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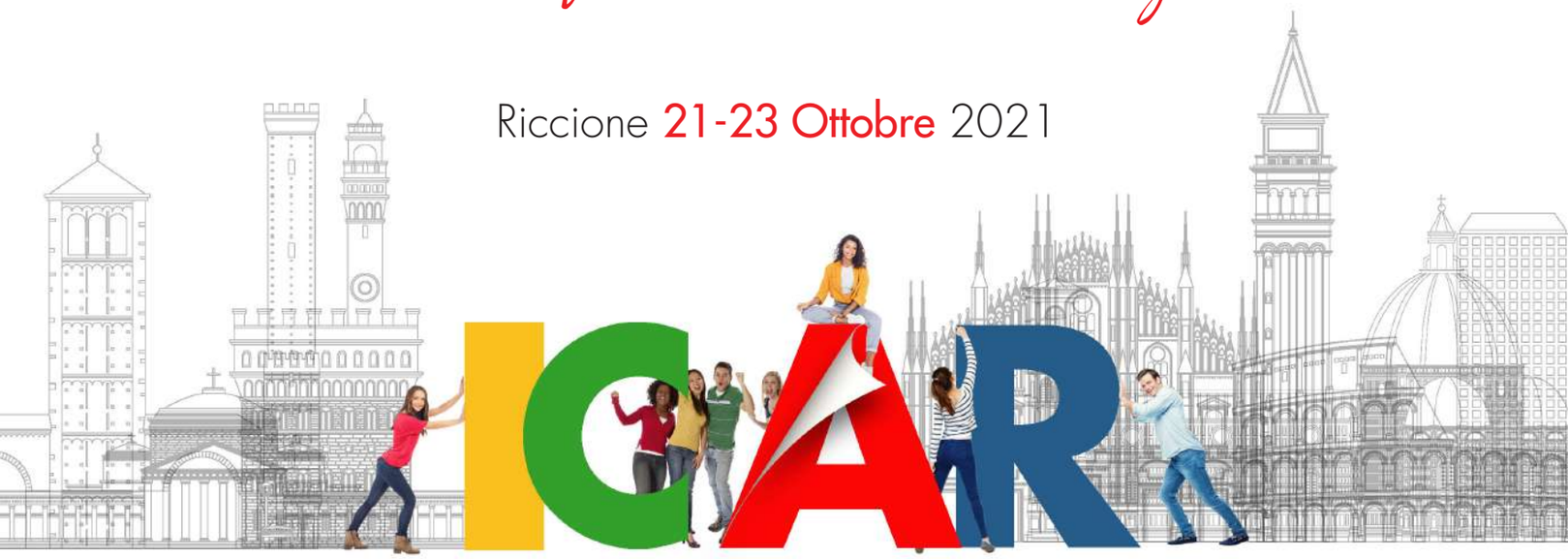
Riccione 21-23 Ottobre 2021



13° CONGRESSO NAZIONALE **Italian Conference** on **AIDS** and **Antiviral Research**

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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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Abstract Book

Clinical HIV

OC 1 COINFECTION WITH HEPATITIS B VIRUS AND/OR HEPATITIS C VIRUS IS A RISK FACTOR FOR HIV VIROLOGICAL REBOUND IN COURSE OF ANTIRETROVIRAL THERAPY

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Background: Coinfection with viral hepatitis B and/or C (HBV and HCV) and HIV is common however, the impact of HBV and HCV coinfection on HIV viremia control during antiretroviral therapy (ART) has yet to be fully understood. The aim of this study was to investigate the impact of viral hepatitis coinfection (included potential occult hepatitis B infection) on the risk of viral rebound (VR) after achieving suppression in real-world data.

Methods: Patients living with HIV (PLWH) from the ICONA Foundation Cohort were prospectively evaluated with aim of assessing whether viral HBV and/or HCV coinfection influenced the risk of VR defined at the time of the first of two consecutive values >50 cp/mL, after achieving a HIV-RNA ≤50 cp / mL also in two consecutive occasions on their first line ART (baseline). Study population was divided in 5 exposure groups: HBsAg+/HIV+, HBsAg-/HBcAb+/HIV+, HCVAb+/HIV +, HCVAb+/HBcAb+/HIV+ and HIV mono-infected patients using all serological test results performed prior to baseline. Nationality, duration of viral suppression, history of virological failure prior to baseline and HIV-RNA at cART initiation ad mode of HIV transmission were identified a key confounders for the association of interest. Standard survival analysis by means of KM curves and Cox regression analysis with time-fixed covariates measured at baseline was employed.

Results: Of a total of 6,380 patients included (Table 1), 4,090 (64%) resulted HIV mono-infected, 308 (5%) HCVAb+, 1,342 (21%) HBcAb+, 410 (6%) HCVAb +/HBcAb+ and 230 (4%) HBsAg +. Regarding the immuno-virological status at baseline, all 4 co-infected groups had CD4+ cell counts lower and HIV-RNA values higher than those seen in HIV mono-infected PLWH. At baseline, almost all groups (98%) were on ART containing NRTIs active against HBV (lamivudine, tenofovir dipivoxil fumarate or alafenamide). Overall, 829 (13%) patients experienced VR over follow-up. By 48 months the risk of VR were the following: 4.8% in mono-infected HIV vs. 12.7% in HCVAb+, 5.9% in HBcAb+, 14.5% in HCVAb +/HBcAb+ and 6.0% in HBsAg+ (log-rank test p<0.0001). After controlling for key confounders, co-infected PLWH showed an increased risk of experiencing VR compared to the mono-infected. In particular, the strongest associations were seen for the HCVAb+ (aHR 1.79 [95%CI 1.25-2.57], p=0.0001) HBcAb+ or HBCAb- (aHR=1.73 [95% CI:1.73–2.45], p=0.002 followed by HBsAg+ (aHR 1.57 [1.04-2.39], p = 0.03), and HBcAb+ group (aHR 1.26 [CI 95% 1.01-1,57], p=0.02, Table 2) the latter showing also a smaller magnitude of the effect.

Conclusions: In our cohort of PLWH, co-infection with all major hepatotropic viruses had an impact on the probability of retaining an HIV-RNA ≤50 cp/mL achieved under first line ART. Particular attention should be paid to PLWH with 'resolved' HBV infection (HBcAb-positive), who, similarly to other PLWH with active hepatotropic coinfection and possibly because of occult infection (OBI), are also likely to be at increased risk of VR.

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Clinical HIV

OC 2 TRANSITIONS IN FRAILTY PHENOTYPE STATES AND ITS ASSOCIATION WITH FRAILTY INDEX: A MULTI-STATE MARKOV MODEL STUDY

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Background: Frailty phenotype (FP) and frailty index (FI) constructs have been applied in the HIV setting, identifying both syndromic and the accumulation of deficit approach to aging. We described longitudinal transitions of FP states in relation to FI at the Modena HIV Metabolic Clinic (MHMC), Italy.

Methods: PLWH with a minimum of two FP and FI measurements and maximum four visits were included. A continuous-time multi-state Markov model describes a process in which an individual moves through a series of states allowing joint analysis of care length, incidence of clinical outcomes and frailty progression or reversion. Next-state transition probabilities were estimated after adjusting for 37-item FI, age, sex, body mass index, CD4 nadir and HIV duration. The probabilities to switch from one state to another were modelled according to an exponential distribution for time-to-event data, which considers censored follow-up times. Time was measured in years and the events were the transitions between the states.

Results: 1325 participants (986 men and 339 women; mean age 53 ± 7,7years) contributing to 3497 observations were included. Median follow up was 2.2 years (range 1 to 12 years). At baseline Mean FI=0,3±0,1, prevalence of 38%, mean duration HIV 21±8,1 years, mean CD4 223,9 ±161,6 µL, BMI 24,3±3,8 kg/m2. Probabilities from fit to prefrail, and fit to frail were 35.7% and 0.4%, respectively. Prefrail had a 24.3% probability of reversal to fit, and a 3.8% risk of progression to frail. Frail had an 56.7% probability of reversal to prefrail and 3.3% to fit. Across the four visits we observed that the percentage of fit subjects decreased from 49.6% in visit 1 to 45.9% in visit 4 while frail patients increased from 1.1% in visit 1 to 3.5% in visit 4 (Figure 1). In the adjusted multi-state Markov model multimorbidity and female sex increased the risk from fit to prefrail only, respectively HR=0.704 (95%CI 0.5, 0.992) and HR=1.457 (95%CI 1.061, 2). Frailty Index predicted both the increased risk of progression from prefrail to frail with an increase of 0.01 of the index (HR 1.053, 95%CI 1.002, 1.106) and reversed transition from prefrail to fit state (HR 0.969, 95%CI 0.95, 0.988). Finally, HIV duration was found to increase the risk of moving) and lowering the probability of transition from prefrail to frail and reversed (HR 0.892, 95%CI 0.798, 0.996; HR 0.876, 95%CI 0.767, 1.000) from prefrail to fit (HR 1.021, 95%CI 1.000, 1.043)

Conclusions: FP states and components are characterized by dynamic longitudinal transitions. Sex and multimorbidity drive initial fit to prefrail state transition, while FI and HIV duration predict both frailty transition and its reversibility. Both FP and FI should be used to monitor aging trajectories in PLWH.

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Clinical HIV

OC 3 INTRAPARTUM USE OF ZIDOVUDINE IN HIV PREGNANT WOMEN IN ITALY. IS IT STILL BEING USED IN THE ERA OF U=U?

L. Taramasso[1], F. Bovis[2], A. di Biagio[3], F. Mignone[4], C. Giaquinto[5], C. Tagliabue[6], V. Giacomet[7], O. Genovese[8], E. Chiappini[9], S. Salomè[10], R. Badolato[11], I. Carloni[12], M. Cellini[13], I. Dodi[14], G. Bossi[15], A. Allodi[16], S. Bernardi[17], R. Consolini[18], M. Dedoni[19], G. Banderali[20], A. Mazza[21], M. De Martino[22], C. Lisi[23], P.A. Tovo[24], M. Bassetti[3], C. Gabiano[24], L. Galli[9], on behalf of The Italian Register for HIV Infection in Children

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Background: Intravenous administration of zidovudine (ZDV) during labor is a key step for mother-to-child HIV transmission (MTCT) prevention, but there is no evidence of benefit when maternal HIV-RNA level at delivery is below 50 copies/mL. The aim of this study is evaluating the appropriateness of intrapartum ZDV use in Italy.
Material and methods: Observational study including mother-infant pairs with perinatal HIV exposure during 2002 -2019, enrolled in the Italian Register for HIV Infection in Children. Univariable and multivariable stepwise logistic regression were used to evaluate factors associated with MTCT.
Results: A total of 3861 infants, born from 3791 pregnancies were included. All mothers received antiretroviral therapy during pregnancy and 3412 (90.0%) received intravenous ZDV during labor. The frequency of ZDV use was 79.9%, 92.1%, 93.7% and 92.8% when HIV-RNA was not available, ≥400 copies, between 50 and 399 copies, and <50 copies/mL. Thirty-three out of 3861 infants were subsequently diagnosed as HIV infected, 25 of them born to mothers receiving intrapartum ZDV, and 31 to mothers with HIV-RNA ≥50 copies/mL or not available. On the other side, two out of the 2306 children born from mothers with HIV-RNA <50 copies/mL at partum, both receiving intrapartum ZDV, were diagnosed as HIV-infected. The adjusted logistic model investigating predictors of MTCT in women with HIV-RNA < 50 copies/mL revealed that ART discontinuation during pregnancy was the strongest risk factor for MTCT (odds ratio, OR, 39.9, 95%CI 3.2-496.6), while a higher gestational age (OR 0.57, 95%CI 0.4-0.8) was protective against HIV transmission. Intrapartum ZDV administration did not influence on the final outcome in this group (Table 1).
Conclusions: In our cohort, intrapartum ZDV use was still inadequate for women with detectable or unknown HIV-RNA. On the other side, IV ZVD in women with undetectable HIV-RNA at delivery must be definitely view as
an overtreatment. The Undetectable=Untransmittable concept needs to be reinforced in health care professionals, as its implementation is crucial to eliminate stigma globally. This should include avoiding the use of intravenous ZDV when peripartum HIV-RNA is undetectable.

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Epidemiology / Social Sciences I

OC 4 LONG-TERM FOLLOW-UP IN A COMMUNITY-BASED PREP COHORT: CONTROLLED INCREASE IN RISK EXPOSURE

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Background: Current research suggests that sexual risk compensation to be associated with PrEP initiation. Data from a longitudinal open cohort of participants in a community-based PrEP Programme (from September 2017 to July 2021) was analysed to investigate the association between PrEP initiation and change in sexual behaviours.
Methods: Participants enter the programme at an evaluation and baseline appointment (T-1), they start PrEP after a 1-month non-exposure timespan (T0) and follow-ups are scheduled 1 month after PrEP start (T1) and then quarterly. In case non-exposure time has been long enough at baseline, PrEP can be started immediately (with T-1 and T0 coinciding). Each appointment entails: completing a questionnaire; a consultation with an infectious diseases doctor; a semi-structured interview with a psychologist/peer counsellor; screening for HIV, syphilis, HCV, C. trachomatis (CT) and N. gonorrhoeae (NG). In addition to descriptive statistics, paired t-tests were used to assess changes over time and Kaplan-Meier survival estimates for incidences of first CT and NG events after PrEP start.
Results: Participants were 534, 96% of them MSM (see Tables 1-2 for socio-demographic characteristics and main risk factors). 415 (78%) participants were in follow-up as of July 2021, 68 (13%) have dropped out of the programme (see Table 3 for detailed reasons) and 51 (9%) have been lost to follow-up. Mean occurrences of condomless anal/vaginal sex in the previous month significantly rose almost two-fold from T-1 to T1, with a less significant change from T-1 to the latest appointment after T1 (T2), yet increasing by more than one third (Table 4). The mean number of occasional partners in the previous month slightly increased at T1 and went back to T-1 levels at T2 (Table 5). Prevalence rates at baseline were 7.4 for CT and 5.7 for NG. Incidence rates after PrEP start were 18.4 per 100 PYFU for CT, 15.7 per 100 PYFU for NG and 32.2 per 100 PYFU cumulatively (Figure 1). All CT and NG infections diagnosed were asymptomatic. Only one seroconversion has been recorded.
Conclusions: A steep and short-term increase in the occurrence of condomless sex was observed immediately after starting PrEP, with a lesser yet relevant increase observed in the long term. Instead, the number of occasional partners has not changed significantly over time, therefore there is only partial evidence for sexual risk compensation. Moreover, most participants that reported stopping PrEP at the same time reported a decrease in perceived risk. With only 9% of participants lost to follow-up this PrEP programme has been effective in retaining in care high-risk participants. Retention in care is essential to assess PrEP uptake, and also to diagnose and treat STIs acquired during PrEP, controlling STIS circulation and any other potential inconvenience. A longer observation time is needed to assess whether the observed sexual behaviour changes are linked to COVID-19 and lockdowns.

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Epidemiology / Social Sciences I

OC 5 CHEMSEX USE IN A HIV PRE-EXPOSURE PROPHYLAXIS (PREP) PROGRAM BASED IN MILAN

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Background: Chemsex, defined as the use of recreational drugs to facilitate sex, is recently increasing among men who have sex with men (MSM). Prevalence and incidence estimates change substantially among different cohorts due to missing standardized definition of chemsex and lack of epidemiological studies in key populations.
Aim of our study is to assess prevalence and incidence of chemsex and define factors associated to its use in a community-based pre-exposure prophylaxis (PrEP) program in Milan.
Methods: Data were collected from self-administered questionnaires filled between December 2017 and July 2021. PrEP users completed a questionnaire at each visit providing data on drug and alcohol use, and sexual behaviors. Chemsex practices included use of crystal methamphetamine, mephedrone, MDMA, ketamine, gamma-hydroxybutyrate (GHB), methylenedioxypyrovalerone (MDPV) and cocaine. Risky alcohol use was defined as alcohol consumption during a sexual intercourse. Participants' characteristics were reported as median (interquartile range) or frequency (%). Logistic regression estimated adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for factors associated with chemsex use.
Results: The analysis included 527 participants with a median age of 44 (31-37) years; 505 (96,2%) were MSM.
Overall, 127 (24.1%) have reported recreational drug use: 61 (11.6%) continuously and 66 (12.5%) occasionally. Eight participants (1.5%) were female and none reported chemsex. Among them, 80 (63.0%) participants reported both illicit drugs and alcohol use while 47 (37.0%) only drugs use (p<0.01). Cocaine was the most consumed: overall, it was taken by 77 (14.6%) PrEP users, followed by GHB and MDMA by 39 (7.4%) and 38 (7.2%), respectively.
Prevalent cases were 86 at the first visit, while incident cases at follow-up visits were 41 with an incidence of 15.5 per 100 person-years of follow up.
Participants who used recreational drugs were more likely to use also erectile dysfunction drugs (aOR 2.77, 95%CI 1.67 -4.60, p<0.001) and alcohol during sexual intercourse (aOR 2.54, 95%CI 1.64-3.94, p<0.001), and to have a higher number of unprotected sexual intercourse (aOR 1.04, 95%CI 1.01-1.09, p=0.022), as showed in Table.
Conclusions: Prevalence and incidence of chemsex use proved to be high among PrEP users in Milan. Recreational drugs are associated with the concomitant use of erectile dysfunction medications and alcohol and with more frequent unprotected sexual intercourses. Routine clinical practice of PrEP programs should include chemsex screening and counseling for a better risk management.

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Epidemiology / Social Sciences I

OC 6 BETWEEN LOSS TO FOLLOW-UP AND PERSISTENCE OF RISKY SEXUAL BEHAVIORS: HOW THE COVID-19 PANDEMIC IMPACTED ACCESS TO PREP

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Introduction: The first wave of COVID-19 pandemic caused the interruption of a multitude of non-essential health services, leading to the loss of previously followed patients in various settings. In our work we analyze how the pandemic and the restrictions have influenced the follow-up of Pre Exposure Prophylaxis (PrEP) users attending the outpatient clinic of the Modena University Hospital.
Methods: All visits of our PrEP outpatient clinic are stored in an electronic database with demographic, clinical and laboratory data, and Sexual Transmitted Infections (STI) events (type and location) are recorded. At each visit, users are tested for renal function, syphilis, HIV, HBV, HCV, and HAV through serologies, as well as for Gonorrhea, Chlamydia, and Mycoplasma genitalium through urine tests, and oral and rectal swabs.
Results: By 08th March 2020, the date of the first national lockdown and suspension of all non-essential outpatient clinics, 37 users were in active follow-up in our PrEP outpatient clinic (at least one control in the previous 3 months). They were all male cisgender, MSM, 84.6% were Italian, median age was 46.5 + 2.12 years
When outpatient visits resumed in October 2020, only 23/37 users returned to regular follow-up (62.2%), while 14/37 users were lost to follow-up (37.8%). Among the 23 users who resumed follow-up, 7/23 (30.4%) reported stopping taking PrEP during the lockdown period, whereas 16/23 (69.6%) continued to take PrEP. Among these, those taking Daily PrEP switched to the On-demand regimen given the inability to obtain a prescription for the drug. During this 7-month period, 10 users continued to receive assistance with telemedicine alone.
10/23 users (43.5%) presented at least one STI at the first post-lockdown visit, 4 users had 2 STIs. The infections found were: 4 rectal Chlamydia, 3 Mycoplasma genitalium (2 rectal, 1 on urine), 4 gonorrhea (3 rectal, 1 pharyngeal), 3 positive serologies for syphilis. Among the 10 users who presented with an STI, 7 had not discontinued PrEP.
Thus, the incidence of STIs during the lockdown period was 3/7 (42%) among those who discontinued PrEP, and 7/16 (43.7%) among those who continued PrEP. No new HIV infection was found.
After lockdown, we had 16 new enrollments.
Conclusion: Lockdown resulted in the loss to follow-up of nearly 40% of PrEP users from the pre-COVID-19 era. Patients who remained followed presented a high incidence of intercurrent STIs after the lockdown period, indicating the persistence of risky sexual behaviors even in times of social restrictions.

Epidemiology / Social Sciences I

OC 7 IMPACT OF COVID PANDEMIC ON SEXUAL HABITS AND PRE-EXPOSURE PROPHYLAXIS RETENTION IN CARE IN A COMMUNITY-BASED SERVICE

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Background: COVID pandemic had a significant impact on most social and medical activities, including sexual habits and access to pre-exposure prophylaxis (PrEP). Social distancing and fear of SARS-CoV-2 infection might have influenced sexual practices. Aims of our study are to describe the number of subjects who discontinued PrEP after the first lockdown and the change of sexual behaviors in those who continued despite COVID-related social restrictions.

Methods: This monocentric, retrospective analysis included all subjects attending a community-based PrEP service who started the prophylaxis before February 2020. Time was stratified in five Periods: 1) before COVID (up to February 2020); 2) during the first lockdown (March-May 2020); 3) after the first lockdown (June-September 2020); 4) autumn lockdown (October 2020-January 2021); 5) vaccine era (February 2021 onwards). Data were collected from self-administered questionnaires providing information about sexual behaviors in the previous three months. Descriptive statistics (median and interquartile range for continuous variables, absolute and relative values for categorical variables) were used. Mean number of sexual partners and unprotected sexual intercourses at each time period were compared with baseline pre-COVID value with t-test. Linear regressions for sexual partners and unprotected sexual intercourses over time were calculated.

Results: The analysis included 158 individuals who started PrEP before February 2020: among them, 39 (25%) did not continue attending visits after the first lockdown. The majority (27, 17%) decided to temporarily postpone prophylaxis until after the end of the pandemic. Ninetyfive subjects continued PrEP: they were mainly MSM (98%), Italians (83%), with a median age of 40 (IQR 31-46) years, without a steady relationship (71%), with a university degree (58%), and with a regular job (89%). They did not show an increased risky behavior: sex workers were 9%, at least one sexually transmitted infection was registered in 28% and Chemsex practices were referred by 18%. In the visits after the first lockdown, the referred sexual habits indicated a tendency towards a reduction in the number of casual sex partners and an increase in unprotected anal/vaginal sexual intercourses (Figure 1). However, at each time point there was not a significant difference compared with pre-COVID behaviors.

Conclusion: COVID-19 had an impact on PrEP users attending a community-based service in terms of persons who stopped the prophylaxis. Nevertheless, in those who decided to continue, sexual habits did not change significantly compared to pre-pandemic period. There is the suggestion that they chose to reduce the number of sexual partners as a possible effect of social distancing, but they increased unprotected intercourses with these selected partners. It would be important to retrieve those who discontinued PrEP that could potentially undergo risky behaviors without its protective effect.

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Epidemiology / Social Sciences I

OC 8 SCHOOL-BASED SEXUALITY EDUCATION IN ITALY 2016-2020: A HIGHLY HETEROGENEOUS SCENARIO

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Background: In Italy, sexuality education (SE) is not part of school curricula. SE and, specifically, comprehensive sexuality education (CSE) as defined by UNESCO, is one of the most important means of promoting sexual well-being among young people and a key component of the global strategy for HIV and sexually transmitted infections' (STIs) prevention in Europe.
School-based SE (SBSE) has the potential to reach the majority of young people, it is cost-effective and valued by students.
This study, funded by the Ministry of Health-General Directorate of Health Prevention, was performed in order to provide an inventory of SBSE carried out in mid and high schools in Italy during the period 2016-2020.
Methods: An online survey was developed and piloted to collect information on duration, providers, objectives, content and methods used to implement and to evaluate SBSE. The survey was disseminated at a national and regional level between July and October 2020, with a focus on 4 regions (Lombardy, Tuscany, Lazio and Puglia) which will be the subject of following interventions. IBM SPSS Statistics 26 was used to perform descriptive analysis of the data, while a framework from UNESCO was adapted to perform a qualitative analysis.
Results: A total of 219 SBSE activities carried out in secondary schools were reported, 3 of which have not been included in the qualitative analysis. The analysis showed a highly heterogeneous scenario in terms of geographical coverage across the country (69% of SBSE delivered in the targeted regions), providers (70% private, 30% public - see Figure 1) and objectives (predominantly informative rather than formative).
The qualitative analysis of content, objectives, and methodology identified 62 SBSE activities (29%) classifiable as CSE, with a median duration of 3 days. The remainder SBSE had a risk-based approach, largely focussing on STIs prevention (35% - see Figure 2). Many SBSE activities (29%) were single-session interventions. The participation of the students and their engagement through the presentation of scientific content in a direct language was reported as a factor positively influencing the activity, while limited time availability for extra-curricular activities was reported as a key challenge. Although 97 SBSE activities performed evaluation (44%), no result was submitted. In 53 SBSE activities (24%) both pre and post assessment surveys were delivered and in 114 (52%) satisfaction was evaluated.
Conclusions: This study showed the absence of a comprehensive and standardised approach to SBSE in Italy.
Italy is one of a few European countries still lacking a dedicated policy for SBSE. According to available data, SBSE is not systematically and equally delivered across the country. The results highlight the need to develop theoretical and practical guidelines for the implementation of CSE in Italy and the integration of sexuality education in school curricula.

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Coinfections and Hepatitis

OC 9 ENRICHMENT OF POSITIVELY CHARGED AMINO ACIDS IN HBSAG C-TERMINUS CORRELATES WITH HBV-INDUCED LIVER CANCER, HAMPERS HBSAG SECRETION AND ALTERS ITS STRUCTURAL STABILITY

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Background: Patients with chronic hepatitis B have a 100-fold increased risk of developing hepatocellular carcinoma (HCC). An impairment in HBsAg secretion is a mechanism mediating HBV related oncogenesis. HBsAg C-terminus is a hydrophobic transmembrane domain, crucial for HBsAg secretion. Gain of charged amino acids (aa) in this domain can alter its folding in the ER membrane, thus hampering HBsAg secretion.
The role of HBsAg C-terminus (aa189-226) mutations, associated with a gain of charged aa, on HBV-induced HCC onset is unknown.
Material and methods: We analyze 807 HBV chronically infected patients from routine clinical practice with an available HBsAg sequence: 28 with HCC (78.6% D; 21.4% A), and 779 patients without HCC (79.8% D; 20.2% A). Multivariable logistic regression model is used to assess association of identified mutations with HCC.
Impact of mutations on HBsAg-secretion is analyzed in vitro by transfecting HepG2 cells with plasmids encoding wt- and mutated-HBsAg. Extracellular and intracellular HBsAg is quantified by an immunoassay (LiaisonXL, Diasorin) and used to define HBsAg secretion factor (ratio between extracellular and intracellular HBsAg). I-Tasser is used to assess HBsAg structures and stability (ΔΔG[wt-mutated]<0 indicating decreased stability in presence of mutation based on Quan,2016).
Results: The acquisition of >1 positively charged aa at HBsAg C-terminus positions 204, 207, and 210 strongly correlates with HCC (71.4% with HCC vs 30.2% without HCC, P<0.001). Multivariable analysis confirms this association stratifying for patients' demographics, HBV genotype, serum HBV-DNA and anti-HBV drugs use (OR[95%CI]:6.3[2.6-15.3], P<0.001). The acquisition of positively charged aa results from S204R, S207R and S210R mutations, found in 14.3%, 28.6% and 28.6% of HCC-patients, respectively.
in vitro, all these mutations determine a significant decrease in extracellular HBsAg amount compared to wt (42% for S204R, 39% for S207R and 32% S210R, P<0.0001 for all comparisons).
Moreover, S204R and S210R also cause a 58% and 28% reduction in HBsAg secretion factor compared to wt (P<0.0001 and P=0.009), further reinforcing their detrimental role in HBsAg release.
In silico, S204R, S207R and S210R decrease HBsAg stability compared to wt (ΔΔG[S204R-wt]=-0.27; ΔΔG[S207R-wt]= -0.11; ΔΔG[S210R-wt]=-0.14) and determine a shortening of membrane-spanning alpha-helix motif (predicted alpha-helix length: aa209-224 for S204R, S207R and S210R vs 205-225 for wt), suggesting an impaired HBsAg C-terminus stability.
Conclusions: Gain of positively charged aa at specific HBsAg C-terminus positions tightly correlates with HCC, hampers HBsAg release in vitro and alters the proper folding of this domain. This could favour an intracellular HBsAg retention, posing the bases for HBV-driven hepatocarcinogenesis.
The detection of these mutations may help identifying patients at higher HCC-risk, deserving more intense liver monitoring.

Coinfections and Hepatitis

OC 10 HBCRAG STRONGLY CORRELATES WITH HIGHER HDV REPLICATIVE ACTIVITY AND WITH ENHANCED LIVER INFLAMMATION AND DAMAGE: IMPLICATIONS FOR HBCRAG AS A BIOMARKER OF DISEASE PROGRESSION IN THE SETTING OF HDV CO-INFECTION

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Background: HBcrAg is a non-invasive biomarker that reflects cccDNA transcriptional activity. Here, we evaluate HBcrAg levels and their correlation with virological and biochemical markers in the so far poorly investigated setting of HBV+HDV coinfection.

Material and methods: This study includes 64 HBeAg-negative patients: 32 co-infected with HDV and 32 HBV mono-infected, matched for patients' demographics. 37.5% of HBV+HDV infected patients is highly-replicating HDV (median [IQR] HDV-RNA: 5.6 [5.1-5.8] log copies/ml) while 62.5% is lowly-replicating HDV (detectable serum HDV-RNA below lower limit of quantification [LLOQ: 640 copies/ml]). HBcrAg is quantified by Lumipulse HBcrAg assay (Fujirebio; LLOQ: 3 logU/mL).

Results: HBV+HDV group has lower serum HBV-DNA and higher HBsAg levels than HBV-monoinfected group (median [IQR]: 22 [<20-136] vs 144 [63-430] IU/ml, P=0.007 for HBV-DNA and median [IQR]: 3.6 [3.1-3.9] vs 2.8 [1.7-3.8] log IU/ml, P=0.002 for HBsAg). HBV+HDV group is also characterized by higher ALT levels (median [IQR]: 42 [24-64] vs 21 [15-27] U/L, P= 0.0002).

Despite lower serum HBV-DNA, the % of patients with HBcrAg>3logU/mL is significantly higher in HBV+HDV-group than in HBV-monoinfected group (53.1% [17/32] vs 21.8% [7/32], P=0.02). Focusing on HBV+HDV group, HBcrAg>3logU/mL is observed more frequently in highly-replicating HDV than in lowly-replicating HDV patients (91.7% [11/12] vs 30% [6/20], P=0.001). Even more, a strong correlation is observed between HBcrAg and serum HDV-RNA levels (Rho=0.77, P=0.006), suggesting that HBcrAg parallels HDV replicative potential. By Auroc, HBcrAg>3logU/mL predicts highly-replicating HDV with a diagnostic accuracy of 78.1% (sensitivity:91.7%, specificity:70%).

Finally, in HBV+HDV group, patients with HBcrAg>3logU/mL are characterized by higher HBsAg levels (median IQR 3.7 [3.6-4.3] vs 3.2 [2.5-3.5] log IU/ml, P=0.02) and, notably, by more elevated ALT and liver stiffness (median [IQR]: 54 [47 -96] vs 25 [15-37] U/L, P=0.001 for ALT and 10.8 [6.1-14.7] vs 7.2 [4.9-8.1] KPa, P=0.02 for liver stiffness).

Conclusions: HBcrAg, a valuable biomarker of cccDNA transcriptional activity, tightly correlates with enhanced HDV replicative potential and an increased liver inflammation. This suggests that an active transcription of cccDNA is required to support an effective HDV pathogenicity. This can have relevant clinical implications for the full effectiveness of novel therapeutic strategies targeting HBV/HDV co-infection.

Coinfections and Hepatitis

OC 11 ENDOCRINE PATHWAYS OF NON-ALCOHOLIC FATTY LIVER DISEASE IN PEOPLE LIVING WITH HIV

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Background: Non-alcoholic fatty liver disease (NAFLD) has multisystemic nature that involves different immuno-metabolic-endocrine pathways. The objective was to explore, using Bayesian networks, the dynamic interplay among endocrine disorders and NAFLD or NAFLD with fibrosis in people living with HIV (PLWH).

Methods: This was a cross-sectional study of PLWH attending Modena HIV Metabolic Clinic, Italy in the period June 2018-January 2020. NAFLD was assessed by transient elastography as controlled attenuation parameter ≥248 dB/m. NAFLD with fibrosis was defined as the contemporary presence of NAFLD and significant liver fibrosis (liver stiffness measurement ≥7.1 kPa). Bayesian networks were applied to identify the relationship among the endocrine disorders and the outcomes through a Directed Acyclic Graph (DAG).

Results: We enrolled 1434 PLWH (75.5% males), mean age of 54.2 years. NAFLD was diagnosed in 39.3%, while NAFLD with fibrosis in 8.2% of PLWH. The DAG model for NAFLD, in which PLWH with IR and diabetes were combined in one variable (IR + diabetes), identified direct associations with age, IR + diabetes, and vitamin D insufficiency (Figure 1A). In the logistic regression model, IR + diabetes was split into three mutually exclusive categories: (i) diabetes alone, (ii) IR alone, (iii) IR + diabetes, while "no IR + no diabetes" was used as a reference. IR alone (OR=2.36, 95%CI: 1.37 - 4.14, p=0.002) was more strongly associated with NAFLD than diabetes alone (OR=1.41, 95%CI: 1.05 - 1.90, p=0.022), while IR + diabetes had an additive effect in predicting NAFLD (OR=2.63, 95%CI: 1.12 - 6.64, p=0.031). In PLWH with age >50 years, vitamin D insufficiency, and both IR and diabetes, the probability of presenting NAFLD was 83.5%. Conversely, if none of the previous was present, the probability of NAFLD decreased to 25.4%. DAG model for NAFLD with fibrosis showed a direct association with IR-diabetes only. Diabetes alone (OR=2.76, 95%CI:1.77-4.24, p<0.001) was associated with NAFLD with fibrosis, while IR alone was not (Figure 1B).

Conclusion: DAG models revealed that IR is more strongly associated with NAFLD than diabetes, while NAFLD with fibrosis is mainly driven by diabetes rather than IR. This suggests a significant role of diabetes on fibrosis progression in PLWH. Vitamin D supplementation might be considered in PLWH with NAFLD.

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Clinical HIV & Clinical Covid I

OC 12 HIGHER RISK OF MABS CLINICAL FAILURE ASSOCIATED TO BAMLANIVIMAB/ETESEVIMAB EXPOSURE AND TO INFECTION BY SARS-COV-2 P.1/GAMMA VARIANT OF CONCERN IN A REAL LIFE SETTING

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Background: Neutralizing monoclonal antibodies (MAbs) against SARS-CoV-2 have received emergency use authorization in Italy for early treatment of outpatients with mild to moderate COVID-19 at high risk of clinical progression and hospitalization. To date, few real-world data about the efficacy of MAbs have been reported. We assessed the impact on hospitalization risk due to COVID-19 of two different MAbs combinations, bamlanivimab+etesevimab (BAM/ETE) and casirivimab+imdevimab (CAS/IMD).

Material and methods: Observational single-center comparative analysis of patients (pts) with mild-to-moderate COVID -19 enrolled within the AIFA MAbs access program. All consecutive pts with SARS-CoV-2 infection, diagnosed by RT-PCR from nasopharyngeal (NP) swab, treated with 1-hour intravenous BAM/ETE (700 mg/1400 mg) or CAS/IMD (1200 mg/1200mg) infusion, were enrolled. To minimize confounders, the two MAbs combo were delivered in a casual modality by alternate day protocol (Mon-Wed-Fri for BAM/ETE and Tue-Thu-Sat for CAS/IMD). Comparisons between the two groups were made by Chi-square for categorical variables and Wilcoxon test for continuous parameters. Primary end point was COVID-19-related clinical failure, defined as 30-day hospitalization or death due to severe COVID-19. Factors associated with primary endpoint were analyzed by fitting a multivariable logistic regression model. Multivariable analysis was adjusted by factors associated at univariable level and by variables with different distribution in two groups of treatment.

Results: A total of 142 pts receiving a MAbs infusion (BAM/ETE=71; CAS/IMD=71) were included. At the time of MAbs infusion, median time from symptoms onset was 4.5 days (IQR 3-6); SpO2 97% (95%-98%); ferritin 215 ng/mL (121 -293); C-reactive protein 1.46 mg/dL (0.48-2.98). 29/142 (20%) developed SARS-CoV-2 infection after vaccination. Main characteristics according to the two treatment groups are reported in Table 1. After 30 days of follow-up, 10/71 (14%) pts treated by BAM/ETE and 2/71 (3%) pts by CAS/IMD experienced COVID-19-related clinical failure (OR 5.66;95%CI 1.19-26.83). Two COVID-19 related deaths were observed, both in the BAM/ETE group. After multivariable adjustment, severe obesity (BMI >35), presence of chronic obstructive pulmonary disease and exposure to BAM/ETE were independently associated to an increased risk of being hospitalized due to severe COVID-19. In a second model, adjusted also for type of SARS-COV-2 variant, exposure to BAM/ETE remain associated to an increased risk of failure (Table 2).

Conclusions: In a real life, not-randomized, observational comparative study, receiving BAM/ETE was associated with a higher risk of clinical progression to severe COVID-19 than CAS/IMD. Infection with P.1/Gamma SARS-CoV-2 variant of concern strongly predicted an increased risk of MAbs failure. The effect of B.1.617.2/Delta VOC on MAbs failure cannot be explored due to still low prevalence of this variant in our cohort.

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Clinical HIV & Clinical Covid I

OC 13 BAMLANIVIMAB AND ETESEVIMAB ADMINISTERED IN AN OUTPATIENT SETTING FOR SARS-COV-2 INFECTION

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Background: The COVID-19 pandemic caused a huge financial and organizational burden on Public Health Systems, due to the wide number of subjects requiring hospitalization. In this setting, early administration of anti-SARS-CoV-2 monoclonal antibodies (mAb) could decrease the risk of developing severe disease and the need of inpatients care. Aim of study was to describe our initial clinical experience with Bamlanivimab and Etesevimab for the treatment of early SARS-CoV-2 infection through an outpatient service.

Material and methods: Patients with confirmed COVID-19 were selected by General Practitioners (GPs) if eligible to mAb administration, according to manufacturer and AIFA (Agenzia Italiana del Farmaco) criteria: i) not hospitalized; ii) with confirmed COVID-19 by RT-PCR testing on nasopharyngeal swab; iii) with at least one mild-moderate COVID-19 symptom within the last 10 days; iv) with at least one risk factor including: Body Mass Index >35 kg/m2, chronic hemodialysis, decompensated diabetes mellitus, primary or secondary immunosuppression, age ≥65 years (with at least one of previous conditions), age ≥55 years (with chronic lung diseases and/or cerebrovascular diseases); v) not requiring oxygen therapy to achieve a room air saturation ≥94%.

If suitability was confirmed by a dedicated Multidisciplinary Team, the patient was admitted to our outpatient within the next 48-72 hours.

On the day of administration, all patients underwent a medical evaluation, followed by mAb infusion. Conversely, if the medical condition had worsened, the patient was hospitalized without mAb administration.

Results: Overall, from March 29th to June 4th, 2021, 106 patients with confirmed COVID-19 were identified by GPs (Figure 1); 26 patients were considered not eligible by a Multidisciplinary Team and then excluded, while 9 refused treatment after the eligibility confirmation. Among the 71 remaining, 6 were not treated with mAb because of worsening of symptoms soon after selection before mAb administration. Finally, 65 received mAb therapy (Table 1). Notably, all patients who underwent mAb survived to COVID-19. However, 2 patients developed adverse events (allergic reaction and atrial fibrillation, respectively) and 6 patients needed oxygen therapy and were hospitalized despite the treatment.

By performing univariate logistic regression analysis, diabetes was the only risk factor for hospitalization after mAb administration [aOR=9.34, 95%CI=1.31-66.49, p=.026]. Importantly, subjects who worsened awaiting mAb were more frequently obese (OR= 16.66, 95%CI=1.80–153.9, p=.013) and received home corticosteroid therapy for COVID-19 (OR=14.11, 95%CI=1.53–129.6, p=.019).

Conclusions: According to our experience, establishing a network among GPs and COVID Units could be an effective strategy to provide mAb treatment to patients with early SARS-CoV-2 infection and high risk of disease progression, in order to reduce hospitalizations and pressure on healthcare systems.

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Clinical HIV & Clinical Covid I

OC 14 REAL LIFE USE OF MONOCLONAL ANTIBODIES AND THEIR IMPACT ON SARS-COV-2 CLEARANCE KINETICS: A SINGLE CENTRE EXPERIENCE

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Background: Real life data on the efficacy/clinical outcome of monoclonal antibodies (MAB) in patients with SARS-CoV -2 infection are scarce. Therefore, our aim was to describe the clinical outcome of our cohort of patients treated with MAB, and the impact of this treatment on viral clearance, measured by rate of positive at SARS-CoV-2 RT-PCR at the different time points and by the cycle threshold values.

Methods: This retrospective cohort study, conducted in Padua, included patients diagnosed with SARS-CoV-2 infections eligible for MAB infusion according to the Italian Drug Agency.

Statistical analyses were performed by Chi-square test or T-Test, as needed. To assess the trend of the percentages of positive subjects over time, we used chi-square test for the linear trend analysis. Temporal trend of CT was assessed by analysis of variance for repeated measures (ANOVA)

Results: From March to May, 2021, 112 patients received MAB, mostly of male gender (67.9%), with a mean age of 64.6 years (SD:13.7). Main risk factors to deem eligibility for treatment with MAB were age (69.1%) and pre-existing cardiovascular diseases (55.4%). Mean time from onset of symptoms to infusion was 5.2 days. Mean time from positivity of testing for SARS-CoV-2 and infusion was 3.6 days. Side effects after infusion were reported in 5.3% cases (fever, chest pain, rash and itching, insomnia, and transitory loss of consciousness). Progression of COVID-19, requiring hospitalization was necessary only for 13/112 (11.6%) patients (11 older and 2 younger than 55 years of age). Two/13 were admitted just for fever after infusion and monitored during the overnight. No patient required intensive care unit admission. Proportion of people with a negative SARS-CoV-2 RT-PCR result from baseline to day 3 was significantly higher in elderly compared to the younger group (32/91, 35.2% vs. 15/21, 71%, p=0.005), but difference disappeared along the follow-up. Mean time to obtain a negative SARS-CoV-2 PCR testing was 16.3 days (SD:6.9) overall, 16.6 days (SD: 6.1) in the elderly group, and 15.5 (SD:9.1) in the young one. Figure 1 shows numbers and proportions of subject by age with a positive SARS-CoV-2 PCR at the different follow-up time points. ANOVA showed a significant reduction of viral replication from baseline to T3 time of follow-up (<0.001), but no statistically significant differences were observed in this trend between young and elderly. No patient reported post COVID-19 syndrome over the three months of follow-up.

Conclusion: Our results showed efficacy of MAB in preventing the severe COVID-19 in a population presenting several risk factors for disease progression and admission to intensive care unit. Furthermore, MAB seemed to be effective also in preventing post-COVID-19 syndrome. Moreover, no differences along follow-up were observed in viral clearance between the elderly and younger group. Our results need to be validated on a greater number of patients.

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Epidemiology / Social Sciences II

OC 15 CORRELATES OF TREATMENT AND DISEASE BURDEN IN PLWH IN ITALY

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Background: People living with HIV (PLWH) today face the disease and treatment burden resulting from the routines associated with taking medicines; adverse events; challenges associated with access to medicines and interference with social activities. This complex concept may definitively impact quality of life. A survey was issued to PLWH within ICONA cohort centres to investigate the correlates of disease burden and health status from the patient's point of view.
Materials and Methods: An online anonymous survey of PLWH on ART was conducted through ICONA Network sites and Patient Group websites between feb-apr, 2021. The HIV Treatment & Diseases Burden (HTDB) has been investigated with a questionnaire containing 31 items -in 7 domains- with 5-point Likert scale answers from 1 (lowest burden) to 5 (highest burden), adapted from DT Eton et al, Qual Life Res 2017, exploring health conditions and care, medications, difficulty with taking medications, medical appointments, monitoring health, exercise or physical therapy, diet, medical equipment, interpersonal challenges, medical/healthcare expenses, confusion/concern about medical information, healthcare providers, difficulty with healthcare services, role and social activity limitations, and physical/mental exhaustion. Data were analysed using descriptive statistics. Respondents were stratified in high burden (H-TDB)/low burden (L-TDB) according with overall TDB mean+1SD. Factors associated with H-TDB has been evaluated with logistic regression model
Results: 531 PLWH completed the questionnaire, 87% were male, 93% Italian nationality, median age 49 years (39-56), 61% were MSM, 88% declared current undetectable HIV-RNA and 57% CD4 cell count >500/mmc, 42% had a university degree level of education, 60% had a stable employment. 64% declared a current regimen containing 3 antiretroviral drugs, 31% only 2 antiretroviral drugs. A single tablet, containing all necessary drugs for a complete antiretroviral regimen, was reported in 74%. The mean TDB was 2.18 (SD=0.76), 99 PLWH had a H-TDB (18.6%). At multivariable regression analysis, after controlling for variables depicted in the Table 1, younger age (HR 0.69, 95%CI 0.55-0.87; p=0.002), not complete treatment satisfaction (HR 2.19, 95%CI 1.28-3.74; p=0.004), the need of a more accurate dialogue with treating physician (HR 2.29, 95%CI 1.21-4.36, p=0.01) and a lower overall Health Status (HR 1.75, 95%CI 1.33-2.32; p=0.002) were all associated with a H-TDB (Table1).
Conclusions: In this self-reported assessment, one out of five PLWH showed a high level of treatment and disease burden. Young age, not complete satisfaction with ART and need of interaction with a tailored health system should be taken into consideration as correlates of treatment and disease burden in a patient-centred approach in order to reduce the negative impact on a self-declared overall health status of the person.

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Epidemiology / Social Sciences II

OC 16 THE FOURTH "95" IS AT REACH

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Background: Measuring progress towards the HIV care cascade allows to identify processes that should be improved to achieve UNAIDS 95-95-95. We focused our attention on the fourth "95": health related quality of life (HRQoL).
Methods: We calculated the number of PLWHIV using the eCDC HIV modelling tool (version 1.3.0) that estimates the size of the undiagnosed population. Data on the diagnosed and treated populations were derived from the clinical database of the only Provincial Center authorized to treat HIV infection. Virologic response to cART was defined according to the last available HIV-RNA measure. HRQoL was assessed by EuroQol 5 Dimensions (EQ-5D) patient questionnaire using EQ-5D index score responses (scale - 0.594 to 1; worst to best health status). We defined as good an HRQoL status with an index score >0.75 that is no more than a modest discomfort in no more than 1 domain.
Results: At January 2021 patients actively followed at our Center were 2824. According to our calculations the total estimated number of PLWHIV was 3371 (figure). All diagnosed and alive subjects were actively taking cART and 98.5% of them had their last viral load < 200 copies/ml. That brought to a final proportion of people living with HIV and virally suppressed of 82.5% just below the 95-95-950 goal. The mean HRQoL was 0.87 (95%CI 0.85-0.89) with 81.2% of persons indicating an index >0.75% thus reaching the threshold for the UNAIDS fourth "95" goal. A severe discomfort was reported by no more than 3.1% of persons in the "usual activities", "pain" and "anxiety/depression" domains, while 52.3% of people indicated a perfect status (index 1). HRQoL was significantly (P=0.037) by age, but more significantly by the number of co-existing chronic diseases (P<0.0001)(figure). Some pathologies were specifically associated with a reduction of HRQoL: bone diseases (P<0.0001), neurological disorders (P<0.0001), psychiatric disorders (P=0.004), neoplastic diseases (P=0.002), cardiovascular diseases (P=0.029), Gastro-enteric diseases (P=0.018) and diabetes (P=0.049). No characteristic of HIV infection including last CD4 or CD8 counts, nadir of CD4, time since infection, type of ARV drugs significantly influenced the reported HRQoL.
Conclusions: Although a high proportion of PLWHIV reported a good HRQoL status compatible with the fourth"95" goal, our data offer hints for reflection. Reported HRQoL was completely independent from the classical tools for describing HIV infection or from the type of ARV therapy. Much more relevant was the weight of some concomitant chronic diseases especially if they could influence one or more specific domains such as "pain" for neurological disorders, bone diseases or "anxiety/depression" for psychiatric disorders, neoplastic diseases, cardiovascular diseases. The "pain" and "anxiety/depression" domains are those with the greatest negative impact on HRQoL and should be addressed carefully.

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Epidemiology / Social Sciences II

OC 17 NARRATIVES OF HIV-POSITIVE PATIENTS IN THE DIAMANTE STUDY

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HIV disease is changed through the years from life-threatening to a chronic condition. Nevertheless, the personal experience of People Living With HIV (PLWH) as well as the doctor-patient relationship are still relatively unexplored and perceived stigma remains a social burden. Narrative Medicine via patients' narrative investigates the perception of illness, focusing on coping defined as the set of conscious strategies used by the patients to accept living with this condition (coping).

The non-interventional DIAMANTE study aimed to collect clinical data and narratives on PLWH treated by D/C/F/TAF, evaluating therapy effectiveness and Patient-Reported Outcomes(PROs). From June 2018 to September 2020 the study involved 18 centers throughout Italy; both naïve or antiretroviral experienced patients were enrolled and followed up for 48 weeks. PROs were collected at enrollment(V1) and at last study visit(V4). Narratives were independently examined to evaluate level of coping by researchers through NVivo10 software based on content analysis.

A total of 243/246 enrolled PLWH have been evaluated: 154(63%) completed the narrative at V1, 125(60%) at V4, and 114(47%) both at V1 and V4. Four narratives were excluded from the analysis both at V1 and V4 due to their shortness and quality of information. Findings show that previous therapy experience do not impact on coping, but patients who still do not accept LWH at V4 reached a lower score(18,9) of HIV Treatment Satisfaction Questionnaire(HIVTSQ) at V4, when compared with those who coped(score 25,7 HIVTSQ) (Fig1A/B). From narratives, which provides deeper insights, the majority of patients evaluated therapy as effective and easy to take, and only 13% of patients who perceived therapy as a doom (always recalling their condition) coped with LWH. Patients did not report any activity limitation from being HIV infected, even though 7% of those who isolated themselves had a lower coping. Stigma perception remains a negative factor at V4 for coping(Fig1D). On the other hand, extroversion[1] represents one of the main drivers in accepting LWH as highlighted through multiple behaviors: the ability to share "the being HIV-positive", the building of positive relationships with family and others, the hope to help others with HIV(Fig1D). Throughout the pathway of care, the emotions(Fig. 1C) evolved from fear and pain after the HIV confirmation test(79%), to relief after first visit(68%), to serenity after V1(38%), confirming that a higher level of information on HIV has a pivotal role in accepting LWH, as well as the overall care pathway.

The extroversion and the care felt as personal growth are key factors in fostering coping, while the fear of stigma and isolation still represent major obstacles in the acceptance of HIV. Educational campaigns focused on the insights that came out from the narratives could help PLWH in improving their quality of life.

[1]Carver et al.Personality and Coping.Annu Rev Psychol.2010.

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Epidemiology / Social Sciences II

OC 18 A TELEPHONE-BASED MULTIDIMENSIONAL INTERVIEW IN ELDERLY PEOPLE LIVING WITH HIV FROM THE GEPPO COHORT

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Background: Elderly people living with HIV (EPLW) show a significant prevalence of multimorbidity, polypharmacy and frailty that increase the risk of disability. Telehealth has been suggested as a new tool to monitor PLWH in the COVID era, but its effectiveness in EPLW is unknown. The aim of this study was two-fold: to explore feasibility of a telephone interview and its capability to collect relevant geriatric outcomes.
Material and Methods: Participants enrolled in the GEPPO cohort in Turin, Brescia and Modena (Italy) were invited to join in a telephone structured interview from October 2020 to March 2021. After acceptance, patients were asked to answer to 63 questions including demographic, clinical, treatment, quality of life (QoL), resilience, frailty and intrinsic capacity (IC) variables and scores. HIV RNA, CD4 cell count and antiretroviral treatment (ART) information in the last 6 months were extracted from the cohort database. QoL was assessed by EQ-5D-5L, resilience by shorten version of CD-RISC -25, frailty by SUNFRAIL questionnaire and IC by 19-item questionnaire developed according to WHO's ICOPE guidelines.
Results: Out of 303 participants, 214 (70.6%) answered and completed the interview, 42 did not answer, 38 did not complete the interview and 9 died. 9 (4.1%) pts resulted to have COVID-19 coinfection. Demographical and clinical characteristics are reported in Table 1.
Average participants' scores were: QoL= 85% (± 14.3), IC=71% (±12.7), resilience 61% (±20.8) and SUNFRAIL 27% (±16.7) and showed average correlations among them (with r values between 0.30 and 0.50) and with working/disability status. Higher QoL and resilience were associated with hours per day spent outside (p values <0.001). Participants with low physical activity or falls had lower score in all explored domains. Anxiety or depression was associated with lower QoL, resilience and IC but not frailty. HIV RNA undetectability was borderline associated with QoL (85.1% vs. 69.2%, p=0.06).
Discussion: A structured telephone call is feasible in EPLW and it was useful for collecting relevant information for geriatric assessment and it may be implemented when face-to-face visits are not needed or discouraged. The management of ART during COVID-19 pandemic needs to be further studied for long term outcomes.
Telemedicine offers the opportunity to collect patients' reported outcomes including intrinsic capacity, resilience and QoL relevant for a multidimensional description of aging in EPWH.

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Antiretroviral Therapy I

OC 19 TRAJECTORIES OF CD4/CD8 RATIO AT 96 WEEKS AFTER SWITCH TO DOLUTEGRAVIR-BASED DUAL THERAPIES IN A MULTICENTRE COHORT OF ART-EXPERIENCED PATIENTS

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Background: Previous cohort studies reported a CD8+T-cell increase and a reduction of CD4/CD8 ratio in people living with HIV (PLWH) treated with dual therapies. Little data are available for these same immunologic endpoints in modern 2-drug regimens (2DR) containing new drugs such as dolutegravir (DTG). Aim of the present study is to evaluate CD4/CD8 dynamics in patients in DTG based 2DR and compare them with DTG containing triple therapies (3DR).

Methods: Prospective observational cohort study in the context of SCOLTA project. All patients with HIV-RNA <50 copies/mL who were switched to a DTG-2DR were included and subsequently compared with patients in treatment with tenofovir/emtricitabine (TDF/FTC) + DTG, tenofovir alafenamide (TAF)/FTC + DTG, and with abacavir/lamivudine (ABC/3TD)/DTG. At least 1-year follow up was requested for study entry. Values were expressed as means± standard deviations.

Results: 533 PLWH were enrolled, 225 in DTG-2DR (120 in DTG+3TC, 38 in DTG+protease inhibitors, PI, and 67 in DTG +rilpivirine, RPV); and 308 in 3DR (49 in TDF/FTC+DTG, 27 in TAF/FTC+DTG and 232 in ABC/3TC/DTG). Patients had similar demographic characteristics and baseline laboratory values in different treatment groups, except for HDL cholesterol in TDF/FTC+DTG group (mean 43± standard deviation 14 mg/dl) and TAF/FTC+DTG group (45±19 mg/dl, vs. 51±15 in DTG-2DR and 51±18 in ABC/3TC/DTG) and for cumulative years in antiretroviral treatment in patients in ABC/3TC/DTG [median 9.2 (interquartile range 4.4-16.5) years vs. 11.2 (3.4-18.1) in TDF/FTC+DTG, 11.3 (5.7-17.7) and 11.1 (6.4-19.1) in DTG-2DR (p=0.01)].

Mean CD4/CD8 ratio at baseline was 1.04±0.64 in DTG-2DR, 0.74±0.47 in TDF/FTC+DTG, 0.88±0.64 in TAF/FTC+DTG and 0.86±0.50 in ABC/3TC/DTG.

At one year of follow up, CD4/CD8 ratio significantly increased in PLWH treated with 3TC/ABC/DTG (+0.08±0.25), TDF/FTC+DTG (+0.1±0.19), and in DTG-2DR with DTG+3TC (+0.08±0.26). Comparison between groups revealed that CD4/CD8 ratio change from baseline was higher in subjects on DTG+3TC as compared to DTG+PI and DTG+ RPV. The CD4/CD8 increase was driven by a significant increase of CD4+T-cells, while CD8+T-cells remained stable, or slightly increased during the follow up, but did not achieve significant reductions in any treatment groups (Table1).

At two years, the CD4/CD8 increase was confirmed significant only in 3DR with DTG+TDF/FTC (0.16±0.28) and 3TC/ABC/DTG (0.1±0.3), while, despite numbers were low, no significant change was observed in any of the DTG-2DR considered (Table 1).

Conclusions: PLWH switched to 2DR in SCOLTA experienced CD4/CD8 increase at one year follow-up only in 3TC+DTG group, while no significant change was observed in DTG+RPV and DTG+PI. Controlled studies with longer follow up will clarify the long-term immunological and clinical impact of DTG-2D.

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Antiretroviral Therapy I

OC 20 INCREASING TREND OF PRETREATMENT INTEGRASE INHIBITORS RESISTANCE IN A COHORT OF ANTIRETROVIRAL THERAPY-NAÏVE PEOPLE LIVING WITH HIV

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Background: Aim of the study was to evaluate prevalence trend of pretreatment integrase strand transfer inhibitor (InSTI) drug resistance and to assess factors associated with pretreatment InSTI resistance among antiretroviral therapy (ART) naïve people living with HIV-1 (PLWH) over the past decade.

Methods: Time-trend study conducted from 2009-2019 on PLWH followed at IRCCS San Raffaele Scientific Institute with genotypic resistance tests (GRT) performed before ART starting. Genotype sequences were analyzed using the Stanford University HIV Drug Resistance Database. Drug resistance (DR) was defined as at least low-level resistance to ≥1 drug of the InSTI class.

All the characteristics were measured at or within 180 days before GRT. Cochrane-Armitage test was used to assess linear trend in pretreatment HIV-1 InSTI DR prevalence over time. A multivariable logistic regression was fitted to determine factors associated with at least low-level INSTI resistance.

Results: Overall, 1223 ART-naïve PLWH were evaluated: 91% were males, median age was 37 (interquartile range, 30 -45) years and HIV-1 subtype (Table 1). At least low-level and at least intermediate InSTI DR were reported in 18 (1.5%) and 5 (0.4%), respectively.

Among PLWH with at least low-level InSTI DR, HIV-1 subtype non-B was found in 8 (44.4%) (p=0.018); G163K, an accessory INSTI mutation previously described as common in subtype non-B viruses from ART-naive patients, was detected in 7/8 (87.5%). Overall, 1/10 (10.0%) of people with HIV-1 subtype B and 1/8 (12.5%) of people with HIV-1 subtype non-B with at least low-level InSTI DR had a strain resistant to more than 1 drug class.

Prevalence of at least low-level InSTI DR was anecdotal between 2009-2013 and then gradually raised from 1.3% in 2014 to 3.9% in 2019 (p-for-trend<0.001); prevalence of at least intermediate InSTI DR increased from 0% in 2009 to 2% in 2019 (p-for-trend=0.188, Figure 1). A significant increase over time in at least low-level DR prevalence has emerged to raltegravir and elvitegravir, not to dolutegravir and bictegravir (p-for-trend<0.001, Figure 2).

At multivariable analysis, HIV-1 subtype non-B vs. B was associated with InSTI resistance [adjusted odds ratio 3.45 (95% CI=1.36-8.85), p=0.011], after adjusting for age and CD4 at baseline.

Conclusions: Prevalence of pretreatment HIV-1 InSTI resistance is rare but has increased in the last years, mainly related to first-generation InSTIs. The only factor associated with InSTI resistance was HIV-1 subtype non-B.

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Antiretroviral Therapy I

OC 21 ROLE OF GENOTYPIC TESTING RESULTS FOR PREDICTING VIROLOGICAL FAILURE IN PERSONS LIVING WITH HIV WITH HIV-RNA ≤50 COPIES/ML WHO REQUIRE AN ART SWITCH

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Background: We sought to investigate whether the genotypic susceptibility score is still relevant for predicting the risk of virological failure (VF) after a therapy switch (TSw) in persons living with HIV (PLWH) with viral load (VL)≤50 cps/mL.
Materials and methods: We designed a matched case-control study nested within EuResist DB of PLWH who had a VL≤50 for >1 month, underwent a TSw and had ≥2 GRTs before TSw. PLWH who, after TSw, ever experienced two consecutive VL>50 cps/mL, or one VL>50 cps/mL followed by TSw, or one VL>1000 cps/mL were cases. Controls were matched by class of the anchor drug in TSw and duration of VL suppression. Conditional logistic regression analysis was used to estimate the odds ratio of VF associated with suboptimal activity of TSw (established by means of the current GSS or the minimum GSS) after further controlling for number of previous VF and mode of HIV transmission. Current GSS of the TSw was obtained using only the results of the most recent GRT prior to the date of TSw. Minimum GSS was calculated as the sum of the minimum predictions ever recorded for each drug in all single GRTs among those available prior to the date of TSw. Suboptimal activity of the TSw was defined as having a GSS of 0-1.75 vs. ≥2. We hypothesised that VL at the time of GRT and length of time from the date of GRT (grouped using the medians) were effect measure modifiers (EMM) for the associations of interest.
Results: We included 205 cases and 565 matched controls. Overall 31% females, 23% MSM, 76% Caucasian and 73% with a B-subtype. Median age (IQR) was 49 (41-54), CD4 count 560 (369-788) cells/mm3, duration of suppression 45 (19-87) months (Table 1A). In the switch regimen INSTI was the anchor drug class in 11.3% of cases, followed by NNRTI (8.2%) PI/r (4.3%) and PI/r+INSTI (1.8%). Participants with suboptimal activity of the TSw were more likely to be PWID (27% vs. 18%, p=0.002), older (52 vs. 48 years, p=0.03), more likely to have a CD4 count ≤200 cells/mm3 at time of TSw (19% vs. 8%, p=0.02), on average, had started ART in less recent years (1998 vs. 2007, p<0.001) and showed a larger number of previous VF (5 vs. 2, p<0.001, Table 1A). The association between current GSS and risk of VF was weak (HR=1.90 95% CI:1.03-3.51) and largely attenuated after controlling for duration of suppression, anchor drug class in TSw, mode of HIV transmission and number of previous VF (HR=1.59, 95% CI:0.84-3.02, Table 1B). The association with minimum GSS appeared to be even less strong. We also found little evidence for EMM by VL at the time of GRT and length of time from the date of GRT (p>0.10).
Conclusions: Our data suggest that, in PLWH switching to modern regimens with a VL≤50 cps/mL, there is little benefit in using current or the minimum GSS to predict the subsequent risk of VF. Further analyses to investigate the predictive role of the more commonly used cumulative GSS, stratifying by concomitant VL and exact timing of GRTs, are warranted.

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Antiretroviral Therapy I

OC 22 EVALUATION OF VIROLOGICAL RESPONSE AND RESISTANCE PROFILE IN VIROLOGICALLY SUPPRESSED HIV-1 INFECTED INDIVIDUALS SWITCHING TO A BICTEGRAVIR BASED REGIMEN IN A REAL-LIFE SETTING

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Background: We evaluated the virological response and resistance profile in virologically suppressed HIV-1 infected individuals who switched to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in a real-life setting.
Material and methods: Survival analysis was used to assess the probability of losing virological control as composite outcome considering individuals who experienced virological rebound (VR, two consecutive viremia >50 cps/mL or one viremia >200 cps/mL) or a viral blip (one single viremia in the range 50-200 cps/mL) after B/F/TAF switch. Cumulative major resistance mutations (MRMs) and cumulative genotypic susceptibility score (cGSS) before switch and resistance after virological rebound were evaluated according to Stanford HIVdb version 9.0.
Results: Overall, 284 individuals exposed to cART since a median (IQR) time of 8 (4-13) years and virologically suppressed for a median (IQR) time of 7 (3-9) years were analyzed. Of them, 82.7% were male, with a median (IQR) age of 50 (42-56) years; 79.2% were infected with HIV-1 B subtype; 20.8% switched to B/F/TAF after first-line treatment; 43.3% experienced at least one failure before switch; 9.2% had a previous experience of failure to INIs. At the moment of switch, 52.8% of individuals had viremia target not-detected and a median (IQR) CD4 count of 662 (505-867) cells/mm3. Eighty-three (29.2%) individuals showed at least 1 cumulative MRM before switch, mainly related to RTIs; 3/146 individuals (2.1%) harbored INI MRMs (N155H, Y143C/H/R). cGSS revealed that 91.9% of individuals had at least two active drugs among B/F/TAF (cGSS≥2); 82.4% of individuals showed a completely active regimen (cGSS=3).
A high percentage (79.2%) of individuals switched to B/F/TAF to increase the genetic barrier of previous INI- or NNRTI-based regimens; other known reasons of switch were: decreasing number of pills and/or drugs (12.7%); increasing number of drugs (4.6%); toxicity (1.8%); clinicians' decision (1.1%).
By 60 weeks after switch, the overall probability of losing virological control was 9.7%; only 8 events of VR (median [IQR] viremia at VR: 274 [204-474] cps/mL) and 16 events of blips were recorded. No significant associations between virological outcomes and genotypic susceptibility to B/F/TAF (P=0.509; Figure 1 panel A) and previous INI failures (P=0.643; Figure 1 panel B) were found.
Almost all individuals (6/8) who experienced VR were previously exposed to first generation INIs, and 2/8 experienced previous virological failure to INIs. Resistance test was performed after VR in 1 individual, no further resistance was accumulated. After VR, viremia was shortly resuppressed in most individuals without treatment change (Table 1).
Conclusions: B/F/TAF treatment switch in virologically suppressed individuals ensures very high rate of virological control regardless previous resistance or failures in clinical settings. Further analyses with longer follow-up are needed to confirm these findings.

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Antiretroviral Therapy I

OC 23 EVALUATION OF TOTAL HIV-DNA AND RESIDUAL VIREMIA IN HIV-1 INFECTED INDIVIDUALS ENROLLED ON THE BE-ONE STUDY WHO CONTINUE A TWO-DRUG REGIMEN WITH DOLUTEGRAVIR PLUS ONE REVERSE TRANSCRIPTASE INHIBITOR OR SWITCH TO ELVITEGRAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR ALAFENAMIDE: RESULTS OVER 96 WEEKS

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Background: To investigate HIV-DNA and residual viremia (RV) levels through 96 weeks (W96) in virologically suppressed HIV-1 infected individuals enrolled in the Be-OnE Study (NCT03493568), randomized to continue a two-drug regimen (2DR) with dolutegravir (DTG) plus one RTI or to switch to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF).

Materials and Methods: Total HIV-DNA (cps/106CD4+T-cells) and plasma HIV-RNA were measured with standardized in-house droplet digital PCR assays. Spearman correlation coefficients (rs) were calculated to assess linear relationship between HIV-DNA, plasma HIV-RNA levels and several immunological parameters (D-Dimer, C-reactive protein [CRP], % CD8+CD38+HLA-DR+, %CD4+CD38+HLA-DR+, CD4+T-cells, CD8+T-cells, CD4/CD8) at baseline (BL), W48 and at W96. Differences in HIV-DNA and RV levels were evaluated by using Wilcoxon signed-rank test among individuals within the same arm or the Mann-Whitney test between the 2 arms.

Results: HIV-DNA and RV measurements at BL and W48 were available for 40/50 individuals, while at W96 for 37/50 individuals (Figure). Overall, median (IQR) HIV-DNA levels were 2247 (767;4268), 1587 (556;3543) and 1076 (512;2345) cps/106CD4+T-cells at BL, W48 and at W96, respectively, while median (IQR) RV levels were 2.9 (1.1;5.3), 4.4 (1.2;9.1) and 2.6 (1.6;3.9) cps/mL, without significant differences between arms (Table).

No significant changes in HIV-DNA levels were found from BL to W48 and from BL to W96 between the two arms. On the other hand, at W48, a modest decrease in HIV-DNA from BL was found: -137 (-983;+133) cps/106CD4+T-cells (p=0.334) in the E/C/F/TAF arm and -226 (-1189;+890) cps/106CD4+T-cells (p=0.465) in DTG+1RTI arm. A further decrease in HIV-DNA levels was found from W48 to W96 in the E/C/F/TAF arm: -285 (-2257;-45) cps/106CD4+T-cells (p=0.010) and -549 (-2269;+307) cps/106CD4+T-cells (p=0.182) in the DTG+1RTI arm.

A significant change in RV was found from BL to W96 in the E/C/F/TAF arm (-1.3 [3.2; -0.1] cps/mL, p=0.007), while RV levels were stable in DTG+1RTI arm. However, no significant changes were found from BL to W48 (p=0.282) and from BL to W96 between the two arms (p=0.371).

Overall, a positive correlation was found between BL HIV-DNA and W96 HIV-DNA (rs: 0.662, p<0.001); this finding was also confirmed within each study arm.

A significant correlation was found between BL HIV-DNA and BL HIV-RNA levels in the E/C/F/TAF arm (rs=0.473, p=0.031), but not in the DTG+1RTI arm (rs=0.049, p=0.841). In general, no significant correlations were found between HIV-DNA, HIV-RNA and the immunological parameters either at BL or W96.

Conclusions: In virologically suppressed individuals, no significant differences were found in the changes of HIV-DNA and plasma HIV-RNA levels from BL to W96 between those treated with a 2DR with DTG+1RTI and individuals who switched to E/C/F/TAF. In spite of that, a small reduction in the residual viremia was found in the E/C/F/TAF arm.

