mg/dL) with a normalization of FeP (19,6%).

Conclusions: Hypophosphatemia per se should not constitute a contraindication for PrEP: tubular function tests are recommended to assess a complete renal function evaluation before PrEP start. Infectious disease specialists and nephrologists should collaborate to ensure safe care of people interested in PrEP and may lead to a potential increase of PrEP use.

PrEP

P 252 PRE-EXPOSURE PROPHYLAXIS (PREP): ACHIEVED RESULTS AND WHAT REMAINS TO BE DONE

L. Coppola[1], M. Iannetta[1,2], L. Campogiani[1], M. Compagno[1], V. Malagnino[1,2], E. Teti[1], L. Ferrari[1], T. Mulas[1], A.R. Cavasio[1,2], N. Braccialarghe[1,2], L. Sarmati[1,2]

[1]Infectious Diseases Clinic, Policlinico Tor Vergata, Rome Italy, [2]Department of System Medicine, Tor Vergata University, Rome, Italy

Background: Pre-exposure prophylaxis (PrEP) demonstrated high efficacy in preventing HIV seroconversion in high incidence groups, expecially among men who have sex with men (MSM). We conducted a retrospective monocentric study, describing the characteristics of behaviour, and the incidence of sexually transmitted diseases (STDs) in subjects enrolled at PrEP center of Policlinico Tor Vergata.

Material and Methods: Among the population treated at our Infectious Diseases Clinic in Tor Vergata Hospital from November 2021 to date, all subjects who agreed to answer a questionnaire on sexual behaviours (including Chem-sex use) were enrolled. Clinical and laboratory data were collected, including basal serological screening for HIV, HBV, HCV and T. pallidum and molecular screening for Chlamydia trachomatis and Neisseria gonorrhaeae on urethral, rectal, and pharyngeal swabs.

Results: Overall, 78 subjects are followed for PrEP prescription: 76 are MSM and 58 (74%) answered to the questionnaire and were enrolled in the study: 53/58 (91%) had a high education level and 13/58 were health professionals (doctors or nurses), median age is 34 years.

High-risk behaviours for HIV infection are common in the study population: 40% of the subjects had the first intercourse at less than 18 years and 24% at less than 14 years old; 86% of men declared more than 100 partners in their lifetime and more than 10 in the last 6 months. Four subjects (7%) use intravenous drugs. 14% of patients said they had practiced Chem-sex in the previous 6 months and 59% had practiced group sex. Condom use is inconsistent in the population: 90% of subjects do not use condom during insertive anal sex and 62% in receptive anal sex, 100% do not use condom in oral sex. HIV test was done in 74% of the population in the previous 24 months.

Only 28% had received information about PrEP from health operators, 40% had been informed by friends and 27% from internet web sites and dating apps.

Serostatus for HAV, HBV, HPV and Monkeypox virus (MPV) was investigated through medical history and/or serological screening. 70% of patients had protective antibodies for HBV (HBsAb positivity), 18% were vaccinated for HAV. Only 30% had started or completed vaccination for HPV and less than 5% for MPV.

In the first screening, 7 patients had a C. trachomatis infection (5 proctitis and 2 urethritis) and 5 patients had N. gonorrhoeae infection (3 proctitis and 2 pharyngitis).

Conclusions: PrEP is a proven effective strategy to prevent HIV infection and to allow early detection of other STDs in high risk populations; it is mainly used by informed persons, mainly italian MSM, often health workers. More efforts should be made to facilitate access to PrEP for other risk groups such as sex workers and the immigrant population. To notice, HPV vaccination is infrequent in this key-population, despite scientific evidence of protection against HPV-related cancer.

PrEP

P 253 HIGH INTEREST IN LONG-ACTING INJECTABLE CABOTEGRAVIR (CAB-LA) AMONG "ON DEMAND" PREP USERS

S. Venturelli[1], D. Ripamonti[1], A.S. Tran[2], L. Comi[1], F. Borghi[1], F. Maggiolo[1], M. Rizzi[1]

[1]UOC Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy, [2]University of Milan, Milano, Italy

Background: Pre-Exposure Prophylaxis (PrEP) is an evidence-based strategy of HIV prevention recommended by the European Centre for Disease Prevention and Control (ECDC) to EU/EEA countries since 2015. In July 2022 WHO released new guidelines for the long-acting cabotegravir (CAB-LA) as PrEP. Our PrEP Clinic has been active for more than 4 years with progressively increasing enrollments. Daily or "on-demand" FTC/TDF is regularly prescribed, while CAB-LA is not available yet.

Methods: Data about individuals who initiated PrEP at our Centre from June 2018 to March 2023 were retrospectively collected. We collected data on demographics, past medical history (PMH), vaccination status, PrEP regimen, PrEP side effects, previous STIs and incident STIs, previous Post-Exposure Prophylaxis (PEP) use and reasons for discontinuation. Follow-up visits at our centre are planned every three or four months. Since 19th January 2023, PrEP users attending follow-up visits were interviewed about their condom use, type of sex, number of partners and also about the interest in CAB-LA as an alternative to oral drug for PrEP strategy. The first 77 questionnaires collected up to 27th March have been evaluated.

Results: Until March 2023, our PrEP cohort included a total of 193 individuals, 98% of which were male (83% MSM, 5% heterosexual and 12% bisexual). Median age was 36 years (IQR 32-45). A total of 69 persons (36%) came from provinces different from Bergamo. A total of 133 users (69%) had no significant PMH. 25 users (13%) reported previous PEP use and 140 users (73%) past STIs with 48% of them with more than one. At their first visit 52%, 90% and 30% of attenders were protected from HAV, HBV and HPV infection, respectively, either for previous infection or vaccination. "On-demand" PrEP was prescribed to 129 persons (68%). Overall, 39 users (20%) complained of adverse events during PrEP use (the most common was nausea) and 164 incident STIs were documented (with rectal chlamydia the most frequent). PrEP was discontinued in 26 users (14%) mainly for users' choice. No incident HIV infection was diagnosed.

Of the first 77 responders to the questionnaire, 75% (58/77) declared having protected anal sex in >70% of sexual encounters before starting PrEP; since PrEP use, the rate of users with such a frequent use of condom in anal sex decreased to 27% (21/77).

A total of 84% users (65/77) declared to be interested in CAB-LA, despite 58% of them (38/65) were on "on-demand" PrEP regimen.

Conclusions: Our preliminary data show a high interest for CAB-LA strategy even in the on-demand PrEP users for whom the appeal of LA seems to overcome the higher drug exposure. This may be due to the need of accurate prediction of sexual encounters and the strict schedule of the event-driven option, without the commitment of the daily option.

PrEP

P 254 PREP IN EASTERN PIEDMONT: STIS AND RENAL SAFETY

F. Rinaldi, O. Bargiacchi, A. Barco, M. Sciarra, A. Rossati, P.L. Garavelli

Infectious Diseases Unit, University Hospital "Maggiore della Carità" Novara

Background: Daily or On Demand Oral Pre-Exposure Phophylaxis (PrEP) with TDF/FTC for HIV infection has been available in Italy since 2017. We observed a cohort of people using PrEP, followed up at the outpatient clinic for Infectious Diseases of University Hospital "Maggiore della Carità" in Novara, a secondary level hospital based in
south-eastern Piedmont.

Material and Methods: We conducted a descriptive analysis of our study population from December 2018 to March 2023, analyzing sexual behavioral risks factors, gender, age, comorbidities, PrEP regimen. We assessed HIV, STIs, renal function, change in PrEP regimen or sexual behavior, before PrEP start and every 3 months thereafter.

Results: Thirty men and one woman accessed our clinic for PrEP prescription (demographic characteristics in Table 1). None of them was a sex worker. Only one subject received Post-Exposure Prophylaxis (PEP) twice before starting PrEP. At baseline, 17 chose daily regimen while 14 preferred on-demand scheme. During follow-up three subjects switched from daily to on-demand regimen due to changes in sexual behavior. All PrEP users received vaccinations for monkeypox, HPV, hepatitis, N. meningitidis and S. pneumoniae. All subjects were followed-up for a median of 5 months. Previous PrEP start 18 individuals reported at least 1 STI (6 syphilis, 4 gonorrohoeae, 9 chlamydial or mycoplasma uretritis/proctitis, one acute HBV infection and one HCV infection).

At baseline two subjects showed positive pharyngeal swab for Neisseria meningitidis, without neurological symptoms and received quinolone prophylaxis. During observation period, 6 subjects contracted a STI: three symptomatic syphilis and three asymptomatic urethritis. Median time from PrEP start to STI event was 5,5 months. None of them seroreverted HIV. Regarding renal function 50% of them presented low level phosphate level at baseline (one patient below 1,5 mg/dL) and underwent nephrologic consultation. During the follow up period none of them showed an increase in creatinine level, four of them (13%) showed a slight decrease in phosphate level, with no evidence of nephropathy, promptly improved with dietary supplementation. None of them interrupted PrEP for renal toxicity issues. Only one of them interrupted PrEP use according to a change in risk behavior (from open to closed sexual relationship).

Conclusions: Our small cohort confirm that PrEP is a safe and valuable preventive measure for HIV infection and ensures STIs screening and treatment for high risk population.

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PrEP

P 255 REASONS FOR LEAVING A PREP COMMUNITY-BASED SERVICE: OUR EXPERIENCE IN BOLOGNA, ITALY

C. Patrucco[1], A. Pozzi[1], S. Mattioli[2], S. Cecere[2], M. Casarini[1], P. Fait[1], D. Marzolla[1], B. Nuti[1], L. Piazza[1], I. Sartini[1], D. Testi[4], V. Gaspari[3], L. Badia[5]

[1]Alma Mater Studiorum University of Bologna, Infectious Disease Department, S.Orsola-Malpighi Hospital, [2]Plus aps, PrEP Point Plus Bologna, [3]Alma Mater Studiorum University of Bologna, Dermatology Department, S.Orsola-Malpighi Hospital, [4]Arcispedale S.Anna, Cona, Ferrara, Infectious Disease Department, [5]Azienda USL di Imola, Infectious Disease Department

Background: Pre-exposure prophylaxis (PrEP) for HIV prevention can be administered in a hospital or extra-hospital setting, as community-based services. In both cases some users may interrupt visits and PrEP use. In one study investigating PrEP discontinuation, most common reasons were: systemic issues, including financial problems, clinic or pharmacy logistics and scheduling barriers; medication concerns i.e. side effects; behavioral factors i.e. sexual behavior changes.

Materials and methods: We conducted a descriptive observational study regarding people taking PrEP in a community-based center in Bologna, Italy. Our aim was to investigate how many users have left the service since it began and the reasons of their choice. We conducted a telephonic survey, administering a questionnaire to each user that has abandoned the service, asking 4 questions: reason for leaving the service, current use of PrEP, current perceived risk of HIV, use of PEP.

Results: 265 have been taking PrEP in the community-based service from February 2018 to March 2023. Ninety-four (36%) have left the service during this period; of these, 74 (79%) answered the survey.

27 (36%) left the service because they moved to another city and/or to another center; 17 (23%) are currently in a monogamous relationship; 6 (8%) use barrier methods (condom); 6 (8%) missed one or more appointments, mostly because of scheduling problems; 4 (5%) were not satisfied at the PrEP point; 2 (2%) had financial difficulties; 1 (1%) experienced PrEP sides effects.

Out of 74 people that answered the questionnaire, 41 (55%) are not taking PrEP anymore, while 33 (45%) are still taking PrEP but in a different setting: 2 (3%) moved to another community center, 24 (32%) moved to a hospital PrEP center, 7 (10%) use PrEP without medical control.

About the current perceived risk of HIV, 52 (70%) consider it low, while 22 (30%) consider it medium or high.

Regarding the use of PEP, 10 of 74 people reported PEP after leaving the community service.

Conclusions: Our study describes the reasons for leaving a PrEP community-based service in Bologna, Italy. It shows that there are PrEP initiators who discontinue it after a certain time, underling that PrEP should not be thought of as a lifelong therapy.

The majority (36%) left the community-based service in Bologna because they moved to another city or to another PrEP center. A lot of people had behavioral changes: some uses barrier methods (8%), others declare to be in monogamous relationships (23%).

Very few people reported side effects or financial problems; the latter is likely related to the mean age of the users of the center, 39 years.

The small but significant percentage of people still taking PrEP without controls after abandoning the planned follow-up underlines the need to implement efforts to avoid use of “savage” PrEP, which gives no guarantees about correct method of administration and can help spread of STIs.

PrEP

P 256 A DESCRIPTIVE ANALYSIS OF SERUM CREATININE VARIATION IN USERS ASSUMING TDF-PREP: A POSSIBLE ROLE OF AGE AND COMEDICATION

M. Albertini, M. Menozzi, E. Martini, M.D. Di Trapani, A. Soffritti, B. Fontana, C. Mussini

Infectious Disease Department, University Hospital of Modena, Italy

Background: Pre-exposure prophylaxis (PrEP), based on the association of tenofovir disoproxil (TDF) /emtricitabine (FTC), is an efficacious strategy to prevent HIV infection in seronegative people. Tenofovir disoproxil may be associated with increase of serum creatinine as a proxy of kidney toxicity. This study aims to describe the population of PrEP users from our centre, focusing on serum creatinine levels trends and the differences between the population aged over and under 50 years old (yo).

Material and methods: We conducted a retrospective observational study reviewing data from the University Hospital of Modena, collected from January 2019 to March 2023. PrEP was dispensed as daily or on-demand regimen. Every 3 months clinical assessment and serum creatinine levels were collected. Nephrotoxicity was defined as at least 20% increase in serum creatinine between basal and last follow-up value. We divided the population by age group at PrEP initiation (<50 yo, >50 yo). A secondary analysis was performed including users aged >50yo only, focusing on nephrotoxicity prevalence in that population.

A descriptive analysis was performed using mean (standard deviations) and number (frequency) for continuous and categorical variables respectively. Comparisons were done with Mann-Whitney U test, ANOVA and Chi-square test according to variable distribution and type.

Results: We collected data of 111 PrEP subjects (tab 1): 109 (98,2%) were males and 2 (1,8%) male-to-female transgenders; among them 23 (20,7%) and 88 (79,3%) users were older and younger than 50 yo, respectively. Ninety-six (86,5%) users were Italian and 90 (81,1%) were men who have sex with men (MSM). On-demand regimen was preferred by 67 (62,6%) of subjects, the daily one by 25 (23,4%), while 15 (14%) used both. Focusing on renal function, data were available for 95 users. Twelve (13,3%) subjects presented nephrotoxicity (tab 2): 7 out of them were using daily regimen, 4 users were on on-demand regimen while 1 used both. Eight users were assuming potentially nephrotoxic comedications, especially antihypertensive drugs. Five (9.6%) and 7 (22.7%) out of 12 were older and younger of 50yo (p=0.104), respectively. The maximum increase was of 0,75 ml/min (from 1,36 ml/min to 2,11 ml/min) in a man undergoing lisinopril comedication, leading to PrEP interruption.

In the secondary analysis among the population over 50 yo including 23 subjects, 5 (21,7%) developed nephrotoxicity (tab 3): 4 of them were on a daily regimen and 3 (60%) users were receiving other potential or known nephrotoxic drugs. None of them experienced an increase in creatinine value that required PrEP interruption. Our analysis did not show any statistically significant difference between the two age groups.

Conclusions: Our data confirm safety of TDF as a PrEP medication, with low interruption rates even in older users. Nevertheless, it remains fundamental to consider concomitant comedications which may increase the risk of renal toxicity and larger cohorts. In this perspective the advent of newer prevention strategies alternative to oral TDF may be considered in some special categories of PrEP users.

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PrEP

P 257 PRE-EXPOSURE PROPHYLAXIS FOR HIV AND RISK OF RECURRENT SEXUALLY TRANSMITTED INFECTIONS

D. Farinacci[1], P.F. Salvo[2], R.J. Steiner[2], A. Ciccullo[3], V. Iannone[2], R.A. Passerotto[2], A. Dusina[4], A. Borghetti[4], S. Di Giambenedetto[2,4], G. Baldin[4]

[1]UOC Medicina Protetta-Malattie Infettive, ASL Viterbo, [2]Dipartimento di Sicurezza e Bioetica, Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, [3]Malattie Infettive, Ospedale San Salvatore, L'Aquila, [4]UOC Malattie Infettive, Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS

Introduction: Pre-exposure prophylaxis (PrEP) is an additional strategy to reduce HIV-1 infections preventing its transmission in high-risk populations such as sexually-active adult men who have sex with men (MSM).
People who decide to start PrEP should be screened for serum creatinine, HIV antibodies, HBV and HCV serologies, and other sexually transmitted diseases (STDs) before starting the regimen.
Methods: We aimed to analyze the main characteristics of the individuals who decided to start PrEP in our Centre between 2019 and 2022, analyzing the incidence of STD acquisition.
Results: We analyzed 170 individuals: 166 were males (97,6%), with a median age of 37 years [IQR 31.00-45.00]. Most of them (n=162, 95.3%) were MSM. The majority were in good shape without comorbidities (91.2%). The main characteristics of the cohort are shown in Table 1.
Most individuals (n=109, 64.1%) preferred a daily dosage, while 61 (35.9%) chose the “on-demand” regimen.
As to previous STDs, 40 patients had at least an old episode of syphilis (23.5%), 10 patients had a previous gonorrhea infection (5.9%), and 5 (2.9%) had previous urethritis from other microbes. Five patients (2.9%) started PrEP after taking Post-exposure prophylaxis (PEP).
During a median period of follow-up of 39.1 weeks [IQR 23.4-104.0] patients were tested for STDs, creatinine, and ALT.
During this period 25 patients were diagnosed with at least one STD (14.7%), in particular, we found 19 new diagnoses of syphilis (11.2%), 12 cases of gonorrhea (7.1%), and 2 cases of chlamydial infection (1.2%). 4 patients were diagnosed with mpox infections (2.4%). 3 patients (1.8%) were diagnosed multiple times with syphilis.
No new HIV, HCV, and HBV infections were detected.
The probability of getting syphilis was estimated as 20% at week 48, with a greater probability in patients that already had syphilis ($p<0.001$)
No significant modifications were detected in serum creatinine and serum ALT during FUP.
Fifty-four (33.5%) patients interrupted prophylaxis and follow-up visits. The estimated probability of not showing to the following FUP was 32% at week 48 with no differences between daily and on-demand groups (log-rank $p=0.413$).
Conclusion: PrEP proved to be an important weapon against the spread of HIV infection in those most at risk, but these subjects represent a high-risk population for STDs in general.
In our cohort, there were no new HIV infections, regardless of the type of regimen used. Despite this, over 10% of patients got at least one STD, often with few or no symptoms, suggesting that this population needs close contact clinics for early diagnosis and treatment. To this proposition, the education of those at risk is fundamental, also given the high number of subjects who tend not to show up for follow-up visits.
Despite this, PrEP continues to be one of the most effective weapons to avoid the risk of HIV infection in subjects with risky behaviors and it is important to increase its use.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 258 IMPACT OF PEER EDUCATION ON SEXUAL HEALTH KNOWLEDGE AMONG ADOLESCENTS AND YOUNG PERSONS IN THE BUEA SUBDIVISION OF THE SOUTH WEST REGION OF CAMEROON: THROUGH VCT CAMPAIGNS

K. Eric Marot, G.T. Ayissi Bella, P. Kuate Tape, R. Ngome

Vision in Action, Presse Jeune Développement, Cameroon National Association for Family Welfare, Alliance for Community Initiative

Background: Generally, social development among young people is largely influenced by their peers. Peer education is a proven and effective approach for promoting reproductive health among young people, especially HIV/AIDS education. This study was campaigns to assess the effectiveness of a peer-led education intervention in addressing sexual and reproductive health related knowledge and concerns among young people in Buea subdivision of the South West region of Cameroon.

Method: A pre and post-test study was conducted among 8930 young people aged 15–24 years who participated in the Peer Education intervention selected from communities in Muyuka. A baseline pretest was conducted before the education program, and it was followed up with a post-test at the end of the five-day long peer education sessions. The project offered services that included voluntary HIV & STI testing, including pre-and post-test counselling, access to HIV prevention tools (condoms, clean injecting equipment, and substitution therapy). The project assigned a central role to supportive counseling as a tool to promote behavior change, beginning with counseling and education after HIV testing, and followed by intensive counseling throughout the management of the case by the peer educators. Data was collected, analyzed, who comprised the focus population. The Health District provided nurses from services and medical experts who offer medical consultations and the dispensation of STI kits.

Results: The campaign was conducted from June 2019 to December 2019. The number of condoms distributed included 2822 male condoms, and 770 female condoms, with192 packages of lubricant. Majority of the adolescents were, 20-24 years old: 1094(72%), 15-19 years old: 228 (15%), Older than 24-year-old: 197.6 (13%). A total of 6099 (68.3%) of the adolescents correctly stated that condoms prevent pregnancy during the campaign compared to 6429 (72.0%) peers during the post test. VCT campaigns total of 680 adolescents were reached (boys 340, girls 340). Nine people (2 boys and 7 girls) tested positive, and were offered treatment boys. STI by 6282 (70.3%) and 6984 (78.2%) of the respondents at pre-test and post-test respectively.

Conclusion and Lesson learn: Sustained exposure and access to informative and enlightening peer education sessions over time have the potential to comprehensively improve SRH knowledge, influence positive opinion change and in turn adoption of positive behaviors among young people. Active screening in adolescents is advocated.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 259 CHEMS & LE HOLOGRAMS

A. Infante

Policlinico Tor Vergata Roma

A counseling theater group is a group of people, with the same kind of experience, who join forces to enrich their lives with new meanings through theatrical techniques. The people is put in the foreground as an active protagonist in the change of one's daily life. Groups are characterized by the fact that knowledge, in these situations, spreads across the board because everyone is on the same level and each person receives and gives support at the same time. This dual role ensures that information circulates faster and more effectively. The set of people to whom this experience was proposed is a group of men who used the methodology of the circularity of experience; led by a figure we will call director, in order to optimize an ultimate goal, not always so evident. Why a group of men? To create a socio-political action in defense of the right to choose and to provide an emotional, rational, emotional basis for men who practice Chemsex. The use of theater allows self-knowledge through experimentation and identification, one acts and recognizes one's own personal direction, feeling authorized to experiment with new behaviors. The path was aimed at men who had expressed the desire to explore a common theme, such as that of Chemsex, but also to imagine new expressive, creative and relational skills to be experimented, then, in their personal life, to improve self-awareness, also in the management of one's own resources and to find a new resilience. The work was mainly experiential. The men had the opportunity to personally experience the potential of theatrical mediation, learn exercises and activations. During the one-year course, the men participated in the construction and interpretation of a theatrical project that allowed them to explore their most intimate personal side. The experience ended with a performance that involved them in a performance open to the public, which I would like to screen in the section dedicated to Chemsex, and all this thanks to Plus Roma, but especially thanks to the esteem and friendship with Giulio Maria Corbelli.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 260 THE. M.A.NNA PROJECT (MAOMETTO ALLA MONTAGNA)

S. Dell'Isola[1], S. Aviani[2], A.M. Ialungo[1], E. Rastrelli[1], G. Starnini[1], L. Caterini[2]

[1]UOC Medicina protetta-Malattie infettive Ospedale Belcolle, Viterbo, [2]UOC Malattie Infettive ASL Ospedale Belcolle, Viterbo

Background: The M.A.NNA. project was developed with an unconditional medical grant by Gilead and had the purpose of implementing an infectious disease surveillance network within the territory of the Local Health Unit of Viterbo. After the long period of COVID-19 there was a significant increase in the proportion of subjects unaware of having blood-borne and sexually-transmitted viral infections, particularly HIV, HCV and HBV While the healthcare situations required emergency measures as of 2020, institutional agencies asked to meet targets that were difficult to reach in real-life practice: eradicate HCV chronic infection and to achieve UNAIDS 90-90-90 target by 2030.
Material and Methods: the healthcare professionals involved in the M.A.NNA project went to a number of meeting places, to perform rapid screening tests and provide brief information on blood-borne/sexually-transmitted diseases. A small mobile clinic was implemented. All subjects voluntarily agreed to being tested anonymously receiving pre- and post-test counselling.
Results: The analysis of data for the six groups observed (university students, GP patients, users of communities for addiction recovery, LGTB subjects, immigrants, pregnant women not screened for infectious diseases) shows that 1.1% of tested subjects were positive and that 0.5% of those tested for HIV were positive, with a large between-group variability (no positive cases among university students and GP patients; 10% HIV-positive and 10% HCV-positive cases among LGTB subjects; 3.2% HIV-positive and 6.4% HCV-positive cases among subjects with addiction-related problems; no HIV-positive and 6.6% HCV-positive cases among foreign subjects). HIV-positive subjects were included into rapid referral outpatient program. Regarding HCV-positive patients with detectable viremia, while they were referred to test-and-treat pathways, they could not reach the hospital and receive treatment due to organizational problems on the part of their Community.
Conclusion: This project is the first joint venture implemented in the territory of the ASL Viterbo, where rapid screening testing for HIV, HBV and HCV has been performed by moving healthcare resources to places where untested subjects can be more easily reached or by performing rapid tests also as an emergency procedure in the hospital setting. The main limitation of our findings relates to the very small number of population samples analyzed, which however suggests that there are still population groups traditionally at risk (LGTB subjects, people with addiction disorders) where the prevalence of blood-born sexually-transmitted diseases is high, and that the implementation of healthcare education and information programs among young subjects (20-30 years) should be a priority. The importance of performing screening tests for infectious diseases outside of the hospital setting is a challenge that must be addressed in order to meet WHO goals by the year 2030.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 261 YOUNG PEOPLE AND HIV - MILLENNIALS ON HIV/AIDS/STI AND EMERGING NEEDS

R. Galipò[1,3], M. Bolletta[10], M. Bononi[4], L. Butini[7], V. Calvino[1], L. Cipriani[9], P. Costa[6], S. De Balzo[2], A. De Faveri[8], S. Negri[5], A. Palummieri[1], B. Marchini[1]

[1]Anlaids Onlus, Roma, [2]Anlaids Campania, Napoli, [3]Anlaids Lazio, Roma, [4]Anlaids Liguria, Genova, [5]Anlaids Lombardia, Milano, [6]Anlaids Mantova, Mantova, [7]Anlaids Marche, Ancona, [8]Anlaids Torino, Torino, [9]Anlaids Treviso, Treviso, [10]Anlaids Umbria, Perugia

Introduction: The School Project has 30 years of experience with adolescents and schools to its credit, with the primary goal of doing prevention with and for young people. Operations are ensured by the territorial branches that carry out the activity in their regions. In view of the epidemiological and social changes, the Project is being updated and renewed with an eye always on the new generations. In light of these changes, data collection tools have also been updated to understand what young people today know about HIV/AIDS/STIs, especially at their sexual debut, and what information needs emerge in reference to sexuality issues.

Method: The interventions are conducted mainly in Secondary Schools and involve in-formative meetings held by physicians, psychologists and educators belonging to 9 Sections of ANLAIDS in 8 Italian Regions. A pre-test questionnaire (regarding young people's knowledge of the issues) is administered before the interventions, followed by a post-test (to assess the effectiveness and usefulness of the interventions). Twelve questions on HIV are proposed in the pre- and post-interventions, and each correct answer is scored for a maximum of 12 points.

Results: In the school year 2022-2023, 6856 questionnaires were completed by boys and girls from 70 secondary schools (72.8% were pre-test). 50.9% of respondents were female; the median age was 16 (range 13-20). 64.8% are from high schools. 74.8% attend 3rd-4th-5th grade classes.

Calculating the difference in mean scores between pre and post, the intervention is effective in both the 1st and 2nd year classes ($M = 5.9$ vs 8.9; $t = -22.299$ $p < .001$) and the 3rd-4th-5th year classes ($M = 6.8$ vs 9.1; $t = -33.212$ $p < .001$).

Older children compared to younger children felt that the interventions were more useful ($M = 3.5$ vs 3.3; $t = 1.990$ $p = .047$), that the work of the providers was more satisfactory ($M = 3.6$ vs 3.4; $t = 2.199$ $p = .028$), and that behaviors could be changed after the intervention ($M = 2.8$ vs 2.6; $t = -2.840$ $p = .005$).

The in-depth topics most requested by the youths are those related to Sexuality and its functions: reproductive and relational (38.7%) and Managing emotions and feelings (29.3%). The test administration activity is still ongoing.

Conclusion: Boys and girls, from the last three years of Grade II Secondary Schools, show more interest in the topics covered in class meetings because the topic of sexuality involves them more closely than their younger classmates. In fact, 33.4% of the older ones have had full sexual intercourse compared to 16.8% of the younger ones. Finally, students express the need to want to address various issues related to sexuality, especially on: Sexuality and its functions: reproductive and relational; management of emotions and feelings; and consent and respect for self, other people and diversity.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 262 BRINGING HIV PREVENTION TO SCHOOLS: DATA ANALYSIS

F. Rossi[1], A. Bianchi[1], P.M. Testoni[1], D. Zagato[1], M. Cernuschi[2]

[1]ASA Associazione Solidarietà ODV, Milano, Italy, [2]San Raffaele Hospital, Milano, Italy

Background: ASA is nonprofit active in HIV infection prevention and support for PLWHIV since ‘85. School project aims to bring the topic of HIV and STIs into schools to raise awareness among adolescents and bring them closer to the world of sexuality in a mature and aware way.

Methods: from Nov ‘22 to March ‘23, students from 4 high schools in Milan aged from 16 to 18 were involved in the project, for a total of 372 people. Each meeting, lasting 2 hours, was conducted by two ASA staff members (a psychologist and a PLWHIV) and covered the main STIs with information (contagion modes, etiology, diagnosis, drug treatment). Social stigma was addressed as well, thanks to the help of video material and the witness of the volunteer. Students' questions were also given the proper time for being answered.This year both a pre-meeting and a post-meeting questionnaire was administered, in order to assess the students' initial knowledge on the topic and subsequently to assess the change in their knowledge and the effectiveness and usefulness of the encounter. The questionnaire consisted of 10 multiple choices questions. Then a satisfaction survey was taken: responses were analyzed in terms of effectiveness, perceived usefulness, and possible need to make changes in the structure of future meetings.