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Epidemiology / Social Sciences III

OC 24 FROM U = U TO BREASTFEEDING OF WOMEN WITH VIROSUPPRESSED HIV

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Background: Vertical transmission of HIV infection can occur in pregnancy, during childbirth or through breastfeeding. In 2017, the EACS considers the possibility of breastfeeding by recommending a precise counseling plan aimed at obtaining therapeutic adherence and a close follow-up for clinical and virological monitoring of both mother and child. Across the ocean, the DHHS guidelines dissociate themselves from the EACS recommendations clearly advising against breastfeeding in this population even in women with a strong desire to breastfeed since the risk of vertical transmission had been highlighted in a percentage lower than 1%.
Aim: Describe the absence of vertical contagion in a cohort of 13 women who, correctly informed about the potential risks of contagion, decided to breastfeed.
Methods: A retrospective study was conducted in a cohort of HIV-infected pregnant women who, despite the information received, decided to breastfeed. The observation was conducted in the period between March 2017 and June 2021. The characteristics of the 13 women are described in table 1. The women delivered, in accordance with the latest guidelines, vaginally since this procedure did not represent an additional risk of infection for the unborn child. Both women with a previous diagnosis and those in whom the diagnosis was made during pregnancy were treated with antiretroviral therapy which, in 100% of cases, resulted in an undetectable viral load (HIV-RNA) and a CD4 + T-Helper lymphocytes> 400 cells / mmc. Adherence was 100% in all patients. Prophylaxis therapy was initiated in all infants at birth, in accordance with treatment guidelines. Breastfeeding time was, on average, 5 months.
Results: All infants were tested for HIV-RNA at birth, 1 and 3 months after birth, and subsequently 1, 3 and 6 months after breastfeeding was stopped. For the last born (April 2021), the control for HIV-RNA is only available in the 3rd month, or after 6 weeks from the suspension of breastfeeding. No contagion was detected.
Conclusions: the data suggest a solicitation to the discussion of the scientific evidence that starting from "Undetectable Equals Untransmittable" (U = U) can open a scientific and cultural review of breastfeeding. From a strictly ethical point of view, the autonomy of women, a fundamental value, must be compared with the principle of precaution and prudence towards the health of the child, balancing the positive effects (in terms of health and well-being) of the choice of breastfeeding. breast, compared to the "predictability" of the negative effects of viral transmission. In this end,is it useful to emphasize the importance of Law 219/2017 (Informed consent and Advance treatment provisions) which highlights the autonomy of the patient who is confronted with the autonomy, competence and responsibility of the doctor. The role of the healthcare professional is to accompany and support the woman's conscious decision, respecting her autonomy.

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Epidemiology / Social Sciences III

OC 25 PREFERENCES IN LONG ACTING AGENTS FOR HIV TREATMENT IN WOMEN LIVING WITH HIV: A CROSS-SECTIONAL EVALUATION AMONG 6 ITALIAN CLINICAL CENTERS

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Background: Long-acting injectable (LAI) antiretroviral therapy (ART) may offer persons living with HIV (PLWH) a challenging alternative to pill-based treatment regimens, but minimal LAI-focused research has occurred among women living with HIV (WLWH) and data on LAI acceptability is lacking in female population. Objective of the study is to identify end-user needs, desires and contexts regarding LAI in WLWH.

Matherials and methods: A cross-sectional structured self-reported questionnaire exploring unmet needs on current ART, desirability and preferences for LAI, was administed to WLWH referring to 6 reference centers in Italy during 2-months period. Preferences for LAI were analyzed grouping WLWH in 2 categories: "dislike injection under any circumstances" (group 1); "prefer injections in any circustances" (group 2). Uni-and multivariate logistic regression analyses were run to evaluate predictors of preferring LAI.

Results: 266 WLWH filled the questionnaire (median age: 52 y [IQR 45-58], 85% were Italian; 75% had level of education < high school; 77% were HIV-infected for >10y; and 72% on ART for >10y; 55% had at least one son; 66% were on menopause. 86% were taking ART with < 2 pills/day, with 9 (8-10) as median VAS of current ART satisfaction. 52% were taking >3 pills/day other than ART. Women who prefer to use LAI were more frequently on reproductive age, had children, had higher level of education, had been living with HIV for a longer time and did not have regular lifestyle habits compared with women who did not prefer LAI (Table 1). Worrying for safety of the drug (61%), difficulties in drug refills (31%) and both (11%) were reported as barriers to LAI; facilitators for LAI were higher freedom (61%), more chances for travelling (35%), confidentiality (22%). 15% of WLWH expected no significant advantage with LAI. At multivariable logistic regression analysis, >2 pills in the ART regimen (AOR 2.44 vs 1 pill, 95%CI 1.12-5.35, p=0.02), were correlated with preference for LAI, menopause (AOR 0.29, 95%CI 0.14-0.64, p=0.002) was related to prefer daily oral pills. ART interference with both social life and job (AOR 2.59 95%CI 0.54-12.41, p=0.23) was related to prefer LAI even if not significantly, possibily due to the low number (n=23) .

Conclusions: In this cross sectional evaluation of potentially users of LAI, we tried to identify a comprehensive profile of WLWH who may prefer to use LAI in the near future. Behavioral and social science research represents an indispensable tool to identify the exact tailoring of long acting regimens in WLWH, which must lead any pathway towards the positioning of long-acting regimens, in order to ensure their correct use and retention in care in the long term.

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Epidemiology / Social Sciences III

OC 26 HCV INFECTION AMONG WOMEN PRISONERS: A SNAPSHOT OF THE ITALIAN ROSE NETWORK

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Women in prison are a minority group with specific characteristics linked to both socio-economic factors and health needs. Hepatitis C virus (HCV) infection, is present at least twice as much in female prisoners as in the male prison population and up to 14 times greater than in the general population.
Therapy with direct-acting antivirals (DAAs) has revolutionized the treatment of HCV much more in prison settings, where by rapid test and treat, the HCV infection eradication becomes an achievable goal.
The italian society of medicine and penitentiary health (SIMSPe) has created a dynamic network that studies the state of health and gender-specific needs for this target population in Italy (ROSE: rete donne simspe).
An 18-month observational study was conducted on 9 prisons to learn about the main characteristics of the HCV cascade of care in women inmates. The only criteria for recruitment were the age of over 18 and acceptance by written informed consent. Viraemic women for HCV were selected; the staging of hepatic fibrosis was assessed both by fibroscan and with the APRI measurement. The therapeutic regimens and the definition of sustained virological response (SVR) and of and evaluation of the efficacy of the therapy followed the standard guidelines. The drop-out was defined as an unplanned interruption or a treatment not started.
From June 2018 of the 486 women enrolled (19% of total women prisoners), 46 were found to be actively infected with HCV and all agreed to initiate treatment. The average age is 45, 44 from Italy and 2 from Eastern European countries. 44 women had a history of intravenous drug dependence and only 2 had had previous treatments for chronic HCV infection. HIV co-infection was present in 3 women (all patients on HAART therapy with suppressed HIV viremia). HCV genotypes observed: 30 patients with genotype 3, 15 patients with genotype 1A and 8 patients with genotype 1B, 1 patient with genotype 2 and 3 patients with genotype 4. Stage of liver fibrosis was evaluated with APRI value (11 patients) or fibroscan (35 patients). The majority of patients (41; 89%) had low fibrosis (APRI score<1.5; METAVIR F0-F1 according to fibroscan). All the 11 women who had F4 fibrosis were greater than 50 years. Only 4 patients did not complete the treatment: 1 for home transfer, 3 for transfer to another institution. Of the 42 women who completed therapy, all achieved SVR 12 weeks after the end of therapy.
Therapy with DAAs is effective and menopause represents the turning point in the evolution of liver fibrosis in chronic HCV infection. Prisoned women often have a history of drug addiction and mental distress, violence and social frailty, all factors that predispose to a greater risk of HCV infection, lack of access to screening and difficulty in retention in care. Gender-specific strategies are needed that reshape the entire treatment process and only by knowing this population in depth can effective actions be implemented.

Clinical HIV & Clinical Covid II

OC 27 IMPACT OF HOME TREATMENT WITH GLUCOCORTICOIDS ON RISK OF IN-HOSPITAL DEATH IN PATIENTS WITH COVID-19 PNEUMONIA

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Background: The Recovery RCT showed that, in patients with COVID-19 disease not requiring oxygen, the use of dexamethasone was associated with higher risk of death. The aim of this analysis was to evaluate whether, in patients with COVID-19 pneumonia admitted to hospital, a history of home prescription (HP) of oral glucocorticoids (OG) was associated with higher risk of in-hospital death.
Materials and Methods: A cohort study of patients with COVID-19 pneumonia, admitted to Modena Hospital over February-December 2020. History of HP was collected at entry in the hospital from A&E records (baseline) and participants were classified according to: no treatment, use of OG and use of other drugs (hydroxychloroquine, heparin, macrolides, beta-lactams). Participants' characteristics at baseline were compared by HP groups. Kaplan-Meier curves were used to estimate day 28 mortality rate by HP groups. A Cox regression analysis was conducted to control for potential key confoundersidentified as the following: BMI, Charlson comorbidity Index (CCI), ethnicity, symptoms and calendar month of enrolment, all fitted as time-fixed covariates measured at baseline.
Results: 1,074 participants were included, 72% males, median age 71 years. Before admission, 812 (76%) were prescribed no treatment, 27 (3%) OG and 235 (22%) other drugs. Several differences by HP groups at baseline were observed: cerebro-vascular disease was more frequent in the OG group (41% vs. 36% in the untreated and 32% in other, p=0.0004). However, compared to other treatment groups, OG had higher neutrophil percentage (79.8% vs. 75.8% in untreated and 78.7% in other, p=0.03) and lower proportion of those with eGFR>60 mL/min (60% vs. 70.4% and 79%, p=0.005) . Also OG treated participants less frequently reported fever than the other drugs group (73% vs. 81%, p=0.05) but more frequently reported cough than the untreated (48% vs. 38%, p=0.02). Furthermore, PaO2/FiO2 tended to be lower in the OG compared to the other groups (223 vs. 272 vs. 264 mmHg; p= 0.13). Overall 74% of those treated with OG were treated in hospital with dexamethasone vs. 54% of the untreated and 64% of those receiving other treatment (p=0.004). There was no difference in mortality by HP group (day 28 KM estimates: 15.9% 95% CI:13.4-18.4 in the untreated, 14.8% 95% CI:1.4-28.2 in OG, 13.2% 95% CI:8.9-17.5 in other treatment; p=0.54, Figure 1). Results were confirmed after controlling for BMI, CCI, ethnicity, symptoms and calendar month of enrolment (Table 1).
Conclusions: In our cohort of patients who developed symptoms leading to hospital admission for Covid-19 there was no evidence that the risk of death differed according to type of HP received. Specifically, under the assumption of a correctly specified model and no unmeasured confounding, our data are compatible with the null hypothesis of no difference in risk of in-hospital death between patients who received OG vs. those who were left untreated.

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Clinical HIV & Clinical Covid II

OC 28 TREATMENT OF COVID-19 SEVERE PNEUMONIA: DO ALL PATIENTS BENEFIT FROM ADDING TOCILIZUMAB TO GLUCOCORTICOIDS? AN OPEN LABEL NON-RANDOMIZED STUDY

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Background: The RECOVERY trial showed an effect of adding tocilizumab to standard of care to reduce day 28-mortality in patients with COVID-19. Most guidelines now suggest glucocorticoids plus tocilizumab as standard of care in the critically ill. However, which patients are likley to benefit the most from a combination of tocilizumab and dexamethasone is still a matter of debate. A post-hoc analysis of the CORIMUNO-TOCI-1 trial showed lower benefit of tocilizumab if treated participants' CRP levels were lower than 15.0 mg/dL.
Methods: This was an observational study of patients with severe COVID-19 pneumonia admitted to University hospital of Modena. Primary endpoint was day-28 mortality. To estimate the effect of intensification on the risk of 28-day death we fitted a marginal structural Cox model by mean of inverse probability weights with the aim of emulating the RECOVERY trial. Intervention was fitted as a time-dependent variable after controlling for both time-fixed and time-varying potential confounding factors. We also investigated the hypothesis that CRP and PaO2/FiO2 were effect measure modifiers (EMM) for the association between intensification with tocilizumab and risk of death. Q1, median, Q3 of the distribution of current values were used to create the strata.
Results: Over the study period, a total of 992 patients with severe COVID-19 pneumonia were admitted to our hospital after June, 2020. Main characteristics of the study population at hospital admission are shown in Table1. All were treated with glucocorticoids and 395 (40%) received intensification with tocilizumab over follow-up. Standard dosage of glucocorticoids was used in 975 participants (98%), 584 (98%) in the no intensification group vs. 391 (99%) in the tocilizumab intensification group (p=0.17). The remaining 91 participants (9%) were treated with high dose methylprednisolone 2 mg/kg/day. The estimated effect of tocilizumab was similar to that estimated in RECOVERY (aHR=0.58; CI: 0.36-0.93; p=0.024, Table 2). Results were similar after removing participants treated with high dose glucocorticoids (aHR= 0.59; p=0.032) and those aged 75+ or with pre-existing solid cancer (aHR=0.39; p=0.064). Overall, although the benefit of intensification with tocilizumab appeared to be greater with higher values of CRP and lower values of PaO2/FiO2 we found no evidence for EEM (p=0.55 and p=0.43 respectively). When we included only participants who started tocilizumab >24h after starting glucocorticoids, the data were more compatible with the hypothesis of EMM by CRP and with a significant benefit received by those starting with >15.0 mg/dL (aHR=0.36, 95% CI:0.14-0.90, Figure 1).
Conclusions: Our data confirms that response to glucocorticoids+ tocilizumab might vary according to patients' level of inflammation. Further studies are needed to better determine whether CRP is the right marker for guiding treatment decisions and above which cut-off we could expect the largest benefit.

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Clinical HIV & Clinical Covid II

OC 29 SARS-COV-2 VIRAL DECAY IN COVID-19 PATIENTS TREATED WITH MONOCLONAL ANTIBODIES IN RELATIONSHIP TO VIRAL VARIANT

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Background: Coronavirus disease (COVID-19) continues to spread worldwide facilitating the diffusion of viral variants. Neutralizing monoclonal antibodies (MAb) have been introduced as part of the treatment for such infection. MAb target the SARS-CoV-2 spike (S) protein.
The aim of the study was to analyse the viral decay in COVID-19 patients after Mab treatment.
Material and methods: Patients referred to Policlinico Tor Vergata with a positive molecular test for SARS-CoV-2 RNA on a nasopharyngeal swab (NPhS) who met the Italian Medicines Agency (AIFA) criteria for Mab therapy, treated with Banlanivimab alone or associated with Etesevimab were enrolled in the study, between April to June 2021. Spike gene was sequenced and SARS-CoV-2 variants were assessed. Clinical and laboratory data were recorded at baseline and during the follow-up, until molecular tests on NPhS were negative. Molecular test on NPhS for SARS-CoV-2 RNA detection were performed using a diagnostic RT-PCR system and an in-house digital-droplet(dd)PCR method targeting the RNA-dependent RNA polymerase (RdRP) gene.
Results: We included 113 patients, 72 males (63.7%). Median age was 63. 110 patients were treated with Banlanivimab and Etesevimab, and 3 received Banlanivimab only.
SARS-CoV-2 infection was mild, lasting less than 10 days (median 7 days).
92 patients (81.4%) were not vaccinated, while 4, 9, 2 and 1 had been vaccinated with ChAdOx1-S (3 double doses, 1 single dose), mRNA BNT162b2, Ad26.COV2.S and COVID-19 mRNA-1273, respectively.
31 patients (27.4%) underwent radiological thoracic examination and only 1 (0,9%) patient did not show any parenchymal abnormality, while 12 (38,7%), 5 (16,1%), 4 (12,9%), 3 (9,7%) and 6 (19,4%) patients showed a parenchymal involvement of 5%, 10%, 20%, 30% and >35%, respectively.
The outcome was favourable for 96 patients (85%), and unfavourable (hospitalization/death) for 10 (8.8%). 7 patients (6.2%) were lost to follow up.
Concerning SARS-CoV-2 variant of concern (VOC), we were able to obtain the sequence of SARS-CoV-2 Spike gene in 70 patients; 45 (64.3%) had a VOC alfa, 18 (25.7%) gamma, 3 (4.3%) beta, 1 (1,4%) delta, and 2 (2,8%) wild type.
NPhSs of 90 patients obtained at Day0 and Day7 (seven days after treatment) were analysed. The median difference between Cycle thresholds (Ct) (Day7-Day0) was 9 cycles (RdRP gene) according to the RT-PCR, while it was -2.8 log (copies/ml) according to the ddPCR. A correlation between the two methods was found (Spearman's rho -0,6, p=0.025).
No difference in the viral load decay was found after stratifying patients according to the VOC (alpha vs non-alpha) and the clinical outcome.
Conclusions: Our analysis suggests that there is no statistically significant association between viral decay after Mab administration and SARS-CoV-2 VOC. Further studies with wider cohorts are needed to assess the effectiveness of Mab treatment on the different viral variant of SARS-CoV-2.

Clinical HIV & Clinical Covid II

OC 30 EFFECTIVENESS OF COVID-19 VACCINE IN HEALTH CARE WORKERS, MILAN, ITALY

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Background: Randomized controlled trials showed efficacy of vaccines against coronavirus disease 19 (COVID-19). There is the need to quantify vaccine effectiveness (VE) in real-word contexts, including people at high risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), such as health care workers (HCWs). Moreover, while RCT showed efficacy against laboratory-confirmed COVID-19 (i.e., symptomatic infections), field studies could contribute to verify VE against asymptomatic SARS-CoV-2infections. Our objective was to evaluate VE against symptomatic and asymptomatic SARS-CoV-2 infections among hospital HCWs.

Material and methods: We performed a cohort study among HCWs of a large University hospital in Milan, Lombardy, Italy by merging routinely collected data on demographics, COVID-19 vaccination, and polymerase chain-reaction (PCR) tests performed on nasopharyngeal swabs. Follow-up started on December 27, 2020 (beginning of vaccination campaign). We included HCWs never PCR-positive before the start date and with at least a PCR test afterwards. Vaccination was treated as a time-dependent variable by calculating person-years (PY) at risk before and after vaccine doses and in selected periods (0-13 days after first dose, 14+ days after second dose, and 7+ days after second dose). The last period was further divided in five periods, each of four weeks. Subjects contributed PY until first positive PCR test (infected cases) or last test (for never positive HCWs), to avoid immortal time bias. We calculated infection rates (cases per 1000 PY), rate ratios (RR, with a Poisson regression model adjusted for gender, age, occupation and 30-day periods), and adjusted vaccine effectiveness (VE = (1 – RR) x 100) and 95% confidence intervals (CI) taking non-vaccinated HCWs (including person-time before first dose for those vaccinated) as reference.

Results: As of July 20, among 3,708 eligible subjects there were 3,408 vaccinated (98% with BNT162b2), 121 with one dose, 3,363 with two doses) and 224 non-vaccinated. The total number of recorded infections (symptomatic or not) was 118, including: 63 (rate 190) among non-vaccinated, 16 (rate 133) in the period 0-13 days after first dose, 6 (rate 48) from day 14 after first dose (VE 75%, CI 40-89%) and 33 (rate 43) from day 7 after second dose (VE 87%, CI 78-92%). Symptomatic infections were 53, 16 of them occurring 7 days after the second dose (VE 92% CI 84-96%). Asymptomatic infections were 65, 17 of them occurring 7 days after the second dose (VE 71% CI 33-88%).

Conclusion: We found high effectiveness of COVID-19 vaccine in HCWs in our hospital, either against symptomatic or asymptomatic infections. Without vaccination, the number of infections would have been 7-8 times larger (i.e., more than 250 cases. Further work is needed to assess long-term effectiveness, also considering new SARS-CoV-2 variants, and better plan future preventive strategies in this high-risk occupational group.

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Clinical HIV & Clinical Covid II

OC 31 IMMUNOGENICITY AND SAFETY OF THE BNT162B2 COVID-19 MRNA VACCINE IN PLWH

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Background: Despite 20 months since the outbreak of the COVID-19 pandemic, if patients who live with HIV (PLWH) have a higher risk of severe COVID-19 is controversial.
Regardless of immune impairment, PLWH may have multiple comorbidities, which represent independent risk factors for severe COVID-19, such as increased cardiovascular risk, lung diseases, diabetes; moreover, PLWH population in our country is getting older.
In March, PLWH were included in risk category of fragile people receiving priority access to vaccination with BNT162b2 vaccine.
The aim of the study was to evaluate the immunogenicity and safety of the two doses regimen.
Material and methods: All outpatients aged ≥18 yrs PLWH who received vaccination between 14th April and 14th May in our Clinic and with a follow-up of at least 2 months, were enrolled in this retrospective observational study. The antibodies title for SARS-CoV-2 was rated with a chemiluminescent microparticle immunoassay after 1 and 2 months since the first administration (positive if ≥ 50 AU/mL). Moreover, information regarding virological (HIV-RNA) and immunological (CD4+ cells, CD4 nadir, CD4/CD8 ratio) conditions at baseline, previous SARS-CoV-2 infection, other immunodeficiency conditions, current ART, comorbidities related to COVID-19 severe outcome (diabetes, hypertension, cardiac comorbidities, COBD) and severe adverse events (sAE) to vaccination were collected.
Results: Among 705 HIV infected patients who received a complete vaccination, 697 patients were tested for antibodies title after 21 days (coincident with the second dose) and were included in the analysis; 577 patients had a second detection, after 30±5 days from the second dose. Baseline characteristics of the study population are reported in Table 1. At time of vaccine administration, all patients were in ART, except one long term nonprogressor; 639 (91.7%) patients had not detectable HIV-RNA; 19 (2.7%) patients were immunosuppressed due to chemotherapy or other immunosuppressive drugs; 345 (49.5%) patients had at least one Covid-19 related comorbidity and 155 (22.2%) had two or more comorbidities.
Final serological results are available for 694 patients after the first dose and 577 after the second one; protective title was demonstrated in 653 (94.1%) and 576 (99.8%) patients, respectively. Among patients who were no-responder at first month (41; 5.9%), 34 (82.9%) showed a protective antibodies title at the second administration; 6 were not tested; only 1 patient was no-responder after completing vaccination, who was a newly diagnosed one, who had 76 CD4 cell (14.6%, 0.3 CD4/CD8 ratio) at time of vaccination, having stated ART only 2 days before. All vaccinations were well tolerated, with no sAE.
Conclusions: PLWH showed a 94.4% of protective antibodies title after first administration and 99.8% of protective title after completed vaccination. High immunogenicity of BNT162b2 mRNA vaccine in PLWH was similar to patients without HIV infection.

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Clinical HIV & Clinical Covid III

OC 32 T-LYMPHOCYTE SUBSET ABSOLUTE COUNTS ASSESSED AT BASELINE REPRESENT A USEFUL TOOL TO PREDICT 30-DAYS MORTALITY IN HOSPITALIZED SARS-COV-2 INFECTED PATIENTS

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T- and B-lymphocytes play a crucial role in the immune response against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Lymphopenia has been consistently reported and associated with the worst manifestation of COVID-19.
The objective of this study was to evaluate the role of baseline lymphocyte subset counts in predicting the 30 days mortality in COVID−19 patients.
We included in a retrospective study SARS-CoV-2 infected patients hospitalized from September to December 2020 in Policlinico Tor Vergata of Rome, for whom T-, B- Natural Killer lymphocyte absolute count assessment (TBNK) was available at baseline. 30-days mortality was recorded (survivors/nonsurvivors) and patients were stratified according to the maximal oxygen support/ ventilation supply required (nonsevere= ambient air [AA] and Venturi Mask [VMK]; severe= Non rebreather mask with reservoir [NRM], noninvasive [NIV] and invasive ventilation [OTI]). Demographics, clinical and laboratory data, were recorded.
Overall, 296 patients were included in the study. The 30-days mortality rate was 22,3%. Male sex (p=0,027), the presence of comorbidities (p=0,002), ICU admission (p<0,001), and the need of noninvasive or invasive ventilation (p<0,001) were associated to increased mortality.
The time from symptom onset to the first positive molecular test for SARS-CoV-2 RNA detection and the first TBNK assessment did not significantly differ after stratifying patients in survivors and nonsurvivors, ruling out a delay in the diagnosis in more severe cases.
Considering the lymphocyte subset absolute counts, total CD3+, CD4+, CD8+, CD4+CD8+ double positive and CD4−CD8− double negative T-lymphocyte were significantly reduced at baseline in nonsurvivors compared to survivors (p<0,001). Conversely, CD3-CD16+CD56+ NK cells and the CD4/CD8 ratio were not significantly different in the two groups.
In a previous work from our group, we identified the cutoffs for T-lymphocyte subset absolute counts, which were predictive of in-hospital mortality (Iannetta et al, Sci Rep. 2021). In the present work, we validated these cutoffs, and estimated for each patient a score, namely the T−lymphocyte subset index (TLSI), which represents the number of T-lymphocyte main subset (CD4+, CD8+) counts below the cutoff. TLSI ranges from 0 (no subsets below the cutoff) to 2 (both CD4+ and CD8+ below the cutoff). After stratifying the patients according to the TLSI, the Kaplan-Meier survival curve analysis showed an increased mortality in patients with a higher TLSI (Log-rank test p<0,0001), with a trend from TLSI=0, through TLSI=1 to TLSI=2 (Log-rank test for trend p<0,0001) (figure1). Considering the 30-days mortality, 6 (6,2%), 14 (18,2%) and 46 deaths (37,7%) were recorded in the group with TLSI=0, TLSI=1 and TLSI=2, respectively.
The evaluation of peripheral T−lymphocyte absolute counts in the early stages of COVID−19 represents a useful tool for identifying patients at increased risk of unfavorable outcome.

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Clinical HIV & Clinical Covid III

OC 33 HIV AND SARS-COV-2 CO-INFECTION: PROTECTIVE ROLE OF IL-10 IN HIV-POSITIVE YOUNG INDIVIDUALS

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Background: While the risk of SARS-CoV-2 infection and/or COVID-19 disease progression in the general population is largely assessed, the impact on HIV-positive individuals remains unclear. This study reports clinical and immunological aspects in a cohort of HIV-infected young individuals and deepens results obtained ex-vivo by an in-vitro HIV/SARS-CoV-2 coinfection assay.

Material and methods: 85 ART-treated HIV-infected young patients (mean age 22.4 years) were enrolled in the study. Real–time PCR was performed to detect SARS-CoV-2 on sputum and plasma samples were tested for anti-SARS-CoV-2-specific antibodies IgG (Euroimmun). HIV-infected young subjects who contracted SARS-CoV-2 infection (H+/S+) were compared to the HIV-positive, SARS-CoV-2 negative ones (H+/S-) and to a cohort of SARS-CoV-2 positive, HIV-negative age-matched patients (H-/S+) (mean age 22.8 years). mRNA expression of factors involved in the anti-viral immune response was performed on Peripheral Blood Mononuclear Cells (PBMCs) upon stimulation with SARS-CoV-2 antigens (Quantigene Plex Gene expression assay). Secreted cytokines/chemokines were quantified on plasma (Multiplex Cytokine Array). An in vitro coinfection assay was performed by challenging PBMCs derived from 10 healthy volunteers with 1 ng/1 × 106 cells of HIV-1BaL and subsequently co-culturing them with a human epithelial cell line from lung adenocarcinoma (CaLu3) infected with SARS-CoV-2 at a multicity of infection (MOI) of 0.015. At 96 hpi (6 days after HIV -1 infection), both PBMCs and CaLu3 cells were harvested for analysis.

Results: 4 out of 85 HIV-infected subjects contracted SARS-CoV-2 infection (H+/S+). H+/S+ did not show any relevant clinical consequence. Cytokines and chemokines production in plasma and mRNA expression were increased in H+/S+ co-infected subjects compared to both H+/S- and H-/S+ individuals, with a significant higher upregulation of IL-10 ($p<0.05$), and this trend was significantly evident by comparing H+/S+ to H-/S+. In-vitro, IL-10 expression was significantly higher in the co-infected condition, in both CaLu3 cells and PBMCs. Strikingly, considering viral loads, we observed a significant reduction of in vitro SARS-CoV-2 replication on Calu3 when exposed to HIV pre-infected PBMCs.

Conclusions: Despite a higher immune activation, HIV-infected subjects did not show any relevant clinical consequence related to SARS-CoV-2 infection. We speculate that this could be justified by the upregulation of IL-10 in H+/S+ subjects, as confirmed in-vitro. Moreover, a dampening in SARS-CoV-2 replication has been observed in the HIV/SARS-CoV-2 co-infected condition, thus confirming the possible protective role of this anti-inflammatory cytokine in HIV positive patients. These results might help defining clinical management of HIV/SARS-CoV-2 co-infected young individuals, or putative indications for vaccination schedules in this population.

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OC 34 SEQUELAE AT 12 MONTHS AFTER COVID-19 IN HOSPITALIZED ADULTS: A MULTICENTER STUDY

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Background: SARS-COV-2 infection can lead not only to an acute disease, but also to a series of long-term complications. The exact nature and prevalence of persistent symptoms after SARS-CoV-2 infection are not known, but in literature a high incidence of sequelae is reported during the convalescence months. The primary goal of this study is to define the incidence and nature of the COVID-19 sequelae encompassed by patients 12 months after their discharge.
Materials and methods: This prospective observational study is included in COVID-19 NETWORK project, a multicenter study promoted by Fondazione IRCSS Ca' Granda Ospedale Maggiore Policlinico di Milano and including some hospitals from Lombardy, Veneto, Abruzzo and Emilia-Romagna. Patients discharged alive within 31st May 2020 were included and were offered a telephone interview in the form of a questionnaire. This survey investigates the state of health 12 months after SARS-COV-2 infection, the need of hospitalization or access to emergency care and the presence of systemic, neurological, respiratory, psychological and gastrointestinal symptoms
Results: Among the 779 patients who were discharged alive, 44 (5.6%) died, 456 subjects (58.5%) completed the questionnaire, 279 (35.8%) were not reachable or refused to join the telephonic follow-up. The population of this last group was represented by older subjects (135/279, 48,4%) and by subjects with more than 3 comorbidities at baseline.
The mean age of the follow-up study population was 59 years (SD 14.1), 10% were transferred in ICU and 70% of them needed oxygen support during hospitalization.
At first analysis 415 (91%) subjects reported at least one symptom at 12 months, 220 (48,2%) reported more than 3 sequelae. The most reported symptom was exertional dyspnea (71,7%) defined by mMRC>1 (modified Medical Research Council Dyspnea Scale) whereas dyspnea at rest was reported by 12.5% of subjects. Fatigue and gastrointestinal symptoms (bowel habit or bloating) were reported by 54,6% and 32,7% of patients respectively. As regards psychiatric symptoms, 32,4% of patients reported sleep disorders during the convalescence months and 23,1% declared episodes of anxiety. For further data see Figure 1.
Severe health issues after discharge including hospitalization or access to emergency room were described by 19.4% of subjects.
Conclusions: Persistent symptoms are found in most individuals even 12 months after hospitalization for COVID-19. Respiratory symptoms and fatigue are the most frequently reported sequelae. Further studies are needed to establish causative and predisposing factors to development of long-term sequelae in SARS-COV-2 infection.

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OC 35 BLOODSTREAM INFECTIONS IN COVID-19 PATIENTS: FIRST-WAVE VERSUS SECOND-WAVE COMPARISON

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Background: Bloodstream infections (BSIs) are the second most common complication in COVID-19 patients. We aimed to compare incidence, timing of development and impact on in-hospital mortality of BSIs in first-wave (January-April,2020) vs. second-wave (October,2020-April,2021) COVID-19 epidemics in Milan.

Material and methods: This retrospective observational study included 3402 adult patients admitted for ≥48 hours to ASST Grande Ospedale Metropolitano Niguarda with a first diagnosis of COVID-19 between January 19, 2020 and March 31, 2021. BSIs were defined by pathogens' isolation in diagnostic blood-cultures. Non-recurrent BSIs were defined by >30 days distance from previous episode, or change in antimicrobial sensitivity pattern. Survival analyses (Kaplan Meyer and Cox) were used to investigate differences in timing of BSIs development and mortality using age and sex as potential confounders. Fisher exact test was used to compare categorical variables.

Results: Out of 3506 patients with a first diagnosis of COVID-19 in the study period, 3402 were included. The median time (IQR) of hospital stay was 14 (9-25) days with no significant differences between 1st and 2nd pandemic waves (p=0.553). 371 BSI events were diagnosed in 261 patients. 114/261(43.7%) patients had more than one BSI event. The OR for multiple BSIs significantly increased for admissions longer than 30 days (OR [95% CI] = 12.510 [8.232-19.012]; p<0.001).

The 40.9% of patients with a BSI within the first 30-days died, vs. the 35.1% of those who had a first BSI after the first 30-days, and the 17.3% of those who never had a BSI. Acquisition of a BSI within the first 30-days increases the risk of death at 30-days (OR 7.9 [95%CI: 5.7-11.0]; p<0.001), independently of age and male sex.

The time-to-first-BSI was significantly shorter during the 1st than during 2nd pandemic wave (p-value = 0.001), as the mean (95% CI) BSI-free survival time was 82 (73-91) vs. 103 (96-110) days, respectively. 30-day survival is significantly lower in the 1st than in the 2nd wave (80.4% vs. 85.5%; p-value= 0.004).

Out of 495 microbial isolates, Gram-negative bacteria and Staphylococcus aureus caused 52.7% and 14.9% of BSI respectively, while 4% were sustained by Candida spp. 246 (66.3%) BSIs were sustained by ESKAPEc pathogens of whom 110 (39.9%) were multi-drug resistant.

Discussion: In our scenario BSI epidemiology significantly changed during the course of COVID-19 pandemics. We observed that compared to the first wave, in second wave COVID-19 patients had a 40% lower risk of developing a BSI, the time-to-first BSI was longer and 30-day survival was significantly higher. The lower risk of the second wave is most likely the result of a lesson learned from the first wave regarding infectious complications management. These findings stress on the importance of a continued vigilance against these infections especially in this pandemic scenario.

Clinical HIV & Clinical Covid III

OC 36 IMPACT OF A PRO-ACTIVE INFECTIOUS DISEASES CONSULTATION FOR THE MANAGEMENT OF A MULTIDRUG-RESISTANT ORGANISMS OUTBREAK IN A COVID-19 HOSPITAL: A THREE-MONTHS QUASI-EXPERIMENTAL PROSPECTIVE STUDY

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Background: Hospitals around the world reported outbreaks of multidrug-resistant organisms (MDROs) during the COVID-19 pandemic. In this setting, the application of antimicrobial stewardship (AS), diagnostic stewardship (DS) and infection control procedures (ICP) through Infectious Diseases (ID) consultation is essential to improve management of MDROs infections and reduce morbidity and mortality caused by secondary infections. Aim of the study was to assess the impact of a pro-active ID consultation on the 28-day mortality risk in patients with a suspected/ confirmed secondary infection during a MDROs outbreak in a COVID-19 hospital.

Material and methods: A quasi-experimental pre-post study was performed in a purposed build COVID-19 Hospital from March to June 2021. All consecutive adult patients with suspected/confirmed infection and/or colonization by MDROs in the study period were included. Patients were managed: i) according to the standard of care during the pre-phase (March 15th - April 25th, 2021); ii) in collaboration with a dedicated ID team performing a pro-active bedside evaluation during the post phase every 48-72 hours (April 26th - June 15th). An audit on ICP and AS principles was also performed before post-phase starting.

Results: A total of 112 patients with a suspected/confirmed secondary infection were included, of whom 89 patients in pre-phase and 45 in post-phase; 22/45, due to the presence of a suspected/confirmed infections in both the pre- and post-phases, were analyzed twice. (Table 1).

Overall, AS included at least one of the following interventions: initiation/improvement of targeted therapy (33%), de-escalation to narrow spectrum (24%), de-escalation to less toxic drugs (20%), discontinuation of antimicrobials (64%). DS included the request of additional microbiologic tests (82%) and instrumental exams (16%).

Univariate and stepwise multivariate Cox regression was performed to assess risk of 28-day mortality: after adjusting for age, sex, COVID-19 severity, infection source, Carbapenem-resistant A.baumannii (CRAB) or KPC-K.pneumoniae as etiological agents, and post-phase attendance, age was associated with increased risk of mortality [aHR: 1.08, 95%CI: 1.03 - 1.13, p<.001], while to be evaluated in the post-phase resulted protective [aHR: 0.31, 95%CI: 0.10 - 0.92, p=.035]. This result was also confirmed by Kaplan-Meiers curves (Log rank p=.021, Figure 1).

Moreover, if compared with pre-phase, post-phase enrollment was associated with an increased number of definitive diagnosis of secondary infections (30% vs 60%, p<.001), a reduction in empirical Colistin use (71% vs 30%, p=.002) and a trend towards reduction of CRAB colonization (79% vs 59%, p=.078).

Conclusions: Implementation of ICP, AS and DS intervention through a pro-active ID team consultation significantly reduced risk of 28-day mortality and improved the diagnostic rate of infections.

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Immunopathogenesis I

OC 37 SARS-COV-2 PLASMATIC VIREMIA AND T-CELL IMMUNE RESPONSE IN HOSPITALIZED COVID-19 PATIENTS

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Background: The delayed onset of critical COVID-19 illness points to a dysfunctional immune response as major correlate of disease severity. Because high SARS-CoV-2 plasma viremia has been linked to tissue damage and mortality, we investigated whether detectable viremia is associated with a hampered SARS-CoV-2 immune response. **Material and methods:** We enrolled 54 hospitalized COVID-19 patients with pneumonia. Plasmatic SARS-CoV-2 viremia, plasma cytokines (IFN-α, IFN-γ, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12p70, IL-17A, TNF- α) and chemokines (GM-CSF) were quantified (RT-PCR and Human MACSPlex, respectively). PBMCs were stained for immunophenotype and intracellular cytokines after stimulation with SARS-CoV-2 peptides pool (Spike, Nucleocapsid, Membrane) or individual peptides. HLA-DR+CD38+ defined activation, GRZB+PRF+ pro-cytolytic T-phenotypes. SARS-CoV-2-specific T cells were determined, after unstimulated subtraction, by means of IL-2, IFN-γ, TNF-α, IL-4, and IL-17A. For CD4+, Th1 polyfunctionality (IL-2, IFN-γ, TNF-α) and integrated MFI (iMFI) were determined. Data were analysed by FlowJo 10.7.2 and GraphPad Prism 9; comparisons with Mann-Whitney U test.
Results: 27/54 patients had a detectable viremia (V+) at a median of 10 days from symptoms onset. A higher proportion of V+ patients required non-invasive/invasive ventilatory support (Fig. 1A). V+ patients presented higher circulating IFN-α and IL-6 (Fig. 1B). Despite comparable total CD4 and CD8%, HLA-DR+CD38+ CD4 and CD8 % was lower in the V+ group (p = 0.01 and 0.02). A trend towards a reduced % of SARS-CoV-2 specific cytokine-producing T cells was observed in the V+ group, reaching statistical significance for CD4 IFN-γ+, CD8 TNF-α+ and CD8 IL-4+ (p = 0.02, 0.04 and 0.04) (Fig. 1C). The same trend was observed after stimulation with individual S- and N-peptides, but not M. To further evaluate whether SARS-CoV-2 viremia is associated with SARS-CoV-2-specific CD4 T-cell functional state, Th1 polyfunctionality was assessed. A trend towards a lower % of bi- and tri-functional SARS-CoV-2-specific CD4 T-cells was observed in V+ patients, reaching significance for IL-2+TNF-α+ CD4 T-cells (p = 0.02). Likewise, iMFI analysis demonstrated a trend towards reduced cytokines production in bi- and tri-functional SARS-CoV-2-specific CD4 in V+ group, reaching significance for IL-2 +TNF-α+ CD4 T cells (p = 0.004 and 0.01).
Conclusions: By showing a more severe disease together with higher circulating pro-inflammatory cytokines and fewer polyfunctional SARS-CoV-2-specific T cells in hospitalized viremic COVID-19 patients, our data suggest an association between systemic SARS-CoV-2 circulation and aberrant adaptive immunity in disease severity. Whether high SARS-CoV-2 viremia hinders the establishment of a virtuous immune response, or a dysfunctional immune response ab initio fails to control viral replication remains to be elucidated, to further inform strategies of targeted therapeutic interventions.

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Immunopathogenesis I

OC 38 T-LYMPHOCYTE SPECIFIC RESPONSE TO SARS-COV-2 PEPTIDES IS DETECTABLE IN PATIENTS WITH MULTIPLE SCLEROSIS UNDER TREATMENT WITH DISEASE MODIFYING THERAPIES, DESPITE ABSENT OR LOW-LEVEL ANTI-SPIKE ANTIBODY TITERS. WHICH ARE THE POSSIBLE CLINICAL IMPLICATIONS?

M. Iannetta[1], D. Landi[2], G. Cola[2], A. Di Lorenzo[1], L. Campogiani[1], I. Spalliera[1], P. Vitale[1], V. Malagnino[1], E. Teti[1], L. Coppola[1], D. Fraboni[3], F. Buccisano[3], S. Grelli[4], G.A. Marfia[2,5], M. Andreoni[1], L. Sarmati[1]

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Little is known about cell-mediated responses in patients receiving disease modifying therapies (DMT) for multiple sclerosis (MS) after severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccination. Achiron et al. showed poor seroconversion rates after SARS-CoV-2 vaccination in MS patients receiving B-cell depleting treatments. The aim of this study was to investigate SARS-CoV-2 specific T- and B-cell responses in MS patients receiving DMTs after vaccination.
MS patients treated with ocrelizumab (OCR) (anti-CD20 drug, causing B-cell depletion), fingolimod (FTY) (anti-S1P1 drug, preventing lymphocyte egress from lymphoid tissues) and natalizumab (NAT) (anti-alpha4 integrin, inhibiting leukocyte migration into the brain), vaccinated with two doses of BNT162b2 vaccine were enrolled in the study. Anti-Spike (S) antibodies (Ab) specific for SARS-CoV-2 were detected with an electrochemiluminescence immunoassay (Elecsys Anti-SARS-CoV-2 S, Roche Diagnostics). Peripheral blood lymphocyte subsets were assessed with a lyse no wash standardized protocol (Multitest 6-Color TBNK and trucount tubes, BD Biosciences). T-lymphocyte specific response was assessed with an in-house interferon (IFN)-gamma release assay (IGRA) after overnight stimulation with SARS-CoV-2 peptide libraries.
30 patients (21 females) with a median age of 41 years were enrolled in the study, (10 OCR, 10 FTY, 10 NAT). No differences were observed in age and sex distribution in the 3 groups. CD3+ T-lymphocyte absolute counts were significantly reduced in FTY group ($p<0,001$), while CD19+ B-lymphocytes were significantly reduced in both FTY and OCR groups compared to NAT group ($p<0,001$). Anti-S Ab were assessed in the 3 groups, and were significantly reduced in OCR and FTY groups compared to NAT group ($p<0,001$ and $p=0,002$, respectively).
Concerning T-cell responses, after whole blood stimulation with the peptide pool libraries specific for SARS-CoV-2, IFN-gamma production was significantly reduced in the FTY group compared to OCR and NAT groups ($p=0,002$ and $p<0,001$, respectively).
In patients receiving B-cell depleting therapies, such as ocrelizumab, despite the absence or low-level titers of anti-S Ab, SARS-CoV-2 specific T-cell response is detectable and comparable to the level observed in patients receiving non depleting therapies, such as natalizumab. Conversely, patients receiving fingolimod, which reduces peripheral blood T- and B-lymphocytes, showed impaired anti-S Ab production together with a reduced IFN-gamma secretion upon peptide stimulation for SARS-CoV-2. Although the protective role of T-cell specific responses after vaccination to prevent SARS-CoV-2 infection needs to be clarified, in a rhesus macaques SARS-CoV-2 infection animal model, McMahan K. et al. showed that depletion of CD8+ T cells in convalescent animals partially abrogated the protective efficacy of natural immunity against SARS-CoV-2 re-challenge. Further studies in humans are needed to clarify this point.

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Comorbidities I

OC 39 SARS-COV-2 INFECTION AND COVID-19 DISEASE IN A LARGE COHORT OF PLWHIV

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Background: Information about incidence, clinical characteristics, and outcomes of HIV-infected individuals with SARS-CoV-2 infection is scarce.

Methods: In a prospective cohort, we included HIV-infected individuals with confirmed SARS-CoV-2 infection and compared them with PLWHIV who tested negative for SARS-CoV-2. Severity of COVID-19 was graded according to NIH classification and data were derived from the clinical data-base of our Institution.

Results: Out of 2898 PLWHIV currently followed, we identified 134 cases of SARS-CoV-2 infection either by RT-PCR test (41.8%) or serology (58.2%). We compared these cases with 307 asymptomatic PLWHIV who tested negative for RT-PCR (31.3%) or serology (68.7%). All of them were on active ARV treatment that continued. Three subject (one positive for SARS-CoV-2 and 2 negative) were diagnosed with HIV during the pandemic and immediately started ARV therapy. Baseline characteristics were not significantly different between SARS-CoV-2 positive and negative patients with the exception of age that was higher in infected patients (P = 0.031)(Figure). Amongst positive cases 20.9% were completely asymptomatic, 46.3% had mild symptoms while 20.9% and 11.9% had a moderate or severe disease, respectively. Only 28 subjects (20.9%) were admitted to hospital. The most common symptom was fever, observed from 88% to 100% of cases according to disease severity (P=0.337), ageusia (P=0.009) and anosmia (P=0.041) were more frequent among patients with mild or moderate disease, while symptoms significantly more frequent in patients with a more serious clinical picture were dyspnea (P<0.0001); cough (P=0.002) and CNS involvement (P=0.028). The only variables associated with a severe clinical picture were male gender (P=0.044) and increasing age (P=0.001)(Figure). Finally 6 patients (5%) died because of Covid-19. All of them were males with a mean age slightly higher (68 years; 95%CI 62-74) compared to survivors (55 years; 95%CI 53-56). Variables associated with the risk of death were the number of chronic co-pathologies (P=0.002) and a lower CD4 count (P=0.034)(Figure). ARV drugs never resulted associated to any of the considered outcomes such as risk of infection, severity of disease and risk of death.

Conclusions: HIV-infected individuals are at risk for SARS-CoV-2 infection . Infection may be asymptomatic in a large proportion of subjects and this variable must be counted when epidemiological studies are implemented in PLWHIV. Furthermore, as barely a fifth of cases are admitted to hospital studies based on hospital admissions may underestimate the problem. Male gender and older age are significantly associated with a more serious disease, while the number of chronic co-morbidities and lower CD4 counts do correlate with mortality. We can exclude any effect of ARV therapy on the risk of acquiring SARS-CoV-2 infection or on the course of COVID-19 disease.

Partially founded by Gilead Fellowship program 2021

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Comorbidities I

OC 40 MENINGOCOCCUS B VACCINATION EFFECTIVENESS AGAINST NEISSERIA GONORRHOEAE INFECTION IN PLWH: A CASE-CONTROL STUDY

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Background: We assessed multicomponent meningococcal serogroup B vaccine (4CMenB) effectiveness against gonorrhoea infection in the setting of people living with HIV (PLWH).
Materials: Case-control study on men who have sex with men (MSM) with HIV-infection, in care at the Infectious Diseases Unit of San Raffaele Institute, Milan, with gonorrhoea, chlamydia, syphilis or HPV between July 2016 (beginning of 4CMenB vaccination) and February 2021. Vaccination status of cases (people with >=1 gonorrhoea infection since July 2016) was compared to two different control groups: group1) people with chlamydia, syphilis or HPV; group2) people with chlamydia or syphilis, since July 2016. Individuals' sexual behaviours were investigated by means of a survey. Those who reported having 0 partners (mean value per month) or 100% use of condom during 2016-2021 were excluded in a second analysis. Univariate logistic regression was applied; odds ratios (ORs) with 95% confidence intervals (95%CI) are reported.
Results: Overall, 1051 individuals (103 cases, 948 controls, Group1) and 732 (103 cases, 629 controls, Group2) were included in the analyses. Median (IQR) follow-up was 3.8 years (2.1-4.3) among 1051 people and 3.9 (2.4-4.3) among 732; 349/1051 (33%) and 221/732 (30%) PLWH received 4CMenB vaccination. Individuals <=44 years (overall median value) were 537/1051 (51%) and 401/732 (55%). Other characteristics in Table1. Vaccinated people were 24 (23%) among cases, 325 (34%) among Group1 and 197 (31%) among Group2. Vaccinated people were less likely to be gonorrhoea cases than controls [analysis with Group1: OR=0.58, 95%CI=0.36-0.94, p=0.027; with Group2: OR=0.67, 95%CI=0.41-1.08, p=0.106]. Among people <=44 years, vaccination was even less likely among cases than controls [13/68 (19%) cases, 168/469 (36%) Group1 controls: OR=0.42, 95%CI=0.22-0.80, p=0.006; 13/68 (19%) cases, 111/333 (33%) Group2 controls: OR=0.47, 95%CI=0.25-0.90, p=0.021]. Among people >44 years we did not find a different risk of vaccination between cases and controls (Figure1A). The survey on sexual behaviours was completed by 580/1051 (55%) PLWH: results in Table2. Overall, 38/580 (7%) reported having 0 partners per month and 134/542 (25%) using always condoms during intercourses. When excluding these two categories, vaccinated individuals were less likely to be gonorrhoea cases than controls [analysis with Group1: OR=0.34, 95%CI=0.16-0.70, p=0.004; with Group2: OR=0.34, 95%CI=0.16-0.71, p=0.004]. Among people <=44 years vaccination was even less likely among cases than controls [analysis with Group1: OR=0.29, 95%CI=0.11-0.75, p=0.011; with Group2: OR=0.28, 95%CI=0.10-0.73, p=0.009]. Among people >44 years we did not find a different risk of vaccination between cases and controls (Figure1B).
Conclusions: 4CMenB vaccination exposure is associated with lower risk of gonorrhoea infection in HIV-infected MSM at high risk of sexually transmitted infections, especially among younger people.

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Comorbidities I

OC 41 A MACHINE LEARNING-BASED MODEL TO PREDICT THE 15-YEAR RISK FOR CARDIOVASCULAR DISEASE IN A COHORT OF PEOPLE LIVING WITH HIV

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Background: Aim of the study was to develop a machine learning-based to predict the 15-year risk for cardiovascular disease (CVD) among people living with HIV-1 infection (PLWH).

Material and Methods: We included PLWH followed at the Infectious Diseases Department of IRCCS San Raffaele Scientific Institute who started antiretroviral therapy (ART) since 1998, had available demographic, clinical and laboratory data at the start of ART (baseline). The primary outcome was the occurrence of major cardiovascular events (MACE, including myocardial infarction, unstable angina, coronary or peripheral arterial revascularization, stroke or transient ischemic attack, peripheral arterial ischemia, cardiac arrest and CVD death) during the 15 years after baseline.

The association of potential predictors and the 15-year CVD risk was assessed using Cox proportional hazard models. A training and using deep learning approach (DeepHit) was applied to improve CVD prediction; DeepHit is a deep neural network that learns the distribution of survival times directly without making specific assumptions on the underlying stochastic process. DeepHit and multivariable Cox regression models adopted the same set of predictors, measured at baseline.

Results: Overall, 4534 PLWH were evaluated: 3586 (84%) were males, with a median age of 38 (interquartile range, IQR 31-44) years.

During a median follow-up of 16.5 (IQR 10.7-22.8) years, 145 (3.2%) PLWH developed MACE in 15 years; median time to first MACE was 9.4 (IQR 6.1-12.3) years.

Factors predicting 15-year MACE risk varied according to the set of predictors considered in the multivariable Cox regression models and included age, hypertension, HDL-cholesterol, hematocrit, CD4/CD8 ratio, HCV and HBV coinfection. DeepHit models generally improved the prediction of Cox predictive risk models, revealing better C-index values. The 15-year PLWH CVD curves according to a multivariable Cox model had a C-statistic of 0.64 that improved to 0.74 using the DeepHit model (Figure 1).

Conclusions: Our findings showed that DeepHit models improve the prediction of 15- year CVD risk in PLWH.

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Immunopathogenesis II

OC 42 THE INTERPLAY BETWEEN SARS-COV-2 INFECTED AIRWAY EPITHELIUM AND IMMUNE CELLS MODULATES THE IMMUNOREGULATORY/INFLAMMATORY SIGNALS

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects primarily the airways tract, inducing the recruitment of inflammatory infiltrates in the alveolar space and a systemic inflammatory cytokine storm. To assess the cross-talk between immune cells and respiratory tract during SARS-CoV-2 dissemination, we analysed the relationships between the inflammatory response induced by SARS-CoV-2 replication and immune cells phenotype in a reconstituted human bronchial epithelium model.

The SARS-CoV-2 infected organotypic human airway epithelium (HAE) was co-cultured with immune cells and the inflammation profile as well as the frequency of immune cell subsets was analyzed. The enriched network and signalling was finally evaluated.

The results indicated that immune cells failed to inhibit SARS-CoV-2 replication in HAE model. In contrast, immune cells strongly affected the inflammatory profile induced by SARS-CoV-2 infection, dampening the production of several immunoregulatory/inflammatory signals (e.g., IL-35, IL-27 and IL-34). Moreover, these mediators were found inversely correlated with innate immune cell frequency (NK and gdT cells) and directly with CD8 T cells. The enriched signals associated to NK and CD8 T cells highlighted the modulation of pathways induced by SARS-CoV-2 infected HAE.

These findings are useful to depict the cell-cell communication mechanisms necessary to develop novel therapeutic strategies aimed in promoting an effective immune response.

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Immunopathogenesis II

OC 43 DETECTION OF SARS-COV-2 RNA AND EVALUATION OF NEUROFILAMENT LIGHT CHAIN IN CEREBROSPINAL FLUID AND PLASMA OF COVID-19 PATIENTS

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Background: Neurofilament light chain (NfL) is considered a specific biomarker of quantitate neuro-axonal damage and normally measured in CSF. Novel methods have given the possibility to measure NfL in plasma instead. Here, we investigated SARS-CoV-2 RNA presence in CSF and plasma samples in COVID-19 patients with neurological symptoms using droplet digital PCR (ddPCR). Moreover, on CSF and plasma samples we assessed NfL levels as well as matrix metalloproteinase-9 (MMP-9), which contributes to blood barrier brain damage, and its specific inhibitor, tissue inhibitor of metalloproteinase-1 (TIMP-1) evaluating the association with disease severity.

Materials and methods: Hospitalized COVID-19 patients with neurological symptoms were enrolled. Plasma and CSF samples were drawn at the acute stage of disease. Using ddPCR viral RNA detection and quantification in CSF and plasma samples were performed. NfL evaluation was assessed using the Simple PlexTM Ella (EllaTM) microfluidic platform. Finally, CSF and plasma levels of MMP-9 and TIMP-1 were evaluated by ELISA. According to the ARDS onset, COVID-19 patients were stratified into ARDS group and non-ARDS group. As control group, we enrolled healthy donors (HD) matched for gender and age to compare NfL, MMP-9 and TIMP-1 plasmatic levels.

Results: Twelve COVID-19 patients with neurological symptoms and 13 HD were enrolled. In CSF and plasma samples viral RNA was detected in 4/12 and 1/12 COVID-19 patients, respectively. According to SARS-CoV-2 detection in CSF samples, not statistically significant differences in NfL, MMP-9 and TIMP-1 levels were found. Otherwise, ARDS group (n=6) showed higher NfL levels and lower MMP-9/TIMP-1 ratio on CSF samples compared to non-ARDS group (n=6) (NfL: 6480 [1512-11012] and 476 [305-2859], p=0.026; MMP-9/TIMP-1 ratio: 0.5 [0.3-0.6] and 0.9 [0.6-0.9], p=0.036).
A positive correlation between NfL levels on CSF and plasma samples (ρ=0.810 p=0.022) was observed. Furthermore, a negative correlation between NfL levels on CSF and MMP-9/TIMP-1 ratio on CSF (ρ=-0.631 p=0.032) was observed.
Finally, COVID-19 patients showed significantly higher plasma levels of NfL, MMP-9 and TIMP-1 compared to HD (NfL: 72 [28-95] and 11 [9-17] pg/ml, p<0.0001; MMP-9: 192 [74-268] and 51 [34-70], p=0.0017; TIMP-1: 319 [201-395] and 61[33-70], p<0.0001). A significantly lower plasma MMP-9/TIMP-1 ratio in COVID-19 patients compared to HD was observed (0.6 [0.4-0.7] and 1.0 [0.6-1.6], respectively, p=0.034).

Discussion and conclusion: Direct invasion of the CNS by SARS-CoV-2 is a controversial issue, with contradictory findings in current literature. As suggest by our data, ARDS is associated to CNS damage and neurological sequelae also in the absence of SARS-CoV-2 detection in CSF. Our data corroborated the clinical relevance of NfL and MMP-9/TIMP-1 in COVID-19 induced neural damage. NfL, MMP-9 and TIMP-1 evaluation on plasma samples can be useful to detect and monitor CNS damage in COVID-19.

Immunopathogenesis II

OC 44 MMP-9 AND TIMP-1 AS A POTENTIAL DISEASE BIOMARKER IN PATIENTS WITH COVID-19 PNEUMONIA

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Background: Matrix metalloproteinases (MMPs) are involved in systemic inflammatory responses and organ failure. The upregulation of MMPs contributes to chronic inflammation, by contrast the increase of TIMPs causes lung fibrosis.
The aim of the study was to evaluate MMP-9 and TIMP-1 plasmatic levels in COVID-19 patients in 2 time-point: at the hospital admission (baseline) and after 3 months of the recovery (T post) comparing the obtaining findings to clinical data.
Materials and methods: On hospitalized COVID-19 patients MMP-9 and TIMP-1 plasmatic levels were evaluated by ELISA. As control group, healthy donors (HD) matched for gender and age were included in the study. Moreover, monocyte/macrophage activation markers such as sCD163 and sCD14 plasmatic levels were evaluated too. For COVID -19 patients, blood samples were taken at two time-points: baseline and T post. According to the severity of the disease, COVID-19 patients were stratified into severe and non-severe groups and the differences were evaluated.
Results: Eighteen-one COVID-19 patients and 34 HD were enrolled. At baseline, MMP-9 and TIMP-1 plasmatic levels were significantly higher in COVID-19 patients compared to HD ($p=0.0002$ and $p<0.0001$, respectively). Stratifying COVID-19 patients according to the severity of the disease, higher MMP-9 and TIMP-1 plasmatic levels in severe group compared to non-severe one was observed ($p=0.047$ and $p=0.0008$, respectively). At baseline, a negative correlation between MMP-9 plasmatic level and P/F ratio ($\rho=-0.274$, $p=0.019$), while positive correlations between MMP-9 plasmatic levels and white blood cell (WBC) absolute count ($\rho=0.558$, $p<0.0001$), neutrophil absolute count ($\rho=0.5590$, $p<0.0001$) and neutrophils/lymphocytes ratio (NLR) ($\rho=0.413$, $p=0.0002$) were observed. Moreover, negative correlations between TIMP-1 plasmatic level and P/F ratio ($\rho=-0.281$, $p=0.0161$) and P/F nadir ($\rho=-0.276$, $p=0.020$) and positive correlations between TIMP-1 plasmatic levels and WBC absolute count ($\rho=0.379$, $p=0.0006$), and neutrophil absolute count ($\rho=0.341$, $p=0.002$) were observed. Finally, a positive correlation between TIMP-1 and sCD14 plasmatic levels ($\rho=0.287$, $p=0.026$) was observed.
At T post, the longitudinal evaluation performed in 54 COVID-19 subjects showed significant reduction in TIMP-1 plasmatic levels and MMP-9/TIMP-1 ratio compared to baseline ($p<0.0001$ and $p<0.0001$, respectively). No differences were observed in MMP-9 plasmatic levels between two time-points.
Discussion and conclusion: The increase in MMP-9 and TIMP-1 plasmatic levels, observed on hospital admission in COVID-19 subjects, especially in those who developed a severe form, and the correlation to monocyte activation marker underline a potential use as prognostic marker and potential therapeutic target in conditions leading to systemic inflammation and acute organ failure.
At T post, the reduction in TIMP-1 plasmatic levels but not in MMP-9 plasmatic levels suggest that inflammation is still ongoing.

Immunopathogenesis II

OC 45 AN NF-KB/JAK/STAT SIGNALING PATHWAYS IS INVOLVED IN APOBEC3A INDUCTION FOLLOWING CCL2 NEUTRALIZATION IN PRIMARY HUMAN MACROPHAGES

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Background: Apolipoprotein B mRNA editing enzyme catalytic polypeptide-like 3 (APOBEC3, A3) family members are cytidine deaminases that play crucial roles in innate responses to retrovirus infection. Among the A3 enzymes, A3A is unique in that it can restrict infection directly in the target cells where it is endogenously expressed, mainly myeloid lineage cells. We previously found that exposure of monocyte derived-macrophages (MDMs) to CCL2 neutralizing antibody (Ab) strongly inhibited HIV-1 replication at post-entry steps of the viral life cycle. This effect was associated with up-regulation of several mRNA coding for factors involved in innate antiviral responses, among which A3A. These transcripts were enriched for RELA and NFKB1 targets, thus suggesting the activation of the canonical NF-kB pathway. This study aimed at identifying the signal transduction pathways involved in the induction of A3A by CCL2 blocking in MDMs.

Material and methods: CD14+ monocytes were isolated from the peripheral blood of healthy donors by immunomagnetic selection and cultivated in vitro for 6 days to obtain MDMs. The signaling pathways underlying CCL2 blocking-mediated induction of A3A were investigated in MDMs exposed to anti-CCL2 Ab by using a combination of pharmacologic inhibition, confocal laser scanner microscopy, qPCR analysis and western blot.

Results: CCL2 neutralization mediated A3A transcripts accumulation was inhibited by actinomycin D and cycloheximide, thus indicating that it requires de novo transcription and protein synthesis. Moreover, exposure of MDMs to anti-CCL2 Ab induced a time dependent phosphorylation of IkB and STAT1, as well as p65 nuclear translocation, thus experimentally confirming activation of the canonical NF-kB pathway and demonstrating triggering of the JAK-STAT signaling pathway as well. In silico analysis revealed the presence of NF-kB and Stat binding sites in the A3A promoter. In keeping with these results, BMS-345541 and Jak inhibitor I strongly reduced A3A transcript accumulation elicited by anti-CCL2 Ab treatment. Interestingly, the inhibitor of I kappa B kinase BMS-345541, as well as Jak inhibitor I, blocked STAT1 phosphorylation. Finally, exposure of MDMs to anti-CCL2 Ab resulted in IL-6 induction and interfering with the IL-6/gp130 axis inhibited A3A up-regulation caused by CCL2 neutralization.

Conclusion: These results provide novel insights into the signal transduction pathways regulating A3A expression in primary human macrophages and unravel new mechanisms by which CCL2 may deregulate macrophage antiviral responses and contribute to AIDS pathogenesis. Therapeutic targeting of CCL2 may thus represent an opportunity to strength host innate immunity and restrict HIV-1 replication.

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Immunopathogenesis II

OC 46 ORAL MUCOSAL IMMUNITY IN SARS-COV-2 INFECTED AND/OR VACCINED SUBJECTS

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Background: SARS-CoV-2 transmission mainly occurs through infected secretions such as saliva, respiratory secretions or respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings. Thus, oral mucosal immunity plays a central role in the early defense against SARS-CoV-2 infection. Though SARS-CoV-2 specific antibody response in serum and plasma samples of SARS-CoV-2 infected patients and/or vaccinees has been extensively investigated, the antibody production in saliva and its relationship to systemic antibody levels needs to be further addressed.

Material and Methods: Here, we fine-tuned a neutralization assay (NTA) to titre neutralizing antibody in plasma and saliva samples of 20 SARS-CoV-2 infected (SI), 28 SARS-CoV-2 vaccinated (SV) and 15 SARS-CoV-2 infected and vaccinated (SIV) subjects using the "wild type" SARS-CoV-2 lineage B.1 (EU): results were considered positive if higher or equal to 1:20 serum titre or 1:2 saliva titre.

Results: Results showed that neutralizing antibodies were present in plasma samples from all the tested subjects, with a higher concentration in SIV compared to both SI and SV ($p<0.0001$ for both). In saliva samples, neutralizing antibodies were detected in 7,1% of SV; 45% of SI and 93,3% of SIV and their presence was positively correlated to the concentration of SARS-CoV-2 systemic antibodies ($p=0.0269$).

Conclusions: Based on these preliminary results, we can hypothesize that vaccine alone is unable to induce the production of a consistent oral immunity, but it can help to reinforce the effects of natural infection on antibody production in the oral mucosa. Moreover, antibody response in saliva may serve as a surrogate measure of previous infection.

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Antiretroviral Therapy II

OC 47 ASSOCIATIONS BETWEEN WEIGHT CHANGES AND PLASMATIC PRO-INFLAMMATORY CYTOKINES IN PLWH FOLLOWING ART INITIATION: DATA FROM THE ICONA COHORT

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Background: The mechanisms by which ART contributes to weight gain (WG) are unknown and larger WG has been observed in persons living with HIV (PLWH) treated with integrase inhibitors (INSTI) or protease inhibitors (PI) vs non-nucleoside reverse transcriptase inhibitors (NNRTI). Pro-inflammatory cytokines (IL-6, TNF-a) are affected by ART and are associated with cachexia. We aimed to estimate the impact of INSTI, IL-6 and TNF-a on WG and evaluate how much of the total effect of INSTI on WG might be mediated by IL-6 and TNF-a.

Material and methods: We studied PLWH enrolled in ICONA starting a first-line ART over 2014-2017. Inclusion criteria were: (i) having a stored plasma sample in the year before ART (T0) and at 11-18 months of ART (T1); (ii) weight measurements at T0-T1; (iii) no modifications in anchor class over T0-T1. We measured plasmatic IL-6 and TNF-a at T0-T1 (ELISA assays). Two linear regressions with T0-T1 WG as the outcome were fitted. The first to relate WG to T0-T1 changes in IL-6 and TNF-a, the second to compare mean WG by anchor class (INSTI vs NNRTI, PI vs NNRTI). Criteria for identification of confounders are described in Figure 1. A mediation analysis assuming no interactions was performed to estimate how much of the total effect associated with INSTI initiation (vs NNRTI) on WG might be mediated by changes in IL-6 and TNF-a.

Results: 151 PLWH started a first-line ART in the study period; median age was 50 (IQR 25-75) years, 18 (12%) were females. Baseline median CD4+ count was 358 cells/mmc (IQR 132-576), HIV-RNA was 4.77 log10 cp/mL (IQR 4.11 -5.24). 76 PLWH (50.3%) started INSTI, 38 (15.2%) NNRTI and 37 (24.5%) PI; 21 (20.5%) started DGT, 114 (75.5%) TDF/FTC, 33 (21.8%) ABC/3TC, 4 (2.65%) TAF/FTC.

T0 weight was 72 (61-80) Kg in INSTI, 71 (60-78) in PI and 73 (65-82) in NNRTI (p=0.507).

PLWH who began INSTI and PI gained significantly more weight compared to NNRTI (INSTI: +3.4 Kg, 95%CI 1.7, 5.1; NNRTI: +0.9 Kg, 95%CI -1.5, +1.7; PI: +3.6 Kg, 95%CI 1.4, 5.8; p=.003). Higher WG in INSTI, but not in PI, was confirmed after controlling for HIV-RNA at T0 (Table 1A). Changes in TNF-a and IL-6 were inversely associated with WG in univariable analysis; after controlling for anchor class and HIV-RNA at T0, only IL-6 retained some independent association with WG (Table 1B-C). After decomposing the total difference in T0-T1 WG between patients initiating INSTI vs NNRTI, only 12.7% (95% CI:6.8-62.1) and 9.1% (95% CI:3.5-70.5) of this total effect could be explained by TNF-a and IL-6, respectively (Table 2).

Conclusions: By 1 year from starting ART, our analysis confirms a higher, although not clinically significant, WG in patients who started INSTI instead of other anchor classes. IL-6 was an independent predictor of WG, but only part of the effect of INSTI on WG appeared to be mediated by peripheral inflammation pathways. Further studies are needed to investigate the role of IL-6/TNF-a as potential mediators of WG in PLWH receiving ART.

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Antiretroviral Therapy II

OC 48 WEIGHT GAIN AFTER SWITCHING FROM EFAVIRENZ/EMTRICITABINE/TENOFOVIR DISOPROXIL FUMARATE (EFV/FTC/TDF) TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) IN PATIENT WITH STABLE VIRAL SUPPRESSION

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Background: In naïve patients bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) initiation has been associated with excess weight gain (WG), but little is known about WG in virologically suppressed patients switched to BIC/FTC/TAF. Aim of this study was to evaluate WG after switching from efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) to BIC/FTC/TAF in patients from the EBONY study.
Material and methods: EBONY is a pilot, single-arm, open-label, prospective study evaluating the efficacy and tolerability of switching from EFV/FTC/TDF to BIC/FTC/TAF in HIV-infected patients with stable viral suppression (HIV-RNA <50 copies/mL for at least 24 weeks). WG was defined as an increase of ≥ 3kg or ≥ 5% of weight or BMI over 2 units from switch (baseline, BL) (outcome 1). A more stringent WG definition (≥10% weight increase or BMI ≥30 from BL), identifying "greater gainers" and treatment-emergent obesity, was also used (outcome 2). Paired t-test was used to compare values at week 24/48 with BL. Factors associated with WG were investigated by multivariable logistic regression.
Results: 214 patients were included, 84.6% males, 87.4% Caucasian; median (IQR) age was 53 (45-58) years; median (IQR) duration of HIV infection was 13 (10-18) years. 15% of patients had a previous AIDS diagnosis. Median (IQR) time of exposure to EFV/FTC/TDF was 8.7 (7.0-10.4) years. Median (IQR) CD4 cell count at BL was 602 (502-869) cells/mmc. Mean weight, BMI, glucose and lipid values at BL and week 24/48, and changes were reported in Table 1. Mean WG was +1.4 kg and +2.0 kg at week 24/48, respectively. No clinically significant change in glucose and lipid values was observed. 43% and 13% of patients experienced outcome 1 and 2, respectively. No factor was found to be associated with outcome 1. Conversely, female gender (OR 3.96; 95%CI 1.25-7.49; p=0.015) and not Caucasian ethnicity [OR 2.66; 95%CI 1.01-7.0; p=0.048) were independently associated with outcome 2.
Conclusions: A clinically negligible, although statistically significant, WG was observed after switch from EFV/FTC/TDF to BIC/FTC/TAF in long-term virologically suppressed patients. No clinically significant change was observed for lipid profile and glucose values. Female gender and not Caucasian ethnicity were associated to WG.

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Comorbidities II

OC 49 VIRAL DYNAMICS IN CEREBROSPINAL FLUID OF PATIENTS WITH PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

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Background: Progressive multifocal leukoencephalopathy (PML) is a severe demyelinating disease caused by the polyomavirus JC (JCV) that affects individuals with a compromised immune system. Being PML a rare disease, studies struggle at including large groups of patients. The aim of this study was to describe the JCV-DNA dynamics in cerebrospinal fluid (CSF) of patients with PML in order to find significant prognostic markers of the disease in terms of both radiological evolution and 1-year survival.