Results: we collected 235 pre-meeting, 364 post-meeting and 311 satisfaction surveys (plus 54 additional comments). Four areas were investigated: overall liking (GS) - scoring 81% of “very informative to extremely informative” response -, clarity of exposition (CE) - 57% rated the presentation from “very to extremely interesting” -, quality of answers given to students' questions (SD) - 80% rated the them as “very clear to extremely clear” - , and usefulness of the meeting (UI) – resulting in 81% of “very or extremely useful”. 17% of the students left additional comments that were consistent with the data collected. Data this year revealed a issue regarding students' difficulty in being serious about filling out the questionnaire, due the perception of the task being a 'homework'; sub-optimal cooperation by teachers in motivating the students worsened this issue. For the first time we witnessed discomfort in dealing with health-related topics: several times there were faintings and manifestations of sickness. This is in line with the accentuated fragility of adolescents observed post COVID, who often developed a defensive retreat in themselves.

Conclusions: students evaluated the activity positively, considering it very useful and interesting, and emerged that the testimony of PLWHIV and the use of audio/visual media captured their attention, and were an added value to decrease stigma. For next school year it is planned to continue the project. To avoid the lack of support by teachers, pre and post questionnaires will be shared directly during the meeting. Furthermore, to create a welcoming emotional climate, each meeting will begin with a short relaxation exercise.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 263 THE NON-ITALIAN MSM POPULATION WITHIN THE ROME CHECKPOINT HIV AND STD SCREENING CONTEXT

F. Angeli

Arcigay Roma, Roma

Background: The analysis proposes a specific focus on the data related to the risky behavior of the non-Italian population within the Roma Checkpoint, an HIV and STD screening service based in Rome and managed by Arcigay Roma and Gay Center.
The time period analyzed is from Nov. 2021 to Mar. 2023, where 188 accesses by non-Italian people were recorded; 140 of those accesses are related to the MSM population, which the survey focuses on.
People were screened with rapid tests for HIV and Syphilis.
The non-Italian percentage represents 15% of Roma Checkpoint accesses.
Material and Methods: The data related to the screened population were collected through a questionnaire on the Cobatest model, available for compilation in both Italian and English.
Each user completed the questionnaire individually, in order to guarantee an additional level of truthfulness and privacy.
Results: Out of 140 non-Italian MSM users, one person tested reactive to HIV, while five people tested reactive to syphilis.
The non-Italian MSM percentage is 74.5% of the overall non-Italian percentage. This data is lower than the average percentage of Roma Checkpoint, which consists for the 82% of MSM people.
Regarding the sexual orientation of the sample, 75% define themselves as homosexual, 20.8% bisexual, 2.1 heterosexual, 2.1% identify with other orientations.
Transgender people are 2.1% of the sample.
The age of the users is divided as follows: 18-25: 33.3%; 26-30: 26.2%; 31-35: 18.4%; 36-40: 11.4%; 41-50: 3.6%; 50+: 7.1%.
85.4% of the sample had already taken an HIV test in the past. 13.9% had never taken a test in the past. 0.7% does not know or does not remember.
12.9% had an STD diagnosed in the last 12 months. 1.3% does not remember and 85.8% have not had a diagnosed STD in the last 12 months.
In the last 12 months from the execution of the screening test, users declare the number of their partners according to this distribution: None: 1.3%; 1: 14.7%; 2-10: 60%; 11-50: 18.7%; 50+: 5.3%.
36% used condoms in all anal intercourses in the 12 months preceding the test. 54.7% did not use a condom at least once in the same time period, 54.7% of them with occasional partners (non-permanent partner). 9.3% does not remember.
During sexual intercourses, 48% never used drugs or alcohol. 46.7% did use them sometimes. 4% often and 1.4% always.
The data related to Sex Workers and IDUs were significant.
9.9% belongs to the Sex Worker (SW) category. The data is higher than the average percentage of Roma Checkpoint, equal to 3% of SW.
4.3% used intravenous drugs (IDU). The data is higher than the general percentage of Roma Checkpoint, equal to 0.4% of injecting drugs users. Furthermore, there are no intravenous drug users in the Italian population of Rome Checkpoint.
Conclusion: The analysis allows us to define the context of the non-Italian MSM population at Rome Checkpoint, with the relevant data of SW and IDU. This makes possible the development of specific strategies in this regard.

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P 264 IO C(')ENTRO HIV CHECKPOINT IN GENOVA, ITALY: RESULTS OF FIRST YEAR EXPERIENCE TOWARDS FUTURE OBJECTIVES AND NEW OPERATIONAL STRATEGIES

E. Terragna, S. Tunesi, A. Chinelli, C. Tosi, G. Notore, U. De Santis, M. Feasi, S. Puppo, D. Fiorellino, E. Pontali, M. Viscoli

Anlaids sezione regionale Ligure Odv, Genova, S.C. Malattie Infettive Ospedale Galliera, Genova, Dipartimento di ricerca traslazionale e delle nuove tecnologie in medicina e chirurgia, Università di Pisa, UOC Malattie infettive, AON SS Antonio e Biagio e Cesare Arrigo, Alessandria

Background: The implementation of community-based centres for HIV screening and sexually transmitted infections (STIs) counselling is increasing in many European countries, Italy included. ANLAIDS Liguria Onlus "Alberto Terragna" inaugurated IO C(')ENTRO – HIV community-based Checkpoint in Genova old town, Italy in December 2021. This is the first report of our results. IO C(')ENTRO is part of COBATEST network, that links organisations across Europe who offer community-based voluntary counselling and STI/HIV testing (CBVCT).
Methods: Data were collected from standard anonymous COBATEST questionnaires from 3/12/2021 to 15/3/2023. Gender, age, sexual orientation and behaviour, risk factors, previous testing and reason to test were the variables considered for the analysis.
Results: During fifteen months of activity, we performed 288 rapid salivar HIV tests.
Almost half of the people tested (51%) identified as males, 48% as females, and 1% transgender.
Most of them (86%) were born in Italy. Considering age, 52% of people were under 25 years old, 36% between 25 and 40 y.o., and the remaining 11% were over 40 y.o.
The majority (51%) of those who visited the Checkpoint had never tested for HIV before.
Standard screening was the main reason to test (58%), while 39% reported risk factors: unprotected penetrative intercourse (63%) and unprotected sex among MSM in the last 12 months (25%). Other reported risk factors were: unprotected sex with sex workers (4 people), drug use (2), sex with HIV positive people (4 people), sex working (7) and using injectable drugs (1) in the last 12 months. Finally, 6% of individuals received an STI diagnosis in the last 12 months.
Almost half of the tests (134/288) were performed during special events outside Checkpoint, such as Pride or World AIDS day initiatives.
Three/288 tests reacted positive and the people were addressed to hospitals for further assessment.
Conclusions: HIV routine screening tests remain low in the general population. However, according to our data, we can assume that a combined in-site and events-associated approach can increase testing, especially for people that have never tested before. Outreach testing is also recommended to engage people in vulnerable situations or at an increased risk of STI/HIV.
Finally, it's relevant to highlight that a large prevalence of young people visited the Checkpoint. This might be due to the fact that they are less subject to HIV stigma and prejudice and/or might be a result of ANLAIDS Liguria effort to engage young people during HIV prevention activities in secondary schools/university and organised events in the regional territory.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 265 THINGS CHANGE. LATEST U=U COMMUNICATION CAMPAIGN OF LILA CAGLIARI

G. Dessì, V. Mascia, B. Mocci, A. Pontis

LILA Cagliari OdV, Cagliari

Background: In 2022, LILA Cagliari (the Italian League for the Fight against AIDS) developed a multi-language communication campaign on TasP (Treatment as Prevention). Since long ago, LILA has committed to hinder stigma towards people living with HIV and, for the forth consecutive year, we paid close attention to U=U. This time we made a campaign in three languages: Italian, English and Sardinian. Among our users there are PLWHIV in their elderly age who has always been more likely to speak Sardinian, hence we launched a campaign which included also this language to make it accessible to everyone.

Material and Methods: The pictures chosen for the campaign are simple ones, but so colourful that they have a strong visual effect. The three subjects are: a 50-year-old man, a guy and a young woman in their 30s. All of them state with spontaneity, and a smile, that "things change", the text combined with the image. For the first time this concept comes on its own with a dot, as to sign a turning point compared to the past campaigns: "Things change.", things are different now. The message is then made explicit with the sentence "People living with HIV do NOT transmit it" in the foreground, and only in the lower part of the image it is clarified further that, thanks to scientific evidence we know PLWHIV, who are on reatment and have undetectable viral load, cannot transmit it even in unprotected sex. It is very important to highlight this essage which cannot be mistaken anymore. The union of image, text and colours makes a strong, complete message hich is addressed to all the population. The therapy is, indeed, effective both in keeping people's state of health and reducing the risk of virus transmission to others. It's a positive, scientifically proven and innovative message in order to banish the fear owards PLWHIV. The bright colours and the relaxed pose of the subjects trigger serenity and strength. The campaign was advertised with large posters affixed in town, online and newspapers' posting, on local and web TVs and conferences where Lila took part. Also, the campaign was spread on all social networks, which allowed it to amplify its communicative power and led people to interact and share the message.

Results: The campaign was quite successful; it has been praised by professionals and organisations that work on these issues. It was advertised on all local media and by the main local newspaper. It held a wide appeal also at an international level and even Bruce Richman, promoter of the worldwide U=U campaign 'Prevention Access Campaign', has mentioned it.

Conclusions: The power of the message generated an effective communication campaign. This has allowed to promote essential concepts that should be commonly known (yet they are not) by the general population.

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P 266 SUPPORTING QUALITY OF LIFE: COMPLEXITIES AND GOALS IN THE EXPERIENCE OF A MINDFULNESS GROUP IN A COMMUNITY SITE

A. Bianchi[1], P. Testoni[1], A. Antonino[1], M. Cernuschi[1,2]

[1]ASA Associazione Solidarietà AIDS ODV, Milan, Italy, [2]San Raffaele Hospital, Milan, Italy

Background: The effectiveness of modern pharmacotherapies makes it possible to take care of the Quality of Life of PLWHIV. ASA ODV has always been interested in both prevention of new infections and support for PLWHIV. It has recently added Mindfulness (M), which consists of a set of practices designed to cultivate awareness of the present experience with acceptance. This discipline was systematized by the (M) Based Stress Reduction program. MBSR consists of 8 weekly sessions. Each class addresses a topic with nonjudgement; it offers meditative practices, followed by sharing one's experience in a group. Homework (exercises, meditative practices) is assigned at each session, with a gradual daily commitment (up to 1 hour/day). The program is effective in reducing stress:it has been clinically proven to be helpful in reducing the multifaceted stress given by living with HIV. ASA has offered MBSR-based programs in both individual and group settings since May '21. The aim of the study is to describe a (M) group experience for PLWHIV to evaluate future interventions.
Methodology: The program had been advertised on ASA's social media as well as proposed by internal psychologists and ID doctors from May '21. It was held in dual mode online/live by an experienced HIV psychotherapist, (M) Teacher. Preliminary talks were led to clarify the course (exercises, commitment needed). The group lasted from May to July '22. An anonymous follow-up survey was emailed to investigate satisfaction with different parts of the program (practices, homework, sharing, nonjudgment) and the specific context.
Results: The program was attended by 5 trainees.(Italians; 3 M, 2 F; mean age 61; 80% HIV+ before 1996). Forming the group had been challenging due to reasons both non-context-specific (logistics; difficulty in taking & pursuing a commitment) and specific (fear of attending a course that included sharing their experience in an "HIV-tagged" space: such that users already frequented the association). 40% followed the whole protocol. 1/5 participated online. From the survey,satisfaction with the exercises and labour in carrying out homework is in line with the results of protocols in non-HIV-related settings.Referring to the mutual sharing of the experience, everyone enjoyed the listening stage; 80% felt heard. 80% of the sample found the theme of self-acceptance and suspension of judgment helpful because "it acknowledges their judgmental side" across the different exercises. 20% found it difficult because "it seems impossible not to judge some things". 60% stated that being in an HIV-related place, together with PLWHIV, allowed them to feel relaxed and safe.
Conclusions: The course has been an opportunity to provide concrete tools for coping with stress in a safe place. The chance to nurture nonjudgment, core to the course and acknowledged by all as an enduring challenge, makes the program particularly useful in fighting internalized stigma, which is still strong towards HIV.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 267 ONE YEAR EXPERIENCE OF THE ANCONA CHECKPOINT: FIRST ANALYSIS OF COBATEST DATA OF POPULATION

S. Caucci[1,3], L. Saracini[2,3], P. Pauri[3], L. Butini[4]

[1]Department of Biomedical Sciences and Public Health, Università Politecnica delle Marche, Ancona, [2]Ass. Opere Caritative Francescane, Ancona, [3]Ancona Checkpoint, Ancona, [4]Immunology Laboratory, Azienda Ospedaliero Universitaria delle Marche, Ancona

Background: On December 03rd, 2021, Ancona signed the Paris Declaration becoming a Fast Track City (FTC) thanks to the cooperation of different association and the municipality. Checkpoint, opened in March 2022, offered rapid STIs tests and free peer counseling promoting a conscious sexuality and access to care for all. The Ancona Checkpoint adhered to community-based testing (COBATEST) network that linked the community-based voluntary counselling and testing (CBVCT) centers promoting STIs tests in Europe and collecting information on reasons for testing, risk behaviors and screening test results.

Material and Methods: Clients scheduled an online anonymous appointment for rapid capillary blood tests: HIV (Ab and p24 antigen detection), HCV (Ab detection) and Syphilis (Ab detection). A trained operator compiled, with client, the COBATEST questionnaire. Tests and questionnaire were free and anonymous. We analyzed data obtaining between March 2022 to March 2023.

Results: In a 12-month period, 540 subjects accessed the service. The population was characterized by 60.56% male, 38.70% female and 0.74% transgender with a median age 29.66, 26.72 and 40.98 respectively. Overall, 84.81% of subjects referred to be Italian and 15.19% of foreign nationality. Reasons for testing were: 16.22% of subjects had risk exposition (36.67% for unprotected vaginal sex, 18.89% for unprotected anal sex, 13.33% for unprotected oral sex), 80.54% for control or screening and 2.88% for other reasons. Limited to subjects with a sexual intercourse in the last 12 months, 20.37% were MSM, 68.7% were heterosexuals and 5.19% did not respond or had no sex. In addition, 50.74% did not use condom in the last penetrative sex. A small percentage of subjects (33.15%) had heard about PrEP of which 67% never consider using it. Knowledge of the Ancona Checkpoint existence was in a large percentage due to the web-based research. During this period a total of 540 HIV tests were performed of which 0.56% were reactive, 100% with a positive confirmatory test and immediately linked to healthcare system. 1.67% and 0.37% of tests performed were syphilis and HCV reactive respectively. The percentage of reactive STIs tests was particularly high among transgender (50%). Those considered foreigners had a higher percentage of reacting screening tests (8.54%) compared to non-foreign born (1.53%). Regarding the transmission group, the higher percentage of reactive screening tests was for MSM with a percentage of 10%.

Conclusions: Our results, together with other studies indicate that check-point service can be a powerful instrument to provide access to STIs testing for high-risk populations such as MSM. Also, counseling represents an additional tool among prevention strategies and sexual health education. Efforts should be concentrated to create structured screening campaigns and to shorten the time between infection and diagnosis improving the activities of our checkpoint.

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P 268 PRISONERS LIVING WITH HIV. RETROSPECTIVE ANALYSIS THE CASCADE OF CARE IN TWO PENITENTIARIES IN NORTHERN ITALY

A. Cambianica[1], F. Pennati[1], A. Faustinelli[1], I. El Hamad[1], F. Roda[2], I. Rossetti[2], B. Fioretti[1], S. Arsuffi[1], S. Fiorentini[3], E. Quiros Roldan[1], F. Castelli[1], E. Focà[1]

[1]Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy, [2]Unit of Prison Health ASST Spedali Civili Hospital, Brescia, Italy, [3]Unit of Microbiology and Virology, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

Background: Compared to the general population, people in prison have a higher prevalence of communicable diseases, including HIV. According to international guidelines, HIV screening should be offered to all people in prison and combined antiretroviral therapy (cART) should be granted to all prisoners with HIV (PrWHIV). However, available data regarding HIV management in prison settings are scarce. Here, we offer an insight of the cascade of care of HIV in two penitentiaries in Brescia, Northern Italy.

Material and Methods: The city of Brescia has two correctional facilities. At admission, a voluntary screening for HIV, HBV, HCV and syphilis is proposed to all prisoners. Treatment and periodical immuno-virological assays are offered to all PrWHIV. Those with positive results at screenings or known HIV infection are referred to the Infectious Disease specialist that performs in-prison consultations. To ensure continuum of care after release, the patients' file is linked to that of the ID Unit. We performed a retrospective observational study including all the subjects admitted annually to the penitentiaries from 01/01/2015 to 31/10/2021 who accepted screening and/or had HIV infection. Socio-demographic, viro-immunological and therapeutic information were analyzed.

Results: During the study period, 5378 accesses were registered. At admission, 2945 (54.8%) screenings for HIV were performed, with a mean of 420.7 tests per year. Overall, 108 PrWHIV were included, 86 (79.6%) of which were already followed at our outpatients' clinic, while 2 (1.9%) were newly diagnosed though screening and 9 (8.3%) were followed at other clinics, previous history is unknown in 11 (10.2%) cases. The number of people who received cART since admission increased from 66.7% (22/33) in 2015 to 92.9% (26/28) in 2021. On the contrary, people not on cART decreased from 6/33 (18.2%) in 2015 to 2/28 (7.1%) in 2021, most of them having self-suspended treatment before admission. The number of virally suppressed patients increased from 40.0% (12/30) in 2015 to 84.0% (21/25) in 2021. Data about CD4+ cell count were available in 58.3% of the cases: sufficient immunological control was obtained in most of the patients during the study period, 67.3% of them having more than 500 cells/ul (Fig. 1). The administration of PI-based regimens was reduced during the years in favor of INSTI-based ones (64% and 28% in 2015 vs. 16% and 60% in 2021 respectively). After release, the percentage of patients retained in care was 65.9%.

Conclusions: We observed poor screening acceptance, which could be improved by opt-out testing strategies. At the end of the study, among PrWHIV, only cART administration reached the 90-90-90 WHO goal, on the contrary more efforts are needed to increase compliance to therapy and thus viral suppression. Retention in care after release was low and may benefit from direct linkage to health structures.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 269 FIFTH YEAR OF MONO SYMPTOMATIC THERAPEUTICAL GROUP FOR CHEMSEX ADDICTION, A ROUNDUP

G. Fracca, M. Manfredini

ASA Associazione Solidarietà AIDS Onlus, Milano

Scope: to offer a place of cure and treatment inside the Milan MSM community, held by a volunteer and a professional psychotherapist.
Objective: to focus on the peculiar elements and dynamics that make the MSM community (and some individuals in particular) vulnerable to problematic chemsex, in order to find specific approach for best practices aimed to cure the addiction.
Description: a weekly semi-open group, aimed mainly but not exclusively to people living with HIV; it has been advertised on the association magazine and website, fliers in gay venues in the Milan area, in HIV clinics, and on grindr. The project had such an echo outside the community that local and national tv and press helped spread the news of its existence.
Over the 5 years we have met over 100 persons and had the chance of identify (locate) some recurrent elements in the structure of personality of MSM that experience problematic chemsex (internalized homophobia, self loathing, loneliness, non affective sexuality among others). We have identified different approaches aimed at freeing the participants from stigma and self-blame by focusing on the cultural and social origins go some of these problems, which can be shared by the whole group, and to possible individual, subjective declinations, which can be rooted in the individual history of each participant.
The structure of the group is the same as the well known “mono symptomatic therapeutical group” used of other addictions such as eating disorders or gambling with some small changes meant to adapt it to the specific needs of our users.
The sharing of experiences and attributions of meaning to the use of substances, and to one's own specific experience is one important step that helps participants to feel empowered and creates authentic interpersonal relationships. Thought the interpretations of the different experiences and affections participants are accompanied to create a new, more positive representation of themselves themselves in their own narrative.
Lessons learned: Due to the specific side and cumulated effects of MDPV such as psychotic and paranoidal episodes, group confrontation appears to be a much more effective tool to control and normalize these feeling, rather than individual therapy.
The synergy between professional figure and a member of the MSM community (although not technically a peer, as not a chemsexuser) has turned out to be fundamental to bridge potential cultural gap between users and therapist. In some cases psychopharmacological support is necessary, it is therefore important that each organization structures itself with one or more psychiatrists informed on this specific addiction.
The setting within an established and historical organization in the Milan MSM scene, helped create a friendly environment that helps participants talk freely, without fear of being judged or stigmatised.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 270 MAPPING THE STATUS OF SERVICES IN THE FIELD OF SEXUAL HEALTH AND HIV MANAGEMENT IN THIRTY-ONE PROVINCIAL CAPITALS OF ITALY

C. Urciuoli, M. Costacurta, M. Marocco, I. Pennini

Arcigay, Bologna

Despite the growing institutional sensitivity towards the inclusion of LGBT+ people (UNAR, 2022; EC, 2018), research on specific populations and community-based services remains marginal in Italy (Aresi, Cuccì, 2018; Van Der Meulen, Muffels, 2016). The present study, which enlisted the participation of the Arcigay territorial network, partially fills this gap by offering a map detailing the current state of services in the field of sexual health and HIV management.

The mapping work was configured as an action research aimed at monitoring healthcare services used by LGBT+ individuals or directed towards them, which allowed for the acquisition, through a judgmental sampling, of data from 31 Italian territories.

Data was collected by the association's operators throughout the national territory between the second and third quarters of 2022 using public communication channels of services. The survey was conducted through a questionnaire divided into nine collection sheets, each for a service category: HIV centers/clinics; Services for people living with HIV; IST & blood sampling centers; PreP, PEP, Vaccines; Psychological, Chems, SerD/SerT, Prisons; Private Social; Local associations health serv.; Local advocacy.

A focus group with operators on the difficulties in obtaining information served to provide an interpretative key to the data.

The situation is problematic, with no differences between North and South, but rather between regional capitals and provincial towns. The former typically serves as a point of reference for services that are lacking in provincial structures and is the destination for cases requiring specialized care: a significant problem for emergencies requiring local services, particularly when the regional capital is – as it happens in most cases - far away.

Exceptions are the large metropolitan cities (Milan, Rome), with a more widespread and diversified distribution of healthcare facilities.

In the last 3 years cases of discrimination have been reported in 19 of the 31 territories examined.

Specific services such as PEP or PrEP are poorly institutionalized or completely absent. In some cases they are contrasted or linked to the sensitivity of a single person who allows, provided that he is present and also through informal channels, the activation of such services.

Vaccination policies for the MSM people are implemented in a very heterogeneous way across the territory, with excellent services in some areas and significant shortcomings in others. Only in Padua and Livorno reception points are provided by private social entitled to problematic Chemsex.

The positive relationship between social actors improves the efficiency of the services provided to the LGBT+ community. The need to institutionalize and extend the work carried out on a national scale was immediately deemed appropriate, not only for the involvement of institutions but also for the benefits brought to the organization of advocacy services dedicated to health.

Attach: https://www.icar2023.it/public/abstract/Attach_ABS_133.png

Social and behavioural science, marginalized groups, community aspects and community surveys

P 271 TAKING IT TO THE STREETS: HIV PREVENTION FOR DRUG USERS THROUGH OUTREACH UNITS IN ROME IN 2022

G. Rodoquino[1], D. Masci[1], B. Colardace[1], P. Sammarco[1], T. Di Giovanni[1], F. Alessi[2], E. Rossi[1], M. Barra[1], M. Zaccarelli[1]

[1]Street Unit and HIV/Infectious Diseases Unit, Villa Maraini Foundation, Italian Red Cross, Rome, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome

Background: The WHO objective to reduce new HIV infection to Zero by 2030 has an intermediate ambitious 2025 target to achieve new 95–95–95 testing, treatment and viral suppression within all demographics, sub-population groups and geographic settings. The 2025 target includes interventions for people who use drugs (PWUD), both injected or non-injected: peer approach, syringes and needle exchange, condoms distribution, overdose interventions, HIV/HCV testing and counselling both for PWID and other population groups, referral to health and social services.

Methods: The Villa Maraini Foundation (VMF), now National Agency for Addictions of the Italian Red Cross, offers a wide range of services with a staff of physicians, psychologists and former IDUs: therapeutic community, OAT, low threshold drop-in and alternative to prison residential center. In order to achieve WHO objectives, both onsite and through two active mobile units within the city of Rome, the organization provides screening for HIV/HCV both for PWUD and other vulnerable population groups as well as linkage to care for patients resulted positive. The Street Unit also offer other specific interventions to reduce transmission among PWUD.

Results: Overall, in 2022, 914 individuals underwent rapid testing both for HIV and HCV, moreover, 50 rapid tests for syphilis were also executed. Only people unaware of their serostatus or previously negative were tested. All subjects who underwent testing, also responded to a short anonymous questionnaire about sexual behaviors and drug use. Four new HIV positive and 33 new HCV positive patients were identified (prevalence 0.44% and 3.61% respectively).

All positive patients were linked to a reference center, and all started specific therapy. More than 2500 information leaflets and over 3000 people received specific counselling about HIV/HCV transmission; 90 patients asked to be followed on-site for psychological support.

In 2022, the staff of Street Unit performed 49 full-blown opioid overdose interventions, using antagonist drugs, and other 311 PWID were assisted for initial overdoses; they distributed 109,249 syringes and 1,187 condoms and collected 88,413 used syringed. Finally, 152 heroin users were sent to the outpatient clinic of VMF for OAT, that has a user service area of about 750 PWUD, with >300 taking methadone daily.

Conclusions: The outreach activity of the VMF has objectives that are in accord with WHO indications for reducing HIV transmission among PWUD and other vulnerable populations. The use of HIV/HCV rapid testing in outreach settings as an effective tool to facilitate access to screening for those ‘out-of-care’ populations, thus ensuring appropriate linkage to care through the collaboration with reference centers for HIV treatment. The high number of people contacted and tested, the overdoses managed and the large amount of syringes collected and exchanged is a demonstration of the usefulness of the program that is ongoing.

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P 272 BREAKING BARRIERS TO HIV AND HCV SCREENING AMONG MIGRANTS IN ROME

D. Masci[1], P. Sammarco[1], T. Di Giovanni[1], G. Rodoquino[1], G.D'Ettorre[2], A. Tullio[1], B. Coladarce[1], E. Rossi[1], M. Barra[1], M. Zaccarelli[1]

[1]HIV/Infectious Diseases Unit & Street Unit, Villa Maraini Foundation, Italian Red Cross, Rome, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome

Background: The use of HIV and HCV rapid testing in in- and outreach settings is an effective tool to facilitate access to screening for marginalized and 'out-of-care' populations, thus identifying positive people and implementing appropriate linkage to care, available through collaboration between treatment reference centers and other Public Health services.
The decentralization of services for HIV/HCV prevention and screening appears necessary in order to achieve the WHO objectives of 95-95-95 for HV and elimination of HCV.
Among vulnerable people, migrants are of relevance for high prevalence and difficulty of reaching.
Methods: Villa Maraini Foundation, with a activity targeted to PWUD, is the National Agency for Addictions of the Italian Red Cross.
The organization is involved in national and international screening campaign for HIV and HCV involving a staff of trained physicians, psychologists and former IDUs. The screening activity started in 2017, both testing onsite the PWUD attending the structure for drug-related treatment as well as, through street unit, with targeted exits addressed to fragile populations, of whom migrants are a crucial subgroup.
The test is free, anonymous and voluntary, it is performed in patients who were previously HIV/HCV negative or unaware of their serostatus.
Results: Overall, 5615 individuals undergo rapid blood test from January 2017 to December 2022, of them 1113 were migrants. The HIV-Ab prevalence among migrant was higher than that found in the Italian citizens tested in the same setting (12/1094, 1.1% vs. 22/4657, 0.5%, p=0.02 at Fisher test). The prevalence of HCV-Ab was also higher as compared with Italians (51/1026, 5.0% vs. 22/4567, 3.3%, p=0.01).
The overall caracteristics of the migrants screened are reported in table 1. The number of subjects tested was lower in 2020-2021 due to pandemic.
Two thirds of migrants were males 4.1% transgenders, they were a young population (median age 32 years), about one third were from East Europe, 7,1% sex-workers, 12.0% reported drug use (3.9% injected). All positive migrants were linked to a reference center in Rome for treatment, overcoming administrative problems.
In general, the screening was well-accepted and raised interest, particularly regarding ways of transmission and preventive measures for HIV and HCV. Lack of knowledge about this topic was evidenced, mainly related to cultural models of many countries, where talking about sexual behavior or drug use is still considered a taboo. This represented a barrier also for the administration of the risk assessment questionnaire, since often people felt embarrassed about questions on sexual practices and drug use.
Conclusions: Despite religious, cultural and language barriers, the high number of positive tests in migrants, found and sent to treatment, supports the need for HIV/HCV screening activities in these subpopulations. The Villa Maraini testing program for marginalized populations is ongoing.

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P 273 TRANSGENDER AND HIV: A CASE FOR AN INCLUSIVE CLINICAL RECORD

L. Brogonzoli[1], M. Errico[2], A. Moznich[2], M. Cascio[2], M. Formisano[2]

[1]Fondazione The Bridge, Milano, [2]NPS Italia aps, Milano

Background: Current health literacy provides evidence of the need to adapt inclusive clinical records; the lack of inclusive tools accentuates the health inequities of the LGBTQIA+ community, starting with the lack of diversity in clinical research data.

As to the transgender population of people with HIV, there is a lack of information, starting from numbers; one of the reasons is linked to the binary approach to clinical records; such approach discourages access to preventive screening and to healthcare services by people who already often experience intersecting stigma, forcing them to maintain a high level of privacy as to identity and clinical condition, penalizing well-being and quality of life.

There are very few experiences in the field, inexistent in Italy.

Material and Methods: NPS Italia has conducted a project aimed at designing a model of inclusive clinical record in HIV.

A multidisciplinary group was set up which, after conducting a literature review, has created a possible model and produced support materials for guidance to clinicians and information to patients.

Following a training course to a group of clinicians, an inclusive clinical record was piloted in three clinical centres using the model for their transgender patients .

Finally, an evaluation of the proposed model was carried out highlighting critical issues, replicability and usability (analysis 27 compiled records) and satisfaction of patients and clinicians (questionnaire)

Results: The international literature review has allowed to extrapolate some recommendations, not all applicable to the Italian context.

The sample was characterized by a strong polarization of AMAB and binary patients, reflecting a willingness to formalize a medical transition pathway; most had already/intended to start a gender affirming pharmacological and/or surgical pathway. More than 50% experienced STI. All were adherent and virally suppressed.

The questionnaire administered to clinical centers has shown a general agreement on the usefulness of making clinical records inclusive and has also shown a positive feedback form patients.

Our analysis has allowed to identify some initial considerations, reviewing the initial model in favor of a system characterized by explicit options and a Two Step process that also includes capturing clinical information related to gender affirming pathways.

Conclusions: Feedback from clinicians indicate strong agreement on the benefits of using an inclusive clinical record as a future management tool. Nevertheless, there is a need for campaigns to raise awareness on the topic directed to healthcare staff and an ad hoc training. The emerging results, even if statistically not relevant, encourage the introduction of such inclusive model in clinical practice.

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P 274 U=U. COSA SAI, COSA NON SAI

A. Zottino[2], M. Cascio[1], M. Errico[1], G.P.Turchi[2], N. Giovannelli[2], D. Manfredotti[2], M. Pellizzato[2], G. Balcan[2], V. Landi[2], A.Moznich[1]

[1]NPS Italia Aps, Milano, [2]Università di Padova, Padova

Background: The research, called “U=U. Cosa sai, cosa non sai”, aims to observe how the community describes a “person with HIV”, framing it under the scientific concept of U=U. This study allows to behold the value of HIV narratives and if it opens to new possibilities, based on the participants’ consideration of HIV as a factual and stagnant reality or as a changeable reality. Moreover, in light of this, anticipating pragmatic fallouts of these discursive productions becomes possible, especially in terms of health promotion and decreasing stigma towards “people with HIV”.

Materials and Methods: The research involved 193 participants, 62 of them were HIV-positive while 131 were HIV-negative (see Table 1) - recruited consensually through social media - to whom an anonymous and open-ended questions protocol was administered in order to detect the language’s use modalities used by participants to describe the positive serostatus considering also U=U concept. Textual data were analyzed using the MADIT methodology, which allows to observe language’s use modalities through the Semi-radial Table of Discursive Repertories (see Figure 1). The language’s use modalities can be distinguished in three classes: stabilization (they tend to offer a unique and hardly changeable narration), generative (they tend to offer a multiple, changeable and open to new possibilities narration), and hybrid (they tend to associate to stabilization or generative modalities increasing their tendency to stability or generativity).

Results: From the textual data analysis a narration tending to a unique and unchangeable vision of HIV emerged - characterized mostly by stigma, discrimination and social isolation - generated by a predominant use of stabilization modalities (see Graph 1, Graph 2, Graph 3). In fact, the capability of producing multiple and changeable narrations measured through MADIT, was medium-low, equal to 0.4 within a scale ranging from 0.1 (maximum stabilization) to 0.9 (maximum generativity) (see Table 2).

Conclusion: The prevalence of stabilization modalities fallouts consists of limiting what could be said regarding HIV exclusively to participants' absolute and static positions (“it is so and could not be otherwise”). This restricts the possibilities of promoting the dissemination of new and health-oriented HIV narrations and highlights how the U=U principle has not yet spread in the community. Therefore, designing interventions to disseminate this principle is necessary in order to encourage open-to-new-possibilities narrations about HIV, contributing to health promotion.

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P 275 LILA TESTING SERVICES IN 2022: OBSERVATIONS FROM EXPERIENCES OF OUR NETWORK

S. Bellini[1], G. Dessi[1], A. Leoni[2], E. Sosio[2]

[1]LILA Nazionale Onlus, Como, [2]Fondazione LILA Milano Onlus, Milano

Background: LILA examined some data from the HIV and STI rapid test services offered by its network in 2022. The services follow the CBVCT (Community Based Voluntary Counseling and Testing) model currently recognized by the Act of the Ministry of Health of 17 March 2021. This exposition examines some data that underline the importance of implementing this type of services.

Methodology: The anonymous and free service is organized with timetables that facilitate access, with broad daily coverage, openings on weekends or in the late evening. Active and non-judgmental listening and the absence of discrimination are the characteristic of the LILA approach. The data was collected through questionnaires provided by trained operators and volunteers during the interview that precedes the execution of the test. The objective of data collection is user-profiling aimed at obtaining information useful for improving prevention actions.

Results: In 2022 LILA reached 1836 people: 18.1% arrived in our services through the positive spread word by friends which is the second source of knowledge of the service, after the internet and social networks. 59.4% of users had tested for a screening check. In particular, 41.1% of users performed the first HIV test in his life. It is interesting to note, compared to the past, the increase in heterosexual users who represent 61.2% of the total and the increase in the number of women (among them, for 52% it was the first meeting about HIV prevention).

Conclusions: Although the restriction of access with a booking system adopted in 2020 due to the Covid-19 pandemic is still in use, requests are reaching numbers comparable to those prior to the lockdowns, demonstrating the usefulness and good functionality of the service. Looking at this data, it can be noted a consolidation of the habit of testing oriented towards sexual well-being, across the general adult population, also the result of a progressive reduction of the stigma towards HIV and STI tests. Therefore it is desirable that the CBVCT method will be further encouraged and supported by institutions with dedicated investments.

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P 276 THE RELATIONSHIP AS OUTCOME INDICATOR: PERSON-BASED APPROACH IN ROME

P. Sammarco, D. Masci, T. Di Giovanni, G.Rodoquino, B. Coladarce, R. Sista, E. Rossi, M. Barra, M. Zaccarelli

HIV/Infectious Diseases Unit & Street Unit, Villa Maraini Foundation, Italian Red Cross, Rome

Background: The Villa Maraini Onlus Foundation, created by Dr Massimo Barra, has been committed to assisting drug users (PWUD) since 1976 and is the first addiction hub in Rome, capable of reaching out to hundreds of people every day, increasing their chances of survival and supporting their access the healthcare system for care and therapy.

PWUD are at greater risk of acquiring and transmitting several infectious diseases, particularly hepatitis C and HIV, related to both drug using practices and unprotected sex, behavior that have significant implications of public health.

Methods: Through the 24-hour onsite Street Unit and Outpatient Clinic, with a team consisting of physicians, psychologists and social and health worker, frequently former drug users, the Foundation offers rapid testing for HIV and HCV and is active 7 days a week. Upon admission, a questionnaire regarding medical history and risk behaviors in the previous months is administered and pre- and post-test counseling is offered. In case of a preliminarily positive test, the team communicates the result, and the patient is sent and often accompanied to a clinical center for confirmatory testing and initiation of treatment with a fast truck route.

Regular follow-up interviews are performed to assess the degree of satisfaction and adherence to treatment.

Results: In 2022, the structure contacted 6,220 individuals, 914 were tested for HIV and HCV, and over 5,000 psychological consultations were conducted both on site and at the street unit. The level of information concerning HIV risk behaviors was generally higher among the LGBTQ and PWUD sub-populations, while the lower knowledge was found in the young people (under 25 years of age). In all patients, a higher level of information was registered at follow-up.

Individuals who were tested positive for HIV and HCV were accompanied to a reference center for confirmation testing. All positives began specific treatment and were supported with advocacy activities in obtaining benefits and bureaucratic processes.

At follow-up, a high level of satisfaction was observed, along with an increased ability to engage with the healthcare context and greater awareness of their own psycho-physical conditions.

Conclusions: The daily commitment with patients belonging to fragile populations is an intense and emotionally engaging activity for the operators of the Villa Maraini Foundation. An approach that involves adapting therapy to the individual, with particular attention to those who are in a condition of greater fragility, thus called 'hard to reach', is adopted and the possibility of establishing a relationship of confidence with them thanks to the daily work into this field. The use of relational strategies aimed at accompanying the person with the activation and reorganization of personal resources improves adherence to treatment and the effectiveness of prevention strategies.

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P 277 "RESILIENCE" – STUDY ON THE PSYCHOLOGICAL AND PRACTICAL IMPACT OF COVID-19 ON THE QUALITY OF LIFE OF PEOPLE LIVING WITH HIV

S. Penon[1], M.L. Cosmaro[1], S. Curridori[1], M. Oldrini[1], D. Savarino[1], S. Mazzilli[2]

[1]Fondazione LILA Milano, [2]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Background: This participatory research, funded by Gilead Community Award 2021 and conducted between 2021 -22, aimed to identify problems that PLHIV had during the first 2 years of the Covid-19 pandemic and possible impact on their mental health due to prolonged lockdowns, social distancing and isolation, fear of acquiring the new disease. Issues related to access to HIV care were also investigated.

Materials and Methods: The study was a cross-sectional participatory research conducted by LILA Milano in 3 phases: (i) a focus group on living with HIV during the pandemic, to collect preliminary information analyzed using thematic analysis; (ii) 12 semi-structured interviews with PLHIV that further investigated themes emerging from the focus group. (iii) a self-administered, anonymous survey disseminated via Google Forms and promoted through LILA's and other NGOs' websites and social media (Aug –Oct 2022). The survey investigated items emerging from the transcripts of the interviews, including: anonymous demographic information; the impact of COVID-19 pandemic on everyday life, access to healthcare, psychological wellbeing and sexual life; sources and quality of information during the pandemic; living with HIV during a new pandemic.

Results: Sample included 171 PLHIV: 26.3% cis women, 72.5% cis men and 1.2% trans women (demographics in attachment). 73.7% respondents reported negative impact of Covid-19 on daily life and 65.5% did not fully recover previous lifestyle. 44.4% agreed that lockdowns influenced number and frequency of sexual acts. Regarding access to HIV care, only 27.5% PLHIV reported negative changes during the pandemic and 73.1% referred no changes in ARV supply. Many declared being satisfied with their HIV specialist (53.8%), general practitioner (45.0%) and hospital management (48.0%) during the emergency. 51.5% affirmed that information spread by mass media was scary. 24% indicated negative changes in access to mental health services. Mean psychological health self-rating was 7.2 (SD: 2.0) during the pre-pandemic period and did not change after two years of pandemic: 7.1 (SD 1.9). 65.5% stated that having HIV prepared them to face the pandemic; 43.9% feared being exposed to greater risks for being HIV positive. 71.9% did not believe that stigma towards PLHIV decreased because of Covid-19.

Conclusions: PLHIV reached through this Italian study proved to be resilient, in line with similar research conducted abroad. Biases related to the small sample - likely in contact with NGOs/NGO websites and more empowered than others - have to be taken into account when analyzing the results. While no major problems emerged in access to HIV care, a minority of respondents had difficulties which need to be addressed. Persistence of stigma, preventing PLHIVs from having positive social and emotional relations is worrying: especially during interviews, many reported not to have suffered from isolation because used to experiencing solitude and loneliness.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 278 CONSCIOUS SEXUALITY AND YOUNG PEOPLE: LET'S TALK ABOUT HIV

A. De Faveri[1], V. Simeone[2]

[1]Anlaids Torino, Torino, [2]Anlaids Torino, Torino

Background: HIV and other STI's are still recognised as a public health problem and, for this reason, it is important to raise awareness of risk behaviours among the younger population and how to protect themselves against infection.
HIV and, more generally, sexual health are topics that are not as widespread as they should be, especially within the school context.
Progetto Scuola Torino works within the school environment to promote a culture of prevention and risk limitation about sexual behaviour in young adolescents.
The objective of Progetto Scuola Torino is to give the opportunity to young people, between the ages of 13 and 18, to address the topic HIV/IST in order to prevent its widespread.
Materials and Method: The sample taken into consideration by Progetto Scuola Torino consists of students (13 -18 years) of 5 Secondary Schools of I and II grade of Piedmont and Aosta Valley.
Initially the theoretical and audiovisual material to be used with students were prepared and selected , 5 schools were contacted and a calendar of meetings was prepared.
The trainers, young volunteers prepared for the meetings by Anlaids Association, met the students in their classes, for a total of 2 hours for each section.
Before and after the meeting, the students were asked to fill in an anonymous questionnaire to evaluate their previous knowledge and the knowledge subsequently acquired and their perception of the usefulness of the meeting.
The meetings followed a non-formal approach and were focused, mainly, on the distinction between HIV-AIDS, and some of the most widespread STIs, how to protect both themselves and others and when and where to carry out screening tests.
Results: From the answers to the questionnaires it emerges that students have acquired or consolidated information on how to protect themselves (condom and PrEP), when to do the test and on the low incidence of HIV mortality. The majority of students believe that the meeting was useful but also that their behaviour will not change after the meeting, which can be explained by the fact that about 84% of the students have not had sexual intercourse yet.
From the questionnaires we also read that about 48% of teenagers would like to talk about sexuality and its functionality in class and that 19.5% of them would like to deepen the management of emotions and feelings.
Conclusion: The meetings in the schools underlined the desire of students to address issues concerning sexuality and interpersonal relationships. The educational offer at school does not provide enough space and time to deepen the themes, so it should be established as an informal space outside school in which young people are able to talk about sexuality.
In order for the theoretical information provided to the students to materialise in field experiences and become so meaningful, it would be important to organise their participation in the informal contexts of the testing evenings.

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P 279 HOW MUCH DOES STIGMA WEIGH IN A MORE INFORMED SETTING? AN ONLINE SURVEY

D. Calzavara[1], R. Rossotti[1,2], G. Federico[3], D. Iannacone[3], D.Buselli[3], S. Bossolasco[1,4], E. Caruso[1], M. Cernuschi[1,4,5]

[1]Milano Check Point ETS, Milano, [2]Grande Ospedale Metropolitano Niguarda, Milano, [3]Gay.it, Milano, [4]IRCCS Ospedale San Raffaele, Milano, [5]ASA Milano ODV, Milano

Background: Despite scientific progress in the management of HIV infection, stigma against people living with HIV (PLWH) still remains a social issue. It is believed that the LBTQ+ community has more sensitivity and greater acceptance for PLWH, but clear evidences in the Italian setting are lacking. Aim of the present study is to measure the level of stigma in this population.

Method: A survey was launched on Gay.it webpage from Nov 24, to Dec 08, 2022. People who access Gay.it's online header are largely LGBT+ or close to the community. The questionnaire was based on a simplified Visser's PRO's Three parallel scale: 12 questions with the option to respond with a value between 1 (not at all agree) and 10 (completely agree). The cumulative score ranged from 12 (no stigma) to 120 (full stigma). Demographic characteristics (age, gender, sexual orientation and education level) were collected. Descriptive statistics and non-parametric tests were used to depict study population. Factors associated to a higher score (i.e., a higher stigma) were tested by mean of Poisson regression.

Results: The survey involved 909 respondents, mostly cisgender men (69%) and women (21%) with a median age of 34 (IQR 24-46) years. Only 11% had heterosexual orientation. Level of education was high (48% had university degree). Study population showed low stigma with a mean score of 21 (IQR 16-27): 15% resulted having no stigma at all. Respondents reported medium/low stigma for all topics, except for the question I think an HIV-positive person should warn me before meeting up for sex, where the mean response was 8 (IQR 3-10). The Poisson regression found that being a trans woman (IRR 0.77, 95%CI 0.63-0.94, p=0.009) and age (IRR 0.98, 95%CI 0.97-0.99, p<0.001) were protective towards stigma, while being gender nonconforming (GNC, IRR 1.31, 95%CI 1.20-1.43, p <0.001), cis male (IRR 1.15, 95%CI 1.09-1.20, p<0.001), bisexual (IRR 1.27, 95%CI 1.10 -1.45, p=0.001), pansexual (IRR 1.22, 95%CI 1.06-1.41, p=0.006), and straight (IRR 1.23, 95%CI 1.07-1.42, p=0.003) were significantly associated to a higher stigma score. Applying the same regression model to the question about partner disclosure before a sexual intercourse, being GNC (IRR 0.81, 95%CI 0.67-0.99, p=0.036) and age (IRR 0.92, 95%CI 0.90-0.94, p<0.001) were associated to a reduced stigma. A lower level of education showed a trend towards a worse score (IRR 1.08, 95%CI 0.99-1.19, p=0.098).

Conclusions: In an informed environment such as that of the Italian LGBT+ population and allies, it appears that stigma persists even if at significantly lower levels than in the general population. The only question that showed low acceptance was about sexual partner disclosure suggesting that there is still a lack of knowledge about U=U. Therefore, educational and awareness actions are essential to break down stigma even in populations that are supposed to be mostly involved and educated on this matter.

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P 280 DIFFICULT TO REACH, FRAGILE KEY POPULATIONS AT HIGH RISK: THE BERGAMO LEAVES NO ONE BEHIND PROJECT

D. Meli[1], P. Meli[1], I. Mercurio[1], F. Maggiolo[2], E. Risi[3], M. Gotti[3] F. Defendi[4], Stefano[4], M. Del Vecchio[5], E. Recanati[5], A. Sarzi Sartori[6], M. Vitali[7], N. Butta[8]

[1]Don Giuseppe Monticelli Società Cooperativa Sociale, [2]ASST Papa Giovanni XXIII, [3]La Melarancia ODV, [4]Fondazione Opera Diocesana Patronato San Vincenzo, [5]Cooperativa di Bessimo Onlus, [6]Fondazione Opera Bonomelli Onlus, [7]Caritas Bergamasca, [8]Arcigay Bergamo Cives

Background: The Bergamo Fast-Track City network started its work on education, information and testing on STIs and HIV proposing tests in public events and in a structured checkpoint. However, it was soon clear that fragile key population might have difficulties in accessing the network.
Methods: The project “Bergamo leaves no one behind” makes available to key populations such as sex-workers, IVDU, migrants, homeless that hardly or not at all interact with structured entities, information about and free tests for STIs and HIV and immediate support. After a training period for volunteers, a structured program has been set up to bring HIV, HCV and syphilis tests in places where these key populations usually gather. The proposal tries to ensure an optimal diffusion of tests in all city contexts. The test is coped with Cobatest questionnaire, which collects personal and behavioral data, previous infections and awareness about STIs and social stigma. In the case of a positive test or of a known infection, volunteers of the project offer help to start the therapeutic process and to favor retention in care.
Results: Six social services dealing with key populations such as sex-workers, IVDU, Migrants, homeless are involved in the project. The test is offered in 7 locations for an average of 23 days a month. Since October 2022, we met 192 people, 182 of whom seeking for testing and 10 asking us treatment support. Among the latter, 5 turned to us asking to be reconnected to treatment and 5 referred difficulties in accessing hospital facilities. Out of the 182 people tested, 6 turned out positive for HIV, 25 for HCV and 6 for syphilis [Panel A]. These data also include people who, aware of their health situation, still wanted to undergo the test. As a matter of fact, only 3 HIV positivities were new diagnoses, 2 of new diagnosis were been linked to care. Six out of the 25 hepatitis C were new diagnosis, three of which were linked to treatment. Among the remaining 19, 15 people were already cured, 4 were diagnosed but never got treated, but only 1 of them accepted to be treated. Finally, out of the 6 positivity to syphilis, the new diagnosis were 4 and all have been successfully linked to care [Panel B].
Conclusion: Our data indicate a positive trend for the Bergamo Leaves No One Behind project. Despite the difficulties in reaching the most fragile populations, we encountered 192 people in the first months of the project. Twenty-seven needed support to access hospital facilities to be treated, 20 effectively started therapy in hospital after testing positive or after turning to us for support (10). A surprising fact is that a few PLWH found in the project a way to re-engage with treatment or to decide to start it. The 7 persons who didn't show up for appointments or who expressed the desire not to treat thier infection, most had previous untreated diagnosis. Hooking up to the care these people will be a further objective in the upcoming months.

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P 281 THE TWO FACES/DIRECTIONS OF THE BERGAMO CHECK POINT: YOUNG PEOPLE AND KEY POPULATIONS

P. Meli[1], D. Meli[1], C. Pellegris[2], F. Maggiolo[3], S. Venturelli[3], I. Mercurio[4], N. Butta[5], R. Carissoli[5], F. Radici[5]

[1]Don Giuseppe Monticelli Società Cooperativa Sociale, [2]Associazione Comunità Emmaus, [3]ASST Papa Giovanni XXIII, [4]Croce Rossa Italiana – Comitato di Bergamo, [5]Arcigay Bergamo Cives

Background: Since 2019 Bergamo has joined the Fast Track City network. One of the main actions developed is the activity of testing for HIV, HCV and Syphilis, which is proposed in a specific location (check point) and on the territory in different settings.
At the network joined 6 public institutions and 13 NGOs and the contribution and specific experience of each one are fundamental to work on the territory, increasing the capacity of the network to deal with the HIV issue.
Materials and Methods: Since November 2021, through the Cobatest questionnaire, we have collected anonymous socio-demographic data and some about sexual health care habits and risk appetite of the population that did the test. From 2019 to 31st March 2023 we met n. 4530 people, carrying out n. 4514 tests for HIV and similar for HCV and Syphilis. The questionnaires collected concern 2124 answers.
Results: Analysing the data from November 2021 to the end of December 2022, 57% of the population is less than 30 years old and most of these are female (Panel A).
42% knew the service in another ways those presented by the questionnaire (Panel B):
- 361 people (16%) met us thanks to an email sent by the Consulta of University of Bergamo twice a year during the European Testing Week and on the occasion of the promotion of the test at university;
- 79 students (8%) decided to take the test after participating in training courses organized at their high schools on the theme of HIV at the check point or directly during two events organized at the same schools.
At the end of 2022, we make a collaboration with the Centro Provincia Istruzione Adulti of Bergamo, which organizes Italian and middle school diploma courses towards an almost completely foreign population. After organizing informative meetings with 540 students, 20% of them took the test directly at school.
The incidence of test reactivity in the youth people is almost nil.
For the key populations we started a project that, in the last three months of 2022, allow us to meet 192 marginalized people (sex workers, DU, homeless, migrants), which allowed us to achieve 6 HIV, 25 HCV and 6 syphilis positivity, attacking people with new infections at the hospital and helping to hang up those who were not being treated or struggling to maintain the therapy (Panel C).
Conclusion: The implementation of different ways of promoting and offering the test allows us to reach the entire population and the collaboration between institutions and NGOs is the key.
Among the younger people there is no positivity, but did the test generated awareness, an increased attention to their sexual health, the propensity to test and stigma reduction.
Among key populations it is much more frequent to find positive results.
The Check Point of Bergamo is doing an important educational role especially with regard to young people and a significant activity to bring out the submerged and support the retention in care of the most fragile people.

Attach: https://www.icar2023.it/public/abstract/Attach_ABS_191.jpg

Social and behavioural science, marginalized groups, community aspects and community surveys

P 282 FOREIGNERS AND THEIR REQUESTS TO LILA HELPLINE FROM 2018 TO 2022: A COMPARATIVE ANALYSIS

A. Castellari[1], A. De Giosa[2], S. Penon[3], M.G. Di Benedetto[1]

[1]LILA ONLUS, Como, [2]LILA Bari, Bari, [3]LILA Milano, Milano

Backgrounds: for over 30 years Lega Italiana per la Lotta contro l'AIDS (LILA) offers a helpline service through its nine territorial offices. The helpline aims at providing information about HIV and sexually transmitted infections (STI) and to give support and guidance on territorial services.
In the last five years, reports have shown a decrease in general calls, with an average decrease of 38.32%. Meanwhile the number of foreign people who contacted us has remained constant with an increase in the incidence of 54.58%, bringing the incidence of total telephone calls from 2.84% to 4.39% on average over the years observed.
Given this evidence, this study aims to analyze in the 2018-2022 period the issues most discussed themes by foreign users to improve the service aimed at this specific population.
Material and Methods: Since 2006 data has been collected in pre-compiled forms during every contact. We have analyzed the period between 2018 and 2022. The analysis of the data is reported every year. Inclusion criteria are being reported as foreign. The number of excluded people based on inclusion criteria is 29370. The total number of included people is 1080.
Results: The population is 32.38% from South America, 22.96% from Europe, 17.78% from Africa, 7.53% from Asia, and 2.03% from North America.
Foreign people contact us mainly from Italy (70.02%), the most represented age group is between 20 and 49 years (59.08%) with the peak 30-39 years (23.78%) and they are mainly men (63.55%) against 34.58% of women.
The data show a preference for contact via phone call, email (23.03%), or face-to-face interview (25.68%). While only 4.48% contact the service through social media.
Most of the population declares that they have already performed an HIV test and 11.82% are waiting to do so. 63,43% of the population lives with HIV, with a rapidly growing trend in the period under analysis going from 60.27% in 2018 to 67.94% in 2022, with a peak of 69.63% in 2021.
Most discussed topics are therapies research (34.69%) and vaccines (36.3%) with an increasing trend of issues related to HIV and immigration (21.84%).
Discussion: Data has highlighted that foreign people usually contact LILA after an HIV diagnosis and ask for support on issues of rights and immigration.
The economic crisis caused by Coronavirus and its repercussions on global health systems has increased the migratory phenomenon. Consequently, it is necessary to increase the identification of tools and methods of welcoming these requests, for example, being able to provide counseling in other languages, prepare memoranda of understanding with the local public social-health services, facilitate the taking charge and access to therapy of foreign people living with HIV in our country.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 283 NO ONE LEFT BEHIND - OMPHALOS LGBTI+ EXPERIENCE, PERUGIA, ITALY. A COMMUNITY-BASED HIV TESTING BEFORE AND AFTER THE CHALLENGING COVID-19 PANDEMIC PERIOD (2020). IT'S TIME TO STRENGTHEN THE DIALOGUE ABOUT SEXUAL HEALTH

A. Zoffoli[1], E. Albertini[2], P. Diana[2], A. Gidari[1], G. Gonnelli[1], S. Tordi[1], D. Francisci[1]

[1]Clinica delle Malattie Infettive, Azienda Ospedaliera di Perugia, Università degli Studi di Perugia, [2]Omphalos LGBTI+, Gruppo Salute

Background: The 95-95-95 UNAIDS to control the transmission of human immunodeficiency virus (HIV) re-enforce the concept of accelerating action to end the AIDS epidemic by 2030. The FAST-TRACK approach involves using rights-based strategies to reach the people who need these services. The community-based testing fights stigma and discrimination, removing social, structural and logistic barriers to HIV testing and standard counselling carried out in a permanent health facility (HTC).

Material and Methods: HIV voluntary testing conducted in a non-medical setting (data retrospectively collected from 1/1/2018 to 31/12/2019 and from 1/1/2021 to 31/12/2022). The aim is to describe a community-based HIV testing (Omphalos LGBTI+ checkpoint) before and after the burden of covid-19 pandemic. Medical doctors provided counselling, rapid HIV testing (Determine™ HIV Early Detect, Abbott) and sexually transmitted infections (STIs) education. Participants completed an anonymous questionnaire and a consent form. The main analysis is descriptive: medians and IQR for quantitative data, numbers and proportions for qualitative data. A univariate statistical analysis was conducted by Mann Whitney test or $\chi 2$ test, as appropriate.

Results: 255 participants were tested in 2021-2022 and 444 in 2018-2019. Epidemiological data are described in table 1. The median time between HIV-tests was 182 days (2018-2019) [IQR 80-322] and 389 days (2021-2022) [IQR 369-463]. The self-reported sexual orientation was significantly different in the two groups (p=0.0009). Participants who reported a STIs (last 12 months) were 55 (12,4%) in 2018-2019 and 14 (5,5%) in 2021-2022 (p=0.0027). In 2021-2022 3 (1,2%) participants declared to be people living with HIV/AIDS (PLWHA) (p=0.02). 58 (22,7%) reported not to remember if they have ever had a diagnosis of HIV (2021-2022), compared to 111 (25%) in 2018-2019, no significative difference. The checkpoint approach was preferred by 180 people (70,6%) after the pandemic (p=0,0001). 164 (64,3%) declared not to use condom (2021-2022), compared to 292 (65,8%) (2018 -2019), no significative difference. No significative difference found in having sex with PLWHA, avoiding sex with PLWHA, practice chemsex and diagnosis of syphilis (last 12 months) in the two analyzed groups.

Conclusions: We registered an access decrease in 2021-2022, a period with few movement restrictions. Globally, almost 1 out 4 declared not to remember if have ever had a diagnosis of HIV and the time passed between the HIV-tests, in those previously tested, was higher after 2020: this support the hypothesis of a more difficult access to HTC and the worrying unawareness about HIV. The community-based approach is significantly preferred in 2021-2022: it is placed in a more accessible location in comparison to the suffering HTC. Unprotected sex is still high. These results can help implementing the community strategies to achieve the global targets and promoting sexual health.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 284 TO DRINK OR NOT TO DRINK. DATA FROM REAL LIFE AND IMPLICATION FOR DIETITIAN COUNSELLING FOR PLWHA

D. Penoncelli[2], A. Pezzana[2], A. Ianniello[1], M. Guastavigna[1], M.C. Ottino[1], G. Orofino[1], G. Calleri[1]

[1]SC Malattie Infettive e Tropicali I, Ospedale Amedeo di Savoia, ASL Città di Torino, [2]SC Nutrizione Clinica, Ospedale Amedeo di Savoia, ASL Città di Torino

Background: Thanks to HAART, HIV infection has become a chronic situation with which the patient lives and ages. European Guidelines and Italian Guidelines on HIV show the importance of treatment of associated non-infectious comorbidities. Among these, cardiovascular diseases have acquired increasing importance in this population. Over 80% of cardiovascular events can be avoided by adopting a correct lifestyle which includes diet, physical activity and stop smoking or alcohol intake. For this reason, our center has decided to investigate the consumption of alcohol in the daily life.