Patients and methods: We reviewed 405 cases of PML that were observed or referred to our Department of Infectious Diseases between 1987 and 2021. Patients were included only if they had at least two CSF samples taken less than 90 days apart. Eighty-seven patients were eligible, including 60 patients with HIV infection (69%). JCV-DNA in CSF was measured by real-time polymerase chain reaction. Patients were stratified into three groups based on the variation of JCV-DNA level over time, expressed as the slope, or angular coefficient (AC) of the curve calculated plotting values at two or more time-points: the Increase Group (IG), including patients with AC>10; the Stable Group (SG), including patients with AC between -10 and 10; the Decrease Group (DG), including patients with AC<-10 (Figure 1). The Chi-square and Kruskall-Wallis tests were used to analyze categorical and continuous variables. The log-rank test was used to assess the probability of 1-year survival; univariate and multivariate Cox proportional hazards models to evaluate the association of different variables with survival.

Results: The median variation between first and last sample was >0.5 log c/mL of JCV-DNA in IG and DG, and <0.5 c/mL in SG. During the time between first and last sample there was progression of Magnetic Resonance Imaging (MRI) lesions in 87% of patients of IG, 73% of SG and 50% of DG, but with no statistically significant difference among the 3 groups. In univariate analyses, survival was significantly different among the three AC groups, with patients belonging to IG showing a reduced one-year survival rate compared to either SG or DG (p=0.04). Type of underlying disease at PML onset, presence of MRI enhancement at time of last sampling, or MRI progression were not significantly associated with survival. In a multivariate analysis model including age, gender, JCV-DNA at first sampling, AC group, HIV infection and administration of cART before PML onset, patients with increasing AC and those with HIV infection had reduced survival. However, the negative prognostic effect of HIV infection disappeared in patients under cART (Table 1).

Conclusions: The lack of association between CSF JCV-DNA dynamics and progression at MRI suggests that the viral load changes in CSF may precede MRI changes. The variation of CSF JCV DNA within 90 days from first sampling, but not CSF JCV-DNA level at first sampling, may be a prognostic marker of survival at one year.

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Comorbidities II

OC 50 SWITCHING TO INSTI OFFSETS NEGATIVE EFFECTS OF WEIGHT GAIN ON INCIDENCE OF INSULIN RESISTANCE IN PEOPLE LIVING WITH HIV

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Background: The objective was to explore weight and BMI changes in a large cohort and in the subsets of individuals without diabetes and insulin resistance (IR) at the time of switch to INSTI, in the attempt to identify the cut-off of weight or BMI increase associated with IR incidence in PLWH switching to INSTI.
Methods: This was a longitudinal matched-cohort study including PLWH attending Modena HIV Metabolic Clinic (MHMC), Italy, divided into two groups: INSTI-naive and INSTI-switchers (INSTI-s) matched for similar observation time since entrance in the cohort. The effect of switching to INSTI on percentage of weight and BMI change was tested through a linear mixed model. A mediation analysis was performed to explore the mediation effect of weight and BMI change in the causal path between the switch to INSTI and IR incidence.
Results: We analyzed 2437 PLWH, respectively 1025 INSTI-s and 1412 INSTI-n, in a total of 54826 weight assessments. At the time of switch, median age was 45 years, 70.1% were males, median BMI was 23.3 kg/m2. In the entire cohort, trends for weight (β 0.386, CI95%: 0.216, 0.555, p<0.001) and BMI (β 0.142, CI95%: 0.080, 0.203, p<0.001) increase were significantly higher in early-INSTI-s (vs. early INSTI-n), but the line slopes of weight and BMI changes in late period of the switch were similar to the trends before the switch for both INSTI-s (β 0.036, CI95%: 0.001, 0.072, p=0.053 for weight and -0.012, CI95%: -0.044, 0.020, p=0.761 for BMI) and INSTI-n (β 0.001, CI95%: -0.086, 0.089, p=1.0 for weight and 0.006, CI95%: -0.007, 0.019, p=0.576 for BMI) (Figure 1A, 1D). Trends for weight (β 0.209, CI95%: 0.023, 0.396, p=0.028), but not BMI (β 0.058, CI95%: -0.009, 0.126, p=0.090), showed a significant increase among INSTI-s with TAF (vs. INSTI-s without TAF). In the subset of PLWH without diabetes at T1, trends for weight and BMI change were similar to the previous model (Figure 1B, 1E). In the subset of PLWH without IR at T1, based on 5261 weight assessments, only trends for weight increase (β 0.633, CI95%: 0.079, 1.186, p=0.025) were significantly higher in early-INSTI-s (vs. early INSTI-n) (Figure 1C, 1F). In the same subset, use of INSTI (HR=0.71, CI95%: 0.52, 0.98, p=0.025) had a protective effect on IR incidence. A weight increase by 1% reduced the total protective effect of INSTI by 21.1% over one year of follow-up, allowing us to identify a 5% weight increase as a clinically meaningful weight gain definition.
Conclusion: This study contributes to a data-driven weight-gain definition in relation to IR as a clinically meaningful endpoint. Switching to INSTI in PLWH without pre-existing metabolic abnormalities offsets negative effects of weight gain on IR incidence, confirming INSTI regimens as a metabolically satisfactory option in PLWH.
Funding: The paper received an independent and unconditional grant by Gilead Sciences.

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Virology and Pharmacology I

OC 51 VIROLOGICAL AND SEROLOGICAL CHARACTERIZATION OF SARS-COV-2 INFECTIONS DIAGNOSED AFTER MRNA BNT162B2 VACCINATION

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Background: Coronavirus disease 2019 (COVID-19) vaccines are proving to be very effective in preventing severe illness; however, although rare, post-vaccine infections have been reported. The present study describes virological aspects of 94 infections, occurred in Lazio Region between December 27 and March 30, 2021, after first or second mRNA BNT162b2 dose administration.

Material and methods: In the frame of the Regional Surveillance programme, naso-pharyngeal swabs (NPS) and possibly sera, collected from individuals who resulted positive for SARS-CoV-2 after vaccination are sent to INMI in Rome, Italy, for further laboratory investigation. NPS (n=94) were tested by RT-PCR to estimate viral loads at the time of diagnosis, by NGS or Sanger sequencing in case of low coverage for the full-genome characterization, to characterize the infecting viral strain, and by viral culture to assess the presence of infectious virus. Serological assays, including anti-N IgG, anti-S IgG, and neutralizing antibodies were performed on the available sera (n=50) collected at the time of infection diagnosis. For 79 individuals, a known date of vaccination was reported and they were classified into three groups: Group 1, individuals tested positive 1 to 15 days after first dose; Group 2, 16 to 30 days after first dose; and Group 3, >30 days from first dose, fully vaccination.

Results: The majority of infections observed in vaccinated individuals in this study had a mild or asymptomatic clinical course (97.6%), and those patients with severe symptoms presented pre-existing co-morbidities and age over 85 years. Median viral load at diagnosis was independent from number and time of vaccine dose administration, despite the higher proportion of samples with low viral load observed in Group 3 . More importantly, infectious virus was cultured from NPS collected from both asymptomatic and symptomatic vaccinated individuals regardless to the time from vaccination, suggesting that they can transmit the infection to susceptible people. Most cases (78%) showed infection in presence of neutralizing antibodies at the time of diagnosis, presumably attributable to vaccination, due to the concomitant absence of anti-N IgG in most cases. Sequencing analysis showed that the proportion of post-vaccine infections attributed to Alpha and Gamma variants was similar to the proportion observed in the contemporary unvaccinated population in Lazio region. In addition, mutational analysis did not suggest enrichment of a defined set of Spike protein substitutions depending on the vaccination status.

Conclusion: Our study confirms the overall vaccine effectiveness against the disease, despite caution is still recommended for vaccinated individuals until adequate vaccination coverage of the population is reached. Overall, this study supports the importance of the characterization of host and virus factors associated with vaccine breakthrough infections, that coupled with intensive and continuous monitoring of involved viral strains, is crucial to adopt informed vaccination strategies

Virology and Pharmacology I

OC 52 CROSS-NEUTRALIZATION OF SARS-COV-2 B.1.1.7 AND P.1 VARIANTS IN VACCINATED, CONVALESCENT AND P.1 INFECTED

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Objectives: The emergence of new variants of concern (VOCs) of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) around the world significantly complicated the exit from Coronavirus disease 2019 (COVID-19) pandemic. The aim of this study was to evaluate the serum neutralizing activity of three cohorts.

Methods: BNT162b2-elicited serum (N=90), candidates as hyper-immune plasma donors (N=90) and patients infected with the SARS-CoV-2 P.1 variant (N=25) were enrolled. Plasma donors had SARS-CoV-2 infection within October 2020, so they presumably were infected by wild-type or 20A.EU1 strains of SARS-CoV-2. Three strains of SARS-CoV-2 have been tested: 20A.EU1, B.1.1.7 and P.1. Neutralizing antibodies (NT-Abs) titers against SARS-CoV-2 were evaluated.

Results: the median NT-Ab titer of BNT162b2-elicited serum was 1:80 (1:40-1:80) when serum was tested with 20A and B.1.1.7 strains. However, when the same sera were tested with P.1 strain the median NT-Ab titer was 1:20 (1:10-1:40) (Figure 1A). The median NT-Ab titer was significantly higher for 20A/B.1.1.7 than for P.1 ($p<0.0001$). The mean titer was 3.3-fold higher for 20A.EU1 than P.1 strain.

The median NT-Ab titer of plasma donors was 1:160 (1:80-1:320), 1:80 (1:80-1:160) and 1:20 (1:10-1:40) when serum was tested with 20A, B.1.1.7, and P.1 strains, respectively (Figure 1B). The median NT-Ab titer was significantly higher for 20A than for B.1.1.7 (mean titer 1.6-fold higher) and P.1 (mean titer 6.7-fold higher) ($p=0.0002$ and $p<0.0001$ respectively). Furthermore, the median NT-Ab titer was significantly higher for B.1.1.7 than for P.1 (mean titer 4.2-fold higher) ($p<0.0001$).

Sera from P.1 infected patients showed a median NT-Ab titer of 1:10 (IQR <1:10-1:30, range <1:10-1:80), 1:10 (IQR 1:5 -1:20, range <1:10-1:80) and 1:80 (IQR 1:40-1:320, range <1:10-1:640) when sera were tested with 20A, B.1.1.7, and P.1 strains, respectively (Figure 1C). The median NT-Ab titer was significantly higher for P.1 than for 20A (mean titer 12.2-fold higher) and B.1.1.7 (mean titer 10.9-fold higher) ($p<0.0001$). The median NT-Ab titer was not significantly different for 20A and B.1.1.7.

Conclusions: The impact of VOCs on serum neutralization activity and protection from SARS-CoV-2 (re)infection needs to be further clarified. Various studies have shown different results and come to different conclusions. Our data corroborate the concept that B.1.1.7 and P.1 are less efficiently neutralized by convalescent sera from subjects infected by the original virus. However, BNT162b2 vaccine-elicited human sera have an equivalent neutralization potency on the B.1.1.7 but lower on the P.1 variant. Convalescent P.1 patients are less protected from other SARS-CoV-2 strains.

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Antiretroviral Therapy III

OC 53 EFFECTIVENESS OF LAMIVUDINE + DOLUTEGRAVIR (3TC+DTG) IN PERSONS LIVING WITH HIV (PLWH) STARTING THEIR FIRST ANTIRETROVIRAL TREATMENT

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Background: The GEMINI RCTs have shown in person living with HIV (PLWH) starting their first line ART, the non-inferiority of 3TC+DTG compared to FTC/TDF+DTG up to 96 weeks. Despite these results, due to the inclusion criteria of the trials, it is unclear whether the same efficacy will be seen in subsets of the ART-naïve who are at higher risk of treatment failure (TF) e.g. those with low CD4 count/AIDS, high HIV-RNA and hepatitis co-infection.
Material and Methods: We included PLWH enrolled in ICONA starting a first-line ART based on 3TC+DTG. TF was defined as having experienced a single HIV-RNA>50 copies/mL or a treatment change regardless of the reason in the window 6-12 months from ART initiation (baseline). Characteristics of PLWH who experienced TF and of those who remained free from TF were compared using chi-square test for categorical and the Mann-Whitney test for numerical variables. A logistic regression analysis was used to estimate unadjusted odds ratios (OR) of TF. Adjusted estimates were obtained after controlling for calendar year of baseline.
Results: We included 142 PLWH of the Icona Foundation Study cohort who started 3TC+DTG as their first-line regimen. Overall, 9% were females, 61% acquired HIV through MSM contacts, 25% were of foreign nationality and had a median age of 38 years (IQR:29-47, Table 1). Risk of TF by 1 year was low at 8.5% (12/142, of whom only 4 due to HIV-RNA>50). Most were pro-active switches but 2 which were due to intolerance/toxicity. The prevalence of baseline characteristics identified as potential risk factors for failing 3TC+DTG was low: 5% (n=7) with a CD4 count ≤200 cells/mm3, <1% with AIDS (n=1), 6% co-infected with HCV (n=6) and 17% (n=24) with HIV-RNA of 100,000-500,000 and 1% (n=2) with HIV-RNA>500,000 copies/mL, most likely present in PLWH who experienced TF. Other factors associated with the risk of TF were a delay in ART initiation (higher risk for longer delay, p=0.02) and calendar year of baseline (lower risk in more recent years, p=0.004, Table 1). PLWH with HIV-RNA>500,000 copies/mL (aOR=36.5 vs. 0 -100,000, 95% CI: 1.70-781.8, p=0.02) showed the greatest difference in risk (Table 2). After controlling for calendar year of treatment initiation, among the key risk factors (CD4 count, HIV-RNA, delay in ART initiation, and HCV coinfection) only the association with the latter was considerably attenuated (Table 2).
Conclusions: In our cohort, the risk of failing first line with 3TC+DTG by 1 year was low and mainly driven by pro-active treatment changes. The data show a reluctance by clinicians in real world to start first-line with 3TC-DTG in advanced patients, which resembles the inclusion criteria of the RCTs. Lower risk of TF was seen in PLWH initiating in more recent years. Larger sample size or longer follow-up is needed to re-evaluate the risk of failure in PLWH with CD4 count ≤200 cells/mm3 and/or HIV-RNA>500,000 copies/mL starting ART with 3TC+DTG.
This study is supported by a grant from ViiV HealthCare.

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Antiretroviral Therapy III

OC 54 REASONS FOR CHOOSING A TAF-BASED 3DR INSTEAD OF A DTG-BASED 2DR AS ART SWITCH STRATEGY FOR VIROLOGICALLY SUPPRESSED PLWH IN ITALY

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Background: Tenofovir alafenamide-based triple regimens (TAF-3DR) and dolutegravir -based dual regimen (DTG-2DR) are two recommended strategies for treatment of person living with HIV (PLWH) with HIV-RNA≤50 copies/mL. Multiple studies have shown high efficacy and tolerability of both combinations. Aim of this analysis was to compare patients' profiles associated with a switch to a TAF-3DR versus a DTG-2DR in a cohort of PLWH with current HIV-RNA≤50 copies/mL.

Methods: We included PLWH from the ICONA Foundation Study cohort who achieved a HIV-RNA≤50 copies/mL (VS) on ART after Jan/2017 and in whom the regimen was subsequently changed to TAF-3DR or DTG-2DR (DTG plus lamivudine [3TC] or DTG plus rilpivirine [RPV]). A cross sectional analysis was performed to compare participants' characteristics at the time of switch. Logistic regression models were used to show the odds ratios (OR) of switching to DTG-2DR vs. TAF -3DR.

Results: 4,291 PLWH were included: n=3,882 (90%) who switched to a TAF-3DR [mostly to RPV/F/TAF (39%) and EVG/c/F/TAF (29%)] and n=409 (10%) to the DTG-2DR group (86% to 3TC+DTG and 14% to DTG+RPV). Selected participants' characteristics are shown in Table 1. Overall, 81% were male with a median age of 46 years (IQR, 37-53) and a median CD4 count of 693/mmc (512-901), 41% had achieved VS on their first-line treatment. TDF- and ABC-based ART before switch were 25% and 46% in DTG-2DR group vs. 90% and 7% in TAF-3DR group, respectively. From fitting a logistic regression model, PLWH who used ABC in the previous regimen [aOR 5.46 vs. TDF (95%CI 4.18, 7.15); p<0.001], had switched more recently [aOR 3.33 per more recent year (95% 2.88, 3.86); p<0.001], had a diagnosis of cardiovascular disease (CVD) [aOR 2.35 vs. no CVD (95% CI 1.16, 4.78); p=0.018], higher levels of total cholesterol at the time of switch [aOR 1.37 per 100 mg/l higher (95% CI 1.02, 1.86); p=0.038] higher CD4 count at the switch [aOR 1.06 per 100 cells/mm3 higher (95% CI 1.01, 1.10); p=0.009] were more likely to be switched to a DTG-2DR regimen. In contrast participants who were enrolled in the South of Italy (vs. North) [aOR 0.32 (95% CI 0.16, 0.63); p=0.001], were less likely to be switched to a DTG-2DR (Figure 1). All other factors considered (listed only at the bottom of Figure 1) did not show an association with the type of switch.

Conclusions: Our real-world data show that the characteristics of PLWH appear to influence the choice of switch therapies at HIV-RNA ≤50 copies/mL. In this setting, in addition to switches that might be partially triggered by cost-saving decisions (e.g. the presence of ABC in previous regimen), other strategies appear to be consistent with the indications coming from the results of recent clinical trials. In particular, among other findings, switches to DTG-2DR based regimens appeared to be enriched in participants showing CVD comorbidities or in those in whom high levels of total cholesterol had been detected.

The project has been partially supported by a Gilead Sciences Medical Grant

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Antiretroviral Therapy III

OC 55 AN ITALIAN NON-INTERVENTIONAL RETROSPECTIVE AND PROSPECTIVE STUDY IN HIV-POSITIVE ADULT OUTPATIENTS TREATED WITH D/C/F/TAF: THE DIAMANTE STUDY

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Background: Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) is a single-tablet regimen based on the protease inhibitor DRV [1]. The high genetic barrier provided by boosted-DRV based regimens ensures a virological suppression also in case of sub-optimal treatment adherence [2].

Material and methods: DIAMANTE is a non-interventional retrospective/prospective study carried on in 18 Italian centers, enrolling HIV-positive adults outpatients treated with D/C/F/TAF as per clinical practice. The patients enrolled in this study belonged to 3 groups: Group1, including patients always treated with a DRV-based ART; Group2, patients switching to D/C/F/TAF from a non DRV-based ART; Group3, naïve patients starting D/C/F/TAF ART at least one month before enrollment. Four visits were scheduled during the study. The primary endpoint was the effectiveness of D/C/F/TAF based treatment, measured as virological suppression at V4 by FDA snapshot algorithm. Due to COVID-19 pandemic statistical plan has been revised extending the V4 (48W±6) window to 8 weeks as per real practice. The safety has been assessed collecting all the AEs, SAEs, ADR, SADR and special situations occurred during the study, started in 2018; the last patient has been enrolled on 09/2019. Three populations have been described: safety (Sp), all patients enrolled in the study; ITT (ITTp), all evaluable patients; and PP (PPp) all patients that during the study did not have protocol violation.

Results: Two-hundred-forty-six patients (Sp) have been enrolled: 81 in Group1, 43 in Group2 and 122 in Group3. Three patients have been excluded from this analysis due to inclusion criteria violation (ITTp).

The last patient last visit was completed was in September 2020. The effectiveness of D/C/F/TAF-based ART measured at V4 by FDA snapshot algorithm and virological response is shown in Figure 1 for ITTp and PPp. Visit schedule of 50 out of 243 (21%) patients was impacted by COVID-19 pandemic: V4 for 40 patients fell into the new range of 2 months; 6 virologically suppressed patients were lost to FU at V4; 4 did not have HIV-RNA measured at V4.

Two-hundred AEs in 246 patients were reported, 158/200 were considered not drug-related. Twenty-one SAEs in 12 patients have been reported, 3/21 lead to study discontinuation. The most frequent AEs reported during the study were hypovitaminosis D (N=9) and hypercholesterolaemia (N=3)

Conclusions: COVID-19 pandemic has impacted study conduction changing visit schedule. Despite that, the ART based on D/C/F/TAF has assured high virological response and good tolerability profile confirming the efficacy and tolerability of DRV-based STR.

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Antiretroviral Therapy III

OC 56 PREVALENCE, CHARACTERISTICS AND OUTCOME OF HEAVILY TREATED EXPERIENCED (HTE) HIV-INFECTED PATIENTS: DATA FROM THE ITALIAN ICONA COHORT

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Background: New regimens are becoming available for heavily treated patients with reduced therapy option. Thus, it becomes important to determine the prevalence and characteristics of this population in the present cART scenario of very potent and safe drugs. We aim to analyse the prevalence as well as the virological and clinical outcomes of heavily treated experienced (HTE) patients who could be eligible for fostemsavir (FTV).

Methods: We included all participants of the Icona cohort with ≥1 clinical visit in 2009-2019. HTE were defined according to the antiretroviral and viro-immunological history (Def1) in participants with unsuppressed or stable HIV-RNA (Def2) who could be eligible for FTV (Fig1A). Prevalence of HTE has been calculated overall and stratified by year and gender. Among HTE, Kaplan-Meier method was used to estimate the cumulative probability of virological failure >200 copies/mL (VF) and of a clinical endpoint including AIDS, severe non-AIDS events (SNAEs by NADC-START definition) and death.

Results: A total of 200/ 13,285 (1.5%) patients were defined as HTE (Fig 1B). Of these, 85 participants satisfied the definition of HTE eligible for FTV (Fig1C). At the last clinical visit, 11/85 (12.9%) had unsuppressed HIV-RNA and 74 were virologically stable but compromised. Main patients' characteristics at baseline, by HTE status are shown in Table 1. Overall, the prevalence of HTE was 0.64% (95%CI 0.51-0.69), and, looking at the different calendar years, it declined from 1.15% (0.82-1.56) in 2009 to 0.68% (0.52-0.87) in 2019. A higher prevalence has been identified in females vs. males (OR=2.82; 95%CI 1.85-4.37).

43/85 of HTE subjects (50.6%) experienced a VF over follow-up; the estimated risk of VF was 43.8% (95% CI 32.9-54.7) by 3-years. The composite endpoint of clinical progression or death was experienced by 23 (27.0%) HTE patients (8 AIDS, 13 SNEAs and 2 deaths), with a cumulative probability of 33.4% (20.6-46.2) by 10-years.

Conclusions: In the era of effective and safe cART regimens, few patients (0.64% of our cohort) satisfy the definition of HTE eligible for FTV therapy. Actually, the prevalence of HTE is declining over calendar year. Although a minority, this population is at high risk of virological failure and clinical progression and new effective therapeutic options are needed.

This study is supported by a grant from ViiV HealthCare.

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Antiretroviral Therapy III

OC 57 BIC/FTC/TAF IS EFFECTIVE ON PLWH WITH LOW CD4 COUNTS: REAL-LIFE DATA FROM THE ICONA COHORT

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Methods: Observational study of patients enrolled in the Icona cohort starting BIC/FTC/TAF as first line or switch ART. Naïve PLWH were defined as late presenters (LP) with CD4<350 and/or AIDS and very-late presenters (VLP) with CD4<200 and/or AIDS. Virologically controlled ART-switching subjects were evaluated according to CD4 cell count at switch (< or>= 350 cells/mmc). Primary endpoint was treatment failure (TF) defined as treatment discontinuation (TD) for any reason or virological failure (VF, 2 consecutive HIV-RNA > 200 copies/ml or 1 HIV-RNA >1000 copies/mL after 6 months for ART-naïve). Statistical analyses included descriptive statistics, and standard survival analysis. Cox-regression models were used to investigate the role of LP/VLP (ART-naïve) and the role of CD4 at switch (ART-experienced) on the risk of TF.

Results: 310 ART-naïve and 1115 virologically controlled ART-experienced patients included (Table1).

ART-Naïve PLWH: median HIV-RNA 4.96-log10 copies/ml (4.39-5.56), median CD4 290 cells/mmc (103-496), 178 subjects LP (57.4%) and 124 VLP (40.0%). In median follow-up of 7.5 months, 38 patients underwent TF (12.2%). TF occurred in 21 LP (11.8%) vs 17 non-LP (12.9%) p=0.77 and in 16 VLP (12.9%) vs 22 non-VLP (11.8%), p=0.78 Out of 38 TF, 4 were VF and 34 were TD; main reasons for TD are showed in Table2A.The overall 1-year probability of TF was 13.2% (95%CI 9.1-19.0). In the Cox regression models after adjusting for HIV-RNA, sex, Italian and mode of HIV transmission there were no significant differences in the risk of TF both for LP (vs non-LP aHR=1.24; 95%CI: 0.61-2.50) and VLP (vs non-VLP aHR=1.76; 95%CI: 0.87-3.56).

ART-experienced PLWH: median CD4 703 cells/mmc (505-933), 120 PLWH had CD4 < 350 cells/mmc (10.8%). In a median follow-up of 13.3 months, 89 PLWH underwent TF (8.0%). 11 events occurred among subjects with baseline CD4 < 350 cells/mmc (9.2%) and 78 (7.8%) among PLWH with CD4>=350 cells/mmc, p=0.61. Out of 89 TF, 12 were VF and 77 as TD, main reasons for TD are showed in Table2B. Overall the 1-year probability of TF was 4.9% (3.7-6.5). In the Cox regression models after adjusting for calendar year of first cART, CD4 nadir and duration of viral suppression, having a CD4 cell count <350 at switch did not affect the risk of TF (aHR=1.29, 95%CI 0.62-2.69).

Conclusions: In this observational real-life setting BIC/FTC/TAF was given to LP in around 60% of cases. This regimen was effective in PLWH with low CD4 both at first and at second lines; a longer follow-up is needed to confirm its effectiveness for VLP. Toxicities and simplification are the main reasons for TF in both lines of ART.

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Antiretroviral Therapy III

OC 58 ART SWITCH FOR PRO-ACTIVE, RE-ACTIVE OR COST-SAVING REASONS: A REAL WORLD EVALUATION OF THE DETERMINANTS OVER THE PERIOD 2017-2020 IN THE VENETO REGION

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Background: ART is for life and with the advent of simpler and more tolerated regimens in recent years an increasing proportion of persons living with HIV (PLWH) undergo treatment switches (TSw). Generally, TSw occur for "pro-active" reasons, such as to prevent long-term toxicity, reduce drug-drug interactions, simplify therapy, and improve adherence, or for re-active reasons typically driven by ongoing toxicities or treatment failure. In addition, ART may be switched for cost saving reasons in absence of other triggers. We aimed to identify patients' profiles more frequently associated with pro-active or re-active TSw vs. those due to cost-saving reasons.

Methods: We included a random samples of patients who underwent a TSw in 6 outpatient's clinic for HIV care in the Veneto Region over 2017-2020. For PLWH who underwent more than one TSw in the same calendar period, only the first of these TSw was included. TSw were classified as i) pro-active (TSw-1), ii) re-active (TSw-2) and iii) cost-saving (TSw-3). The proportion of type of TSw by calendar period were described. We also calculated the frequency of TSw according to participants' characteristics at time of switch and compared them using a chi-square test. A multinomial logistic regression was used to evaluate the association between a selected number of participants' characteristics and the probability of switching for pro-active or re-active vs. cost-saving reasons. Separate multivariable models were fitted for each of the characteristics after controlling model-specific confounding variables.

Results: We included 405 TSw occurring in the same number of unique PLWH. Demographic and clinical characteristics are reported in Table 1. TSw-3 were more prevalent in 2019-2020 (29%) vs. 2017-2018 (17%) when the TSw-1 were more frequent (34% vs. 22%) (p=0.004). The most prevalent TSw regimen was 3TC-DTG (33% of TSw-3, 31% of the TSw -1 and 12% of TSw-2). In the TSw-2 group, 14% switched to TAF/FTC/RPV, 12% to ABC/3TC/DTG and 10% to TAF/FTC/DRV/Coci. Compared to TSw-3, factors associated with TSw-1 were: dyslipidaemia (30% vs. 7%, p<0.001), TDF in previous regimen (40% vs 18%) and DTG in previous regimen (21% vs. 43%). Of note, 53% of PLWH previously on TDF were switched to a Descovy-based regimen and 55% of those previously on ABC were switched to 3TC-DTG for cost-saving reasons. Factors associated with TSw-2 vs. TSw-3 were: no. of tablets in previous regimen (2 vs. 1), ABC in previous regimen (23% vs 43%) and DTG in previous regimen (12% vs. 43%, Table 1). Associations remained strong after controlling for confounding factors (Table 2).

Conclusions: In our analysis, cost-saving TSw appeared to be most prevalent in recent years. Pro-active TSw appeared to be mainly driven by detection of dyslipidaemia and previous use of TDF (50% were switched to TAF). In contrast, use of DTG very infrequently led to pro-active or re-active changes and ABC was mainly replaced with the aim of reducing costs.

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Antiretroviral Therapy III

OC 59 SWITCHING TO EMTRICITABILE/TENOFOVIR ALAFENAMIDE/BICTEGRAVIR ON METABOLIC AND HEPATIC SAFETY: PRELIMINARY DATA FROM SURVEILLANCE COHORT LONG-TERM TOXICITY ANTIRETROVIRALS/ANTIVIRALS (SCOLTA) PROJECT

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Background: Our aim was to investigate the role of switching to Emtricitabile/Tenofovir Alafenamide/Bictegravir (FTC/TAF/BIC) on metabolic and hepatic safety in a real life setting.
Material and methods: Consecutive patients with HIV infection enrolled in SCOLTA project switching or initiating FTC/TAF/BIC were included. T0 and T1 were defined as results at baseline and 6-month follow-up respectively.
Results: 316 people living with HIV (PLWH) initiating FTC/TAF/BIC were enrolled. 245 (77.5%) were male, 42 (13.3%) were naive to combination antiretroviral treatment (cART).
At T0 main characteristics were (mean ± standard deviation [SD]) the following: age 48.8 ±11.8 years, CD4 cell count 644 ±345 cell/µL, BMI 25 ±4.3 kg/m2, total cholesterol (TC) 191.2 ±42.9 mg/dL, HDL cholesterol (HDL-c) 49.1 ±16.3 mg/dL, glucose 97.1 ±25 mg/dL. Triglycerides [TRG] median value 114 mg/dL (interquartile range [IQR] 81-173), AST 23.0 U/L (IQR 19-29), ALT 22.5 U/L (IQR 17-32).
At T1, 113 PLWH completed follow-up: 97 were experienced (14 patients with detectable viral load) and 16 naïve to cART. 53 PLWH (46.9%) were switched from FTC/TAF/elvitegravir/cobicistat (ELV/COBI), 14 (12.4%) from FTC/TAF/dolutegravir (DTG) and 30 (26.6%) from other regimens.
Main characteristics at T1 were: mean age 48.4 ±12 years, CD4 cell count 634 ±347 cell/µL, BMI 25.6 ±3.9 kg/m2, TC 192.5 ±43.3 mg/dL, HDL-c 49.6 ±12.5 mg/dL, glucose 97.6 ±31.1 mg/dL. Median TRG 114 mg/dL (IQR 91-170), AST 23.0 U/L (IQR 19-28), ALT 23 U/L (IQR 18-32).
83 (85.6%) of experienced PLWH and 12 (75%) of naive PLWH had HIV-RNA < 50 copies/mL.
At T1 eleven (11) experienced PLWH had HIV-RNA >50 copies/mL: three PLWH had HIV-viral load ≥ 200 copies/mL.
At T1, experienced PLWH showed a significant variation in TRG (mean change -20 ± 62.2 mg/dL, p=0.003) and glucose (+5.67 ± 19.5 mg/dL, p=0.01)
Splitting for previous regimen, patients that were on FTC/TAF/DTG had a significant variation in TC (+15,6 ± 26.4 mg/dl, p=0.05) and HDL-c (+2.5 ± 3.9 mg/dL, p=0.04) while PLWH that were on FTC/TAF/ELV/COBI experienced significant changes in TC (-15,1 ± 26.8 mg/dL, p=0.0003), TRG (-29.2 ± 39.9 mg/dL, p<0.001), glucose (+6.4 ± 19.7 mg/dL, p=0.03). Excluding 5 PLWH with diabetes' diagnosis at T0, no significant change in glucose in PLWH previously on FTC/TAF/ELV/COBI were found.
In naive PLWH the following significant changes were observed at T1: TC (+23 ± 33.9 mg/dL, p=0.03), HDL-c (+8.7 ± 12.9 mg/dL, p=0.03), AST (-19.3 ± 27.1 U/L, p=0.04)
Four PLWH interrupted treatment: one for muscular pain, one for piastrinopenia, two for central nervous system adverse events (1 insomnia, 1 nervousness)
Conclusions: Experienced PLWH switching to FTC/TAF/BIC improved their lipid profile, especially if previous treatment was FTC/TAF/ELV/COBI. A trend to increase of TC and HDL-c was found in PLWH with FTC/TAF/DTG as previous treatment. No impact on AST/ALT was observed.

Virology and Pharmacology II

OC 60 EVALUATION OF FACTORS POTENTIALLY ASSOCIATED WITH LOW-LEVEL VIREMIA IN PLWH FROM THE ITALIAN ARCA COHORT: A MATCHED CASE-CONTROL STUDY

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Background: ART is able to effectively suppress plasma HIV-RNA to an undetectable level in most HIV-infected people. However, a subset of PLWH on ART still experience a persistent low-level-viremia (LLV); but its cause remains a challenging issue for clinicians. Thus, the present study aimed to investigate the impact of pre-existing drug resistance and other factors on PLWH with LLV compared to those who maintain viral suppression (VS).

Materials and methods: A matched case-control study design was used. We selected ART-experienced subjects from ARCA database followed in the period 2009-2019, and with at least one plasma genotypic resistance test (GRT) for protease/reverse transcriptase and integrase (when available). Cases (LLV) were subjects who had at least one episode of LLV after at least 6 months of VS, defined as having at least two consecutive viremia values between 50 and 1000 cps/mL; controls (VS) included patients with viremia <50 cps/mL since 6 months, for at least as long as the median duration of the period of observation (OP) of LLV in the cases. The beginning of OP was defined as baseline (BL). Once cases were identified, eligible controls were matched 1:1 to the cases by calendar year of the first therapy and by drug class-based regimen at BL. The pre-existing drug resistance was measured by cumulative GSS score that was calculated based on the regimen at BL and treated as a binary variable (GSS <2 and ≥2). To explore the effect of cumulative GSS score and other factors on LLV, a logistic regression analysis was performed.

Results: A total of 552 PLWH (276 cases and 276 controls), mainly Italians, heterosexuals, and infected by HIV-1 subtype B were analysed (Table 1). Median (IQR) nadir and BL CD4 count (cells/mm3) were 172 (58-280) and 570 (373 -768), respectively; median (IQR) zenith and BL viremia (cps/mL) were 5.0 (4.1-5.5) and 1.4 (1.2-1.6), respectively. They started their first therapy in 2000 (1997-2008), the time from first regimen to BL was 11 (3-16) years. A high percentage of them (72.5%) had a GSS ≥2. Compared to controls, cases showed higher median age, higher proportion of non-Italians, longer time since HIV diagnosis, lower CD4 cell count nadir and a higher zenith and BL viremia. By evaluating factors potentially associated with LLV, at multivariate analysis we found that age (AOR [95% CI]: 1.32 [1.08-1.62], p=0.008), non-B subtype (1.87 [1.14-3.05], p=0.012), zenith viremia (1.51 [1.34-1.71], p<0.001) and number of drugs previously administered (1.07 [1.01-1.13], p=0.016) independently predicted LLV. No association of cumulative GSS and LLV was found.

Conclusions: In ART-experienced PLWH the presence of pre-existing drug resistance, i.e. having a cumulative GSS score <2 (not fully active regimen) did not affect LLV. These data also suggest that age, pre-therapy viral load (zenith), harbouring a non-B subtype and exposure to a largest number of drugs are associated with an increased risk of occurrence of LLV.

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Virology and Pharmacology II

OC 61 DISTRIBUTION OF TENOFOVIR PLASMA TROUGH CONCENTRATIONS IN PLWH TREATED WITH DORAVIRINE

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Background: Consistent evidence is available in literature showing that coadministration of cobicistat or ritonavir resulted in significantly higher tenofovir concentrations and higher tenofovir disoproxil fumarate (TDF) discontinuation compared with other antiretroviral regimens.
Studies in healthy volunteers have shown that concomitant administration of doravirine (DOR) had no meaningful effects on the pharmacokinetics of tenofovir from TDF. However, data in people living with HIV (PLWH) are still lacking. Here, we sought to compare the pharmacokinetics of tenofovir in PLWH treated with DOR versus other TDF-based antiretroviral regimens in a real-life setting.
Material and methods: PLWH receiving TDF-containing antiretroviral regimens for at least 3 months and with at least 1 assessment of tenofovir plasma trough concentrations were included in the study. The distribution of tenofovir concentrations was stratified according to the main antiretroviral drug classes as follows: DOR, PIs/ritonavir or cobicistat, NNRTIs, INIs and ELV/cobicistat. The reference range for tenofovir trough concentrations adopted in our center was 40 -180 ng/mL.
Results: 50 PLWH concomitantly treated with TDF/3TC and DOR were identified. They were mostly men (74%), with mean age of 48±11 years, optimal immuno-virologic control (98% had HIV viral load <20 copies/mL; CD4+: 723±232 cells/mL), and a preserved renal function (serum creatinine: 0.9±0.2 mg/dL). Patients' demographic and clinical characteristics were comparable to those from PLWH (n=533) treated with other TDF-based antiretroviral regimens.
Overall, a wide distribution in the tenofovir plasma trough concentrations was observed, with values ranging from 10 to 783 ng/mL. As shown in the Figure, the highest tenofovir concentrations were measured in PLWH given ELV/COBI (n=82; 167±126 ng/mL; 24% of assessments >180 ng/mL) or PI/ritonavir (n=218; 146±124 ng/mL; 24% of assessments >180 ng/mL), being significantly higher than values measured in patients given INIs (n=53; 112±70 ng/mL; 10% of assessments >180 ng/mL), NNRTIs (n=180; 108±62 ng/mL; 11% of assessments >180 ng/mL) or DOR (104±42 ng/mL; 6% of assessments >180 ng/mL).
Co-administration with DOR was also associated with a reduced interpatient variability in the tenofovir trough concentrations (40%) compared with other regimens (PI/ritonavir: 85%; ELV/cobicistat: 75%; INI: 63%; NNRTI: 57%).
Discussion: Concomitant administration of DOR resulted in significantly lower tenofovir concentrations compared with boosted-based antiretroviral regimens, and a reduced interpatient pharmacokinetic drug variability compared with all other TDF-based antiretroviral regimens. Less than 10% of PLWH treated with DOR had tenofovir concentrations above the safety threshold of 180 ng/mL, posing indirect, preliminary pharmacokinetic-driven evidence for a potential less renal toxicity of this novel co-formulation.

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Virology and Pharmacology II

OC 62 SNP-168 OF THE PROTEIN KINASE AND CD4 OR CD8 DYNAMIC IN HIV-1 PATIENTS

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Background: Protein kinase R (PKR) may be activated during virus infection and thus plays a pivotal role in the regulation of protein synthesis in infected cells. TAR-RNA binds to and activates PKR, thus leading to the inhibition of protein synthesis and controlling HIV replication.
Objective: To evaluate the role of variant alleles SNP-168 of the promoter region of a double-stranded RNA (dsRNA)-dependent PKR in shaping the dynamics of CD4 and CD8 counts in patients living with HIV (PLWH)
Methods: Clinical data of HIV-1 infected patients were collected since year 2005 (baseline BL evaluation) as part of routine clinical care and recorded in the database of the Division of Infectious Diseases of the San Raffaele Hospital (CSLHIV Cohort). Single nucleotide polymorphism at position -168 of the PKR promoter was investigated by means of direct sequence analysis. Latent class mixed effects models were estimated to model longitudinally measured immunologic biomarkers while accounting for nonlinearity of the outcome variable. In the initial model the following covariates were entered: gender, age, duration of the infection, AIDS diagnosis, co-infection with hepatitis C, risk factor for HIV-1 infection, SNP-168, CD4 nadir and ARV treatment. The time of measurement was also considered along with a time updated categorical version of HIV-1 load (VL) time updated (VL zero, e.g, equal to 0.9; residual, e.g., 0.9-49 cp/mL; >50 cp/mL but lower than 595 cp/mL, which is the median value of the detectable VL over time; >595 cp/mL). The final model was obtained using backward procedures.
Results: Demographic and clinical baseline characteristics of 95 HIV-1 patients are reported in Table 1. Patients had in median, 35 repeated measurements for CD4 and 29 for CD8. AIDS diagnosis and age were negatively associated with the outcome CD4 cells count (p=0.008 and p=0.004, respectively). Patients with higher levels of viral load (higher than the median value, 595 cp/mL) showed lower CD4 cells count (p<0.0001), compared to those having VL zero (reference category). Moreover, CD4 cells count significantly increased over time but only in patients with SNP-168 CT variant (p<0.0001). Patients with CT variant showed on average higher CD8 cells count, (p=0.011). CD8 cells count was positively and significantly related to HIV load.
Conclusions: The SNP -168, clinical characteristics and HIV load dynamic seemed to influence the immunological status of HIV-1 infected patients.

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Virology and Pharmacology II

OC 63 INTERPATIENT VARIABILITY IN THE PHARMACOKINETICS OF THE REMDESIVIR AND MAIN METABOLITE GS-441524 IN TREATED COVID-19 SUBJECTS

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Background: Remdesivir (RDV) is a pro-drug of the nucleoside analogue GS-441524. RDV is the first antiviral drug against SARS-CoV-2 approved for use in hospitalized COVID-19 patients. Nevertheless, data from clinical trials failed to give definitive results on RDV effectiveness in treating COVID-19. Aim of this work was to study the pharmacokinetic (PK) of RDV and its main metabolite GS-441524 in a real-world setting of COVID-19 patients, and to identify possible associations with different demographic,biochemical and virological factors.

Method: SARS-CoV-2 positive hospitalized patients, undergoing RDV treatment, were prospectively enrolled. RDV was intravenous (IV) administered at 200 mg loading dose on the first day followed by 5 or 10 days of 100 mg. Blood samples were collected on day 4, immediately (C0) at 1 (C1), and 24 (C24) hours after administration. RDV and GS -441524 concentrations was measured using a validated UHPLC-MS/MS method and the Area Under Curve (AUC) was calculated.

At baseline, the COVID-19 severity [intensive care unit (ICU) or no-ICU], sex, age, renal (eGFR) and liver (ALT) functions were assessed. One week after the end of treatment (EOT), SARS-CoV-2 RNA was evaluated in nasopharyngeal swabs. Mann-Whitney and Pearson rank tests were used for statistical comparisons.

Results: Seventy-nine patients were included, 70.8% of subjects showed a SARS-CoV-2 RNA negative NP swab after EOT. The mean and CV% of RDV were: C0 2737 (97.2) ng/mL, C1 136.8 (283.6) ng/mL and AUC 2740 (182.7) h*ng/mL and undetectable at 24 h after IV. The mean and CV% of GS-441524 were: C0 90.6 (51.0) ng/mL, C1 104.6 (48.0) ng/mL, C24 58.7 (68.7) ng/mL, and AUC 1976 (54.3) h*ng/mL.

PK data from COVID-19 patients showed a similar level but higher CV% than those described by manufacturer for a population of healthy adults. The univariate regression model showed no statistically significant associations between RDV PK parameters and all variables evaluated (figure 1 panel A). Of note, statistically significant correlations between GS -441524 plasmatic exposure vs age or renal function were observed; in particular, age directly correlated with AUC and with all-time points, while the eGFR at baseline inversely correlated with GS-441524 AUC and with all-time points (figure 1 panel B).

At EOT, patients with SARS-CoV-2 RNA negative swabs showed a slight higher AUC ($p=0.03$), C0 ($p=0.02$), C1 ($p=0.04$) and C24 ($p=<0.04$) of GS-441524 when compared with persistent SARS-CoV-2 RNA positive patients.

Conclusion: Our results showed a high interpatient variability of RDV and GS-441524 that can be at least partially due to age and renal function in COVID-19 patients. Moreover, RDV metabolite exposure appears to affect viral clearance. Further research is mandatory to identify other factors that may influence the PK of RDV and its metabolites, in order to define possible host factors potentially affecting the efficacy of RDV treatment.

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Virology and Pharmacology II

OC 64 TEMPORAL TREND OF DRUG-RESISTANCE AND APOBEC EDITING IN PBMC GENOTYPIC RESISTANCE TESTS ON ISOLATES WITH CONTEXTUAL UNDETECTABLE HIV-1 PLASMA VIRAL LOAD PERFORMED FOR CLINICAL ROUTINE

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Background: In the context of treatment optimization, the usage of genotypic resistance test (GRT) on PBMC has been increased in clinical practice, especially in subjects with poor information about previous resistance. However, no data about temporal trends of resistance in PBMC compartment are available. Moreover, information retrieved from HIV-DNA are useful to explore the extent of APOBEC editing in PBMC and evaluate its potential temporal fluctuations. Thus, the aim of this study is to evaluate the temporal trend of drug-resistance and APOBEC editing in the context of suppressed viremia.
Material and methods: We included 1141 protease (PR)/reverse-transcriptase (RT) and 693 integrase Sanger GRTs on PBMC from 1030 HIV-1 infected virologically suppressed individuals. GRTs were performed for clinical routine over the period 2010-2020. Major resistance mutations (MRM) to PI, NRTI, NNRTI and INI and the presence of APOBEC-related mutations (APO-M) were evaluated over time according to Stanford HIVbd version 9.0. APO-M related to stop codons and to drug resistance mutations were considered.
Results: At GRT, patient's characteristics [median (IQR)] were: age: 50 (42-56) years; time of previous virological suppression: 46 (8-102) months; number of regimens previously experienced: 4 (2-7); nadir CD4 count: 176 (60-296) cells/mm3; zenith viremia: 5.3 (4.7-5.7) log10 copies/mL. At GRT, the majority of isolates (63.8%) was from individuals receiving a 3-drugs based regimen (26.8% PI-, 22.8% NNRTI- and 14.2% INI-based), while, 16.7% of isolates were from individuals receiving a dual regimen. Concerning resistance, 36.9% of isolates harboured at least one MRM (8.2% to PI, 24.8% to NRTI, 20.0% to NNRTI and 0.6% to INI). Resistance to 1, 2 and at least 3 classes was detected in 23.3%, 10.0%, 3.6% of isolates, respectively, while 63.1% of isolates did not show any resistance. Concerning APOBEC-editing, 16.0% of isolates harboured APO-M related to drug resistance, while in 6.7% APO-M related to stop codons in PR/RT were detected.
In general, resistance prevalence to PI, NRTI, NNRTI and INI was stable over time, though a slight decrease was observed in 2020 for NRTI and NNRTI resistance (Figure Panel A). Similarly, no significant differences in the prevalence of resistance to 1, 2 and at least 3 were observed in the observation period (Figure panel B). Stable trends were also found by considering the prevalence of APO-M, as both mutations associated with resistance and stop codons (Figure panel C).
Conclusions: In isolates from HIV-1 virologically suppressed individuals, resistance in PBMC and the extent of APOBEC editing were stable in the last decade. The low and stable prevalence of APOBEC related stop codons underlines that Sanger DNA GRT provides information with acceptable reliability to manage treatment switch in individuals under virological control.

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Epidemiology / Social Sciences IV

OC 65 INTEREST IN INJECTING LONG-ACTING AGENTS BY PEOPLE LIVING WITH HIV IN ITALY: A PICTURE FROM THE ICONA NETWORK

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Background: Long-acting formulations of antiretroviral therapies (ART) can deliver drugs that can last for months, freeing people from daily regimens of pills, and will enter soon in clinical routine. The aim of this study is to understand reasons for people living with HIV (PLWH) to ask for an injecting Long-Acting agents (iLAA).
Methods: an online anonymous survey of PLWH on ART was conducted through ICONA Network sites and Patient Group websites between February and April 2021. The HIV Treatment & Diseases Burden has been investigated with a questionnaire containing 31 items -in 7 domains- with 5-point Likert scale answers from 1 (lowest burden) to 5 (highest burden), adapted from DT Eton et al, Qual Life Res 2017. Data were analysed using descriptive statistics. Weighted mean and linear regression models with weights were used to evaluate the differences according to interest in iLAA, overall in the HIV Treatment & Diseases Burden and in each domain of the questionnaire.
Results: 580 PLWH completed the questionnaire, 86% male, 14% female, mean age: 48 years (±11), 87% declared an undetectable HIV-RNA (8% unknown current HIV-RNA). Other characteristics are shown in Table1. Subjects interested in iLLA were younger (p<.001), with a higher education level (p=0.02), with more recent HIV diagnosis (p<.001), afraid to disclose serostatus (p=0.002) with a higher proportion of subjects without comorbidity (p<0.001) and not completely satisfied with the ongoing ART (p<.001). There were no differences in the overall 'HIV Treatment and Diseases Burden' and in the different domains between the two groups (Table2). While analysing the single items, subjects interested in iLLA declare higher issues in their daily organization for taking ART (p=0.026), were more bothered by having to rely on the ART medications (p<.001) and more frequently felt frustrated by their HIV status (p=0.041).
Conclusions: Young age, recent HIV diagnosis and disclosure issues seem to profile the patient most interested in taking iLLA in the future. Overall treatment and diseases burden does not seem to have a significant impact on preference, except for some aspects related to daily organization and the constrain of ARV therapy.

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Epidemiology / Social Sciences IV

OC 66 MILAN FAST TRACK CITY: STUDY ON HIV PREVALENCE IN TWO DIFFERENT SETTINGS

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Rationale: we aim to compare the prevalence of HIV among subjects with risky behaviors attending the Milan check-point to be screened for HIV and among patients screened for HIV because hospitalized for HIV-indicator diseases (HIV-ID), in Milan.

Methods: Two different data-sets, both prior to COVID-19 epidemics (affecting HIV testing due to lockdown):
- the check-point data-set, including all individuals undergoing HIV testing at Milan check-point from February 1st, 2019 to January 31, 2020.
- the ICEBERG study, including all the patients with HIV-IDs (Raben et al, 2019) hospitalized at San Paolo hospital in the same calendar period.

Data on age, sex and nation of birth were collected. Risky behaviors were collected for the check-point group, HIV-ID for the Iceberg group. CD4, HIV-RNA and AIDS were collected in HIV pos individuals of both settings.

Results: In February 2019-January 2020 a total of 1,271 subjects attended the check-point to be tested for HIV and 381 were tested for HIV because hospitalized for 458 indicator diseases (HIV-IDs): 314 (82.4%) presented with 1 HIV-ID, 57/381 (15.0%) with 2, and 10 (2.6%) with 3.

Patients with HIV-ID were more frequently males, non-Italian and older than check-point ones (Table 1).

Overall, HIV was detected in 15/1,271 (1.2%) persons tested for HIV at the Milan check-point, and in 15/381 (3.9%) patients with HIV-IDs (P<.001), with 10/15 of the latter group being AIDS-presenters. In detail, HIV was detected in 8/314 (2.5%) individuals with one HIV-IDs, 2/57 (3.5%) with two and 5/10 (50%) with three HIV-IDs (P<.001). Table 2 shows the prevalence of HIV in relation to risky behaviors (2a-check-point group) or HIV-ID (2b-Iceberg group).

8/ 237 iceberg patients with STD diagnosis were HIV positive (3.4%), but after restricting to the 205 subjects that had STDs and no other HIV-IDs, the prevalence dropped to 1% (n=2), similar to check-point one.

Among the subjects diagnosed with HIV, those diagnosed for HIV-ID were older, less frequently males, less frequently MSM. While CD4 counts were lower in the Iceberg patients, mostly below 200 cells/ml, HIV-RNA were high in both population, indicating the high risk of transmitting the infection in both settings (Table 3).

Conclusions: Even if the prevalence of HIV among subjects tested for risky behaviors is around 1%, it reached the 2.1% among MSM, and was even higher in a setting of patients hospitalized for selected indicator-diseases (3.9%). Subjects unaware of HIV are spreading the virus since many years and constitute a possible source of maintaining HIV in the population. In contrast, widespread virologically effective ART and PrEP could constitute a curb to HIV circulation in persons with risky behaviors.

As fast track city initiative, it's crucial to pursue the HIV prevention campaigns both in subjects with risky behavior and in those who do not perceive themselves currently at risk, and are not targeted by Milan Checkpoint initiatives.

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Epidemiology / Social Sciences IV

OC 67 IMPACT OF COVID-19 ON HIV TESTING AND COUNSELLING SERVICES IN LAZIO REGION

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Background: HIV testing and counselling is the gateway for people to reach HIV treatment, care, and the full range of prevention options, for other sexually transmitted infections as well. The COVID-19 pandemic has required rapid adaptation of health systems, at a scale never previously witnessed, and, according to a recent survey of WHO, HIV/hepatitis health services are among the most extensively affected by the COVID-19 pandemic. Many people, particularly key populations, may have experienced further reduced access to testing and other essential services than before the pandemic.

Setting: Lazio Region, including the metropolitan area of Rome, has the highest incidence of HIV in Italy. Local HIV policies, updated in 2018, ask every health district to implement one or more public HIV testing and counseling sites (HTCS) to offer HIV/STI screening, based on a global approach to prevention. Presently, 27 public HTCS are recognized: 15 are departmental facilities for prevention services (DPS) and 12 are in AIDS clinical centers (ACC) providing comprehensive inpatient and outpatient medical care to people living with HIV. All the HTCS are in a network coordinated by the Regional AIDS Reference Center (RARC) of the National Institute for Infectious Diseases L. Spallanzani, in order to refer and promptly link persons to appropriate HIV care.

Methods: A survey was conducted in July 2020-March 2021 among the Lazio HTCS to investigate the local impact of COVID-19 pandemic on utilization of HTCS. Key questions comprised the quantitative impact, from March to May 2020, on HIV testing volume (compared with the same period in 2019) and measures put in place to address such an unexpected challenge.

Results: 22/27 (81.5%) HCTS responded to the survey. 10 were ACC (4 located outside Rome, and 6 within the city), and 12 were DPS. 13 of respondent stated that HCTS personnel and resources were involved in COVID care (8 ACC and 5 DPS); 3 of them stated their services had been closed and 10 that were functioning only on an appointment basis.

Number of attenders and HIV tests undertaken by HTCS in 2020, as compared with the same period in 2019, decreased significantly (-50% and -36%, respectively), mainly in HTCS of ACC ($p<0,001$), many of them disproportionally involved in COVID-19 management. No difference was observed in the proportion of new HIV diagnoses between 2020 and 2019 (0.9% for both periods).

Conclusions: The COVID-19 pandemic has had considerable impact on the accessibility to HCTS with a presumable effect on the continuum of HIV prevention, early diagnosis and linkage to care. With the COVID-19 pandemic still spreading, HIV testing should be routinely offered in all settings and with different approaches to reach all people, especially key populations.

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Epidemiology / Social Sciences IV

OC 68 ESTIMATION OF THE PROPORTION OF PEOPLE LIVING WITH HIV IN ART AND VIRALLY SUPPRESSED, USING SURVEILLANCE AND COHORT DATA. ITALY, 2012-2019

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Background: The progress of the United Nations Programme on HIV/AIDS (UNAIDS) "90-90-90" target needs to be systematically monitored. To this purpose, the European Centre for Disease Prevention and Control (ECDC) carried out projects to implement standardized methodologies to obtain such estimate, relying on public health surveillance data and HIV study cohorts.

Our aim was to estimate, for the years 2012-2019, based on an approach already published (Gourlay et al. CID 2017; https://doi.org/10.1093/cid/cix212), the last two 90s, that is the proportion of people living with HIV (PLHIV) who: ever initiated ART and was virally suppressed.

Material and Methods: According to the methodology used, PLHIV whoever initiated ART were defined as ever treated, regardless of treatment guidelines, antiretroviral drug regimens or number of drugs, treatment interruptions or discontinuations, and subjects having at the last visit of the year a viral load ≤200 copies/mL as virally suppressed. We used data from ICONA Foundation cohort study, weighted using official data obtained from Italian National HIV surveillance system in order to adjust for the different distribution of age, sex, country of origin, transmission mode, and CD4 cell count at diagnosis. The methodology used allowed the production of high and low estimates (when considering or not those lost to follow-up) and preferred estimates were the mid-point between the high and low estimates.

Results: Preferred estimate of proportion of PLHIV ever treated increased steadily from 74.6% in 2012, to 93.4% in 2019 (Fig.1 A). Notwithstanding a moderate lower proportion on ART among males and foreign born PLHIV in the first years, from 2017 onwards this target was reached without difference according to country of origin and gender. Regarding transmission mode, only people who inject drugs (PWID) had a wide range estimate, and the preferred estimate never reached the 90%. Among PLHIV ever treated, the preferred estimate of PLHIV virally suppressed increased overall from 86.6% in 2012 to 92.3% in 2019 (Fig.1B), reaching the 90% target starting from 2015. However lower proportions of virally suppressed were found for females and foreign born PLHIV and, again, for PWID who never reached the 90% target.

Conclusions: In Italy, global estimate of the last two UNAIDS targets, increased steadily from 2012 to 2019. The achievement of the 90% of PLHIV ever treated seems assured from 2017 onwards and of virally suppressed PLHIV from 2015 onwards. Only the proportions for PWID reaching the two outcomes remained lower than 90% throughout the entire period examined, and the proportion of virally suppressed in females, foreign born and PWID still needs to be improved to reach the 90% target. Our finding suggests an overall effective ART coverage but the need of public efforts toward retention in care of selected subpopulations.

Project funded by Minister of Health - CCM.

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Epidemiology / Social Sciences IV

OC 69 PREVALENCE OF HIV INFECTION IN THE PIPSA PROJECT CARRIED OUT IN LUANDA, ANGOLA. DATA ANALYSIS BY SEX AND AGE GROUP

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Introduction: In recent years, great improvements in the response to HIV/AIDS have been made, and the numbers of new HIV infections and AIDS-related deaths have declined. However, in recent times, countries, including Angola, have experienced an increase in HIV prevalence. HIV prevention programs reduce the risk of new infections; an important part of prevention is treatment; when taken consistently reduces the risk of illness among PLWHA, and viral load to undetectable level that prevents HIV sexual transmission.
Since 2017 Angola has joined the WHO "Test and Treat" strategy. To support the country in overcoming these challenges, the PIPSA project implemented an “HIV prevention/test/treat" program carried out in a hospital, four health posts and four health centers in the municipality of Kilamba Kiaxi, Luanda.
Objective: To assess overall and stratified HIV prevalence among the active sexual age group (18-47 years) using data from the PIPSA project.
Methods and materials. The PIPSA project has recruited and trained ten activists who informed and tested daily in the centers. Testagem was preceded by group counselling, and result was delivered through individual counseling.
HIV test was performed with Determine and Unigold tests.
Data were analysed using Chi Square test, Fisher’s exact test, R 4.0 (R Foundation for Statistical Computing).
Results: A total of 24,860 subjects (67% F and 33% M) were tested from November 2018 to October 2020, HIV prevalence was 4.3% (95% CI 4.1 to 4.6%).
21,192 subjects, 85.2%, were 18-47 years old, HIV prevalence was 4.1% (95% CI 3.8 to 4.3%), data from age and sex subgroups are reported in Table 1 and 2.
Conclusions: In this study, HIV prevalence was 4.3%, higher than the official country data of 1.9% (UNAIDS 2020); either because data come from people intercepted at the health centers, therefore not in good health, or for a real increase in HIV spreading in the country.
In people aged between 18 and 47, the prevalence was 4.1%; in this group the prevalence increases significantly in each subgroup, from 1.5% to 9.2% (p <0.0001); this may be due to: people increase sexual activity over time but not the use of condoms; older people may have had less access to information; and possibly polygamy.
When comparing men, women and pregnant women, a difference in HIV prevalence was found in the subgroup aged 18 -27 years, higher among pregnant women (p <0.0001); it may be due to: beginning of sexual activity, obviously without condom use; women are more likely to contract the infection; gender gap in sex negotiation.
The data presented need to be validated by more extensive investigations; they are still very important to set up secondary prevention campaigns that take into consideration target groups.
The PIPSA (Integral Protection of Seropositive People in Angola) project is funded by Agenzia Italiana per la Cooperazione e lo Sviluppo and is carried out by Unione Medico Missionaria Italiana and CUAMM - Medici con l'Africa.

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Epidemiology / Social Sciences IV

OC 70 HIGH PREVALENCE OF MENTAL HEALTH DISORDERS IN HIV POSITIVE ADOLESCENTS AND YOUTHS: AN OBSERVATIONAL STUDY FROM 8 HEALTH SERVICES IN BEIRA DISTRICT, MOZAMBIQUE

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Introduction: Adolescent mental health is a significant public health concern, which is extremely relevant when referring to adolescents living with HIV. Adolescence is a critical phase of physical, emotional and social changes, which may impact adherence to HIV care and ART. Mozambique has contemporary 52% of its population aged under 18y and the world's 8th highest HIV prevalence. Notably, 120,000 HIV-positive adolescents live in the country. In order to better understand the proper intervention to deliver, we performed an observational study to evaluate anxiety, depression, post-traumatic stress disorder and alcohol-drug abuse in adolescents and youth assessing health services in Beira district, Mozambique.

Methods: From 20 November 2019 to 20 June 2021, all adolescents and youth (10-24y) accessing one of the psychological services offered at 8 Servicios Amigos dos Adolescentes (SAAJ) of the Beira District, were screened by a trained psychologist using the following standardized tools: GAD-7 for anxiety, PHQ-9 for depression, PC-PTSD-5 for post-traumatic stress disorder, CAGE-AID for alcohol -drug abuse.Data from the psychological consultation were recorded on an open-source platform (Kobo Tool). HIV positive and negative subjects were compared and characteristics potentially associated with anxiety status (GAD-7>10), depression (PHQ-9 11), post-traumatic stress disorder (PTSD-5 3) and substance abuse (CAGE 2) were evaluated using a multivariable logistic regression model.

Results: Overall, 1,811 adolescents and youth were included in the study (63% F, median age: 19 years [IQR:16-21]). Of them, 934 (52%) were HIV positive. When comparing scores of HIV positive subjects to negative ones, the median values were: 6 (IQR:4-9) vs 3 (IQR:1-6) for GAD-7, p-value<0.01; 5 (IQR:3-7) vs 3 (IQR:1-5) for PHQ-9, p-value<0.01; 1 (IQR:1-2) vs 0 (IQR:0-1) for PTSD-5, p-value<0.01; 1 (IQR:1-2) vs 0 (IQR:0-1) for CAGE, p<0.01.

The multivariable logistic regressions showed a greater probability to be GAD-7>10 for women vs men [(AOR): 1.46, 95% CI: 1.01-2.10, p-value=0.042], for workers vs unemployed (AOR: 2.18, 95%CI: 1.12-4.23, p-value 0.022) and for people HIV+ vs negative (AOR: 1.78, 95%CI 1.25-2.54, p-value<0.01). Also, women and workers had greater probability (AOR:1.67, 95%CI: 1.11-2.50, p-value 0.013 and AOR:2.80, 95%CI: 1.33-5.92, p-value 0.007, respectively) to score 11 at PHQ-9. Higher values of CAGE (2) and PTSD (3) seemed to be associated only with HIV positive condition (AOR:4.87, 95%CI: 3.72-6.38, p-value<0.01 and AOR:1.73, 95%CI: 1.28-237, p-value<0.01, respectively).

Conclusion: In our study, the first to our knowledge investigating HIV adolescent mental health in Mozambique, HIV positive adolescent and youth had the worst scores of all the administered mental health screening tools. According to our results, public health policies and intervention targeted to the metal health of this fragile group should be addressed with priority.

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Epidemiology / Social Sciences IV

OC 71 HIGH PREVALENCE OF ASYMPTOMATIC SARS-COV2 INFECTION IN THE COHORT OF LIVER TRANSPLANT RECIPIENTS AT INMI SPALLANZANI

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Asymptomatic subjects account for approximately 25% to 45% of SARS-CoV-2 infections, and in particular, subjects on mild immunosuppressive therapy may have had the symptoms masked and spread the virus for an extended period.
A prospective clinical and serosurvey study was conducted in a cohort of 278 liver transplant recipients (LTR) in Rome, Italy, to determine the cumulative incidence of symptomatic and asymptomatic COViD-19 cases and evaluate both clinical features and associated risk factors. Three serologic tests were performed each on 259 LTRs.
Two different ELISA tests, one based on raw extract of whole- SARS-CoV-2 virus and another on specific viral antigens (N and S proteins), were used to detect specific IgG, IgM and IgA.
Twelve COVID cases were identified through standard screening procedures (molecular testing in case of symptoms or exposition to COVID-19 cases) and 7 of whom were asymptomatic. SARS-CoV-2 serology screening allowed also to diagnose an unexpected asymptomatic case and 17 subjects with a previously treated/cured infection.
SARS-CoV-2 cases were mainly (78.3%) diagnosed during the second semester of epidemic that reflected the epidemic curve in Italy.
The COVID-19 cases in our cohort were not categorized according to gender, age, obesity, diabetes, renal impairment, type of antirejection therapy nor to the span of time since the transplantation. Asymptomatic cases were compared to symptomatic cases and classified/organized by male gender and age range.
In conclusion, combining standard diagnostic protocols with repeated serology it increased the cumulative incidence of SARS-CoV-2 infection from 5.1% to 10.9% in our LTR cohort, while/whereas a minor number of asymptomatic subjects (6%) were found to carry Sars-Cov2 in respiratory tract at the moment of serologic diagnosis.

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Antiretroviral Therapy I

OP 1 REAL-LIFE EXPERIENCE WITH DOLUTEGRAVIR-BASED TWO-DRUG REGIMENS

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Background: Two-drug regimens (2DR) with dolutegravir (DTG), with either lamivudine (3TC) or rilpivirine (RPV) are considered a innovative, effective and well tolerated therapeutic strategy in people living with HIV (PLWH). Aim of this study is to describe a cohort of patients switching to DTG containing 2DR.
Materials and methods: Single center, observational, retrospective study including all patients treated with a DTG-based 2DR, in combination with either 3TC or RPV, in the period 2016-2021. A descriptive analysis of the cohort was performed and resistance-associated mutations (RAMs) were recorded. Significant RAMs were defined according to the International Antiviral Society-USA (IAS-USA), which includes, for 3TC the presence of K65R/E/N or M184V/I and, for RPV, the presence of L100I, K101E/P, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188L, H221Y, F227C or M230I/L.
Results: One-hundred and seventy-five PLWH were enrolled. Characteristics of the study population are shown in Table 1. The median age was 60 years (IQR 54-64), also including two youth patients (9 and 11 years-old, respectively). 26% of patients were previously diagnosed with AIDS and 42% had experienced virological failures before switching to 2DR. The median time since HIV diagnosis was 19 years (IQR 9-24), with a median time of ART of 19 years (IQR 9-24). At the time of switch to 2DR, the median CD4 were 686/mmc (IQR 519-941); one hundred thirty-five patients (77%) had HIV-RNA ≤ 50 copies/mL; 5 patients (3%) had HIV-RNA between 50 and 200 copies/mL; 8 patients (5%) switched to 2DR after virological failure (HIV-RNA > 200 copies/mL). Among PLWH with available GRT, 19% of PLWH in the DTG+RPV group had at least one relevant RPV-RAM, and 4% in the DTG+3TC group had at least one relevant 3TC-RAM; no significant DTG-RAM was reported. None of the PLWH harboring RAMs experienced virological failure over a median follow up of 114 (IQR 72-189) weeks. 2 patients discontinued therapy during the period of observation, one in the DTG+3TC group and one in the DTG+RPV group. Reasons for discontinuation were virological failure (1 patient, DTG+RPV group) and patient's preference (1 patient, DTG+3TC group); there were no reports of adverse events overall.
Conclusions: In this cohort of highly experienced PLWH, switching to DTG-based 2DR was safe and well tolerated. Despite the presence of significant RAMs in a non-negligible proportion of patients and 8% of therapeutic switches in patients with HIV-RNA > 50 copies/mL, we report a low rate of discontinuations due to virological failure. Considering the need for lifelong antiretroviral therapy, 2DR might be a suitable option in terms of tolerability and also in different settings than the one highlighted in clinical trials.

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Antiretroviral Therapy I

OP 2 COMPARISON OF EFFICACY AND TOLERABILITY OF DOLUTEGRAVIR / RILPIVIRINE OR DOLUTEGRAVIR / LAMIVUDINE IN EXPERIENCED HIV-1 POSITIVE PATIENTS SWITCHED FROM A THREE-DRUG REGIMEN BASED ON NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS IN A SINGLE CENTER IN ITALY

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Background: Clinical studies show that switching to DTG/RPV or DTG/3TC once daily is effective and well-tolerated. However, a head-to-head comparison between DTG plus RPV or 3TC is missed in trials, and real-life data is limited. Notably, specific data about patients who switched from a standard 3-drug regimen based on 1 NNRTI (Non-Nucleoside Reverse Transcriptase Inhibitor) + 2 NRTI (Nucleoside Reverse Transcriptase T-Inhibitor) is lacking.
Objectives: To compare the efficacy, tolerability, and discontinuation rate due to all causes of two-drug therapy based on DTG/3TC or DTG/RPV in a population of HIV-1 positive patients (PLHIV) who switched from a standard 3-drug regimen based on 1 NNRTI + 2 NRTI with HIV-RNA <50 copies/mL.
Methods: A single-centre cohort retrospective study was carried out on all PLHIV with HIV-RNA <50 copies/mL, over 18-year-old in care at the Azienda Ospedaliera Careggi (AOU) switched to DTG/RPV or DTG/3TC from any three-drug NNRTI-based regimen
Results: Of the 79 patients included in the study, 40 (50.6%) took DTG/3TC while 39 (49.4%) took DTG/RPV. The follow-up time was 62.97 py in the DTG/3TC and 64.99 py in the DTG/RPV group. Cisgender men were 64 (81.0%). The median age was 55 years (IQR 49-59 years). Sixty-nine (87.3%) were Italian. Thirteen (16.5%) had an AIDS diagnosis. The median nadir of CD4 was 307 cells/µL [IQR 187-460], the median zenith of HIV-RNA 5.04 copies/mL Log10. No differences in the baseline clinical/demographic characteristics were observed (Table 1). Notably, about half of the patients in both groups had more than three lines of treatment. The most frequent pre-switch therapy was TAF/FTC/RPV in both groups, taken by 22 (53.6%) in the DTG/3TC group and 28 (66.8%) in DTG/RPV group. Overall, 9 patients (11.4%) discontinued the treatment: 2 in the DTG/RPV arm and 7 in the DTG/3TC arm (log-rank p= 0.0654). We observed only one confirmed failure in 3TC/DTG arm and no adverse event above grade 2. The patient with virologic failure (VF) had no resistance mutations at baseline for study drugs. The discontinuation rate ratio for DTG/RPV compared to DTG/3TC adjusted for gender, age origin, cumulative number of the previous regimen was HR 0.16 [95% CI 0.03-1.05; p= 0.056]. We did not observe any significant difference in CD4 counts, renal function, and lipid parameters in the two treatment groups from the baseline to the 24 and 48 weeks.
Conclusion: The results of this study showed that treatment with a two-drug regimen of DTG/3TC or DTG/RPV in clinical practice is characterized by a low rate of VF and a high rate of viral suppression in pre-treated PLHIV with HIV viremia <50 copies/mL. However, multi-treated PLHIV, virologically suppressed by taking an ART regimen based on NNRTIs who switch to DTG/3TC show a tendency to discontinue more than those who switch to DTG/RPV. This result needs to be confirmed on extended series.
Support: The study was conducted with unconditional support from ViiV Healtcare

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Antiretroviral Therapy I

OP 3 EFFICACY AND SAFETY OF SWITCHING FROM EFAVIRENZ/EMTRICITABINE/TENOFOVIR DISOPROXIL FUMARATE (EFV/FTC/TDF) TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) IN VIROLOGICALLY-SUPPRESSED HIV PATIENTS (EBONY STUDY)

S. Cicalini, P. Lorenzini, E. Grilli, S. Ottou, M.M. Plazzi, F. De Zottis, M. Camici, M. Fusto, R. Gagliardini, R. Bellagamba, A. Antinori
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Background: Aim of this study was to evaluate efficacy and safety of switching from efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) given once daily (QD) or on alternate days (QOD), to bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) in HIV-suppressed patients from the EBONY study.
Materials and methods: EBONY is a pilot, 48-week, single-arm, open-label, prospective study in which patients with stable viral suppression (HIV-RNA<50 copies/mL for >24 weeks) on EFV/FTC/TDF QD or QOD, without drug resistance mutations (DRM) or history of previous virological failure were switched to BIC/FTC/TAF. HIV-RNA and HIV-DNA levels, immunological parameters, renal function and metabolic profiles were monitored. Estimated glomerular filtration rate was evaluated by CKD-Epi. Virological rebound (VR) was defined as two consecutive HIV-RNA ≥50 copies/ml. Treatment failure (TF) was defined as VR or treatment discontinuation (TD) and time-to-TF was estimated by Kaplan-Meier method. Factors associated with TF were investigated by multivariate Cox regression.
Results: 234 patients were enrolled; 190 completed week 48. At switch (baseline, BL) 84.2% of patients were males, 87.6% Caucasian, 47.9% MSM. Median (IQR) age was 52 (45-58) years. Median (IQR) duration of HIV infection was 13 (10-18) years, 14.4% of patients had a previous AIDS diagnosis. Median (IQR) time of exposure to EFV/FTC/TDF was 8.8 (7.0-10.4) years. 69.7% of patients switched from EFV/FCT/TDF QD and 30.3% from EFV/FTC/TDF QOD. Only 2/234 (0.8%) patients experienced VR and 5/232 (2.2%) experienced TF. No patient developed DRM. The 1-year probability of TF was 2.3% (95%CI 1.0-5.6). No factors were associated with TF. Mean HIV-DNA, CD4/CD8 counts, glucose, lipid and renal values at BL and week 24/48, and changes are reported in Table 1. CD4 count significantly increased over time. A modest but statistically significant increase in creatinine level was observed at week 24/48 (p<0.001 for both), while the proportion of patients with proteinuria remained stable. No clinically significant changes in lipids were observed. There were no adverse events leading to discontinuation of study drug.
Conclusions: Our preliminary data showed that switching from EFV/FTC/TDF to BIC/FTC/TAF was highly effective and safe with 99% viral suppression and significant increase of CD4 cell count. A mild increase in blood creatinine was observed, probably due to the inhibition of OCT2 by BIC.
This study was funded by a Gilead Sciences Inc. unrestricted grant

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Antiretroviral Therapy I

OP 4 EFFICACY AND TOLERABILITY OF A SWITCH TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE IN VIRALLY SUPPRESSED PLWH

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Background: Since bictegravir (BIC)/emtricitabine (FTC)/tenofovir alafenamide (TAF) has been authorized from the Italian Medicines Agency in June 2019, our institute has established a prearranged switch from elvitegravir/cobicistat (EVG/c)-based regimens in virally suppressed PLWH and, based on a case-by-case evaluation, from other regimens. Aim of this study was to define the efficacy and tolerability of BIC/FTC/TAF in a real-life setting.

Methods: Retrospective cohort study including PLWH who switched to BIC/FTC/TAF while with HIV-RNA <50 copies/mL and having at least one HIVRNA value within 12 months after switch. Virological failure (VF) was defined as two consecutive HIV-RNA ≥50 copies/mL or a single HIV-RNA >400 copies/mL. Treatment failure (TF) included VF or discontinuation for any reason. Data are reported as median (IQR). Probabilities of VF or TF were estimated by Kaplan-Meier curves.

Results: 974 people were enrolled (characteristics in Fig.1 Panel A). At availability of BIC/FTC/TAF, most patients on treatment with EVG/c/FTC/TAF were switched [N=678 (69.6%)]. Switches to BIC/FTC/TAF from different regimens [N=296 (30.4%)] were due to: treatment simplification (83.7%), toxicity (9.5%), other causes (6.8%).

During 10,249 person-months of follow-up (PMFU), 71 TF occurred for an incidence rate of 6.9 [95% confidence interval (CI) 5.3-8.5] per 1000-PMFU. The estimated 6- and 12- month probabilities of TF were 4.3% (95%CI 3.2-5.9) and 7.7% (95%CI 6.0-9.2) (Fig.1 Panel B). TF occurred after a median of 5.2 months (IQR 3.1-9.6) for: simplification to dual therapy (14%), CNS toxicity (17%, overall incidence 1.2%), other toxicity (24%), other causes (12.7%), death (5.6%), and VF (30.9%, overall incidence 2.3%).

VF occurred after a median of 5.8 months (IQR 3.1-11.1) and the median HIV-RNA was 76 (63-130) copies/mL. The cumulative probabilities of VF were 1.2% and 2.1% at 6 and 12 months, respectively (Figure 1 Panel B). Of 18 VF, eight (44%) occurred in PLWH who already experienced at least one VF with previous regimens. In ten cases (56%), after two consecutive HIV-RNA ≥50 copies/mL (eight cases) or a single HIV-RNA >400 copies/mL (two cases), HIV-RNA spontaneously returned <50 copies/mL maintaining BIC/FTC/TAF; in four cases (22%) undetectability was achieved after a switch; four cases are under management for poor treatment adherence. It was possible to obtain results of genotypic resistance testing in four cases: no one highlighted resistance mutations to InSTIs and NRTIs. TF and VF occurrence did not change significantly according to the regimen used before BIC/FTC/TAF.

Conclusions: In a large sample of suppressed PLWH followed in a real-life setting, one-year cumulative probability of BIC/FTC/TAF treatment failure was low (7%) with 2% of virological failure, suggesting that the switch is effective and safe.

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Antiretroviral Therapy I

OP 5 EFFICACY, SAFETY AND FEASIBILITY OF A RAPID ANTIRETROVIRAL THERAPY STARTING B/F/TAF IN ADVANCED HIV DISEASE (RAINBOW STUDY)

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Background: A rapid ART initiation in subjects with advanced HIV disease could improve the outcomes. Data on this strategy are lacking. The primary endpoint of Rainbow study was to evaluate time-to-clinical or virologic failure in enrolled patients. The w24 interim analysis of the study is shown.

Material and Methods: Pilot, monocentric, single-arm, prospective, phase IV clinical trial enrolling 30 ART-naïve subjects presenting at HIV-1 diagnosis with an advanced disease described as the presence of an AIDS-defining event and/or CD4 cell count <200 µL. Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg was started within 7 days from HIV diagnosis. Exclusion criteria were: CrCl < 30 mL/min, severe hepatic impairment, active tuberculosis, cryptococcosis, pregnant/breastfeeding women, systemic cancer chemotherapy. BL resistance genotype was unknown before ART initiation.

Results: Among 116 new HIV diagnosis at INMI Spallanzani from May 2020-January 2021, 40 (34%) had advanced HIV disease. 30 fulfilled eligibility criteria for this study and were enrolled. Major reasons for being ineligible were time needed to exclude active tuberculosis or a delay in referral HIV diagnosis. The included patients presented similar clinical characteristics to those not enrolled. 16.7% were female, 90% caucasian, median age 45yrs (38-58), the most prevalent risk factor was heterosexual intercourse (33%). 43% presented CDC stage C: 7 Pneumocystis pneumonia, 5 Kaposi's sarcoma, 1 HIV-associated encephalopathy. At BL median CD4 cells was 90 cells/µL (39-147), CD8 499 (357-940), CD4/CD8 ratio 0.14 (0.09-0.24), HIV RNA log10 cp /ml 6.0 (5.4-6.4), HIV DNA log10 cp /106 PBMC 4.1 (3.8-4.4). Median days from the first HIV test to BL were 6 (5-7). 40% of patients had ≥ 1 comorbidity and 1 (3.3%) was HCV coinfected.

Proportion of participants with HIV-RNA < 50 copies/mL increased during the observational period. It was 9/26 (35%) at w4, 19/30 (63%) at w12 and 16/18 (89%) at w24 (Figure 1). To date, all participants have achieved virological response (HIV-RNA reduction > 1 log 10 copies/ml) at W12 and no viral rebound was observed. The proportion of partecipants with CD4 > 200 cells/µL was 2/30 (7%) at BL, 14/23 (61%) at w4, 17/29 (59%) at w12 and 9/19 (47%) at w24 (Figure 2). During the 24w follow-up, no ART discontinuation was observed due to toxicity or virological failure and no ART modification was performed once GRT was reviewed [no NRTI mutations, 3 accessory INSTI mutations (E157Q, G163K, L74I)].

SAE were: 1 IRIS+ PML (week, w4), seizures (w4 and w12), all in the same patient, a clinical worsening/suspected IRIS (w4) and a disseminated tuberculosis + IRIS (w2), that needed an ART switch.

Conclusions: Preliminary results of Rainbow study provide the first evidence supporting the feasibility of B/F/TAF test and treat strategy in advanced HIV subjects.

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Antiretroviral Therapy I

OP 6 EFFECTIVENESS, SAFETY AND TOLERABILITY OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (B/F/TAF) IN PEOPLE LIVING WITH HIV (PLWH) IN ROUTINE CLINICAL PRACTICE: 6-MONTH RESULTS OF THE ITALIAN BICSTAR COHORT

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Background: BICSTaR is an ongoing, multinational, prospective cohort study in HIV-1 treatment-naïve (TN) or treatment-experienced (TE) adults receiving B/F/TAF in routine clinical care. Real-world data on virologic and safety parameters are being collected. Here we present the preliminary month 6 (M6) results from the Italian cohort (GS-EU-380-4472).
Material and methods: M6 evaluation included data from PLWH with either a M6 visit at time of data cut-off (Feb -2021) or an early termination prior to M6. Outcomes of interest were viral suppression (HIV-1 RNA <50 copies/mL using a missing/discontinuation=excluded analysis), drug-related non-serious and serious adverse events (DRAEs, DRSAEs) and treatment persistence.
Results: A total of 97 PLWH (8 TN, 89 TE) were analyzed: 81% male; 42% ≥50 years of age. Baseline demographic and HIV-related characteristics are shown in Table 1. Comorbidities were documented in 65% of participants, with 51% receiving concomitant medication. Comorbidities (in ≥10%) included hyperlipidemia (31%), osteopathic disorder (20%), hypertension (18%), and other cardiovascular disorders (10%).
TE participants had a median of 3 previous antiretroviral regimens (Q1, Q3 [2.0, 6.0]); 20% had a history of virologic failure, 13% harbored major resistance-associated mutations (RAMs); 97% were on suppressive ART prior to switch, most commonly elvitegravir/cobicistat/F/TAF (55%), dolutegravir+F/TAF (12%) and rilpivirine/F/TAF (8%).
Of participants with available HIV-1 RNA data at M6 (n=85), HIV-1 RNA was <50 cp/mL in 6/6 (100%) TN and in 79/79 (100%) TE participants. No major RAMs to components of B/F/TAF emerged.
M6 retention in the study and persistence on B/F/TAF was 96% (1 drug-related B/F/TAF/study discontinuation [due to DRAE] and 1 study discontinuation due to participant decision; 2 cases were lost to follow-up). There was no discontinuation due to renal, hepatic or bone AEs.
Overall, 6 DRAEs (no DRSAEs) were reported in 4 (4%) participants (one leading to B/F/TAF discontinuation). At M6, the median weight change in TE participants was 0.1 kg (Q1, Q3 [-1.0, +2.0]) (n=28). A weight gain of > 5% and >10% was reported in 2 and 0 TE participants, respectively. Median BMI change in TE was 0.0 kg/m2 (Q1, Q3 [0.4, +0.7]) (n=28).
Conclusion: Consistent with randomized controlled trials and other national BICSTaR cohorts, preliminary data from this real-world Italian cohort confirmed the well-established safety profile of B/F/TAF. B/F/TAF also demonstrated high virologic effectiveness and treatment persistence in this population of PLWH characterized by multiple treatment changes and in some cases history of virologic failure with major RAMs.

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Comorbidities / Miscellaneous

OP 7 MARAND-X: CLINICAL TRIAL ON THE USE OF LESS NEUROTOXIC ANTIRETROVIRALS IN HAND

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Background: Despite a high prevalence (30-50%) HIV-associated neurocognitive disorders (HAND) pathogenesis is incompletely understood and antiretrovirals (ARV) neurotoxicity has been suggested as a potential mechanism. We designed a pilot, randomized, prospective, single-blind clinical trial to assess changes in neurocognitive function in people living with HIV (PLWH) with HAND randomized to a less neurotoxic ARV regimen (darunavir/cobicistat, maraviroc, emtricitabine: "MARAND") or to continue their treatment.

Method: PLWH were screened from clinical records and subsequently studied with an array of 23 neuropsychological (NPS) tests and lumbar puncture: only PLWH with HAND, on efavirenz/darunavir-free ARV regimens, with R5-tropic infection susceptible to MARAND and HIV-RNA <50 copies/mL on both plasma and CSF were enrolled. After 1:1 randomization, NPS tests were repeated after 24 weeks. A Global Deficit Score was calculated as average of the deficit scores of the following NPS tests: Rey Figure Copy, Rey Figure Delayed Recall, Digit Span Backward, Trail Making A, Frontal Assessment Battery. Resting state electroencephalography (rsEEG) waves were analyzed through the LORETA©® freeware at both study time points. Data are expressed as median (interquartile range). Non-parametric tests (Mann-Whitney and Wilcoxon's) were used. Variables difference between two time points (delta) was calculated. Planned sample size was 76.

Results: In June 2020 the study was prematurely terminated for slow accrual when 38 participants were enrolled and 28 completed the follow-up. Male (75%) and European ancestry (89%) were prevalent: median age was 56 years (7.5); median CD4+ count was 706 cell/μL (413). Baseline characteristics were similar between study arms. We did not measure a significant change in GDS within both study arms (MARAND arm: -0.2; p 0.08; control arm: - 0.4 p=0.14), without a significant difference between them (delta GDS: p=0.66). The memory-assessing tests Digit Span Backward (p=0.01) and Immediate Free and Cued Selective Reminding (p=0.02) improved in the MARAND arm only, but not in the control arm. No changes in rsEEG waves were detected between the two study time points within both study arms. A linear logistic regression identified estimated creatinine clearance, BMI and baseline plasma HIV-RNA >20 copies/mL as independent predictors of GDS change at week 24.

Conclusion: In this small but well controlled study, the use of less neurotoxic ARV showed no beneficial effect over unchanged ARV regimen, as assessed by NPS tests and rsEEG. Baseline features as renal function, BMI and virological control were independent predictors of GDS change at week 24.

The beneficial effects in the memory domain observed in the experimental arm warrant further prospective studies.

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Comorbidities / Miscellaneous

OP 8 MANAGEMENT OF DIABETES MELLITUS IN PEOPLE LIVING WITH HIV AND DIABETES: A SINGLE-CENTER EXPERIENCE

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Background: Diabetes mellitus (DM) is a major public health problem with a worldwide prevalence in the general population close to 10%. Previous studies have shown that DM is 4-fold more common in people living with HIV (PLWH) than in HIV-negative persons, posing these population at high risk of micro- and macrovascular complications. International guidelines for DM management in PLWH are similar to those in the general population. However, the adoption of these guidelines and the response of PLWH and diabetes to glucose-lowering therapies in real-life settings remain ill defined.
Material and methods: The database of our clinic, with nearly 2500 PLWH on active follow-up, was retrospectively investigated to search for PLWH with a diagnosis of DM. Data on demographic characteristics, hematochemical analyses and medications at the last available follow-up were collected. Optimal control of DM was defined as having fasting glucose <130 mg/dL or HbA1c <53 mmol/mol. The distribution of glucose-lowering therapies in our patients were compared with those from the annual report of the national registry on the consumption of drugs in Italy.
Results: 200 PLWH and DM were identified. They were mostly men (82.5%), with mean age of 64±9 years and a mean follow-up of 8.2±6.3 years after the diagnosis of DM. The majority were treated with triple antiretroviral regimens (66%), based on tenofovir (43%) and integrase inhibitors (70%). The patients had good immune-virologic control (95% had HIV-RNA < 20 copies/mL; CD4+ 720+361 cells/microL), preserved renal (serum creatinine 1.2±1.7 mg/L) and liver (AST 37 ±35 IU/mL) functions. Mean total fasting glucose and HbA1C were 143±50 mg/dL (51% exceeding the 130 mg/dL cutoff) and 51 ±16 mmol/mol (30% exceeding the 53 mmol/mol cutoff), respectively. Mean total cholesterol, triglycerides and LDL were 173±44, 178 ±135 and 95±38 mg/dL, respectively. 25%, 63% and 86% had, respectively, LDL <70 mg/dL, <100 mg/dL and <130 mg/dL.
Some differences were found in the use of glucose-lowering drugs between PLWH and DM and HIV-negative patients (Table 1). In particular, incretin mimetics (GLP-1 analogues and/or DPP4 inhibitors) were used less frequently in PLWH and DM compared with HIV-negative patients (6.1% versus 15.5%), compared to a trend for a greater consumption of metformin in the formers (53.7% versus 37.7%). No differences were found on glifozins (7.1% versus 4.0%) or insulins use (26.4% versus 24.1%).
Discussion: A good glycemic control was observed, with a large part of PLWH and DM reaching the HbA1c targets established by international guidelines. The same trend was observed also for dyslipidemia, although the ambitious target of LDL <70 mg/dL was reached only by 25% of patients. It remains to be established whether the limited use of incretin mimetics in PLWH compared with HIV-negative patients was driven by the fear of potential DDIs with the antiretroviral therapies.

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Comorbidities / Miscellaneous

OP 9 THE INTERPLAY BETWEEN RESILIENCE AND HEALTH RELATED QUALITY OF LIFE IN PLWH DURING THE COVID ERA: A COMPARISON OF A GERIATRIC COHORT WITH A COHORT OF PLWH YOUNGER THAN 65 YEARS

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Background: Resilience is defined as an individual's positive adaptation to stressors. COVID pandemic represents a generalized stressor which may impact differently older people living with HIV (PLWH). The objective of this study was to compare resilience in PLWH older or younger than 65 years with particular regards to its impact on quality of life (QoL).
Methods: Participants enrolled in the GEPPO cohort (including PLWH aged >65 years) in Turin, Brescia and Modena HIV Metabolic Clinic (MHMC) (Italy) were invited to join in a telephone structured interview from October 2020 to March 2021. They were compared with PLWH aged <65 years from MHMC assessed in the same period. Resilience was measured through a short version of the CD-RISC-25 questionnaire and HRQoL with EQ5D5L. Resilience was defined as a the 5-level score of 5 questions above the mean (ranging from 0 to 20). HRQoL>89.7 % was used as validated cut-off for optimal QoL.
Results: 214 geriatric patients were compared wtith 534 PLWH aged <65 years. The relationship between resilience and HRQoL is depicted with linear regression in the two groups (R=0.42 in young and 0.21 in geriatric participants). Predictors of optimal QoL at multivariable logistic regression are shown in Figure 2 comparing geriatric vs PLWH age<65 years (panel A) and in the GEPPO cohort only (panel B).
Conclusion: Resilience but not age>65 years impact QoL in PLWH. The relationship between resiliance and QoL underline the need to better characterize this construct in different age groups. Properly designed intervention to address resilience should be studied but immediate actions to tackle sedentary life and polipharmacy should be considered to improve QoL in PLWH in the COVID era.

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Comorbidities / Miscellaneous

OP 10 EFFICACY AND TOLERABILITY OF DORAVIRINE + RALTEGRAVIR COMBINATION REGIMEN AS THERAPY OF SWITCH IN ART EXPERIENCED PLWHIV: THE DOR-INI EXPERIENCE

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Introduction: Dual antiretroviral regimens have gained growing importance as a therapeutic option for HIV chronic infection given reduced side-effects, lower costs, and lighter pharmacologic burden. In particular, the combination of an Integrase Strand Inhibitor (INI) plus a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) as switching therapy in virally suppressed People Living with HIV (PLWHIV) has been recognized as having high effectiveness, poor metabolic side effects, and few drug interactions. This study aimed to evaluate if the same advantages were observed in a cohort of undetectable PLWHIV switching to a dual regimen based on the association of Raltegravir -Doravirine (RAL+DOR).

Methods: Demographic, clinical, and immune-virological data regarding all patients switched from effective 3-drugs, RAL-based, antiretroviral therapy to RAL+DOR dual regimen were retrospectively collected. Descriptive statistics and paired Student t-test/ Mann Whitney Wilcoxon test were performed, as appropriate, to compare CD4+count, viral load, blood cholesterol, glucose and triglycerides levels, body weight, and waist circumference measured before the switch and at the follow-up (FU) visit. A p value <0.05 was considered statistically significant.

Results: From September 2020 to May 2021, a total of 28 patients (pts) were switched to RAL+DOR. They were all Italians, mainly males (57%), mean (±SD) age of 55.6 (±8) years, diagnosed with HIV from a mean of 19 (±8) years. Clinical and immune-virological features of the study population are reported in Table 1. Comorbidities were reported for 16 pts (57%), particularly dyslipidemia (15 pts, 53%). At the moment of the switch, all patients were virologically suppressed from a mean of 11.4 (±5.9) years. In all cases, avoiding potential NRTI-related drug toxicity was the reason for the switch. Notably, patients had experienced a mean number of 3.82 (±2.6) previous ART regimens, and 28% (8) of them had reported at least one virological failure. Genotypic Resistance Test was available for 15 pts (53%), 25% of whom presented drug-resistance associated mutations, (Table 1). After a median FU of 23.7 (±12.8) weeks, persistent virological suppression was observed in all subjects. No significant variations in CD4+count, blood cholesterol, glucose and triglycerides levels, body weight, and waist circumference were observed, as reported in Table 2.

Conclusions: According to our preliminary observation, a combination regimen of RAL+ DOR may represent an efficacious and well-tolerated treatment switch, NRTI sparing, option, with low impact on metabolic profile. PLWHIV with a long history of HIV infection, presence of comorbidities, and previous episodes of virological failures due to drug resistance-associated mutations could represent ideal targets for this regimen, even though more extensive studies are warranted to confirm this data.

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Comorbidities / Miscellaneous

OP 11 TRENDS OF POLYPHARMACY AND 2DR ANTIRETROVIRAL USE: A 15-YEAR OBSERVATIONAL MATCHED-COHORT STUDY

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Background: The objective of the study was to describe prevalence and risk factors for polypharmacy (PP) and two-drug regimens (2DR) antiretroviral therapy (ART) in the period 2006-2020. PLWH were divided into two groups: residents (non-switchers) and migrants (2DR switchers). Four phenotypes of PLWH were analyzed: healthy residents (without 2DR and multimorbidity), unhealthy residents (without 2DR and with multimorbidity), healthy migrants (2DR without multimorbidity) and unhealthy migrants (2DR with multimorbidity).
Methods: This was a longitudinal matched-cohort study that included ART-experienced PLWH, 2DR-naïve at baseline, with at least three visits at Modena HIV Metabolic Clinic (MHMC), Italy, from January 2006 to December 2020. The groups were matched for similar observation time since entrance in the MHMC cohort (T1-T0). Multimorbidity was defined as ≥ 3 co-morbidities. PP was defined as the use of >5 drugs other that ART. Logistic regression identified predictors of both PP and 2DR switch.
Results: The prevalence of polypharmacy increased from 2.6% in 2006 to 16.1% in 2020, as well as the use of 2DR regimens, that increased from 1.7% in 2006 to 26.1% in 2020 (Figure 1). 385 PLWH (75.6% males), respectively 162 migrants and 223 residents, were analyzed. The median age was 51.9 ± 8.4 years, median CD4 was 680 (526.3 – 852.3) and HIV RNA viral load was undetectable in 370 (96.1%) at T1. Migrants were older than residents (53.2 vs. 51.1 years, p=0.02) and had longer HIV exposure (22.0 vs. 19.0 years, p=0.02). The mean number of drugs to treat co-morbidities was higher in migrants (3.3 vs. 2.7, p=0.03), but PP did not show statistically significant differences between the two groups (17% vs 11.7%, p=0.16). Risk factors for PP were short physical performance battery (OR=0.72, 0.54 -0.97, p=0.032), BMI (OR=1.17, 1.04-1.32, p=0.008), HIV duration (OR=1.08, 1.02-1.15, p=0.008), age (OR=1.08, 1.02-1.15, p=0.012) and male sex (OR=6.18, 1.42-26.9, p=0.015). Four phenotypes were analyzed: 118 healthy residents (without 2DR and multimorbidity), 105 unhealthy residents (without 2DR and with multimorbidity), 77 healthy migrants (2DR without multimorbidity) and 85 unhealthy migrants (2DR with multimorbidity). PP was predicted by unhealthy migrants (OR=3.3, 1.23-8.85, p=0.017) and unhealthy residents (OR=4.0, 1.58-10.13, p=0.004) phenotypes while 2DR was not associated with this outcome.
Conclusions: A parallel increase in 2DR and PP trends was observed in the period 2006-2020. PLWH switching to 2DR are heterogenous population in which PP does not represent a major driver for switch. 2DR should be considered a deprescribing option in the management of PP.
Supported by ViiV Italy.

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Comorbidities / Miscellaneous

OP 12 RAPID, DRUG-RESISTANCE-DRIVEN, START OF ANTIRETROVIRAL THERAPY: AN OPEN-LABEL, PROSPECTIVE, PROOF-OF-CONCEPT, CLINICAL STUDY (TWODAY STUDY)

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Background: Rapid starting of antiretroviral therapy (ART) has been associated with improved clinical outcomes. A two-drug regimen (2DR) with dolutegravir (DTG)/lamivudine (3TC) proved as safe and effective as a regimen of three drugs (3DR) in treatment-naïve patients (pts). However, to start ART with this 2DR, all of the following information are needed: HIV susceptibility to both DTG and 3TC, CD4+ cell count, HIV-RNA, HBsAg. We hypothesized that a tailored regimen (2DR when clinically feasible or a 3DR otherwise) started very soon after laboratory testing might reduce the frequency of regimen change in the first month. The primary aim of this study was thus to evaluate, among pts who start ART very rapidly, the proportion who needs to modify treatment within one month from ART start.

Material and methods: Open-label, prospective, proof-of-concept, single center, clinical study. All ART-naïve pts who presented at our center were considered for this study. Those with CD4+ >200 cells/mL and HIV-RNA <500,000 copies/mL, no transmitted drug resistance (TDR) to DTG or 3TC, undetectable HBsAg, started ART with a 2DR of DTG/3TC. When either CD4+ count <200 cells/mL or HIV-RNA >500,000 copies/mL or detectable TDR to either DTG or 3TC, or detectable HBsAg, ART was started with a 3DR recommended by Italian guidelines, accounting for drug resistance. FU: 4, 12, 24 weeks. No comparisons between regimens were anticipated.

Results: 32 pts have been enrolled; 28 (88%) males, 25 (78%) MSM, with a median (Q1-Q3) age of 41.4 (35-47) years; 7 (22%) had CD4+ counts <200 cells/μL and 15 (47%) HIV-RNA >5 log10 copies/mL. Further baseline characteristics are reported in the figure.

At baseline genotypic resistance testing (GRT), we never detected mutations associated to resistance to DTG or bictegravir; 2 pts harbored variants with reduced susceptibility to raltegravir/elvitegravir (67A mutation in one, 163K in the other); 3 harbored variants with reduced susceptibility to rilpivirine (138A mutation); 1 harbored a variant with reduced susceptibility to some NRTIs (67N, 215S, 219E mutations).

Median time from GRT sampling to ART start was 5 days (5-5).

Based on laboratory results, 21 (66%) pts were eligible for 2DR; 20 (63%) started DTG/3TC, 12 (37%) started a 3DR. One patient eligible for 2DR received an InSTI-free 3DR because of history of suicide attempt.

No regimen modification occurred within one month.

SAEs occurred in 2 patients, requiring hospitalization: opportunistic infection a few days after ART start for one receiving 3DR and traumatic displaced arm fracture for one on 2DR.

The figure shows changes in HIV-RNA, CD4+ cell counts, HIV-DNA, weight, abdominal circumference, through 24 weeks of FU.

Conclusions: No regimen modification was needed within the first month of treatment. A 2DR can be started within a few days after HIV diagnosis, relying upon complete results of the needed laboratory tests (including GRT).

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HIV & Covid I

OP 13 UV IRRADIATION AND SARS-COV-2: A FOCUS ON UVA/UVB/UVC -INACTIVATION ON VIRAL REPLICATION

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Abstract: UV radiation is one of the most reliable and recognised microbicide approach, whose application has been widely employed since the last century. Recent publications quantified the UV-C dose at 254 nm necessary to completely inactivate SARS-CoV-2, confirming the highly virucidal effect of such radiation(1). Moreover, there are clues that SARS-CoV-2 virulence is strongly reduced during the summer season in many populous cities of the world, indicating that sunlight could play a role in the occurrence, spread rate and duration of coronavirus pandemic(2).
Since solar UV-C light is filtered out by the ozone layer of the stratosphere, the possible virucidal effect could be caused by UV light in the range 290-320 nm (UV-B) and 320-400 nm (UV-A)(3).
Herein, we report the effect of different quasi-monochromatic UV-A/B/C irradiation on SARS-CoV-2. Experiments were conducted using a custom-designed lamp based on 278 nm (UV-C), 308 nm (UV-B) and 366 nm (UV-A) LEDs. According to the irradiance at the different wavelengths, three exposure times were set to provide three different UV-doses. Vero E6 cells were infected with UV-irradiated SARS-CoV-2 at a concentration resembling the one found in the sputum of COVID-19 patients. Cells were observed daily for cytopathic effect while cell culture supernatants were harvested at 24, 48, 72 hours to measure viral replication by SARS-CoV-2 nucleocapsid absolute copy number quantification (qRT-PCR). Fluorescence in situ hybridization (FISH) approach was used to further endorse the effect of UV-irradiation on viral replication.
Results showed that an UV-A dose of 4000 mJ/cm2 and of 200 mJ/cm2 for the UV-B are sufficient to completely inhibit the replication of SARS-CoV-2. As expected, a much lower UV-C dose (4 mJ/cm2) was necessary to achieve the same effect. Data were confirmed by analysing SARS-CoV-2-induced cytopathic effect and by FISH analyses. Moreover, the comparison of the UV action spectrum on SARS-CoV-2 to previous results obtained on other pathogens suggests that RNA viruses might be particularly sensitive to long UV wavelengths.
These outcomes are crucial for the development of novel sterilizing methods based on UV-C technology to contain SARS-CoV-2 infection and could contemporary contribute to the explanation of seasonal fluctuations in COVID-19 epidemiological trends.

1Biasin, M. et al. UV-C irradiation is highly effective in inactivating SARS-CoV-2 replication. https://doi.org/10.1101/2020.06.05.20123463
2Nicastro, F. et al. Modulation of COVID-19 Epidemiology by UV-B and -A Photons from the Sun. https://doi.org/10.1101/2020.06.03.20121392
3Sagripanti, Lytle. Estimated inactivation of Coronaviruses by solar radiation with special reference to COVID-19. https://doi.org/10.1111/php.13293

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HIV & Covid I

OP 14 DETERMINANTS AND CHARACTERISTICS OF PROGRESSOR AND NON PROGRESSOR SARS COV-2 INFECTED PATIENTS

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Background: In most cases COVID 19 presents with mild flu clinical manifestations but even initially mild cases can progress towards severe cases with major complications such as ARDS, MOF and death. The aim of the study is to identify clinical-laboratory determinants in the severe progression of COVID-19 disease in a cohort of patients who presented a mild initial clinical features at the time of hospital admission.

Materials and methods: All patients admitted at the S.M. Goretti hospital with pneumonia with a P/F ratio ≥300, were enrolled and were stratified into progressor and non progressor subjects. All the patients were treated the same due the protocol. The progression was defined by achieving ARDS condition in the subsequent in-hospital staying.

The results were analyzed using Graph Prism and R. A stepwise logistc regression analysis was performed to investigate the relatioship between the risk of having ARDS and age, gender, symptoms, comorbidities, Neuthrophilis% (N%), Glycemia.

Results: Among 929 patients, 552 had a P/F≥300 and 295 are defined as Progressor and 257 as Non progressor. Progressors are more synthomatic than non progressor (p=0.001), in particular they have fever (p<0.001), cough (p=0.038) and dyspnea (p=0.004). Regarding comorbidities, progressor have more comorbidity than non progressor (p=0.017), such as hypertension (p=0.043), cardiovascular diseases (p=0.04) and dementia (p=0.003).

Progressor at baseline have higher levels of N% (p<0.0001), glycemia (p<0.0001), LDH (p<0.0001), ferritin (p<0.0001), PCR (p<0.0001), VES (p<0.0001), fibrinogen (p<0.0001) and d-dimer (p<0.0001) than non progressor.

Finally, the stepwise logistic regression analysis found that gender (p=0.0007; OR 2.006), age (p <0.001; OR 1.041), symptoms (p=0.00005; OR 3.479), N% (p <0.001; OR 1.038) and glycemia (p=0.0078; OR 1.007) independently increase the risk to develop ARDS.

Conclusions: Early detection of patients at high risk of progression to severe SARS COV-2 disease is essential in order to improve their outcome and identify subjects who can be promptly treated with antivirals or monoclonal Ab.

The study points out specific clinical characteristics of the progressor subject that may be used in the future in order to identify a specific and standardized score that can direct towards optimal management of the subject, identify the patient who needs hospitalization and the choice of treatment, also in according to the new therapies.

HIV & Covid I

OP 15 METABOLIC ASSOCIATED FATTY LIVER DISEASE IS HIGHLY PREVALENT IN THE POST-ACUTE COVID SYNDROME

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Background: This study aims to determine the prevalence of metabolic associated fatty liver disease (MAFLD) in patients with post-acute COVID syndrome (PACS) and its association with PACS-cluster phenotypes.
Methods: We included 235 consecutive patients followed at the Modena post-acute COVID syndrome (PACS) clinic (MPC) from 15 July 2020 to 30 April 2021. The diagnosis of PACS was based on ≥1 cluster of symptoms: respiratory, neurocognitive, musculoskeletal, psychological, sensory, dermatological signs and symptoms. The primary outcome was prevalence of MAFLD detected by transient elastography during the first MPC visit. The prevalence of MAFLD at the time of hospital admission was estimated retrospectively using the hepatic steatosis index (HSI). Logistic regression analysis to identify independent predictors of MAFLD, and Pearson correlation coefficient to explore correlations among different PACS clusters and MAFLD were implemented.
Results: Of 235 patients, 162 (69%) were men (median age 61). The prevalence of MAFLD at MPC visit was 55.3%. The estimated prevalence of MAFLD on admission was 37.3% (vs. 55.3% p<0.001). Homeostasis model of insulin resistance (OR=1.5, 95%CI: 1.14-1.96), body mass index BMI (OR=1.14, 95%CI: 1.04-1.24), and the metabolic syndrome (OR=2.54, 95%CI: 1.13-5.68), were independent predictors of MAFLD; the number of PACS clusters was inversely associated with MAFLD (OR=0.86, 95%CI: 0.76-0.97). Thirty-one patients (13.2%) had MAFLD with no other associated PACS clusters. Each correlation between MAFLD and other PACS clusters was weak to very weak (Figure 1).
Conclusions: MAFLD was highly prevalent at follow-up after hospital discharge and may represent a specific PACS-cluster phenotype, with potential metabolic and cardiovascular health implications.

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HIV & Covid I

OP 16 ASSESSMENT OF WELL-BEING, RESILIENCE AND INTRINSIC CAPACITY IN PATIENTS WITH POST-ACUTE COVID-19 SYNDROME

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Background: Resilience is defined as an individual's positive adaptation to stressors. COVID-19 pandemic represents a generalized stressor which may impact differently people with post-acute COVID-19 syndrome (PACS). The objective of this study was to characterize resilience in people with PACS with particular regards to the identification of frailty-resilience phenotypes, which may differently impact quality of life (QoL). The objective of this study was to characterize resilience in people who were hospitalized for severe COVID-19 disease with particular regards to the identification of frailty-resilience phenotypes, which may differently impact Intrinsic Capacity (IC) and quality of life (QoL).

Methods: This was an observational study of people recovered with COVID-19 attending Modena PACS Clinic. Frailty was assessed after discharge by using Frailty Phenotype (FP) ranging from 0 to 5. FP score was categorized as fit (from 0 to 2) or frail (≥3). People with PACS were offered to complete a set of electronic questionnaires including the CD-RISC-25 for resilience and Short Form 36 Health Survey Questionnaire and EQ-5D-5L for HRQoL. Resilience was defined as CD-RISC-25 score >60.0 (ranging from 0 to 100); while Health-related quality of life (HRQoL), as Short Form 36 (SF-36) Health Survey Questionnaire score>61.6 (ranging from 0 to 100) and with EQ-5D-5L>89.7% (ranging from 0 to 100).

Results: In the period July 2020 - April 2021, 232 patients were evaluated at MPC, median age was 58.0 (IQR: 50.0 - 67.0) years. Prevalence of non-resilience was 114 [49.14%], while prevalence of frailty was 72 [31.03%]. Prevalence of PACS was 173 [74.57%], specifically respiratory cluster was represented in 128 [55.17%], MAFLD 93 [40.09%], neurocognitive in 82 [35.34 %], psychological 79 [34.05%], musculoskeletal 67 [28.88%], sensory 49 [21.12%], other 42 [18.1%]. Impaired IC was associated with the phenotypes "frail/non-resilient" (OR=7.39, 95% CI, 3.20; 17.07, p<0.001), and the phenotypes "fit/non-resilient" (OR=4.34, 95% CI, 2.16; 8.71, p<0.001). Predictors for EQ-5D-5L <89.7% were the phenotypes "frail/non-resilient" (OR=5.93, 95% CI, 2.64; 13.33), "frail/resilient" (OR=5.66, 95% CI, 1.93; 16.54, p<0.01) (Figure 1A). Predictors for SF-36 Health Survey Questionnaire score <61.60 were the phenotypes "frail/non-resilient" (OR=4.69, 95% CI, 2.08; 10.55, p<0.01) "fit/non-resilient" (OR=2.79, 95% CI, 1.00; 7.73, p=0.04) (Figure 1B).

Conclusion: Resilience characterizes well-being of people hospitalized for severe COVID-19, highlighting that this construct is complementary to frailty in the identification of clinical phenotypes with different impacts on relevant clinical outcomes including IC and HRQoL.

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HIV & Covid I

OP 17 ACHIEVING VIROLOGICAL CONTROL IN PAN-RESISTANT HIV-1 INFECTION

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Background: HIV-1 pan-resistance is anecdotal and refers to a reduced susceptibility to NRTIs, NNRTIs, PIs and InSTIs. As a challenge both for individual management and public health, it highlights the need for drugs with original mechanisms of action, such as fostemsavir, lenacapavir, islatravir, and ibalizumab (IBA). In this case series, we propose a strategy to improve virological control in HIV-1 pan-resistant infections, which takes into account both a deep assessment of the historical and current resistance mutations to tailor an optimized background regimen (OBR) and a new therapeutic approach including IBA and recycled enfuvirtide (ENF).

Methods: Three PLWH with pan-resistance documented by GRT on plasma HIV-RNA and peripheral blood mononuclear cell (PBMC) HIV-DNA (Figure 1-2-3, panels A) were recruited. From baseline (BL, defined as starting date of IBA plus OBR), IBA was administered intravenously (2 gr loading dose followed by 800 mg every 14 days), ENF was injected subcutaneously (90 mg twice daily) until stable virological control, and the OBR consisted of approved antiretrovirals at the recommended dosage tailored based on GRT-driven susceptibility prediction, clinical and pharmacological history. Since BL, HIV-RNA has been quantified biweekly using PCR Cobas® HIV-1 test 6800 Systems, Roche Diagnostics; undetectable viral load was defined as HIV-RNA <50 copies/mL. GRT on plasma RNA and PBMC DNA were interpreted according to the Stanford HIVDb version 9.0 (last updated on 2021-02-22). The follow-up was censored at data freezing (16 January, 2021).

Results: HIV-RNA and CD4+ cell count collected before and after BL are reported in Figure 1-2-3, panels B. Case 1, with a BL HIV-RNA of 275,000 copies/mL, fell between 100 and 600 copies/mL from week 10 and, at week 76, showed a HIV-RNA of 948 copies/mL. Case 2 had HIV-RNA 62,600 copies/mL at BL, then reached values permanently <100 copies/mL from week 4 and, at week 76, was steadily <50 copies/mL. Case 3 started with HIV-RNA 21,966 copies/mL at BL, reached HIV-RNA levels below 200 copies/mL after a single loading dose of IBA, frequently achieved HIV-RNA <50 copies/mL and, at week 98, had a HIV-RNA of 84 copies/mL.

Conclusions: the combination of a GRT-driven strategy to build OBR, recycling of ENF, a new drug free from cross-resistance with all the antiretrovirals available, and a close monitoring attributable to a route of administration that ensure patient adherence, has revealed to be a turning point in achieving virological control in heavily-treated PLWH who have experienced repeated ART failure on any number of prior regimens over a 20-30 year period, up to develop HIV-1 pan-resistant infection.

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HIV & Covid I

OP 18 RESILIENCE AND FRAILTY IN PEOPLE LIVING WITH HIV DURING THE COVID ERA: TWO COMPLEMENTARY CONSTRUCTS ASSOCIATED WITH HEALTH-RELATED QUALITY OF LIFE

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Background: Resilience is defined as an individual's positive adaptation to stressors. COVID pandemic represents a generalized stressor which may impact differently people living with HIV (PLWH). The objective of this study was to characterize resilience in PLWH with particular regards to the identification of frailty-resilience phenotypes, which may differently impact quality of life (QoL).

Methods: This was an observational study of PLWH attending Modena HIV Metabolic Clinic. Frailty was assessed in 2019, prior to the onset of COVID pandemic by using 37-Item frailty index (FI) ranging from 0 to 1. FI score was categorized as fit (<0.25) or frail (>0.25). In January 2021, PLWH were offered to complete a set of electronic questionnaires including the CD-RISC-25 for resilience and EQ-5D5L and SF-36 for QoL. Resilience was defined as CD-RISC -25 score >75.7 (ranging from 0 to 100).

Results: Out of 800 PLWH reached via mail, 575 (72%) completed the questionnaires. Median age and HIV duration were 54.5 and 24.3 years, respectively. Prevalence of frailty using 37-FI cut-off >0.25 was 45.9%. Frail PLWH were significantly older (56.6 vs 52.7), had lower CD4 nadir (191 µL vs 254 µL), higher BMI (25.0 kg/m2 vs 23.5 kg/m2) and higher multimorbidity (91.8% vs 69.1%). Regarding geriatric syndromes, higher burden of polypharmacy (56.8% vs 28.3%) and falls (15.2% vs 9.0%) was observed, while there was no difference in loneliness (23.9% vs 19.3%). Prevalence of impaired resilience using CD-RISC-25 cut-off <75.7 was 79.3%. PLWH with impaired resilience had similar age (54.5 vs 54.6), had lower CD4 nadir (222.5 µL vs 221 µL), BMI (23.8 kg/m2 vs 24.6 kg/m2) and multimorbidity (79.4% vs 82.4%). Regarding geriatric syndromes similar burden of polypharmacy (42.1% vs 38.7%) we observed while there were significant difference in falls (13.6% vs 5.0%) and loneliness (24.6% vs 9.2%). Impaired resilience was associated with loneliness (OR=2.39; 1.20;4.76, p<0.001). Predictors for EQ-5D5L <89.7% were the phenotypes "frail/non-resilient" (OR=5.21, 95% CI: 2.62; 10.33) and "fit/non-resilient" (OR=5.48, 95% CI: 2.8; 10.74) (Figure 1A). Predictors for SF-36 <64.40 were the phenotypes "frail/non-resilient" (OR=7.43, 95% CI: 2.57; 21.22), "fit/non-resilient" (OR=6.27, 95% CI: 2.17; 18.16) (Figure 1B). Both models were corrected for age, sex, HIV duration and nadir CD4.

Conclusion: Resilience characterizes well-being of PLWH during COVID crisis. This construct is complementary to frailty in the identification of clinical phenotypes with different impacts on QoL.

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Coinfections and Hepatitis

OP 19 IMPACT OF POLYPHARMACY AND AGING ON THE RISK OF MULTIPLE DRUG-DRUG INTERACTIONS (DDIS) IN HCV PATIENTS TREATED WITH PANGENOTYPIC DIRECT-ACTING ANTIVIRALS (PDAA)

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Background: Recent studies suggest that sofosbuvir-based regimens are preferred in HCV elderly patients, based on the slightly more user-friendly DDI profile when compared to protease inhibitor (PI)-based regimens Our aim was to explore the impact of polymedication and aging in the prevalence of multiple DDIs of patients treated with sofosbuvir/velpatasvir (SOF/VEL) or glecaprevir/pibrentasvir (GLE/PIB).

Methods: Retrospective observational study from an Italian database covering a total of 6.9 million health-assisted individuals and including patients treated with SOF/VEL or GLE/PIB (2017-2020). Demographics, comedications, and DDIs were evaluated in the overall population and in patients receiving ≥ 2 comedications showing DDIs with the pDAA. DDI severity and the effect of multiple DDI (in terms of increase in comedication concentration, decrease or increase in DAA) were identified using the Liverpool University tool.

Results: 4,185 HCV patients were included; 2,057 treated with SOF/VEL and 2,128 with GLE/PIB. Male ratio was similar in both groups (60% vs 61%, ns), while the median age was 56 vs 52 years old (p<0.001), with a higher percentage of patients over 50 yo in SOF/VEL vs GLE/PIB (72% vs 58%, p<0.001).In terms of comedications, the most prescribed drugs were cardiovascular drugs (43% SOF/VEL;24% GLE/PIB), alimentary (37% SOF/VEL; 21% GLE/PIB) and nervous system (25% SOF/VEL; 15% GLE/PIB). The use of comedications (≥1 comed) was higher in SOF/VEL vs GLE/PIB (72% vs 50%, p<0.001), as well as the number of patients receiving ≥2 comed (57% vs 32%, p<0.001). Number of patients receiving ≥ 2 comed at risk of multi-DDI with pDAAs was 270 (14.6%, overall), 135 (12%) with SOF/VEL and 135 (20%) with GLE/PIB (p<0.001). Male ratio was similar in both groups receiving ≥ 2 comed at risk of multi-DDI (61% vs 57%, ns), with a slightly higher median age in SOF/VEL (74 vs 67 years old, p<0.001), confirming the same trend observed in the overall population over 50 yo (94% vs 79%, p<0.001). Interestingly, the number of patients under 50 yo with multiple DDIs was three times more in GLE/PIB vs SOF/VEL (21% vs 6%, p<0.05). The effects of multiple DDIs are shown in figure 1.

Conclusion: In our sample population, PI-free pDAA regimen seems to be preferred in elderly patients particularly in those with≥ 2 comed at risk of multi-DDI. The effects of DDIs are mainly related to increase of comedications among patients treated with PI-based pDAA.

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Coinfections and Hepatitis

OP 20 HBEAG LEVELS VARY ACROSS THE DIFFERENT PHASES OF HBV INFECTION, AND CAN BE PREDICTIVE OF THERAPEUTIC OUTCOME IN THE SETTING OF IMMUNOSUPPRESSION-DRIVEN HBV REACTIVATION

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Background: HBeAg is a marker of active HBV-replication and HBeAg-loss is an important end-point, associated with a favourable clinical outcome. Here, we quantify HBeAg in different phases of HBV infection, its correlation with virological/biochemical markers and its role in predicting virological response to treatment.

Material and methods: This study includes 109 HBeAg+ patients: 20 with acute-infection (HBcIgM+, median[IQR] HBV-DNA:8.3[7.9-8.7]logIU/mL, ALT:1556[142-2027]U/L), 28 with HBeAg+ chronic-infection (median[IQR] HBV-DNA:8.2[8.0 -8.4]logIU/mL, ALT<40U/L), 32 with HBeAg+ chronic-hepatitis (median[IQR] HBV-DNA:8.2[7.1-8.6]logIU/mL, ALT:85[62 -179]U/L) and 29 patients with immunosuppression-driven HBV-reactivation (HBV-R) (median[IQR] HBV-DNA:6.8[5.5-8] logIU/mL, ALT:143[40-528]U/L, pre-reactivation status HBcAb+/HBsAg-). 15/29 patients with HBV-R were monitored for >12months after starting TDF/ETV (median[min-max] follow-up: 21[12-54] months). Quantitative HBeAg (qHBeAg) is assessed by DiaSorin LIAISON assay. Association of qHBeAg at HBV-R with the achievement of HBeAg-loss after starting treatment is assessed by Fisher exact test.

Results: qHBeAg is higher in patients with HBV-R and acute-infection (median [IQR] 930 [206-1945] and 754 [210-3379] PEIU/mL) and decreases in patients with chronic infection (648 [7-1490] PEIU/mL, reaching the lowest levels in chronic hepatitis (481 [28-1393] PEIU/mL).

qHBeAg shows strong positive correlation with qHBsAg in HBV-R (Rho=0.61, P=0.003), acute infection (Rho=0.78, P<0.001) and chronic hepatitis (Rho=0.75, P<0.001) while weaker correlation is observed with serum HBV-DNA. Notably, among the virological biomarkers, qHBeAg shows the strongest negative correlations with ALT specifically in acute infection (Rho=-0.66, P=0.006) and chronic hepatitis (Rho=-035; P=0.05), reflecting a modulation in HBeAg production by the extent of immune response. Furthermore, in the setting of acute infection, the 3 patients developing chronicity are characterized by higher HBeAg levels at diagnosis than patients resolving HBV infection (2555[1365-2555] vs 299[189 -3203] PEIU/mL).

Focusing on 15 patients with HBV-R starting TDF/ETV for >12 months, ALT normalization is achieved in 93% of patients while virological suppression and HBeAg-loss in 60% and 53.3%, respectively. The combination of qHBeAg >2000PEIU/mL + qHBsAg >52000IU/mL at HBV-R is the only factor predicting the lack of HBeAg-loss during treatment (HBeAg-loss achieved in 0% patients with qHBeAg>2000 PEIU/mL + qHBsAg > 52000IU/mL vs 72.7% patients without this combination, P=0.01, result not significant considering qHBeAg and qHBsAg separately).

Conclusions: HBeAg levels differ during the natural history of HBV-infection and according to the extent of immunological pressure. In the setting of HBV reactivation, qHBeAg can be useful in predicting virological response to treatment under iatrogenic immunosuppression.

Coinfections and Hepatitis

OP 21 HCV KNOWLEDGE AND AWARNESS AMONG INJECTING DRUG USERS IN THE DIRECT ACTING ANTIVIRALS ERA

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Background: We investigated the knowledge of HCV transmission-related behaviours in PWID admitted in a therapeutic Community to understand better why HCV prevalence remains high, even in those who deny sharing syringes.
Methods: From January-2018 to January 2021, trained interviewers administered a face-to-face interview to PWID at admission in San Patrignano (Italy) TC, focusing on knowledge of transmission pathway and long term effects of HCV-infection, according their HCV status knowledge (HCVAb-pos vs. HCVAb-neg/unknown).
Results: 388/401 PWID (96%) adhered to the study: 74.2% males, median age 19 years (IQR: 16-22) at first drug injection and 29 years (IQR: 24-37) at TC-admission. 276 (71.1%) were heroin and cocaine injectors, 90 (23.2%) heroin only and 22 cocaine only (5.7%). 204 individuals were already aware of being HCVAb-pos at TC-admission (52.6%), while among the remaining 184, 94 (24.2%) were previously screened resulting HCVAb-neg and 90 (23.2%) were never screened before. HCV Ab prevalence was 40.5% in those who denied receptive sharing of syringes (81/204 individuals), 66.3% in those who admitted it but only with intimate partner or trusty friends (110/166) and 64.7% (11/17) in those who shared syringes with other people. Seven persons were HIV-pos (1.8%, of which 6 also HCVAb-pos at TC-entry). Knowledge of HCV-related diseases and modality of transmission was statistically higher among HCVAb-pos ($p<0.001$). There were large gaps in HCV knowledge, lower in those aware of being HCVAb-pos (Fig 1). In particular some injecting-related practices, like dividing doses through syringes and paraphernalia (other than syringes) sharing, proven as risky for HCV transmission, were not sufficiently recognized as dangerous by our PWID population.
Conclusions: Even if in recent years most of PWID avoid sharing of syringes, or share only with intimate partner or trusty friend, HCV prevalence remains high in this population, whereas HIV diffusion is ending. Accurate HCV information is failing to reach PWID, and/or they may not value the little information they do receive. Supported by: Grant Gilead IN-IT-987-5396, part of the LEGA-C™ program.

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Coinfections and Hepatitis

OP 22 A PILOT INTERVENTION FOR HCV ELIMINATION AMONG MSM IN ROME: AN UPDATE ON MORE THAN 1200 SCREENED INDIVIDUALS

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Background: HCV prevalence among men who have sex with men (MSM) is not negligible, however information on this issue in Italy is scarce, particularly for HIV-uninfected MSM. An HCV screening program targeted to MSM in Rome started in July 2019 in two hospitals and one urban community setting run by an NGO. The program is based on the offer of rapid tests for HCV antibodies, aimed at identifying, linking to care and treating with Direct Acting Antivirals (DAA), MSM with previously undiagnosed HCV infection.

Methods: Adult (>18 years old) males reporting same-gender sex in the previous 12 months attending the study sites were invited to undergo, after providing written informed consent, a free-of-charge rapid HCV Antibody test (OraQuick HCV®). For all participants, demographic, clinical and behavioral data were collected using an anonymous questionnaire. Free confirmatory standard serology tests were guaranteed to those found reactive to rapid HCV test. Individuals with confirmed HCV-infection, were referred through a dedicated "fast track" pathway for further clinical and laboratory assessment and DAA-treatment according to Italian treatment guidelines.

Results: From July 2019 to June 2021, 1213 MSM agreed to be screened for HCV infection (89.0% Italians, median age 40 years, interquartile range, IQR: 32-48), mostly (90.5%) tested in the two clinical centers. HIV-infection was reported by 301 (24.8%) MSM and 51.2% of all participants reported a previous HCV negative test. Overall, 4 MSM (all enrolled in clinical centers) were reactive at rapid test (overall prevalence 0.33%, 95% Confidence Intervals, CI: 0.10-0.79).

HCV prevalence among HIV-infected and HIV-uninfected individuals was 1.0% (3/301, CI: 0.25%-2.69%) and 0.11% (1/912, C.I.: 0.01-0.54), respectively.

Two of the HCV-Ab positive individuals reported a previous negative HCV test and all four individuals resulted as newly-diagnosed HCV infections. All cases were confirmed being viraemic (range 1.7x106-23.7x106 UI/mL) harboring HCV genotype 1a (3 cases) or 4 (1 case), with a mild-moderate liver fibrosis. All cases were linked to care, underwent clinical assessment and completed DAA treatment (8 weeks protocol with glecaprevir/pibrentasvir, GLE/PIB) started within 4 to 12 weeks after HCV diagnosis. Three cases (2 HIV-infected) reached Sustained Viral Response (SVR) at 12 weeks after end of treatment (EOT), while one had suppressed viraemia at EOT (EOT response, EOTR) (see Figure 1).

Conclusions: These data show the feasibility and potential effectiveness of a program which combines HCV screening and effective linkage to care and treatment to unearth the presence of HCV in the MSM community. Overall, HCV prevalence in this population is quite low, although it is 9-times higher in HIV-infected MSM. 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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Coinfections and Hepatitis

OP 23 HUMORAL RESPONSE TO MRNA SARS-COV-2 VACCINE IN CIRRHOTIC PATIENTS WITHOUT PRIOR EXPOSURE TO THE VIRUS

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Background: SARS-CoV-2 infection and the resulting disease, COVID-19, is associated with increased morbidity and mortality in cirrhotic patients. Despite that, cirrhotic subjects were not enrolled in phase 3 studies of SARS-CoV-2 vaccines, therefore currently no efficacy, immunogenicity, or safety data are available for this vulnerable population with any of the approved COVID-19 vaccines. The aim of the present study was to quantify the humoral response following full vaccination with the Moderna m-RNA-1273 SARS-CoV-2 vaccine in a cohort of cirrhotic patients.
Material and methods: Cirrhotic patients, who were routinely followed in the hepatologic unit of INMI Lazzaro Spallanzani, were consecutively enrolled. All participants were vaccinated with the Moderna m-RNA-1273 SARS-CoV-2 vaccine, with the recommended dosing interval of 28 days between the two doses. The blood samples were collected before the first (T0) and the second dose (T1) of vaccination and 15 days after the second vaccine dose injection (T2). SARS-CoV-2 S1/S2 IgG chemiluminescent assay was used according to the manufacture instructions to detect IgG antibodies directed against a recombinant S protein (S1/S2). Every participant was asked to report the side effects after each dose of the vaccine (during 7 days following every dose). Continuous variables were summarized as mean ± standard deviation and categorical data as counts and percentages.
Results: One hundred cirrhotic patients were enrolled, nine of them were excluded from further analysis due to positive IgG antibodies to SARS-CoV-2 nucleocapsid protein. The mean age was 59.9 ± 9 years, the majority of them were males (68.1%) and the mean BMI was 26.7 ± 4.6 Kg/m2. The most common etiology of cirrhosis was viral (81.3%), 14.3% of them had hepatocellular carcinoma (HCC) and 7.8% were infected with HIV. Co-morbidities were common, including hypertension (21.1%), diabetes (15.6%), obesity (8.8%), chronic respiratory diseases (6.7%) and cardiovascular diseases (5.6%). The majority of patients had a Child-Pugh A cirrhosis (87.9%) and the mean MELD value was 9.15 ± 3.1 (Table 1). All the patients tested negative for SARS-CoV-2 N-protein IgG serology at T0, two patients tested positive during follow-up (one at T1 and one at T2). A positive antibody response to spike protein was detected in 91% (75/82) of patients at T1 with a mean IgG anti-spike level of 177 ± 256 bau/ml and in 100% (79/79) at T2 with a mean IgG anti-spike level of 3377.2 ± 27.8 bau/ml. No major adverse events to the vaccine were reported, the most common local side effect was local pain (71.4%), the most common systemic effect was fatigue (37.4%) followed by arthralgia (19.8%) and myalgia (18.7%) (Table 2).
Conclusions: The present study demonstrate an optimal humoral response to the Moderna m-RNA-1273 SARS-CoV-2 vaccine in a cohort of cirrhotic patients with no major adverse events to the vaccine. Study limitations include a small sample size and short follow-up period.

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Coinfections and Hepatitis

OP 24 SYPHILIS REINFECTION IN PEOPLE LIVING WITH HIV (PLWH): A MONOCENTRIC RETROSPECTIVE STUDY

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Background: Syphilis still represents a major public health concern. The infection does not lead to immunity against reinfection and repeated episodes of syphilis occurs predominantly in people living with HIV (PLWH). The aim of this study is to evaluate the incidence of syphilis reinfections in PLWH in our Centre.

Methods: Our Infectious Disease Unit assists 3841 HIV patients, with a dedicated clinic for sexually transmitted diseases (STIs) which is part of the Italian Sentinel Surveillance System (SSS). We offer syphilis test to all newly diagnosed with HIV or STIs, in presence of symptoms or as periodical annual screening. We retrospectively evaluated syphilis notifications from 2013 to 2020 matching them to our electronic health record system. We considered as inclusion criteria: HIV infection, documented history of previously treated syphilis, one or more episodes of syphilis reinfection. Demographical and clinical characteristics, risky habits, number of reinfections and serological response were considered. We defined as a serological-non-responder (SNR) a ≤ 4-fold decrease in non-treponemal titres after an appropriate treatment. We recorded also if a lumbar puncture (LP) was performed, according to guidelines.

Results: In the study period 68 PLWH presented at least one episode of reinfection/failure (range 2-12) accounting for 210 recurrences, with a mean of 3.1 episodes per each patient. All patients were male, 59 (86.8%) had European origins, and 58 (85.3%) were homosexual/bisexual. Through annual screening, 54 (86.8%) recurrences were diagnosed in asymptomatic patients. At first diagnosis of reinfection, 21 (30.8%) were classified as indeterminate late syphilis and 20 (29.4%) were secondary syphilis. After treatment, 15 patients (22.1%) resulted in serological-non-response at least in one episode (5.4% of all notified cases in the study population). LP was performed in 10 (14.7%) patients, 3 SNR patients and 5 with CD4 count ≤350/microL. Two neurosyphilis were diagnosed.

Discussion: Syphilis reinfection occurs predominantly in men who have sex with men (MSM). Most reinfections were detected during periodical screening in asymptomatic patients, in line with literature, suggesting that clinical findings in subsequent episodes of syphilis may be rare. Data regarding serological response in repeated episodes are discordant, but each additional episode of syphilis may result in a more attenuated immune response. The low rate of SNR in our study supports reinfection rather than treatment failure, despite the reluctance in exposing sexual habits it is known to undermine the exact diagnosis. LP acceptance was low, possibly due to the asymptomatic or mild symptomatic presentation, although presenting high diagnosis rate (20%) in case of acceptance. The high rate of asymptomatic presentation supports the role of periodical screening in PLWH, as well as the need of an appropriate counselling to increase the acceptance LP, if indicated.

Immunopathogenesis I

OP 25 DECREASED NEUTRALIZATION OF THE B.1.525 (NIGERIAN) SARS-COV-2 VARIANT BY SERA OF PREVIOUSLY INFECTED AND UNINFECTED VACCINATED INDIVIDUALS

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Background: Emergent SARS-CoV-2 variants of concern (VOC) and variants of interest (VOI) are challenging the immune protection resulting from natural and artificial immunization with the original B.1 virus variant. The VOI B.1.525 combines relevant spike mutations detected in several VOC, yet its potential for vaccine escape has been poorly investigated. Aim of this study was to determine serum neutralizing antibody (NtAb) response to B.1.525, as well as to other viral variants, in a cohort of health care workers (HCWs) including both previously infected and uninfected individuals, all vaccinated with two doses of the BNT162b2 COVID-19 mRNA vaccine.

Materials and Methods: 15 previously infected HCWs tested at baseline (T0inf) and 17±6 days after receiving the second vaccine dose (T2inf), and 15 uninfected HCWs tested 18±4 days after the second dose vaccination (T2uninf) were enrolled. The infected group had median age [IQR] of 38 [31-52] years, included 8 females and was infected during the first wave of the pandemic. The uninfected group had a median age of 38 [29-59] years with 11 females. NtAb titer to live virus variants belonging to lineage B.1, P.1, B.1.1.7 and B.1.525 was determined by a microneutralization assay performed in VERO E6 cells using as readout the quantification of cell viability (CellTiter-Glo® 2.0, Promega). The NtAb titer was defined as the reciprocal value of the sample dilution that showed a 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. Statistical analyses were performed using IBM SPSS Statistics, version 20.

Results: In previously infected HCWs, NtAb titres to all viral variants significantly increased at T2inf with respect to T0inf ($p < 0.001$). Also, the median NtAb titer after the second dose vaccination was higher in the previously infected compared with the uninfected group ($p < 0.001$) (Figure 1). Overall, NtAb titres to the B.1.525 strain (63 [7-323] ID50) correlated well with those to B.1 (133 [9-456], P.1 (148 [46-988]) and B.1.1.7 (87 [5-681]) ($p<0.001$ for all comparisons). NtAb titres to B.1.525 were significantly lower with respect to those obtained for each variant ($p<0.001$). Anti-spike protein Abs also correlated with NtAb titres to B.1 (rho = 0.934), P.1 (rho = 0.914), B.1.1.7 (rho = 0.913) and B.1.525 (rho = 0.918) viruses ($p<0.001$ for all comparisons). Also, a significant increase was observed when comparing the anti-spike Ab median titres at T2inf and at T0inf (27763 [18282-46108] vs. 1.7 [0.5-4.4]; $p=0.001$).

Conclusions: NtAb elicited by natural or artificial immunisation with the original B.1 lineage cross-neutralize multiple viral variants. However, neutralization of B.1.525 is significantly reduced with respect to other variants. Indeed, NtAb titres could be ranked with the definite order P.1>B.1=B.1.1.7>B.1.525. Despite reassuring in vitro data, in vivo protection remains to be confirmed.

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Immunopathogenesis I

OP 26 SEVERITY OF COVID-19 PATIENTS PREDICTED BY SERUM SPHINGOLIPIDS SIGNATURE

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Background: The coronavirus disease 2019 (COVID-19) is an ongoing pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The reason behind the high inter-individual variability in response to virus infection is poorly understood, as well as the possible patient's outcome. Most people experience mild to moderate illness whereas 20% of patients progress into severe or critical phase. Mortality risk increases in subjects with comorbidities, however persistent symptoms and long term effects can affect also patients with mild symptoms. The aim of our study was to get better insight into changes in the sphingolipid (SL) composition of COVID-19 patients characterized by different disease severity and relate changes in SL profile to the development of serious illness. SLs are bioactive lipids acting as modulator of cell to cell interactions being the major components of the plasma membrane. Changes in SL composition may affect the structure of the plasma membrane promoting cell signaling translation and influencing specific responses.

Materials and Methods: SLs were extracted from sera of 24 healthy controls and 59 COVID-19 patients (11 mild, 28 moderate, 12 severe and 8 critical). The extracts were analyzed by untargeted and targeted mass spectrometry and levels of enzymes involved in SL metabolism as acid sphingomyelinase (aSMase) and serine palmitoyltransferase (SPTLC1) were assessed by ELISA. Caspase 3 levels were assessed as marker of cell death in relation to COVID-19 severity. Spearman correlations were performed to show the association between SLs and IL-6, C-reactive protein, ferritin, D-dimer, lactate dehydrogenase and liver enzymes (ALT, AST, GGT).

Results: Results indicated a progressive increase of dihydrosphingosine (DhSph), dihydroceramides (DhCers), ceramides (Cers), sphingosine (Sph) according to disease severity, together with a decrease of sphingomyelins (SMs) and sphingosine-1-phosphate (S1P). These results matched with an activation of the de-novo synthesis of Cers, confirmed by high levels of SPTLC1 and by the loss of the protective effect of S1P. In addition, severe patients showed high level of aSMase, that affects Cers and GM3s levels, supporting a shift towards apoptosis, confirmed by high levels of Caspase 3. Critical patients were characterized by high levels of DhSph and DhCers but not of glycosphingolipids. Cers, DhCers, DhSph, Sph, glycosphingolipids, SPTLC1, aSMAse and Caspase 3 were positively associated with inflammatory markers whereas SMs and S1P were negatively correlated.

Conclusions: In severe and critical patients, unbalanced lipid metabolism induces lipid raft structural remodeling leading to cell apoptosis and immunoescape suggesting an active SL participation to viral infection. Therefore, counteracting the SL metabolic rewiring characteristic of severe illness may influence patient's prognosis and decrease viral load thus aSMase, GM3 and SPTLC1 can be potential therapeutic targets.

Immunopathogenesis I

OP 27 EXPANSION OF MYELOID DERIVED SUPPRESSOR CELLS CONTRIBUTE TO PLATELET ACTIVATION BY L-ARGININE DEPRIVATION DURING SARS-COV-2 INFECTION

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Background: A massive platelets activation and thrombotic events characterize severe COVID-19, highlighting their critical role in SARS-CoV-2-induced immunopathology. Since the massive expansion of myeloid-derived suppressor cells (MDSC) described in severe COVID-19, herein we evaluated their possible role in platelet activation during SARS-CoV-2 infection.

Methods: SARS-CoV-2 infected patients (n=62) were enrolled at the INMI "Lazzaro Spallanzani" in Rome. All patients were symptomatic, ranging from moderate (PO2/FIO2>200, n=31, no ICU) to severe (n=31, requiring intensive care unit admission, ICU). Median age was 65 years (range 22-95), 60% were males. Healthy individuals (HD, n=9) were included as controls. The frequency of MDSC and platelets activation (PAC-1 expression) were evaluated by multiparametric flow cytometry and the plasmatic concentration of L-Arginin was evaluated by UPLC-MS/MS Mass-Spectometry. In the vitro experiments, MDSC were isolated by magnetic purification.

Results: During COVID-19, a lower plasmatic L-arginine level was observed compared to healthy donors, which was correlated with MDSC frequency. Additionally, platelets activation, monitored by PAC-1 expression, was higher in severe COVID-19 patients compared to healthy controls, and inversely correlated with L-arginine plasmatic concentration. Notably, MDSC were able to induce platelet PAC-1 expression in vitro by reducing L-arginine, indicating a direct role of expanded MDSC in platelet activation. Accordingly, we found a positive correlation between ex vivo platelet PAC-1 expression and MDSC frequency.

Conclusions: Overall, our data demonstrate the involvement of MDSC in triggering platelet activation during COVID-19, highlighting a novel role of MDSC in driving COVID-19 pathogenesis.

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Immunopathogenesis I

OP 28 CYSTEAMINE IS AN APPROVED DRUG WITH ANTIVIRAL AND IMMUNOMODULATORY PROPERTIES PROMISING FOR COVID-19 TREATMENT

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Background: The aminothiol cysteamine, derived from coenzyme A degradation in mammalian cells, and its disulfide product of oxidation cystamine have been demonstrated to have anti-infective properties targeting viruses, bacteria and even the malaria parasite. To determine whether cysteamine and cystamine exert an antiviral action against SARS-CoV-2, the causative agent of COVID-19, we tested their efficacy in cell-based assays. Moreover, since cysteamine has also immune-modulatory activity, as shown in humans with cystic fibrosis and in mice, we investigated their ability to modulate the SARS-CoV-2-specific immune response in COVID-19 patients.