Materials and Methods: In January, February and March 2023, the questionnaire "Abitudini alcoliche - Audit C" of the ISS was administered to patients with HIV-1 infection afferent to the Infectious Diseases Clinic and at their first Nutritional visit of the Amedeo di Savoia Hospital in Turin.

Results: A total of 528 patients (358 males and 170 females) were enrolled; 51.14% (270) doesn't consume alcohol and 48.86% (258) consume alcohol. Of these, 202 patients are males and 56 females (80% Italian and 20% foreign) with a mean age of 53 ± SD 11.16.

Of the 258 patients, 110 (group A) consumed alcohol 1 to 4 times a month (76 males and 34 females) and their mean BMI is 26.52 kg/m2 ± SD 5.45. Of the subjects in group A, 98 take 10-20 g of alcohol a day and 12 patients take 30-40 g of alcohol a day. None of them drink >60 g of alcohol on a single occasion.

The group B (148) drinks alcohol 2 to 4 or more times a week (126 males and 22 females) and their mean BMI is 26.48 Kg/m2 ± SD 5.48. Of the subjects in group B, 100 take 10-20 g of alcohol a day, 44 patients take 30-40 g of alcohol a day and 4 take 50-60 g of alcohol a day. 28 of these patients drink > 60 g of alcohol a day on a single occasion.

No statistically significant difference between the BMI of group A and group B (P = 0.4) was found.

Conclusions: About 50% of PLWHA consume alcohol, and in 9% of patients the threshold is ≥ 30 g/day. Although the EACS Guidelines allow 20-40 g/day for male and 10-20 g/day for female, more restrictive indications are assumed in dietitian counseling (threshold of 10 g/day for females and 20 g/day for males) in view of the carcinogenicity of alcohol and its relationship with a lot of metabolic alterations.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 285 ASSOCIATION BETWEEN LOCUS OF CONTROL, HEALTH LOCUS OF CONTROL, COPING AND RESILIENCE IN AN ITALIAN COHORT OF PEOPLE LIVING WITH HIV

V. Massaroni[1], V. Delle Donne[1], R. Jo Steiner[1,2], R. Passerotto[1,2], A. Dusina[2], G. Baldin[2], P.F. Salvo[1,2], F. Lamanna[1,2], S. Di Giambenedetto[1,2], A. Borghetti[2]

[1]Infectious Diseases Institute, Department of Safety and Bioethics, Catholic University of Sacred Heart, Rome, Italy, [2]UOC Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Background: Locus of Control (LOC) allows people to assess the degree to which they believe their behaviours are controlled by internal or external factors. People with an internal LOC believe that they can control their actions and behaviours, while people with an external LOC believe that their behaviour depends on external factors. This study aims to assess LOC in people living with HIV (PLWH) and its interaction with Health Locus of Control (HLC), coping strategies and resilience.

Material and Methods: We conduct a cross-sectional survey enrolling 150 PLWH. Exclusion criteria were age <18 years and difficulties with the Italian language. LOC was measured using the Italian version of the internal-external (I-E) control scale. High scores in I-E scale indicate an external LOC. For the HLC measure, PLWH were asked the following question: "Do you believe you can do something to preserve a good health status?" Patients could choose from the following response alternatives "Yes to a very high extent", "Yes to some extent" or "No one's results are not important." PLWH who chose the first alternative were framed with an internal HLC, those who chose the other two alternatives with an external HLC. The Italian version of the Coping Orientation to the Problems Experienced (COPE-NVI) was used to measure patients' coping strategies. For the resilience measure, we used the Italian version of Resilience Scale. We explored factor associated to external LOC and the relationship between different scales.

Results: Many of PLWH were male (65.3%, n=98), aged 51 to 60 (38.7%, n=58), with upper secondary school degree (46.0%, n=69). Most of PLWH (65.3%, n=98) were >10 years ago diagnosed with HIV and 62.7% (n=94) of them received >10 years ago for the first time ART. 84.0% (n=126) reported HIV-RNA<50 copies/Ml. 52.7% (n=79) reported an excellent adherence. The PLWH mean reported on the I-E scale was 18.22 (SD 2.06), demonstrating an external LOC in our patients. 134 PLWH (89.3%) reported external HLC. Sixty percent of the respondents (n=90) reported good resilience. The coping strategy with the highest mean reported was avoidance (mean 30.39, SD 8.22). PLWH with poor adherence and resilience, who frequently forget to take therapy and who miss more than one visit a year show an external LOC (p=0.014; p=0.002; p=0.009; p=0.003 respectively). There was a positive correlation between external LOC and the avoidance coping strategy (r=0.172; p=0.035).

Conclusion: In conclusion, our results emphasize that our PLWH have an external LOC and HLC. PLWH with poor adherence, resilience, forgetting to take therapy and skipping doctor visits show external LOC. In addition, there is a positive correlation between external LOC and an avoidance coping strategy. Thus, it is important to identify PLWH with an external LOC in order to build interventions to help them adhere to their treatment regimen, implement appropriate behaviours to manage their disease and to improve their quality of life.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 286 THE ROLE OF EMOTION DYSREGULATION IN PATIENT HEALTH ENGAGEMENT AND HIV-RELATED SYMPTOM DISTRESS IN AN ITALIAN COHORT OF PEOPLE LIVING WITH HIV

V. Delle Donne[1], V. Massaroni[1], P.F. Salvo[1,2], V. Iannone[1,2], D. Farinacci[2], A. Ciccullo[3], A. Borghetti[2], A. Carbone[1,2], S. Di Giambenedetto[1,2], F. Lombardi[2]

[1]Infectious Diseases Institute, Department of Safety and Bioethics, Catholic University of Sacred Heart, Rome, Italy, [2]UOC Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [3]UOC Infectious Diseases, Ospedale S. Salvatore, L'Aquila; Italy

Background: Emotion dysregulation (ED) refers to difficulties in the self-regulation of affective states and engaging in goal-directed behaviour. To date, only few studies have examined the role of ED among people living with HIV (PLWH). This study aimed to explore the role that ED may play in health engagement and HIV-related symptom distress (HSD) in a cohort of PLWH.

Material and Methods: We conducted a cross-sectional survey enrolling 152 PLWH on cART. Exclusion criteria were age <18 years and difficulties with the Italian language. We assessed ED using the "Difficulties in Emotion Regulation Scale" (DERS). The "patient health engagement scale" (PHE-S) was used to measure the patient's active involvement in the treatment process. We administered "HIV Symptoms Distress Module" (HIV-SDM) to measure the global burden of symptoms during the past 4 weeks. We examined the distribution of DERS scores between different engagement positions of PHE, between different levels of HIV-SDM and quality of adherence to cART and visits.

Results: Many of PLWH were male (66%), aged 51 to 60 years (39%), with upper secondary school degree (46%). Most of the respondents (66%) were>10 years ago diagnosed with HIV and received>10 years ago for the first time cART (63%). Mean DERS scores were significantly higher in women than in men (91.35vs68.78, p=0.003), in PLWH with pre-existing psychiatric conditions compared to those who had none (94.21vs71.40, p=0.008) and in PLWH who were past injecting drug users compared to those who have not been (102.39vs73.75, p=0.029). Mean DERS values were significantly higher in PLWH in the blackout phase of PHE compared with patients in the arousal, adhesion and eudamonic phase (120.50vs110.50,62.92and 44.71 respectively,p<0.001). Furthermore, mean DERS scores were significantly higher in PLWH with a high level of distress on the HIV-SDM compared to those with a low level (120.70vs65.63,p<0.001) and in PLWH with optimal cART adherence compared to those with poor adherence (129.35vs65.60,p<0.001).In particular, mean DERS scores were significantly higher in PLWH who forgot or mistimed taking cART (87.40vs63.73,p<0.001 and 90.81vs58.82, p<0.001, respectively), suspended cART on personal initiative for at least 2 days (118.68v64.35,p<0.001) or missed at least 1 outpatient visit in the last year (111.87vs64.71,p<0.001) compared to those who did not.

Conclusion: In conclusion, our findings highlight that high ED might be associated to high levels of HSD and poor engagement to care in PLWH. Specifically, PLWH with poor adherence to cART and to outpatient visits showed higher ED. Moreover, our results suggest that among PLWH women, those with pre-existing psychiatric conditions and past injecting drug users might suffer greater ED. Therefore, this overview underlines the importance of assess and target ED to improve the psychological wellbeing of PLWH, to facilitate care engagement and to increase appropriate behaviour for maintaining good health.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 287 SEARCHING FOR HCV INFECTION: INVOLVEMENT OF THERAPEUTICAL COMMUNITIES IS MANDATORY!

A. Floriani[1], J. Sechi[2], C.M. Bruno[2], V. Vivaldi[3], M. Gladioro[3], M. Ciccone[4], G. Lizzio[4], D. Fiorellino[5], N. Bobbio[5], F. Del Puente[5], M. Feasi[5], E. Pontali[5]

[1]SERD Interno C.C. Genova-Marassi ASL3 Genovese, Genova, [2]C.T. San Benedetto, Genova, [3]C.T. Ma.Ris, Isola del Cantone (GE), [4]C.T. CEIS 'Trasta', Genova, [5]S.C. Malattie Infettive, E.O. Ospedali Galliera, Genova

Introduction: The current target to eliminate HCV as a public health problem is undermined by the difficulty to diagnose all HCV cases in the community. There is a large number of people who are currently undiagnosed for various reasons. One of the largest reservoir of infection includes those previously used or currently are using drugs. Among the settings that concentrate this population are Therapeutical Communities.

Methods: The 3 Therapeutical Communities insisting on our territory (C.T. Ma.Ris; C.T. CEIS 'Trasta'; C.T. San Benedetto) were involved in 3 training activities on HCV diagnosis, management and training, one per Therapeutical Community at their site. Each event involved two infectious diseases specialist and a nurse from our hospital; a drug addiction specialist working in the local prison; all staff and guests of each Therapeutical Community.

Results: The three meetings reached 72 people: 20 staff and 52 guests (from 10 to 25 for each meeting). During the month following the meeting, guests could come to our outpatient unit to be tested. Results of 9 testing were: 2 already HCV-treated were tested for HCV-RNA and were still negative; 7 without evidence of previous HCV serological status were tested (3 positive with HCV-RNA negative; one positive with HCV-RNA positive and later treated and cured; one with pending results; two negative). Nine other guests already knew their status and did not come for testing. In addition, two HIV-HCV co-infected patients started again their follow up (lost more than 2 years before); their Therapeutical Communities were unaware of their HIV status.

Discussion: This kind of initiative is time consuming for health staff, but it can be very cost-effective. The possibility to re-engage two HIV-HCV co-infected patients was of crucial importance for them and from a public health point of view (interruption of chain of transmission). The opportunity to train together staff and guests was essential to create an 'easy going' climate between health staff and guests. Even if immediately after the initiative, there was a relatively low number of people coming for testing, a seed of knowledge on HCV transmission, diagnosis and management was planted. This can be seen as an investment for the future, new guests and staff members will be informed by a shared knowledge within the Therapeutical Community. Our plan for the future is to meet again the 3 Therapeutical Communities and, in consideration of the turnover in staff and guests, to check what has remained of this initiative in terms of knowledge.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 288 HIV AND HCV AWARENESS AND KNOWLEDGE AMONG THE GENERAL POPULATION IN BRESCIA, NORTHERN ITALY

F. Viola, S. Arsuffi, B. Formenti, P. Magro, I. Polesini, E. Focà, F. Castelli, E. Quiros-Roldan for FAST-TRACT CITY Brescia Group

Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy

Introduction: During the European Testing Week in May 2022 and the World AIDS Day on the 1st of December 2022, the Infectious and Tropical Diseases Clinic of the ASST Spedali Civili of Brescia, together with the Municipality of Brescia, Northern Italy, and local civil societies, organized four days of free rapid screening tests for HIV and HCV. We report the results of a questionnaire that was offered to the participants to investigate knowledge on HIV and HCV.

Methods: This is a cross-sectional study based on an anonymous, multiple-choice self-completion questionnaire administered to everyone who performed the screening test or requested a consultation. We compare the answers between four sub-groups, people aged 18-40 vs >40 years old and heterosexual vs LGBTQ+ (lesbian, gay, bisexual, transgender, queer), to evaluate whether there was one or more groups more in need of tailored preventive strategies.

Results: Overall, 333 questionnaires were completed: 171 (51%) were female, 257 (77%) 18-40 years old and 264 (79%) heterosexuals. Overall, about half of respondents never performed an HIV test before (n=183, 54.95%). Those aged >40 years old performed the lowest results: in this group only 6 (7.8%) knew the ways of HIV transmission (vs n=101, 39% in the younger group), only 15 (19.7%) were aware that undetectable=untransmittable (vs n=123, 47.9% in the younger group) and only 7 (9.21%) knew PrEP (vs n=68, 26.5% in the younger group). Analyzing the results in the LGBTQ+ group, we evidenced that 28 (44.4%) knew the ways of HIV transmission (vs n=79, 30% in the heterosexual group), only 34 (53.9%) subjects were aware that undetectable=untrasmittable (vs n=104, 39.4% in the heterosexual group) and PrEP was known from 27 (42.8%) individuals (vs n=48, 18.2% in the heterosexual group). Finally, about 65% and 70% respectively of young and LGBTQ+ people would cohabit with PLHIV, and only 35.5% of >40 years old and 55.6% heterosexuals would do it. Moreover, comparing the four common questions for HIV and HCV, we evidenced that only 56 (16.82%) individuals answered correctly to all the questions on HIV (high knowledge level). A much lower proportion of subjects had similar knowledge on HCV (n=11, 3.3%). The population with medium-high knowledge was mostly composed of women (78%), under 40 years old (96.9%), university students or graduates (87.5%).

Conclusion: The deepest gaps in knowledge of HIV and HCV were found in the over 40 years old group. Among all, this group would mostly benefit from tailored preventive initiatives, also considering that in Italy the median age at HIV diagnosis is 40 years old. HIV stigma is still strongly present among different strata of the population and should be urgently addressed. Moreover, knowledge about HIV is wider than knowledge about HCV, although its prevalence is estimated to be lower, also among high-risk populations, such as older people, who would benefit the most from educational and prevention interventions.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 289 LATE-PRESENTER PERSON LIVING WITH HIV IN DETENTION INSTITUTE. CASE REPORT

A. D'Angelillo[1], D. Farinacci[1], E. Rastrelli[1], C. Lupan[1], A. Sanvito[3], A.M. Ialungo[1], C. Viti[3], G. Starnini[1]

[1]UOC Medicina Protetta-Malattie Infettive, Belcolle Hospital, Viterbo, Italy, [2]UOS Medicina Penitenziaria Territoriale, ASL Viterbo, Italy, [3]UOC Otorinolaringoiatria, Belcolle Hospital, Viterbo, Italy

Background: For people in detention, international guidelines suggest informed counseling for being screened for sexually transmitted diseases [1]. Despite this, not all facilities are equipped: both for the absence of experienced and dedicated staff and the lack of adequate tools. These problems often result in missed diagnoses in at-risk individuals and limited treatment options. [2]

Methods: In this work, we wanted to describe a case of diagnosis of a late-presenter patient from a correctional institution admitted to our Unit.

Case Report: 27-year-old Nigerian patient at his first detention, which began in 2021. The patient reported that he refused to perform infectious disease screening tests upon entering the prison. In history, he reported an episode of itchy skin rash for which he had been treated as per skin scabies in the summer of 2022 without clinical benefit. From October 2022 he began to complain of the appearance of pharyngodynia for which he was subjected to antibiotic treatment with amoxicillin-clavulanate and later with ceftriaxone and metronidazole, also without benefit. Given the lack of clinical response, blood tests were performed with leukopenia and lymphopenia for which an HIV test was proposed with a positive result. At this point, the patient was admitted to our ward where blood tests revealed a viremia of 516.000 copies/mL with CD4 lymphocytes of 9 cells/mm3 and positivity of HBsAg.

Over the skin, there was the persistence of diffuse maculopapular skin lesions, the presence of marked unilateral tonsillar swelling covered with yellowish exudate, and a hyperemic mucous thickening of the soft palate. After a tonsillar excision and a biopsy of the palatal lesion, the presence of a nodular lesion compatible with Kaposi's sarcoma, with positive immunostaining for HHV8, was demonstrated. The gastroscopy demonstrated the presence of mammillary and ulcerated mucosa both in the esophagus and in the stomach, these lesions were compatible with visceral Kaposi's sarcoma.

Conclusions: We wanted to analyze the case of a young prisoner with HIV infection in an advanced stage, who, despite staying in a detention institution, which should be considered, in this population at risk, the first contact with healthcare facilities, the diagnosis was very delayed probably due to the patient's lack of awareness of the disease, the long-term risks related to the infection itself and the lack of tools within the detention institution.

In the general population, we are witnessing, in recent years, a new increase in the diagnosis of HIV infection, especially in young subjects and very often in advanced stages of the disease. [3] It is therefore essential in the subcategories, particularly at risk, and therefore also in subjects who access certain facilities such as detention institutions, to implement awareness of the disease and the tools useful for early identification of infections, to guarantee early access to treatments and limit the spread.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 290 A FRIENDLY, RAPID TESTING AND COUNSELING APPROACH TO IMPROVE LINKAGE TO CARE: A TWO YEAR EXPERIENCE AT CHECKPOINT AND HOSPITAL CENTER

G. Mancarella[1], S. Garattini[1], A, Gasperin[1], A. Destro[1], F. Izzo[1], L. De Martino[1], D. Di Trento[1], S. Corazza[1], S. De Maria[1], A. Parente[1], A. Grimaldi[1], L. Battisti[1], S. Cacace[1], A. Carraro[2], R. Marocco[2], V. Rossi[2], M. D'Achille[2], A. Petrillo[3], V. Vitale[3], A. Girardi[3], M. Lichtner[1]

[1]Università la Sapienza, Latina, [2]Infectious disease department, Latina, [3]Arcigay - Sei come sei, Latina

Introduction: In the last three years, the SARS-CoV2 pandemic had an heavy impact on chronic illness management and diagnosis, HIV infection being one of them. On a national and local level, the majority of the newly diagnosed people are late presenters, so it became mandatory to increase our effort to create structured screening campaigns and obtain early diagnosis. Two years ago, the city of Latina joined the Fast Track Cities network and the Checkpoint initiative, a place outside hospital where everyone can be tested for sexually transmitted disease and receive sexual health education with particular focus on PrEP and PEP. In this work, we want to talk about the last year and a half experience.

Methods: People wanting to be tested in our Checkpoint need to schedule an online anonymous appointment and choose between the available rapid capillary blood tests: HIV, HCV, syphilis or all of them. At first, we administer a community-based counseling and then perform the HIV test(Ab and p24 antigen detection), HCV(Ab Detection) and Syphilis(Ab detection). Results are given in 15 minutes and uploaded on the COBATEST website.

On the other hand, testing in our clinic does not need a scheduled appointment, requires a phlebotomy and results are available in 3 days. Counseling is conducted by ID specialists and written in the patient's anonymous medical record. Unlike last year, all three tests are now offered. Data was collected through the COBATEST export tool and compared with the one from our clinic.

Chi square and Student t tests were used for data analysis.

Results: From January 2022 until now, in our Checkpoint 248 people have been tested for HIV, HCV and syphilis. All HIV tests resulted negative, whereas 1 HCV test and 2 syphilis tests resulted positive and promptly treated. The population was characterized as shown in table 1.

Although the majority of people at Checkpoint does not say to have sexual risk behaviours, a very low number of it says to use condoms. On the contrary, patients in the clinic reported more unprotected sex ($p<0.00001$).

People tested at Checkpoint are younger than in the clinic ($p <0.0001$). It also appares that people interested in beginning PrEP medication come at checkpoint to be tested and get info($p=0.008$), whereas people who are already on PrEP choose to be tested in our clinic ($p=0.036$).

Conclusion: These sixteen months of testing and counseling in our Checkpoint highlighted the great role that this service has in the community in terms of prevention and linkage to care. We should put our effort in educating people about the tools we now have to prevent HIV transmission such as PrEP and PEP. Furthermore, as a great number of people is not using condom and does not feel at risk, we also have to raise sexual health awareness. Improving the activities of our checkpoint, working side by side with Arcigay volunteers, will certainly help us getting closer to the Fast Track Cities goal of ending the HIV epidemic.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 291 COMPREHENSIVE SEXUALITY EDUCATION (CSE) IN ITALIAN SECONDARY SCHOOLS: PRELIMINARY RESULTS OF EDUFORIST2 PILOT ACTIVITY

A. Chinelli[1], R. Galipò[2], P. Meli[3], S. Bellini[4], N. Catucci[5], M. Farinella[6], L. Rancilio[7], A. Camposeragna[8], G. Paparatto[1], A. Musco[9], E. Torri[1], M. Ubbiali[10], M.C. Salfa[11], B. Suligoi[11], A. Caraglia[12], D. Martinelli[9], L. Tavoschi[1]

[1]Dipartimento di ricerca traslazionale e delle nuove tecnologie in medicina e chirurgia, Università di Pisa, [2]ANLAIDS, Roma, [3]CICA, Bergamo, [4]LILA, Firenze, [5]LILA, Bar, [6]Circolo di cultura omosessuale Mario Mieli, Roma, [7]Caritas Ambrosiana, Milano, [8]CNCA, Roma, [9]Dipartimento di Scienze Mediche e Chirurgiche, Università di Foggia, [10]Dipartimento di Scienze Umane, Università di Verona, [11]Centro operativo AIDS, Dipartimento Malattie Infettive, Istituto Superiore di Sanità, Roma, [12]Direzione Generale della prevenzione sanitaria, Ministero della Salute, Roma

Background: Comprehensive Sexuality Education (CSE) is internationally recognised to be an important strategy to promote sexual and reproductive health (SRH), included sexually transmitted infections (STIs) and HIV prevention. Schools are considered to be the most appropriate context to promote SRH interventions, which are demanded also by students. In Italy, CSE is not part of school curricula. This study describes the preliminary results of EduForIST2 CSE pilot activity in upper secondary schools (USS), in 4 Italian regions (Lombardy, Tuscany, Lazio and Apulia). EduForIST2 is a project funded by the Ministry of Health.

Methods: The pilot activity has been developed by an interdisciplinary team of academics, public health professionals and civil society organisations (CSOs) with expertise in SRH promotion in schools. External experts assisted in the definition of structure and content. The pilot activity consisted of 5 interventions with students on the following topics: 1) changes in adolescence and healthy relationships; 2) sexual identity and diversity; 3) consent and contraception; 4) STIs prevention and sexual health services; 5) insights into topics decided by the students. Meetings with families and teachers were also organised. Educators belonging to CSOs, appropriately trained, have conducted the activity. The evaluation consisted of pre-post tests on knowledge and satisfaction.

Results: The results refer to preliminary analysis of 546 pre tests (from 12 schools in 4 regions) and 236 post tests (from 6/12 schools in 3/4 regions). Knowledge increased in all the 15 items investigated, with a significant ($p<.05$) increase in 11. Highest increment of correct answers was found in 2 items: “The need to pee often with burning may be an STI symptom” (+45.9%) and "There are drugs that enable people with HIV not to get AIDS and not to transmit the infection to other people” (+35.2%). The items with less increment of correct answers were “The timing of physical changes during adolescence is the same for everyone” (+3.8%) and "A stereotype is a rigid, generalised opinion” (+1.1%). Pre-post tests also asked to provide a definition of sexuality by answering the question: “What is sexuality?”. Early content analysis showed that post-test answers were broader than pre-test and answers like “I don’t know” were less frequent (9,1% vs 1,7%). Satisfaction questionnaires were completed by 171 students. On average, 73% appreciated “very much” talking about the topics of the activity (especially STIs) and 74% liked the possibility to talk to adults other than teachers.

Conclusions: This study represents one of the first CSE interventions in USS in Italy. The early results report that the intervention was effective in enhancing knowledge and decreasing uncertainty, especially on the topics of STIs prevention. More data are needed to support evidence-based interdisciplinary and comprehensive activities on SRH to be introduced in Italian schools.

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P 292 WEB LISTENING TO IDENTIFY THE INFORMATION NEEDS OF DIFFERENT TARGETS AND DETECTED THE BARRIERS TO THE MODIFICATION OF THE HIV BEHAVIORS

A. Colucci[1], A. D'Ari[2], F. Furiozzi[2], P. Gallo[1], M. Mirabile[2], G. Santolini[2], E. Fanales Belasio[1], R. Dalla Torre[1], A. D'Agostini[1], E. Fedele[2], T. Bertani[2], M. Schwarz[1], R. Valli[1], L. Bertinato[3], S. Iavicoli[2]

[1]Unità Operativa Ricerca psico-socio-comportamentale, Comunicazione, Formazione Dipartimento Malattie Infettive – Istituto Superiore di Sanità, Rome, Italy, [2]Direzione Generale della Comunicazione e dei Rapporti Europei ed Internazionali – Ministero della Salute, Rome, Italy, [3]Segreteria Scientifica Presidenza - Istituto Superiore di Sanità, Rome, Italy

Background: Institutional communication on HIV and STI requires the knowledge of people information needs and tools mainly used for information on health issues. To this goal, an analysis of web listening, aimed to improve the effectiveness of the communication campaigns of the Ministry of Health through the identification of the information needs of different target groups and of barriers affecting HIV risk behaviors, was conducted by Istituto Superiore di Sanità jointly with the Ministry of Health and field experts.

Material and methods: All the spontaneous listening on the web and on social channels, in relation to conversations in Italian referring to HIV, AIDS or Sexually Transmitted Diseases, was recorded through the Blogmeter Suite, which is an integrated Social Listening platform. Between 1 October 2021 and 30 September 2022, a database of over 2 billion indexed documents, traceable and readable texts (sources: Facebook, Twitter, Instagram, YouTube, TikTok, Twitch, forums, blogs, news and apps review sites as Google Play and App Store) containing at least one selected keyword on AIDS, HIV, HIV, HIV test, sexually transmitted diseases, was scanned and analyzed. To detect the level of knowledge attitudes and behaviors regarding prevention, stigma and HIV testing, the following interest areas have been identified: STI and HIV/AIDS reference scenario, being HIV positive and HIV test.

Results: Reference scenario: Web conversation on STI took place mainly on Facebook, which is the source of almost half of the contents and of the 66% of the buzz. However, Instagram and TikTok were the sources where most users interacted. The mostly used terms on the web were HIV and AIDS.

Being HIV positive: HIV-positive people expose themselves very scarcely on the public web places. In the public sphere, AIDS and HIV are faced impersonally, with opinion based on theoretical knowledge.

The HIV test: The cost of the test wass the most mentioned topic, and anonymity was a critical issue. Very few people knew about self testing.

Conclusions: Data analysis shows how the perception and discussions on HIV and AIDS are different among the general population compared to HIV+ persons. ForHIV- people, the recurring elements of the analysis are seasonality, attention to news events, knowledge of HIV and AIDS linked to the past. There was little knowledge of the methods of transmission, and availability of the test.

For HIV+ people, the main concerns were therapy and drugs, followed by the need to maintain anonymity at the place of work.

Stigma is certainly present, and HIV+ people do not expose themselves publicly, using more protected web places and implementing protecting behaviors as changing doctors, activating forms of health tourism, avoid disclosing their status.

Furthermore, the web listening analysis showed that young people have very little awareness of the risks and are poorly informed, representing a target for prevention campaigns.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 293 IMPACT OF COVID-19 ON THE MANAGEMENT OF THEIR DISEASE IN PEOPLE LIVING WITH HIV: PRELIMINARY RESULTS OF SEMI-STRUCTURED INTERVIEWS

A. Camposeragna[1], L. Cosmaro[2], P. Piselli[3], C. Cimaglia[3], A. Nappo[3], M. Farinella[4], L. Rancilio[5], S. Mattioli[6], V. Calvino[7], D. Zagato[8], D. Masci[9], P. Meli[10], J. Testa[11], N. Piazza[12], M. Errico[13], A. Caraglia[14], E. Girardi[1] for the Working Group of the project "The impact of COVID-19 on the processes and outcomes of care of people with HIV"

[1]CNCA, Rome, [2]LILA Milano, Milan, [3]INMI L. Spallanzani, Rome, [4]Circolo di Cultura Omosessuale "Mario Mieli", Rome, [5]CARITAS Ambrosiana, Milan, [6]PLUS, Bologna, [7]ANLAIDS Onlus-ETS, Rome, [8]Associazione Solidarietà AIDS odv, Milan, [9]Villa Maraini, Rome, [10]CICA, Bergamo, [11]Italian Society of Migration Medicine - SIMM, Rome, [12]Arcigay, Bologna, [13]NPS Italia, Naples, [14]Ministero della Salute, Rome

Background: People Living with HIV (PLWHIV) are one of the groups of people for whom the Covid-19 pandemic could have represented a major obstacle to maintain an effective continuum of care.
Aims: To investigate how the pandemic affected PLWHIV in terms of quality of life and access to treatment, to know their opinion about the use of telemedicine and how it can be improved, how pandemic affected new HIV diagnosis and linkage to care
Material and methods: A sample of 36 subjects, of which 12 new HIV diagnosis, was interviewed by NGOs trained workers. The semi structured interview focused on their experience as patients during the pandemic, the support offered by NGOs and PLWHIV community and their suggestions on how to tackle a new pandemic, from the perspective of HIV patients. The interviews were conducted in March 2023.
Results: The sample consists of 10 women, 5 transgenders 21 men aged mostly 30-44 yrs. One third was diagnosed with HIV after October 2019 and were therefore considered as recently diagnosed during the pandemic period. A preliminary qualitative analysis highlights the difficulties in getting in touch with their HIV clinics, in particular with their referring doctor. It is evident that scheduled visits were frequently delayed, causing concerns and worries about their care. None of the respondents reported ART interruption, since a 3-months pills provision has been established and is still in place, representing for the respondents an important positive improvement in the management of their disease. Respondents referred that telemedicine could represent a relevant improvement able to reduce time to get prescriptions but a de visu contact with their doctor is still considered a fundamental aspect for their continuum of care. The support received from NGOs during the pandemic was fundamental mostly in obtaining information about their condition, especially in terms of psychological support to face isolation due to lockdown measures. Lack of Information on potential effect of COVID-19 on their condition.
Conclusion: In this preliminary analysis of interviews conducted in a group of PLWHIV, it emerged that (i) the pandemic had a big impact on their life, mainly in terms of lack of information, health assistance and perceived psychological distress; (ii) telemedicine could represent a support for the management of their disease but cannot completely substitute a more intensive in person assistance.
Project funded by the Minister of Health (ref 4023).

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P 294 THE ROLE OF THE PSYCHO-SOCIAL TEAM OF THE C.A.M.A. ODV, IN 25 YEARS OF ACTIVITY IN THE "HOME TREATMENT OF PEOPLE SUFFERING FROM AIDS AND RELATED PATHOLOGIES" - INTERVENTIONS IN IMPLEMENTATION OF THE PRESIDENTIAL DECREE 09.14.1991 AND MINISTERIAL DECREE 09.13.1991

A. Calluso, N. Catucci, M. Di Tullio, R. Giusto, S. Loiudice, C. Michelucci, I. Lanera, M. Potenza, A. Scavo, P. Tomasicchio

C.A.M.A (Centro Assistenza Malati Aids) OdV ETS

Introduction: The funds are foreseen by Law 135/90. In June 1995, the Puglia Region, with resolution no. 96, approves the «Home care treatment of patients affected by AIDS and related pathologies».
In 1998, the voluntary association C.A.M.A. is awarded the service, through a regular call for tenders, announced by the Local Health Authority BA/4. In November of the same year, the President of the C.A.M.A., Dr. Angela Calluso, signs the first agreement which has so far given the possibility to 16 people with full-blown AIDS and residing in the province of Bari to use the ADI-AIDS service.
Methods: The ADI provides both medical and psycho-social support. The integration system is developed through the following roles: the ASL BA maintains management, control and health responsibility; The Home Care Unit (UAD), managed by the Infectious Diseases Unit of the AUO Polyclinic of Bari, has the responsibility of continuing, at the patient's home, the therapies started during hospitalization, also providing nursing assistance and The C.A. M.A. carries out the psycho-social-assistance part. From 1998 to today, n. 105 assistance plans have been activated.
The team is made up of the following professional figures: Coordinator; n. 2 psychologists; Social Worker; Nurse; n. 5 Social Health Operators
The Psycho-social team of the C.A.M.A. performs the service through:
- Direct dispensing on the user: drug administration control; rehabilitation services; psychological support; social and domestic assistance; accompaniment to hospital and socialization facilities; health education of the user and family members.
- Indirect delivery for the user: handling of bureaucratic procedures; research and/or activation of solutions for maintenance and/or job placement; participation in supervision with the health and management managers of the ASL and the UAD; writing reports; use of the information technologies of the Association; weekly feedback meetings; drug supply; planning and coordination of work with ASL and UAD operators.
Results: The goal was to create an integrated care model that took into account both the health needs and the psycho-social problems of people with full-blown AIDS. In fact, a service has been created that is able to improve the quality of life of the user and favoring a suitable stay of the assisted at home, also giving support to the family unit.
Conclusions: The advantages brought to the assisted, during these 25 years of psycho-social activity of the C.A. M.A. in the ADI AIDS, were as follows:
limitation of hospital stays; improvement of therapeutic compliance; improvement of the quality of life; improvement of the family environment, since the whole household is supported in dealing with the weight of the various health, psychological and social problems that assistance to the person suffering from AIDS entails.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 295 THE PREVENTION OF SEXUALLY TRANSMITTED INFECTIONS (STIS) IN NEW MIGRANT POPULATIONS. DATA FROM THE PERUGIA OUTPATIENTS CLINIC

M. Ramadori, V. Suriani, S. Tordi, A. Bernardelli

USL Umbria 1

Introduction: The outpatient clinic for migrants in Perugia was established in 1999 thanks to the collaboration between the Umbria 1 USL health authority and Anlaids Umbria. The outpatient clinic offers free medical services to everyone (migrants and non-migrants, resident foreigners, people temporarily present in the territory, even irregular ones), which consist of an initial physical examination (also on immediate arrival), the prescription of drugs or further specialist examinations through the national health service, a psychotherapeutic assistance, rapid HIV and HCV tests, the delivery of condoms and information materials. The clinic registered 184 users in the period February 2021-February 2022.

Methods: This is a retrospective observational study analysing the epidemiological and clinical data of patients who underwent at least one medical examination in the period February 2022-February 2023.

Data were extracted from the electronic medical records (Docunque) or from paper records for patients who had only performed HIV/HCV tests (anonymous). The main analysis was descriptive: mean and SD for quantitative data, numbers and proportions for qualitative data.

Results: In the period analyzed, accesses to the outpatient clinic were 429, with a mean of 1.35 accesses per patient (SD ±1.00). A total of 318 patients were registered; of these, 292 patients had an electronic medical record, as 26 had only an anonymous HIV/HCV test.

Among the 292 patients we considered, 28.76 % were female; the mean age was 32.7 years (SD ±16.42) and the most represented nationalities were: Pakistan (18%), Bangladesh (10%), Nigeria (8%), Egypt (5%), China (4%), Ivory Coast (4%) Spain (4%), Afghanistan (3%), Cameroon (3%), Ethiopia (3%), Morocco (3%), Tunisia (3%), Ukraine (2%), other (39%).

The most frequent clinical problems were dermatological (9.7%), first general medical examination (8.2%), chronic orthopaedic and postraumatic conditions (7.4%), scabies (5.3%), gastrointestinal problems (4.7%), respiratory (4.7%), dental care (3.2%), certificate requests (3.2%) other and unknown (53.6%). A total of 297 patients were referred to the psychological service by both territorial health services and this outpatient service.

Overall, 46 HIV/HCV tests were performed, of which 1 (2.17%) HIV test was positive and 1 (2.17%). HCV positive.

Conclusions: There has been an increase in the number of users compared to previous 12 months (+72,8%) due to improved association communication strategies, but also as a result of the lack of dedicated territorial health services post covid pandemic. Furthermore, an exponential increase in the number of migrants entering by sea has occurred, according to the Ministry of the Interior. For this population, the outpatient clinic for migrants represented the only way to access to a medical services, including prevention of STIs.

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P 296 QUALITY OF PRE- AND POST-COVID-19 HEALTHCARE: THE POINT OF VIEW OF WOMEN LIVING WITH HIV

A. Bove[1], M. Cernuschi[2], A. Cervo[3], C. Pinnetti[4], A. Perziano[5], M. Errico[6], G.V. Calvino[7], M. Giglia[8], M. Guastavigna[9], D. Canetti[10], A. Di Biagio[11], M.L. Cosmaro[12], A. Cingolani[13] for Icona Foundation Study Group

[1]Circolo di Cultura Omosessuale Mario Mieli, Roma, [2]Associazione Solidarietà Aids, Milano, [3]Department of Infectious Diseases, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy, [4]Clinical and Research Department, National Institute for Infectious Diseases 'Lazzaro Spallanzani' IRCCS, Rome, Italy, [5]Associazione Arcobaleno AIDS, Torino, [6]Network Persone Sieropositive, Milano, [7]Anlaids Onlus-ETS, Roma, [8]Department of Medical and Surgical Sciences, Clinics of Infectious Diseases, S. Orsola-Malpighi Hospital, 'Alma Mater Studiorum' University of Bologna, Bologna, Italy, [9]Unit of Infectious Diseases, "Divisione A", Amedeo di Savoia Hospital, Torino, Italy, [10]Infectious Diseases Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy, [11]Infectious Diseases Clinic, Policlinico San Martino Hospital, Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [12]Fondazione LILA Milano, Milano, [13]Infectious Diseases Unit, Fondazione Policlinico Universitario A.Gemelli IRCCS, Catholic University of the Sacred Heart,Rome, Italy

Background: Due to the COVID19 pandemic, the offer of health services had to change either to ensure continuity in the doctor-patient relationship or to respond to the care needs of people living with HIV, both being fundamental to their physical and psychological health. This is particularly true for WLWH who can require care due to pregnancy, menopause, and depressive symptoms.

Methods: An anonymous nationwide web survey created by the Community Advisory Board of Icona has been spread through the centers of its network and through the CBVTC websites and social media.73 questions exploring several aspects including socio-demographic characteristics, HIV-related health data, information on disclosure of HIV, perceptions of stigma and self-stigma, and female specific health aspect such as pregnancy, menopause, contraception and cancer's screenings. The online RedCap survey has been conducted from Jun22 to Mar23.

Results: The sample comprises 210 WLWH, median age 52 (IQR 29-62), medium-high cultural level, mainly living in northern Italian towns, and economically independent in 63.3% of cases. 7.9% initiated their HIV treatment during the pandemic. In most cases, HIV diagnosis was made more than ten years earlier, with an average of 19 years. 78.6% of WLWH reported a 'good' or 'optimal' opinion on the healthcare received in their center. For 80.9% of cases, the judgment on their clinical center has not changed after the pandemic (only 1.3% reported an improvement). There was a similar judgment in the quality of services provided after the pandemic (no critical issues 60.4% pre-COVID19 period and 57.6% post-COVID19 period, p=0.257). 10.9% pre- and 12.8% post-COVID19 reported a difficulty of being heard (p=0.366). 4.5% decided to change center after the pandemic - Table 1.

Conclusions: The examined women sample shows a relatively stable relationship with reference clinical center during pre-and post COVID19. They maintain the chance to meet the doctor, with low concerns in schedule the appointment. Satisfaction derives from the possibility of reaching health figures on the phone; few problems were reported in the time devoted to the visit, and waiting times, while half of the women reported critical issues with respect to drug procurement, regardless of the pandemic period. The sample may not be representative of the reality of Italian WLWH, as they have a long history of HIV and thus are more confident with health care personel. Main respondents were women followed in larger centers where critical issues due to pandemic may have been more mitigated. The present analysis does not reveal major critical issues in the utilization of the health care system by WLWH with an old HIV diagnosis in the pandemic period.

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STIs, Sexually transmitted infections

P 297 UREAPLASMA UREALYTICUM: A CONTROVERSIAL PATHOGEN TO TREAT. THE EXPERIENCE FROM A DIFFICULT-TO-REACH POPULATION

A. Colpani[1], A. Donisi[2], A. De Vito[1], N. Geremia[3], B. Zauli[1], V. Fiore[1], S. Babudieri[1], G. Madeddu[1]

[1]Unit of Infectious Diseases, Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, [2]Migration Health Unit, Primary Health Care Department, AUSL Piacenza, Piacenza, [3]Unit of Infectious Diseases, Department of Clinical Medicine, Ospedale "Dell'Angelo", Venice, Italy

Background: Ureaplasma urelaytitcum has a controversial pathogenetic role. Its transmission occurs mainly through sexual intercourse. While its treatment is discouraged among the general population, special groups of population may benefit of antibiotic treatment, both for individual and public health concerns. We studied prevalence, treatment, and recurrence of U.urelyticum among a population of undocumented migrants sex workers in Piacenza, Italy in a 20 years' timeframe.

Materials and Methods: We collected medical records from the outpatients' clinic for undocumented migrants in Piacenza, Italy from 1999 until 2021. Only sex workers records were included. Results from cervical swabs and antimicrobial susceptibility (AS) tests were analysed, with a particular focus on U.urealyticum. Clinical and/or microbiological failure was the main outcome. Clinical failure was defined as persistence or presence of symptoms after receiving antibiotic treatment. Microbiological failure was defined as the isolation of U.urealyticum at the follow-up (FU) swab after treatment, with the same AS pattern previously isolated or with just one category (sensitive, intermediate, resistant) variation per single antibiotic or with newly identified resistance according to the prescribed antibiotic (Figure 1). Quantitative variables were summarized as mean and standard deviation (SD), qualitative ones by absolute and relative frequencies. Logistic regression analysis was performed to assess the relationship between sociodemographic, clinical variables and outcome.

Results: Overall, data from 319 women with U.urealyticum were collected. Two-hundred-sixty-seven AS tests were collected, showing high sensitivity rates for doxycycline, josamicine, and other tetracyclines, and high resistance to ciprofloxacin(Figure 2). One-hundred-eighty-seven received antibiotic treatment and 132 were lost to FU(LFU). No variables were significantly associated with LFU. Regarding outcome, having a previous sexually transmitted infection was associated with failure(p=0.033). All antibiotics were associated with higher risk of failure when compared with doxycycline(Table 1). Of the 62 failed patients, 32 did not have AS testing, thus failure rate could be overestimated.

Conclusions: Our data show a good performance of doxycycline in the treatment of U.urealyticum. Its pathogenetic role is controversial, however data regarding particularly at-risk populations are missing. Further study to establish cost-effectiveness of test and treatment of U.urealyticum among sex workers are needed.

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STIs, Sexually transmitted infections

P 298 REDUCTION OF SEXUAL RISKY BEHAVIOR AND VACCINATION DO NOT EXPLAIN DECREASED INCIDENCE OF MPOX AMONG PREP USERS ATTENDING A COMMUNITY-BASED FACILITY

R. Rossotti[1,2], D. Calzavara[2], M. Cernuschi[2,3], A. De Bona[2,4], A. Tavelli[5], S. Bossolasco[2,3], C. Muccini[2,3], D. Tesoro[2,4], D. Moschese[2,6], G. Mulé[2,4], A. d'Arminio Monforte[7]

[1]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [2]Milano Checkpoint, Milan, Italy, [3]San Raffaele Scientific Institute, Milan, Italy, [4]ASST Santi Paolo e Carlo, Milan, Italy, [5]ICONA Foundation, Milan, Italy, [6]ASST Fatebenefratelli Sacco, Milan, Italy, [7]University of Milan, Milan, Italy

Background: The Italian monkeypox (MPX) outbreak involved essentially the Milan area starting from mid-June 2022. As observed in other European regions, new cases decreased significantly by October but no reasons for this epidemiologic trend have been established yet. We aimed to assess whether reduction in sexual activity and at-risk behaviors and/or vaccination might explain this finding in PrEP users attending a community-based service.
Methods: Milano Checkpoint provides assistance to the largest Italian cohort of PrEP users. At each visit clients are tested for sexually transmitted infections (STIs) and fill self-administered questionnaires about their behavior in the previous 3 months. Subjects with a visit in July to November 2022 were selected: overall and condomless sexual intercourses, chemsex practices, and STIs incidence were compared to what registered in the previous visit. Descriptive statistics and non-parametric tests (Pearson's Chi-square, Mann-Withney U, McNemar exact, and Wilcoxon signed-rank) were used to compare groups, while incidence rates of STIs and incidence rate ratio (IRR) were calculated. Logistic regression model was built to describe factors associated to change in sexual encounters.
Results: We selected 435 individuals: Table 1 describes features of study population. Smallpox vaccine was available from the second half of August and only a minority (26.2%) completed the full course. A reduction in the number of intercourses was observed in 174 (40.0%) PrEP users, but the majority did not change the number of sex acts during the MPX outbreak: the overall number of sexual contacts arose from 11 (IQR 5-25) to 12 (IQR 5 -26) in the epidemic months (p=0.070). Condomless intercourses and use of chemsex did not change (p=0.459 and p=0.766, respectively). The incidence of STIs was 87.3 per 100 PYFU in the pre-epidemic versus 84.8 per 100 PYFU in the epidemic period (IRR 1.03, 95% CI 0.80-1.32, p=0.813). The only factor associated to reduction in sexual activity was a lower level of education (OR 0.69, 95% CI 0.54-0.86, p=0.001). Sexual behavior did not change after vaccination (p=0.593) nor a diagnosis of MPX (p=0.856).
Conclusions: Both reduction of risky sexual behavior and MPX vaccination do not explain the vanishing of epidemics. Saturation of high-risk groups or hesitancy to contact health facilities to avoid quarantining policies should be investigated.

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STIs, Sexually transmitted infections

P 299 MONKEYPOX IN A WOMAN WITH HIV INFECTION: A CASE REPORT

S.M. Susini[1], A. Maddaloni[2], P. Bellopede[2], M. Talamo[2], S. Parente[2], A. Giaccone[2], A. Gallicchio[2], A.R. Buonomo[1], I. Gentile[1], A. Franco[2]

[1]AOU Federico II, U.O.C. Malattie Infettive e Tropicali, Napoli, [2]AORN Ospedale dei Colli, Ospedale D. Cotugno, U.O.C. Malattie Infettive dell'Età Geriatrica, Napoli

Background: Monkeypox is a zoonotic infection caused by Monkeypox virus, an Orthopoxvirus similar to smallpox. In May 2022 for the first time many outbreaks were reported worldwide and Monkeypox was soon declared by the WHO a public health emergency of international concern (PHEIC), reaching 86,500 confirmed cases globally by February 2023, the majority of whom being observed among men who have sex with men (MSM).

Case Presentation: A 33-year-old woman with HIV-1 infection and undetectable HIV RNA, CD4+ T lymphocytes count 913/µl, sought medical attention in August 2022 for mild fever with chills, painful and swollen cervical and axillary lymph nodes and headache, followed by the onset of vesicular rash and odynophagia. Skin lesions were localized in the armpit and they were characterized by multiple vesicles with a synchronous evolution towards itchy scabs within one week. The patient reported unprotected heterosexual intercourses in the previous two weeks. The patient tested positive for Monkeypox DNA on blood sample and molecular swab performed on vesicular lesions. The patient was therefore isolated at home for 21 days, until lesions spontaneously disappeared. Contact tracing was carried out, but not secondary contagions were reported.

Discussion: Only a minority of cases has been reported among heterosexual patients, especially women. Furthermore the armpit is an uncommon localization for Monkeypox lesions as they are mostly localized in the genital area or extremities. No specific treatment has been approved for Monkeypox so far. Antiviral drugs such as tecovirimat may be recommended for patients who are more likely to become seriously ill, such as patients with acquired or primitive immunodeficiency, hematological patients and patients on immunosuppressant drugs. In Italy Monkeypox vaccine is currently recommended for MSM patients, however it should be taken into consideration for non MSM patients with HIV infection or people with multiple sexual partners.

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STIs, Sexually transmitted infections

P 300 DOXYCYCLINE ORAL TREATMENT FOR LATENT SYPHILIS: EVALUATION OF OUTCOMES AND TOLERABILITY

M.L.Colombo[1,2], D. Moschese[3], A. Rizzo[4], F. Petri[5], G. Carrozzo[1,2], M.V. Cossu[3], G. Rizzardini[3], A. Gori[2,5], S. Antinori[1,2]

[1]III Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [2]Università degli Studi di Milano, DIBIC Luigi Sacco, Milan, Italy, [3]I Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [4]Laboratory of Clinical Microbiology, Virology and Bioemergencies, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy, [5]II Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Milan, Italy

Background: Syphilis is a sexually transmitted infection (STI) that can cause serious health problems if left untreated. When neurological involvement and pregnancy are excluded, first-line treatment in case of latent syphilis consists of penicillin G benzathine (BPG). In case of penicillin allergy or refusal of injections, doxycycline is an alternative treatment, but data on its efficacy, especially against late latent syphilis, are limited. We describe our experience of doxycycline treatment for latent syphilis in our STI outpatient clinic in the year 2022.

Material and Methods: In the presented experience, we included consecutive subjects diagnosed with latent syphilis at our STI outpatient clinic from January to December 2022 who could not receive first-line treatment due to allergy to beta-lactam or refusal of injections. All subjects were followed until 31st March 2023, for at least 5 months after treatment. We collected demographic characteristics.

Second-line treatment with doxycycline 100 mg every 12 hours (14 days for early latent infection, 28 days for late latent infection) was prescribed to all subjects. We assessed doxycycline treatment efficacy in both late and early latent syphilis. The efficacy of treatment was evaluated in terms of a negative nontreponemal quantitative test by rapid plasma reagin (RPR) or a reduction of at least 4 times (2 dilutions) of its titre.

Results: A total of 21 subjects were diagnosed with latent syphilis at our STI outpatient clinic and received treatment with doxycycline. They were prevalently males (90.4%) with a median age of 42 (IQR, 35 - 47). Most of the subjects were people living with HIV (57.1%), all of them on antiretroviral therapy and a CD4+ cell count > 350/mmc (Table 1).

As shown in Figure 1, a total of 17 subjects (81%) were classified as early latent and 4 (19%) as late latent infection. Compliance with doxycycline was 95.2%, with 1 treatment interruption due to gastrointestinal adverse effects (early latent group). 4 patients with early latent infection failed to assess a post-treatment RPR and were thus excluded. For early latent patients, the treatment efficacy rate was 83.3%: 10 patients achieved therapeutic success while 2 patients showed a decline of 1 dilution in RPR titres at month 5 (Figure 2). Among late latent infections, the treatment efficacy rate was 75%: 3 patients achieved therapeutic success while for 1 patient post-treatment RPR declined by 1 dilution after five months of follow-up.

Conclusions: Our experience showed favourable outcomes after doxycycline treatment in both early and late latent syphilis. Even though our experience was limited, the findings are consistent with the literature. Moreover, a shorter follow-up of only five months may have hidden a potentially favourable outcome at month six. Our findings reinforce that, when first-line treatment is not possible, doxycycline can be considered as an option for the treatment of both early and late latent syphilis.

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STIs, Sexually transmitted infections

P 301 LUETIC INFECTION IN THE PRESENT DAY: CHARACTERISTICS OF A COHORT OF PATIENTS DIAGNOSED WITH SYPHILIS IN THE ROMAN SUBURBS

M. Zordan, M. Compagno, A. Di Lorenzo, L. Ansaldo, D. Checchi, L. Ferrari, E. Teti, M. Iannetta, L. Sarmati

Roma, Università di Tor Vergata

Introduction: Syphilis is a sexually transmitted infection (STI) caused by Treponema pallidum. Although considered to be less common than in the past, it remains a global public health problem that should not be underestimated due to its possible serious consequences.

Methods: In this single-centre retrospective study, we analysed the characteristics of patients diagnosed with syphilis at the Infectious Diseases Clinic of Tor Vergata Hospital (Rome) between January 2018 and December 2022.

Results: We included 151 patients who received a diagnosis of syphilis in the period of observation, with a major reduction of new cases in 2020 due to COVID-19 pandemic [Tab.1]. They were predominantly men (84.1%), Italian (74.2%), male-male-sexuals (MSM) (55%) and with a median age of 39 years (IQR 31-47) [Tab.2]. 62 patients (41.1%) were people living with HIV (PLWH), 9 (6%) had chronic HBV infection and 10 (6%) had HCV antibodies, 6 (3.8%) of them had detectable HCV-RNA.

25 (16.5%) patients presented with symptoms related to luetic infection, while 105 (69.5%) had no symptoms; for 21 (13.5%) of them no data about symptoms were available. Latent syphilis was the most frequent form (late in 64.6% and early in 6.6%) followed by secondary (8.6%), primary (7.3%) and tertiary (1.3%)[Tab.3]. 9 patients (6%) were simultaneously diagnosed with HIV and 26 (17.2%) with another STI. 58 patients (38.4%) had already received a syphilis diagnosis in the past (prior to the observation period), more frequently among PLWH ($p<0.001$). 19 patients (12.6%) were diagnosed with luetic reinfection in the observation; the diagnosis of reinfection was more frequent in PLWH ($p=0.037$) [Tab.4]. The majority of patients were treated with benzathine benzylpenicillin in single (19.2%) or triple (59.2%) administrations, 5.3% with doxycycline and 2.3% with ceftriaxone; data were not available in 13.9% of cases. [Tab.5].

Conclusions: Syphilis is still a frequent infection and PLWH are at higher risk of contagion. The majority of our patients were diagnosed at an asymptomatic stage of the disease, which is why it is necessary to increase the habit of regular screening especially in high risk populations, even in the absence of compatible symptoms.

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STIs, Sexually transmitted infections

P 302 PREVALENCE OF HUMAN PAPILLOMAVIRUS (HPV) IN THE ORAL SWABS OF PATIENTS AT UNIVERSITY HOSPITAL OF BARI

D. Nesta[1], V. De Laurentiis[1], E. Milano[2], M. Lorusso[1], S. Piccolo[1], L. Capozzi[1], M. Mastria[1], S. Garzone[1], E.M. Ranieri[1], S. Stolfa[1], F. Romanelli[1], S. Denicolò[1], L. Nisi[1], M.T.Montagna[3], A. Saracino[2], A. Mosca[1], R. Del Prete[1], A. Visceglia[1], L. Ronga[1]

[1]UOC Microbiology and Virology, University "Aldo Moro", Bari, [2]Clinic of Infectious Diseases, University "Aldo Moro", Bari, [3]Department of Biomedical Sciences and Human Oncology, Section of Hygiene, University "Aldo Moro", Bari

Background: Human Papillomavirus (HPV) is one of the most common sexually transmitted pathogens, accounting for 5% of all cancers worldwide. HPV is associated with both benign lesions and with neoplastic diseases, such as oropharyngeal cancer. Although the presence of oral HPV has been investigated in several studies, data from the literature is limited so better understanding of its epidemiology and infection-related characteristics is crucial for effective and targeted prevention efforts.
The purpose of this study is to assess the prevalence of HPV in oral swabs in a population referred to the University Hospital of Bari.
Material and Methods: All the results obtained from 174 oral swabs analyzed for HPV detection from February 2017 to December 2022 were retrospectively collected. DNA was extracted using MagNa Pure Compact Nucleic Acid Isolation Kit I by the MagNa Pure Compact System (Roche Diagnostics). DNA amplification was performed by Anyplex™ HPV28 Detection (Seegene).
The patient dataset was built after removal of duplicated of the same patients. Statistical analysis was performed by the open-source environment R 4.2.1.
Results: The samples have been collected from a cohort of 78 females and 74 males, with median age of 53 (IQR:35-69) and 51 (IQR: 38.5-60.75), respectively. Median age of female and male patients was not statistically different (Kruskal-Wallis p-value=0.350).
As suggested by loess non-parametric regression and confirmed by two negative binomial regression models on both the patients and samples datasets, the monthly number of patients abruptly decreased after Covid-19 social distancing measures.
Oral HPV has been detected in 14 out of 152 patients (9.21%, 95%CI: 5.32%-15.26%) without any difference among females and males (6.41% Vs 12.16%, Fisher's exact test p-value=0.268).
In total, the following HPV-genotypes have been detected: HPV-16 (3, 1.97%), HPV-33 (2, 1.32%), HPV-35 (1, 0.66%), HPV-39 (2, 1.32%), HPV-42 (3, 1.97%), HPV-51 (1, 0.66%), HPV-56 (2, 1.32%), and HPV-6 (4, 2.62%). Only one multiple infection (5 different genotypes) has been detected. Median age has not been different between HPV positive and negative patients (53 Vs 40, Kruskal-Wallis p-value=0.084).
Prevalence of HPV infection has not been statistically different before and after the Covid-19 social distancing measures (10.26% Vs 5.71% Fisher's exact test p-value=0.524).
Discussion: HPV oral prevalence (~10%) is consistent with the medical literature, and it has not modified by the Covid-19 social distancing measures, despite the reduced testing. As HPV infection is thought to cause 70% of oropharyngeal cancers in the United States, the impact on people's health is quite evident, therefore necessitating vaccine coverage to prevent oropharyngeal cancer. At the same time, increased screening is required to both detect symptomatic and asymptomatic HPV-infected individuals as the overall testing is below the average of the pre-Covid-19 age.

STIs, Sexually transmitted infections

P 303 PREVALENCE OF SEVEN SEXUALLY TRANSMITTED PATHOGENS IN ORAL CAVITY AND THE IMPACT OF A NEW DEDICATED AMBULATORY FOR STI AND PRE-EXPOSURE PROPHYLAXIS (PREP) IN BARI

M. Lorusso[1], L. Ronga[1], E. Milano[2], V. De Laurentiis[1], M. Mastria[1], S. Garzone[1], F. Indraccolo[1], S. Stolfa[1], F. Romanelli[1], S. Denicolò[1], L. Nisi[1], M.T. Montagna[3], A. Saracino[2], A. Mosca[1], R. Del Prete[1]

[1]UOC Microbiology and Virology, University "Aldo Moro", Bari, [2]Clinic of Infectious Diseases, University "Aldo Moro", Bari, [3]Department of Biomedical Sciences and Human Oncology, Section of Hygiene, University "Aldo Moro", Bari

Background: Sexually transmitted infections (STIs) are a considerable public health issue with high prevalence and incidence. From January 1991 to the end of 2019, the Italian sentinel surveillance system for STIs recorded 140.874 cases, with males accounting for 71.5% of the cases.
The purpose of this study is to estimate the prevalence of seven bacterial sexually transmitted pathogens detected from oral swabs, and to evaluate the impact of a new ambulatory for STIs at the Infectious Disease Clinic at the University Hospital of Bari.
Material and Methods: All the results obtained from the oral swabs analyzed for STIs detection were retrospectively collected. Duplicated of the same patient were removed from the final dataset.
DNA was extracted using MagNa Pure Compact Nucleic Acid Isolation Kit I (Roche Diagnostics) by the MagNa Pure Compact System (Roche Diagnostics). DNA amplification was performed by AnyplexTM II, STI-7 Detection Kit (Seegene). The kit is able to identify Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG) (b), Ureaplasma urealyticum (UU), Ureaplasma parvum (UP), Mycoplasma hominis (MH), Mycoplasma genitalium (MG), Trichomonas vaginalis (TV).
One sample collected from a female subject was processed by the Genexpert CT/NG (Cepheid).
Statistical analysis was performed by the open-source environment R 4.2.1.
Results: The results of 130 oral swabs collected from an equal number of patients (16 females and 114 males) from January 2015 to December 2022 were analyzed. Overall median age was 37.5 (IQR: 28.25-47.00), while the median age of females and males was 54.50 (IQR: 32-65.50) and 36.50 (IQR: 28.25-46.00) without any statistically significant difference (Kruskal-Wallis p-value=0.060, Hedge's g=0.11).
The opening of the STIs ambulatory in November 2021 was associated with a level increase of the monthly time-series of patients, as confirmed by a Negative Binomial GAM model. But only among male patients did the number of testing continue to rise. (Fig. 1).
In 32 patients (32/130=24.6%), at least an infection was detected. In particular the prevalence was:
NG – 6.15%;
UU – 5.43%;
UP – 0.76%;
MH – 3.88%;
TV – 15.50%.
A comparison by sex wasn't done due to the small amount of females and the unique positive result due to TV (1/15, 6.67%). The prevalence of the detected microorganisms was also not significantly different before and after opening.
Discussion: The new STIs ambulatory significantly increased the monthly number of patients who underwent the oral swab to identify seven non-viral pathogens, despite the non-significant difference in prevalence before and after the ambulatory opening.
Overall, the female patients remained constantly low with time. Concerning implications for female patients' health and the epidemiological spread of non-symptomatic infections call for quick action to ensure equal access to the healthcare systems.