Methods: Cysteamine and cystamine antiviral effect was evaluated using either the kidney epithelial African green monkey-derived VERO-E6 cells (i.e. cytopathic effect (CPE) inhibition assay; SARS-CoV-2 virus yield assay; electron microscopy) or human epithelial lung adenocarcinoma Calu-3 cells (SARS-CoV-2 virus yield assay). The SARS-CoV-2-specific immunomodulatory effects of these compounds were assessed in COVID-19 patients measuring the levels of interferon (IFN)- in an ex vivo whole-blood assay.

Results: We found that in SARS-CoV-2-infected Vero-E6 cells cysteamine and cystamine decrease the virus-induced cytopathic effects, with IC50 values of 180±53 and 80± 39μM, respectively. Moreover, these compounds significantly decreased the in vitro viral production in both the VeroE6 and in Calu-3 cells. Interestingly, cysteamine and cystamine exert their antiviral action independently of treatment time respect to SARS-CoV-2 infection; similar magnitude of CPE inhibitory effects were observed when Vero E6 cells were treated before, together or after infection.

We also found that cysteamine and cystamine significantly decreased the magnitude of IFN- production induced by SARS-CoV-2 specific peptides in COVID-19 patients.

Conclusions: Overall, our findings suggest that cysteamine, an already human applied drug, and cystamine exert an anti-viral effect against SARS-CoV-2 and have immunomodulatory effect in vitro, thus providing a rationale to test these compounds as novel therapy for COVID-19.

Immunopathogenesis I

OP 29 HIGH CD169 MONOCYTE/LYMPHOCYTE RATIO REFLECTS THE IMMUNO-PHENOTYPING DISRUPTION AND PREDICTS OXYGEN NEED IN COVID-19 PATIENTS

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Background: The COVID-19 is an acute infectious disease caused by the SARS-CoV-2 virus. To date, a standard therapeutic approach for COVID-19 patients (COV) has not been established and the identification of early biomarkers to predict disease progression is needed. Recently, was suggest that SARS-CoV-2 infects CD169 macrophages in the spleen and lymphonodes playing a central role in mediating SARS-CoV-2 translocation. Moreover, CD169 was strongly overexpressed in the blood of confirmed COV. To clarify whether CD169 was activated by SARS-CoV2 stimulation, Peripheral Blood Mononuclear Cells (PBMCs) from HDs were stimulated in vitro with SARS CoV-2 Spike protein for 24 hours and CD169 RMFI and mRNA expression were evaluated. Then, we analysed CD169 in blood cells of COV admitted to the hospital during the COVID-19 outbreak and correlated its expression with clinical characteristics.
Material and Methods: The ratio of the Median Fluorescence Intensity (MFI) of CD169 between monocytes and lymphocytes (CD169 RMFI) was used to screening blood samples of Healthy Donors (HDs) and COV by flow cytometry, and its correlation with clinical signs, inflammatory markers, cytokines mRNA expression, and disease progression was evaluated.
Results: In vitro stimulation of PBMCs from HDs with SARS-CoV-2 Spike protein induced a significant increase in CD169 RMFI in a dose-dependent manner with a significantly increase of IL-6 and IL-10 gene expression. CD169 RMFI was also highly expressed in the macrophages of COV but not in those of HDs, especially in untreated patients at sampling. In CD4 + T cells of untreated patients, CD169 RMFI inversely correlates with the expression of central memory (CD45RA- CCR7+) and effector memory (CD45RA- CCR7-) cells and directly correlated with exhaustion markers (CD57+ PD1+). In CD8+ T cells, its expression was associated with the decrease of naive (CD45RA+ CCR7+) and increase in EM (CD45RA- CCR7-) cells. Finally, CD169 RMFI positively correlated with the senescence marker CD57+. Moreover, the CD169 RMFI correlated with inflammatory markers, blood cytokine levels, and pneumonia severity in the untreated group of COV at sampling. Notably, in this group, CD169 reflects the respiratory outcome of patients during hospitalization.
Conclusion: our data highlighted the association between CD169 expression and clinical status, inflammatory markers, and respiratory outcome and considering the immunological role of CD169 and its involvement during the infection and the progression of COVID-19, it could be considered as an early biomarker of disease progression.

Immunopathogenesis I

OP 30 EFFECT OF SARS-COV-2 SEQUENCES ON IMMUNE RESPONSE IN A549-ACE2 LUNG CELLS

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Background: Phylogenetic analysis of the full-length Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genome showed that, RaTG13 is one of its closest relatives. The SARS-CoV-2 genome encodes 16 nonstructural proteins, 4 structural proteins (spike; envelop; membrane; nucleocapsid) and at least 8 accessory proteins (ORF3a, ORF3c, ORF6, ORF7a, ORF7b, ORF8, ORF9b and ORF10). As these proteins may contribute to host adaptation and the modulation of immune responses, we applied a multidisciplinary approach to verify SARS-CoV-2 and BatCoV RaTG13 ORF transfection effect on specific cellular pathways involved in the antiviral and immune response.

Methods: 48-hours post viral protein transfection in A549-ACE2 lung cells we analysed: 1) Gene expression profiles of 80 genes involved in the immune and antiviral response (QuantiGene Plex assays); 2) the release of 27 soluble factors including caspases and cytokines in the supernatants (Multiplex ELISA). Simultaneously, A549-ACE2 lung cells were in vitro infected with 0.1 MOI of SARS-CoV-2.

Results: Preliminary results show that: following SARS-CoV-2 infection Type I Interferon (IFN) and inflammatory response are significantly upregulated. Conversely, ORF9b and N transfection was accompanied by an activation of the inflammatory process (IL1 , IL-6, IL-8, IL-12B, CCL3) and a reduced expression of both Interferon Stimulated Genes (IFITM1, IFITM3, IFIT1, STAT1, STAT2) and antigen presentation pathway (HLA-A and ERAP2). Notably, the trend of the different targets was comparable following the transfection of ORF sequences from SARS-CoV-2 and BatCoV RaTG13 .

Conclusions: Though preliminary, these results suggest that coronavirus accessory proteins contribute to the activation of immune response at different levels. Further analyses will be necessary to validate the results obtained in different cell lines and to verify the effect of SARS-CoV-2 proteins carrying positively selected variants mainly those unique to the new emerging variants of concerns (VOC). This study will allow to clarify the mechanisms of immunopathogenesis induced by the different SARS-CoV-2 sequences and to identify potential therapeutic molecules.

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Epidemiology / Social Sciences I

OP 31 SARS-COV-2 EVOLUTIONARY DYNAMICS IN THE FIRST PHASE OF THE EPIDEMIC IN ITALY

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Background: The COVID-19 pandemic represents an unprecedented challenge for global public health with the continuous emergence of new genetic viral variants and the related implications like their potentially increased pathogenicity or transmissibility and, possibly, vaccine escape. Presently no comprehensive data are available to establish the lineage of SARS-CoV-2 strains circulating in Italy and their population dynamics. Considering that Italy has been the first and one of the main incubators for the epidemic spread in Europe and in the United States, the analysis of SARS-CoV -2 molecular epidemiology since the first wave of the epidemic in Italy is of particular interest.
The aim of this study was the reconstruction of SARS-CoV-2 evolutionary dynamics in time and space in Italy and Europe.
Materials and Methods: Whole Genome Sequences and epidemiological data were collected at the centres participating to the collaborative group SCIRE (SARS-CoV-2 Italian Research Enterprise) between 24th February and 18th June 2020. Two dataset were analysed, the first including only Italian sequences (n=479) and the second including also European and Chinese genomes (n=1,375). The maximum likelihood trees were estimated using IQ-TREE v.1.6.12. The Italian dataset was also analysed by BEAST v.1.10 in order to estimate the tMRCAs of the main clades. The phylogeography was reconstructed using PastML.
Results: The most prevalent lineages were B.1 (n=222, 47.7% including 32 lineages derived from B.1), and B.1.1 (n=141, 30.3%, including 19 lineages derived from B.1.1) followed by the lineages B (n=73, 15.7%) and B.1.1.1 (n=29, 6.2%).
A total of 80 (80/465, 17.2%) Italian isolates were included in 22 highly supported clusters, while most of the Italian strains were intermixed in the whole tree. While the clusters observed in the first weeks of the epidemic included frequently international isolates, only pure Italian clusters were observed mainly after the lockdown and distancing measures were adopted. Lineage B and B.1 spread between late January and early February 2020, from China to Veneto and Lombardy, respectively. Lineage B.1 spread further to other Italian regions (mainly in the North) and other European countries. Lineage B.1.1 most probably evolved within Italy and spread from central to other Italian regions, particularly in the South, and to European countries. The lineage B.1.1.1 developed most probably in other European countries entering Italy only in the second half of March and remained apparently localized in Piedmont until June 2020.
Conclusions: The reconstructed ancestral scenario suggests a central role played by China and Italy in the widespread diffusion of the highly transmissible D614G variant in Europe in the early phase of the pandemic. More dispersed exchanges involved several European countries from the second half of March 2020.

Epidemiology / Social Sciences I

OP 32 CHARACTERIZATION OF SARS-COV-2 VARIANTS CIRCULATING IN CENTRAL ITALY BY DEEP-SEQUENCING OF FULL-LENGTH S GENE

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Background: The spread of SARS-CoV-2 variants of concern (VOC) has led to increased attention on the spike glycoprotein (S). Our aim was an in-deep characterization of S variants circulating in Central Italy by deep-sequencing.
Methods: Nasopharyngeal-swabs (NS) of SARS-CoV-2 infected patients (pts) were collected from June 2020 to June 2021. Full-length S gene was performed using MiSeq (Illumina-Inc) with home-made protocols. Mutations were defined according to their intra-host prevalence as: major (>99%), minority (2-20%), intermediate (>20-70%). All pts had NS RT-PCR positive for 3 genes: envelope(E), nucleocapsid(N) and RNA-dependent-RNA-polymerase(RdRp) with Cycle-Threshold (Ct) values <35. Mann-Whitney and Kruskal-Wallis tests were used for statistical analyses.
Results: S sequences were characterized in 207 pts, 108 (52.2%) hospitalized and 99 (47.8%) non-hospitalized; 62.3% were males and 83.6% with Italian ethnicity. Higher Ct values were observed in hospitalized vs non-hospitalized pts [median(IQR) NS Ct of E-N-RdRp was 25(21-28)-24(20-27)-25(22-28) vs 22(17-25)-20(17-25)-22(18-26), respectively, all p<0.001].
Overall, 163(78.7%) pts were infected with a VOC, with B.1.1.7 (63.8%) most prevalent, followed by P.1 (30.7%), B.1.351 (4.3%) and B.1.617.2 (1.2%) (Fig 1). 23.1% of pts with B.1.1.7 showed at least 1 additional major S mutation vs 38% with P.1 [with a high frequency (11/19) of S640F mutation], 1(14.3%) with B.1.351 and 2/2 B.1.617.2 (with G142D mutation in the known position).
Also, several variants of interest (VOIs) were observed: 3(1.4%) B.1.258 characterized by N439K+D614G, 2(1.5%) B.1.525, and 1 B1.160 characterized by S477N+D614G (Fig2). Until February, EU1 variants were observed (13.0%) with A222V+D614G, of them 70.4% showed also A262S+P272L.
Presence of minority mutations were observed in 73 pts [35.3%, median(IQR) 2(1-3) mutations]; while 10 pts showed 1-2 mutations with intermediate prevalence.
Stratifying pts according to type of unknown additional mutations [minority+/-major (mMa,N=73), only major additional (Ma,N=42) and without additional mutations (Wa,N=92)] significant higher Ct-values were observed in pts with mMa mutations vs all other groups (Tab1).
Interestingly, Δdays from first COVID19 symptoms to NS tended to be longer in pts with mMa respect to others [median (IQR) mMa: 10(7-12) days vs Ma: 5(4-10) days vs Wa: 9(5-10) days, p=0.006].
In addition, 24(11.6%) pts were vaccinated, of them 8 pts were hospitalized and overall 58.3% carried B.1.1.7, 29.2% P.1, 8.3% B.1.525 and 4.2% B.1.617.2 VOCs. According to additional mutations 8 showed mMa, 4 Ma, and 12 Wa.
Conclusion: We confirmed a rapid spread of VOCs, more than half characterized by the presence of additional mutations. In the case of minority mutations, higher Ct values were observed and correlated with a longer duration of infection and lower viral load, suggesting an intra-host evolution regardless of the type of VOC.

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Epidemiology / Social Sciences I

OP 33 IMPACT OF COVID PANDEMIC AND ANTI-SARS-COV-2 IMMUNIZATION ON VACCINATION AGAINST SEXUALLY TRANSMITTED INFECTIONS

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Background: Vaccination against sexually transmitted infections (STIs) is a major objective for any STI Clinic. Immunization for HAV, HBV and HPV is free for subjects at high risk of infection; anti-meningococcal vaccinations are recommended under special conditions. The start of COVID pandemic in February 2020 had a significant impact on most medical procedures, including vaccination activity. Additionally, anti-SARS-CoV-2 vaccinations require some weeks of distance from the other immunizations. Herein we describe the impact of COVID pandemic and immunization on our vaccination activity in HIV-positive patients, PrEP users and subjects attending the Clinic for STI screening.

Methods: This monocentric, retrospective analysis included all subjects attending our STI Clinic who were evaluated for vaccination from 2018 onwards. Time was stratified in three Periods: 1) before COVID start (up to February 2020); 2) during COVID diffusion (from March 2020 to March 2021); 3) from SARS-CoV-2 vaccines availability (from March 2021 onwards). Vaccine schedules were related to these 3 periods. Delay in vaccine schedule and course fulfillment were evaluated. Descriptive statistics (median and interquartile range for continuous variables, absolute and relative values for categorical variables) were used. Mann Whitney U and Kruskal-Wallis for continuous variables, and Chi-square tests for categorical variables were applied.

Results: The analysis included 572 individuals: they were mainly males (84%), Italians (82%) and with a median age of 44 (IQR 36-53) years. The majority was HIV-infected (75%), the others were PrEP users (20%) and subjects attending STI screening (5%). During the study period 611 first doses and 813 booster doses were administered. The number of dose administrations was almost stable from January 2018 to February 2020, fell dramatically during the first lockdown (when only 21 doses were administered) and increased from May 2020 onwards to values higher than the pre-COVID period (Figure 1). The median delay in vaccine completion was 27 (IQR 3-85) days in Period 1, 37 (IQR 6-66) in Period 2 and 11 (IQR 3-31) in Period 3 ($p=0.006$). The rate of course non completion was 30.2% in Period 1, 33.7% in Period 2 and 62.0% in Period 3 ($p<0.001$). Nevertheless, excluding the last Period that is still ongoing, the rate of fulfillment was not different between Period 1 and 2 ($p=0.332$).

Conclusion: Vaccination activity suffered a significant decrease throughout the first lockdown. Nevertheless, during the following months the number of administered doses increased noticeably to made up for what went missed during the first lockdown, although with a significant delay. So far, it does not seem that anti-SARS-CoV-2 vaccinations had an impact on STI vaccination schedule. However, COVID immunization campaign is still ongoing and its full effect on the management of the other vaccines should be evaluated in the following months.

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Epidemiology / Social Sciences I

OP 34 INFLUENZA VACCINE: KNOWLEDGE AND BELIEFS AMONG ADHERENT PLWH DURING THE FIRST SEASONAL CAMPAIGN OF THE COVID-19 ERA

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Background: Influenza is a common pathogen of the respiratory tract that can cause serious respiratory issues, especially in people living with HIV (PLWH). Despite flu-vaccine being recommended by international guidelines, there is scarce data about the attitudes and practices of HIV-infected patients towards influenza vaccination during the COVID-19 pandemic. The aim of the study was to gain a better understanding of the determining factors that drive PLWH to influenza vaccination, focusing particularly on whether the COVID-19 pandemic influenced the patients' willingness to vaccinate.
Methods: A questionnaire was administered via telephone, evaluating the subjects' adherence (over the last 3 years), while also investigating their knowledge and beliefs about influenza vaccination, focusing on how the pandemic influenced their willingness to vaccinate. The population was divided into two groups based on adherence to vaccination: full adherence (all 3 years), non-full adherence (1 or 2 years). Patients' comorbidities and key clinical information (i.e., CD4+ count, age, HIV-vl) were obtained from the records of their clinical consultation. Data were analysed using the Chi-squared and Mann Whitney U tests.
Results: Patients assisted by our clinic in December 2020 amounted to 3841: 388 (10.1%) booked the administration of the influenza vaccine at our facility. Two hundred nineteen patients participated in the survey. Mean age was 53 years, 76.3% (167/219) were male, 76.5% (58/219) had at least one comorbidity. All of them achieved viral suppression, only 3.7% (8/219) presenting a CD4 count < 200 cell/mm3. Comorbidities did not positively influence the adherence to vaccination (p>0.2). The COVID-19 pandemic did not significantly impact the willingness to vaccinate, and adherence was not different between the two groups (p=1). Several misbeliefs about the vaccine emerged: influenza vaccine was considered protective against both influenza and SARS-CoV 2 by almost a quarter (22.8%) of the population, and half (49.3%) was convinced that vaccination could permanently raise their CD4+ count, especially among fully adherent patients (p=0.015). Only half of the population (111/219 50.7%) was brought to vaccination by the counselling offered by healthcare professionals. Among the non-fully adherent population, 90/107 (88.2%) patients did not know they needed to vaccinate against influenza. Finally, it emerged from the survey that 25/102 (24.5%) from the non-adherent group would not have been vaccinated in a location other than our clinic (p<0.05).
Conclusions: Despite a generally positive attitude toward vaccination, healthcare professionals must offer better counselling, to improve the patients' understanding of the vaccination and its benefits, especially during the time of the COVID-19 pandemic. A secure and private space for vaccination seems to encourage immunization, especially among less adherent people, possibly because of the HIV stigma.

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Epidemiology / Social Sciences I

OP 35 RESULTS OF A SARS-COV-2 WORKER SCREENING IN THE MARCHE NORD COMPANIES TO PREVENT VIRUS INFECTION IN THE WORKPLACE

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Background: During the first months of the SARS-CoV-2 pandemic, the Covid-Lab of University of Urbino and the Confindustria Pesaro Urbino association signed an agreement to support the Marche Nord companies in the adoption of anti-contagion safety protocols. A double step procedure involves a positive serological rapid test (presence of IgM / IgG or both antibodies), followed by a nasopharyngeal swab (NPS) for the SARS-CoV-2.

Material/Methods: The detection of IgG and IgM Ab was performed using a rapid immunochromatographic test marketed by Diatheva, CE-IVD certified. Total RNA from NPS was subjected to a one-step real-time RT-PCR multiplex for the detection of RNA-dependent RNA polymerase (RdRp) specific gene and envelope gene (E) of the SARS-CoV-2, and the internal control (human RNase P) (COVID-19 PCR DIATHEVA Detection kit, CE-IVD certified). The results were considered valid when the cycle threshold (Ct) value of the internal control was ≤ 40 and were considered positive when the Ct values of RdRp target gene were ≤ 45, negative when > 45.

Results: Between May 2020 and Apr 2021, over 10000 rapid serological tests had been carried out on workers of 35 companies associated with Confindustria, and in 5% of cases IgG or IgM were found (519). All the 519 swabs gave a valid result (RNAse P Ct ≤ 40, mean±SD 30.10±3.98) with 105 positive results (20%) for SARS-CoV-2 with a Ct value ≤ 45 (mean±SD 23.13±7.24). Overall, only 1% of samples resulted positive for viral RNA (105/10000): in the months May-Sept 2020, the positivity rate was 0% (0/107 swabs), Oct-Dec 2020 19% (64/329) and in the months Jan-Apr 2021 49% (41/83). The number of "very low positive" samples with RdRp Ct value ≥ 35 were 11 (10%) (AMCLI, Indicazioni operative 001-2021).

We compared NPS collected in two different viral transport medium [Zymo Research (1 ml fill) and Jiangsu Rongye Tecnology (3 ml fill)] and in samples from "3 ml swab" significantly higher RNAseP Ct values were obtained (ΔCt 6.1, p<0.0001). The spectrophotometric analysis confirmed that using "3 ml swab", RNA samples had a lower concentration (14±6 ng/µl vs 52±19 ng/µl, p<0.0001) and consequently as might be expected, a lower amount of RNA were used for subsequent RT-PCR test (72±30 ng vs 259±95 ng, p<0.0001).

Conclusion: The University of Urbino set up a rapid-response (within 24 h, generally <6 h) diagnostic centre for RNA of SARS-CoV-2 detection (Covid-Lab) allowing the companies to activate the optimal safety path to ensure the health and safety of workers in the workplace. Our observations during this first year of activity, highlight that in the workplace, the infection does not seem to spread if precautionary measures are followed and only 1% (1 worker out of 100) tested positive for the SARS-CoV-2 virus.

Due to the variety of swabs available on the market, to avoid false negative results and problems due to low sensitivity with low viral load samples, the use of high-performance PCR kits is recommended.

Epidemiology / Social Sciences I

OP 36 A MIXED METHOD OF FOLLOW-UP WITH TOTAL PATIENT CARE PROVIDED CONTINUUM WITH SAVING OF HOSPITAL CHECKS DURING THE COVID-19 PANDEMIC

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Background: One of the biggest challenges in the COVID-19 era is to provide assistance to a great number of inpatients with severe COVID-19 infection, at the same time assuring the continuum of care for patients living with HIV. In this work we assessed resilience of our system in providing the continuum of care and results in Calabria. In this region, for a matter of reasons, resilience of the health care system as a whole was severely challenged especially during the first wave of the pandemic.

Material and Methods: HIV patients followed in our centre were included from January 2019 to March 2020 (pre-pandemic era, PPE) and from April 2020 to July 22nd, 2021 (pandemic era, PE). We estimated the intensity of follow-up as the mean interval of days between patient checks (performed as day-hospital admissions), adjusted for the length of follow-up in both eras. Results of HIV-RNA, CD4+ T-cell counts, and cART regimens were also analysed.

Results: 69 patients were studied, 52 already seen in PPE and 17 newly entered in PE, the majority of them (15/17) being already experienced for cART. Eight patients in PPE and 5 in PE were missed along the follow-up, including 2 patients who died (1 in each era). The remaining 56 patients are still followed-up using a mixed method (phone contact and direct consultations) at the date of the present analysis. Intensity of follow-up decreased, with a mean interval between patient checks of 92 days (min-max: 13-228) in PPE to 161days (min-max: 16-478) in PE. At last evaluation, HIV-RNA was undetectable in 51/56 (91%) patients, being most of them (33/56, 59%) on cART including DTG. In a sub-analysis, among 30 patients with available evaluations both in PPE and in PE maintaining the same cART (except 1 who underwent simplification), 28 remained with undetectable HIV-RNA, while 1 patient continued to have low-level viraemia (from 50 to 100 copies/mL), and only 1 patient had a virological failure. CD4+ T-cell count ranked as for clinical risk (<200/mm3vs. greater values) remained stable.

Conclusions: Despite reduction in the intensity of follow-up, an effective continuum of care was guaranteed using a tailored approach with phone contacts and day-hospital admissions. Although administratively inappropriate, day-hospital appeared to be useful in health crisis providing a setting where consultations and exams could be performed simultaneously as needed without sending patients to multiple outpatient services. It remains to be seen whether such an approach is feasible and acceptable even in centres with a greater number of patients on follow-up. Also, optimized regimens with high genetic barrier could have played a positive role.

Epidemiology / Social Sciences II

OP 37 HIV-RELATED INTERNALIZED STIGMA AND PATIENT HEALTH ENGAGEMENT (PHE) MODEL IN AN ITALIAN COHORT OF PEOPLE LIVING WITH HIV

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Background: The care engagement of People living with HIV (PLWH) measured with the patient health engagement (PHE) model and its association with HIV-related are not well established. Indeed, currently there is no data yet about the engagement of PLWH measured with the PHE model. This study aimed to evaluate the effects of HIV-related internalized stigma on care engagement and mental health and to fill the lack of data on PHE model applied to PLWH.

Material And Methods: We conduct a cross-sectional survey consecutively enrolling 82 PLWH. Exclusion criteria were age <18 years and difficulties with the Italian language. Each participant completed an anonymous 46-item online survey. Internalized HIV-related stigma was measured using the modified six-item internalized AIDS-related stigma scale (IA-RSS). The patient health engagement scale (PHE-S) was used to measure the patient's active involvement in the treatment process. Zung Depression Scale was also administered.

We investigated significant difference among different engagement positions of the IA-RSS and compared different frequencies in engagement positions according to demographic and clinical variables. Futhermore factor associated to IA-RSS were explored.

Results: Many of PLWH were male (73.2%), aged 51 to 60 years (45.1%), with upper secondary school degree (47.6%) and employed (53.7%). Most of the respondents (63.4%) were between 5 and 10 years ago diagnosed with HIV and received between 5 and 10 years ago for the first time ART (57.3%). Overall, 74.4% reported HIV-RNA<50 copies/mL and the mean adherence to ART was 9.37 (SD 0.91) on a 0-10 scale.

Higher IA-RSS scores were positively associated to depression scores (β 0.07; 95% CI 0.03/0.10; p<0.001) after adjusting for time from HIV diagnosis (β 0.86; 95% CI -0.22/1.95; p=0.0119) and heterosexual transmission risk factor (β 0.72; 95% CI -0.05/1.50; p=0.067).

The mean IA-RSS value was significantly higher in PLWH in the blackout and arousal phase of PHE compared with patients in the adhesion (mean 5.5 [SD 0.8] vs 2.95 [SD 1.5]; p=0.003 and mean 4.16 [SD 1.4] vs 2.95 [SD 1.5]; p=0.006 respectively) and eudamonic phase (mean 5.5 [SD 0.8] vs 2.09 [SD 1.1]; p<0.001 and mean 4.16 [SD 1.4] vs 2.09 [SD 1.1]; p<0.001 respectively). Furthermore, we identified a higher percentage of patients with elevated depressive symptoms in the blackout phase of PHE [p <0.001; 60% (n=3/5)] compared with PLWH in the arousal, adhesion (both 20%, n= 1/5) and eudamonic phase (0%, n=0/5).

Conclusion: In conclusion, our findings highlight that HIV-related stigma might be associate to higher levels of depression and poor engagement to care in PLWH. Therefore, this overview describes for the first time the engagement in care of PLWH measured with PHE and underlines the importance of improving the psychological wellbeing of PLWH and fight HIV-related stigma to facilitate care engagement, a fundamental step for a population with chronic disease involved in long-life treatment to maintain quality of life.

Epidemiology / Social Sciences II

OP 38 TALKING ABOUT STIGMA AND HIV PREVENTION, THE ARTISTS' CONTRIBUTION

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Lila Cagliari OdV, Cagliari

Background: In 2019 Lila Cagliari OdV (member of LILA - Italian League for fighting AIDS) handled the first HIV prevention campaign unded by the Autonomous Region of Sardinia. At the beginning, it was realised a conventional communication campaign and then, since WAD 2020, thanks to the participation and the contribution of many different artists, a series of multimedia contents were published. The campaign, called "With a little help from our friends", is a joint action to speak about HIV by using different types of languages and includes 16 video spots. Addressed to the youth population, it deals with the use of condom and invite them to get tested; moreover it promotes the concept of U=U, in order to make it accessible to anyone and foster a culture of non-discrimination towards PLWHIV.
Methods and Materials: Lila Cagliari has contacted several local artists, many of whom are well-known worldwide (Paolo Fresu, Carolina Melis). We have reached directors, actors, musicians, performers, cartoonists, writers who could attract with various artistic languages and convey the message. Thus far the artists involved have been 31 and the materials and methods used are as numerous as the works realised by them. The contents are available on Lila Cagliari website, social media and at the meetings with the high school students within our project EducAids 2021. Some of the most appreciated artists among the youth have been invited to talk about HIV at these meetings.
Results: The works realised highlight the variety of contents linked to HIV which, no matter how complex they are, they could be communicated through different artlangs. Each artist has focused on a theme, such as U=U, the importance of knowing your own status, the promotion of femidom, the fight against stigma. Some artists have given their contribution by revealing themselves as people living with HIV. This campaign has enabled us to come into contact with loads of young people: it was a great chance to talk about conscious sexuality and stigma. It was favourably unexpected the artists'immediate response and their wish to do something through this form of "social art" which they all felt as a mission. All the works realised on video have been endorsed by the Società Umanitaria Cineteca Sarda and Sardegna Film Commission Foundation, which have promoted these videos within their film festivals and those in which they took part.
Conclusion: The communication campaign has overall enjoyed widespread appreciation and in particular by the PLWHIV in contact with our organisation and by the artists' admirers involved. Each contribution has helped in the fight against stigma and discrimination and has achieved the goal to inform about HIV key subjects and promote HIV testing. Above all, that allow us to reach different target groups and build further relations between the artists and our organisation, and among the same artists.

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Epidemiology / Social Sciences II

OP 39 A VISUAL SCALE TO EVALUATE THE QUALITY OF LIFE IN PLWHA. FOURTH-90, UTOPIA OR REALITY?

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Background: Over the past decade, advances in HIV treatment have resulted in major changes in the lives of people living with HIV/AIDS (PLWHA). Considering the low toxicity of present therapies and the growing simplicity in their formulation, the future aim will be the so-called "fourth 90", that is the psychological, physical and social well-being of PLWHA. Several tests were proposed to investigate the quality of life (QoL) of PLWHA, but they mostly resulted too complex and not adequately effective to be routinely used in clinical practice. Recently, an Australian study - the PozQoL study – reported on a quick, inexpensive and easy-to-understand test aimed at assessing the QoL of PLWHA. Here we described our experience in PLWHA' QoL evaluation using a questionnaire inspired by PozQoL in Central Italy.
Matherials and methods: A questionnaire was proposed to PLWHA during routine visits at our centres from January to June 2021. The questionnaire consisted of 13 multiple-choice questions divided in 4 main domains (health, psychological, social and functional aspects, Table 1). The possible answers were collected by a visual scale. It consisted of 5 coloured face emoticons expressing 5 different grades of concern (from a green smiling face representing no concern at all – grade 1 – to a red sad and worried face representing serious concern – grade 5). Grade 1 and 2 were considered as "low concern" while grade 3 to 5 as "moderate to serious concern". We separately evaluated each question; in case of >33% grade 3-5 answers, a univariate and multivariate analysis for risk factors were performed.
Results: We enrolled 322 patients, 37 remained anonymous and, therefore, final analysis include the remaing 285 patients. The main characteristics of the study population are described in Table 2. Question 10 about HIV stigma reached the most percentage of worrisome answers (56%) followed by question 3 and 2 (49% and 48%, respectively); also questions 1, 6, 8, 11 and 12 underwent further analysis that are reported in table 3. Stigma was not associated to any risk factor. In the health domain (question 1 to 3), PLHIV with a recent diagnosis were more concerned about their status.
Conclusions: In our experience, this visual scale appeared easy to be understood, administered and capable to quickly evaluate different domain of well-being (fourth 90). PLWHA were mostly concerned about the HIV-related social aspects, especially stigma and discrimination. No specific risk factors were highlighted. The fourth 90 is still far to be reached. A global approach involving the whole society should be taken into account.

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Epidemiology / Social Sciences II

OP 40 HEALTH-RELATED QUALITY OF LIFE (HRQOL) FROM HIV PATIENTS' PERSPECTIVE: COMPARISON OF PATIENTS-REPORTED OUTCOME (PRO) MEASURES AMONG PEOPLE LIVING WITH HIV (PLWH) AND OTHER CHRONIC CLINICAL CONDITIONS

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Objectives: To perform a comprehensive assessment of patient's reported outcomes measures (PROMs) among PLWH and patients affected by other chronic conditions (OC) such as diabetes mellitus type 1, rheumatoid arthritis, breast cancer in hormonal therapy, and to investigate factors associated with different PROMs outcomes.
Methods: Cross-sectional observational study. Questionnaires investigating quality of life (Medical Outcomes Study Short Form 36-item Health Survey), work productivity (WPI), adherence (Morinsky), health status (Eq-5D-3L), treatment satisfaction (TSQ) were administered to pts consecutively observed at a single Universitary Hospital during a 2 month period, with comparable disease related aspects. Logistic regression analysis was used to analyze the association between disease group (HIV vs OC) and PROMs.
Results: 230 patients were enrolled (89 PLWH, 143 OC). Mean age: 49 y (SD 10), mean time of disease 12y (10), 96% were Caucasian, 35% assumed polypharmacy, 42% of male were PLWH vs 16% OC ($p<0.001$), 19% PLWH vs 6% OC had clinical complications ($p<0.001$). HIV infection was independently associated to a better quality of life in several domains compared with the other conditions, except in mental health, whereas a worst quality of life in most domains was reported by older patients and those experiencing polypharmacy.
Conclusions: In this cohort of patients with chronic conditions followed within the same health setting, PLWH showed better self-reported health outcomes compared to other chronic conditions considered as a whole, with comparable characteristics of chronicity. The independent detrimental role of older age and polypharmacy in most outcomes suggests the need of longitudinal assessment of PROMs in clinical practice.

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Epidemiology / Social Sciences II

OP 41 USING TECHNOLOGY TO SUPPORT VULNERABLE PLWHIV AT THE TIME OF CORONAVIRUS

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Using technology to support vulnerable PLWHIV at the time of coronavirus

Introduction: At times of social and health crises, the gap between those moving forward and those at a standstill broadens. Considering this period, defined by the SarsCov2 pandemic, to be particularly challenging for vulnerable subjects, our Association, with the unconditioned help of Gilead Science, set up a project: NOT TO BE LEFT BEHIND Supporting vulnerable PLWHIV at the time of coronavirus.

Materials and methods: The project's target were PLWHIV in the Turin metropolitan area, on whose lives the pandemic had had an especially negative impact, increasing difficulties in handling daily routines and causing a drop in the quality of life. The project provided individuals with support on various levels – health, psychological, social and economic – thanks to a multidisciplinary team made up of an infectious diseases specialist, a nurse, two psychologists, three counsellors (one a peer counsellor), a computer expert, a coordinator, and a volunteer. Due to the epidemic, technological devices – smartphones, tablets, Zoom – with the backing of a computer expert, were used to contact and support individuals.

Results: Activities began in June 2020. Upon indication of the doctors of the Amedeo di Savoia hospital, 16 people were contacted and 14 through the Association's helpline: 16 men and 14 women; 22 heterosexuals, 8 homosexuals (MSM), 26 Italians, 4 Latin Americans. A total of 346 interventions were carried out: 274 by counsellors, 46 by psychologists, 14 by the computer expert, 12 by a volunteer. Telephone and video interviews, as well as vocal and written messages, helped not only to make the people contacted feel less alone and less isolated, but they also made it possible to build trust based on listening, allowing individuals to talk about themselves and bring to our attention any critical points that might be dealt with thanks to the help of our counsellors and psychologists. Counsellors identified 6 cases for referral to the psychologists; in 4 cases they identified economic difficulties, resulting in a volunteer delivering shopping vouchers on a monthly basis. 2 people entered the Association's self-help group; 2 women were invited to join the support group for HIV + women. The project closed on 15 December 2020.

Conclusions: Despite the use of such uncommon means of contact, the individuals supported made their appreciation apparent. Networking and strong bonds with the doctors and nurses of the Amedeo di Savoia hospital proved to be winning elements in the project. The presence of an HIV+ counsellor, a self-help group and a group of women supported by a psychologist represented further resources.

Epidemiology / Social Sciences II

OP 42 IMPACT OF SARS-COV-2 PANDEMIC ON QUALITY OF LIFE IN PEOPLE WITH HIV

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Background: Since the start of the SARS-CoV-2 pandemic, many hospital wards have been transformed into COVID-19 wards. Also, outpatient services, including HIV outpatients clinics, have been closed. For this reason, access to care for people with HIV (PWH) has been challenging. Therefore, our study aims to evaluate the quality of life change in PWH during the pandemia.
Material and methods: Before the pandemia, we proposed four questionnaires (CES depression scale, Hamilton anxiety rating scale, mini nutritional assessment, Pittsburgh sleep quality scale) to PWH followed in our outpatient clinic as part of clinical routine evaluation. Between June and July 2021, we re-proposed the questionnaires to the same patients. Furthermore, we investigated the subjective perception of lack of medical attention antiretroviral therapy collection. We also recorded clinical and viro-immunological data.. Continuous variables with non-parametric distribution were compared with the Wilcoxon Rank Sum test. P-value was considered significant when <0.05.
Results: Sixty-four patients agreed to complete the questionnaire before the pandemic. Unfortunately, two patients died during the pandemic, and six refused to complete the questionnaires again.
Overall, 56 patients have been included in the study, with a median age of 58 (IQR 50-0.5) years. Of them, 43 (74.2%) were male. The main characteristics are summarized in table 1.
Since the start of the pandemia, only nine PWH have changed the treatment, in particular, five patients started a dual-regimen with 3TC/DTG, and four PWH stopped treatment with TAF/FTC/EVG/c and started TAF/FTC/BIC. Before the pandemia, seven patients had a detectable HIV-RNA vs. two at the last control (p=0.16).
Regarding CES-D, the median score was 13(IQR 6-18) before the pandemia and 10 (IQR 4-20); the number of people with a score above 16 (minimum score to suspect the presence of depression) was 23 before and 21 after. About HAM-A the median score was 9 (IQR 4.5-9.5) before and 10(IQR 3.5-17) after the pandemic, with a p-value=0.0158. Furthermore, the sleep quality changed significantly (p=0.0160); the median score of the Pittsburgh scale was 6(IQR 3-9) and 7(IQR 3.5-11) before and after the pandemic, respectively. We observed a decreased MNI score, especially in patients who had a worsening of CES-D and HAM-A scores. The median score was 14(IQR13-14) before and 13(IQR 12 -14) after (Table 2).
Finally, 18(32%) patients reported a lack of medical assistance during these months. In particular, people who had this feeling had significantly higher HAM-A and CES-D scores (p=0.015 and p=0.005, respectively). However, only 5(9%) patients reporting issues with the ART collection.
Conclusions: Although the pandemic had no impact on viral suppression rates, we observed increased anxiety and worsening of sleep quality and nutrition. Thus, a better management strategy is needed to provide better care and avoid the decrease in quality of life in PWH.

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Antiretroviral Therapy II

OP 43 CHANGES IN SERUM INFLAMMATORY AND IMMUNE ACTIVATION MARKERS ASSOCIATED WITH LAMIVUDINE/DOLUTEGRAVIR AND TENOFOVIR ALAFENAMIDE/EMTRICITABINE/BICTEGRAVIR AS INITIAL ANTIRETROVIRAL TREATMENT

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Objectives: The use of dual antiretroviral therapies could reduce the toxicity of antiretroviral treatment in HIV-1-infected patients, but it's unknown still today if reducing the number of drugs could lead to an adverse increase in inflammation and immune activation markers.

Methods: Prospective cohort study of adult HIV-infected patients naïve to combination antiretroviral therapy (cART), who started as initial regimen lamivudine/dolutegravir 300/50 mg daily (3TC/DTG) or tenofovir alafenamide/emtricitabine/bictegravir 25/200/50 mg daily (T/F/BIC), and were followed-up for 12 months. The primary endpoint was change in serum levels of inflammation markers: high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL -6), tumor necrosis factor-α (TNF- α), and D-dimer. The secondary endpoint was change in the CD4+/CD8+ T lymphocyte ratio.

Results: On the whole, 84 patients were enrolled in the study: 39 in the 3TC/DTG group and 45 in the T/F/BIC group. Overall 83% were men, 95% Caucasian, and the mean age was 45.3 years. The baseline mean CD4 T lymphocyte count was 414 cells/mm3, and the baseline mean log10 HIV RNA was 4.2 copies/mL; 16 patients (19%) had CD4+ T lymphocyte count <200 cells/mmc, and 22 (26%) had plasma HIV RNA >100,000 copies/mL. Comorbidities included hypertension in 19 cases, diabetes mellitus in 9, and obesity in 8. After 12 months, 3TC/DTG produced a significant decrease in median serum levels of IL-6 (-2.5 pg/mL; 95% CI, -3.9, -1.4; p=0.012), TNF-α (-6.9 pg/mL; 95% CI, -9.8, -3.5; p=0.017), and D-dimer (-0.28 pg/mL; 95% CI, -0.37, -0.19; p=0.041), while decrease in median serum levels of hsCRP was not significant (-0.16 mg/dL; 95% CI -0.27, -0.04; p=0.067). After 12 months, T/F/BIC produced a significant decrease in median serum levels of IL-6 (-2.9 pg/mL; 95% CI, -4.2, -1.6; p=0.009), TNF-α (-7.2 pg/mL; 95% CI, -10.5, -4.1; p=0.017), and D-dimer (-0.33 pg/mL; 95% CI, -0.46, -0.22; p=0.039), while decrease in median serum levels of hsCRP was not significant (-0.11 mg/dL; 95% CI -0.22, -0.03; p=0.098). Changes in serum levels of all biomarkers were comparable in patients treated with 3TC/DTG or T/F/BIC. After 12 months, increase in mean CD4+/CD8+ T lymphocyte ratio was significant (+0.22; 95% CI +0.09, +0.43; p=0.031), and this change too was comparable in both groups. Finally, at month 12 plasma virological efficacy was also comparable in both groups: 36 patients (92%) treated with 3TC/DTG and 43 (96%) treated with T/F/BIC has plasma HIV RNA <20 copies/mL.

Conclusion: Our findings suggest that initial antiretroviral therapy with 3TC/DTG or T/F/BIC leads to a significant reduction in mean plasma concentration of main inflammation markers, and to a significant increase in mean CD4+/CD8+ T lymphocyte ratio. The 12-month changes in serum inflammatory and immune activation markers were comparable in subjects treated with dual or triple therapy.

Antiretroviral Therapy II

OP 44 CARDIOVASCULAR RISK AND LIPID PROFILE AFTER SWITCHING TO TAF/FTC/RPV OR TAF/FTC/EVG/COBI IN PEOPLE LIVING WITH HIV AND CONTROLLED PLASMA VIREMIA

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Aim: We aimed to assess the overall cardiovascular and metabolic effect of the switch to tenofovir alafenamide (TAF) based single tablet regimens (STRs) [TAF/emtricitabine/rilpivirine (TAF/FTC/RPV), TAF/FTC/elvitegravir/cobi (TAF/FTC/EVG/cobi)] in a cohort of people living with HIV/AIDS (PLWH) under effective ART.

Methods

All PLWH aged above 18 years on antiretroviral treatment with an HIV-RNA <50 cp/mL at the time of the switch to TAF/FTC/RPV and TAF/FTC/EVG/cobi were retrospectively included in this analysis. Framingham risk score modification after 12 months from the switch as well as lipid profile and body weight modification were assessed. The change from baseline to 12 months in mean cardiovascular risk and body weight in each of the STR's group was assessed by means of Wilcoxon signed-rank test, whereas a mixed regression model was used to assess variation in lipid levels.

Results: One hundred and seventy PLWH were switched to TAF/FTC/EVG/cobi and 191 to TAF/FTC/RPV (Table). No difference in the Framingham cardiovascular risk score was observed after 12 months from the switch in each of the STR's groups (Figure). A significant increase in total cholesterol levels 12 months after the switch was observed in PLWH switched to TAF/FTC/EVG/cobi [192 (SD 34) mg/dl vs 208 (SD 40) mg/dl; p<0.0001] and TAF/FTC/RPV [187 (SD 34) mg/dl vs 195 (SD 35) mg/dl; p=0.027]. Moreover, a significant variation in the mean body weight from baseline to 12 months was observed in PLWH switched to TAF/FTC/EVG/cobi [72.2 (SD 13.5) kilograms vs 74.6 (SD 14.3) kilograms; p<0.0001] and TAF/FTC/RPV [73.4 (SD 11.6) kilograms vs 75.6 (SD 11.8) kilograms; p<0.0001].

Conclusion: No difference in the cardiovascular risk after one year from the switch to these STRs were observed. PLWH switched to TAF/FTC/EVG/cobi and TAF/FTC/RPV showed an increase in total cholesterol levels and body weight 12 months after the switch. This phenomenon could be likely due to the fact that the majority of our patients switched from a TDF-based regimen, which is known to have an impact on lipids and weight gain.

Aknowledgement

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Antiretroviral Therapy II

OP 45 WHO COULD BE ELIGIBLE FOR LONG-ACTING ANTIRETROVIRAL TREATMENT? A SNAPCHAT FROM ANTIVIRAL RESPONSE COHORT ANALYSIS (ARCA) ITALIAN COHORT

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Background: Thanks to the introduction of antiretroviral regimens (ART), HIV infection has become a chronic condition in which therapy should be continued lifelong. Therefore, in the last years, long-acting (LA) formulation with cabotegravir (CAB) and rilpivirine (RPV) have been approved by Food and Drug Administration and European Medicines Agency, and it is recommended in adults with HIV who are on ART, with HIV RNA levels <50 copies/mL.
Our purpose was to estimate patients eligible for the novel LA therapy with CAB+RPV in an Italian perspective based on the Antiviral Response Cohort Analysis (ARCA) cohort.
Material and methods: From ARCA database, we selected all people with HIV (PWH) with more than 18 years, having at least one follow-up in the last 24 months. We excluded patients with HbsAg positivity, evidence of rilpivirine and integrase inhibitors mutations, last HIV-RNA > 50 copies/mL.
Results: Four thousand one hundred three patients are currently followed in ARCA. Overall,1641(39.9%) patients have been included. Of them, 1163 (70.9%) were males, 1399 were Caucasian (85.3%), of which 1291 (92%) were Italian born. Of 474 eligible women, about 12.2% have less than 50 years with childbearing potential. The median length of HIV infection was 10.2 years (IQR 6.3-16.3), with the median of CD4 cells count nadir was 238 (106-366) cell/mm3, and the median of last available CD4 cells count was 706 (509-944) cells/mm3; only 48 (2.9%) of the participants had less than 200 CD4 cells/mm3. The characteristics of eligible PWH are summarized in Table 1.
The majority of PWH were treated with a three-drug regimen (n=1116, 68%); in particular, 568 (34.6%) PWH were treated with 2NRTI + INSTI, 420 (25.6%) with 2NRTI + NNRTI, and 128 (7.8%) with 2NRTI and PI. Among the 525 (30,3%) patients treated with two-drug regimens (2DRs), 325 (18.1%) were treated with lamivudine (3TC) and dolutegravir (DTG) and only 84 (5.1%) with RPV and DTG.
Conclusion: According to our Snapchat on ARCA cohort, about 39.9% of virological suppressed patients may be suitable candidates to long-acting CAB+RPV. Eligible patients are mainly men with a sexually acquired infection, a median last CD4 cell count superior to 500/mm3 and a prior ART with three-drug-regimen including NNRTI and INSTIs.

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Antiretroviral Therapy II

OP 46 HIV-DNA DECAY IN ART-NAÏVE PATIENTS STARTING DOLUTEGRAVIR PLUS LAMIVUDINE VS TRIPLE THERAPY

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Background: Data are lacking regarding the HIV-DNA decay in ART-naïve patients starting a dolutegravir (DTG) plus lamivudine (3TC) dual regimen. Our aim was to compare the HIV-DNA dynamics in ART-naïve patients starting a DTG-based triple regimen vs DTG plus 3TC dual regimen.
Methods: This was a prospective, longitudinal study enrolling patients who started a triple regimen combining DTG with emtricitabine/tenofovir alafenamide or tenofovir disoproxil fumarate (3-drug regimen group, 3DR), and patients who initiated a dual regimen combining DTG 50mg plus 3TC 300mg once daily (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/10^6 leukocytes) at two time-points: before starting therapy (baseline, BL) and at virological success (VS) (HIV-RNA <50 copies/mL). Results were expressed as log10 HIV-DNA copies/10^6 leukocytes.
Results: We included 38 ART-naïve patients, 19 in 3DR and 19 in 2DR: mostly males (89.5%), median age was 35 years (IQR 27-44). As compared to 3DR, patients in 2DR were younger (31 years, IQR 23-39 vs 39, IQR 32-48, p=0.053), with higher CD4 cell/mm3 (397, IQR 247-516 vs 251, IQR 77-421, p=0.061), higher CD4/CD8 ratio (0.47, IQR 0.34-0.60 vs 0.24, IQR 0.12-0.29, p<0.001). In 3DR, 31.6% of patients had an AIDS event. Figure shows the dynamics in HIV-RNA and HIV-DNA levels according to the two groups. Whereas 3DR displayed higher viremia than 2DR, at BL Log10 HIV-DNA levels were similar between two groups. HIV-RNA significantly decreased at VS in the 2 groups to a comparable level, thus 3DR group showed a more marked delta change than 2DR (-4.23 log10 copies/mL, IQR -5.15/-3.48 vs -3.62, IQR -3.9/-3.09, p=0.057). There was a significantly HIV-DNA levels reduction at VS, which reached a comparable level between groups, and with a similar delta change (2DR: -0.27 log10 HIV-DNA copies/10^6 leukocytes, IQR-0.48/-0.06 vs 3DR: -0.27, IQR -0.55/-0.04, p=0.863). At VS, both CD4 cells and CD4/CD8 ratio maintained higher levels in 2DR than 3DR (p=0.025 and p=0.010, respectively). Time to reach VS was similar between groups (2DR: 55 days, IQR 29-134 vs 3DR: 64, IQR 29-135, p=0.916). By regression analysis, any explanatory variable resulted to be correlated with either HIV-DNA and HIV-RNA decay; a direct correlation between BL HIV-RNA and BL HIV-DNA levels (r=0.319, p=0.051) was observed.
Conclusion: In ART-naïve patients, starting a DTG plus 3TC dual regimen did not show differences regarding the HIV-DNA dynamics as compared to starting a DTG-based triple regimen, in this setting. Our results add important new data that support the effectiveness of this approach on the cellular reservoir, which needs to be confirmed in larger cohorts.

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Antiretroviral Therapy II

OP 47 REAL-LIFE IMPACT OF DRUG TOXICITY ON DOLUTEGRAVIR TOLERABILITY: CLINICAL PRACTICE DATA FROM A MULTICENTER ITALIAN COHORT

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Background: Dolutegravir (DTG) is currently one of the most used Integrase inhibitors (INI) in antiretroviral therapies (ARV) in both naïve and experienced HIV-infected patients (pts).
Materials and Methods: We analyzed a multicenter cohort of HIV-infected pts, both naïve and experienced, starting a ARV including DTG. Censor was defined as death, suspension of DTG (changes in concomitant ARV drugs was not considered a suspension) or the date of the last virological determination. Chi-square test and non-parametric tests were used to assess differences in categorical and continuous variables, respectively. Kaplan-Meyer survival analysis were performed to estimate the probability of maintaining the study-drug and Cox-regression analysis to evaluate predictors of discontinuation.
Results: We enrolled 3442 pts: 2521 (73.2%) were males, with a median age of 50 yrs (IQR 41-56). Naïve pts were 653 (19.0%), of whom 115 (17.6%) were AIDS-presenters. As to experienced pts, median time from HIV diagnosis was 16.5 yrs (8.5-23.7) while median time on ARV was 12.6 yrs (6.1-19.1); 1652 (60.3%) had a HIV-RNA>50cp/mL at baseline. Full patients' characteristics are shown in Table1. During 16981 PYFU, we observed 726 discontinuations (4.3 per 100 PYFU); main reasons for DTG discontinuation were: toxicity (40,7% of total discontinuations, with CNS toxicity alone accounting for 16.5%), simplification (19.4%) and treatment intensification (12.0%). Estimated probabilities of maintaining DTG at 3 and 5 yrs were 79.1% (SD ±0.8%) and 74.2% (SD ±0.9%), respectively. Treatment-naïve pts showed a lower probability of maintaining DTG at 3 and 5 yrs (72.2% and 68.8%, respectively) compared to treatment-experienced pts (log-rank p<0.001). At a multivariate analysis, a longer time of virological suppression resulted protective against DTG discontinuation (per 10 months more, B -0.03, aHR 0.997, 95%CI 0.994-0.999, p=0.016) after adjusting for CDC stage, previous virological failure, peak HIV-RNA and nadir CD4+ cell count. The vast majority of discontinuations (722/726, 99.4%) happened within the first 12 months of DTG initiation. In a specific survival analysis, probability of not discontinuing DTG due to neuropsychiatric toxicity was 85.9% at 1 yrs, 71.4% at 3 yrs and 69.4% at 5 yrs; no differences in this regard were observed between naïve or experienced pts. All discontinuations due to CNS toxicity were observed in the first year since DTG initiation.
Conclusions: Our data confirm the overall good tolerability of DTG in clinical practice, with a low rate of discontinuations. CNS toxicity resulted the main reason for DTG discontinuation with all related interruptions happening in the first year from DTG introduction.

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Antiretroviral Therapy II

OP 48 PREVALENCE AND INCIDENCE OF MULTIDRUG RESISTANCE IN THE ARCA DATABASE, 2020 UPDATE

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Background: Despite the increasingly high rate of success of antiretroviral therapy (ART), a suppressive ART regimen cannot be constructed for a minor proportion of HIV patients due to multidrug resistance (MDR). The aim of this work was to estimate the prevalence and incidence of MDR in the nationwide ARCA database.

Materials and methods: Adult patients with at least one HIV genotype up to April 15, 2020 were included. MDR was defined as intermediate or high-level resistance to at least one drug in ≥3 of the key antiretroviral classes (NRTIs, NNRTIs, PIs, INSTIs), based on the Stanford HIVdb 8.9-1 algorithm, in the cumulative genotype. Due to the paucity of integrase genotypes and the negligible prevalence of transmitted INSTI resistance, patients never exposed to INSTI were assumed to harbour an INSTI susceptible virus unless there was genotypic evidence of INSTI resistance. Factors associated with development of MDR were analysed through logistic regression.

Results: The analysis included 29,184 patients (67% males, median [IQR] age 41 [35-48] years at first genotype, 71% harbouring subtype B virus), tested from 1997 to 2020. Over time, MDR emerged in 2,171 patients (7.4%). The prevalence of MDR increased sharply in the first 4 years and topped at 15.0% in 2001, then remained at the same level for 4 years and started to decline from 2006 (14.0%) to 2011 (8.6%). A consistent decline was confirmed in the following decade although with a flatter slope ending at 5.7% in 2020. The incidence of MDR also sharply increased in the first 3 years and topped at 7.4% in 2000, then declined steeply through 2008 (1.4%) and finally plateaued at <1% in the last decade. Predictors of MDR at multivariate analysis included male gender (AOR 1.20, 95% CI 1.08-1.34; p=0.001), exposure to mono NRTI (AOR 2.00, 95% CI 1.76-2.27; p<0.001) or dual NRTI (AOR 1.36, 95% CI 1.19-1.54; p<0.001), pre-ART CD4 counts (AOR 0.49, 95% CI 0.38-0.63; p<0.001 for >500 vs. <200 cells/microliter), subtype non-B (AOR 0.67, 95% CI 0.48-0.93; p=0.017), year of first genotype (AOR 0.15, 95% CI 0.12-0.18; p<0.001 for 2009-2013 vs. <2004).

Conclusions: Both the prevalence and incidence of MDR have topped around the early 2000s, followed by a biphasic decay down to current <6% and <1%, respectively. Major drivers for development of MDR include obsolete factors not impacting recent and future ART such as exposure to suboptimal therapy but also remaining risk factors such as low pre-ART CD4 counts. Thanks to current effective ART, newly emergent MDR is expected to be a very rare event, however a proportion of patients harbouring MDR virus remain where a key role can be played by drugs from novel classes such as fostemsavir, ibalizumab and possibly the maturation and capsid inhibitors currently under development.

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HIV & Covid II

OP 49 REAL LIFE USE OF THE ANTI-SARS COV-2 MONOCLONAL ANTIBODIES IN THE EARLY PHASE OF INFECTION: PLANNING, ENROLLMENT, ADMINISTRATION AND MONITORING

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Background and Objectives: Patients with underlying medical conditions are at increased risk for severe Covid19. Recent studies demonstrated efficacy of using neutralizing monoclonal antibodies (MAbs), which provides immediate passive immunity, in the early stage of infection, to stop clinical evolution and reduce hospitalization and lethality rates.
Materials and methods: Since 22/03/2021, a dedicated 7-day-service for anti-SARS CoV-2 MAbs administration was set up based on a medical-nurse-pharmacology team. Patients were enrolled upon notification by general practitioner or service physician after confirmation of a positive nasopharyngeal swab and the infusion was made not over 24h. If patients couldn't reach hospital independently, they were carried by local transport team. The drugs used were bamlanivimab, bamlanivimab/etesevimab and casirivimab/imdevimab, whose infusion lasted 1h and then patients remained in observation for the next hour. If respiratory failure emerged, hemogasanalysis and lung CT were performed and, if necessary, patients were hospitalized. After the infusion, a service of telemonitoring was activated for most patients. Follow-ups at 7, 14 and 30 days were performed on the total of patients using as main outcomes 28-days-survival, progression to a moderate disease and hospitalization. Adverse reactions emerged during or after administration were also analyzed. A comparison between the two treatments was performed.
Results: A total number of 179 subjects were included. In 32 cases active transport service was performed. GP referred 54% of subjects, 35% were auto-referred and 10% contracted the virus in non-COVID in-hospital stay. At the hospital admission, 25 subjects presented COVID-19 pneumonia, so they were hospitalized and evaluated separately. At 30 days out of a total of 148 patients treated, 76% had no clinical evolution of disease, 19% developed mild symptoms. The overall survival was 99%. The progression to a moderate disease was 17%. The hospitalization rate was 2%. 22 (12%) patients resulted negative after 7 days, 61 (35%) at 14 days, 127 (86%) at 30 days. Regarding safety, in 98% of cases, no adverse reactions were recorded, only in 1 case the drug was suspended for hypotension. In 76% cases, there was fever in the hours following the administration with self-resolution.
Non-significant statistical differences in outcomes were observed between the two groups of treatment (tab.1).
Conclusions: Our real-life use of MAbs confirms a favorable outcome with an exceptional safety profile, encouraging more efficacious strategies to reach all high-risk patients. Even in patients admitted to the hospital for complications we observed no death and no need of invasive ventilation. Organizational measures to reduce the interval time between symptom onset, diagnosis and MAbs administration, are urgent needed. The use of MAbs requires a "test and treat" strategy, therefore a close interaction between local medicine and hospital is necessary to treat suitable patients as soon as possible.

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HIV & Covid II

OP 50 LEARNING BY DOING: EFFECTS OF MONOCLONAL ANTIBODY TREATMENT ON THE OUTCOME OF AMBULATORY PATIENTS WITH COVID-19

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Background: Since the beginning of the SARS-CoV2 pandemic, the research for effective therapies has been a major issue for the scientific community worldwide. At the time of writing, neutralizing monoclonal antibodies (mAbs) represent a targeted therapy for patients with mild symptoms and a strategy to prevent the spreading of the virus and the progression to a severe COVID-19 presentation. We report our first experience on the use of Bamlanivimab/Etesevimab (Bam/Ete) and Casirivimab/Imdevimab (Cas/Imd) in a cohort of not-hospitalized SARS-CoV2 infected patients.
Material and methods: We conducted a real-life retrospective, single-center study at the University Hospital Policlinico Umberto I of Rome and included patients with a recent diagnosis of SARS-CoV2 infection. Patients involved in the study showed from mild to moderate symptoms and answered to at least one of these inclusion criteria: severe obesity, diabetes mellitus, chronic cardiovascular diseases, chronic lung diseases and primary or secondary immunosuppression. On day 1 RT-PCR for SARS-CoV2 on nasopharyngeal swab was performed to all patients and a single intravenous dose of neutralizing antibodies was administered. On day 10 a follow-up examination and a RT-PCR for SARS-CoV2 on nasopharyngeal swab were performed.
Results: A total of 116 patients were included in the study, 57 females and 59 males. Overall, the median age was 65.5 years old (IQR 57-73.7), cardiovascular disease was the most frequent comorbidity (62.9%). [Table1] The median number of days the mAbs were administered was 4 days from the onset of symptoms (IQR 3-6) and 3 days from the first positive RT-PCR nasopharyngeal swab (IQR 2-4). Fifty-eight doses of Bam/Ete and 58 doses of Cas/Imd were randomly administered. Among our patients, 4.3% were hospitalized due to the progression of the infection, while 95.7% fully recovered. Within ten days from the infusion, the 58.6% of patients treated with Bam/Ete was asymptomatic, compared to the 50% of patients treated with Cas/Imd. No adverse events were reported. Ten days after the infusion of Bam/Ete, 48.28% of patients tested positive at the nasopharyngeal swab, 22.41% positive with a very low viral load and 24.14% negative; at day 20, the percentage of negative patients increased to 53.45%. Ten days after the infusion of Cas/Imd 36.7% tested positive, 39.66% positive with a very low viral load and 24.14% negative; at day 20, the percentage of negative patients increased to 50%.
Conclusions: Our real-life experience suggests that mAbs treatment is well tolerated and reduces hospitalization and progression of the infection in patients with well-known risk factors for the development of a severe form of COVID-19, as shown in previous studies. According to our experience, there was no significant difference between the two combinations of mAbs, except a relative earlier reduction of the viral load with Casirivimab/Imdevimab. Additional studies with a larger number of patients are warranted to evaluate the effectiveness of mAbs treatment.

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HIV & Covid II

OP 51 EFFICACY, SAFETY AND VIROLOGICAL CLEARANCE IN COURSE OF TREATMENT WITH ANTI-SARS-COV-2 MONOCLONAL ANTIBODIES IN PATIENTS DIAGNOSED WITH MILD-MODERATE COVID-19

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Background: Anti-SARS-CoV-2 monoclonal antibodies (mAbs) have shown efficacy and tolerability in high-risk outpatients with mild-moderate COVID-19. AIFA indicated mAbs in non-hospitalized patients with ≥1 risk factor for disease progression within 10 days from symptom onset. Real-life data are still lacking. We hereby report mAbs efficacy and safety data in a cohort of SARS-COV-2-infected patients at risk for a negative outcome. We also explored the association between baseline nasopharyngeal (NP) viral load and virological clearance at 7 days after treatment.

Materials and methods: We enrolled high-risk patients with mild-moderate COVID-19. High-risk patients were defined according to AIFA (BMI ≥35, dialysis, diabetes, immunodeficiencies, age ≥55 with cardio-cerebrovascular or chronic pulmonary disease). Patients requiring hospitalization for COVID-19 were excluded, except for those hospitalized for other reasons. Patients were treated with bamlanivimab, bamlanivimab/etesevimab or casirivimab/imdevimab in a dedicated outpatient service. Clinical recovery was defined as apyrexia and SO2 >95% in room air; virological clearance was declared with 1 PCR-negative NP swab.

Patients underwent NP swab at T0 (infusion) and after 7 days (T7); if still PCR-positive at T7, they underwent weekly swabs up to negativity. According to guidelines, isolation was discontinued in asymptomatic PCR-positive patients at day 21 from symptom onset. Blood tests were performed at T0-T7; viral load was measured on NP swab (RT-PCR) at T0-T7 in a subgroup of unselected patients. Chi-square, Mann-Whitney, Wilcoxon tests and logistic regression were used for the analyses.

Results: 69 patients were included [Table 1]. MAbs showed efficacy in 64 (92.7%) patients: 55 (79.7%) patients reached clinical and virological clearance, 9 (13%) were released from isolation even though persistently PCR-positive, 2 (2.9%) were lost to follow-up, 1 (1.4%) has not completed the follow-up yet, 2 (2.9%) were hospitalized after infusion for respiratory failure (1 required CPAP, 1 high-flow oxygen therapy). 19 (27.5%) patients displayed mild adverse effects (no SAE were reported), most commonly fever (16, 23.2%) and nausea/vomiting (2, 2.9%). Lymphocyte and platelet counts normalized at T7 [Table 2].

Median NP viral load significantly decreased from T0 to T7 [Figure 1]. At T7 20/67 (29.9%) patients obtained virological clearance; higher NP viral load at T0 and lower baseline lymphocyte counts were associated with a lower probability of virological clearance at T7 [Table 3-4].

Conclusions: Despite the lack of a control group, our real-life data confirm that anti-SARS-COV-2 mAbs can be safely administered in outpatient settings. By identifying higher viral loads in the nasopharynx and lower basal lymphocyte counts as factors associated with delayed virological clearance, our data add to our understanding of the role of mAb therapy in the most efficacious treatment and containment of COVID-19 pandemic.

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HIV & Covid II

OP 52 EX VIVO EFFICACY OF CURRENTLY LICENSED ANTI-SARS-COV-2 MONOCLONAL ANTIBODIES

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Background: Two monoclonal antibody (mAb) cocktails, namely LY-CoV555/LY-CoV016 by Eli-Lilly (LYC) and REGN-COV2 by Regeneron (REG) have received emergency use authorization from the FDA for early treatment of mild to moderate COVID-19 in patients at high risk for progressing to severe COVID-19. The rapid emergence of SARS-CoV-2 variants is challenging the efficacy of mAbs designed based on the formerly prevalent B.1 lineage. The aim of this work was to test the efficacy of LYC and REG treatment in a small population of infected patients from clinical practice. The virus neutralization capacity of patient serum was determined against the wild type B.1 variant and against the paired individual variant isolated from each patient to assess mAb activity ex vivo.

Materials and Methods: Of 19 patients studied (9 males, mean (SD) age 62.4 ± 16.7 years), one was asymptomatic while the others developed mild symptoms such as cough (n=13), headache (n=10), fever (n=9), dysgeusia (n=3), dyspnoea or gastrointestinal symptoms (n=2). Two patients had received one and two SARS-CoV-2 mRNA vaccine doses. Patients were randomly treated with LYC (n=10) or REG (n=9) 2.9 ± 1.6 days from diagnosis. Sera were collected 1 hour before (baseline) and 1 hour post mAbs infusion. NtAb titres were determined in a live virus microneutralization assay performed in VERO E6 cell line using a quantitative readout based on cell viability. NtAb titres were defined as the reciprocal value of the sample dilution that showed a 50% protection of virus-induced cytopathic effect (ID50) and determined against the wild type lineage and the paired isolate from each patient.

Results: None of the patients required mechanical ventilation or hospitalisation. Seventeen and 2 patients harboured the alpha and gamma virus, respectively. All patients but the one completing two-dose vaccination (ID50 = 70) were negative for NtAb at baseline. The median [IQR] post-infusion NtAb titres were significantly higher ($p<0.001$) in REG vs LYC recipients against the wild type virus (20,820 [17,388-27,651] for REG vs 6,792 [4,736-7,777] for LYC) and even more against paired individual variants (117,453 [51,200-128,000] for REG vs 9,512 [4,878-17037] for LYC). However, the time from diagnosis to SARS-CoV-2 RNA negativization was not significantly different ($p=0.182$) with the two cocktails (17 vs 13 days; LYC vs REG) and was not correlated with NtAb titres both for wild type and for paired individual variant. Overall, the neutralization capacity was higher to the patient paired virus than to the wild type virus (18,558 [7,620 -117,453] vs. 8,931 [6,461-20,820], $p=0.001$) but titres were highly correlated (rho = 0.728, $p<0.001$). One notable exception were the two gamma variants which were not neutralized by the LYC cocktail (Figure 1).

Conclusions: Both LYC and REG infusion achieve high virus neutralization capacity in vivo against currently prevalent variants, however the gamma lineage appears to be resistant to LYC.

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HIV & Covid II

OP 53 REAL-LIFE USE OF REMDESIVIR-CONTAINING REGIMENS IN CORONAVIRUS DISEASE-2019: A RETROSPECTIVE CASE-CONTROL STUDY

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Background: Remdesivir (REM), a nucleotide analogue drug that inhibits viral RNA polymerases, has shown potent antiviral activity in vitro and efficacy in animal models of COVID-19; nevertheless, clinical trials and real-life reports have shown conflicting data on its effectiveness. Aims of the study were to evaluate the impact of REM on Intensive Care Unit (ICU) admission, need for orotracheal intubation (OTI) and in-hospital mortality. Furthermore, we estimated the kinetic of several laboratory parameters at days 0-6-10 and assessed the risk factors for in-hospital mortality in patients treated with REM.

Methods: We conducted a retrospective, single-center, case-control (1:1) study including hospitalized patients with confirmed SARS-COV2 infection. Cases were patients treated with REM for 5 days, controls were patients not receiving REM. REM was used in patients with radiologic evidence of pneumonia and receiving oxygen support. Cases and controls were matched for age, sex, duration of symptoms (days) and severity of infection at admission (expressed by PaO2/FiO2). Univariate and multivariable analyses were performed to explore the effect of REM on ICU admission, need for OTI and in-hospital mortality as well as the mortality risk factors in the REM-population.

Results: A total of 192 patients (96 cases and 96 controls) were included in the study, 134 males and 58 females, 13.5% were admitted to ICU with a mortality of 14.1%. Overall, median (IQR) age was 64 years (56-72), duration of symptoms was 6 days (3-8) and PaO2/FiO2 at admission was 279 (211-337). Patients receiving REM had a lower rate of ICU admission (p: 0.003) and need for OTI (p: 0.028) than controls, whereas no difference between cases and controls were observed as for mortality rate (p: 0.14). However, at multivariable analysis only high CRP (p: 0.006), severity of infection (p: 0.015) and haematological malignancies (p: 0.011) were independently associated with ICU admission. Likewise, presence of haematological malignancies (p: 0.001), lower duration of symptoms (p: 0.012), higher severity of infection (p: 0.001) and low lymphocytes count (p: 0.036) at admission were independently associated with in-hospital mortality. No association was observed as for the need for OTI. In patients treated with REM, a significant increase of absolute count of lymphocytes B, CD4+ and CD8+ T-cells from day1 to day10 of REM therapy was observed (figure 1). At multivariable analysis, a low albumin value at admission (p: 0.016) and a lymphocytes count lower than 725 cells/mmc for more than 6 days (p: 0.002) were significantly associated with mortality.

Conclusions: Our real-life study showed that therapy with REM did not have any impact on either ICU admission, need for OTI or in-hospital mortality. The duration of lymphopenia was independently associated with mortality in patients treated with REM. Additional prospective studies are warranted to evaluate the efficacy of REM in COVID-19 patients.

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HIV & Covid II

OP 54 SARS-COV-2 INFECTION AMONG PERSONS LIVING WITH HIV

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Background: Available data suggest that HIV does not increase the risk for SARS-CoV-2 infection or predispose to poor outcomes from COVID-19 compared to the general population. However, what happens when SARS-CoV-2 meets HIV is not entirely understood.
Aim Of The Study: This study aimed to evaluate the proportion of PLWH who developed COVID-19 or asymptomatic infection in a cohort of HIV-positive subjects in charge of the outpatient service of Infectious Diseases Unit, Policlinico Riuniti, Foggia. In patients with COVID-19, we further evaluated the clinical features and outcome of the disease.
Results: From March 2020 to May 2021, 225 consecutive HIV-positive subjects were enrolled. The median age was 52 (SD± 11,9) years, 153 patients(68%) were male; all received antiretroviral therapy with a viral load of < 50 copies per ml and a median CD4 count of 631cells per µl.
During the observation period, 8 HIV-positive people were diagnosed with COVID-19. The characteristics of these patients are shown in the Table. All had mild disease, and no one required hospitalization. Among the remaining 217 subjects, 38 tested positive for SARS-CoV-2 IgG and IgM, of whom 6 had a nasal swab positive for SARS-CoV-2 infection. None developed symptoms of COVID-19. The overall proportion of HIV-positive patients with SARS-CoV-2 infection was 19.5%; a similar seroprevalence was found in a cohort of blood donors tested in the same period in our area.
Conclusions: Although preliminary and limited to a small number of patients, the data from this study show that PLWH do not have a higher risk of acquiring SARS-CoV-2 infection. Moreover, our results suggest that HIV-positive subjects with COVID-19 do not have a greater risk of serious illness than HIV-negative subjects.

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Immunopathogenesis II

OP 55 INCREASED RATES OF INDETERMINATE QUANTIFERON-TB GOLD PLUS ASSAY IN SEVERE COVID-19 PATIENTS REFLECT AN IMPAIRED INTERFERON-GAMMA SECRETION AND CORRELATE WITH THE PROFOUND REDUCTION OF T-LYMPHOCYTE SUBSETS IN PERIPHERAL BLOOD

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Previous studies have shown an increased number of indeterminate QuantiFERON-TB Gold Plus (QFT-P) assay results in patients hospitalized for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS–CoV–2), due to a profound dysregulation of the immune system. Our study aimed to define the prevalence of indeterminate QFT-P assay in patients hospitalized because of SARS-CoV-2 infection and to evaluate its possible correlation with the outcome, the severity of the disease and the peripheral blood lymphocyte subsets.

A retrospective study was performed from March to May 2020 on patients hospitalized with SARS–CoV–2 infection in Policlinico Tor Vergata. Demographics, clinical and laboratory data were collected. Patients were divided into two groups according to the severity of the disease: non-severe if oxygen was not needed or Venturi mask (VMK) was required; severe if Non-Rebreather Mask (NRM), non-invasive ventilation (NIV) or orotracheal intubation (OTI) were necessary. Statistical analysis was performed using JASP.

During the study period, 150 patients were included in the analysis. Median age was 61 years (interquartile range [IQR] 49-79), median time between symptoms' onset and blood sampling for QFT-P assay was 10 days (IQR 6-16). 130 patients had a positive or negative QFT-P assay, while 20 patients had an indeterminate QFT-P assay. After stratifying patients according to sex, need of intensive cares, outcome (survivors vs nonsurvivors) no differences in the rate of indeterminate QFT-P assay were found (p=0.58, p=0.90 and p=0.45, respectively). Conversely, severe patients had increased rate of indeterminate QFT-P assay compared to nonsevere (23% vs 7%, p=0.02). Considering the Mitogen-Nil condition in the QFT-P assay, which is a measure of the nonspecific T-cell stimulation, a significantly lower level of interferon (IFN)-gamma production was found in patients with severe compared to nonsevere disease (3.2 IU/ml vs 9.6 IU/ml, p<0.001). A decreasing trend of IFN-gamma production in the Mitogen-Nil condition was found proceeding from patients who did not need oxygen therapy, through patients with VMK, NRM and NIV, to patients who underwent OTI for mechanical ventilation. Furthermore, a direct correlation between the IFN-gamma levels in the Mitogen-Nil condition and the absolute count of total lymphocytes (Spearman's rho 0.464, p <0.001), CD3+ (Spearman's rho 0.504, p<0.001), CD4+ (Spearman's rho 0.410, p<0.001) and CD8+ (Spearman's rho 0.555, p <0.001) T-lymphocytes was found.

Our study provides some evidence of a correlation between indeterminate QFT-P assay and severe SARS-CoV-2 infection and between IFN-gamma production in the Mitogen-Nil condition and the immune status of the patient. This leads to conclusion that the indeterminate QFT-P result depends on the lymphopenia found in the most severe cases of SARS-CoV-2 infection, while it is not possible to determine whether lymphocyte dysfunction is involved.

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Immunopathogenesis II

OP 56 ROLE OF SERUM E-SELECTIN AS A BIOMARKER OF INFECTION SEVERITY IN CORONAVIRUS DISEASE-19

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Background: E-selectin is a recognized marker of endothelial activation which has been studied in cardiovascular disease; however, its place in Coronavirus Disease-19 (COVID-19) has not been explored yet. The aims of the study were to compare sE-selectin values among ICU admitted and non-admitted, survived and non-survived patients as well as subjects developing or not thrombosis.
Methods: A single-centre, retrospective study of patients with COVID-19 hospitalized at Policlinico Umberto I, Sapienza University of Rome from March to May 2020 was performed. Demographic, clinic, laboratory, including E-selectin data were anonymously collected. Simple and multiple logistic regression models were developed.
Results: A total of 100 patients with a COVID-19 diagnosis were included. The median age (IQR) was 65 years (58-78), 62 (62%) were men. Of these, 29 (29%) were admitted to ICU, 28 (28%) died and 19 (19%) had a thrombotic event during hospitalization. The median value (IQR) of sE-selectin was 26.1 ng/ml (18.1-35). Median sE-selectin values did not differ between deceased and survivors (27.1 [22.4-41.7] vs. 25.2 [17.1-32.6] ng/ml, p = .06) and among patients having a thrombotic event and who did not (32.1 [23.5-39.9] vs. 26.1 [17.5-34.4] ng/ml, p = .22) (Fig.1A/1B). Compared with patients who did not receive ICU treatments, patients requiring ICU care had higher levels of sE-selectin (36.6 [25.8-47.1] vs. 24.1 [17.0-30.1] ng/ml; p < .001) (Fig.2). The simple logistic regression model showed that each increment of 1 ng/ml of sE-selectin level was associated with a higher risk of ICU care (OR 1.07, 95% CI, 1.03-1.12). The AUC of the ROC curve was 0.75 (95% CI, 0.64-0.87). In the multiple logistic regression model, a value of sE-selectin levels greater than 33 ng/ml (OR 13.7 [95% CI, 3.2-81.9]), PaO2/FiO2 ratio <200 (OR 80.3 [95% CI, 14.4-716.2]) and PaO2/FiO2 ratio between 200 and 300 (OR 9.1 [95% CI, 1.7-62.1]) were found to be significantly associated with an increased risk of ICU admission, after adjusted for sex, Lactate dehydrogenase levels and neutrophils count (Fig.3). The AUC of the ROC curve was 0.90 (95% CI, 0.83-0.98). sE-selectin values significantly correlated with PMNL count (R = 0.32 [p = .001]) and the number of days from symptoms onset to hospitalization (R =0.28 [p = .004]).
Conclusions: sE-selectin levels are predictive of ICU admission in COVID-19 patients. Indeed, compared to patients who did not require ICU treatment, we found higher levels of sE-selectin in ICU admitted patients. Besides, a positive correlation between neutrophils and sE-selectin values and time from symptoms onset to hospitalisation and sE-selectin was found. Since data on the relation between sE-selectin and COVID-19 are absent, this study aimed to contribute toward the comprehension of pathogenic aspects of this disease, giving a possible clinical marker able to predict its severity.

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Immunopathogenesis II

OP 57 EFFECTS OF VIREMIA AND CD4 RECOVERY ON THE GUT "MICROBIOME-IMMUNITY" AXIS IN NAÏVE HIV-1 PATIENTS UNDERGOING ART THERAPY

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Background: HIV-1 infection is characterized by persistent systemic inflammation and immune activation, even in patients receiving effective antiretroviral therapy (ART). Converging data from many cross-sectional studies suggest that the gut microbiota changes can occur throughout HIV infection, treated by ART, however the results are contrasting. For the first time, we compared the fecal microbial composition, serum, and fecal microbial metabolites and serum cytokines' profile of naïve patients before starting ART and after reaching virological suppression after 24 weeks of ART therapy. In addition, we compared the microbiota composition, microbial metabolites, and cytokines' profile of patients with CD4/CD8 ratio <1 (Immunological non-responders-INR) and CD4/CD8 >1 (Immunological responders-IR) after 24 weeks of ART therapy.
Methods: We enrolled 12 HIV- naïve patients receiving ART, mainly based on integrase inhibitors. Fecal microbiota composition was assessed through Next Generation Sequencing. A comprehensive analysis of a blood broad-spectrum cytokines' panel was performed through a multiplex approach. At the same time, serum free fatty acid (FFA) levels and fecal Short Chain Fatty Acid (SCFAs) were obtained through GC-MS.
Results: We observed modest change of microbiota (increase of Ruminococcus and Succinivibrio and decrease of Intestinibacter), increased serum propionic and butirric acids, a reduction of serum IP-10 and an increase of IL-8 levels, at viral suppression condition.
In addition, we detected a reduction of Faecalibacterium, an increase of Alistipes, fecal isobutyric, isovaleric and 2-methylbutyric acids in Immunological non-responders.
Conclusion: Our results provided an additional perspective about the impact of HIV infection, ART, and immune recovery in the microbiota-immunity axis at the metabolism level, which are an indicator of the active processes occurring in the gastrointestinal tract. Individuals with HIV-1 infection, before ART and after reaching virological suppression with 24 weeks of ART, displayed a microbiota with unchanged overall bacterial diversity and the systemic inflammatory status, not completely restored. In addition, we confirmed the role of the gut microbiota metabolites in immune reconstitution.

Immunopathogenesis II

OP 58 CYTOKINE PROFILE OF COVID-19 PATIENTS WITH AND WITHOUT ACTIVE TUBERCULOSIS

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Background: Tuberculosis (TB) and coronavirus disease 2019 (COVID-19) are infectious diseases affecting primarily the lungs and sharing some pathogenetic mechanisms. For both diseases, the immunopathogenesis has been carefully described but there are no data on their interaction in co-infected hosts. Several cases of TB and COVID-19 co-infection have been reported but hosts' cytokine profile has not been described. This study aims at assessing selected cytokine response in COVID-19 patients with and without TB co-infection.

Methods: We collected sera, on days 7 and 14 after COVID-19 diagnosis, from 20 COVID-19/TB co-infected patients and 12 COVID-19 patients, with a mild form of disease and not exposed to immunosuppressive drugs. Sera were analysed using the Luminex platform assessing the values of C-X-C motif chemokine ligand-10 (CXCL-10), interleukin-6 (IL-6), and interleukin-10 (IL-10). The study protocol was approved by the Ethics Committee of Monza e Brianza (code no. 3377). Statistical differences were evaluated using the Mann-Whitney U test with R software version 4.0.3.

Results: Among 32 patients with COVID-19 or COVID-19/TB infection, a total of 57 sera samples were analysed (38 from co-infected and 19 from non-co-infected patients). On day 7 significant differences between co-infected and non-co-infected patients were observed for all three cytokines analysed, with reduced levels of IL-6 (11.5 vs. 41.7 pg/mL; p=0.008) and IL-10 (15.4 vs. 30.0 pg/mL; p=0.031), and higher CXCL-10 levels in the co-infected group (241.8 vs. 112.0 pg/mL; p=0.020) (Figure). On day 14, differences in serum levels of IL-6 (18.0 vs. 11.7 pg/mL; p=0.155) and IL-10 (15.9 vs. 10.8 pg/mL; p=0.375) were no more significant, while CXCL-10 levels remained significantly higher in co-infected patients (227.5 vs 67.1 pg/mL; p<0.001).

Conclusions: COVID-19/TB co-infected patients displayed lower levels of IL-6 and IL-10 on day 7 compared to the non-co-infected, suggesting a more vigorous early immune response. On day 14, however, while no more differences existed for IL-6 and IL-10, CXCL-10 remained significantly higher in the COVID-19/TB co-infected persons, as expected in pulmonary TB. Although bias risk was reduced by selecting a homogeneous control group of non-co-infected subjects, our study has several limitations including the small sample size, missing sera samples (10.9%; 2/40 and 5/24 from co-infected and non-coinfected patients, respectively), and the narrow range of cytokines examined. Further studies are required to unfold any important immunological changes among COVID-19/TB co-infected patients.

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Immunopathogenesis II

OP 59 ROLE OF TOCILIZUMAB IN DOWN REGULATING THE CONCENTRATION OF SCD163 IN A COHORT OF SARS-COV 2 INFECTED PATIENTS WITH VARYING SEVERITY

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Background: Cytokine storm is a major phenomenon associated with the immunopathogenesis of SARS-COV-2. Elevated levels of sCD163 in the plasma are associated with macrophage activation and in eliciting systemic immune response. Elevated levels of D-dimer, LDH and ferritin also correspond to disease severity, indicating the need to study them. The aim of this study was to analyse the effect of tocilizumab on the sCD163 levels at various time intervals in a population severely infected with SARS-CoV-2.

Methods: The study population consisted of COVID-19 patients treated with tocilizumab (Tocilizumab) and not treated with tocilizumab (Controls) and healthy donors (HD). The patients were also categorised into ARDS and Non-ARDS based on severity of the disease. COVID-19 was confirmed by RT-PCR following an elevation in the CRP values. Patients were classified into ARDS and NON-ARDS and type of ventilation AA, CPAP, VMK, IOT was decided based on P/F ratio. Ferritin, LDH, D-DIMER, CD4 counts were administered on admission as per the standard clinical examination protocol. sCD163 was measured using ELISA (R&D Systems) in plasma taken before (T0) and 7 and 45 days after tocilizumab therapy (T7, T45). Tocilizumab group was then classified into responders (R) and non-responders (NR) based on patient response to therapy.

Results: Seventy COVID-19 patients and 47 age matched healthy donors (HD) were enrolled. Among COVID-19 patients, 45 were treated with tocilizumab [tocilizumab group] while 25 were not treated with tocilizumab. At T0, the overall sCD163 levels were high in COVID-19 patients in comparison to HD ($p<0.0001$) also sCD163 was higher in ARDS patients as compared to Non-ARDS ($p=0.002$). At T0, no differences were observed in sCD163 levels between tocilizumab and controls groups. The longitudinal evaluation of sCD163 levels showed a significant reduction in tocilizumab group ($p=0.003$) while no differences were observed in control group. Tocilizumab treated patients were divided into responders and non-responders based on survival or death.

Non-Responders in accordance with Responders didn't show significant differences in the level of sCD163 at T0 and T7 even though sCD163 levels reduced markedly in both the populations at all time points including T45 in responders when analysed longitudinally ($p=0.02$ and $p=0.01$).

Conclusion: It can be concluded that sCD163 plays a significant role in eliciting an immune response in COVID-19 population and hence, it is also associated with the phenomenon of cytokine storm. The blood biomarkers such as ferritin, LDH etc seem to be of utmost importance in deciding the clinical epidemiology of the patients. Tocilizumab therapy can be an effective method to control the heightened immune response in majority of the infected subjects even though a complete normalisation seems to be absent.

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Immunopathogenesis II

OP 60 CLINICAL AND IMMUNOLOGICAL CHARACTERIZATION OF SARS-COV-2 INFECTION IN CHILDREN

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Background: Recent reports support the general claim that children affected by the coronavirus disease 19 (COVID-19) are more likely to develop mild or asymptomatic clinical presentation compared with adults. Nonetheless, exhaustive reports on specific immune responses to SARS-CoV-2 in paediatric patients remain scarce, posing an unprecedented challenge to clinicians.
The present study aims to characterize the immunological profile in a cohort of SARS-CoV-2-infected children at different ages with different clinical manifestations, ranging from mild to critical.
Material and methods: From February to May, 2020, 18 SARS-CoV-2-infected children were enrolled in the study and were compared to 13 age- and sex-matched healthy controls. According to established diagnostic criteria, patients were defined as pauci-symptomatic/moderate (55,6%), and severe/critical (44,5%), respectively. These two groups were further categorized into acute and subacute according to the time from symptoms onset (cut-off 7 days). Eventually, patients were categorized into three groups according to age, namely infants (1-12 months, 39%), children (1-12 years, 44%), and adolescents (>12 years, 17%). SARS-CoV-2 infection was confirmed by real–time PCR on nasopharyngeal swab. Specific antibodies to different SARS-CoV-2 antigens, to HCoV-OC43 and HCoV-HKU1 beta coronaviruses, and to H1N1 virus were tested in plasma by LIPS assay. A lentiviral vector–based SARS-CoV-2 neutralization assay was used to evaluate Nab responses.
Anti-viral immune response was evaluated by gene expression analysis (Quantigene Plex Gene expression assay) and by secretome characterization (Multiplex Cytokine Array) of peripheral blood mononuclear cells (PBMCs) both unstimulated and upon stimulation with SARS-CoV-2-specific antigens.
Results: Independently of clinical severity, SARS-CoV-2 infection in paediatric patients results in hyperactivation of immune response in comparison to the healthy counterpart, along with an increase of pro-inflammatory markers (IL-2, IL-6, IL-8, IL-17, MCP-1, MIP-1β, TNF-α) both at RNA and protein level ($p < 0.05$). Further increases in SARS-CoV-2-specific immunological markers of cytokine storm, T cell activation, and inflammasome components occur in the severe cases, acute cases and in infants, unraveling potential correlations with clinical severity and age. Specifically, when further analyzing data distinguishing patients based on age, a hyper-inflammatory profile emerged in infants, which is reminiscent of that observed in severe and acute cases. as evident by the presence of SARS-CoV-2-specific antibodies.
Conclusions: In the present study, we characterized immunological aspects in a cohort of SARS-CoV-2-infected children. Our data suggest the existence of specific SARS-CoV-2-induced cytokine/immunological profiles potentially correlating with clinical severity, time to symptoms onset and, importantly, age, which deserves to be further investigated in larger cohort studies.

Immunopathogenesis III

OP 61 BINDING AND NEUTRALIZING ANTIBODIES TO INTERFERON (IFN) A/B AND DEFECTIVE IFN TRANSCRIPTIONAL PROFILE IN COVID-19 PATIENTS

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Background: Heterogeneous patterns of type I interferon (IFN-I) response in COVID-19 patients have been associated to COVID-19 severity. Notably, compared with mild or moderate cases, severe and critically ill patients have a profoundly impaired IFN-I response. A possible cause of IFN deficiency is the generation of antibodies that target IFN-I – a form of autoimmunity. Therefore, in order to provide additional insights to the immunopathogenesis of SARS-CoV-2 infection, we investigated the serum prevalence of natural anti-IFN-I-antibodies (e.g., binding antibodies/BABs and neutralizing antibodies/NABs) in COVID-19 patients. The relationship between the presence of anti-IFN NAB and the IFN-I signature was also characterized.

Methods: Anti-IFN-α/β-BABs and NABs were examined in serum samples collected from a large cohort of COVID-19 patients (n=368). The analysis of anti-IFN alpha and beta BABs were performed using ELISA assays (Human Anti-IFN alpha ELISA Kit, Thermo Fisher Scientific, Waltham, MA; Human Anti-IFN Beta Antibody ELISA Kit, Cloud-Clone Corp. CCC, USA). All BABs positive serum samples were processed to explore anti IFN-I NABs, using a bioassay based on IFN-induced inhibition of virus cytopathic effect on human cells in culture (EMC virus and A549 cells). The titer of neutralizing antibodies was expressed in TRU/ml (Tenfold Reduction Units)/ml, TRU/ml being the serum dilution able to reduce IFN-I titer from 10 to 1 LU/ml). Transcript levels of IFN-alfa, IFN-beta, IFN-omega and IFN stimulated genes (ISGs: ISG15 and ISG56) were analyzed in NAB positive patients and compared with those obtained from NAB negative patients and healthy controls through RT/Real Time PCR.

Results: Our results showed that 6.8% (n=25/368) of COVID-19 patients had anti IFN-alpha BABs while 10% (n=37/368) were positive to anti IFN-beta BABs. About half (44%, n=11/25) of IFN-alpha BABs positive patients showed high titer [>10 (range 13.3 – 34133.3) TRU/ml] of anti IFN-alpha NABs. By contrast, only 1 patient out of 37 IFN-beta BABs positive individuals showed anti-IFN-beta NABs (100 TRU/ml). A cross reactivity of anti-IFN-alpha/beta NABs to neutralize IFN-omega was detected. Notably, NAB positive patients had a decreased transcript expression of IFN-alfa, IFN-beta, IFN-omega, ISG15 and ISG56 mRNA levels than healthy controls ($p<0.05$ for all genes). Also, ISG15-mRNA levels were reduced in COVID-19 patients positive for anti IFN-I NABs compared to those without NABs ($p=<0.05$).

Conclusions: Our findings demonstrate that COVID-19 patients had high titer of natural antibodies that recognized and/or neutralized IFN-I. Anti IFN-I NABs are associated with a defective production of circulating IFN-I blood levels and might contribute to impairment of the antiviral innate response in COVID-19.

Immunopathogenesis III

OP 62 PLASMA CYTOKINE LANDSCAPE REVEALS THE IMPORTANCE OF DIFFERENT MOLECULAR PATHWAYS IN PREDICTING COVID-19 SEVERITY AND SURVIVAL

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Background: The pathways and molecular mechanisms driving severity and clinical outcome of COVID-19 remain poorly understood. Thus, we quantified a total of 62 cytokines, chemokines and other factors involved in inflammation and immunity in plasma from 80 hospitalized patients with severe disease who were stratified on the basis of the pO2/FiO2 or on the basis of clinical outcome.

Methods: We used a Luminex platform (R&D System, Minneapolis, MN) for the simultaneous quantification of the following molecules: a proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), bone morphogenetic protein (BMP)2, BMP4, BMP7, CD40L, CCL2, CCL3, CCL4, CCL5, CCL11, CCL19, CCL20, CXCL1, CXCL2, CXCL10, CX3CL1, EGF, FGF basic, G-CSF, GM-CSF, interferon (IFN)-alpha, IFN-beta, IFN-gamma, IL-1-alpha, IL-1 receptor antagonist (IL -1RA), IL-1-beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-6RA, IL-7, IL-10, IL-11, IL-12p70, IL-13, IL-15, IL-17, IL-17C, IL-17E, IL-18, IL-19, IL-23, IL-27, IL-33, FAS, FAS Ligand, FLT-3 ligand, granzyme B (GRZB), leptin (lep), leptin R (lep-R), optineurin (OPN), PD-L1, platelet derived growth factor (PDGF)-AA, PDGF-AB/BB, TGF-beta, transmembrane activator and CAML interactor (TACI), TNF, TNF-related apoptosis-inducing ligand (TRAIL), vascular endothelial growth factor (VEGF), according to the manufacturer's instruction. Participants were classified according to whether over the 28 days duration of the study had ever received invasive mechanical ventilation (MV) or died (cases) or not (controls). Median levels of molecules have been compared between cases and controls using the Mann-Whitney test. To determine the relationship of multiple molecules with the risk of MV/death, we took advantage of a priori identification of molecules functional groupings. A global test procedure by means of logistic regression analysis proposed by O'Brien for multiple endpoints was used.

Results: Median of age of cases was 72 years, controls 60 (P=0.008); all other clinical characteristics were similar. Cases presented significantly higher plasma levels of lep-R, CCL20, CXC3CL1, CXCL10, OPN, IL-11, IL-18, IFN-g, IL-13 and reduced levels of FASL, FAS, IL-5, CXCL1, TRAIL, IL-15, IL-27, IL-2, EGF, IL-17, IL-1a, IFN-b, IL-14 vs. controls. As shown in the Table, by functional grouping, comparing 3rd with 1st tertile of ranks, cases also had lower levels of molecules related to apoptosis (P=0.0167), to interferon response (P=0.0079), and to TH2 regulation (P=0.0116), and higher levels of molecules related to cell metabolism (P=0.0258) compared to controls.

Discussion: The distinction between patients who more likely progress to critical or fatal COVID-19 and those who more likely do not progress could be relevant for a timely therapeutic intervention. We identify a number of plasma biomarkers that may help identifying patients with critical or life-threatening COVID-19. Further studies are needed to confirm the biological value of our observations.

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Immunopathogenesis III

OP 63 PREGNANT WOMEN DEVELOP A SPECIFIC IMMUNOLOGICAL LONG-LIVED MEMORY AGAINST SARS-COV -2

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Background: It is well established that pregnancy induces deep changes in the immune system. This is part of the physiological adaptation of the female organism to the pregnancy and the immunological tolerance toward the fetus. Indeed the suppressive T regulatory lymphocytes are progressively more represented, while the expression of co-stimulatory molecules decreases overtime. Such adaptations relate to an increased risk of infections and progression to severe disease in pregnant women, potentially resulting in an altered generation of long-lived specific immunological memory of infection contracted during pregnancy. How potent is the immune response against SARS-CoV-2 in infected pregnant women and how long the specific SARS-CoV-2 immunity might last need to be addressed, especially considering the current vaccinal campaign.

Material and Methods: This is an observational longitudinal study performed on 47 pregnant women with SARS-CoV-2-positive first diagnosis when admitted at delivery. Blood samples were collected at time of delivery, after 2, 4 and 24 weeks (w) post-delivery. Plasma was employed to profile a 27-cytokines/chemokines panel, to perform the SARS-CoV-2 specific antibody titer (T0 to T4) and to perform the in vitro neutralization assay (T4 only). PBMCs were stimulated in vitro with SARS-CoV-2 antigen to analyze CD4+ and CD8+ memory subsets (naïve, central memory, effector memory and TEMRA). Moreover, mRNA expression of 74 genes involved in the inflammatory antiviral response was analyzed simultaneously.

Results: Results show that 80% developed an anti-SARS-CoV-2-specific IgG response, comparable with the non-pregnant population. While IgG were present only in 50% of the asymptomatic subjects, the antibody production was elicited by infection in all the mild-to-critical patients. IgG peaked at w4. The in vitro neutralization ability significantly correlated with the antibody titer in this cohort. The specific T-cell subsets showed traits of a functional and responsive adaptive immune response against SARS-CoV-2 infection, which then rebalanced over-time. The analyses of the pro-inflammatory profile triggered by specific SARS-CoV-2 stimulation, both as mRNA expression and plasmatic cytokines/chemokines release, showed an intense pro-inflammatory activity, which then faded away over-time.

Conclusions: A picture of an intense inflammation is clearly detectable in pregnant women during the peri-partum period, consistently with the traits of SARS-CoV-2 infection, fading away after partum and during convalescence. Our results show that inflammation is greatly diminished within two weeks after delivery and completely resolved by month six after delivery, but a specific memory is maintained.

These results shed light on SARS-CoV-2-specific immunity in pregnant women; understanding the immunological dynamics in response to SARS-CoV-2 is essential for defining proper obstetric management of pregnant women and gender-specific vaccinal plans.

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Immunopathogenesis III

OP 64 ROLE OF TYPE-I AND -II INTERFERONS IN SARS-COV-2 INFECTION: CONVERGENT EFFECT, DIFFERENT MECHANISMS

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Background: Since the outbreak of Coronavirus Disease 19 (COVID-19) by the Severe Acute Respiratory Coronavirus-2 (SARS-CoV-2), immense efforts have been made by the scientific community to uncover its viral mechanisms of action, and factors controlling the susceptibility/outcome of the infection. A decrease in the innate antiviral response, hyper-inflammation, and exhaustion of effector T-cells are considered as major determinants of COVID-19 severity. Recent studies highlight the dynamic nature of virus-host interaction during SARS-CoV-2 infection, raising intriguing questions about the role and timing of interferon (IFN) responses. In fact, SARS-CoV-2 infection delays/antagonizes Type-I, and to a definitely lesser extent, Type II-IFNs. While paving the way for potential antiviral therapies based on innate immune activation, the molecular mechanisms linking different IFN pathways to SARS-CoV-2 susceptibility remain to be elucidated. Therefore, the present study investigates the role of Type-I and -II IFNs in SARS-CoV-2 replication in vitro.
Methods: Human pulmonary (CaLu3) and intestinal (CaCo2) cell lines were pretreated with either IFN-a, -b (10 and 100 IU/ml) or –g (100 and 1000 IU/ml), O.N. Cells were infected with SARS-CoV-2 (MOI 0.05) for 3h, and IFNs were added during infection. Supernatants were harvested at 24 and 48h post-infection to assess viral replication by RT-qPCR, and to quantify the levels of cytokines/chemokines through Multiplex assay. RNA extracted form cell lines was retrotranscribed to perform qPCR. In parallel, MTT was performed to assess cell viability.
Results: We provide evidence that Type-I and -II IFNs dramatically reduce SARS-CoV-2 replication in CaLu3 and CaCo2 cells, with IFN-b and -g showing the most prominent, long-lasting anti-viral effects. None the IFNs tested was toxic at the concentrations employed. Analysis of innumerous transcriptional targets associated with innate and adaptive immune functions, paralleled by quantification of cytokines/chemokines in the supernatants, unraveled different mechanisms underlying the anti-replicative effects of Type-I vs -II IFNs. In detail, IFN-a and –b were mostly efficient in controlling IFN stimulating genes (ISGs), pro-inflammatory cytokine/chemokine levels and associated transcription factors, such as MX-1, IFITM-1, RANTES, ACE2, RIG-1, and STAT1. On the other hand, IFN-g dramatically enhanced the expression of genes associated with the antigen processing/presentation pathway, including HLA, TAP, endoplasmic reticulum aminopeptidases, and the immunoproteasome. Convergent effects of Type-I and -II IFNs were also identified, which consist of reducing IL-6 and TNFR expression, along with targeting SARS-CoV-2-induced alterations in cholesterol metabolism.
Conclusions: These preliminary results suggest that boosting IFN responses in the course of SARS-CoV-2 infection may halt viral replication by acting at several levels, including activation of antiviral ISGs, strengthening of the adaptive immune response through the antigen processing pathway, and modulation of cholesterol metabolism, which may influence viral replication within membranous cell compartments.

Immunopathogenesis III

OP 65 PERSISTENCE OF HUMORAL IMMUNE RESPONSE AFTER ONE YEAR FROM COVID-19 DIAGNOSIS: EVIDENCE FROM A MONOCENTRIC STUDY

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Background: Knowledge regarding the durability of humoral immune response against SARS-CoV-2 infection is limited. Currently, there are contrasting evidence of antibodies' durability with evidence from SARS suggesting >12-month persistence, although humoral immunity against seasonal coronaviruses start decreasing after 6 months from infection. For COVID-19, only one study has reported evidence of humoral immunity at 8 months after diagnosis. In our study we sought to assess the persistence of anti-SARS-CoV-2 antibodies in subjects diagnosed, 12 months before, with COVID-19 and explore whether antibodies titers were associated to hosts' immune status.

Methods: We performed an observational cohort study considering patients, with at least 18 years of age, previously diagnosed with COVID-19 at Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico. The study was approved by the Ethics Committee of Milano Area 2 (no. 241_2020) with informed consent waived in all cases. To ascertain the influence of hosts' immune status, we developed a composite indicator based on subjects' co-morbidities (ie, HIV infection, diabetes, history of organ transplantation, documentation of active cancer) and the exposure to immunosuppressive therapy (eg, chemotherapy, biological drugs, corticosteroids). To limit the impact of confounders (ie, anti-COVID-19 vaccination), we measured anti-nucleocapsid (N) titres in all the subjects, using Roche Elecsys® immunoassay, rather than anti-spike ones. A gamma regression model was used to test whether anti-N titres were associated to hosts' immune status. Data was analyzed using R version 4.0.3.

Results: A total of 128 patients, 51 (40%) women and 77 (60%) men with a median age of 58 (IQR 50-65) years, were tested for at 12-month after COVID-19 diagnosis. Of them, 111 (87%) were hospitalized and 13 (10%) were admitted to the intensive care unit (ICU). Overall, 22 (17%) have been classified as immunocompromised (ID) because either had diabetes (59%), solid organ transplantation (14%), active cancer (18%), or have been exposed to immunosuppressive treatment (36%). Subjects ID were generally older (61.7 vs 56.3 years; p=0.009), although none were admitted to ICU. Although, only 4 subjected tested negatives for anti-N antibodies (ie, <1AU/ml), median anti-N titres were lower in ID subjects (17.5 vs. 68.6 AU/ml, p<0.001) (figure, A). The immune status, in the regression model, resulted significant (exp β=0.47 [95CI: 0.32–0.72], p<0.001) and remained so when controlling for age, sex, and ICU admission (exp adj-β=0.38 [95%CI: 0.25–0.61], p<0.001), the latter used as a proxy of disease severity (figure, B).

Conclusions: To our best knowledge, this is the first study reporting data after 12 months from COVID-19 diagnosis with anti-N titers ≥1AU/ml in all but 4 ID subjects. Our finding highlights the significant reduction of anti-N antibodies in ID subjects, also when controlling for confounding factors.

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Immunopathogenesis III

OP 66 IMMUNOGENICITY AND SAFETY OF TWO DOSES OF BNT162B2 VACCINE IN VERY ELDERLY SUBJECTS

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Background: COVID-19 has severely affected elderly living in nursing homes (NH) with deaths accounting for nearly half of the global number. This is a strong rationale for prioritization of NH residents and staff during early vaccination campaigns. However, data on immunogenicity and safety of COVID-19 vaccines in elderly population have not been well investigated. Here, we aimed to assess the humoral response and the short-term tolerability to BNT162b2 vaccine in residents of a NH and in staff.

Material and methods: This is a cohort study conducted between February 1 and May 31. All NH residents and staff were offered 2 doses of the mRNA vaccine BNT162b2 (Pfizer-BioNTech). Who accepted to be vaccinated were invited to participate in the 3-month serological survey. Serum samples for the assessment of SARS-CoV-2 antibodies production were collected immediately before from the first dose of the vaccine (T0), after 3 weeks at the time of second dose (T1) and after 12 weeks from baseline (T2) using the VITROS Anti-SARS-CoV-2 IgG 2 (Ortho-Clinical Diagnostics, CEDEX, France). Information regarding any new symptoms occurred after the administration of the first and second dose were also collected. SARS-CoV-2 antibody production and vaccine tolerability of the residents were compared with those from the staff.

Results: 61 (median [IQR] age: 91 [87-94] yrs) of the 64 residents and all the 50 members of staff (median [IQR] age: 50 [43-57] yrs) accepted to participate. The serological assessment at T0 showed that 47 (76%) of the residents and 28 (56%) of the staff were positive for anti-SARS-CoV-2 IgG. All residents tested positive at T0 had a previous history of COVID-19; however, 8 residents tested negative had a previous history of disease. 6 of 28 staff members tested positive at T0 had always had negative surveillance nasal swabs performed fortnightly from July 2020.

The % of anti-SARS-CoV-2 IgG positive subjects increased both among residents and staff after the first vaccination dose and reached the 98% in residents and 100% in staff.

At T0 residents and staff showed a significant difference in the median [IQR] S/C signal, (6.9 [1.5-11.3] vs 2.1 [0.0-8.1], p=0.001), with higher IgG S/C signal in residents than in staff, but this difference disappears when only residents and staff members with a previous history of COVID-19 were compared (8.4 [2.5-11.4] vs 8.0 [3.2-9.5], p=0.525). At T1 and T2 no differences in anti-SARS-CoV-2 IgG S/C signal were found between residents and staff (17.3 [15.4-18.1] vs 16.4 [9.9 -18.0], p= 0.160 and 18.7 [16.4-19.4] vs 17.3 [14.9-18.6], p=0.151, respectively).

Side effects (mainly pain at the site of injection) were significantly more frequent in staff members than residents either after the first (98% vs 48%, p<0.01) and the second (92% vs 56%, p<0.05) dose of the vaccine. No severe side effects were registered.

Conclusions: Our data support the use of vaccination programs against SARS-CoV-2 in very elderly subjects.

Social Sciences / Miscellaneous

OP 67 PATIENT OUTREACH STRATEGY TO ENHANCE RETENTION TO CARE OF HIV-POSITIVE ADOLESCENT AND YOUTHS: EXPERIENCE FROM HIV HIGH BURDEN SETTING

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Introduction: Patients lost to follow-up (LTFU) at different stages of the HIV cascade may increase HIV transmission, mortality and morbidity rates as well as hinder efforts to control the HIV epidemic, especially in a youth and adolescent populations. In Mozambique, retention in care after 3 years on antiretroviral therapy (ART) is around 44%, in a country where 52% of its population aged under 18y and around 120,000 adolescents living with HIV.
Methods: From 1 June 2019 to 20 June 2021, an intervention was piloted in Beira District (Mozambique) with the aim to bring back on care adolescents and youths LTFU or discontinuous with therapy. With the support of 4 local activists' associations phone calls were made to all LTFU and discontinuous patients identified in the lists of 8 HIV local health services of the Beira District. Home visits were made after unsuccessful calls, to patients without telephone contact or to whom have consented to the visit. Intervention was considered successful if the patient returned to visit and to ART within the next 60 days from the contact with the activist.
Results: Overall, 3314 adolescents and youths living with HIV were included in the study (67% F, median age 19 ys [IQR 15-21]). A telephone contact was performed for 58%, while home visits for 42% of the sample. The searching action was efficacy for the 86% of the population. LTFU compared with discontinuous patients were statistically significant (p-value< 0.005) mostly: older, female, no students, without an income and education, with a greater number of partners, with lower use of condom, with more alcohol consumption; even a smaller percentage of them were taking their medication. Among women, there were more pregnant and lactating women; they needed more active research with home visit, with more attempts and the action was efficacy for a lower percentage (72% vs 89%, p-value< 0.001). The multivariable logistic regressions show a greater probability of efficacy of the intervention for those who used condom "sometimes/always" compared with those who never used it [OR: 23.9, 95%CI: 15.7-36.5, p-value<0.01], and for those who have received a telephone contact (OR: 1.38, 95%CI: 1.02-1.87, p-value 0.038); lower values are obtained for age (OR:0.84, 95%CI: 0.81-0.87, p-value <0.01), smokers and drinkers (OR: 0.11, 95%CI: 0.06-0.22, p value<0.01 and OR: 0.04, 95%CI: 0.03-0.06, p-value<0.01, respectively) and for number of attempts >1 compared with one attempt (OR: 0.44, 95%CI:0.31 -0.63, p-value<0.01 and OR: 0.17, 95%CI: 0.11-0.26, p-value<0.01 for 2 and 3 attempts, respectively).
Conclusion: Our study described the typical profile of a huge sample adolescents and youths LTFU or discontinuous with therapy in Mozambique; also highlighted how a strategy made by community engagement, patients' outreach and the active involvement of activists in the recovery of patients LTFU can plays a central role in HIV control with a special focus to retention to care.

Social Sciences / Miscellaneous

OP 68 KNOWLEDGE OF HIV AND STIS: WHICH ARE THE MOST VULNERABLE POPULATIONS? RESULTS FROM A WEB-BASED SURVEY IN ITALY

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Introduction: Prevention campaigns have led to a significant decrease in new HIV diagnoses, while other sexual transmitted infections (STIs) show an opposite trend. In addition, several educational programs are promoted among young students, whereas informational campaigns addressing the general population are scarce or have little effectiveness. Therefore, we aimed to investigate the level of awareness regarding STIs among the general population.
Methods: We proposed a questionnaire regarding STIs and HIV to the general population in Italy.
We assigned 1 point to correct, 0.5 point to partially correct, and 0 point to wrong answers. The maximum feasible score was 10. We analysed the score differences based on sex, sexual orientation, age, region of origin, level of education, occupation, use of condoms, and prior training on HIV and STIs.
Results: Overall, 2183 people answered the questionnaire, with a mean age of 39.8±12.8 years. One-thousand-seven-hundreds thirteen (78.5%) were female, 457 (20.9%) were male. Overall, the mean score was 7.62 ± 1.42. The score of each separate category is reported in Table 1.
Regarding the score differences among variables, females answered better than males (p=0.02), whereas sexual orientation was not associated with a statistically significant difference. When considering sexual behaviour, no use of condoms was associated with worse scores.
Regarding the level of education, a higher degree of education was associated with better scores; the wider the educational level gap, the more significant was the difference in scoring. Furthermore, we compared health workers, not health workers, retired, unemployed, and students. Health workers obtained the highest mean score (8.42±1.22), while retired people showed the worst performance. The analysis by age group reinforces this data since people aged over 60 years old performed worse than anyone else. In addition, people aged over 50 years old had worse scores than younger people. On the contrary, people aged under 20 years old gained worse scores than people aged 20-49 years old, even if this difference is not statistically significant.
Furthermore, we aimed to assess the level of awareness about the U=U campaigns, and only 357 (16.4%) people already knew about it.
Conclusion: In conclusion, our study reveals several gaps in knowledge about HIV and STIs among the general population, especially among people aged over 50 years old. Furthermore, lack of awareness about HIV and STIs seems to be associated with a precarious use of condoms.

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Social Sciences / Miscellaneous

OP 69 HIV AND ADOLESCENTS. EVALUATION OF AN HIV AND STI PREVENTION PROJECT FOR HIGH SCHOOL STUDENTS

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Background: ASA, Associazione Solidarietà AIDS (AIDS Solidarity Association), is a voluntary association that since 1985 has been active in the prevention of HIV infection and in the support of HIV-positive people. The school project aims to bring the topic of HIV infection and sexually transmitted infections (STIs) within the school context because adolescents are a particularly vulnerable population as they are involved in their first sexual experiences.
Methods: from November 2020 to June 2021, students from three high schools in Milan, aged 16-18 years, participated in the project. Due to the Covid 19 pandemic, it was not possible to hold in-person meetings with students; this obstacle was overcome through remote meetings using Google's Meet platform. Each meeting, lasting two hours, was conducted by a psychologist for the information and a volunteer who told his experience of living with the virus. Space was left for questions from students. After the meeting, a link was sent by e-mail to access an online questionnaire and to leave a comment on the activity carried out. The questionnaire consists of 7 single-answer questions to be chosen from those proposed. The answers received were analyzed to get feedback in terms of effectiveness and perceived usefulness.
Results: with about 300 students involved, 250 responses to the anonymous questionnaire and 42 comments were sent. The questionnaire investigated four areas: overall satisfaction, clarity of presentation, quality of the answers given to the students' questions, usefulness of the meeting. Regarding the area of overall satisfaction, 73% rated the meeting as very informative to extremely informative. Regarding the clarity of exposition assessed through the presentation of the slides, 85% found the presentation from fairly to very interesting. 77% of students rated the explanations following the questions asked as very clear to extremely clear. Finally, with regard to the usefulness of the meeting, 80% found the meeting between very and extremely useful. 16.80% of the students left comments that are consistent with the data that emerged from the questionnaires. Among these were: "it was very useful because in these times there is a lot of misinformation on the subject", "the testimony was very useful and it made us understand what to do if we tested positive".
Conclusions: students found the meeting interesting and useful. As evidenced by comments such as "The fact that we are now older, and that we have taken up the subject, makes me realize that it is not something far from me and that it can never happen", the meetings are a valuable tool for awareness, prevention and fight against stigma.

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Social Sciences / Miscellaneous

OP 70 SARS-COV-2 VARIANTS SURVEILLACE HIGHLIGHTS LOCAL EMERGENCE OF DIFFERENT GENOTYPES

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Background: Since late 2020 the emergence of SARS-CoV-2 'variants of concern' (VOCs) challenged the effort to contain the pandemic because mutations in the Spike protein may affect virus transmissibility and antigenicity. Here, we report on the sequencing of the SARS-CoV-2 genome in a cohort of patients in Calabria (South Italy) from March to July 2021.

Material and Methods: RNA was extracted from 271 nasopharyngeal swabs. Sequencing of the S gene was performed by Sanger method. Whole-genome sequencing (WGS) analysis of 30 representative SARS-CoV-2 variants was performed with Ion Torrent technology using the Ion AmpliSeq SARS-CoV-2 Research Panel on the Gene Studio S5.

Results: Sequencing analysis identified 12% of the samples belonging to B.1 lineage, 5% of which showed at least one additional mutation in the S gene such as S477N, initially identified in the United States as a subtype of the Iota variant (VUM, B.1.256.2) and together with other mutations (E484K, P681H) defines a subtype of the Kappa variant (VOI, B.1.620). Approximately 2% of the samples of the B.1 lineage are characterized by the combination of two different mutations in the Spike protein - 69/70 deletion and N439K- initially identified in Denmark.

From March to July 2021, more than 80% of all variants identified in Calabria, are of the Alpha variant. Some of these variants (3.3%) are characterized by one additional mutation in the S gene, A701S, a position typically mutated in B.1.351 (Beta). Gamma variant was detected in 7.5% of cases, with one showing an additional mutation (P681H) characteristic of the Alpha variant and 2 samples showing Q677H and L452R mutations. Q677H is typical of the Eta variant (B.1.525) while L452R was identified in the Iota (VUM, B.1.526.1) and in the Delta variant (B.1.617.2).

Subsequently, to further characterise the identified variants, we performed WGS analysis on 30 representative samples. This analysis led us to identify 17 novel substitutions throughout the entire SARS-Cov2 genome (E102K, D1639N, D2980N, D3222N, S3687L, L3691S, A3623S, V5168, D5429Y, K5542R, E5585A in ORF1ab, S253P in ORF3a, P30L in ORF8, I82T in M, L139F in N and 2 substitutions upstream of the N gene). In B.1 lineage 5 samples, characterized by Q675H mutations in the S protein, showed A3623S in ORF1ab, P30L in ORF8 and A220V in N protein. Two samples with S477N in S protein showed V5168L, K5542R, E5585A mutations in ORF1ab. In the Alpha variant group three samples with A701S mutation in S protein showed upstream gene variant (c.-3delA) in the N gene. In Gamma variant samples all six showed S253P in ORF3a and an insertion (c.-12_-11insAACA) in the N gene.

Conclusions: SARS-CoV-2 variants monitoring highlighted the emergence of different genotypes some of which characterized by co-existing of multiple mutations typical of different variants at the same time. This evidence confirms a persistent viral genome evolution into more contagious forms.

Social Sciences / Miscellaneous

OP 71 ACCESS TO HIV TESTING BEFORE AND AFTER SARS-COV-2 PANDEMIC IN MILAN: COMPARISON BETWEEN A HEALTH-CARE SETTING AND A COMMUNITY SETTING

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Background: SARS-CoV-2 pandemic had a huge negative impact on health systems worldwide, not only in terms of non-COVID diagnostic and therapeutic services but also in terms of prevention, including HIV screening. This represents one of the most important secondary prevention strategies to reduce the spread of the infection and the related disease burden. In this study we evaluated and compared the impact of SARS-CoV-2 pandemic on HIV testing in health-care and community settings in Milan.

Methods: We extracted the HIV screening tests performed between 01/01/2019 and 10/ 06/2021 from the databases of two local hospital-based STIs outpatient clinic (S. Paolo and Niguarda Hospitals) and a community-based HIV testing facility (Milano Checkpoint). The tests performed before Mar-2020 were considered "pre-COVID", the others were considered "post-COVID". We then compared the two settings in these two frames of time in terms of number of tests performed, test results and age, sex and nationality of the subjects who got tested.

Results: Globally, 4106 HIV screening tests have been performed, 1263 (30.8%) in a health-care setting and 2843 (69.2%) in a community setting.

Comparing the two settings, in the whole period considered the community setting tested younger subjects (p<0.001), a higher percentage of females (p<0.001) and a lower percentage of foreigners (p<0.001), with a lower HIV prevalence (p<0.001) (Tab.1).

In the health-care setting, in the post-COVID period there has been a decrease in the number of tests performed, from a mean of 50.3 to 37.0 HIV-test/month (-26.4%) (Tab.4). A lower percentage of females (13.3% vs 20.1%, p=0.001) and a higher median age (31 vs 34 years, p=0.001) have been found in the post-COVID period (Tab.2). HIV prevalence remained quite high (2.4% vs 3.9%, p=0.470) (Tab.3).

In the community-setting, in the post-COVID period there has been also a relative decrease in the number of tests performed (from 120.8 to 85.0 HIV-test/month, -29.6%), mostly due to the stop of the activities of this facility during lockdown (Mar-Jun2020, Fig.1). Indeed, after restricting to the period of Jul2020-Jun2021 the average number of HIV-test/month reached the 114.9 similar to pre-COVID era. A lower percentage of females (33.8% vs 27.8%, p=0.001), a lower median age (30 vs 29 years, p=0.009) and a lower HIV prevalence (1.0% vs 0.1%, p=0.001) have been found in post-COVID period.

Conclusions: Both settings have reduced their activity due to the pandemic, particularly during the lockdown, but they have now reached the same numbers of pre-COVID era. The prevalence of HIV was high in the health-care setting, possibly because of subjects attending the service while symptomatic and/or at higher risk. The differences between the subjects tested in the two settings demonstrate how they reach different populations, underlining the importance of an integrated approach to ensure greater coverage and effectiveness of HIV screening campaigns.

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Social Sciences / Miscellaneous

OP 72 CHARACTERIZATION OF PLWH WITH LOW-LEVEL VIREMIA: RESULTS FROM THE ITALIAN ARCA COHORT

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Background: Despite the success of antiretroviral therapy (ART) for suppressing virus replication, some people living with HIV (PLWH) maintain a low-levels viremia (LLV). The clinical significance of LLV remains unclear. Aim of the present study is to characterize PLWH with LLV compared to those who maintain virological suppression (VS).

Material and methods: We selected PLWH enrolled in ARCA cohort between 2009 and 2019 with at least one genotypic resistance test (GRT) for protease/reverse transcriptase and integrase (when available) from plasma samples before ART start. In Group 1 (G1), we included PLWH with LLV (at least two consecutive plasma HIV-1 RNA values between 50 and 1000 copies/mL) occurring after at least 6 months of virosuppression. In Group 2 (G2), we included patients with HIV-1 RNA <50 copies/mL since 6 months with a duration equal or superior to the median duration of the LLV period observed in G1 with non-consecutive blips allowed. Observation period (OP) was defined as the time corresponding to the duration of LLV or VS. Potential differences between the two groups were evaluated by T-test or Mann-Whitney exact test for quantitative variables and Chi-squared or Fisher's exact test for qualitative variables, as appropriate.

Results: Among 2103 PLWH, 340 belonged to G1 with a median duration of LLV of 182 days (interquartile range, IQR: 131-252); 179 (52.7%) had all viremia values during the OP between 50 and 200 copies/mL. PLWH in G2 were 1763, with a median duration of VS of 1182 days (IQR: 735-2317) ($p < 0.001$). The median year of OP start was in 2013 (IQR: 2011-2016) and 2012 (IQR: 2010-2016), respectively. PLWH in G1 were significantly older, more frequently injective drug users and coinfected with HBV or HCV than those in G2. Consistently, in G1, history of HIV infection was longer, with lower CD4+ T cell count at nadir and higher zenith viremia; first-line ART was started earlier with a heavier exposure to different ART regimens, particularly including non-nucleoside reverse transcriptase inhibitors (NNRTI), protease inhibitors (PI) and integrase inhibitors (INI). By evaluating the pre-existent resistance, a significantly higher proportion of individuals with resistance associated mutations for PI, NNRTI and NRTI before the OP was found in those with LLV compared to those on VS, evaluated both as cumulative resistance (63.8% vs. 44.6%, $p<0.001$) and as resistance detected at the last GRT before the OP (18.8% vs. 2.0%, $p<0.001$) (Figure 1). A trend towards significance for higher prevalence of pre-existent resistance to INI was also found in G1 (cumulative INI-resistance: 21.9% in G1 vs. 9.1% in G2, $p=0.061$; INI-resistance at the last GRT pre-OP: 18.8% in G1 vs. 9.1% in G2, $p=0.124$).

Conclusions: PLWH who experienced LLV were shown to have longer history of HIV infection and exposure to different ART regimens and a higher prevalence of pre-existent resistance compared to those who maintain virological suppression.

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Epidemiology / Social Sciences III

OP 73 PRE-EXPOSURE PROPHYLAXIS (PREP) THOUGH THE SARS-COV-2 PANDEMIC PERIOD: THE EXPERIENCE OF THE DEDICATED SERVICE OF TUSCANY REGION IN S.M.ANNUNZIATA HOSPITAL, FLORENCE

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Background: Pre-Exposure Prophylaxis (PrEP) is currently a consolidated strategy for prevention of HIV infection in high-risk populations. The Infectious Diseases Unit of S.M.Annunziata Hospital (Azienda USL Toscana Centro), Florence, set up the first PrEP service of Tuscany Region.
Methods: In December 2018 Azienda USL Toscana Centro created a dedicated e-mail account for people requiring PrEP information profilassipreesposizione.firenze@uslcentro.toscana.it, that was published on HIV associations' websites, brochures and on social media.
The account was daily managed by dedicated medical doctors of the Unit.
Users performed a baseline screening for renal function, HIV, HAV, HBV, HCV, Syphilis and other sexually transmitted infections (STIs), and received a counseling for PrEP evaluation.
For those beginning PrEP, follow-up exams and visits were planned every 3 months.
People susceptible for vaccinations were referred to a dedicated service that was organized in our Unit. During the months of reduced hospital accesses due to SARS-CoV-2 pandemic, first visits and vaccinations were postponed, but to all people already on PrEP, continuation of therapy was guaranteed.
When necessary, the prescription for treatment was directly brought by medical doctors from the hospital to territorial pharmacies.
Results: From January 2019 to July 2021 57 people performed a first visit and baseline screening; 56 males and a transgender woman, median age 39.6 yrs, 91.5% MSM, 35.6% coming from other Tuscan cities or other regions; 74.5% had a high-level instruction (degree), 33.8% reported at least one previous episode of post-exposure prophylaxis (PEP) and 52.5% a previously diagnosed STI. At baseline, one patient had a first diagnosis of HIV infection showing a recent seroconversion, and 8 cases of undiagnosed STIs were identified. The 30.5% of users was susceptible to HBV and 49.1% to HAV.
Nine people (15.7%) were lost-to-follow-up (LTFU) immediatly after the baseline visit (before starting PrEP); of the 48 people who proceeded with follow-up, PrEP was prescribed in 40 cases (83.4%), 57.5% on-demand. Of these, 65% is stably on follow-up, while the 35% was LTFU (64.2% before the beginning of SARS-CoV-2 pandemic).
In one case PrEP had to be stopped because of renal failure development; no acute HIV, HBV, HCV and HAV infections were observed.
During follow-up, 14 cases of STIs were diagnosed (4 C.trachomatis, 3 Syphilis, 1 N.gonorrhoeae, 3 U.urealyticum, 3 M. hominis).
Conclusions: Despite the SARS-CoV-2 pandemic period, our internal organization guaranteed continuity of care to all people already on PrEP who required the continuation of therapy; a high level of retention in care was obtained.
In our experience PrEP confirmed effectiveness in HIV prevention; moreover, the required baseline and follow-up screenings proved to be an important instrument for the identification of people susceptible for vaccinations, and for the quick diagnosis and treatment of STIs.

Epidemiology / Social Sciences III

OP 74 PREP EXPERIENCE AT MILANO CHECKPOINT: PROMOTING HEALTH AND WELL-BEING THROUGH THE INTEGRATION OF COMPLEMENTARY SKILLS

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Background: Properly taken,PrEP is useful to reduce new Hiv infections.Since Sept. 2017 ASA offered a service on appointment aimed to counteract DOIY PrEP, which is potentially able to increase Hiv and other STIs spread.During the 1st appointment,after a rapid Hiv test, an ID doctor informs them about medication, how to take it and how to care against other STIs, eventually by vaccines. HCV,syphilis, and-since Feb.2019, after service's merging into Milano Checkpoint-ct and ng rapid tests are also offered at the same time. A psychologist faces motivations leading to PrEP, sexual behavior (also chemsex), attitude towards Hiv, thoughts and expectations regarding medication, giving opportunity to reflect over themselves. Both specialists stress that PrEP cannot substitute condoms.Psychologist assures attention to emotional aspects connected to PrEP in the firsts 3 appointments; then is substituted by a trained peer.Appointments has been paused from Mar. to June 2020, due to Covid-19 restrictions. Since July 2020, the 1st appointment is preceded by a screening Skype call by higly skilled peer, who also stresses that mandatory condition to start taking PrEP are 2 weeks having only safe sex.
Method: Self-administered questionnaires (January 2020-July 2021) have been analyzed by descriptive statistics. Bio-psycho-social & medical features,sexual habits and risk behaviors are observed. Qualitative analysis on interviews with counselors have been conducted.
Results: 467 users (M 98%; 26-40 53%; homosexual 88%; graduated and over 67,3%; Italians 82%; using Chems 19,5%). During the 1st appointment we mainly analyze sexual habits, how & until when they will remain on PrEP. Particular focus on Hiv fears and motivation to PrEP path. Following appointments are devoted to their own relationship with PrEP taking and changes in sexual life.
Conclusions: more than half of the sample take PrEP as "precaution, supplementary care". To take PrEP is easy for everybody and produces positive fallout on sex emotional aspects. Along the way, 30% of the users reduce condom use. Among those who suspended or shifted the way of taking the medication, it was mostly because of decreased dating: this is easily related to the restrictions & concerns about Covid-19. Stigma is confirmed to be lower (32%) at baseline when compared to early analysis,and decreases further along the path (this shows that PreP is a catalyst for virtuous circles in the fight against stigma). In the first talks, users speak not only about their sexuality but also about their relationships and identity. A few feel the need to talk about their psychotherapies, and a portion asks our counselors (psychologists or peers) for contacts in order to start. The PreP process in this way structured, with medical follow-ups and interviews dealing with the emotional aspects, thus recognises the needs of the service users, who are interested not only in protecting themselves and living a satisfactory, albeit monitored, sexuality, but also in promoting their own well-being.

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Epidemiology / Social Sciences III

OP 75 RAPID TESTS IN THE PANDEMIC: THE "CONTINUUM OF CARE" OF VILLA MARAINI DURING THE COVID-19 EMERGENCY

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Background: The Covid-19 pandemic has led to the overshadowing of other diseases, including HIV and chronic liver diseases, generating a reduction in the quality of life for patients for whom one aspect, that of taking charge and care, is fundamental. Social distancing made difficult to carry out rapid screening tests for diseases such as HIV and HCV. Fewer tests, fewer early diagnoses, fewer options for a cure. Villa Maraini Foundation has continued with the testing activity also during the lockdown, with the necessary changes to ensure safe execution for patients and operators.

Methods: The team is represented by a doctor and a psychologist / socio-health worker, frequently a former drug addict. Rapid tests are on a capillary blood sample: HIV, HCV and Syphilis tests. PPE are used: ffp2 mask and sterile gloves for the doctor and mandatory surgical mask for the patient. The rooms are sufficiently ventilated and the surfaces are disinfected regularly. Tests were also carried out outdoors, in the Foundation's green spaces or at the Tor Bella Monaca park where the Road Unit operates. First of all the patient's temperature is taken, then a pre-test counseling is carried out through a questionnaire regarding clinical history and risk behaviors in the previous 6 months. The doctor carries out the test and communicates the results: in case of negativity, the patient is informed about the possibility of repeating it or not, in the event of a preliminary positive test the patient is sent to the Infectious Diseases Clinic of Tor Vergata Polyclinic for sampling confirmation and the beginning of the treatment.

Results: From March 2020 to June 2021, 311 people were tested, of which 76 were women and 235 men.

Of the women, 72 took the HIV test, 69 negative and 3 positive, 62 the HCV test, 51 negative and 11 positive, and 49 the Syphilis test, 48 negative and 1 positive.

Of the men, 211 took the HIV test, 207 negative and 4 positive, 187 the HCV test, 148 negative and 39 positive, and 117 the Syphilis test, 113 negative and 4 positive. 100% of the positives for HIV and HCV have been sent to specialized centers for the execution of the confirmation sampling, and to date 100% of patients tested with positive results have started specific treatment.

Conclusions: from the point of view of the "continuum of care" in which Villa Maraini has always believed, it was essential to be able to guarantee the execution of rapid screening tests for MTS to our patients. The closure of many clinics and the lengthening of waiting times for taking care and the start of treatment have created many difficulties, but the constant presence of a trained team, former operators with their communicative and empathic skills, the availability of a 24-hour service were the strengths of our work.

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Epidemiology / Social Sciences III

OP 76 COVID-19 IN HIV/AIDS OUT-OF-HOSPITAL FACILITIES IN LOMBARDY

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Background: The impact of Sars-CoV2 on people living with HIV/AIDS in the Lombardy out-of-hospital facilities (Homes, henceforth) was a feared event both for the epidemiological trend in Lombardy region and for the consequences that could exist for people with AIDS and comorbidities.
Objectives: The aim was to evalue the spread of SarsCoV2 inside the Lombardy Homes, since the Coordinamento delle Case Alloggio della Lombardia had frequently met the team managers and provided operational directions based on the health authorities' guidelines and the available literature.
Methods: In May 2021, a survey was conducted in the 21 Homes managed by C.R.C.A members (Fig.1).
Results: Between 1st February 2020 and 30th April 2021, 204 bed-places and 32 places for daytime guests were available. During this time, 280 guests, 226 healthcare operators, and 12 volunteers were present overall. Since March 2020, daytime guests have had no access to the Homes: they have either switched to home visits or been hosted inside.
25/280 guests and 31/238 operators had a Covid-19 diagnosis by symptoms and/or RNA-PCR positive swab test (Fig. 2 -3). 5/25 guests were diagnosed while hospitalized for other reasons. In 3/21 Homes, neither guests nor operators were affected by Covid-19. During these months, 11/280 guests died, but only 1 because of Covid-19.
On average, guests with Covid-19 were older than the operators and had more severe clinical courses. 9 guests were asymptomatic. 11/20 guests diagnosed in a Home were later hospitalized, and 10/11 needed oxygen supplementation. Of the nine guests isolated in the facility, only 1 needed oxygen.
Among the operators, 27/31 were isolated at home: 6 remained asymptomatic, 20 had a mild and 1 a moderate Covid -19. 4/31 were hospitalized, 3/4 needed oxygen supplementation (Fig. 4).
When someone tested positive in the facility, all the operators and guests were tested by nasopharyngeal swabs, even repeatedly. This measure allowed minimizing the spread of the virus. 22/31 operators (71%) had Covid-19 in spring 2020, while 14/25 guests (56%) had Covid-19 in the autumn. In autumn, three different clusters affected 11 guests and 6 operators in total (Fig. 5).
Conclusions: the measures implemented allowed to contain the spread of the infection in the Homes, especially during the so-called "first wave". Another helping factor is the small size of the communities. In the autumn, weaker attention on the precautionary measures might have favoured the Sars-CoV2 diffusion in some contexts. This situation led to reintroduce stricter measures. Consequently, the number of new positive cases decreased significantly in the first months of 2021. A factor contributing greatly to this result is the beginning of the vaccination campaign, first for the healthcare operators and later for the guests. Indeed, at the end of April 2021, most operators and guests received at least one dose of the vaccine (Fig. 6).

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Epidemiology / Social Sciences III

OP 77 THE COVID-19 PANDEMIC IMPACT ON RETENTION IN CARE AND VIRAL SUPPRESSION AT THE INFECTIOUS DISEASES UNIT OF S. M. ANNUNZIATA HOSPITAL, FLORENCE: COMPARING 2019 AND 2020 DATA

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Background: The primary objective of our analysis was to evaluate the impact of the first year of COVID-19 pandemic on retention in care and sustained viral load suppression of people living with HIV (PLWH) followed by the Infectious Diseases (ID) Department of S. M. Annunziata Hospital (OSMA), Florence.
Materials and methods: Data on PLWH that were dispensed antiretroviral (ARV) medications by the OSMA ID Unit in 2019 (01/01 to 31/12) and 2020 (01/01 to 31/12) were extracted from the database of OSMA hospital pharmacy. A single HIV-1 RNA measurement per semester in 2019 and 2020 was collected from the OSMA Laboratory database. Patients were stratified according to: - type of ARV treatment (single tablet regimen [STR] versus multiple tablet regimen and dual/3-drugs/4-drugs regimen); - HIV-1 RNA measurement (20, 20-50, 51-200, >200 cp/ml); - sex, age and geographical origin. 2019 and 2020 data were collected and analysed by an Excel database.
Results: Patients who were dispensed ARVs at least once a year by the hospital Pharmacy were 755 (177 [23%] female, median age 52.3 years) in 2019 and 803 (177 [22%] female, median age 52.3 years) in 2020. Subjects with viral load (VL) <20 cp/ml were 597 (79%) in 2019 vs 658 (82%) in 2020; in 2020 93% of HIV+ individuals (n=750) had VL<50 cp/ml, versus 90% (n=681) in 2019. 53 patients (7%) were switched to a different ARV regimen between 2019 and 2020. Patients on dual regimens were 12% and 13% in 2019 and 2020 respectively; 47 versus 23 individuals were given dolutegravir-based STR dual combinations in 2020 and 2019 respectively. Considering the foreigners subgroup, in 2020 the hospital Pharmacy dispensed ARV drugs to 153 (19%) patients born in countries other than Italy. As well as the total population, this subgroup showed good adherence, with 90.8% of individuals with VL<50 cp/ml (88% in females and 92.5% in males). The median age of individuals receiving dual regimens was higher than patients who were given 3/4-drugs regimens, probably due to clinical considerations on comorbidities and polypharmacy in elderly individuals.
Conclusions: We conducted this data analysis hypothesizing the following critical aspects deriving from 2020 COVID-19 pandemic: a more difficult access to hospital pharmacy/outpatient clinic and a subsequent decrease in treatment adherence, viral suppression and chances of optimizing ARV treatments according to 2019 EASL Guidelines. Unlike what was expected, we observed between 2019 and 2020 a 3% increase in viral suppression among the considered population (90% vs 93% VL <50 cp/ml in 2019 and 2020 respectively). The fact that during the lockdown in spring 2020 the hospital pharmacy started dispensing a larger amount of ARV medications at each access than in 2019 could represent one of the reasons why the pandemic did not affect the adherence in our HIV population. To conclude, the COVID-19 pandemic did not have a negative impact on retention in care in our setting.

Epidemiology / Social Sciences III

OP 78 REACHING 90-90-90 IN THE MUNICIPALITY OF KILAMBA KIAXI, LUANDA, ANGOLA. THE EXPERIENCE OF PIPSA PROJECT

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Background: Since 2018 the Angolan government has undertaken the "test and treat" policy to realize the UNAIDS HIV/AIDS target of 90-90-90.
To date, despite the availability of antiretroviral therapy (ART), in sub-Saharan countries adherence is not optimal and people, often, abandon therapy.
In this context an "HIV Prevent/Test/Treat" program, aimed to comunity, to provide information on HIV, increase HIV counseling and testing and support those who tested positive was implemented (PIPSA project).
The project takes place in the municipality of Kilamba Kiaxi, Luanda, and this study was carried out in three health centers, (Palanca II, Kilometro 9A and Whegi Maka).
Methods and materials: Ten community activists, three nurses and a psychologist were recruited and trained.
Activists, daily, go to clinics and use peer-oriented intervention to: inform persons about HIV prevention and importance of getting tested; test persons who agree to be tested; follow up and support, through counseling, those who tested positive in initiating ART.
Address and telephone numbers of the positive persons are recorded, then the activists perform home visits and phone calls to HIV-positives to reinforce them on the importance of: adhering and retain themselves in care; not abandoning ART; and to disclose HIV status to sexual partner and relatives. Some persons, on a team decisions basis, receive more home visit.
In addition, the nurses of the project call people who have missed the visit to book another appointment and the doctor carries out a weekly visit in each center.
Objective: Follow up of people tested positive from november 2018 to august 2020.
Results: During the project observation period: 890 persons tested positive; activists carried out 2094 home visits and 11040 phone calls; nurses made 3548 phone calls; and doctor performed 382 visit.
The results of follow up are showed in Table 1 and 2.
Conclusions: Several studies carried out in sub-Saharan countries have investigated the factors that prevent adherence to ART among PLWHA. Mobility is the first barrier and is due to economic insecurity and social precariousness. Other barriers are stigma, side effects of ART, difficulties in reaching the health center, lack of information, assistance and support and negligence. Improving support of HIV-positive people, through the interventions of community activists (peer operators) and the emotional interest of nurses, psychologists and doctors, may achieve strong reduction in the abandons of therapy and high retention in care rate (90%).
Our observation has several biases, the most important of which are the shortness of the observation time and the fact that the persons in treatment lived fairly close to the health center.
The PIPSA (Integral Protection of Seropositive People in Angola) project is funded by Agenzia Italiana per la Cooperazione e lo Sviluppo and is carried out by Unione Medico Missionaria Italiana and CUAMM - Medici con l'Africa.

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Virology

OP 79 MOLECULAR EVIDENCE OF HIV-1 TRANSMISSION IN A CRIMINAL CASE IN ITALY

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Background: Intentional transmission of HIV between individuals has important legal implications and therefore may come to require forensic investigation based upon molecular data. This study describes the use of phylogenetic analysis as forensic evidence in a criminal HIV transmission prosecution that was used for the first time in court of low in Italy.
Materials and Methods: The investigation started in November 2015 with the charge of a woman who discovered by chance her HIV seropositivity. The analysis was extended to other people possibly involved, by retrieving pol sequences from anonymous regional HIV drug resistance databases. Subtype B sequences were selected with a genetic distance ≤2% compared to the defendant HIV-1 pol sequence. Phylogenetic analysis was conducted by using Maximum Likelihood and Bayesian methods. Cluster evolutionary rate and dating was also estimated. In addiction, to gain insights on possible paraphyletic relationships among the accused and the possible victims, ultra-deep pyrosequencing of env region was performed on the available stored residual plasma samples from subjects harbouring a similar virus compared to that of the defendant.
Results: On a total of 12,755 pol sequences analysed, collected from the Lazio area in the same time period by different HIV reference centers, 35 individuals were discovered to be directly involved in this transmission cluster (bootstrap value of 100% and a posterior probability of 1). Five subjects, although identified for harbouring a similar virus, were excluded from the criminal case by the phylogenetic analysis. Individuals were 85.7% heterosexual females, median (IQR) age: 31 (26-33). Median (IQR) viral load and CD4 cell count were: 4.74 (3.98–5.43) log copies/mL and 323 (121–460) cells/mm3. The tree was scaled by calendar year, from which the period of cluster transmissions can be inferred. Estimated mean time of the Most Recent Common Ancestor of the cluster was 19.5 years before 2016 (95% HPD: 14.0-26.7), suggesting that it was originated around the end of 1997 (95% HDP: 1989–2002). The env ultra-deep phylogenetic tree, constructed with all the representative subject sequences, revealed a complete mixture of quasispecies among the accused and the other subjects involved in the criminal case, but a complete segregation from another subject with a similar virus, but not related to the legal proceeding.
Conclusions: This study described the phylogenetic investigation on the largest voluntary criminal case of HIV transmission in Italy, in which a man, although being aware of its HIV-1 seropositivity, voluntarily transmitted the virus during the course of various sexual relationships to dozens of victims. In fact, the molecular investigation submitted to the prosecutor office as substantial forensic evidence, in addiction to several reports from victims, led to a decisive conviction of the accused.