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STIs, Sexually transmitted infections

P 304 NEISSERIA MENINGITIDIS IN PREP USERS: SEXUAL TRANSMISSION AND ISOLATION OF AN ESBL POSITIVE STRAIN

G. Gamboni[1], C. Pallotto[1], C. Papalini[1], A. Repetto[2], F. Allegrucci[2], E. Schiaroli[1], D. Francisci[1]

[1]Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy, [2]Department of Medicine and Surgery, Medical Microbiology Section, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy

Background: N. meningitidis (Nm) sexual transmission has been recently described in several studies, especially in MSM population. Nm showed a remarkable genic plasticity due to the capability of genetic exchange with other pathogenic and non-pathogenic bacteria. The acquisition of additional resistance mechanisms, the emergence of hypervirulent groups and the ability to colonize extra-pharyngeal mucosal surfaces can be explained by this process. In the last decade outbreaks of Nm invasive disease in MSM communities were reported in North America and Europe and the incidence of Nm urethritis and proctitis in STI prevention setting, such as PrEP clinics, is increasing. We describe a case series of a Nm cluster observed in the PrEP outpatient clinic of Perugia, a medium size southern european setting.

Materials and Methods: We retrospectively analyzed all the patients with Nm isolation in pharyngeal, urethral and anal samples.

Results: From October 2022 to February 2023 we isolated Nm in 6 patients grouped in 2 different small clusters. Main characteristics of the patients were summarized in table 1. They were all PrEP users except for one patient who was on post-exposure prophylaxis. Five patients reported a previous STI; every patient suffered from a concomitant STI in addition to Nm infection/colonization. The first cluster consisted of 3 cases: one symptomatic proctitis and 2 asymptomatic pharyngeal colonizations. The patient with Nm proctitis presented with asthenia, anal tenesmus and fever. The direct microscopic examination of the anal swab showed an inflammatory pattern. The second cluster consisted of a symptomatic Nm pharyngitis and 2 further asymptomatic pharyngeal colonizations. We identified an ESBL producer Nm in a patient coming from England while the remaining isolates were susceptible to ceftriaxone. The symptomatic patients were treated for 7 days. The asymptomatic patients received a prophylaxis with ciprofloxacin when cetfriaxone was not prescribed to treat a concomitant infection.

Conclusions: Although a strict indication to treat Nm colonizations is not available, we administered in such cases a prophylaxis to reduce the potential Nm spreading in a community with an elevated frequency of sexual contacts. Few data are available about Nm proctitis, and it is still difficult to clarify his burden in clinical infection or its potential role in facilitating acquisition of an additional STI as demonstrated for N. gonorrhoeae. Our findings, according with other studies in literature, underline the importance of a meningococcal screening in higher risk population, like PrEP users, to adopt the correct clinical practices and strategies in public health prevention.

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STIs, Sexually transmitted infections

P 305 HIV AND SYPHILIS RAPID TESTS AMONG UNIVERSITY STUDENTS: A PREVENTION AND AWARENESS CAMPAIGN TOWARDS SEXUALLY TRANSMITTED INFECTIONS

F. De Gregorio, M. Niglio, C. Grillo, R. Papale, M. Caggese, F.R.P. Ieva, A. Narducci, E.P. Drago, T.A. Santantonio, S. Lo Caputo

Infectious Disease Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy

Introduction: Rates of new sexually transmitted infections (STIs), such as HIV, syphilis, chlamydia, and gonorrhea, are rising among adolescents and young adults worldwide. To improve knowledge of STIs and testing behaviors, we launched a campaign for prevention and awareness among students of the University of Foggia. The project named “Educate-Prevent-Test” was realized by residents in Infectious Disease, University of Foggia.
Methods: The project, still ongoing, started on December 2022 and targets all students of the University of Foggia. All participants were administered two questionnaires, one concerning general STI knowledge (10 items) and the other about sexual habits. In addition, the execution of rapid tests (Abbott kits DETERMINE antigenic tests for HIV EARLY DETECT and SYPHILIS TP) for Syphilis and HIV infections is offered, previous a signed informed consent.
Results: 270 subjects were tested: 170 women (63%), the age distribution was: 18 -20 years =81 (30%), 21-25 years=127 (47%) over 25 years=60 (22%). The STI general knowledge questionnaire showed that 230 (85%) students knew the risk of STIs transmission by oral practices, 243 (90%) knew the efficacy of cART to inhibit HIV replication, but 114 (42%) didn't know the correlation between cART efficacy and HIV infection transmission (U=U definition). Moreover, 235 (87%) knew that contraceptive pills do not protect against STI transmission, and 27 (10%) didn’t know which vaccines for STIs are now available. Sexual behaviors questionnaire revealed that 58/270 students (21%) had performed test for HIV or Syphilis previously; 167 of them (62%) had 1 sexual partner for a year, 81 (30%) had from 2 to 5 sexual partners for the year, and only 16 subjects (6%) had more than 5 sexual partners for the year. Furthermore, 89 of 270 tested students (33%) habitually practiced unsafe sex, and only 12 (4%) reported previous treatment for STI. None of the tested students showed a positive test for HIV or syphilis.
Conclusion: From our preliminary data, we observed that larger campaigns for STIs screening by rapid exams, can be considered a great opportunity for early diagnosis. Besides, we think that "peer to peer" test execution may ensure a higher rate of project adherence, to improve knowledge about sexual risk behaviors and to raise awareness about STIs in our study population.

STIs, Sexually transmitted infections

P 306 DISTINCT MUCOSAL INTERFERON RESPONSE TO MPXV, HIV AND HPV INFECTIONS IN ANAL CELLS FROM MSM

M. Fracella[1], L. Maddaloni[2], A. D'Auria[1], F. Frasca[1], L. Santinelli[2], C. Bitossi[1], N. Cavallari[2], P. Mazzetti[3], A. Pierangeli[1], C.M. Mastroianni[2], M. Pistello[3], G. Antonelli[1], G. D'Ettorre[2], C. Scagnolari[1]

[1]Laboratory of Virology, Department of Molecular Medicine, Sapienza University of Rome, Rome, Italy, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy, [3]Virology Section and Retrovirus Centre, Department of Biomedicine, University of Pisa, Pisa, Italy

Background: The recent outbreak of monkeypox virus (MPXV) in non-endemic countries and its biological implications on human health have aroused wide concern. The possibility of MPXV sexual transmission is being investigated, as transmission rate appears to be elevated in men who have sex with men (MSM) and has been associated with unexpected anal and genital lesions. Previous studies have reported that poxviruses use a multitude of strategies to disable host innate immunity, including Interferon (IFN) response. It is well documented that sexually transmitted infections (STIs) modify the mucosal environment; notably, HIV may alter the epithelial integrity, favoring HPV infection on basal cells, where it dysregulates cell division and local immunity. To gain insight into the mucosal immunity to MPXV, in comparison with HIV and HPV infections, we investigated the expression levels of type I and III IFNs related genes in anal cells from MSM.
Methods: Forty-five anal canal brushing samples were collected from MSM patients attending a proctology clinic. Detection of HPV and MPXV DNA was performed by RT-PCR. From purified cellular RNA, transcripts of genes coding for type I IFNs (α2A, β) and their receptor subunits (IFNAR1/-2), for type III IFNs (λ1 to 3) and their receptor subunit (IL28R1) and for ISGs (ISG15 and ISG56) were measured by quantitative RT-PCR assays and normalized to the housekeeping GUS gene (the 2^−ΔCt method).
Results: Five MPXV(+) men (that were HIV and HPV negative), 10 HIV(+)/HPV(-) men, 10 HIV(-)/HPV(+) men, 10 HIV(+)/HPV(+) men and 10 healthy controls (HC) were enrolled in this study. Comparing groups, IFN-AR1, IFN-AR2, ISG15 and ISG56 [$p<0.05$; Kruskal-Wallis (KW) test)] were highly expressed in MPXV(+) patients, while IFN-λ3 ($p< 0.001$ KW test) was drastically down-regulated. MPXV group also showed lower levels of IFN-λ1 mRNA [$p<0.05$; Mann-Whitney (MW) test] compared to HIV(+)/HPV(-) and HIV(+)/HPV(+) men. Moreover, IFN-α2A and IFN-β ($p<0.05$; MW test) decreased in MPXV(+) patients compared to HC. Comparing HIV(+)/HPV(+) men and HC, IFN-β and IFN-λ2 ($p<0.05$; MW test) were less expressed in co-infected patients. In addition, HPV(+)/HIV(-) patients had lower levels of IFN-α2A and IFN-β mRNA as opposed to other groups ($p<0.05$; KW test).
Conclusions: Our data indicated a differential and dysregulated expression of IFNs and ISGs genes in anal cells of MPXV(+) patients, supporting the notion that down-regulation of type III IFNs with the activation of heterogeneous patterns of IFN expression, including ISG15 and ISG56, may be associated to disease severity. Also, our investigations on HPV(+)/HIV(+) co-infected men reported a significant downregulation of IFN genes that may facilitate both HIV spread to adjacent cells and HPV persistence. Hence, clarifying IFN pathway dysregulation in MSM during STIs may help in devising immunotherapeutic strategies to limit the risk of HPV/HIV-related anal cancer and MPXV disease severity.

STIs, Sexually transmitted infections

P 307 RAPID INCREASE IN SYPHILIS DIAGNOSES IN ROME DURING THE FIRST QUARTER OF 2023

C. Stingone, M. Giuliani, L. Gianserra, M.G. Donà, E. Giuliani, F. Pimpinelli, A. Latini

San Gallicano Dermatological Institute IRCCS of Rome, Italy

Background: Syphilis and gonorrhea are robust biological indicators of recent risky sexual behavior, and the increase in their incidence is associated with significant changes in the sexual behaviors toward unsafe sexual practices. A significant increase in syphilis incidence has been recorded in recent years in core communities such as MSM, also related to the use of pre-exposure prophylaxis (PReP) to prevent HIV. Recently, a dramatic increase in diagnoses of syphilis has been observed at the STI Center of S. Gallicano Dermatological Institute of Rome, Italy.

Material and methods: From the computerized archive of STI cases, all syphilis and gonorrhea diagnoses (pharyngeal, rectal and urethral infections) from September 2022 to March 2023 were retrieved, from both, HIV positive and negative populations. All cases of primary, secondary, and recent latent (< 1 year since infection) syphilis were identified as recent syphilis (RS). Data were recorded by month of diagnosis.

Results: A total amount of 123 syphilis diagnoses were recorded over the study period. Of those, 104 have been identified as RS (84.6%). HIV infected patients accounted for 38/123 (30.9%) and 34/104 (32.7%) cases, respectively. While the number of cases was stable until January 2023, a dramatic increase has been observed in February, when a peak was reached: 36 total diagnoses, of which 31 RS. The large majority of infections was observed in MSM population.

On the other hand, Gonococcal disease did not show a similar increase remaining stable over the entire observation period.

Conclusions: The observed increase in both total syphilis and RS diagnoses during the first quarter of 2023 compared to the previous months suggests that an outbreak is ongoing in the MSM roman community. The observed increase has prompted us to alert LGBT+ associations in order to spread information and maximize the syphilis' screening, also in the context of POCs through rapid tests.

STIs, Sexually transmitted infections

P 308 WHEN IT RAINS, IT POURS: EARLY TREATMENT WITH TECOVIRIMAT OF MYOPERICARDITIS ASSOCIATED WITH MONKEYPOX INFECTION IN A PERSON WITH HIV AND PREVIOUSLY UNDIAGNOSED LYME DISEASE

G. Formica[2], F. Lagi[1], A. Rostagno[2], A. Milia[3], S. Pradella[4], G. Guazzini[3], S. Tekle Kiros[2], P. Corsi[1], A. Bartoloni[1,2], F. Pieralli[3]

[1]Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, Italy, [2]Department of Clinical and experimental medicine, University of Florence, Florence, Italy, [3]Intermediate Care Unit, Careggi University Hospital, Florence, Italy, [4]Department of Radiology, Careggi University Hospital, Florence, Italy

Background: Since early May 2022, cases of monkeypox (Mpox) have been reported from countries where the disease is not endemic, and continue to be reported in several endemic countries. Common manifestations are rash with umbilicated vesicles and systemic symptoms. Serious complications like secondary skin infections, pneumonia, encephalitis, and myocarditis can occur. We present a case of Mpox infection complicated by myopericarditis in a person living with HIV with a previously undiagnosed Lyme disease.

Case Report: The patient was a 42-years old man, MSM, with undetectable HIV-RNA for more than 10 years, stable CD4 cell count, and in treatment with TAF/FTC/RPV.

We evaluated him in the outpatient clinic because of the appearance of low-grade fever and some skin lesions on the genitals. The polymerase chain reaction (PCR) for Mpox DNA from skin lesions tested positive. In the absence of other symptoms, he was isolated at home. Two days after the first evaluation, the patient reported a rise in body temperature up to 39°C, chest pain without irradiation, and shortness of breath. The patient was then referred to the emergency department (ED) and then hospitalized on suspicion of myopericarditis. We found an increase in troponin level, a slight reduction in ejection fraction, and grade 2 AV block (Mobitz 1 and 2) with frequent sinus pauses (the longest of 10.1 s). Colchicine, ibuprofen, and antiviral therapy with tecovirimat 600 mg bid were started. Low-dose dopamine was administered due to hypotension in bradycardia. Cardiac MRI with gadolinium showed mild interstitial edema with mild pericardial enhancement. The patient was discharged from the intermediate care unit on the 19th day. The 2:1 AV block was still recorded on the Holter ECG performed on day 26. Considering that high-degree AV block is the most common presentation of Lyme carditis, the patient was investigated for Lyme disease. Serological results evidenced a previous Borrelia burgdorferi senso latu, hence we decided to treat the patient with antibiotic therapy, although it was not possible to determine a role of a previous Lyme disease in the cardiac abnormalities observed during the Mpox acute infection. At the evaluation on day 44, the patient appeared in good condition no indications for PM implantation were given by the cardiologists.

Discussion: Myocarditis and pericarditis are possible severe complications with very few described cases in the literature. Tecovirimat is an antiviral specifically designed to inhibit smallpox infection diffusion and its efficacy in Mpox-infected patients is not well established and a randomized clinical trial in humans with Mpox infection is currently ongoing.

The potential risk of serious complications from Mpox infection may warrant special attention and monitoring since the isolation phase at home.

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STIs, Sexually transmitted infections

P 309 NEISSERIA GONORRHOEAE IN A LOCALIZED SEPTIC ARTHRITIS: AN UNUSUAL AETIOLOGY

M. Zagarrigo, S. Tedeschi, E. Zamparini, A. Cascavilla, G. Fornaro, A. Zuppiroli, P. Viale

Infectious Diseases Unit, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

Background: Disseminated gonococcal infection is caused by the hematogenic diffusion of N. gonorrhoeae. It represents a complication in 0.5-3% of gonococcal infections, mostly in patients younger than 40 years old.
Spectrum of manifestations ranges from suppurative arthritis to tenosynovitis-dermatitis-polyarthralgias triad with systemic symptoms.
The diagnosis is clinical and laboratoristic, searching for N. gonorrhoeae in blood, pharynx, rectum and genital samples, urine and synovial fluid. The culture of the latter is positive in less than 50% of the cases of suppurative arthritis and even lower in the triad.
Treatment is usually with surgical debridement followed by intravenous cephalosporin.
Case Report: A 30-years-old male suffered a traumatic injury of the right hand and left knee at the beginning of Oct. 2022. After 10 days, he experienced a strong pain in the injured knee, associated with fever up to 38.5°C, nausea, vomiting and diarrhoea.
After 3 days he went to the E.R. of an orthopedics-specialized hospital, where he underwent blood cultures (resulted negative) and arthrocentesis that showed high proteins (5.3 g/dL) and leucocytes (86'350/mmc, 92% polymorphonucleates) and low glucose. The synovial fluid was cultured as well.
The arthroscopic debridement surgery was performed the same day and showed hemarthrosis, intraarticular fibrosis, synovial pseudomembranes and chondropathy. Surgical-obtained synovial fluid analysis confirmed the previous findings. Broad spectrum antibiotic therapy with daptomycin plus piperacillin/tazobactam was started immediately after surgery upon Infectious diseases consultation, but was stopped after a few days because of hypertransaminasemia.
After 8 days, the culture of only one sample of synovial fluid out of all the other samples resulted positive for N. gonorrhoeae (ciprofloxacin resistant, ceftriaxone susceptible).
The patient was then transferred to our Infectious Diseases Ward, where he was given a ceftriaxone-based treatment and was checked up for STDs. When asked, the patient reported unprotected sexual intercourses with multiple partners. The patient refused to undergo pharyngeal and rectal swabs for PCR search of chlamydia and N. gonorrhoeae DNA, so only the PCR on the urine sample was performed and was negative. HIV, major hepatotropic viruses, syphilis, CMV and EBV testings were negative as well.
The treatment with ceftriaxone was continued in a Day Hospital regimen for a total of 18 days, with clinical and laboratoristic improvement.
Conclusion: Gonococcal septic arthritis may cause joint damage if treatment is inadequate or if left untreated. Since the fastidious nature of gonococci in cultures and the lately increasing rate of multi-resistant strains, it is important to test for N. gonorrhoeae also the urogenital and extra-genital sites in sexually active patients at high risk with suspected disseminated gonococcal infection, along with an accurate sexual history of the patient.

STIs, Sexually transmitted infections

P 310 ANALYSIS OF STIS INCIDENCE AND RISK FACTORS IN A COHORT OF MSM ATTENDING A PREP COMMUNITY-BASED CENTER AND THE STD OUTPATIENT CLINIC OF THE DERMATOLOGY DEPARTMENT OF S.ORSOLA-MALPIGHI HOSPITAL IN BOLOGNA. ONE YEAR FOLLOW-UP DATA FROM SEX-CHECK-PLUS STUDY

P. Fait[1], M. Casarini[1], D. Marzolla[1], S. Cretella[1], D. Testi[1], B. Nuti[1], A. Pozzi[1], C. Patrucco[1], L. Piazza[1], I. Sartini[1], L. Rapparini[2], S. Mattioli[3], M. Pedone[3], S. Cecere[3], L. Badia[4], V. Gaspari[2]

[1]Alma Mater Studiorum University, Infectious Disease Department, S.Orsola-Malpighi Hospital, Bologna, [2]Alma Mater Studiorum University, Dermatology Department, S.Orsola-Malpighi Hospital, Bologna, [3]Plus aps, PrEP Point Plus, Bologna, [4]Infectious Disease Department, Azienda USL di Imola

Background: Men who have sex with men (MSM) are at high risk of HIV and other sexually transmitted infections (STIs). Pre-exposure prophylaxis (PrEP) is effective in reducing HIV risk but does not protect from other STIs; indeed, concerns remain that PrEP use may lead to increased STIs acquisition. Frequent screening and early detection remain a key prevention tool; intra and extra-hospital settings both represent, in this scenario, a valuable help.

Materials and methods: We conducted a retrospective study through the analysis of two cohorts. The first (cohort 1) consists of HIV-negative cisgender MSM subjects receiving PrEP at a community service in Bologna, Italy. These subjects were followed up with a visit every three months consisting of a counseling session, the administration of an anonymous questionnaire on sexual habits and self-perception of risk, and rapid diagnostic tests for HIV, HCV, syphilis, Chlamydia trachomatis, and Neisseria gonorrhoeae (CT/NG) on urine, rectum, and oropharyngeal swab samples.

The second group (cohort 2) consists of HIV-negative cisgender MSM subjects not taking PrEP who attended the STD outpatient clinic of the hospital's Dermatology Department. These patients were not included in a standardized STIs screening, but went to the clinic according to their needs.

In both groups, we analyzed data from subjects who made three or four accesses in the time period between December 2020 and March 2022.

Results: A total of 192 MSM were enrolled; 96 subjects took PrEP at some point during the study, while 96 never took it. The mean age was 43 years (IQR 26-64). In cohort 1 37% of the respondents reported >10 different sexual partners in the previous 3 months; 36% and 33% reported condom use in less then 50% of insertive and receptive anal intercourses respectively; 40% reported sex without a condom with 1-5 partners of unknown serostatus in the previous 3 months.

Regarding chemsex habits, we found that 32% of the respondents had sex under the influence of drugs.

During the study period, in the cohort 1 we diagnosed 25 infections caused by CT (including 1 reinfection), 19 caused by NG (including 3 reinfections) and 4 syphilis; no HIV infections were diagnosed. The cumulative incidence of STIs was 46% over the analyzed time period. The annual incidence rate was 0,6.

Conclusions: Data collected within our cohorts show a high incidence of STIs, demonstrating how close monitoring in both hospital and community-based approaches are important in managing populations with specific risk factors.

STIs, Sexually transmitted infections

P 311 SYPHILIS IN PREP USERS AND PLWH ATTENDING AN OUTPATIENT CLINIC OF A LARGE CLINICAL CENTRE IN ROME

R.J. Steiner[1], P.F. Salvo[1], D. Zjalic[2], D. Farinacci[3], C. Savoia[2], G. Baldin[4], A. Ciccullo[5], A. D'angelillo[3], F. Lamanna[1], S. Di Giambenedetto[1,4], A. Borghetti[4]

[1]Dipartimento di Sicurezza e Bioetica, Sezione di Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, [2]Sezione di Igiene, Dipartimento di Scienze della Vita e Sanità Pubblica, Università Cattolica del Sacro Cuore, Roma, [3]UOC Medicina Protetta - ASL Viterbo, Viterbo, [4]UOC Malattie Infettive, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, [5]Malattie Infettive, Ospedale San Salvatore, L'Aquila

Background: In the last years the incidence of syphilis have been increasing substantially, especially among men who have sex with men (MSM), either living with HIV or in Pre-Exposure Prophylaxis (PrEP). We aimed to assess syphilis incidence for these two groups in the years between 2019 and 2022 and assess if there were differences between the two groups.

Material and methods: We enrolled 2600 and 152 PrEP users followed by our clinic between 2019 and 2022, All the enrolled patients were tested for syphilis with VDRL and TPHA test performed every 6 months.

Results: Among PLWH, the incidences of infection were 1,12%, 0,81%, 0,85%, and 0,81% for 2019, 2020, 2021, and 2022 respectively. In the PrEP group, the incidences were 1,97 %, 5,92%, 6,58%, and 5,92% for 2019, 2020, 2021, and 2022 respectively. Among PLWH, the incidences of re-infection were of 0,23%, 0,19%, 0,31%, and 0,35% for 2019, 2020, 2021, and 2022 respectively. In the PrEP group, the incidences were 3,29%, 0,66%, 2,63%, and 1,97% for 2019, 2020, 2021, and 2022 respectively.

Among PLWH group, 57/220 (25,9%) were symptomatic, while in the other group all the infected patients showed no symptoms.

We have prescribed 220 treatments in the PLWH population, mostly with intramuscular penicillin (204 – 92.7%), while for PrEP users we prescribed 45 treatments, 44 with intramuscular penicillin (97.8%) and 1 with doxycycline due to a reported penicillin allergy.

Conclusions: In the studied population, syphilis incidence have been increased in the observed period of time in the PrEP users population. In that group we also observed a drastic reduction of reinfections in 2020, followed by a rapid increase in the next year. This could be due to the emergence of the SARS-CoV-2 pandemic. Conversely, in PLWH the infections seem to be decreasing and re-infections increased only slightly after 2020. All the PrEP infected users were asymptomatic, suggesting the importance of screening among this population at high risk of STDs.

STIs, Sexually transmitted infections

P 312 A CASE OF OTIC INVOLVEMENT IN SECONDARY SYPHILIS

M. Abbott, A. Gizzi, F. Guida Marascia, D. Spicola, A. Sanfilippo, C. Buscemi, F. Di Lorenzo, C. Iaria

UOC Malattie Infettive e Tropicali, ARNAS Civico, Palermo

Background: With the advent of antibiotic era neurosyphilis has become a rare diagnosis but can lead to irreversible sequelae. There is the asymptomatic involvement (the most common, with spontaneous resolution and no inflammatory response), the early neurosyphilis phase (meningeal NS and meningo-vascular NS) and a late symptomatic phase (tabe dorsalis and general paresis). CNS involvement also includes otosyphilis (OS), it can occur in any stage and lead to irreversible neurosensorial hearing loss, vertigo and gait instability. The diagnosis is difficult to make because clinical manifestations may mimic other causes of hearing loss. The CDC recommends all patients with suspect OS to undergo a lumbar puncture, however the inconsistency of CSF findings does not exclude the diagnosis of OS and should not delay treatment. We report a case of otic involvement in early secondary syphilis.

Case report: A 30-year-old Caucasian male came to the ER with a disseminated non-itchy maculo-papular rash spread through the body (atypically sparing hands and feet) with peripheral scale, cervical lymphadenopathy and a history of high fever (max 41°C), weight loss, night sweats two months before and left-side hearing loss within the last 20. The suspicion of syphilitic rash was confirmed by positive VDRL testing (1:128) and TPPA (1:40960), negative HIV Ab. Due to high-risk sexual behavior history we ran a full STD panel (negative). A single injection of 2.4 mU of im benzathine penicillin was administered. Even if the patient was immunocompetent the extensively disseminated rash and the hearing loss complaint raised the suspicion of CNS involvement. A brain MRI showed bilateral pachimeningeal inflammation with post-contrastographic enhancement, but LP showed no CSF abnormalities and RPR test on CSF was negative. The audiometry confirmed the neurosensorial hearing loss. Treatment for OS was started with ceftriaxone iv 2g daily for 14 days.

Discussion and Conclusions: The suspicion of CNS involvement arises with risk factors, such as HIV+ with low CD4 count with neurological signs and positive serology, but the immunocompetent status should not stop further testing. The utility of CSF findings is controversial as non treponemic serology testing in CSF is not sensitive enough and does not rule out the possibility of NS. Prevalence data of NS and OS are hold back by lack of consistent reports and it is vital to acknowledge these manifestations as syphilis incidence continues to increase all around the world.

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STIs, Sexually transmitted infections

P 313 CASE REPORT: A NOVEL PRESENTATION OF NEUROSYPHILIS IN A HIV-UNINFECTED PATIENT WITH FRONTO-TEMPORAL-PARIETAL CEREBRAL ATROPHY

E. Matteini[1], A. Dusina[1], F. Sanmartin[1], A. Carbone[1], E. Rando[1], G. Maiuro[1], A. Cingolani[1], V. Guglielmi[2], P. Del Giacomo[1]

[1]Dipartimento di Sicurezza e Bioetica, Università Cattolica del Sacro Cuore, Rome (IT), [2]Fondazione Pol. A. Gemelli IRCCS, Neurology Unit, Rome (IT)

Introduction: Neurosyphilis refers to the infection of the central nervous system by Treponema pallidum. It can occur at any time after initial infection. Recently, different presentations of this condition have been identified. The clinical and radiological features of neurosyphilis as cerebral atrophy have not been described in current literature.
Material and Methods: We report a novel case of a 70-years old HIV-uninfected man who came to our attention with progressively worsening speech disorder characterized by anomia and low-fluency. After excluding behavioral disorders and neurodegenerative dementia (negativity of Alzheimer's Disease biomarkers, including Beta Amyloid, total TAU Protein and Fosfo TAU Protein), he underwent MRI: it showed atrophy of fronto-temporo-parietal left lobe associated to widening of the local-regional periencephalic liquor spaces and ex-vacuous dilation of the left lateral ventricle, especially in the temporal horn". Spine MRI showed no signal changes.
Lumbar puncture was performed: hyperproteinorrachia (92 mg/dL), hyperglycorrachia (103 mg/dL), hypercellularity (22/mm3), VDRL ++, TPHA positive with a title of 1/5120; IgG 341 mg/L, albumin 431 mg/L, with IgG index 2.0 and IgG/Alb 79.1. Filmarray negative.
On blood tests, syphilis FTA-AbS +++, VDRL positive with a title of 1/16 and TPHA 1/5120.
HIV-Ab test was confirmed as negative.
Antimicrobial therapy with crystalline G penicillin (6 million units intravenous every four hours) for 14 days was set up.
During the hospitalization the patient was periodically referred for logopedic examination, pointing out a persistent lack of lexical retrieval (isolated words, poorly informative), while the apraxic-articulatory aspect improved gradually.
Results: Once the treatment was over, the patient was followed in ambulatorial setting with clinical improvement: neurologists observed an improved fluency and ability to convey information, together with resolution of ideomotor apraxia. However, fatuous attitude and deficit in repetition of sentences were still described, along with episodic memory disorder.
Follow up includes MRI and lumbar puncture at 6 months apart.
Conclusion: This case may be considered a form of meningovascular neurosyphilis, a possible presentation of early neurosyphilis. It can cause an infectious arteritis of subarachnoid vessels, resulting in thrombosis, ischemia, or infarction. Its manifestations may be acute or chronic and the neurological deficits reflect the territory of the vessel involved.
The CSF abnormalities are generally less severe than in acute meningitis, with lymphocytic pleocytosis between 10 to 100 cells/microL and protein concentration of 100 to 200 mg/dL. CSF-VDRL is usually but not always reactive.
The case illustrates the broad spectrum and different course of neurosyphilis, highlighting the importance of considering it in differential diagnosis with other neurological diseases.