Virology

OP 80 ASSESSMENT OF SPECIFIC IMMUNOLOGICAL RESPONSE AFTER ADMINISTRATION OF ANTI-MENINGOCOCCAL QUADRIVALENT CONJUGATE VACCINE MENVEO® IN A POPULATION WITH VERTICALLY-TRANSMITTED HIV INFECTION

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Background: In HIV-infected patients, high incidence of invasive meningococcal disease is reported. Moreover, HIV-subjects, because of immune abnormalities, may undergo impaired vaccine response. Our study aims to assess the immunologic response after the administration of a quadrivalent meningococcal conjugate vaccine Menveo® (MenACWY-CRM, GlaxoSmithKline Vaccines) in HIV-infected young patients.

Material and Methods: We carried out a controlled, non-randomized, observational and prospected study, involving 27 HIV-infected patients aged 9–30 years, reporting vertically-transmitted HIV infection and followed at the Pediatric Infective Disease Clinic of ASST FBF-Sacco, Milan Italy. All patients enrolled were on HAART, and 25 out of 27 presented optimal immunological and viral response. Each subject received the vaccine Menveo (0,5 ml i.m.). MenACWY-specific Ab titer, viral load and CD4+ T cells count were measured at baseline (T0), T3, T6 and T12 months post vaccination. In 14 patients, MenACWY-specific cell-mediated immune responses were evaluated at the same time points.

Results: Menveo induced seroconversion in all subjects except one. We divided our cohort in different subgroups: Responders (R), reporting seroconversion at T3, Highly-Responders (HR) with a high Ab titer at T0, and Non-Responders (NR). The administration of the vaccine induced MenACWY-specific cell-mediated immunity at T12 mainly in HRs (Effector Memory CD4+T cells). MenACWY-specific IL2-secreting CD4+ T and CD8+ T cells were slightly increased in both HRs and Rs. In the NR group, terminally-differentiated CD4+ and CD8+ T cells were the only parameters modified.

Conclusions: The administration of Menveo® vaccine, considering both R and HR subgroups, induced a valid antibody-mediated protection. Moreover, we observed the development of a stable T cell-mediated immune memory that lasted robustly up to one year since vaccination in most of the subjects analyzed. The NR showed instead a peculiar immune phenotype, correlated to an unsuccessful response to the vaccine. Notably, the NR was characterized by high viremia and low compliance to the therapy throughout the whole study period. Our data indicate that alternate immunization schedules need to be considered in ART-non-responder patients.

Virology

OP 81 REGULATION OF M6A METHYLATION AS NEW THERAPEUTIC OPTION AGAINST COVID-19

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Background. Coronavirus Disease 2019 (COVID-19) appeared for the first time in Wuhan, China, at the end of 2019 and then bursted all over the world. The causative agent has been described as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel member of Coronaviridae family, responsible to date for 192,284,207 confirmed cases including 4,136,518 deaths. Vaccines are offering a way out of the COVID-19 pandemic, but other alternative strategies, such as human monoclonal antibodies able of neutralizing the virus, are also being extensively investigated. Furthermore, repurposing molecules, e.g. remdesivir, lopinavir-ritonavir, hydroxychloroquine, are being experimentally used, and there is a non-stop search for prophylactic and therapeutic interventions. The epigenetic machinery contributes in SARS-CoV-2 replication and should be explored more deeply. In this scenario a recently discovered post-transcriptional regulation is the N6-methyladenosine (m6A), a RNA modification that affects both cellular and viral transcripts with important implications for RNA fate and function. Only few evidence demonstrated the role of m6A methylation in SARS-CoV-2 infection, indicating that this type of modification interferes negatively with the viral replication.

Material and Methods: Vero cells (ATCC CCL-81) were treated with rhein (R7269, Sigma-Aldrich) at not cytotoxic concentrations and simultaneously infected with SARS-CoV-2 (clinical isolate gently donated by Hospital Lazzaro Spallanzani, Rome, Italy) for 2 hours at 37°C. Two days post-infection, viral plaques were stained and microscopically scored. The same experiment was repeated and RNA was collected by TRI Reagent (T9424, Sigma-Aldrich) after 48 hours. m6A levels were analyzed by m6A RNA methylation assay kit (ab185912, Abcam).

Results: To evaluate if m6A methylation could have a direct regulatory role in coronavirus infection, a natural anthraquinone called rhein was used. Rhein's biological activity includes a wide range of fields, including the FTO inhibition, that is the main demethylase enzyme involved in m6A pathway. The drug (from 0.39 to 200 µg/mL) was added simultaneously with SARS-CoV-2 on the Vero cell monolayer and viral plaques were counted after 48 hours. Rhein interfered with SARS-CoV-2 life cycle starting from 25 µg/mL and completely blocked the infection at 200 µg/mL. Furthermore, results revealed that rhein at 200 µg/mL caused a two-fold increase in the methylation levels compared to the not treated cells.

Conclusions: Our study for the first time demonstrates that the inactivation of m6A demethylation pathway via chemical drugs could restrict SARS-CoV-2 replication. The overall results indicate that m6A key enzymes could be exploited as potential therapeutic options in the fight against COVID-19.

Virology

OP 82 CHARACTERIZATION OF HUMORAL AND CELLULAR IMMUNE RESPONSE AFTER SARS-COV-2 MRNA VACCINE IN HIV-1 INFECTED PATIENTS

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Background: Although HIV-1 infection was not initially considered as a risk factor for a severe COVID-19, recent studies suggest that people living with HIV (PLWH) (particularly with low CD4 cell counts or untreated HIV infection) might have a more severe clinical course than HIV-negative people. While the SARS-CoV-2 mRNA vaccine trials found near-universal robust immune responses in the general population, the antibody levels and immunogenicity to SARS-CoV-2 vaccination has not been fully reported in PLWH. Therefore, this study aimed to characterize the neutralizing antibodies titers and the immunophenotype and activation of T and B cells after two-dose SARS-CoV-2 mRNA vaccine among HIV-1 infected patients.

Material and Methods: Blood samples were collected from 20 successfully ART treated HIV-1 infected males at baseline (T0, not vaccinated) and 1 month after the second dose (T2) of Pfizer/BioNTech BNT162b2 vaccine. Anti-spike-Nab titers were assessed using a replication-competent VSV-pseudovirus expressing the SARS-CoV-2 spike protein. Two-fold serial dilutions of patient's plasma were pre-incubated with 10^2TCID50/100 µL and added to cell monolayers. CPE was scored at 48 hours post-infection. To characterize the T and B subpopulations and their activation levels, thawed PBMCs were stained with Viobility, CD3, CD4, CD8, CD19, CD45Ro, CD27, HLADR, CD38 and CD24 (Miltenyi Biotec). The data acquisition was done using Gallios Flow Cytometer and the analysis were conducted using the Kaluza software (Beckman Coulter). Statistical analysis was performed using PRISM v.8.0.

Results: At baseline, HIV-1 infected patients, mean age 53 ±10 years, were all under ART from at least 10 years (median:16; IQR:10-21 years); the HIV viral load was < 37 copies/mL in all patients and the median CD4 T cell count was 612 (IQR:490-765) cell/mm3. After one month from the second dose of vaccine (T2), 4 subjects out of 20 (20%) did not develop neutralizing antibodies, 7 subjects (35%) had antibodies with neutralizing activity against SARS-CoV-2 below 1:80. 9 (45%) subjects had a neutralizing antibody titer over 1:80. The vaccine side effects and reactions were mild, and no adverse events occurred. No statistically significant differences were observed between the baseline and T2 frequencies of circulating CD4-T, CD8-T and B subpopulations ($p>0.05$). Moreover, the expression levels of CD38 and HLADR, on naïve, TCM and TEM CD4 and CD8 T cells and CD38 and CD24 markers on B cells at baseline were similar to those observed after anti-SARS-CoV-2 vaccination (T0 vs T2: $p>0.05$).

Conclusions: Two-dose SARS-CoV-2 mRNA vaccination promote an Anti-Spike-neutralizing activity in virologically suppressed PLWH (80%) but may not have an impact on cellular immune frequencies and activation. Considering these preliminary results, further studies, including healthy subjects, are needed to better delineate the specific anti SARS-CoV-2 immunological profile among HIV-1 infected subjects.

Virology

OP 83 SAFETY AND TOLERABILITY OF THE PFIZER-BIONTECH BNT162B2 COVID-19 VACCINE IN A DIVERSE COHORT OF PEOPLE WITH HIV (PWH)

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Background: The pivotal BNT162b2 trials reported that in the 7 days after vaccination, common side effects comprised pain at the injection site, tiredness, headache, muscle/joint pain, chills and fever (dose-2 > dose-1). Reported data included only ~60 vaccine recipients with HIV. We systematically evaluated solicited and unsolicited side effects after 2 vaccine doses (3 weeks apart) in PWH with diverse risk groups, HIV history and comorbidities.
Methods: Consecutive PWH attending for vaccination prospectively completed a structured questionnaire reporting side effects experienced in the 7 days after each vaccine dose. Findings in the cohort were related to data from the total BNT162b2 trial population (ref: FDA submission, Nov 2020).
Results: In this interim analysis, the population totalled 197 PWH. Baseline characteristics: 71% males, median age 48 years (IQR 40-56), 78% Italy-born, 44% MSM, 15% IDU, 76% smokers, 28% prior AIDS-diagnoses, >99% on ART, 96% viral load <50 copies/ml, median nadir CD4 count 258 cells/mm3 (81-426), current CD4 count 723 cells/mm3 (509-954), CD4:CD8 ratio 0.8 (0.6-1.2). Prevalent comorbidities: hypertension (25%), cardiovascular disease (10%), diabetes (7%), chronic renal disease (4%). Prior COVID-19 diagnosis: 7%. After dose-1 vs. dose-2, solicited local and systemic reactions overall occurred in 71% vs. 65% (p=0.07) and 50% vs. 63% (p=0.01), respectively. Figures 1-2 show side effects by dose, severity and duration. Unsolicited symptoms (>1% of participants) comprised light-headedness (3%), nausea (2%), and oral disturbances (1.5%), typically mild-moderate and short-lived. One patient developed a superficial upper leg thrombophlebitis on day 8 after dose 1 immediately following a 3hr car journey. There were no serious adverse events.
Conclusions: The BNT162b2 vaccine was well tolerated. Fatigue, muscle/joint aches, chills and fever increased in incidence after dose-2, as did the taking of pain relief medication. Side effects were mainly similar to those reported in general trial populations, albeit with significantly more injection site swelling and less injection site pain, chills and headache. The study, including pre- and post-vaccination antibody testing, is ongoing.

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Virology

OP 84 DIFFERENCES IN RESPONSE TO MRNA BNT162B2 VACCINE AMONG A COHORT OF HEALTH CARE WORKERS (HCWS): INSIGHTS INTO THE POTENTIAL OF A BOOSTER DOSE

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Background: HCWs are at high risk of contracting SARS-CoV-2 infection and have therefore been a priority target group for vaccination. Given the widespread diffusion of SARS-CoV-2 variants of concern (VOC), potentially less responsive to vaccines, it may be useful to identify HCWs with short-lasting immune response possible candidate to a booster dose.
We aimed to study HCWs with a decreased response to vaccine, and to identify their characteristics.
Methods: We studied 392 HCWs receiving mRNA BNT162b2 vaccination; anti-spike IgG antibodies (Elecsys, Roche) were tested at baseline (first dose of vaccine, T1), at second dose (T2), 1 month after the second dose (T3) and 6 months thereafter (T4). Antibodies responses were divided into strata: negative (<0.4 U/ml), <100 U/ml, 100-500 U/ml, 500 -1000 U/ml, 1000-2000 U/ml, >2000 U/ml. We considered an impaired response displaying antibodies titers <500 U/ml one month after completing the cycle, and a sustained one antibodies >1000 U/ml 6 months after.
Predictors of anti-SARS CoV-2 antibodies one and 6 months after completing the vaccination cycle were analyzed by logistic and linear regression analyses. Changes across the different timepoints has been evaluated using Wilcoxon signed-rank test for paired data.
Results: A total of 392 HCWs entered the study (293 F, 74.7%; median age 47 years -IQR:34-54); 147 subjects (37.5%) had known COVID-19 diagnosis before vaccination, 4 HCWs (1.0%) after the first dose and 23 (5.9%) showed positive anti-S antibodies at T1, indicative of previous undiagnosed SARS-CoV-2. Median values and strata of anti SARS-CoV-2 IgG titers at different timepoints are showed in Table1 and Figure1. Overall the anti SARS-CoV-2 IgG titers peaked at T3 and started to decline at 6 months (T4), p=0.023. At both T3 and T4 none of the HCWs tested were non responders.
A total of 53/319 (16.6%) showed anti SARS-CoV-2 Ab<500 U/ml one month after completing the cycle, whereas 31/87 (35.6%) showed antibodies >1000 U/ml at 6 months. Predictors are shown in Table 2. Age older than 50 years was predictive of impaired after one (anti -S <500 U/ml: AOR 3.26; 95%CI 1.72-3.20) and after 6 months (anti-S >1000 UI/ml: AOR 0.19, 95% CI: 0.06-0.55); previous COVID-19 disease was associated with prolonged sustained response (6 months anti-S>1000 U/ml: AOR 4.2, 95%CI: 1,13-13.4). Also the results from the multivariable linear models (Table 3), showed the inverse correlation for age and positive correlation for previous SARS-CoV-2 infection at the T3 and T4 anti SARS-CoV-2 response.
Conclusions: At 6 months after mRNA-based vaccination, only 1% of study participants presented very weak response, with anti-S <100 U/ml, while more than one third presented titres > 500 U/ml. In this relatively young population, being older than 50 years old and not having a previous COVID-19 diagnosis were independently associated with a lower probability of a sustained anti-S total IgG response over time. The role of cellular immunity in preventing SARS CoV-2 infection and disease in vaccinated individuals also in the presence of weak antibody formation still remains to be clarified, and will inform on the need and timing of a booster dose.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 1 SWITCHING TO BICTEGRAVIR IN ELDERLY PEOPLE LIVING WITH HIV-1 UNDER VIROLOGIC CONTROL: A RETROSPECTIVE DATA ANALYSIS (BICTEL COHORT)

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Background: People living with HIV-1 (PLWH) have a life expectancy as long as general population and an increasing cut of them is aging, thanks continuous advance in antiretroviral therapy (ART). However, non-AIDS comorbidities appear earlier and the pill burden rises sooner compared to healthy peers. Thus, a single-tablet regimen with high genetic barrier, low drug-drug interaction and a good toxicity profile seems to be an optimal choice for elderly PLWH.
Methods: This is a 48 weeks real life observational retrospective cohort of PLWH >= 55 years who were switched to a BIC/FTC/TAF regimen, independently from the previous ART. Data were collected from medical records.
Primary objective was to compare changes in HIV-RNA levels from baseline to week 48. Secondary objectives were: virological failure (HIV-RNA > 50 copies/ml), changes in immune and metabolic profile, reasons to switch, occurrence of sign or symptoms related to central nervous system (CNS), safety and adherence to ART (according to a self-reported questionnaire).
Baseline characteristics are described as mean values ± standard deviation (SD), simple frequencies (n) and percentages (%). Changes from baseline of continuous variables were assessed by the paired Student's t-test. All tests were two-sided and p-values (p) < 0.05 were considered statistically significant.
Results: 128 PLWH were included in this 48-week follow-up. Baseline demographic, immunovirological and therapeutic data are shown in Table 1.
After 48 weeks of follow-up, no virological failure was detected, and subjects with HIV-RNA <50 copies/ml increased from 119 (94%) to 126 (99%). CD4+ T cells count increased from 622.68 ± 303.34 to 818.5 ± 343.2 (p <0.001); CD4/CD8 ratio increased from 0.73 to 0.93 (p <0.001).
Total cholesterol significantly decreased from 194.8 ± 35.9 mg/dl to 185 ± 39.1 mg/dl (p 0.049), whereas LDL and HDL cholesterol levels did not change significantly, as well as AST, ALT and creatinine values. Total body weight increased, despite not significantly, from 77.3 ± 17.5 kg to 79 ± 17.9 kg (p 0.189), with a parallel rise of BMI (from 22.6 ± 4.3 to 24.6 ± 94; p 0.189).
No adverse effects attributed to BIC/FTC/TAF use were reported in the medical records, including signs or symptoms related to CNS disorders.
Average baseline adherence of the enrolled subjects was 76/128 (59%), and significantly increased to 123/128 (96%) (p 0.025).
Conclusions: BIC/FTC/TAF is safe and well tolerated in PLWH >= 55 years. We observed a significant reduction in total cholesterol, without an increase in body weight and BMI. All subjects maintained the virological suppression with a significant improvement of CD4+ T cells count and CD4+/CD8+ ratio from baseline. Finally, all patients' self-reported questionnaires showed a significantly higher adherence profile compared to baseline.
The project has been partially supported by a Gilead Sciences Medical grant.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 2 WHEN THE COLOR MATTERS: DRUG INDUCED HYPERSENSITIVITY TO DTG/RPV COFORMULATION

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Background: Two-drug antiretroviral therapies (ART) based on dolutegravir are recommended for naive and/or virologically suppressed HIV-1 infected patients and they are generally safe[1,2]. One of the dual therapies available in single tablet regimen (STR) is dolutegravir (DTG)/rilpivirine (RPV), (commercial name: Juluca). STR has been associated with significantly higher adherence[3]. However, some authors expressed concern about cutaneous drug-induced hypersensitivity (DIH) associated with STR[4]. Several reports of skin rash induced by STR already exist, but none investigated the tolerance to the single components of the regimen.

Case Report: We observed two cases of drug-induced hypersensitivity occurred after two-drug STR administration. Following the DIH event, the patients continued to receive uneventfully the same molecules as separate pills. The first case is a 38-year-old woman with HIV-1 infection since 2012. Her comorbidities included allergic asthma and sensitization to environmental allergens, but not previous DIH. In March 2019, her ART was switched from abacavir (ABC)/lamivudine (3TC) plus atazanavir boosted with cobicistat (ATV/c) to DTG plus RPV. The regimen was administered in separate pills because DTG/RPV coformulation (Juluca) was not available at the time. The patient received DTG/RPV coformulation in one single pill for the first time in October 2020. Three hours after ingestion, she developed a mild-moderate diffuse allergic rash. She denied use of any other new substance. The second case is a 75-years-old male patient, with HIV-1 infection since 2001. He had no history of previous allergies. His ART was switched from raltegravir plus ATV boosted with ritonavir to DTG plus RPV in separate tablets in July 2018. The patient received the DTG/RPV coformulation for the first time in March 2020. Upper extremities allergic rash, diffuse itching and lip edema appeared ten days after STR initiation. The patient denied use of any further new medication. In both cases ongoing DTG/RPV coformulation was discontinued, and ART switched to DTG plus RPV in separate pills. According to Naranjo's score, the observed DIH is classified as "probably" associated with the introduction of DTG/RPV coformulation[5]. The product labels of DTG (single pill), RPV (single pill) and DTG/RPV coformulation were compared in order to determine if different excipients could justify the DIH reaction towards DTG/RPV coformulation only. The only difference in composition was the presence of iron oxide red (E172) in the coformulation film-coating. This excipient is a synthetic colorant known to be a potential skin sensitiser[6]. It might be implicated in a previous case of DIH not related to ART[7].

Conclusions: This is the first observation of DIH induced by a synthetic colorant contained in the DTG/RPV coformulation. Allergic tests are needed for confirmation. This report may be useful in the era of ART simplification to two-drug regimens.

Antiretroviral therapy

Issues on antiretroviral therapy

P 3 AN EXTENDED FOLLOW-UP OF NAÏVE PATIENTS WITH <100,000 COPIES/ML HIV-RNA TREATED WITH DOLUTEGRAVIR MONOTHERAPY

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Background: We previously reported our experience in 20 HIV-infected patients, naïve to HAART and with a zenith HIV RNA<100,000 copies/ml, followed at the Infectious Diseases Outpatient Department of G.B. Rossi Hospital in Verona, Italy, who started dolutegravir (DGT) monotherapy after refusing nucleoside reverse transcriptase inhibitors [1]. We now report the results of an extended follow-up.
Material and methods: Baseline characteristic of the patients were reported previously [1].
Results: After a mean duration of follow-up of 66.6 months (range 56-74), 13 patients are still on DGT monotherapy. Their mean CD4 cell count was, when last determined, 735/mm3 (range 262-1281) with an undetectable HIV RNA (10 with undetectable HIV RNA and 3 with <20 copies/mL) (table 1). As previously reported [1], one patient developed an enanthema that led to dolutegravir discontinuation after few days. Six patients developed virological failure after a mean time of 32.5 months (range 7-47); HIV RNA levels were, at virological failure, over 1000 copies/mL. After intensification, all patients were virologically suppressed again. We also compared body weight and BMI at baseline, at 12 months and after over 55 months using a paired sample t test (p value of less than 0.005 was considered statistically significant). The mean body weight at baseline was 71.9 Kg (range 57.5-96.5) with a mean BMI of 23.78 Kg/m2 (22.39-26.38). After one year of treatment the mean body weight was 76.06 (62-99) and the mean BMI 25.16 (22.39-28.34), with a mean weight gain of 4.077 Kg (p 0.0000036) and a rise in BMI of 1.37 Kg/m2 (p 0.0000075). After over 55 months, the mean body weight rose to 79.030 (60-91) with a mean BMI of 26.21 (22.53-32.27). The mean increase in body weight was 7.03 Kg in respect of baseline (p 0.00080) and the mean rise of BMI was 2.49 Kg/m2 (p 0.0000075). At baseline, four patients were overweight; after 12 months, seven were overweight, and after over 55 months five patients were still overweight and two had become obese. Lipids and glucose values showed the development of LDL-hypercholesterolemia (>130 mg/dL) in three patients (no patients are on statins because they refused the treatment) and of hyperglicemia (blood glucose values between 100 and 125 mg/dL) in two patients (table 2).
Conclusions: Even though dolutegravir monotherapy is not recommended in naïve patients, in this small cohort its efficacy after over 55 months of follow-up is comparable to clinical studies [2,3] and real word data using recommended regimens [4]. Our extend follow-up confirms the association between integrase inhibitors and body weight gain that was however not linked to an increased risk of metabolic complications in our small patient cohort

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Antiretroviral therapy

Issues on antiretroviral therapy

P 4 IMMUNOLOGICAL OUTCOMES OF PERSONS RECEIVING DOLUTEGRAVIR-BASED ANTIRETROVIRAL THERAPY FOR TREATMENT OF HIV IN THE ITALIAN MASTER COHORT

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Background: The integrase strand transferase inhibitor (INSTI) dolutegravir (DTG) is approved to treat HIV as a first-line and salvage antiretroviral therapy [ART] agent. Although this drug demonstrates strong efficacy at reducing HIV RNA viral load in clinical studies, research is needed to better understand the impact of DTG-based regimens on immunological outcomes, including CD4 T cells, CD8 T cells, and CD4:CD8 T cell ratio.
Material and Methods: Participants from the Italian MaSTER cohort who initiated a DTG-based ART regimen either at first-line ART or following a major regimen switch were included. Multivariable regression models were fitted to evaluate the association between patient demographic and clinical factors and immunological outcomes. Immunological outcomes were coded as binary: CD4 <500 (poor response), CD8>500 (poor response), and CD4:CD8<1.2 (poor response). Covariates included age, sex, nationality, transmission risk (intravenous drug use, heterosexual sex, men who have sex with men, or other), baseline HIV RNA viral load, hepatitis (B or C) coinfection, diagnosis year, ART status (experienced vs. naïve) and treatment regimen (three-drug [3D] vs two-drug combinations [2D].
Results: There were 3,830 individuals who received a DTG-based therapy in the Italian MaSTER cohort between 2009 -2017. The population was majority male (73.7%), of mean age 49.6 years (sd=13.9), Italian nationality (88.1%), with heterosexual transmission risk (35.9%), ART-experienced (83.4%), and receiving 3D regimen (75%). Compared to females, males had significantly higher odds of poor immunological outcomes. Increasing age, baseline viral load, and non-Italian nationality were associated with higher odds of poor CD4 response and CD4:CD8 ratio. Individuals with IDU risk had higher odds of poor CD4 response and conversely lower odds of poor CD8 response compared to individuals with heterosexual risk. ART-naïve individuals had higher odds of poor CD4 response compared to ART-experienced individuals. Compared to 2D regimens, 3D regimens were associated with higher odds of poor CD4 response (odds ratio [OR]=1.35; 95% confidence interval [CI]=1.09-1.66), low CD4:CD8 ratio (OR=1.37; CI=1.06-1.78) and lower odds of poor CD8 response (OR=0.69 CI=0.52-0.90)]. No statistically significant differences were found for other covariates (Table 1).
Conclusion: Males, older individuals, non-Italian nationals, ART-naïve people, and individuals receiving 3D regimens were more likely to experience poor immunological outcomes in this study. The DTG+3TC combination, currently the most frequently recommended 2D regimens, counted for about half of all 2D regimens in this population. We plan to analyze prospectively the immunological outcomes on an increasing proportion of people receiving this combination.

The data analysis included in this study were funded with the support of ViiVHealthcare.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 5 PRELIMINARY FINDINGS ON THE EFFICACY AND SAFETY OF A 2DR WITH DOLUTEGRAVIR PLUS DORAVIRINE IN CLINICAL PRACTICE

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Background: Doravirine (DOR) is a novel NNRTI, with good tolerability and a higher genetic barrier compared with other NNRTI. In this study we aimed to analyze the efficacy and safety of a dual regimen with DOR plus dolutegravir (DTG) as a switch strategy.

Material and methods: In our multicenter cohort we enrolled all treatment-experienced PLWHIV starting a 2DR with DOR+DTG. Primary endpoint was time to virological failure (VF, defined by a single HIV-RNA ≥1,000 copies/mL or by two consecutive HIV-RNA ≥ 50 copies/mL). We also collected viro-immunological and metabolic parameters at baseline and during follow-up visits, comparing variables using parametric and non-parametric tests, as appropriate.

Results : We analyzed 14 pts: 9 (64%) were males, with a median age of 56 years (IQR 47-63). Median time from HIV diagnosis was 25 years (IQR 19-29) while median time from ARV initiation was 17 years (IQR 6-24). Nine pts (64.3%) had experienced at least one VF in their clinical history and 5 pts (35.7%) had a previous AIDS-defining event. Reasons for starting DOR+DTG were: intensification of existing regimen in 5 cases (35.7%), proactive switch (5, 35.7%) and reduction of pill burden in 4 cases (28.6%). Five pts had a baseline HIV-RNA > 50 copies/mL. During a cumulative observation time of 7.77 PYFU, we observed 1 discontinuation due to VF in a patient with a known history of poor adherence to ARV; all other 13 pts achieved or maintained virological suppression during follow-up. The pt experiencing VF presented a HIV-RNA >1000 copies/ml after 6 months of therapy; of note, he had a viral load of 2296 copies/ml at baseline and after failure was switched to BIC/FTC/TAF. Estimated probability of maintaining study regimen at 24 weeks was 86%. Two pts in our cohort presented known resistance mutations (RAMs) to NNRTIs: one pt had both the K101P and the K103N, RAMs that show high resistance to rilpivirine and efavirenz; the other pt had the Y181C, a mutation that reduced susceptibility to NNRTIs. Both this pts were virologically suppressed at baseline and switched from a 2DR with a PI plus DTG; they remained virologically suppressed during follow-up. Finally, we did not observe significative changes in immunological or metabolic parameters.

Conclusions: Preliminary data from our cohort show that a 2DR with DOR+DTG may be a safe and effective choice both as a proactive switch strategy and as a rescue regimen. Results from larger studies and/or clinical trials are needed to properly assess this strategy.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 6 DELAYED SEROCONVERSION IN PATIENT WITH ACUTE HIV INFECTION IN EARLY TARV

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Introduction: Nowadays, the diagnosis of HIV infection is based on fourth generation tests, which are able to identify both antibodies produced against the virus and the viral antigen p24. The use of these tests makes the diagnosis of HIV infection possible even at a very early stage.
With regard to acute HIV infections, the 2019 EACS guidelines call for starting TARV as soon as possible in order to lower viremia, reducing the chances of transmission, viral reservoir formation and chronic inflammatory stimulus.
The effect of initiating ART during acute infection on the immune response remains unclear, but an impact on the production and longevity of antibodies produced is hypothesized.
Clinical Case: We present the clinical case of G:C (M, 26 years old), who came to our attention on Jan. 8th 2021 for HIV testing because of a perceived risk. The fourth generation test performed on that date came back as negative. The same test, performed on the partner on the same day, came back as positive. The last sexual intercourse at risk was about 3 days earlier. In addition, the patient reported fever, asthenia and loss of appetite. At the physical examination there were subcentimetric lymphadenopathies in the laterocervical district bilaterally and also under the chin. Given the symptoms and the concomitant new diagnosis in the partner, on Jan. 12th it was performed an HIV RNA test, wich shows the presence of the virus in the blood (3498 copies/mL). From Jan 13th on, the patient started TARV with BIC/TAF/FTC. The lymphocyte typization found 1279/mmc CD4 T lymphocytes (37%, ratio 0.93). On Feb. 1st the CD4+ T lymphocytes value was 905/mmc (24%, ratio 0.52), with the viremia reduced to 166 copies/mL. The HIV test repeated on Feb. 12th came back as negative again. On Feb. 25th the enzyme immunoassay was weakly reactive, but the Western Blot was still negative, while the HIV RNA was not detected (< 20 cp/mL). Also an HIV 1 DNA test was performed, which came out negative. The HIV test and the search for HIV DNA were repeated in the same way on Mar. 16th and May 14th, without any change in the results. The patient is currently continuing the follow-up with a periodic repetition of the HIV test in order to identify the precise timing of the seroconversion.
Conclusions: Although in a single observed case, we can hypothesize that there is an effective correlation between the early initiation of TARV and the failure to seroconvert during acute HIV infection. Considering that the enzyme immunoassays search for the serological markers, this situation can limit the correct classification of an HIV infection, reducing the usefulness of first and second level diagnostic tests.

Antiretroviral therapy

Issues on antiretroviral therapy

P 7 SWITCHING FROM FTC/TAF TO DOR/3TC/TDF: EFFECTS ON LIPID METABOLISM AND RENAL FUNCTION ON A SMALL CASE-SERIES

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Background: We aimed to assess the impact on lipid metabolism and renal function of switching from a tenofovir alafenamide fumarate (TAF) regimen to a tenofovir disoproxil fumarate (TDF) regimen in a small case-series of HIV patients.

Materials and Methods: All patients older than 18 years, switching to doravirine (DOR) / lamivudine (3TC) / TDF from a TAF based regimen, who were not on a treatment with a statin drug, were included in this study. We collected data about: date of diagnosis, date of beginning of the previous regimen, date of switch; plasma viral load, CD4+ T-lymphocyte count, triglycerides, total cholesterol, LDL, HDL, creatinine and eGFR 6 months before switch, at switch and 6 months after switch.

Results: We collected data about 7 patients, 5 males (71.4%) and 2 females (28.6%). Median age was 48.62 years (IQR 48.03-55.96), and they were diagnosed with HIV for a median time of 15.28 years (IQR 12.11-30.67). Four patients (57.1%) were not smokers, while 3 (42.9%) of them were. The third drug was bictegravir (BIC) for 2 of them (28.6%), dolutegravir (DTG) for 1 (14.3%) of them, nevirapine (NVP) for 2 (28.6%) of them and rilpivirine (RPV) for 2 (28.6%) of them, and their previous regimen lasted for a median time of 27.20 months (IQR 11.80-28.93).

There is no correlation between total cholesterol values 6 months before the switch (median 246 mg/dL, IQR 223-276) and at switch (median 256 mg/dL, IQR 214-285) (p value = 0.802); however, we highlighted a strong correlation between total cholesterol levels at switch and at 6 months post-switch (median 179 mg/dL, IQR 162-211) (p value = 0.008). We did not highlight any correlation between creatinine levels at switch (median 0.8450, IQR 0.7500-0.9875) and 6 months post-switch (median 0.8400, IQR 0.7500-0.8900) (p value = 0.428). (figure 1)

Conclusions: Although our data are preliminary and on a small number of patients, therefore our statistics are strongly influenced by the size of the sample, they highlight a tendency towards normalization of total cholesterol in patients switched from TAF to TDF. This is unsurprising, due to the re-known statin-like effect of TDF, although it remarks how TAF might not be the right choice in patients affected by disorders of the lipid metabolism. Moreover, despite TDF being set aside because of its known effects on renal function, we did not highlight any worrying increase of creatinine or decrease of eGFR, although this could be just the effect of the short period of observation. Further studies, with higher numbers and longer periods of observation are needed to establish if our observations are to be confirmed.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 8 EFFECTS OF LOCKDOWN IN A COHORT OF HIV SUBJECTS

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Background: SARS-CoV-2 is responsible for COVID-19, a disease that in a few months has become pandemic. This infection, characterized by an airborne transmission, forced a social reorganization with general lockdowns in most of the counties of the five continents, in order to limit the spread of the infection.
For greater safety, a reorganization was necessary not only in the work activities of individual citizens, but also and above all in hospital activities with a redistribution of spaces and a reduction in interventions, guaranteeing only those urgent and that cannot be deferred.
Therefore, the biggest part of day hospital activities, including that dedicated to the follow-up of people living with HIV were reduced.
Material and methods: This is a single center, retrospective, observational study, conducted enrolling all HIV patients, followed by the DH of the Infectious Diseases Clinic of Chieti, Italy, who made at least two accesses in the first 6 months of 2020, of which at least one before the start of the lockdown. Aim of this study is to evaluate the clinical and laboratory characteristics of HIV-positive patients during lockdown period.
Results: We enrolled 178 HIV patients and 140 of them were male; we selected only the subjects who did not experienced an increase of the viremia in the year before the enrollment; a viremic blip was found in 29 patients during lockdown. 17 of them were on single tablet regimen (STR) while 12 were on a multi-drug regimen.
80% of patients in a multi-drug regimen had already shown viremic blips, while in the STR group only 53% had at least one previous viremic blip.
Looking at the variations of the laboratory parameters, only CD4 percentage lymphocytes sub-populations, LDL, and CRP showed a multiplicative effect for the interaction among viremia increase, type of pharmacological approach, and time of the study (p-value = 0.006; p-value=0.05; p-value=0.005, respectively). The subjects with an increase in the viremia, treated with multiple pharmacological approach, showed a reduction in the CD4 percentage, an increase in the CRP, and higher level of LDL. The patients treated with a single-tablet regimen we noticed a stability in CD4 percentage and CRP values.
Conclusions: The main results of the study highlighted that the subjects in single-therapy seem to be more protect against viremic-blip compared to multiple therapy. Nevertheless some of them experienced a blip for the first time.
All this can be explained by an incorrect treatment adherence that took place during the lockdown.
The reduction in hospital visits probably affected the viremic blip. We believe that the counseling represents a strong support system that allows the early identification and resolution of the reasons that can lead to non-optimal adherence, playing an important role in preventing failure.
Non-adherence to therapy is also reflected in increase in LDL and CRP in blip group, as to signal a change in habits and lifestyle.

Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 9 TOWARDS "FAST-TRACK CITIES" AT THE TIME OF SARS-COV2 PANDEMIC: THE COMBINATION OF HIV BLOOD TEST AND NASOPHARYNGEAL SWAB ON 1ST DECEMBER 2020 WORLD AIDS DAY

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Background: The COVID-19 pandemic is expected to have a far-reaching impact on both our Health Care System and in chronic illness management. Infectious Diseases specialists' work was for a long time mainly centered on COVID-19 patients and the widespread feeling was of a slowdown in HIV screening and Linkage to care. On World AIDS Day 2020, WHO called for global solidarity to maintain HIV service.
On December 17th 2020, the municipality of Latina signed the Paris Declaration, joining the more than 300 cities and municipalities included in the Fast-Track Cities network, working in solidarity towards the goal of ending urban HIV epidemics by 2030.
When access to Hospitals was very restricted due to distancing rules, on 1st December 2020 World AIDS Day we proposed both a SARS-CoV-2 free of charge nasopharyngeal swab and HIV testing and counseling in our Clinical Reference Centre for HIV Cure.
Materials and Methods: To increase attendance at the event, a press release was made on the main local media and on a facebook dedicated page. Online booking through a QR Code link was required to participate in order to schedule the appointments throughout the day.
An exhibition of canvases by Silver, the author of Lupo Alberto, was organized in some of the locals of Infectious Diseases Clinic, for that date only dedicated to the World AIDS Day.
From 6 pm, a music show and a debate about HIV prevention and treatment through COVID times was live streamed on the Facebook page. Many experts (Clinicians, Virologists), young doctors actively involved in COVID patients' care, musicians and dancers took part in the show "HIV and Covid: two pandemics compared" that totalized 1684 views.
Results: The number of participants was 60, all of whom underwent nasopharyngeal swabbing and blood testing after a brief counseling, which was then registered on an anonymous chart. SARS-CoV-2 was determined with STANDARD F COVID-19 Ag FIA(SD BIOSENSOR,Inc), a rapid fluorescent immunoassay that gives results in 30 minutes allowing subsequent medical care. All SARS-CoV-2 test turned negative.
The mean age of participants was 31(20-65 years), 27(45%) were females and 33(55%) males. 28(47%) of them had an HIV test for the first time. Although drug-related risk factor was not detected, 30(50%) participants needed advice about risky sexual behavior and prevention of STD. All HIV tests resulted negative.
Conclusions: In our experience, combining SARS-CoV-2 and HIV testing was the driver to the success of the initiative.
Free of charge nasopharyngeal swab for SARS-Cov-2 has warranted the safety of the event and constituted a useful mean to attract and ease HIV testing and STD counseling. The hope is that in the future, together with the support of the Fast-Track Cities initiative, structured screening and counseling will be part of the multidisciplinary efforts for HIV+ subjects inclusion and care, testing with a friendly, beyond hospital walls approach, yet respecting social distancing rules.

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Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 10 THE IMPACT OF INFECTION WITH SARS-COV2 AMONG PEOPLE LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS (PLWH)

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Background: The acute phase of SARS-Cov2 is associated with a severe reduction of T cells in the blood, especially of CD4+ T cells. However, it is unknown the role of chronic low-grade inflammation in people living with HIV (PLWH) on infection with SARS-CoV-2 and the severity of COVID-19 once PLWH are infected.
Material and methods: The medical records of PLWH followed in regimen of Day Hospital (DH) were examined to identify patients who contracted the SARS-Cov2. These last underwent a telephone questionnaire with prior consent, concerning their period of co-infection. Then, these laboratory data have been collected: BMI, viral load, absolute lymphocytes, B lymphocytes, CD4+ T lymphocytes, CD4/CD8 ratio, NK cells, Neutrophil-Lymphocyte Ratio (NLR).
Results: From February 24, 2020 to July 1, 2021, 12 of all the 248 PLWHs contracted SARS-Cov2 infection. Percentage of infection of SARS-Cov2 among the PLWH was slightly lower than in the general Italian population: 4.8% versus 7.1%. About the period of infection: 1 patient in the first wave (form February 24, 2020), 6 patients in the second wave (from October 5, 2020), 5 patients in the third wave (from February 8, 2021). Mean age was 55 years, there was a male prevalence (7 men, 5 women), mean BMI was 26.7 (obesity in 2 patients). The stage of HIV was A in 8 PLWH and C in 4 PLWH: all of them were on "triple therapy" regimen. Most common comorbidities were hypovitaminosis D, dyslipidemia, arterial hypertension and hepatic steatosis. 10 patients reported mild symptoms of COVID-19 (fever, cough, asthenia, ageusia, anosmia), mainly treated with antipyretics, corticosteroids and pidotimod; 2 patients were asymptomatic. Among PLWH COIVD+, 1 patient died of advanced hepatocellular carcinoma and 1 patient was subjected to monoclonal antibodies with excellent results. In all of them these post-infection values were substantially unchanged compared to pre-infection period: absolute lymphocytes (delta: 40 cells/ul), CD4/CD8 ratio (delta: 0.1) and NLR (delta: 0.63). In only 2 patients there was a reduction of both CD4+ T lymphocytes and B lymphocytes. After infection of SARS-Cov2, only 2 PLWH had a viremic blip (89.8 and 48 copies/ml).
Conclusions: There was not an increased risk of severe COVID-19 among PLWH in Day Hospital: probably because they had well-controlled HIV on antiretroviral therapy (ART), CD4+ T lymphocytes > 200 cells/ul, more controlled comorbidities than in the general population. SARS-Cov2 infection, or more generally lockdown, did not affect compliance with ART or routine access to DH or daily life (2 patients had insomnia and anxiety, 1 patient had attention deficit). The number of PLWH COVID+ is certainly underestimated: maybe because some PLWH did not underwent follow-up visits in DH during the lockdown. Furthermore, the data refer to patients on ART, therefore the rate of infection in people with unrecognized or untreated HIV infection has not been investigated.

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Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 11 DID LOCKDOWN DUE TO SARS-COV-2 PANDEMIC JEOPARDIZE THE EFFICACY OF ANTIRETROVIRAL THERAPY?

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Background: Since March 2020, the SARS-Cov-2 pandemic in Italy led to difficulties in providing full HIV services to HIV-infected people. Lombardy underwent lockdown during the first wave of the SARS-Cov-2 pandemic (March-May 2020), leading to closure of ambulatory activities (visits and laboratory monitoring). However, in our center, to avoid treatment interruption, from March 2020 to the end of May 2020 most recent laboratory results were checked and antiretroviral therapy (ART) was prescribed and provided despite lack of visits. Aim of this study was to evaluate whether the lockdown due to SARS-Cov-2 pandemic jeopardized the efficacy of ART in a single clinical center in Lombardy.

Methods: All HIV-infected people enrolled in the HIVCSL Cohort Study with at least one viral load measured both between June 1, 2019 and December 31, 2019 ("preCov-period") and between June 1, 2020 and December 31, 2020 ("postCov-period") were included in this analysis.

Primary outcome: incidence rate (IR) of virological failure (VF), defined as either two consecutive HIV-RNA values >50 copies/mL or a single HIV-RNA values >400 copies/mL.

Secondary outcomes: IR of HIV-RNA values ranging between 50-400 copies/mL; IR of VF in people who were on the same ART during the preCov and the postCov period.

Univariable Poisson regression applied to estimates IRs of VF and the corresponding relative risk (RR) with the 95% confidence intervals (CIs).

Results: The baseline characteristics of the 1381 people who fulfilled inclusion criteria are summarized in Figure (Table 1). 16 people (during 5570 person-months of follow-up PMFU) failed in the preCov-period; preCov IR (95%CI) of VF: 2.87 (1.64 – 4.45) per 1000-PMFU; during 6000 PMFU in the postCov-period, 14 failures occurred; IR: 2.33 (1.27 – 3.72) per 1000-PMFU; RR 1.23 (0.60-2.52); p=0.569.

Results were similar when considering IRs for any HIV-RNA 50-400 copies/mL (Figure, Table 2) or only people who were on the same ART during preCov- and postCov-period (Figure, Table 3).

Characteristics of people who failed in the preCov-period did not differ from those of people showing VF in the postCov-period (Figure, Table 4).

Conclusions: Three months of lockdown did not jeopardize the efficacy of ART in people followed in our center. Regular provision of ART despite lack of clinical monitoring is an effective strategy for preventing VF during relatively brief lockdown periods. Whether this holds true also during longer periods requires further investigation.

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Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 12 COVID-19 AND HIV CARE: DIAGNOSTIC DELAYS

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Background: The SARS-CoV-2 infection has forced a social reorganization with general lockdowns in most counties, in order to limit the spread of the infection.
For greater general safety, a reorganization was necessary not only in the work activities of individual citizens, but also and above all in hospital activities with a redistribution of spaces and a reduction in interventions, guaranteeing only those urgent and that cannot be deferred.
Therefore, the biggest part of day hospital activities, including that dedicated to the follow-up of people living with HIV (PLWH), have been reduced (Lancet HIV,2020).
Although some international institutions, in collaboration with governments, are working to sustain HIV service provision for people living with HIV, the COVID-19 pandemic presents several barriers and challenges to the HIV care continuum (Guaraldi et al, 2019).
We present a case of late diagnosis of carcinoma of the hypopharynx in a patient with HIV.
Case Report: 68 years old male patient with HIV infection group C3 (wasting syndrome), followed by the DH of the SS. Annunziata Hospital of Chieti since 2014. At diagnosis, the CD4 + count showed 11 cell /mmc, while HIV-RNA was 3,231,000 cp/ml. He presented with sebopsoriasis, mucocutaneous candidiasis, but no opportunistic infection. He started cART on 17.10.14 with ABC/3TC/ATV/r+ RAL, then, on March 2017, it was changed with ABC / 3TC / DTG in STR. The patient underwent about six checks per year during the follow-up.
From March 2020 the patient began to accuse aphonia, pharyngodynia, dysphagia for solid food. Thus, he performed several antibiotic therapies and corticosteroid therapies without benefit. Despite needing it, during the first 5 months of 2020, when lockdown measures in Italy were very stringent, the patient did not carry out any clinical checks.
In June 2020, he returns to carry out medical checks at DH and, through an ENT consultation, a new formation of the posterior larynx is discovered. It was confirmed at TC scan with dimensions of approximately 5.2 cm x 3.6 cm x 5 cm. In light of this, the patient underwent positioning of subystmic tracheostomy and multiple biopsy samples of neoformation. Because of the extension of the lesion, ENT consultant excluded the possibility of surgery treatment and redirected the patient to Radiotherapy Department.
In August 2020 despite the need for radiation treatment, the waiting lists were very long due to delays of pandemic era. Therefore, with difficulty, the patient had to go to multiple extra-regional radiotherapy centers in order to be treated.
Conclusions: As COVID-19 continues to spread around the world, many locations are facing the risk of SARS-CoV-2 infection and barriers and challenges for maintaining the HIV care continuum. We recommend that governments and international partners should work together to maintain the HIV care continuum during the COVID-19 pandemic, with particular efforts made to ensure timely access to, and to avoid disruption of routine HIV services.

Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 13 FLORENCE FAST-TRACK CITIES ACTIVITIES DURING THE SARS-COVID 19 PERIOD

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Background: The city of Florence joined the Fast-Track Cities protocol in November 2019 with the support of all the Third Sector Organizations (ETS) dealing with HIV, the Infectious Diseases clinical centers of the local health unit "Toscana Centro" and of the Universities. The municipal commitment has made it possible to share on a more organized level the objectives that the ETS network and clinical centers were already carrying out and to consolidate the HIV coordination table within the Health Society of Florence.

Material and methods: Each association has carried out its activities according with Covid 19 emergency rules. During the web conferences with the municipal authorities, priorities have been decided: information, prevention and communication campaigns. Screenings are carried out following the community-based VCT protocol of the European COBATEST network. Relations with clinical centers for the Linkage to Care of people found reactive to screening for HIV and STI or suitable for PrEP have been maintained. With CME courses, updates and training of operators on HIV and anti-Covid regulations were made to perform the services safely. Online meetings were organized to raise awareness on prevention issues in the population. A public website about Fast-Track was built and we are working on an integrated service charter.

Results: During the first year of the FTC, despite the necessary interruptions due to the Covid pandemic, HIV and STI screening were carried out also on vulnerable populations (85 HIV-HCV tests, 20 for Syphilis), prevention and harm reduction actions (2023 brochures on HIV, 8012 condoms distributed to sexworkers, IDUs, migrants and young people, 696 lubricants, 2807 syringes and 180 free foils for inhaling substances, 45 accompaniments to health services), psychological support for people with HIV (100 interviews conducted), helpline service (597 calls received), projects with high schools (a total of 200 students), research with clinical centers, integrated management projects for the PrEP (41 people involved). The screening activities detected 2 HIV positive people and 1 positive person was tested for Syphilis among sex workers.

Conclusions: We obtained good results but there's still a lot to do. There is a lack of dedicated structural funds despite the signing of the FTC protocol and too much is entrusted to the work of ETS. Although they are able and willing to provide continuous and quality services, they rely on volunteering and self-finance. This is a significant limit on the pursuit of the WHO goals. It has not yet been possible to find the location for a checkpoint that brings together the services and allows the activation of large-scale communication campaigns. This shared commitment to build a network that can contribute to everyone's health has yet to make a qualitative leap to be considered a collective priority and we trust that this can be achieved by being part of the international network of FTC.

Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 14 RISK FACTORS FOR SEVERE COVID-19 AND POST-COVID-19 SYNDROME IN A COHORT OF PLWH ON TREATMENT

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Background: According to WHO recent statement, HIV increases risk of mortality due to COVID-19 among hospitalised patients, but whether it increases the risk of severe COVID-19 is still unclear. We aimed at assessing the relationship between clinical/HIV-related characteristics and the outcomes of SARS-CoV-2 infection (disease severity and post-COVID -19 syndrome) in our cohort.

Materials and Methods: Retrospective cohort study in PLWH linked to care at our centre (Infectious and Tropical Diseases Unit, Padova, Italy) and who were diagnosed with SARS-CoV-2/COVID-19 (both by serology or RT-PCR on nasopharyngeal swab) from the beginning of the epidemics to (March 2020). Demographic and clinical data were retrieved from medical records. COVID-19 severity was defined based on WHO criteria; post-COVID-19 syndrome included SARS-CoV-2-related signs or new symptoms appeared after SARS-CoV-2 diagnosis. Non-parametric tests were used for the statistical analysis and binary logistic regression was modelled on biologically and statistically significant variables at univariable model.

Results: 106 patients tested positive for SARS-CoV-2, median age was 52 years (IQR:42-59), 80.2% were males. All were on cART. Median length of HIV infection was 11 years (IQR:5-18), 93.4% patients had undetectable HIV-RNA, and median CD4+ cell count was 559 cells/mmc (IQR: 444-783) at the moment of SARS-CoV-2 infection. 49.4% were asymptomatic infection, while 24.5% presented a moderate or severe COVID-19, and 3.8% were hospitalized and died. At univariate, moderate-severe COVID-19 cases showed increased number of signs/symptoms at diagnosis (p<0.001), larger number of comedications (p.013), more commonly previous history for pulmonary AIDS events (p.039), pulmonary diseases (p.003), neurological disorders (p.009), and cancer (p.010). No differences were observed for viro-immunological parameters. At multivariate (Table 1), only the number of COVID-19-related signs/symptoms at diagnosis (p<0.001) and of non-antiretroviral comedications (p=0.048) were linked with the odd of moderate-severe COVID-19, regardless of age, sex, plasma HIV-RNA, CD4/CD8 ratio, previous AIDS episodes and comorbidites which were significant at the univariate analysis. The risk of post COVID-19 syndrome was more common among moderate-severe COVID-19 cases (p=0.005), and it was associated with lower platelets count (p=0.011) and larger number of signs/symptoms at presentation (p=0.002).

Conclusion: Among "well-controlled" PLWH the severity of SARS-CoV-2 infection and the likelihood of developing post-COVID-19 syndrome appear to be related to the same factors identified in the general population and they are not influenced by variables related to HIV. The possible role of the previous pulmonary AIDS events (significant only at the univariate) and the low platelet count should be further investigated, as well as further studies in different HIV-positive populations are required to challenge our results.

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Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 15 PROLONGED SARS-COV-2 B.1.177 LINEAGE INFECTION IN A HIV ADVANCED NAÏVE PATIENT

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Background: If HIV/SARS-CoV-2 coinfection is associated with a worse evolution of COVID-19 is still uncertain. However, chronic COVID-19 is described in severe immune-suppressed people. Herein, we report the case of a woman, newly diagnosed at advanced stage of HIV infection, presenting a prolonged (7 months to date) SARS-CoV-2 infection.
Case Report: In January 2021, a 30-year-old woman with a previous diagnosis of undifferentiated connectivitis treated with immunosuppressive drugs for one year and tested negative for HIV three years before, after a contact with a COVID+ case, resulted positive for SARS-CoV-2. From then, until March she was subjected to 6 nasopharyngeal swabs, all positive, without complaining any COVID-19-related symptom. On March 25th she presented with fever and cough with dyspnea and was admitted to Policlinico of Bari with a peripheral saturation of 89%. A chest CT scan was performed revealing multiple widespread areas of increased parenchymal density, like "ground glass", disseminated in both lungs; respiratory exchanges worsened, requiring an increasing oxygen support until placement of noninvasive mechanical ventilation and transferal to Intensive Care Unit. On 2nd April, Cytomegalovirus DNA on blood specimen was detected by real time PCR (32,439 copies/ml) and therapy with Ganciclovir was started. Then, a HIV-test was performed, resulting positive, so the patient was moved to the Infectious Disease Department. HIV Viral load (VL) was 23,545 cp/ml and CD4+ 12.7 cell/mm3 (2%). Since the possible source of HIV infection was a previous partner already in follow-up and resulting not adherent, ART regimen with DRV/cobi/TAF/FTC was initiated. A bronchoalveolar lavage was performed and P.jirovecii PCR-DNA resulted positive, so Cotrimoxazole was started. In the following days, the patient showed improvement of clinical conditions and respiratory function, and reduction of the inflammatory markers with undetectable CMV-DNA on blood specimen. During hospitalization, 6 nasopharyngeal swabs for SARS-CoV-2 were performed, always resulting positive with low value of cycle threshold (Ct) indicating persisting high replication (Table I). IgG anti-SARS-CoV-2 antibody test was negative. The patient was discharged at the end of May; with indication to home isolation and ambulatory follow-up; 3 additional nasopharyngeal swabs were repeated in June and July, still positive, while last CD4+ cell count was 34/mm3. Whole-genome sequencing performed on the sample of 24 May 2021 revealed that strains belonged to B.1.177 lineage.
Conclusions: Low CD4+ cell count may influence the clearance of SARS-CoV-2 in HIV-infected patients causing chronic infection. The additional role of previous corticosteroid therapy should be considered. In the light of this background, it would be interesting to know if antiviral drugs, like Remdesivir or monoclonal antibodies, also after seven months of SARS-CoV-2 infection, could help to speed up virological recovery.

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Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 16 HIV VIRAL LOAD AND COVID-19 PANDEMIC: FINDINGS OF AN HIV REFERENCE CENTER IN ROME

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Background: COVID-19 pandemic has reduced the access of people living with HIV (PLWH) to reference centers. However, retention-in-care is critical to maintain adherence to therapy and viral suppression. Maintenance of viral suppression in PLWH is critical for health and prevention purposes. Few studies have evaluated the effect of the COVID-19 pandemic on treatment-experienced patients in terms of adherence to antiretroviral therapy. During lockdown in Italy, our center implemented several measures to ensure HIV-care continuum, such as home delivery of therapy and teleconsulting.
Material and methods: To evaluate whether the changes in clinical assistance introduced by this measures during lockdown might have affected care outcomes, the trend of HIV-1 viral load (HIV-RNA copies/ml) was investigated during a one-year period, including: September-November 2019 (no-COVID-19 months); December 2019-February 2020 (pre-COVID-19 months); March-April 2020 (lockdown months); May 2020 (partial-lockdown month) and June-August 2020 (post-lockdown months). Changes of HIV-1 viremia by month were evaluated. Specifically, HIV-1 viral loads performed during the one-year observation in patients in steady antiretroviral treatment for at least six months were recorded. The proportion of undetectable viral loads (HIV-RNA <30 copies/ml) by month and quarters was assessed.
Results: Overall, 1,233 viral loads from 453 patients were included. Overtime, no significant changes were observed in the proportion of undetectable HIV viral loads either by month or by quarter (p=0.268 and p=0.393, respectively). During the 2-month lockdown, the proportion of undetectable results remained in line with the previous months, despite the fact that the number of tests performed was lower. In fact, viral load testing was postponed for patients in stable suppression who, during teleconsulting, declared to be scared of getting SARS-CoV-2 infection by attending the hospital. A sharp increase in measurements in May 2020 was observed. Rescheduling of clinical activities for stably suppressed HIV patients who postponed their visit caused this rebound of attendees. Among these patients, viral loads remained undetectable, in line with previous months.
Conclusions: No significant changes in the proportion of undetectable HIV-RNA were observed over the one-year period that encompassed no-COVID-19 months up to post-lockdown months. Continuity of service, ensured also by the implementation of new tools for PLWH care and assistance, made it possible to maintain viral suppression in our patients.

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Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 17 SYPHILIS DIAGNOSES AMONG HIV-INFECTED AND HIV-UNINFECTED INDIVIDUALS DURING A YEAR OF SARS-COV-2 PANDEMIC: THE EXPERIENCE OF AN HIV/STI REFERENCE CENTER IN ROME

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Background: COVID-19 pandemic has impacted the prevention, diagnosis, and treatment of Sexually Transmitted Infections (STIs). To investigate whether the pandemic and lockdown restrictions adopted in Italy affected the diagnosis of syphilis in people living with HIV (PLWH) and HIV-negative individuals, a retrospective study was conducted at the largest STI center in Rome, which is also an HIV regional reference center. The center always remained open for visits and testing during the lockdown period.

Material and methods: All syphilis cases diagnosed in 2017-2018-2019 (pre-pandemic years) and in 2020 (pandemic year) were retrieved from our records. Date of diagnosis, stage, age, gender, transmission group and HIV status were collected. Diagnoses of infectious syphilis (primary and secondary/recent) in the pandemic year were compared with those in the pre-pandemic period. The mean number of cases diagnosed by month in the pre-pandemic years and the corresponding p for trend were calculated. Statistical correlations were assessed using Fisher exact test and chi-square test. A p value <0.05 was considered as significant.

Results: Overall, 166 cases were diagnosed in 2020, mostly (92.8%) among men who have sex with men (MSM). Late syphilis was more frequently diagnosed among HIV-infected patients (p<0.001), whereas primary and secondary/recent syphilis cases were significantly more frequent among HIV-uninfected subjects (p<0.01). During this year, we observed three peaks in syphilis diagnoses: the main one in February, the pre-pandemic month, a second one in June, during the post-nationwide lockdown period, and a more modest peak in November. The increase of diagnoses in June might be due to the patients' fear of attending the hospital during the first lockdown (March-May 2020), which prevented them from seek healthcare, and to infections acquired during the lockdown period despite the restrictions. We also noted an overall decrease of infectious syphilis (n=81) in 2020, compared to 2017-2019 (n=106 on average, with no significant change by month, p for trend=0.40), an observation that made us to consider the possibility of a reduction in sexual encounters during the pandemic year. Out of the 81 cases of infectious syphilis recorded in 2020, 19 were diagnosed in HIV-infected subjects (23.5%), with no significant difference compared to 2017-2019 (86/318, 27.0%), p=0.43. Men, MSM and HIV-negative subjects accounted for the majority of infectious syphilis cases both in 2020 and in the pre-pandemic years.

Conclusions: In conclusion, the fraction of syphilis cases diagnosed among HIV-infected individuals did not significantly change in the pandemic year compared to the previous three years. Late syphilis diagnoses were significantly more frequent among HIV-infected subjects than HIV-uninfected individuals in 2020. Syphilis trend in 2020 has been definitely influenced by COVID-19 pandemic and consequent restrictions adopted in Italy.

Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 18 COVID-19 IN A PATIENT WITH HIV INFECTION: MONOCLONAL ANTIBODY AS A NEW THERAPEUTIC STRATEGY?

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Background: Global spread of SARS-CoV-2 and the subsequent COronaVirus Disease 19 (COVID-19) pandemic had a huge impact on everyone's life, especially on frail patients and on those with chronic conditions. It is widely known that some risk factors could worsen the progression of some infectious diseases. Obesity, for instance, can be considered a crucial factor for the clinical deterioration of patients tested positive for SARS-CoV-2. Furthermore, recent studies highlighted that HIV-positive patients, even if with a complete viral load suppression, face an increased risk to develop severe COVID-19 than HIV-negative people. Thanks to recently introduced therapies, such as Monoclonal Antibody (MAb), we indeed prevented a severe progression of COVID-19 in a patient with a critical clinical history that could have led to a potentially fatal outcome.
Case Report: We report the case of a 63-year old patient, followed-up in our clinic of Infectious Disease, with history of HIV infection, Pneumocystis pneumonia (PJP), obesity, diabetes, hypertension, chronic kidney disease (CKD), dyslipidemia, hypovitaminosis D, hepatic steatosis, renal lithiasis, diverticulosis, previous hepatitis B, esophageal candidiasis, HIV-associated progressive multifocal leukoencephalopathy. On March 20th 2021 the patient reported cough, fever and gastrointestinal symptoms and on March 23rd 2021 he tested positive for SARS-CoV-2. According to Italian Medicine Agency inclusion criteria, the patient was eligible for MAb administration because of the presence of comorbidities and no need for hospitalization. The administration was performed in outpatient procedure on March 27th 2021. Before MAb infusion, the patient underwent preliminary blood test and pulmonary echography that showed minimal interstitial disease with Lung Ultrasound Score (LUS) = 2/36. The treatment consisted of the combination of casirivimab 1200 mg and imdevimab 1200 mg infused for about 40 minutes followed by 1 hour observation period. At the end of the procedure, the patient was discharged with the prescription of a 7-days therapy with Low Molecular Weight Heparin (LMWH) in addition to usual home therapy. In the following days the patient was daily monitored by territorial healthcare network until he tested negative for SARS-CoV-2 on April 6th 2021.
Conclusions: Obesity and HIV infection are risk factors for developing severe COVID-19 in patients tested positive for SARS-CoV-2. So our patient was at higher risk for adverse outcome. In fact, the mortality due to COVID-19 is way higher in HIV-positive than HIV-negative people. Despite expectations, our patient fully recovered after MAb therapy. SARS-CoV -2 infection in HIV-positive people could lead to severe COVID-19. The administration of target therapy in the first phase of the infection, such as Monoclonal Antibody, could represent an important tool to prevent the progression of COVID-19 and its complications leading to a prompt recovery.

Clinical HIV, Clinical COVID-19

HIV and COVID-19

P 19 PHARMACOECONOMICS ASSESSMENTS DURING THE SARS-COVID 19 PANDEMIC COMPARING PHARMACEUTICAL EXPENDITURE FOR ANTIRETROVIRAL THERAPY (ART) BETWEEN 2019 AND 2020: IMPACT OF THE LOCKDOWN IN THE INFECTIOUS DISEASE CENTER IN FLORENCE

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Background: Verify the effects of the SarsCov2 pandemic (especially spring 2020 lockdown), and the consequent changes in the organization of the Infectious Diseases (ID) Department of the S.M. Annunziata Hospital (OSMA) in the assistance to HIV positive patients (PLWH), with the reduction of the timing of visits and the possible trend, given the key objective of guaranteeing adherence to ART, to avoid therapy changes until normal follow-up is restored, evaluating the pharmacoeconomic impact.

Material and methods: Data on PLWH about dispensed ART by the OSMA ID Unit in 2019 (01/01 to 31/12) and 2020 (01/01 to 31/12) were extracted from the hospital pharmacy database on medications directly dispensed. Patients were stratified according to the regimes with annual cost ranges established by the Region (1 range <5000 €, 2 5000 -7000 €, 3 7000-9000 €, 4 >9000 €), by ART regimen (dual, 3-drugs, >=4-drug), by VL value (<20, 20-50, 51- 200, > 200), by age and sex. 2019 and 2020 data were collected and analysed in an Excel db.

Results: In 2020 compared to 2019, 53 patients (7%) changed ART, of these: 6 went from DUAL of two tablets to dual STR, 4 from STR of 3 drugs to dual STR, 4 from multi-drugs regimen (MTR) to dual regimens, 19 from MTR to 3-drug STRs. The increase in DUAL therapies is 1% (from 12% to 13%), but if we identify patients treated with the DUALs STR indicated in the guidelines these doubled from 23 in 2019 to 47 in 2020. Regimens were re-evaluated, considering also the cost-effectiveness ratio of the existing treatment compared to the possible new one. If proven effective and well tolerated, apparently obsolete treatments (with often cheaper generic drugs) contained costs, bringing this center to have the lowest average annual patient cost among the other facilities of Center Tuscany. 30 patients are treated with the EFV/FTC/TDF and another 67 with regimens containing the generic backbone FTC/TDF, obtaining a savings of 471,000 €/year. In 2020, compared to 2019, despite the decrease of range 4 drug prescriptions, the cost for ARV apparently increased by 18%. This is explained by the average increase in DDD/patient dispensed in 2020, 26% more in the January-May period and 13% more in the October-December period, compared to 2019, a "hidden" saving of 8%.

Conclusions: Given the reduction of outpatient visits induced by the pandemic, the Pharmacy of our Center has dispensed on average a quantity of drugs higher than the norm to promote adherence to ART and thus keeping the effectiveness of the treatment itself. Furthermore, there was an increase in access to the Pharmacy by PLWH and in the optimization of therapeutic regimens, determining more patients with undetectable viremias and a significant annual saving in the cost of ART. Moreover the savings given by the use of equivalent drugs were considerable in the two years analyzed, while still maintaining viraemie values that are completely overlapping, if not better, than other regimens.

Clinical HIV, Clinical COVID-19

Issues on COVID-19 therapy

P 20 REMDESIVIR FOR THE TREATMENT OF COVID-19: DATA FROM A REAL-LIFE EXPERIENCE

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Introduction: Clinical trials show Remdesivir efficacy in shortening time to recovery from Sars-COV-2 pneumonia, at the condition of being prescribed in patients with recent infection requiring low-flow oxygen. Nevertheless, despite early symptom onset, rapid evolution of COVID-19 is often observed in clinical practice. Aim of this study is to describe clinical features and evolution of a monocentric, real-life cohort of patients treated with Remdesivir.

Methods: Data regarding sex, age, co-morbidities, clinical presentation of COVID-19, , time of antiviral administration from symptoms onset and concomitant medications of all COVID-19 patients treated with Remdesivir in our Unit were retrospectively collected and described as number and percentages for categorical variables and as median (Inter Quartile Range-IQR) for continuous, non-normal, variables. Primary endpoint was outlining a correlation between diverse patients features at baseline and i) rate of recovery ii) duration of hospital stay iii) time to Sars-COV-2 nasal swab negativization. To this aim, Spearman's rank correlation coefficient was calculated. Secondary endpoint was to detect changes in eGFR and blood AST, ALT, GGT levels before and after antiviral treatment. Wilcoxon sign-rank paired t-test was performed. A $p<0.05$ was considered statistically significant.

Results: From October 2020 to June 2021, a total of 202 subjects with Sars-COV-2 pneumonia were hospitalized in our Unit, 170 of whom, beside standard treatment, underwent Remdesivir administration. Clinical presentation and respective outcomes of study cohort are described in Figure 1. Patients (mainly males, 65.3%, older than 50 years, 81.1%, 68% requiring low flow oxygen), received Remdesivir after a median of 7 (IQR 5.75) days from symptom onset. After a median hospital stay of 16 (IQR 13.5) days, a relatively high rate of recovery was reported (87.6%). In 101 pts, a negative Sars-COV-2 nasal swab was obtained before discharge, after a median of 21 (IQR 15.8) days from first positive RT-PCR. At univariate analysis, no association was outlined between time of Remdesivir administration and outcome, neither with duration of hospital stay, nor with time to Sars-COV-2 nasal swab negativization. Conversely, age, severity of disease and elevated markers of inflammation at baseline were significantly associated to the previous endpoints (Table 1). A slight improvement was observed between AST (median 31 vs 27.4, p=0.001) and eGFR (median 87.3 vs 96.0, p=0.001) levels before and after antiviral administration.

Conclusions: Indication for Remdesivir treatment include timing of symptoms onset and oxygen flow required. Nevertheless, in real-life settings, a rapid worsening in patient's status could impair the latter condition. In our experience, only a negligible proportion of COVID-19, real-life patients treated with Remdesivir with mild/moderate presentation progressed towards more severe forms of disease. No significant drug-toxicity was reported.

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Clinical HIV, Clinical COVID-19

Issues on COVID-19 therapy

P 21 EARLY TREATMENT WITH BAMLANIVIMAB ALONE DOES NOT PREVENT COVID-19 HOSPITALIZATION AND ITS POST-ACUTE SEQUELAE. A REAL EXPERIENCE IN UMBRIA, ITALY

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Background: Bamlanivimab as monotherapy had been authorized by FDA on November 2020 and in Italy on February 2021 in patients with mild /moderate COVID-19 and at high risk of progression to severe disease, but its utilization was revoked on April 2021. Aim of our study is to describe its clinical use in Umbria as monotherapy during authorization period and to evaluate clinical outcome according to the time of infusion.

Materials and Methods: Demographic, clinical history, virological and clinical outcomes of patients admitted to the Infectious Diseases Clinic of Perugia and to the COVID Hospitals of Spoleto and Città di Castello, in order to receive a single 700 mg IV infusion of bamlanivimab alone according to AIFA criteria, are described. The timeliness of the treatment (within 72 hours) was evaluated. Thirty days after the infusion, patients were interviewed about their health state, the results of subsequent nasopharyngeal swabs and any change in pre and post-treatment symptoms.

Results: 39 patients (51.3% male), mean age 63±15.8 received bamlanivimab. Cardiovascular disease was the main risk factor (51%). The most represented COVID-19 related symptoms were fever (46%), cough (59%), myalgia (54%) and asthenia (51.3%). Genes N, S, and E were detected by a PCR assay, in 38/39, 1/39 and 29/39 patients respectively (Table 1). Four patients had been vaccinated, 2 with two doses. In these two, COVID-19 arose > 15 days after the second dose, while in the other 2 the disease arose after 8 and 2 days after the first dose. The average time between the onset of symptoms and treatment was 4.23±1.73 days (range 1-8). During and up to one hour after the end of the bamlanivimab infusion, vital signs remained stable and the patients were discharged in good health. No adverse events were documented. The hospitalization rate for any reason was 20 % (8 pts), 10% for COVID-19 pneumonia (4), 10% for worsening of an underlying disease (thrombocytopenia, diabetic ketoacidosis, acute renal failure in chronic kidney disease, bacterial pneumonia). At 30 days from the infusion, patients reported an increase in symptoms such as asthenia (77 vs 51%), dyspnea (38.5 vs 23 %), tachypnea (44 vs 33.3%) compared to baseline, and the onset of a new symptom: insomnia in 41% (Figure 1). The comparison between patients early (within 3 days) vs later treated showed no differences regarding COVID-19 pneumonia hospitalization (3/15 vs 2/24 p=0.289) or the nasopharyngeal swabs time negativization (mean 16.58±4.10 vs 16.70±4.63 days p=0.942).