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STIs, Sexually transmitted infections

P 314 EFFECTIVENESS OF THE MPOX VACCINATION CAMPAIGN AND VACCINE SAFETY PROFILE – EXPERIENCE OF A STI CLINIC DURING 2022 EPIDEMIC

D. Tesoro[1], G. Mulè[1], D. Barbanotti[1], R. Castoldi[1], L. Biasioli[1], S. Pettenuzzo[1], N. Gemignani[1], F. Molà[1], L.B. Lundgren[1], A. De Bona[1], A. d'Arminio Monforte[2], G.C. Marchetti[1]

[1]ASST Santi Paolo e Carlo, Milano, [2]Fondazione ICONA

Background: Since May 2022, cases of mpox (MPX) have been reported from many non-endemic countries, especially in the U.S. and Europe. Most cases involved MSM, often being reported through STI clinics. In August, a vaccination campaign with an attenuated vaccine was started in Lombardy, Italy. Here we describe (I) characteristics and risk factors of vaccinees at our STI Clinic in San Paolo Hospital, Milan; (II) effectiveness of the campaign in reaching higher-risk individuals; (III) side effects of the vaccine.

Materials and methods: Retrospective observational study. We considered all subjects who received a first shot in our Clinic during the first and second vaccinal sessions (August 2022 vs. September-October 2022). In the first one, a 0.5ml intramuscular shot was used; in the second session, based on most recent evidence from the literature, a 0.1 ml subcutaneous shot was given. Demographics, sexual behaviour and risk factors for infection were collected at the first visit, side effects were collected at the recall visit. Due to overall scarcity of vaccines, regional guidelines to select individuals at risk were used (i.e. at least 1 among 5 prespecified risk factors). Primary endpoint was prevalence of higher-risk individuals (≥3 risk factors) in each session. Secondary endpoint was prevalence of each side effect. We used non-parametric test and chi-square to compare subgroups, and logistic regressions to correlate number of risk factors and vaccinal session.

Results: 817 subjects received a first shot of vaccine, 223 in August and 594 in September-October. Demographics, sexual behaviour and risk factors are shown in Table 1. Subjects in the first session were more likely to have ≥3 risk factors (30.4% vs. 14.3%, OR 2.61 [95% CI, 1.810-3.763], p<0.001). Systemic adverse reactions were uncommon both after intramuscular and subcutaneous shot (fatigue 9.5% vs. 6.2%; fever 3.6% vs. 2.2%; headache 1.5% both). Local adverse reactions were different based on administration route: pain (50% vs. 15.7%, p<0.000), swelling (15.3% vs. 63.9%, p<0.000), redness (2.7% vs. 54%, p<0.000), and itching (2.7% vs. 27.5%, p<0.000). None of these was severe.

Conclusions: By following regional guidelines, MPX vaccination campaign in our Centre was effective in prioritising subjects at higher risk for infection. MPX vaccine was generally well tolerated, with frequent, yet mild, local adverse reactions with both administration routes.

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STIs, Sexually transmitted infections

P 315 THE IMPACT OF COVID-19 PANDEMIC ON STI TRENDS AND AT-RISK SEXUAL BEHAVIORS. A NATIONAL MULTICENTER STUDY

M. Giuliani[1], A. Latini[1], C. Negri[2], C. Colli[3], M. Grandolfo[4], M.G. Donà[1], C. Stingone[1], E. Giuliani[1], M. Farinella[5], A. Caraglia[6]

[1]Istituto Dermatologico San Gallicano, IRCCS, Rome, [2]Centro CMST/AIDS Gorizia Monfalcone, [3]Centro MTS UCO Clinica Dermatologica ASU Giuliano-Isontina, [4]Centro MST Clinica Dermatologica Università di Bari, [5]Circolo di Cultura Omosessuale "Mario Mieli", Rome, [6]Ministero della Salute, Rome

Background: Lockdown, mobility restrictions, physical distancing norms and use of personal protective equipment (PPE) imposed by COVID-19 pandemic control, may have affected people's sexual behavior, especially in individuals at risk of sexually transmitted infections (STIs) and that of higher risk communities; such as men who have sex with men (MSM), commercial sex workers (CSW) and disadvantaged social minorities. However, there are still few studies that have measured in sexually active populations, changes in STI trends and in sexual behaviors during COVID-19 pandemic.

To address this hypothesis, a multicenter study founded by Italian Ministry of Health was started in 2023 January, with the aim of assessing "how much and how" the COVID-19 pandemic may have affected STI trends observed in recent years in Italy and the sexual habits of groups at higher risk for STIs and social fragility.

Objectives:

- to assess variations in the frequency of STI diagnoses in selected public clinical centers for STI by geographic representativeness, catchment area and standard of care, during the pre-pandemic (2018-2019), pandemic (2020 -2021) and post-pandemic (2022-2023) periods;
- to investigate quantitative-qualitative variations in specific parameters of the sexual behavior during the three periods among people attending STI centers and interviewed in diagnostic POCs during screening activities.

Methods: The analysis of the STI trends will be conducted comparing the annual reporting cases diagnosed during the three selected periods in the STI centers according to the diagnosis criteria already defined by the Sentinel Surveillance System of STI-ISS. The behavioral investigation will be conducted by a structured interview, based on a validated questionnaire administrated to all attendees of the clinical centers and diagnostic POCs in collaboration with local NGOs. The STI centers were selected according to the following criteria:

- documented activities accredited by Italian Institute of Health;
- representativeness of the three geographical areas of the country;
- ensure standardized data on annual STI diagnoses over the three periods of interest of the study;
- ensure a population of attendees with sexual risk characteristics useful for conducting the behavioral study;
- staff with documented expertise in epidemiological studies;
- documented expertise in STI screening programs also in collaboration with local NGOs and diagnostic POC-based.

Expected Results: The data collected by this multicenter study may be useful in guiding and complementing existing regional STI prevention plans and provide insights for specific post-COVID19 campaigns, targeted to higher risk population groups.

Virology and Pharmacology

P 316 EXTENSIVE VIROLOGIC CHARACTERIZATION IN AN HIV-INFECTED INDIVIDUAL WITH APPARENT HIV REMISSION FOR 2 YEARS AFTER ALLOGENEIC STEM CELL TRANSPLANTATION WITH CCR5 WILD-TYPE CELLS: A CASE STUDY

I. Vicenti[1], S. Piemontese[2], L. Fiaschi[1], C. Biba[1], A. Cervo[3], I. Varasi[1], F. Saladini[1], G. Leonardi[4], C.F. Perno[5], C. Mussini[6], M. Zazzi[1], V. Borghi[6]

[1]Department of Medical Biotechnologies, University of Siena, Siena, [2]Hematology and Bone Marrow Transplantation Unit, IRCCS San Raffaele Hospital, Milan, [3]Infectious Diseases Unit, Department of Health Promotion Sciences and Mother and Child Care "Giuseppe D'Alessandro" (PROMISE), University of Palermo, Palermo, [4]Hematology Unit and Chair, Department of Medical and Surgical Sciences, Azienda Ospedaliera Universitaria Di Modena, University of Modena and Reggio Emilia, Modena, [5]Multimodal Research Area, Unit of Microbiology and Diagnostics in Immunology, Bambino Gesù Children's Hospital, IRCCS, Rome, [6]UO of infectious Diseases, University of Modena and Reggio Emilia, Modena

Background and aim: Allogenic hematopoietic stem cell transplantation (allo-HSCT) with homozygous CCR5Δ32 donor cells is the only potentially HIV-1 curative intervention. However, allo-HSCT has been associated with a drastic reduction in the HIV reservoir independently of engraftment with CCR5Δ32 or CCR5 wild-type cells. In this study, we investigated ex-vivo the reservoir of an HIV-1 infected individual with no evidence of infection at 2 years after allo-HSCT with wild-type CCR5 genotype.

Case Report: The study participant was an adult male, HIV-1 infected since 1994 with 5 antiretroviral class multidrug resistance strain and under treatment with ART. On January 2020, at the age of 58, he received an allo-HSCT from an HLA-identical sibling donor for a Hodgkin lymphoma in second complete remission after 24 cycles of therapy with the anti- PD1 pembrolizumab. The patient received a reduced toxicity conditioning regimen, based on fludarabine and treosulfan at myeloablative dosage, and was discharge on day 47 after transplant without major complications. He never developed graft-versus-host disease, neither acute nor chronic. Despite positive HIV-1 serology, he maintained undetectable viremia and he was negative for HIV-1 DNA by routine diagnostic analysis. In March 2022 CD4+ T cells were isolated after leukapheresis and maintained in culture to determine: (i) the CCR5 genotype by Sanger sequencing, (ii) the amount of cell-associated HIV-1 DNA (CAD) and cell-associated HIV-1 RNA (CAR) by digital droplet PCR at baseline and after ex-vivo stimulation with ionomycin (ION, 1 µg/ml) plus phorbol-myristate-acetate (PMA, 50 ng/ml). Briefly, 2-days post induction (dpi) 4 x 107 patient derived CD4+ were co-cultivated with MOLT-4 CCR5, a cell line permissive for HIV-1 infection. CAR and CAD were quantified at baseline (T0) and 2-7-14-21 dpi (T2, T7, T14, T21). At T7, T14 and T21, the infectivity of the CD4+T/MOLT-4 CCR5 co-cultures was evaluated using a modified TZM-bl based assay (TZA) protocol. In addition, a positive control of 1.2 x 106 CD4+ T cells, deriving from an HIV-1 positive, virologically suppressed patient was analysed in parallel.

DNA sequencing confirmed a wild type homozygous CCR5. CAR and CAD were negative at baseline and at all time points analysed. The CD4+T/MOLT-4 CCR5 co-cultures were not infectious in TZA at T7, T14 and T21. The HIV-1 positive control was quantifiable in CAD at T7, T14 and T21 with 931.2 ± 400.1, 68.9 ± 10.1, 128.6 ± 15.3 HIV-1 copies per 106 CD4+ T cells respectively and in TZA at T21 with 16.1 [5.4-47.8] IUPM/cells.

Conclusions: Two years after wild-type CCR5 allo-HSCT, the patient remained without measurable or inducible HIV-1 DNA and RNA in the blood compartment by multiple ultrasensitive assays on a total of 40 million CD4+ T cells. However, the presence of the virus in other tissues was unexplored. Ultimately, only analytical treatment interruption may reveal whether full remission has been achieved.

Virology and Pharmacology

P 317 SAFETY EVALUATION OF CABOTEGRAVIR IN ZEBRAFISH EMBRYOS

S. Ferretti[1], D. Zizioli[1], I. Zanella[1], L. Mignani[1], M. Degli Antoni[2], F. Castelli[2], E. Quiros-Roldan[2]

[1]Department of Molecular and Translational Medicine, University of Brescia, Brescia, [2]University Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia

Background: Zebrafish has been widely accepted as an alternative vertebrate animal model for in vivo assessment of chemical and new drug toxicity. Cabotegravir is one of the newest drug approved for clinical use in HIV-infected patients. It belongs to the INSTI class and is an analog of dolutegravir. Embryo-fetal toxicity studies with cabotegravir were conducted in rats and rabbits without evidence of treatment-related increase of fetal anomaly incidence at any dose, while dolutegravir treatment was associated with increased risk of neural tube defects in zebrafish embryos but not in humans. We tested cabotegravir safety in zebrafish embryos by measuring survival, morphologic development and behavior.

Methods: Wild-type zebrafish embryos were exposed to cabotegravir doses in the range 5-500 μM from gastrula stage (4 hpf) up to 120 hpf (human Cmax 20 μM). Survival rate and gross morphology were evaluated. Neurodevelopment was analyzed by Whole Mount In situ hybridization (WISH) with an RNA probe revealing the expression of the gene neurod, a transcription factor used as marker of neuronal differentiation. Locomotor activity and adaptability to environmental stimuli was analyzed by registering larval swimming in a 2h trial period under dark/light cycling.

Results: Survival was unaffected by all cabotegravir doses up to 25X the human Cmax. No gross morphology changes were as well observed, except for a slightly reduced body length at doses higher than the Cmax. Considering the strict chemical similarities between cabotegravir and dolutegravir, to verify if not macroscopically evident but more subtle effects of cabotegravir on zebrafish embryo neurodevelopment exist, by WISH we analyzed the expression of a known marker of differentiated neurons (neurod) at 96 hpf and found that cabotegravir treatment (10-20 μM) resulted in a reduced expression in regions corresponding to the diencephalon (d), midbrain/hindbrain boundary (mhb) and craniofacial ganglia (cfg). Behavioral studies revealed that locomotor activity was severely reduced (>60%) from the lower doses used in the study.

Conclusions: Cabotegravir does not modify survival or gross morphology of zebrafish embryos up to very high doses. Notwithstanding, we observed defects on neuronal differentiation and at doses from 4x lower than the human Cmax movement alterations.

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Virology and Pharmacology

P 318 EFFECT OF DORAVIRINE ON DOLUTEGRAVIR TROUGH CONCENTRATIONS IN PEOPLE WITH HIV SWITCHED FROM DARUNAVIR/COBICISTAT

S. Pagano[1], C. Gervasoni[1,2], S. Antinori[1], V. Micheli[3], A. Gori[2], D. Cattaneo[1,2]

[1]Department of Infectious Diseases, ASST Fatebenefratelli-Sacco University Hospital, Milan, Italy, [2]Gestione Ambulatoriale Politerapie (GAP) Outpatient Clinic, ASST Fatebenefratelli-Sacco University Hospital, Milan, Italy, [3]Laboratory of Clinical Microbiology, Virology and Bioemergencies, ASST Fatebenefratelli Sacco University hospital, Milan, Italy

Background: Dolutegravir and doravirine are individually safe and potent ARV therapy components, but their combined use has not been studied in clinical trials. Real-life experiences in small cohorts of highly treatment experienced PWH have shown that combined treatment of dolutegravir with doravirine was well tolerated, achieving virologic suppression in most cases. In healthy volunteers doravirine co-administration increased dolutegravir exposure by about 25-35%, a difference that was considered as not clinically relevant.

Objective: To exclude that the co-administration of dolutegravir and doravirine in PWH may result in a different magnitude of DDI.

Methods: A consecutive series of PWH with history of good adherence and undergoing TDM of dolutegravir plasma trough concentrations as routine clinical practice before and after the switch from darunavir/cobicistat to doravirine were considered. The second TDM assessment was performed at least 14 days after the switch to ensure steady state conditions and to minimize any potential effect of cobicistat. Collected blood samples were taken 24 hours after the last drug intake (patient self-report). Drug concentrations were assessed by high performance liquid chromatography method with ultraviolet detection. Comparisons between the two visits were performed by paired t-tests.

Results: Enrolled patients (n=13; 7 males, 6 females) were all Caucasians, with mean age of 54±9 years, body weight and body mass index of 70±14 Kg and 24.5±3.6 Kg/m2, respectively, and a diagnosis of HIV of 21±7 years. They had good viro-immunological status (CD4 cell count: 764±269; viral load: <20 copies/mL in 11 out of the 13 patients; the remaining two had 25 and 28 copies/mL). The reasons for the switch from darunavir/cobicistat to doravirine were: removal of the booster (n=6), comorbidities (n=4) or risk of DDI (n=3).

The first and second TDM were performed at 1042±873 days or at 333±181 days after starting dolutegravir plus darunavir/cobicistat or dolutegravir plus doravirine, respectively. As shown in the Figure, the switch from darunavir/cobicistat to doravirine resulted in a significant increase of dolutegravir trough concentrations (from 1363 ±570 to 1909±848 ng/mL, +57%, p=0.025). No significant variations in the viro-immunological status was observed after the switch (CD4 cell count: 896±488 cells/mm3; viral load: <20 copies/mL in 12 out of the 13 patients; the remaining patient had 26 copies/mL). No discontinuations for drug-related adverse events occurred.

Conclusions: We have documented that doravirine significantly increased dolutegravir concentration in PWH previously treated with darunavir/cobicistat. Accordingly, doravirine might be advantageous when the dose of dolutegravir should be doubled such as in patients carrying resistance to integrase inhibitors or when medications known to reduce dolutegravir absorption (i.e. mineral supplements) are co-administered.

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Virology and Pharmacology

P 319 SINGLE-CELL TRANSCRIPTOMICS OF CSF AND PBMC IN A PRIMARY HIV INFECTION OF A SUBJECT ALREADY AFFECTED BY MULTIPLE SCLEROSIS

C. Pinnetti[1], F. Messina[2], G. Rozera[2], P. Spezia[3], I. Mastrarosa[1], A. Vergori[1], A. Antinori[1], E. Girardi[4], F. Vaia[5], F. Maggi[2], I. Abbate[2]

[1]Clinical and Research Infectious Department, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Virology Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [3]Department of Translational Research, Retrovirus Center - University of Pisa, [4]Scientific Direction, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [5]General Direction, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy

Background: In infected patients, HIV early invades the central nervous system where it can persist, evolve, and become compartmentalized. Although productive infection in this district is low, the presence of the virus, together with local inflammation, may lead to neurodegenerative disorders. Analyzing the cell types present in the cerebrospinal fluid (CSF), with their-specific transcriptomes, could shed light on the events involved in the genesis of the neuro damage. The study aimed to establish single-cell transcriptomes in CSF and PBMC in a patient with an HIV primary infection, to find viral transcripts in the cells under study, and to associate, whenever possible, the presence of HIV transcripts with impaired transcriptomic profiles.

Materials and Methods: A primary HIV infection of a 37 years old male with a previous diagnosis of multiple sclerosis was studied. For single-cell transcriptomics, 5,000 cells from CSF and PBMC were subjected to reverse transcription and barcoding using Single Cell 3' Reagent Kit and 10x Chromium platform (10x Genomics, USA); cDNA libraries were sequenced on the Illumina platform. Clustering analysis was performed and the expression of some specific genes was compared among the clusters. The presence of HIV-1 transcripts was investigated by a bioinformatic pipeline.

Results: HIV-1 viral load was 69,396 and 7,195 copies/ml in plasma and CSF, respectively; gag, pol, and env sequencing assigned an HIV-1 subtype G. In peripheral blood, CD4 T cells were 323/μL (CD4/CD8 ratio 0.63). High-quality cDNA was obtained from single-cell whole transcriptomes, producing a mean of 1,594 transcripts/cell in CSF and 6,255 transcripts/cell in PBMC. Single-cell transcriptomes derived from CSF (1446) and PBMCs (4647) were put together for unsupervised cluster analysis that identified a total of 16 cell clusters, mainly representing distinct cell subsets. Thereafter, differences in cellular distributions between CSF and PBMC were evaluated (Figure 1). In CSF, CD8 T cells were the most represented (52%), with a small population of pDC cells (0.4%): when compared with blood, CSF contained higher proportions of plasmacells (2,21%). At the first analysis, no separated cell cluster showed an up-regulated expression of genes related to neurodegenerative diseases. Some HIV-1 transcripts were found, mainly in CSF, which mapped preferentially to the HIV-1 pol region. Due to the low number of infected cells observed, it was not possible to appreciate altered cell host transcription due to the presence of the virus.

Conclusions: Although limited to a single case, these preliminary data allow us to glimpse the power of this experimental approach for the understanding of the pathogenetic events involved at the single cell level between host and viruses. Efforts are however needed to improve the sensitivity of the detection of the viral transcripts among host cellular transcriptome.

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Virology and Pharmacology

P 320 USE OF HIV GENOTYPE RESISTANCE TEST IN ITALY: A NATIONAL SURVEY

A. De Vito[1], A. Bezenchek[2], R. Scutari[3,4], L. Colagrossi[4,5], G. Valenti[6], M.C. Bellocchi[7], L. Pipitò[6], S. Ferrara[8], S. Malandrin[9], M. Tallarita[9], A. Cozzi-Lepri[10], F. Ceccherini Silberstein[7], S. Lo Caputo[8], S. Rusconi[11]

[1]Unit of Infectious Diseases, Department of Medicine, Surgery, and Pharmacy, University of Sassari, Sassari, Italy, [2]IPRO-InformaPRO S.r.l., Rome, Italy; EuResist Network GEIE, Rome, Italy, Italy, [3]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy, [4]Multimodal Research Area, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [5]Microbiology and Diagnostics of Immunology Unit, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [6]Infectious and Tropical Diseases Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy, [7]Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy, [8]S.C. Malattie Infettive, Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Foggia, Foggia, Italy, [9]Microbiology and Virology Unit, ASST Ospedale San Gerardo, Monza, Italy, [10]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME) Institute for Global Health UCL, London, UK, [11]Unit of Infectious Diseases, University of Milano and ASST Fatebenefratelli "L. Sacco" Hospital, Milan, Italy

Background: HIV genotype resistance test (GRT) has played a key role in managing people living with HIV (PLWH). However, due to early antiretroviral strategy, and the presence of new drugs with a high genetic barrier, the necessity of GRT has been questioned. On the contrary, GRT represents a fundamental item for dual-regimens and injectable treatment prescriptions.
Our study aims to understand the use and attitude towards GRT among Infectious Diseases Units in Italy.
Methods: We performed a cross-sectional study, asking each Infectious Diseases Unit in Italy to complete a questionnaire. We promoted a web-based survey through a google form, which was spread by e-mail or cellphone. The centers that did not perform the GRT were excluded from the second part of the questionnaire.
Results: We collected answers from 97 Infectious Diseases Units. The majority of the centers followed at least 500 PLWH. Among the 97 centers, only six (6.2%) answered that they do not perform GRT on any occasion. Regarding the 91 centers that prescribe GRTs, 50 (56.0%) sent the blood samples to an external laboratory; in particular, only 5/28 (17.9%) small centers have an internal laboratory, compared to 13/34 (38.2%) medium centers and 22/24 (91.7%) large centers (p<0.001).
Most centers prescribe the GRT in drug-naïve people, and all centers in case of virological failure; only 24 (26.4%) prescribe the GRT before a treatment change in selected PLWH. Regarding the virological failure, the majority of centers (37) prescribe the GRT when the HIV-RNA is > 200 copies/mL; 25 (27.5%) prescribe it when the HIV-RNA is > 50 copies/mL, while 17 (18.7%) and 12 (13.2%), prescribe the GRT when the HIV-RNA is > 500 copies/mL and 1000 copies/mL, respectively. In addition, 84 (92.3%) centers receive the integrase resistance test in naïve PLWH.
Regarding which GRT test is used in the laboratory, 34 (37.3%) did not know which one was used. In 15 (16.5%) cases, the answer was that the laboratory used both NGS and Sanger, while 28 (30.8%) answered only NGS, and 14 (15.4%) only Sanger.
About the timeline, most centers can have the GRT result within one month (n=70, 78.0%); in particular, 21 (23.1%) received the results within two weeks. On the contrary, 21 (23.1%) centers typically wait more than one month. The answers to the questionnaire are summarized in Table 1.
Finally, the majority of participants (83) consider the GRT test for naïve PLWH a fundamental routine exam.
Conclusion: Our study shows that most Italian Infectious Diseases Units prescribe the GRT in clinical practice and believe it represents a fundamental exam for new HIV diagnoses. On the contrary, the use of GRT on HIV-DNA is still limited. Further efforts are needed to reduce the time in those centers that received the result after more than one month.

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Virology and Pharmacology

P 321 EVALUATION OF ELITE INGENIUS® INTEGRATED SYSTEM FOR DETECTION, QUANTIFICATION AND MONITORING OF HIV-1 RNA IN CEREBROSPINAL FLUID

P. Paba[1], G. Costanza[1], S. Grelli[1,2]

[1]Unit of Virology, Policlinic of Tor Vergata, Rome, Italy, [2]Department of Experimental Medicine, the University of Rome Tor Vergata, Rome, Italy

Background: In patients under Antiretroviral Therapy (ART), the HIV-1 virus is suppressed in the blood, but remains present in some tissues and body fluids (HIV escape), such as cerebrospinal fluid (CSF). Recently, small footprint fully automatic systems became available for quantification of HIV-1 in plasma or serum, but not CSF. Standardized quantification in matrices different of blood is essential for monitoring HIV-1 re-activation under ART. ELITE InGenius® is an integrated platform, which sequentially performs extraction, amplification, and interpretation of results. The system is CE-IVD marked for quantification of HIV-1 in plasma. This study aims to compare the performance of the ELITE InGenius® and Roche Cobas® system, which is used for investigating HIV-1 in CSF in many laboratories.

Methods: We processed CSF leftover previously characterized by the Roche Cobas® HIV-1 assay, to test the systems' agreement. The CSF samples included: 10 HIV-1 positive and 10 HIV-1 negative HIV-1 patients positive in plasma, and 10 HIV-1 negative from non-HIV-1 patients. To evaluate the sensitivity and reproducibility, we created serial dilutions of HIV-1 (from 2500 IU/mL to 10IU/mL) by spiking a pool of HIV-1 negative CSF with the 4th WHO International Standard. Each dilution was processed in parallel with the two systems in 3 independent runs. Descriptive statistical analyses, correlation analysis, and method agreement were performed. Sensitivity was evaluated as the percentage of positive samples detected/total number of positive samples. P values <0.05 were considered significant. Statistical analyses were conducted with Minitab19 Software.

Results: All the HIV-1 negative CSF samples from ART patients (n=10) and non-HIV-1 patients (n=10) tested negative at the ELITE MGB® and Roche Cobas® HIV-1 assays. HIV-1 positive CSF samples (n=10) from ART patients, confirmed positive in CSF and PL by the Roche Cobas® system, were also positive at the ELITE InGenius®. Among these, just one was detectable but non-quantifiable with both systems. A series of medium low-titer spiked samples were tested to simulate low-viral load conditions. The sample at 10IU/mL was detected in only one replicate run with each system. The mean difference in quantification between systems was not-significant ($p<0.37$), while the correlation by the Spearman rank test was statistically significant ($rho=0.943$; $p<0.001$).

Conclusions: For the detection of HIV-1 in CSF, the HIV1 ELITE MGB® assay was specific when compared to the routine test Cobas® HIV-1 (Roche). The two systems were equivalent in sensitivity and repeatability for quantifying HIV-1 RNA in CSF samples. The availability of small-footprint systems, such as the ELITE InGenius®, should induce the laboratory to reconsider the methods for HIV-1 RNA detection in CSF samples, by analyzing several aspects, including workflow optimization, costs of instruments and consumables, processivity, and logistics.

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Virology and Pharmacology

P 322 COMPARISON OF DEVELOPMENTAL SAFETY BETWEEN DORAVIRINE AND EFAVIRENZ IN ZEBRAFISH (DANIO RERIO) EMBRYOS

S. Ferretti[1], S. Storti[2], D. Zizioli[1], I. Zanella[3], F. Castelli[2], E. Quiros-Roldan[2]

[1]Department of Molecular and Translational Medicine, University of Brescia, [2]Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, [3]Department of Molecular and Translational Medicine, University of Brescia and Clinical Chemistry Laboratory, ASST Spedali Civili di Brescia

Background: In clinical trials (DRIVE-FORWARD vs. ritonavir-boosted darunavir and DRIVE-AHEAD vs. efavirenz, EFV), doravirine (DOR), the most novel non-nucleoside reverse transcriptase inhibitor (NNRTI), demonstrated a better safety profile than the older antiretroviral drugs like EFV without sacrificing efficacy. Preclinical safety studies demonstrated that DOR is not mutagenic or genotoxic in vitro genetic toxicity assays. However, preclinical studies in rats and rabbits showed maternal toxicity during pregnancy (body weight loss), associated with concomitant fetal toxicity (skull malformations). Little information about in-utero safety exposition is however available and, further, few preclinical studies have focused on DOR developmental toxicity. In this study, zebrafish (Danio rerio) embryos were chosen as an in vivo model to further investigate the developmental toxicity of DOR, compared with EFV.

Methods: DOR and EFV exposure effects during development were assessed and compared in zebrafish embryos by the Fish Embryo Toxicity test, after their exposure to subtherapeutic doses and up to 25X(DOR)-5X (EFV) the human C max. Viability, hatching rate and gross morphology of embryos were recorded. Larvae' behaviour was assessed by the light-dark locomotion test.

Results: DOR exposure did not significantly affect survival rate at 24 and 48 hours post fertilization (hpf) at doses up to 25X the human C max and did not induce any gross morphological defects at 24 and 72 hpf at doses up to 25X the human C max (Figure 1). On the contrary, EFV exposure resulted in a low survival and developmental and hatching rate delay even at subtherapeutic doses. Interestingly, the locomotor response of DOR-exposed embryos to light-dark stimuli followed a trend resembling an inverse U-shaped curve with increased locomotion up to 2.5X the therapeutic dose, followed by decreased locomotion at 10X the therapeutic dose, while EFV-treated embryos showed reduced locomotion already at 0.5X the human C-max.

Conclusions: Our findings in zebrafish embryos add further information about developmental DOR safety, confirming its better safety developmental profile compared to EFV. Further studies are however needed to expand our understanding regarding DOR embryo exposure behavioural effects.

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Virology and Pharmacology

P 323 LARGE PROPORTION OF NEW HIV DIAGNOSES IN NORTHERN ITALY SUSTAINED BY NON-B SUBTYPES WITH HIGHER HIV DNA IN THE EFFECTOR MEMORY SUBSET

G. Bozzi[1] , M. Centazzo[1,2], P. Saltini[1,3], G.M. Butta[1,2], A. Liparoti[1,3], C. Bobbio[1], A. Muscatello[1], A. Gori[3], A. Bandera[1,3], L. Manganaro[2,3]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Infectious Diseases, Milano, Italy, [2]INGM - Istituto Nazionale di Genetica Molecolare - Milan, Virology Unit, Milano, Italy, [3]Unimi - Università degli Studi di Milano, Milano, Italy

Background: Non-B HIV-1 subtypes, once rare in Europe, are becoming established. For subtype C, altered susceptibility to RT inhibitors is described, and CCR5-expressing CD4 subsets are more susceptible to infection; other subtypes are less characterized. We conducted a sub-analysis of a study investigating latency in CD4 subsets, and compared newly diagnosed individuals carrying B and non-B subtypes.

Methods: Sub-analysis of GR-2018-12365699 study enrolling naïve outpatients newly diagnosed with HIV from 11/2019 at IRCCS Policlinico, Milan. Subtyping through REGA on GTR sequences. Pre-ART CD4 immunophenotype determined after cell-surface staining allowing discrimination among subsets; cells acquired on BD-Symphony, and data analyzed on FlowJo. Cell associated HIV-1 DNA was measured through ddPCR (Bio-Rad QX200 System; LTR and CCR5
copy quantification).

Results: Thirty-five individuals with new HIV diagnoses were analyzed, 17 with primary (compatible Western blot, known time of seroconversion and/or clinical syndrome) and 18 with chronic infection. Median age was 36 [IQR 30.5 - 42], males were 33/35 (94%). Route of transmission was MSM in 24/35 (73%) and HE in 9/35 (27%). Median CD4 count was 376/mcL [293 - 720] and median plasma HIV RNA was 55600 cp/mL [32100 - 136000] at diagnosis. Twelve (34%) individuals harbored non-B subtypes: 4 CRF02_AG; 2 A1; 2 C, 1 F1, 3 recombinants. None had transmitted drug resistance, while 4/23 with clade B had TDR. Carrying non-B subtypes did not show association to primary infection, route of transmission, country of birth or baseline CD4 count. Instead, it was associated to plasma HIV RNA levels at diagnosis (p=0.034), with higher loads for non-B patients. Immunophenotyping analysis revealed significantly lower counts in the Effector Memory subset in individuals with primary infection with non-B subtypes compared to B subtype. In a subset of 20 individuals, total HIV
DNA was significantly higher in the Effector Memory and Transitional Memory subsets of individuals harboring non-B versus B clade.

Conclusions: Our monocentric cohort confirms that non-B subtypes are sustaining large shares of new HIV-1 diagnoses and becoming endemic in Italy. Significantly different proportions in the Effector Memory subset, with higher HIV DNA, might reflect discrepancies in natural history and even impact drug susceptibility.

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P 324 DOES PROVIRAL DNA-NGS MATCH HISTORICAL GENOTYPE?

F. Stefanelli[3], A. Chiara Russo[1,2], L. Labate[1,2], C. Fraccalvieri[3], M. Cerchiaro[1,2], M. Bavastro[1,2], L. Taramasso[1], M. Bassetti[1,2], B. Bruzzone[3], A. Di Biagio[1,2]

[1]Infectious Diseases Unit, Policlinico San Martino Hospital-IRCCS, Genoa, Italy, [2]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [3]Hygiene Laboratory Unit, Policlinico San Martino Hospital-IRCCS, Genoa, Italy

Background: The importance of genotypic analysis of resistance associated mutations (RAMs) in the optimization of antiretroviral treatment has never been questioned.The most common and worldwide used method to detect RAMs is the Sanger Sequencing (SS), able to identify only variants with >20% prevalence, and only when a certain amount of virus is present.If a treatment switch is needed in patients with undetectable virus, for reasons other than viral failure, the cumulative historical genotype (HG) can be useful, if available. When the HG is lacking, RAMs detection by SS in proviral DNA instead of plasma viral RNA may in part overcome the problem, although controversial results have been reported. In this study, proviral DNA samples belonging to antiretroviral experienced patients, with a history of virological failure and HG were selected and tested by next generation sequencing method (NGS). The resistance profile was compared with HG.

Material and Methods: Patients were selected in the Infectious Disease Unit, San Martino Hospital (Genoa, Italy). Proviral DNA was extracted from 14 EDTA containing tubes at Hygiene Laboratory, San Martino Hospital (Genoa, Italy) using QIAamp® Blood Mini kit (Qiagen). Library preparation for NGS was performed using the commercial kit AD4SEQ HIV-1 Solution v2 (Arrow Diagnostics) following manufacturer's specific instructions for DNA and sequenced on iSeq100 platform (Illumina). FastQ files were analysed on SmartVir (SmartSeq S.r.l.) software for RAMs inference.

Results: An optimal coverage was obtained in 11/14 (79%) samples. The patients' characteristics are described in table 1. Summarizing, patient characteristics identify a person who started antiretroviral therapy many years ago, and failed several therapeutic lines (assesed by many SS), becoming resistant to different drugs. All were infected by subtypes B virus. Concordance between RAMs present in HG and detected in NGS was, for PI, NRTI and NNRTI respectively, 70%, 86% and 52% with >20% threshold (Ct) and 96%, 94%, and 74% with >5% (Ct). RAMs present in HG e in NGS are listed in figure 1. The RAMs in positions 41, 67, 70, 210, 215 and 219 known as TAMS and the RAMs in positions 103 and 184 were the most represented both in HG and in NGS. Correlation between HG and NGS was 100% for most TAMs at 5% (Ct), slightly lower for the TAM in position 41 at the RAMs in positions 103 and 184 and 20% (Ct).

Discussion: The good correlation between RAMs detected by proviral NGS and HG allowed us to demonstrate that NGS can be used as a tool, in selected cases, to describe the RAMs history of a patient. As it could be expected (see the patients' characteristics), the TAMs and the RAMs in position 103 and 184 were the most frequently detected in NGS and also present in HG, as a consequence of exposition to the relative drugs in the partially effective regimens of the first decade of HAART, creating a heavily mutated prevalent viral population which loaded the DNA reservoir.

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Virology and Pharmacology

P 325 THE EFFECTS OF COGNATE PEPTIDE RECOGNITION ON PROVIRUSES IN EXPANDED T CELL CLONES IN AN ELITE CONTROLLER

F. Dragoni[1,2], A.K. Kwaa[1], C.C. Garliss[1], R.T. Veenhuis[1], B.A. Woldemeskel[1], A. Camilo-Contreras[1], H. Raymond[3], A.G. Dykema[1], E.P. Scully[1], A.M. Rosecrans[1], K.N. Smith[1], F.D. Bushman[3], F.R. Simonetti[1], J.N. Blankson[1]

[1]Johns Hopkins University School of Medicine, Baltimore, MD, USA, [2]Department of Medical Biotechnologies, University of Siena, Italy, [3]Department of Microbiology, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, USA

Background: Clonal expansion of HIV-1-infected CD4+ T cells is a major cause of latent reservoir persistence. Growing evidence suggests that intact proviruses integrated into specific chromosomal locations, like Zinc Finger (ZN) genes, are more likely to evade immune surveillance and be selected over time. However, which factors regulate viral transcription and cell proliferation are not fully understood. To elucidate these mechanisms, we studied the dynamics of infected clones in an Elite Controller (EC) undergoing chemoradiation.

Material and Methods: We characterized HIV-1 integration sites and we quantified total and specific infected T cell clones in an EC before and after he received ART, chemoradiation and immunotherapy for a metastatic lung cancer. By CD8-depleted PBMCs stimulation experiments with common chronic antigens (i.e. CMV and HIV Gag peptides), we resolved the T cell specificity at the epitope level of two infected clones. Finally, we evaluated the impact of immune recognition by autologous CD8+ T cells following stimulation with their cognate peptides.

Results: We detected a marked yet transient contraction in the number of expanded infected clones after chemoradiation, along with a modest decline in both total and intact HIV DNA. At the end of the follow-up, total HIV DNA returned to pre-treatment levels, but intact HIV DNA increased significantly. Of note, plasma HIV RNA remained undetectable (<20 copies/ml) throughout the study. We observed that the proviral landscape was dominated by two large clones with replication-competent proviruses integrated into ZNF genes, in locations previously associated with deeper latency. One clone, with a provirus integrated into ZNF470, was stable during treatment. In contrast the other clone, which had a provirus integrated in ZNF721 (ZNF721i) and recognized the Gag peptide STLQEQIGWMTNNPP (241-255), underwent a 70-fold expansion after chemotherapy was completed. We found a third nearly intact provirus (Chr7.d11sc), integrated into an intergenic site, which recognized two overlapping Gag peptides, EKAFSPEVIPMFSAL (162-176) and SPEVIPMFSALSEGA (166-180). Upon stimulation of CD8-depleted PBMCs with cognate Gag peptides, we observed that ZNF721i was 200-fold less inducible than Chr7.d11sc, despite extensive clonal proliferation. Interestingly, in the presence of activated CD8+ T cells, both virus production and cell proliferation of cells carrying Chr7.d11sc were significantly more impacted than ZNF721i, which proliferated while eluding immune engagement.

Conclusions: These results demonstrate that the lower inducibility of the ZNF721i provirus resulted in immune evasion from CD8+ T cells by cell proliferation with negligible expression of viral antigens. The lower inducibility of ZN721i could explain its marked clonal expansion observed in vivo after chemotherapy.

Virology and Pharmacology

P 326 HIV DRUG RESISTANCE: SANGER SEQUENCING VERSUS NEXT GENERATION SEQUENCING

N. Randazzo[1], G. Garzillo[2], M. Lucente[1], G. Cendarello[4], V. Bartolacci[5], P. De Leo[6], E. Pontali[7], A. Di Biagio[2,3], S. Artioli[7], B. Bruzzone[2]

[1]Hygiene Laboratory Unit, Policlinico San Martino Hospital-IRCCS, Genoa, Italy, [2]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [3]Infectious Diseases Unit, Policlinico San Martino Hospital-IRCCS, Genoa, Italy, [4]Infectious Diseases Unit, Sanremo Hospital, Imperia, Italy, [5]Infectious Diseases Unit, S. Corona Hospital, Pietra Ligure, Italy, [6]Infectious Diseases Unit, San Paolo Hospital, Savona, Italy, [6]Infectious Diseases Unit, Galliera Hospital, Genoa, Italy, [7]Infectious Diseases Unit, S. Andrea, La Spezia, Italy

Background: Genotypic HIV drug resistance (HIVDR) testing plays a role in the standard of care for the clinical management of HIV-infected patients, that helps to assess the role of resistance associated mutations (RAMs) in virologic failure, optimize the selection of the appropriate drug regimen and survey transmitted RAMs among the population. So far, Sanger Sequencing (SS) has been the gold standard method for drug resistance monitoring in clinical setting. However, the advent of Next Generation Sequencing (NGS) has revolutionised the detection and characterization of RAMs leading to detection of RAMs harbored in minority viral populations whose clinical meaning is still unknown. In the present study a comparison of RAMs at 20% and 5-20% threshold obtained by Sanger Sequencing and NGS was made.

Materials and Methods: Viral RNA was extracted from clinical specimens collected at Hygiene Laboratory, San Martino Hospital (Genoa, Italy) using the EZ1&2 Virus Mini Kit v2.0 on automated platform. Sanger sequencing was carried out by an in-house method based on nested amplification of two distinct amplicons for RT-Protease and Integrase. Following sequencing reaction, electropherograms were manually corrected on SeqScape v4 (Applied Biosystem) and the consensus was analysed on HIV Drug Resistance Database (HIVdb) developed by Stanford University. Library preparation for NGS was performed using the commercial kit AD4SEQ HIV-1 Solution v2 (Arrow Diagnostics) and sequenced on iSeq100 platform (illumina). FastQ files were analysed on SmartVir (SmartSeq S.r.l.) software for RAMs inference.

Results: A total of 65 HIV-1 positive samples were tested for RAMs. The patients' characteristics are described in Table 1. The samples' viral loads ranged from 1.5 to 6.8 log10 copies/mL (IQR 1.9 [3.8-5.7]). Concordance on the subtypes was 98%, with one discrepant attribution (SS = B; NGS = CRF24_BG), possibly due to the greater chance of detecting minority variants with NGS. As for the metrics, the average coverage at 100x was 98% for Protease (PR), 96% for Reverse Transcriptase (RT), and 94% for Integrase (IN) region. All samples had coverage of at least 30x in important RAMs positions and thus considered to be valid. When considering the 20% threshold, both technologies were able to correctly detect all the mutations, whereas, decreasing the threshold to up to 5%, 3 patients (5%) showed some major NNRTI or INSTI mutations.

The patients with resistance to at least one class of drugs were 19, 19 and 22 when using Sanger, NGS >20% and NGS >5%, respectively (Table 2).

Discussion: Overall, our results show a total correlation between SS and NGS sequencing when a 20% threshold is applied. As expected, NGS can identify less represented viral populations harboring RAMs, which SS cannot detect under a 20% threshold. However, the clinical weight of these mutations is yet to be determined, and such speculations go beyond the purpose of this report.

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Virology and Pharmacology

P 327 A NOVEL NANOBRET PROTEASE SENSOR TO SENSE HIV-1 PR ACTIVITY IN LIVING CELLS

M. Centazzo[1,2], A.V.V. Djossou[1], G. Alvisi[1]

[1]Department of Molecular Medicine, University of Padova, Padova Italy, [2]Current address INGM, Istituto Nazionale Genetica Molecolare "Romeo ed Enrica Invernizzi", Milan, Italy

Background: HIV-1 protease (PR) activity is still largely unknown, while its role in viral maturation has been long characterized, its ability to interfere with the host machinery to better suit the viral life cycle remains understudied. To this end we developed a new NanoBRET sensor by fusing NanoLuc and mNeonGreen via an HIV-1 PR cleavable peptide linker, allowing to monitor PR activity in real time in living cells with extraordinary sensitivity.

Materials and Methods: BRET Assays

HEK293T cells were seeded in in 24 well plates and transfected with the target plasmids. 48h post transfection cells were processed for BRET measurements (VICTOR X2 Plate Reader, Perkin Elmer, Waltham, MA, USA). Fluorescence signals (mNeonGreen net) relative to mNeonGreen were acquired using a fluorometric excitation filter (band pass 485 ± 14 nm) and a fluorometric emission filter (band pass 535 ± 25 nm). Luminometric readings were performed 15 min after addition of Coelenterazine H (PJK Biotech, 5 µM in PBS), using a luminometric 535 ± 25 nm emission filter (mNeonGreen) and a luminometric 460 ± 25 nm emission filter (NanoLuc). Luminometric data were used to calculate the ratio between the mNeonGreen and NanoLuc signals relative to each NanoBRET probe.

Western Blotting

HEK293T cells were seeded in in 6 well plates and transfected with the target expression plasmids (2 µg/well) in the absence or presence of Lopinavir (S1380, Selleckchem; 10 mM). 48h pt cells were lysed and subjected to SDS PAGE/Western blotting on 12% bis-tris acrylammyde gels. Proteins were transferred to PVDF membranes (RPN303F, GE Healthcare, Chicago, IL, USA) and visualized after incubation with the primary mouse monoclonal antibodies anti mNeonGreen (32F6, Chromotek; 1:500), and anti HVI-1 PR (1696, Thermofisher Scientific; 1:2000) and with goat anti mouse alkaline phosphatase conjugated secondary antibody (Santa Cruz Biotech, sc-2055; 1:10,000), followed by incubation with an enhanced chemiluminescence substrate (ECL Prime Western Blotting Detection Reagent, RPN2236, GE Healthcare). Signals were acquired using an imaging system (Alliance Mini, Uvitec, Cambridge, UK).

Results: Our sensor showed a threefold increase in signal to noise ratio as compared to traditional RLuc-YFP based BRET probes. Expression of wild type but not catalytically inactive protease resulted in a significant decrease of the BRET ratio, and allowed validation of the inhibitory activity of several well-known protease inhibitors. WB analysis confirmed the ability of the wt protease but not the catalytically inactive one to cleave the sensor.

Conclusions: Our probe offers a new, sensitive and easy-to-use way to study the activity of the HIV-1 PR. Additionally, the design of this molecular probe makes it possible to rapidly exchange the protease-cleavable linker. As a proof of principle, we developed different probes sensitive to proteases from different viruses, putting this kind of design on the forefront of current research in virology.

Virology and Pharmacology

P 328 EVALUATION OF A NEW AUTOMATED REAL-TIME PCR COMMERCIAL TEST FOR HIV-DNA QUANTIFICATION IN PBMC AND WHOLE BLOOD SAMPLES

T. Allice[1], F. Cerutti[1], M.G. Milia[1], G. Gregori[1], E. Burdino[1], A. Pilone[1], M. Cazzadore[1], E. Scuccimarra[1], M. Ferrara[2], S. Bonora[2], V. Ghisetti[1]

[1]Laboratory of Microbiology and Virology, ASL Città di Torino, Italy, [2]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Italy

Introduction: Quantification of total HIV-1 DNA from peripheral blood mononuclear cells (PBMC) of patients via polymerase chain reaction (PCR) provides a useful tool to monitor the size of the viral reservoir. Standardized methods for the total HIV-1 DNA quantification are currently lacking and several discordant results are still present in different studies.

Aim of this work was to analyze the performances of an automated commercial total HIV-DNA assay for the measurement of total HIV-1 DNA in PBMCs and/or Whole Blood (WB) samples from HIV-1 positive patients.

Materials and Methods: We analyzed 28 PBMC and WB samples derived from 28 HIV-1 patients (26 patients with viremiae <20 copies/ml and 2 with HIV-RNA of 29 and 19000 copies/ml, respectively) with the HIV-1 DNA Test PRO (Diatheva) processed in automation with Elite InGenius platform (Elitech).

The HIV-1 DNA Test PRO is a real time PCR that allow the simultaneous amplification of total HIV-DNA (target gene LTR) and Human Telomerase Reverse Transcriptase (hTERT) from WB and PBMC samples. The endogenous gene amplification is used to verify DNA-extraction success, to determine the presence of PCR inhibitor and to obtain HIV-DNA copies without cellular DNA quantification. Moreover this test is performed totally in automation in the Elite InGenius platform starting from samples extraction, amplification and quantification.

Results: Total HIV-1 DNA were detected in WB and PBMCs in 25 patients with a quantity within 5 to 1126 copies/10^6 cells and 5 to 1335 copies/10^6 cells, in PBMCs and WB, respectively. In three patients HIV-1 DNA resulted undetectable in PBMCs and WB samples. Correlation between PBMCs and WB HIV-DNA quantification, was 0.91. With the Bland-Altman analysis the mean difference between HIV-DNA quantification in PBMCs and in WB samples was 0.22: total HIV-1 DNA resulted underestimated less than a quarter when we evaluated WB samples in respect to PBMCs quantification.

Conclusions: Performances of HIV-1 DNA Test PRO assay processed in automation with Elite InGenius platform, for the measurement of total HIV-DNA in PBMCs and WB samples of HIV-1 positive patients, resulted good. In particular, we observed an acceptable correlation in HIV-1 DNA quantification starting from PBMCs and WB samples: by using WB samples , total HIV-1 DNA was underestimated less than a quarter in respect to PBMCs quantification. Moreover this assay is performed totally in automation and use an endogenous gene amplification to avoid cellular DNA quantification.

Therefore, this new commercial assays could be considered a valid molecular test for the detection and quantification of HIV-1 DNA in human blood.

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P 329 EVALUATION OF THE HIV1 ELITE MGB ASSAY FOR HIV-1 RNA QUANTIFICATION: COMPARISON WITH THE COBAS HIV-1 TEST

T. Allice, F. Cerutti, M.G. Milia, G. Gregori, B. Simoncelli, A. Ognibene, P. Tremante, A. Bottoni, S. Monteleone, V. Ghisetti

Laboratory of Microbiology and Virology, ASL Città di Torino, Torino, Italy

Introduction: HIV-1 RNA quantification by nucleic acid testing (NAT) is a key component for controlling the HIV epidemic, as NAT can be used both for HIV diagnosis and for treatment monitoring among people living with HIV who receive antiretroviral therapy (ART). Currently, HIV-1 viral load assays are available on high-throughput platforms. A rapid and user-friendly viral load test could be important to clinical decision making in the definition of HIV acute infection and in out-reach patients.

The aim of this study was to compare the performance of the HIV1 ELITe MGB kit (Elitech) with the COBAS HIV -1 test.

Materials and Methods: Thirthy HIV-1 plasma samples derived from HIV positive patients representing different subtypes of HIV-1 group M (B=18, F=4, G=2, CRF02_AG=3 and 4 not genotyped) were tested for HIV-1 viral load with the routine laboratory COBAS HIV-1 test (Roche) and with HIV1 ELITe MGB assay (Elitech) on the Elit InGenius platform (limit of quantification 26 cp/ml, limit of detection 17 cp/ml).

Results: HIV1 ELITe MGB kit, identified 23/25 HIV-1 RNA positive and 5/5 negative samples. With Elite test two samples resulted not detected (HIV-RNA viremia was 23 and 101 copies/ml with COBAS test), 5 samples resulted below the limit of quantification of the method (<26 cp/ml) and 18 samples with HIV-1 RNA load ranged from 32 to 944783 (and from 23 to 789000cp/ml with COBAS assay).

Correlation between COBAS Test and HIV1 ELITe MGB kit was 0.98 (Spearman rank test). Using a Bland-Altman analysis, we observed a close quantification of all samples since the mean of differences was 0.24. All ELITe results showed a lower viral load than COBAS test with exception of 4 samples (with viremia higher than 1500 cp/ml). When comparing individual viral load values, differences exceeding 0.5 Log were found for 3/18 (38%) samples (mean difference 0.6). The maximum difference observed in HIV-1 load was 0.66 log.

Conclusion: In this study, the HIV1 ELITe MGB assay showed a good performance in the quantification of a wide HIV-1 variants from clinical samples. This automated test could be used for treatment monitoring HIV positive patients in ART but also for rapid assessment in case of suspected acute infection or in the management of potential mother-to child transmission.

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P 330 RITONAVIR-BOOSTED ATAZANAVIR DOSE ESCALATION TO OVERCOME THE DRUG-DRUG INTERACTION WITH RIFAMPICIN: EFFECTIVENESS ON INTRACELLULAR AND PLASMA DRUG CONCENTRATIONS

A. De Nicolò[1], E. De Vivo[1], H. Mugerwa[2], S. Nakabuye[2], J. Namusanje[2], J. Kobusingye[2], P. Denti[3], K. Gausi[3], C. Waitt[4], A. D'Avolio[1]

[1]University of Turin, Dept. of Medical Sciences, [2]Joint Clinical Research Centre, Kampala, Uganda, [3]University of Cape Town, Cape Town, South Africa, [4]University of Liverpool, Dept. of Pharmacology and Therapeutics, Liverpool, UK

Background: Ritonavir-boosted atazanavir (ATV/r) is an important component of combination antiretroviral therapy (cART). ATV/r is prone to drug-drug-interactions with cytochrome inducers, such as rifampicin (RIF). Therefore, a dose escalation study was planned to assess the pharmacokinetic effectiveness and safety of administering ATV/r twice-daily(bid) to overcome RIF inducing effect. In this work, the intermediate analysis of the first half of the enrolment are reported

Methods: Healthy, HIV-positive volunteers with suppressed viral load on ATV/r containing regimens were enrolled (final scheduled number, 28). The trial consisted of sequential periods: PK1) participants on ATV/r 300/100mg once-daily (qd, NRTI backbone) for the first week, PK2) RIF 600mg qd and dolutegravir (DTG) 50mg bid were added (2 weeks), PK3) ATV/r increased to 300/100mg bid (1 week), PK4) RIF dose was doubled (1 week). Then, RIF was withdrawn. ATV, RTV and DTG were quantified in plasma and peripheral blood mononuclear cells (PBMC) by a LC-MS/MS validated method at the end of each period (PK1 to PK4), to evaluate the steady-state trough concentrations.

Results: By preliminary analysis, the plasma concentrations of ATV/r in the first 5 patients were severely reduced after the addition of RIF (ATV geometric-mean-ratio [GMR, all compared to PK1] 0.034, CI90%0.026–0.045), with all patients under the 150 ng/mL MEC value, but ATV/r escalation did compensate efficiently for RIF effect (ATV GMR 1.04, CI90% 0.598–1.830). No Grade 3 or 4 safety events were observed. Only 1 patient out of 5 had plasma concentrations near to the literature reported MEC of 150 ng/mL for trough concentrations.

Within PBMC, preliminary analysis on 15 patients confirmed that the drop in ATV/r concentrations is present also at intracellular level, although less marked (ATV GMR 0.14, CI90% 0.09–0.27) as compared to plasma (median ratio increased from 1.2 to 3.1 from PK1 to PK2). Again, increasing ATV/r dose overcame the pharmacokinetic interaction (ATV GMR 1.14 CI90% 0.74–1.76, PK3 vs PK1). Further increasing RIF dose did not show any further significant impact (ATV GMR PK4/PK3 0.93, CI90% 0.71–1.22), probably denoting a ceiling effect for enzyme induction by RIF (Figure 1). DTG concentrations, on the other hand, appeared significantly increased after ATV/r dose escalation (GMR PK3/PK2 1.37, CI90% 1.37–3.53); in this case, RIF 1200 mg reduced this effect to a not significant value (GMR PK4/PK2 1.53, CI90% 0.98–2.40).

By a virological point of view, all the patients maintained virological suppression throughout the protocol.

Conclusion: These preliminary data suggest the theoretical pharmacokinetics effectiveness and the safety of increasing ATV/r dose to overcome the effect of RIF. Completion of the full study shall confirm these encouraging data.

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P 331 THE APPLICATION OF HIV-1 GENOTYPE RESISTANCE TEST: A MULTICENTRE ITALIAN VIROLOGY LABORATORY EXPERIENCE

R. Scutari[1,2], L. Colagrossi[2,3], A.Bezenchek[4], A. De Vito[5], G. Valenti[6], M.C. Bellocchi[7], L. Pipitò[6], S. Ferrara[8], S. Malandrin[9], M. Tallarita[9], A. Cozzi-Lepri[10], S. Lo Caputo[8], S. Rusconi[11], M. Zazzi[12], F. Ceccherini-Silberstein[7]

[1]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy, [2]Multimodal Research Area, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [3]Microbiology and Diagnostics of Immunology Unit, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [4]IPRO-InformaPRO S.r.l., Rome, Italy; EuResist Network GEIE, Rome, Italy, Italy, [5]Unit of Infectious Diseases, Department of Medicine, Surgery, and Pharmacy, University of Sassari, Sassari, Italy, [6]Infectious and Tropical Diseases Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy, [7]Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy, [8]S.C. Malattie Infettive, Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Foggia, Foggia, Italy, [9]Microbiology and Virology Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, [10]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME) Institute for Global Health UCL, London, UK, [11]Unit of Infectious Diseases, University of Milano and ASST Fatebenefratelli "L. Sacco" Hospital, Milan, Italy, [12]Department of Medical Biotechnologies, University of Siena, Siena, Italy

Background: Resistance to HIV-1 antiretroviral therapy has significant clinical implications for choosing effective antiretroviral regimens. For this reason, the use of HIV-1 genotype resistance test (GRT) should be an integral diagnostic part of HIV care. Despite this, doubts remain about how to do, when and how to interpret the results. Therefore, we aimed to provide an overview of the GRT methods used in Italy by focusing on crucial points in the entire diagnostic process.

Material and methods: A virological questionnaire containing 19 key questions on using and interpreting HIV-1 GRT was submitted to Italian virological centres, identified by consulting HIV clinical and virological networks and associations.

Results: Out of 35 centres that answered to the questionnaire, the majority (N=16, 45.7%) perform 50-200 HIV-1 GRTs per year, followed by 12 centres (34.3%) performing >200 GRTs and 7 (20.0%) performing <50 GRTs (see figures). All participants perform both HIV-1 DNA/RNA GRT. The protease/reverse-transcriptase (PR/RT), integrase (INT) ± V3 regions, which represent the main targets of antiretroviral therapy, are the most sequenced portions (N=30, 85.7%). Furthermore, 11 centres sequence other HIV-1 regions (gp41:9, gp120:8, env:5 and gag:3) and 2 centres perform the HIV-1 full-length. Fourteen centres use NGS platform, 10 use Sanger while 11 centres use both methods. Most centres using Sanger exploit home-made protocols (N=14). For HIV-1 clade interpretation, 24 centres use PR/RT/INT sequences while 10 use only PR/RT region. Stanford is the software of first choice for HIV-1 clade analysis (N=30) followed by Rega (N=12), phylogenetic analysis (N=7) and others (e.g., COMET and Geno2pheno, N=6).

Regarding NGS, most centres (N=22/25, 88%) use an Illumina platform with Arrow assay. The analysis of PR/RT and INT sequences generated by NGS is mainly done by using SmartVir and Stanford software (N=18 and 21, respectively). Regarding NGS sequencing of V3/Env, for tropism interpretation, 11 centres apply a combined analysis system (SmartVir+Geno2pheno), the remaining use a single system (N=6 Geno2pheno and N=7 SmartVir). Looking at minority mutations provided by NGS, more than half of the centres (N=15) indicate in the report the mutations with their percentage, while 8 centres indicate only their presence and 2 centres do not report this information.

Moreover, most of participants declare to give GRT results within 3 weeks (N=26, 74.3%).

Noteworthy is the influence of COVID-19 in the use of the NGS method in clinical practice; in fact, half of the centres saw the implementation of this method also in HIV-1 drug resistance.

Conclusions: Most Italian virology diagnostic centres perform HIV-1 GRT from both DNA and RNA using next-generation systems, providing a deeper characterization of the viral genome. Despite this, it is necessary to standardize experimental and analytic systems to identify a unique diagnostic process common to all national centres.

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