Conclusions: Despite recent several outbreaks of gamma variant in Umbria, bamlanivimab in monotherapy has been taken by patients largely infected by alpha variant that seems to be susceptible to bamlanivimab. However, respect to a virological response, an aggravation of some baseline symptoms as well as in the 41% of patient the onset of a new symptom: a non-restorative sleep was observed.

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Clinical HIV, Clinical COVID-19

Issues on COVID-19 therapy

P 22 HEART RATE CHANGES IN PATIENTS TREATED WITH REMDESIVIR FOR COVID-19

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Introduction: Cardiac rhythm abnormalities, including sinus bradycardia and QTc interval- prolongation, have been reported in some patients during treatment with Remdesivir, requiring close cardiac rhythm monitoring. This study aimed to assess through daily Electrocardiogram (ECG) examination the occurrence of heart rate abnormalities in a cohort of COVID-19 patients treated with Remdesivir and identify potential clinical predictors.
Methods: A subset of 88 subjects out of 170 COVID-19 patients (pts) treated with Remdesivir in our Unit from November 2020 to June 2021 was included in the study (63% males, 80% older than 50years, 86% with mild-moderate severity COVID-19 at admission). All patients underwent ECG examination at baseline, each day during Remdesivir treatment, and at discharge. Over time, heart rate changes were recorded and compared with non-parametric ANOVA; differences were confirmed by post-hoc Tukey analysis. Patients features at admission (sex, age, comorbidities, laboratory test including IL-6, RPC, D-dimers, High-sensitive Troponin-I) and clinical presentation of COVID-19, were collected and correlated to heart rate reductions by Spearman's rank correlation coefficient calculation. A $p<0.05$ was considered statistically significant.
Results: A median of 6 ECGs (IQR 2) during the five days of antiviral treatment was performed. Baseline mean heart rate was 82.2 bpm (±SD 17.2). Compared to baseline, a significant reduction of heart rate after administration of Remdesivir was observed until discharge (median heart rate of 66 bpm (IQR 11.3). The reduction was particularly noticed during the first two days of treatment (ANOVA $p<0.001$, Figure 1). Lowest mean heart rate recorded was 58.4 (±10.3) bpm. Prolongation of QTC Interval >450 msc was observed in 34 cases, while 11 pts experienced new-onset heart rhythm abnormalities in the course of COVID-19. At correlation matrix including age, gender, cardiovascular risk factors, presence of ischemic heart disease, atrial fibrillation, troponin, inflammation markers at admission, COVID-19 severity of disease, only baseline heart rate resulted significantly related to lower heart rate levels observed after Remdesivir administration (Spearman's rho: 0.342, $p=0.001$).
Conclusions: Our data confirmed the occurrence of transient bradycardia in the course of treatment with Remdesivir. Daily ECG monitoring highlighted a peculiar trend in heart rate reduction, characterized by a decrease during the first two days of treatment and followed by a plateau. In any case, symptomatic bradycardia or arrhythmias implying Remdesivir discontinuation nor cases of QTc prolongation occurred. According to our data, Remdesivir showed a good cardiovascular safety that could justify its use even in subjects with a high prevalence of cardiovascular comorbidities.

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Clinical HIV, Clinical COVID-19

Issues on COVID-19 therapy

P 23 INFLUENCE OF EARLY CORTICOSTEROIDS THERAPY IN COVID-19 DISEASE PROGRESSION

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Background: The progression of COVID-19 disease is associated with the proinflammatory host response, and the role of immunomodulatory therapy has been evaluated during the pandemic. In the RECOVERY trial, the use of Dexamethasone seems to reduce the mortality in patients who require supplemental oxygen. However, no data are available regarding the early use of domiciliary corticosteroids in patients with Sars-CoV-2 infection. Herein, we aim to investigate if the previous use of steroids at home, in the first week from the symptom onset, may correlate with the worsening of critical outcomes in patients with COVID-19 disease.
Materials and methods: A monocentric retrospective case series of patients hospitalized in our Infectious Disease Unit between July 2020 and April 2021 with confirmed Covid-19 by RT-PCR testing on nasopharyngeal swab were included. Data regarding early corticosteroids use before hospitalization were retrieved; the cohort was divided in two groups, those who received early corticosteroids (less than 7 days from symptoms onset) (group A) and those who did not (group B). Pearson's $\chi 2$ test or Kruskal Wallis were used as appropriate to compare variables. Univariate and multivariate logistic regression were used to investigate predictors of critical outcomes.
Results: Overall, 394 patients were enrolled, 125 (32%) in group A and 269 (68%) in group B. General characteristics of patients at admission were compared: importantly, no significant differences were evidenced in terms of age, sex and comorbidities. However, patients in group A showed more frequently fever (84% vs 74%, p=.024) and cough (50% vs 35%, p=.006). Moreover, the incidence of acute respiratory failure requiring O2-therapy was significantly higher in patients who received early corticosteroid therapy (92% vs 67%, p<.001); similarly, the need of noninvasive/invasive ventilation was significantly higher in this group (31% vs 19%, p=.007). Finally, 28-day mortality risk was compared; a trend towards an increased mortality was found in group A (10% vs 6%, p=.089). By performing a univariate and a stepwise multivariate logistic regression (Table I), independent predictors at admission of noninvasive/invasive ventilation were male sex (aOR=2.49, 95% CI=1.41-4.40, p=.002), obesity (aOR=2.56, 95% CI=1.44-4.54, p=.001), heart failure (aOR=7.05, 95% CI=1.09-45.27, p=.040), bacterial sepsis (aOR=3.70, 95% CI=1.44-9.48, p=.006) and early corticosteroid therapy (aOR=1.97, 95% CI=1.16-3.33, p=.011). However, multivariate analysis failed to show a significant association between early corticosteroid therapy and mortality.
Conclusions: Early corticosteroid therapy significantly correlates with a high risk of severe lung failure in course of Covid -19. Therefore, according to this finding, the use of corticosteroids in the early phase of the disease should be discouraged.

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Clinical HIV, Clinical COVID-19

Issues on COVID-19 therapy

P 24 REMDESIVIR MILK LEVELS IN A COVID INFECTED-BREASTFEDING WOMAN: A CASE REPORT

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Background: Remdesivir (GS-5734), a nucleoside analogue, and has inhibitory effects human highly pathogenic coronaviruses, including SARS-CoV2 [1]. No information is available on the use of remdesivir during breastfeeding [2]. Remdesivir (RDV) is given intravenously because it is poorly absorbed orally, so infants are not likely to absorb clinically important amounts of the drug from milk. In addition, newborn infants have received intravenous RDV therapy for Ebola with no serious adverse drug reactions [4,5]. Given this limited information, it does not appear that mothers receiving RDV need to avoid nursing, but until more data are available, RDV should be used cautiously with infant monitoring during breastfeeding [6]. RDV is extensively metabolized by hydrolases in nucleoside metabolite GS-441524 in plasma. The most common adverse effects reported after intravenous infusion include elevated aminotransferase and bilirubin levels and other liver enzyme elevations, diarrhea, rash, renal impairment and hypotension. Moreover, no data were available in the literature about breast milk concentration.

Materials and methods: We analyzed plasma and milk levels of RDV and its metabolyte GS 441524 in a 35-years old woman with SARS COV-2 interstitial pneumonia after delivery and treated with RDV from day 1 to 5. Milk samples were collected the 3rd and 5th day since drug start at 1-3-7-21-24 hours from drug administration, plasma sample at 3rd and 5th day were also analysed. Drug levels were sent to the Clinical Pharmacology and Pharmacogenetic Laboratory in Turin and analyzed with UHPLC-MS/MS

Results: In all milk samples GS 441524 was isolated. The concentrations were steady during the first 24 hours from the administration with a maximum concentration after three hours after the administration (118 ng/mL). The plasma concentration after three hours from administration was 113 ng/ml (Table 1).

Conclusions: Breast milk concentrations were similar to those in plasma. Our results show that RDV is highly present in woman breastmilk with similar plasma values.

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Clinical HIV, Clinical COVID-19

Issues on COVID-19 therapy

P 25 CONVALESCENT HYPERIMMUNE PLASMA USE: A CASE SERIES OF 6 IMMUNOCOMPROMISED PATIENTS

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Background: Since the start of this pandemic, administration of convalescent plasma has been proposed in patients with COVID19. Efficacy data is based mainly on reports of improved clinical outcome. There are few randomized trials, the one from the PlasmAR Study Group showed no difference between placebo and plasma in severe COVID19 patients. A randomized and controlled clinical trial TSUNAMI showed no benefits in terms of reducing the risk of respiratory worsening or death in the first thirty days. Recently neutralizing monoclonal antibodies were proposed for immunocompromised patients who continue to be positive to SARS-CoV2 PCR tests. We report our experience with convalescent plasma at the Infectious Diseases Unit of Santa Maria Goretti Hospital of Latina in a special setting of immunocompromised hosts.

Materials and methods: All patients who received convalescent plasma for COVID19 from the 1st of September 2020 were included. Plasma from patients younger than 60 years, previous SARS-CoV2 infection, negative nasal swab and neutralizing antibody titer of at least 1:160 was collected. The decision to use plasma was based on the immunocompromised status of patients and the severity of disease, in order to provide additional support to both recovery and eradicate the infection. All patients received at least 2 units of plasma, one at day 1 and one at day 3. Mortality at 28 days was assessed.

Results: All 6 patients (age range 56-83 years, 2 women) were on supplemental oxygen support (2 CPAP Helmets, 1 HFNO, 1 Venturi mask, 2 nasal oxygen flow) at the time of treatment and underwent local standard of therapy for including steroids/immunomodulators and remdesivir. Convalescent plasma was administered on day 1 and day 3, 3 patients had another dose at day 5. 4 patients had hematological malignancy and 2 had common variable immunodeficiency (CVID). 3 patients had specific COVI19 serum immunoglobulin prior to treatment. Only one patient obtained negative PCR testing for SARS-CoV2 on nasal swab after 60 days. Recovery from ARDS was obtained in all patient and mortality at 28 days after admission was zero. There were no safety concerns. The primary cerebral lymphoma patient had a story of long COVID with persistent radiological findings of pneumonia and positive BAL specimens. Plasma treatment was given with the intention to obtain virologic negativity. 2 patients died three months later due to complications related to their hematological disorders.

Conclusions: In this case series of patients with COVID-19 and immunodeficiency, administration of convalescent plasma containing neutralizing antibodies was followed by an improvement on their clinical status. Efficacy evaluation is limited by the small number of patients. More data is needed which could suggest whether convalescent plasma may have a role in immunocompromised patients, who are frequently excluded from invasive respiratory supportive care.

Clinical HIV, Clinical COVID-19

Management of COVID-19

P 26 COMPARISON BETWEEN ANTIGEN AND MOLECULAR TESTS FOR THE DETECTION OF SARS-COV-2 INFECTION: A RETROSPECTIVE CLINICAL STUDY

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Background: To date, real time (RT)-PCR testing is the gold standard for the diagnosis of an active infection with SARS-CoV-2. However, to expand testing capacity in the outpatient setting, new SARS-CoV-2 rapid antigen tests (RATs) have also been implemented. RAT is more rapid, but less reliable in terms of sensitivity. However, real-life data on the performance of the RAT in comparison with RT-PCR test are lacking. Therefore, we aimed at assessing the diagnostic performance of third-generation LumiraDx antigen test compared to RT-PCR SARS-CoV-2 in a retrospective cohort of patients attending the Infectious Diseases Unit of Padua during the second wave of Covid-19 pandemic.
Methods: From January 30th to May 30th, 2021, we collected respiratory samples from individuals who had COVID-19 symptoms or who were eligible for SARS-CoV-2 testing (i.e., close contacts with infected subjects). The subjects were tested simultaneously for SARS-CoV-2 both by RAT and RT-PCR. In addition, SARS-CoV-2 cycle-threshold (CT) values of RT-PCR were compared with the results of the antigenic tests, in order to test whether positivity to RAT could have been associated with higher levels of viral replication (i.e., lower CT). Demographic, clinical characteristics of the patients, time between SARS-CoV-2 testing and onset of symptoms were recorded. Data were analyzed with ad-hoc packages of the programming language Python and with the statistical software R.
Results: Over the study period, 282 consecutive individuals were tested for SARS-CoV-2 both by RT- PCR and LumiraDx RAT, mean age was 61 years (95% C.I. 58-63), and mainly of male gender (177/10, 63%). Thirty-two subjects were asymptomatic (21.4%) and 250 (88.6%) were symptomatic. Among subjects who had symptoms, 84 had pneumonia and 1 neurological manifestation of SARS-CoV-2. Overall, 228 (80.5%) and 177 (62.7%) subjects tested positive for SARS-CoV-2 by RT-PCR and Lumira RAT, respectively (Fig.1). Lumira RAT showed a sensibility and a specificity of 76% (95% C.I 71% - 82%) and 94% (95% C.I. 88% - 100%) in diagnosing SARS-CoV-2 infection, compared to the standard of care. The sensitivity was higher than 91% when symptom onset was < 10 days. CT values ranged from 14 to 38. False negative RAT results were significantly associated with high CT values, and to a far testing from symptoms' onset ($p<0.05$).
Conclusion: The 3rd generation RAT LumiraDx assay performed an overall specificity and sensitivity of 94% and 76%, respectively. However, when used in the early COVID-19 onset its sensitivity significantly improved, showing that it is heavily influenced by the high SARS-CoV-2 viral load. This result highlights the importance to perform a timely screening in people who develop symptoms. In addition, since the results can be obtained quickly and the number of false positive results is negligible, this assay can be considered as good tool for the use in the first aid setting for a fast-track path to the COVID-19-hospital.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 27 BMI CHANGES AND WEIGHT LOSS IN PATIENTS HOSPITALIZED FOR COVID-19: A SINGLE-CENTRE EXPERIENCE

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Background: Patients with COVID-19 experience an increased risk of malnutrition and unintentional weight loss. Many factors are involved into body wasting in COVID-19: loss of appetite, dysgeusia, fever, immobilization, need of oxygen supplementation, catabolic–anabolic imbalance, endocrine dysfunction and other organ-specific complications such as cardiac and renal dysfunction. The European Society for Clinical Nutrition and Metabolism (ESPEN) published a practical guidance to manage this clinical issue. The aim of this study was to assess unintentional weight loss in a cohort of COVID -19 patients admitted to a third level hospital in Italy during the first wave of the pandemic (1st-31st March 2020).

Materials and methods: We included all patients older than 18 years with a confirmed diagnosis of COVID-19 pneumonia, and who were admitted to the Infectious Diseases Unit of Padova University Hospital over the study period. Demographic and clinical characteristics of the patients, including the measure of body weight (BW), the height and body mass index (BMI, kg/m2) at hospital admission and discharge were recorded.

Results: Two hundred and nineteen patients were included, 63% were male, mean age was 67.7 years [IQR: 64.7 -70.59, CI 95%]. The mean duration of hospitalization was 16 days [IQR:14-18, CI 95%]. The mean BMI value at admission was 27.2 kg/m2 [IQR:26.2-28.1, CI 95%], 26% of patients were obese, 31% overweighted, 42% had a normal BW, and 1%patients were underweighted. The mean BMI value at discharge was 25.6 kg/m2 [IQR:24.7-26.5, CI 95%], with a mean BMI loss of -1.56 kg/m2 [IQR:-1.85,-1.27, CI 95%] and a mean weight loss of -4.6 Kg [IQR:-5.4;-3.6, CI 95%] (Fig 1A). Males were more likely to experience weight loss compared to females (U=2065, p-value=0.008) (Fig.1B). In addition, BMI loss negatively correlated with the length of hospitalization (r= -0.3924, p-value < 0.0001), but it was not correlated with patient's age (-0.01427746, p-value = 0.8775).

Conclusion: Our study confirmed that the length of stay significantly contributed to both weight loss and BMI value decrease in patients with COVID-19 pneumonia. Prolonged bed immobilization may cause loss of muscle mass, especially in more severe cases, even though other pathogenetic mechanisms (such as the cytokine storm) may play a crucial role. Greater decreased of BMI in males than in females is probably because men have a greater quantity of muscle mass than women. Interestingly, we did not find any correlation between the reduction of BMI and age. Our findings highlight the need of implementation of both nutritional support strategies and an early physical rehabilitation in patients with COVID -19, especially among those whose length of stay is supposed to be particularly long. Further studies will help in characterizing this phenomenon and identifying targetable biologic mechanisms of COVID-19 weight loss.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 28 FACTORS ASSOCIATED WITH MORTALITY IN PATIENTS AGED OVER 65 YEARS WITH SARS-COV-2 INFECTION

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Background: Since the outbreak of the SARS-CoV-2 pandemic, millions of people died, especially among elderly people. Many risk factors associated with a higher mortality have been investigated in COVID-19 patients. The aim of our study is to evaluate all in and outpatients with more than 65 years followed by our Unit and identify the risk factors for death.
Material and methods: We conducted a retrospective study to evaluate which risk and preventive factors played a role on mortality rates of SARS-CoV-2 positive patients with more than 65 years. We included all SARS-CoV-2 infected patients followed by our Unit between 07/03/2020 and 31/03/2021. We excluded patients with missing data. Qualitative and quantitative variables were summarized with frequencies and means. Logistic regression analysis was performed to assess the relationship between clinical and epidemiological variables and mortality.
Results: A total of 552 SARS-CoV-2 infected elderly patients were recruited, with 231 (41.8%) males and a mean age of 81.3 (± 8.2) years. Overall, 308 patients (55.8%) were hospitalized, and 133 (24.1%) died. The most common comorbidity was hypertension (n=385, 69.7%), followed by cardiovascular diseases (CHD), neurological, and psychiatric disorders (225, 182 and 178 cases, respectively). The main characteristics are summarized in Table 1.
At logistic regression, older people had an increased risk of death [OR 1.1 (95%CI 1.02-1.09) p=0.004]. Regarding comorbidities, none of them seemed to affect mortality rates in a multivariate analysis, except from BMI ≥ 30 Kg/m2 [OR 2.1 (95%CI 1.23-3.48) p=0.006]. Fever and dyspnea were the only symptoms associated with increased risk of mortality.
Furthermore, in regard to treatment, remdesivir [0.3 (95%CI 0.11-0.73) p=0.009] and heparin [OR 0.3 (95%CI 0.18 -0.54) p<0.001] showed a lower risk of death. Furthermore, at the Kaplan-Meier survival analysis people treated with heparin (log-rank 0.004) and remdesivir (log-rank 0.001) had a lower 28-days mortality.
Conclusions: We highlighted factors, such as age and high BMI, associated with risk of death in a fragile cohort such as people older than 65 years. On the contrary, treatment with heparin and remdesivir was associated with a lower mortality risk. Thus, further studies are needed to establish the best treatment strategy for elderly people with COVID-19.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 29 POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) AND COVID-19: A CASE REPORT

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Background: Encephalopathy is a common complication of COVID-19. Although the encephalopathy is idiopathic in many cases, posterior reversible encephalopathy syndrome (PRES) has been reported in more than one percent of patients with COVID-19. PRES is a clinico-radiological entity associated with a wide array of clinical presentations including headaches, focal neurological deficits, seizures, visual disturbances, and encephalopathy. In the setting of COVID-19 SARS CoV2 contributes, via binding to ACE-2 and induction of the cytokine-mediated inflammatory response, to the impairment of cerebrovascular autoregulation. There is no specific treatment for PRES, but symptoms are thought to be reversible once the underlying cause is removed. It is widely believed that appropriate treatment of hypertension, and associated inflammation is of great importance for treating PRES.
Materials and methods: Here we present a case of a 29-year-old female COVID-19 patient, who had given birth, with clinical and radiological findings of PRES, and describe the diagnostic and therapeutic procedure of this syndrome.
Results: The patient presented with respiratory failure, arterial hypertension (maximum value 170/100 mmHg), intense frontal headache, subintrant tonic-clonic seizures and mnestic alterations. Her blood examination displayed elevated C-reactive protein (84.1 mg/L compared to expected <5 mg/L) and D-Dimer (1988 µg/ml compared to expected <500 µg/ml), decreased lymphocyte count (0.57). Renal and hepatic function indices were normal. Urinalysis showed no proteinuria. Physical-chemical examination of CSF showed only increase in proteins. Brain MRI showed: cortical subcortical areas of hyperintense signal in TR sequences long areas, in cerebellar hemispheric, occipital and fronto-parietal areas on both sides; edema vasogenic with initial signs of cortical cytotoxic edema due to ischemic suffering appreciable in the sequences diffusion-weighted sequences in some brain sites; in perfusion sequence, hyperemia and slowing of blood flow with an increase in cerebral blood flow in the areas described above; corticopial contrastographic impregnation in the right temporo-occipital and left high fronto-parietal area, sites of incipient interruption of the blood-brain barrier. In addition to antithrombotic prophylaxis (enoxaparin), antibiotic prophylaxis of bacterial pulmonary superinfections (piperacillin/tazobactam) and antiepileptic treatment (levetiracetam), the patient was treated for PRES triggers with nifedipine, mannitol and dexamethasone. Clinical neurological conditions improved markedly, concomitant with the improvement of respiratory function and the normalization of hematochemical examinations.
Conclusions: Posterior reversible encephalopathy syndrome should be considered in COVID-19 patients with hypertension and neurologic symptoms such as seizures and focal neurologic signs, in order to treat their triggers early, thereby preventing complications.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 30 CLINICAL CHARACTERISTICS OF HEALTHCARE WORKERS WITH SARS-COV-2 INFECTION AFTER VACCINATION WITH BNT162B2 VACCINE

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Background: The pandemic of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has hardly affected the entire world. Vaccines against COVID-19 appear as a tool able to curb out the mortality and to reduce the circulation of the virus. Consequently, mass vaccination campaigns are ongoing worldwide. Little is known so far about the clinical characteristics of individuals who developed SARS-CoV-2 infection after having received the vaccination, as well as the temporal relationship between vaccine administration and symptoms onset.
Materials and methods: Retrospective cohort study among the healthcare workers (HCWs) of the Fondazione IRCCS Ospedale Maggiore Policlinico of Milano, vaccinated with the BNT162b2 vaccine who developed SARS-CoV-2 infection (documented through positive RT-PCR on NPSs). We collected the demographic, clinic and virologic characteristics through a specific questionnaire.
Results: Overall, we have identified 15 HCWs with SARS-CoV-2 infection after vaccination, 7 (46.7%) of them were male and the mean age was 38.4 years (SD 14). In 4 of them the presence of SARS-CoV-2 anti-nucleocapside (anti-N) antibodies was assessed before vaccination and resulted positive in 1 case. In all HCWs the presence of SARS-CoV-2 anti-spike (anti-S1) antibodies was assessed, in average 42.2 days after the completion of vaccination, with a mean value of 2,055 U/mL (SD 1,927.3). SARS-CoV-2 infection was ascertained in average 56.2 days after vaccination. The mean cycle threshold (Ct) of SARS-CoV-2 PCR was 26.4, the lineage was characterized in 9 HCWs (table 1). None of the HCWs reported a primary or secondary immunodeficiency. Regarding symptoms, they were reported only by 7 (46.7%) HCWs and appeared on average 55 days after the second dose of vaccination. Of those who reported symptoms, one (14.3%) had fever, 7 (100%) rhinitis/conjunctivitis, 4 (57.1%) taste and smell alterations, none had respiratory symptoms, 4 headache/arthralgia (57.1%) and 1 gastrointestinal symptoms (14.3%). All symptoms disappeared in a few days and no other unclassified symptoms were reported
Conclusions: Infections occurring after vaccination with BNT162b2 vaccine are mostly asymptomatic and are not associated with the serum titre of anti-S1 antibodies. The absence of important symptoms is a reassuring finding, which confirms the data about efficacy of the BNT162b2 vaccine in preventing the severe form of COVID-19 reported in registration studies. We did not find a predominance of a specific viral variants, with several lineages represented. This is in accordance with published data, which highlighted a reduced but still efficacious immune response against viral variants in those vaccinated with BNT162b2 and suggest that the risk of infection after vaccination is not currently related to the viral genotype but to other variables yet to be uncovered.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 31 MEDIASTINAL ADIPOSE TISSUE AS INFLAMMATORY BIOMARKER IN COVID19 PNEUMONIAE

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Background: SarsCoV2 is an RNA virus that acts through its S protein link to ACE2 receptor which is expressed by the epithelial alveolar cells. ACE2r is also found in the visceral adipose tissue (VAT) that can produce proinflammatory cytokines. Study aim is to evaluate the mediastinal VAT involvement in SarsCov2 pneumoniae as inflammatory tissue.
Material and methods: We observed 47 outpatients which had Covid19 pneumoniae confirmed by molecular SarsCov2 nasopharyngeal swab and CT chest imaging. At the follow-up, the patients underwent a chest CT to evaluate pneumoniae outcome, and these results were retrospectively compared to chest CT hospital admissions. Moreover, it was studied the mediastinal VAT. Axial chest CT images values were obtained from thick overlapped slices of 2,5mm (120-140 kV, 10-40 mAs, pitch <1) and from sub-millimetric reconstructions that used high-definition contrast algorithms and then were optimized for soft tissue evaluation. CT images were elaborated to identify and measure the mediastinal fat volume by setting the tomodensitometry values between -25/-95 Hounsfield Unit (UH). The total mediastinal fat volume was expressed in cm3and evaluated for each patient. CT image results were correlated to inflammatory biomarkers variations
Results: Among the 47 patients evaluated in a median timespan of 107 (50-168) days from discharge, 23.4 % were female and 76.6% male; the median age was 60 years old (49-67); the median BMI was 26.6 (24.8-31.6). All patients had O2 therapy and only 12 (25.5%) had been on mechanical ventilation either CPAP or NIV support. PCR, IL6, LDH and ferritin were the parameters more constantly altered in the acute phase and without differences between patients on mechanical ventilation and those on vent mask O2 therapy. Instead, mediastinal Vat volume values were higher in patients on CPAP/NIV support compared to those on vent mask (235.9 [96.4-250.4] vs 141.4 [93.9-186.3] p=0.075). VAT volume parameters reduced significantly at the follow-up imaging (t-test VAT at T0 146.2 [93.8-219.4] vs T1= p < 0,0001).
Conclusions: Many studies showed VAT involvement in the systemic inflammation responsible for Covid19 respiratory manifestations and our results support this hypothesis. We observed a significantly increase of VAT volume, measured at mediastinal level in acute phase of Covid19 pneumoniae and especially in patients with severe respiratory distress, and return to a normal range at the follow-up control. This trend seems to be more stable than other inflammatory modified biomarkers values and to be independent from them. In our opinion, the mediastinal VAT volume measurement should be evaluated as well the pulmonary parenchyma in Covid19 pneumoniae. Our data have limits -small sample size, bias of selection and retrospective approach- so prospective studies with larger sample size are warranted to further investigate the VAT's role in the systemic inflammation activation and its implications.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 32 EARLY PREDICTORS OF CLINICAL DETERIORATION OF COVID-19 IN A COHORT OF OUT-PATIENTS IN SOUTHERN ITALY: A MULTICENTER OBSERVATIONAL STUDY

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Background: Data regarding early predictors of clinical deterioration in patients with infection of SARS-CoV-2 is still scarce. The aim of the study was to identify early symptoms related to a worsening of clinical presentation of the novel coronavirus disease 2019 (COVID-19).

Methods: We conducted a multicenter observational study on a cohort of patients with COVID-19 in home isolation. Study period was from March 2020 to October 2020. We assessed and collected clinical data, i.e. fever, dyspnoea, and need for hospitalization, everyday through phone calls. Then we focused on 3 time-points, i.e. the beginning of symptoms, 3 days (t3) and 7 days (t7) after the onset of symptoms.

We defined mild and non-mild COVID-19. Mild COVID-19 included patients who did not require oxygen supplementation and/or had a Modified Early Warning Score below 3 points, whereas non-mild COVID-19 included those with severe or critical disease, according to the World Health Organization definition.

We compared patients with mild infection to those with non-mild infection, and then evaluated which factors were independently related to a non-mild COVID-19 through a logistic regression model.

Results: We included 189 patients with COVID-19: 108 (57.1%) were males, mean age was 52.1 years ± 17 SD, and median Charlson Comorbidity Index was 2 (0-3) (table1). Of the 189 patients enrolled, 118 (62.4%) had a mild and 71 (37.6%) a non-mild infection, and 88 (46.6%) needed hospitalization (table1).

Compared to patients with mild COVID-19, patients with non-mild COVID-19 were more frequently males (p 0.05), older (p<0.001) and had more comorbidities, especially hypertension (p<0.001), cardiovascular diseases (p 0.01) and type 2 diabetes mellitus (0.001) (table1). Moreover, patients with non-mild COVID-19 showed a different distribution of fever and dyspnea at the 3 different time-points, with a higher rate of persistent fever and dyspnea at t3 and t7 (table1).

At the multivariate analysis, factors independently associated to a non-mild presentation at t3 and t7 were age (OR 1.07, 95%CI 1.03-1.10 and OR 1.06, 95%CI 1.03-1.11 respectively) and persisting fever (37-38°C: OR 13.71, 95%CI 5.16 -35.74 and OR 19.5, 95%CI 7.36-51.62 respectively at t3 and t7; ≥38°C: OR 5.98, 95%CI 1.39-25.74 and OR 5.15,95%CI 1.34-19.86 respectively at t3 and t7) (tables 2a,2b).

Conclusions: Persisting fever at t3 and t7 seems to be related to a more severe clinical presentation of COVID-19. Although the limitation of the study, these results may be useful to assess hospitalization criteria and optimize use of resources in the out-patient setting. However, further studies are needed.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 33 COVID-19 AND MYOTONIC DYSTROPHY: CASE REPORTS AND SYSTEMATIC REVIEW

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Background: Steinert's disease, also known as myotonic dystrophy type 1 (MD1), is a rare genetic disorder involving muscles characterised by progressive myotonia and multi-organ damage. It is associated and complicated by respiratory and cardiological complications that often lead patients to exitus. These conditions have also been recognised as traditional risk factor for a severe COVID-19. SARS-CoV-2 pandemic had a huge impact on people with chronic disease, but the real impact on people with Steinert's disease has not yet been fully defined. To the best of our knowledge, only a few cases of Steinert's disease and COVID-19 have been described and more data is needed to understand whether this genetic disease is a risk factor for more serious evolution or death in patients with COVID-19.
Methods: Therefore, the aim of this work was to describe two cases of patients with SD and COVID-19 and to summarise available evidences of clinical outcome of COVID-19 in patients with Steinert's disease, by performing a systematic review of the literature (following PRISMA statements and performing PROSPERO registration).
Results: We admitted two patients with Steinert's diseased and COVID-19 (87-year-old male and 58-year old male), who with an early hospitalization and timely treatment, survived. To date, only five cases were described worldwide (Table 1). Our analysis reported a high mortality rate (80%) in patients with both Steinert's disease and COVID-19. It mainly suggests and highlights the importance of strengthening prevention strategies in this populations, especially vaccination. Indeed, all these patients should be early identified and treated to avoid complications. It is still unknown which treatment regimen is best to be given in those patients. Further studies on a greater number of patients are necessary to provide clinicians with further evidence.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 34 MONOCYTES CD169 AND HLADR EXPRESSION IN SARS-COV2 INFECTION

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Introduction: CD169 (sialoadhesin or Siglec-1) is a type I interferon-inducible receptor, and its expression is up-regulated on monocytes in viral infections. It is reported that monocyte CD169 (moCD169) expression is increased also in SARS-CoV2 infection. HLA-DR is an immune status marker. Over stimulation or immune exhaustion induce the decrease of HLADR expression on monocytes. Several studies proposed the reduced monocyte HLA-DR (moHLA-DR) expression as an unfavorable biomarker of infection.
The aim of our study was to evaluate the expression of moCD169 and moHLA-DR in patients with severe COVID-19.
Methods: Forty-two patients with COVID-19-related respiratory distress were enrolled. In most of them intubation or ventilatory support was required. In 20 patients (47%) moCD169 and moHLA-DR expression were monitored during the hospitalization, at 10-15 days intervals in most cases. In addition, 10 healthy donors were included as the normal control group (NC). Flow cytometric IO Test myeloid activation kit (Beckman Coulter), including a cocktail of CD169-PE, HLADR-APC and CD64-PB markers was used in peripheral blood samples. The moCD169 expression was expressed as the ratio between CD169 intensity on monocytes divided by the CD169 expression on lymphocytes, used as the negative control. The moHLA-DR intensity was reported as Geo Mean.
Results: At hospitalization 35 patients (83%) showed moCD169 ratios significantly higher than NC (185 vs 8.01, p: 0.01) and in 29 cases a decreased moHLA-DR expression was found (Geo Mean 8413 vs 28241 in NC, p< 0.001). Only one patient showed an increased moHLA-DR expression (Geo Mean: 50340). The remaining 7 patients showed moCD169 ratios comparable to NC and 2 of them had weakly positive SARS-CoV-2 PCR. In 4 patients with normal moCD169 ratio moHLA-DR expression was severely decreased (Geo Mean: 940). Three other patients with suspected COVID-19 pneumonia were characterized by high moCD169 ratios, negative SARS-CoV-2 nucleic acid RT-PCR of nasal-throat swab specimens, but positive molecular detection of BAL samples.
During the follow-up, the down-regulation of moCD169 was associated with the reduction or the negativity of SARS-CoV-2 molecular detection with a median moCD169 ratio of 4.3. Interestingly, in four cases the persistence of a high moCD169 ratio was associated with a sustained positivity of SARS-CoV-2 molecular nasal-throat swabs. The moHLA-DR expression persisted low (Mean 7386) during the follow-up in 18 patients. Only in 2 cases the moHLA-DR expression was increased with values comparable to NC and an improvement of respiratory conditions.
Conclusion: This study indicates that moCD169 and moHLADR may be used in COVID-19 patients as a possible predictive biomarker of the SARS-CoV-2 infection. In particular moHLADR expression may be useful to identify patients with a poor outcome.

Clinical HIV, Clinical COVID-19

Management of COVID-19

P 35 USE OF NASAL SWAB AS A PREDICTOR OF MRSA SUPERINFECTION IN SARS-COV-2 RELATED PNEUMONIA

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Background: During the current pandemic, it was evidenced that up to 71% of patients admitted with COVID-19 had received broad-spectrum antibiotic therapy, which was prescribed for the suspicion of pulmonary bacterial superinfections (also by MRSA). In clinical practice, linezolid and/or vancomycin are frequently used in empirical CAP/HAP therapy, even in the absence of a confirmed diagnosis of MRSA infection, as current IDSA/ATS guidelines suggest the use of anti-MRSA antibiotics in patients with specific risk factors including recent influenza-like illness. However, as shown in the literature, the systematic use of these drugs is associated with an increase in hospital costs and the risk of iatrogenic toxicity, without a gain in survival. Therefore, the use of nasal swabs for culture testing has already been suggested as a negative predictor of pneumonia by MRSA and as a tool for rapid de-escalation of antibiotic therapy which could be particularly useful in Europe, where the presence of MRSA is less marked than in American territory.
The objective of the study is to evaluate the use of nasal swab as a predictor of MRSA superinfection in SARS COV-2 related pneumonia.
Material and methods: From March to June 2021, patients admitted to our hospital with clinical and radiological diagnoses of COVID-19 pneumonia and suspected lung bacterial secondary/co-infection were enrolled. All patients were subjected to microbiologic diagnostic investigations for bacterial pneumonia, including nasal swab for detection of common bacteria and fungi within 72 hours of the start of empirical antibiotic therapy according to clinical judgment.
Results: Overall, 50 patients were enrolled, 53% males, with a median (q1-q3) age of 67 (57-79) years (Table 1). Importantly, at nasal swab screening, only one patient resulted positive for MRSA, 4 patients resulted positive for methicillin sensitive-S. aureus, and the remaining resulted negative.
In 14/50 (28%) patients a secondary infection was confirmed by microbiologic investigations, including 5/14 bloodstream infections by gram negative bacteria (GNBs), 3/14 BSI by Enterococcus spp. and/or Candida spp., 2/14 urinary tract infections, 2/14 pneumonia by GNBs, 1 case of C. difficile colitis and 1 case of Aspergillosis.
Independently from nasal swab result, 5/50 (10%) received an empirical anti-MRSA antibiotic coverage when the secondary infection was suspected. Interestingly, no cases of secondary infections caused by MRSA were documented at admission or during hospitalization.
Conclusions: According to the low prevalence of colonization to nasal swab found in our center, the use of empirical anti-MRSA therapy was not justified in patient with COVD-19 pneumonia, especially early during admission.
Considering the high negative predictive value, screening for MRSA at the time of hospitalization or clinical worsening could be a strategy of antimicrobial stewardship to mitigate the negative consequences of antibiotic therapy.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 36 COMPARISON BETWEEN COVID-19 PATIENTS HARBORING VARIANTS OF SARS-COV-2 AND A POPULATION FROM THE FIRST PANDEMIC WAVE

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Background and Aims: In this last year across the world, several variants of SARS-CoV-2 emerged. Among these, three new variants have rapidly become dominant, spreading also in Italy and arousing concerns: α (UK), β (South Africa), and γ (Brazil). The recently emerged SARS-CoV-2 variants harbor several mutations at the receptor binding domain in the spike (S) glycoprotein that may alter virus-host cell interactions, contributing to immune escape, increased transmissibility and conferring resistance to inhibitors and antibodies. Aim of the study was to investigate differences in clinical, laboratory and radiological findings in patients with coronavirus disease 2019 (COVID-19) comparing patients harboring a wild-type SARSCoV-2 and patients with new emerged variants.

Methodology: We included 224 nasopharyngeal swabs from COVID-19 patients admitted to University Hospital "Policlinico Umberto I" in Rome. To define the SARS-CoV-2 genotype, S gene was sequenced using Sanger method. Patients were stratified into two groups: wild-type group (N=148), patients harboring wild-type SARS-CoV-2 hospitalized from March 2020 since April 2020, and variant group (N=76), patients infected with new emerged variants enrolled from March 2021 since April 2021. Laboratory and clinical data and imaging findings from chest computed tomography (CT), were also collected and evaluated.

Results: One hundred and fifty patients (60 females, 90 males) with a median age of 56 (IQR: 48-62) were included in the wild-type group and 76 patients (24 females, 52 males) with a median age of 52 (IQR: 40- 68) were included in the variant group. According to clinical outcome, a significant high percentage of patients with Acute respiratory distress syndrome in the variant group compared to the wild-type group was observed (56.5% vs 37,3%, respectively; p= 0.0282). At admission, the absolute number of white blood cells (WBC), neutrophils and the neutrophil/lymphocyte ratio (NLR) were significantly higher in variant groups than in the wild-type group. [WBC: 6.4 (IQR: 5.1-9.4) vs 4.8 (IQR: 3.8 -5.6), p=0.0002; neutrophils 5.7 (IQR:3.8-7.1) vs 2.8, (IQR: 2.2-3.8), p<0.0001].

Conclusions: Our preliminary data showed higher chest CT score, absolute count of WBC and neutrophils, and NRL in the variant group compared to the wild-type one suggesting that the high chest CT score observed in variant group may be due to an increased neutrophils mediated organ damage.

Clinical HIV, Clinical COVID-19

Management of COVID-19

P 37 RADIOLOGICAL AND CLINICAL SEQUELAE IN PATIENTS WITH MILD/MODERATE COVID-19 DISEASE

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Background: The coronavirus disease 2019 (COVID-19) is a viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).Although extrapulmonary manifestations are frequent,this virus is essentially responsible for a lung disease.Chest x-rays may be normal in early or mild disease;when alterations are present,these are more often represented on both x-ray and CT scan by consolidation or ground-glass opacification with generally bilateral,peripheral and predominant distribution in lower areas.According to preliminary studies,complete radiological resolution is observed four weeks or more after the symptom onset,although alterations persist in more than half of patients within three months and are mainly represented by the persistence of ground glass area and fibrotic outcomes.Our aim was to describe clinical and radiological sequelae in the first month after discharge in patients with mild/moderate disease.
Material and methods: Patients admitted to our centre from March to May 2020 were re-evaluated 14 and 30 days after discharge.Patients with mild/moderate clinical form (defined by the presence of clinical or radiographic evidence of pneumonia with SpO2 ≥ 90% on room air) were included.All patients underwent radiological examination at admission. Temperature,blood pressure,heart rate,peripheral oxygen saturation by pulse oximeter,respiratory rate and thoracic examination were evaluated at each reassessment;a questionnaire on any persisting or arising symptom after discharge was administered.At the 30-day follow-up patients were also subjected to a control CT scan and blood tests.
Results: A total of 161 patients referred to our centre in the study period whose characteristics and outcomes are summarized in Table 1.While patients with severe disease were directed to cardio-pulmonary post Covid Unit,a total of 101 patients with mild/moderate disease were re-evaluated 14 days after discharge at our Centre;of these,55 patients also attended a second follow up visit at 30 days.None presented significant changes in vital parameters.Symptoms reported at 14- and 30-days follow-up are shown in Figure 1. At 30 days, only 3/55 patients had alterations in blood chemistry, in all three cases represented by a modest increase in D-dimers.CT scan performed at 30-days showed that most patients (67%) had persistent radiological changes represented by fibrotic outcomes (40%) and ground glass areas (84%). No new thromboembolic events were detected (Figure 2). Three patients repeated a chest CT scan at 6 months and only in one case the persistence of unilateral ground glass areas was highlighted.
Conclusions: According to previous reports, 67% of patients with mild clinical disease still presented radiological changes at one month, mainly represented by the persistence of ground glass areas. Therefore, a chest image should be repeated in these patients not earlier than 3 months to assess what may be the actual persistent pathological alterations.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 38 COVID-19 INFECTION AND A SEVERE AUTOIMMUNE HEMOLYTIC ANEMIA CASE: A CASE REPORT AND REVIEW OF THE LITERATURE

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At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan. Its rapid spreading caused an epidemic throughout China first, and then a global pandemic. To date, there are several data in literature regarding the complications that have developed due to or during COVID19. Among these, several cases of autoimmune hemolytic anemia have been reported in SARS-CoV-2 swab positive patients from 2020 to date. We present the case of a woman in her early 60s with jaundice and asthenia. She had had respiratory symptoms 2 weeks prior to admission and two positive nasopharyngeal swabs (RT-PCR) for Sars-CoV-2. Medical history included asthma, hypertension and thyroid cancer. Her initial blood tests showed hyperbilirubinemia and severe macrocytic anemia. Chest X-ray was positive for features suggestive of COVID-19. Further blood tests showed a significant drop in haemoglobin and direct Coombs test (DAT) resulted positive. We also performed a search for english articles with “SARS-CoV-2” plus “anemia” as main topics, considering only the cases with a positive DAT, mainly from PubMed and PMC. There are many cases reported in literature of autoimmune diseases secondary to COVID19 and few with AIHA as either onset of COVID19 or late manifestation of the viral infection. We considered 29 cases of AIHA concomitant to COVID19, including the patient we treated in our Unit. We observed both wAIHA and CAD in cases reported in literature, but there’s a significant prevalence of CADs, with 14 cases out of 29 of CAD (48,3%), 7 case of wAIHA (24,1%), 1 case of mAIHA (3,4%), and 7 cases (24,1%) where titration was not performed. Most common diseases in medical history included: hypertension, diabetes, chronic renal disease, obesity. Out of the cases examined 16 patients were treated with steroids, 13 received blood transfusion, rituximab was added in 4 cases, in most cases after failure with first line treatment with corticosteroids. In most cases, 18 out of 29, there was a full recovery, 3 patients out of 29 died, there are no data about the outcome for 8 cases. While thrombocytopenia remains the most common autoimmune disease during SARS-CoV-2 infection, the growing number of reported cases of AIHA has become a cause for concern and interest. Although the mechanisms of the interaction between SARS-CoV-2 and haemolytic anemia are still not fully understood and further studies are certainly needed to evaluate them, the possible correlation between COVID19 and AIHA cannot be ignored.

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Management of COVID-19

P 39 THE ROLE OF TOCILIZUMAB IN THE TREATMENT OF COVID-19 ASSOCIATED PERSISTENT HICCUPS: CASE REPORT AND CONCISE REVIEW

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Hiccups are involuntary diaphragmatic muscle contractions with early glottis closure terminating inspiration. To date there are eight cases of persistent hiccups described as a symptom of onset in patients with the novel coronavirus disease (COVID-19). A 70-year-old man with a medical history of hypertension presented to our hospital with a chief complaint of persistent hiccups, fever, asthenia, muscle weakness and anorexia. Four days earlier, the patient had developed fever without localizing symptoms followed by the onset of hiccups. His fever partially improved with paracetamol, however, the hiccups persisted and increased in severity and frequency. The hiccup became so intense that it prevented feeding and forced the patient to go to the emergency room (ER). On arrival at the ER, he was febrile to 38.7 °C with a heart rate of 89 beats per minute, blood pressure of 130/75 mmHg, respiratory rate of 19 breaths per minute, and oxygen saturation of 94% on room air. Computed tomography (CT) scan of the chest showed bilateral subpleural areas of ground-glass attenuation and crazy paving pattern (Fig. 1). Laboratory values were remarkable for elevated C-reactive protein (54 mg/L), ferritin (1227 ng/mL), and lactate dehydrogenase (LDH) (294 U/L) levels, a nasopharyngeal swab for Sars-CoV2 was positive. Medical treatment was immediately set (proton pump inhibitors, remdesivir, dexamethasone , enoxaparin, metoclopramide twice a day iv and oxygen support). Nasogastric tube was also placed without any benefit. After two days the hiccups got worse; we also noticed a worsening of respiratory failure (oxygen flow from 1 to 4 l / min) myalgia and asthenia, weight loss (2 kg), intermittent fever and a significant increase in CRP (142 mg/L). Therefore in order to reduce this hyperinflammatory response, we introduced Tocilizumab 8 mg / kg in a single dose; patient's informed consent and the authorization of the local healthcare authority were obtained.. As early as four hours after the end of the tocilizumab administration, in an unexpected and dramatic way, the patient had a complete resolution of the hiccups. Control chest CT after seven days showed bilateral basal fibrosis (Fig.1). After a ten days we suspended medical therapy for COVID-19 and oxygen support; the patient was discharged asymptomatic.

To our knowledge, this is the first case report of successful treatment with Tocilizumab of persistent hiccups as an atypical presenting complaint of COVID-19. In fact only four hours after the iv administration of tocilizumab, there was a rapid and persistent resolution of the hiccups, accompanied, after 24 hours by a drastic reduction in CRP and other markers of inflammation. Therefore we reasonably hypothesize that the IL-6 inhibitor resolved the lower lobes inflammation (likely parapneumonic pleuritis) causing irritation of the phrenic nerve and its pericardial branches and the diaphragm are thought to be potential causes of hiccups.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 40 IVERMECTIN USE IN COVID-19: A CASE-CONTROL RETROSPECTIVE STUDY

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Background: Ivermectin (IVM) is a broad-spectrum antiparasitic drug approved for the treatment of onchocerciasis and other worm infestations. We aimed to assess the effectiveness of ivermectin (IVM) on a small cohort of COVID-19 cases in terms of mortality, length of stay and time to negative nasopharyngeal swab, and to see if IVM + Standard of Care (SoC) was more effective than SoC alone by comparing our cases with COVID-19 controls. Standard of Care at our center was defined at the time of observation as a 5-day course of remdesivir + dexamethasone.

Materials and Methods: All patients older than 18 years and experimentally treated with IVM + SoC were included in this study and retrospectively matched with a 1:1 ratio by age, sex, comorbidities, and WHO eight-category scale value at admission to COVID-19 patients only treated with SoC. We collected data about: sex, age, comorbidities, symptoms of COVID-19, oxygen-therapy, chest x-ray at admission and at 7 days, outcome, time to outcome, time to negative nasopharyngeal swab.

Results: We included 23 cases, 9 females (39.1%) and 14 males (60.9%), and 23 controls. Median age for cases was 52 years (IQR 47-74), while median age for controls was 53 years (IQR 47-74). At the time of admission, 20 patients (87.0%) in each group were affected by pneumonia. However, there was a statistically significant difference in PaO2/FiO2 ratio in cases (median 165, IQR 136-305) and controls (median 362.7, IQR 309-400) ($p < 0.001$). This difference is not highlighted at t1 (7 days since admission), t2 (14 days since admission), t3 (28 days since admission) ($p = 0.122$, $p = 0.646$, $p = 0.873$ respectively).

Although the time to the first negative nasopharyngeal swab is not significantly different between cases and controls ($p = 0.344$), the percentage of cases discharged with a negative swab (69.6%) is significantly higher than the percentage of controls (39.1%) ($p = 0.038$).

We used a Kaplan-Meier survival curve to determine the chance of a case or a control to improve their condition within 28 days since admission. Using the worsening of clinical conditions as the event, as we did not observe any death among both cases and controls, we observed a statistically significant difference in chances at clinical improvement in cases than in controls ($p = 0.022$). (Figure 1)

Conclusions: Although our data are preliminary and on a small number of patients, therefore our statistics might be influenced by the size of the sample, we observed that IVM shows promising and exciting results in treatment of COVID -19, both in terms of rate of virologic recovery and in terms of chances of clinical improvement. A limitation of our study was in selection of patients, the differences in PaO2/FiO2 ratio highlight how our group was in favor of administering IVM to more severe cases. Further studies are needed to establish if our observations are to be confirmed.

Attach: https://www.icar2021.it/public/abstract/Attach_ABS_239.tiff

Clinical HIV, Clinical COVID-19

Management of COVID-19

P 41 CHARACTERIZATION OF LONG-COVID SYMPTOMS IN AN ITALIAN CLINICAL CENTER

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Background: Recent studies have highlighted that significant number of patients with COVID-19 may experience prolonged symptoms, known as long-COVID. We aimed to characterize this condition in our cohort of recovered COVID -19 patients.

Material and methods: Patients who recovered from COVID-19 underwent a dedicated questionnaire, in order to assess the presence and frequency of symptoms. Data about medical history, COVID-related hospitalization and long-COVID symptoms were collected; symptoms staging was expressed in terms of frequency ranging from 0 (never) to 3 (severe, almost everyday). The 3-level version of Euro-Quality of Life (EQ-5D-3L) was administered to investigate five dimensions (Usual activities, Self care . Mobility, Pain/Disconfort, Anxiety/Depression). Patients performed a global healt status self-evaluation on a scale from 1 to 100%. Descriptive analysis was performed and predictors of long-COVID symptoms were searched via regression analysis. Chi-square test was used to compare frequency distributions.

Results: We analyzed data from 168 patients: 103 (61.3%) were males and median age was 58 years (50-66). One hundred-eighteen (70.2%) were hospitalized and more than half of patients (56%) had pneumonia; of these, 77% requiring oxygen support. The majority of patients (65, 38.7%) had a severe form of the disease according to WHO criteria. Through the EQ-5D-3L test, we observed that about 10% of patients experienced moderate to severe pain/discomfort. Median perceived health status was 80 (IQR 70-90). Full patients' characteristics are available in Table1.
The most frequently long-COVID symptoms observed was asthenia (109 cases, 64.9%), followed by exertional dyspnea (83, 49.4%) and arthralgia (72, 42.9%). Symptoms reported most frequently as moderate or severe were asthenia (43.5%), exertional dyspnea (31.5%), arthralgia (27%). As to neuropsychiatric symptoms, sleep disorders (overall 39.3%, moderate/severe 26,2%) and amnesia (overall 33.9%, moderate/severe 24.4%) were the most prevalent. Remarkably, four patients (2.4%) reported the onset of suicidal ideation.
In our chi-square analysis, we observed that non-hospitalized patients had a higher prevalence of moderate to severe neuropsychiatric symptoms (vs hospitalized patients, p=0.009) as well as mood disorders (p=0.026) and palpitations (p=0.002). There were no difference in terms of post-COVID-19 symptoms in different disease severity groups.

Conclusions: Our results suggest that the morbidity of COVID-19 extends beyond the recovery from the acute phase. The syndrome known as long COVID may result in significant impact to patients' lives and livelihoods. In particular, respiratory and neuropsychiatric symptoms seem to have a major role in terms of frequency and severity. Severity of acute disease could not be related with post-COVID-19 symptoms intensity. Patients who experienced domestic isolation instead of hospitalization could experience a deeper neuropsychiatric damage.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 42 MANAGEMENT OF SARS-COV-2 PERSISTENCY IN A 20-YEAR-OLD MALE AFFECTED BY AGAMMAGLOBULINEMIA: A CASE REPORT

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Immunocompromised people are at major risk of developing serious manifestations of SARS-CoV-2 infection and prolonged viral shedding. Some cases of symptomatic infection with several days of persistent shedding in immunocompromised host have been described.
Here we report the case of a 20-year-old male affected by unclassified agammaglobulinemia, diagnosed with SARS-CoV-2 infection on January 7, 2021. He was hospitalized on February 24 with CT scan evidence of interstitial pneumonia. He received a 5-days cycle of remdesivir and steroid therapy with rapid apyrexia. He was discharged with persistently positive SARS-CoV-2 swab and sputum with viral quantification of Log107,55 copies/ml and Log106,22 copies/ml respectively. D69-70 deletion, E484K and N501Y mutations were not detected at genotyping with Allples SARS-CoV-2 Variants I Assay, Seegene Inc. With AIFA authorization, on March 24 he received monoclonal antibody bamlanivimab due to SARS-CoV-2 persistency. On April 9 a new hospitalization occurred due to fever, with CT scan evidence of pneumonia with a different distribution of ground-glass alterations. SARS-CoV-2 swab was negative, while sputum and bronchoalveolar lavage fluid were positive with Log103,11 copies/mL and Log103,49 copies/ml respectively. Lineage B.1.177.52 with E484K mutation was identified at genotyping. He received a second 5-day-cycle of remdesivir with apirexia after few days. He was discharged persistently positive on sputum. After two days he developed fever and was hospitalized with Log104,5 copies/mL of SARS-CoV-2 on sputum. He was tested for blood cultures, HIV, herpes viruses, fungal markers (serum cryptococcal and galactomannan antigens, serum β-D-glucan, P. jiroveci amplification on sputum), IGRA. All blood tests were negative except for β-D-glucan considered as a false-positive due to immunoglobulin administration, and RT-PCR of SARS-CoV-2 on sputum and nasal swab. He performed ophthalmological evaluation, transthoracic echocardiography and full body CT scan. Interstitial pneumonia with a different distribution from previous radiological exams was the only pathological alteration. After AIFA agreement, he received a 10-days-cycle of remdesivir followed by monocolonal antibodies casirivimab/imdevimab. Stable apyrexia started from May 5. SARS-CoV-2 on sputum and nasal swab testes negative on May 12 and he was discharged. To this date, no more symptoms have been reported at follow-up. Given the lack of symptoms no nasal swab was repeated.
SARS-CoV-2 persistency in immunocompromised host should be considered life-threatening. In individuals with humoral response deficiency, SARS-CoV-2 may not lead to a self-limiting infection; persistent viral replication could lead to indefinite relapses. A different therapeutic schedule may be indicated for these patients. In our case, a longer remdesivir cycle followed by combined monoclonal antibodies seem to have been effective, but further studies are needed.

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Clinical HIV, Clinical COVID-19

Management of COVID-19

P 43 CHARACTERISTICS AND TREATMENT RESPONSE OF PATIENTS WITH SARS-COV-2 INFECTION TREATED WITH MONOCLONAL ANTIBODIES IN TWO REFERENCE HOSPITALS IN CATANZARO (SOUTHERN ITALY)

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Background: Monoclonal antibodies (moAbs) for SARS-COV-2 are used in current clinical practice to treat patients, whose characteristics may be however different from the inclusion criteria of RCT's, which led to rapid approval of these drugs. For instance, duration of infection was restricted in trials within a maximum of three days from the positive swab in the BLAZE-1 trial, while the Italian Medicinal Agency (AIFA) indicated 10 days from symptom onset as a cut-off beyond which moAbs should not be prescribed. Also, patient characteristics (age, comorbid diseases, etc.) could influence tolerability/safety profiles. The objective of this work (ongoing) was to explore effectiveness and safety of moAbs in current clinical practice.

Materials and Methods: We set-up a collaborative prospective cohort of patients in two hospitals in Catanzaro. For this analysis we included all patients treated so far according with the AIFA criteria. We described demographic, laboratory and clinical characteristics of patients at baseline. Prospective follow-up was performed using negative nasopharyngeal swab for SARS-CoV-2 RNA as main outcome. Laboratory exams were performed at one point after negativization. Written consent to data processing was obtained from participants.

Results: 23 patients were treated (10 M, 13 F). Their median age was 64 years (range: 17-91). Median duration of SARS-CoV-2 positivity at the time of moAbs administration was 3 days (range: 1-9). Main comorbidities were obesity in 7/23 (30.4%) and immunocompromising conditions in 6/23 (26%) patients. Nasopharyngeal swab turned out to be negative for SARS-CoV-2 RNA within a median of 21 days (range: 4-28) except from a 60 years-old woman treated with rituximab for severe autoimmune anemia secondary to systemic lupus erythematosus whose nasopharyngeal swab is still positive after 55 days from therapy with moAbs, and notwithstanding repetition of moAbs in combination with remdesivir (this case will be described in details in the conference paper). No serious adverse reactions requiring medical interventions were observed during infusion for all patients or thereafter. Only one patient died for a reason unrelated to treatment. For 16 patients with the check of the exams performed at a median time of 28 days (range: 11-42) after the first negative swab for SARS-CoV-2 RNA, increases with respect to baseline were found for red (p=0.001) and white (p=0.007) blood cell, lymphocyte (p=0.001) and platelet (p=0.002) counts.

Conclusions: With this small longitudinal study we confirm effectiveness and safety profiles of moAbs in a real-life setting. However, since far more patients had a diagnosis of SARS-CoV-2 infection than the minority of those who received moAbs in the same period, and the interval between diagnosis and treatment was longer than that used in RCT's, we conclude that more efforts should be put to promote treatment access of those in need.

Clinical HIV, Clinical COVID-19

Management of COVID-19

P 44 DON'T FORGET MIS-C : A TYPICAL CASE IN A 16YA OBESE BOY

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is spreading through the human population presenting a large variety of clinical features.
In Italy and across Europe and the US, in association with outbreaks of Covid-19 cases, lots of young patients diagnosed with Kawasaki disease-like were detected. The cause of the diseases is assumed to be a post-infectious inflammatory response following SARS-CoV-2 infection, named by the WHO as "multisystem inflammatory syndrome in children and adolescents temporarily related to covid-19 (MIS-C)".
Case report: An obese 16-year-old boy presented to our Emergency Department (ED) with fevers and malaise. The patient presented an urticarial rash on his trunk and legs. He was diagnosed on his initial visit with an acute bacterial infection: we proposed to hospitalize because of 2 points at qSOFA score (high respiratory rate and hypotension). At blood test C-reactive protein and white-blood count were both significantly elevated at 130 mg/L and 16.32 x 10^9/L respectively, we found altered coagulations parameters (d-dimer 9116 ug/L). Antibiotic therapy with ceftriaxone was empirically started. During hospitalization fever continued and he developed gastrointestinal symptoms such as vomiting and diarrhea and oral mucosal swelling. For a persistent tachycardia at rest with an abnormal ECG with long QT the patient performed an echocardiography which showed no pathological findings. There are no other significant microbiological findings. A subsequent COVID-19 immunoglobulin G testing was positive. Waiting for the results of the diagnostics set, the patient has gradually improved without specific therapy.
Discussion: MIS-C is a recently recognized pediatric illness spectrum in association with SARS-CoV-2 infection. Diagnosis is done in children and adolescents 0–19 years of age with fever > 3 days + multi-organ involvement (two of the following: rash or conjunctivitis or muco-cutaneous inflammation signs, hypotension or shock, features of cardiac dysfunction, coagulopathy, acute gastrointestinal problems) + elevated markers of inflammation + evidence of COVID-19 (RT-PCR, antigen test or serology positive). Differential diagnosis has to be done with infectious form (bacterial sepsis, septic shock-like syndrome, toxic shock syndrome, acute rheumatic fever) or vasculitis such as Kawasaki Disease.
Our case was a mild form of MIS-C: no treatment was needed for the complete recovery of the patient.

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Clinical HIV, Clinical COVID-19

Management of HIV infection

P 45 A EU COLLABORATIVE PARTNERSHIP FOR ACTIVE LIFESTYLES FOR THE ADHERENCE TO THE HIV THERAPY AND TO PROMOTE FITNESS AS THERAPY

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Context: As stressed in the EU Physical Activity Guidelines, regular physical activity can prevent or delay the onset of certain illnesses. Thus, the ARIE project promotes fitness therapy for people living with HIV/AIDS. ARIE offers an innovative fitness protocol helping PLHIV to accept and reconnect with their bodies. With the symptomatology of HIV being altered since the advent of antiretroviral therapy (ART), we are now learning about associated metabolic changes with negative and possibly fatal implications. A combination of aerobic and resistance exercise can help modify these risk factors.
Introduction: ARIE outlines the goals of a fitness therapy capable of inducing physiological adaptations to exercise in PLHIV through pleasant, engaging and motivating exercise. The ability of professionals, properly trained to identify the exercises specific to patients' needs, ensures each lesson is a real therapy session, complementing or replacing a normal rehabilitation activity performed in a clinical environment. In addition, fitness is cheaper than a health system's rehabilitation programme.
Aims: ARIE purpose is to examine the health benefits from regular exercise training among PLHIV on ART. An overview of the findings indicates that physical activity and exercise are both safe and effective in improving cardiorespiratory fitness, metabolic profile, and quality of life. Today, movement therapy is a well-recognised form of complementary therapy used in hospitals and comprehensive HIV clinics.
The project will implement:
- a EU innovative protocol to promote fitness to HIV+ people aged 18-50 to be involved in a moderate/vigorous physical activity;
- a 'Train the Trainers' EU course for health professionals and trainers from the project partners' countries on the protocol application, to educate PLHIV about the importance of physical activity for their recovery and well-being.

Method: ARIE activities will be carried out in consecutive stages, while management, quality control and dissemination will be ongoing and involve every aspect of the project. Each activity will include preparation, design, implementation, validation and finalisation stages. The quality of work will be supervised by all project partners and discussed at project meetings. Project partners will give feedback on interim results, research plans, report drafts, and publications.
Results: The project to evaluate improvements, results will be assessed through quantitative and qualitative indicators. Data will be collected using quality instruments provided during the project implementation, and through other sources of information, which may include feedback from:
- Attendees taking the ' T-t-T' courses;
- Participants in the project pilot;
- Followers on social media and visitors to partners' websites;
- Participants in the dissemination events.

Recommendations
- Encourage physical activity as therapy;
- Apply the ARIE protocol.

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Clinical HIV, Clinical COVID-19

Management of HIV infection

P 46 SILENCE MAY KILL YOU

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Background: Only about 75% of heterosexual HIV-infected patients are seropositive for CMV. HIV-infected patients with CD4+ T-cell counts < 50 cells/ml are often viremic and viruric with CMV, which does not imply that they have disease due to CMV. Isolation of CMV from BAL specimens is relatively common in HIV-patients with viral PNA . Diagnosis of CMV pneumonia is confirmed when histopathology shows intracellular lesions typical of CMV.
Material and Methods: The patient underwent laboratory and radiological examinations. In addition, consultations were carried out by pulmonologists, cardiologists, resuscitators and ophthalmologists.
Results: On 19/08 a 47-year-old patient suspected of a viral pathology was admitted to our ward. The patient had a silent remote medical history. He went to the emergency room for fever and diarrhea, which arose on 18/07. For this symptomatology he had taken various antibiotics without obtaining improvements. He presented with: lymphomonocytosis, neutropenia, increased CRP and PCT and positive serology for CMV and EBV. He also had a chest CT scan which showed emphysema, but no inflammatory lesions. Upon entering the ward, the patient presented with significant respiratory failure; therefore oxygen-therapy with VMK 15 L/min was started. During the hospital stay it was necessary to resort to NIMV with CPAP and HFNC. On 19/08 CMV-DNA on plasma was 413900 copies/ml. This data combined with the clinic made us think of an acquired immunodeficiency even if no risk factor emerged from the medical history. In fact, on 20/09 the serology and western blotting for HIV were positive, HIV-DNA on plasma 145400 copies/ml and CD4 + 328 cells/ml. Meanwhile, respiratory function had worsened and bilateral ground-glass lesions appeared on chest CT. On 22/08 the CMV-Dna on BAL was 235800 copies/ml. Culture of CMV or CMV PCR from tissue, secretions or excretions is insufficiently specific for CMV-caused disease to be used as a basis for therapy except in the case of neurological disease. Lung biopsies were not performed at our hospital. Diagnostic tests for PCP, mycobacterial pneumonia, and bacterial pneumonia were all negative. We therefore diagnosed CMV pneumonia. Ganciclovir therapy was started on 23/08. On 09/02 CMV-DNA on plasma was absent. On 03/09 ART was started with TAF + FTC + DRV / COBI, a treatment with a very high genetic barrier. On 17/09 the patient was discharged with maintenance therapy for CMV pneumonia and without oxygen therapy.
Conclusions: The case is a clear example of how dangerous the lack of information can be in the medical field. The patient had made no mention of risky sexual behavior and this led to the delay in the diagnosis of HIV infection. Furthermore, the clinical presentation of CMV pneumonia was not characteristic and it was necessary to make a diagnosis by exclusion, which consequently postponed the start of effective therapy, which could only take place with a very advanced clinical picture.

Clinical HIV, Clinical COVID-19

Pediatric, adolescent, maternal, fetal aspects in HIV

P 47 WEIGHT GAIN IN A COHORT OF PREGNANT WOMEN LIVING WITH HIV

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Background: Overweight and obesity are increasing among people living with HIV, thus rising attention on possible factors that are associated to weight gain, including antiretroviral therapy (ART). Currently, little data are available on weight gain during pregnancy in women treated with different ART regimens.
In this retrospective cohort study, we aimed at describing the trend of weight gain during pregnancies in women followed by our outpatient HIV service in a North-West University Hospital in Italy.
Material and methods: We included all pregnancies followed in the period 2014-2021 in our outpatient HIV service. We collected women's weight before pregnancy and at the first, second and third trimester of gestation. We collected demographic data (age at pregnancy, ethnicity), virological data (ART during pregnancy, viral load at delivery), data on gestational hypertension and diabetes, hypercholesterolemia and hypertriglyceridemia and neonatal weight.
Difference in baseline weight and weight change during pregnancy were compared in PI and non-PI containing ART regimens, as well as in INI and non-INI containing regimens, using Mann-Whitney U test.
Results: Thirty-three pregnancies were included in the study, of which three were twin pregnancies. Median age of women was 32.3 (±3.8) years. Fourteen (42%) were Caucasian, 9 (27%) African origin, 8 (24%) South American and 2 (6%) Asian. Eight out of 33 women started their first line ART during pregnancy (range 8-17 weeks). Eight women (23%) received a protease inhibitor (PI) containing regimen, twelve (36%) an integrase inhibitor (INI), nine (27%) a non-nucleoside reverse transcriptase inhibitor (NNRTI), three (9%) a PI+INI containing regimen and one (3%) PI+INI+NNRTI. All had HIV-RNA <200 copies/mL at delivery.
Mean weight before gestation was 62 (±10.7) kg, and absolute total weight gain was 9.6 (±4.4) kg during pregnancy. Women who received an INI-based ART showed a tendency toward greater weight gain during the second (+8.2 ±3.6 kg) and third (+11.1 ±3.6 kg) trimester compared to others (p=0.022 and p=0.076, respectively). Mean weight gain per trimester and according to ART regimen is outlined in Table 1. The mean weight of newborns did not differ significantly among treatment groups.
None of the study participants developed gestational hypertension, while 2 (6%) had fasting glycemia > 110 mg/dL, 10 (30%) hypercholesterolemia and 5 (15%) hypertriglyceridemia, with a frequency that was not significantly different among the considered ART regimens.
Conclusions: In our cohort, weight gain in pregnancy was slightly more pronounced in women treated with INI during the second and the third trimester when compared to other regimens. However, mean weight gain was within the physiological range expected in course of pregnancy. No difference in newborn weight and in the frequency of hypertension, dyslipidemia or diabetes was observed in women undergoing different ART strategies in course of pregnancy.

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Coinfections and Hepatitis

Bacterial and fungal infections in immunocompromised host

P 48 A CASE OF COMPLICATED TRICUSPIDALIC ENDOCARDITIS IN A PATIENT WITH UNDIAGNOSED HIV AND HCV INFECTIONS

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Background: People who inject drugs (PWID) have always been a group at hight risk of infective endocarditis (IE), that have special characteristics: younger patients, community-acquired, right-sided native valve involved (mostly tricuspid valve), most often caused by Staphylococcus aureus, usually associated with human immunodeficiency virus (HIV) and hepatitis C (HCV) coinfection.
Immunocompromised patients , with HIV and HCV coinfection, have a major risk to develope complicated infective endocarditis, often first sign of their basic condition.
Case Report: We present a case of complicated tricuspidalic endocarditis caused by methicillin-sensible Staphylococcus aureus (MSSA) in a patient with undiagnosed HIV and HCV infections.
On march 24 of present year a 33 years old patient came to our Emergency Room with generalized malaise, fever(BT 39,5°)and atypical chest pain, from ten-twelve days. He belonged to PWID.
The initial laboratory results were: c-reactive protein (CRP) 319 mg/L, procalcitonin 3,2 ng/mL , D-dimer 4,56 mg/L, neutrophilia (7980/uL) and leukopenia(560/uL), arterial blood gas analysis with pO2 60 mmHg. Chest computed tomography (CT) revealed multiples pulmonary nodularities with excavations, strongly suspicious for septic embolizations, and also hepato-splenomegaly. Given his radiographic findings along with his clinical picture we suspected endocarditis in PWID, following which we performed:
blood cultures, with isolation of a methicillin-sensible Staphylococcus aureus (MSSA);
transthoracic echocardiography(TTE) with findings of multiples tricuspidal formations(the biggest was about 3 cm in its major diameter), suggestive for endocarditic vegetations, that cause mild tricuspidalic insufficience;
serology and PCR exams in order to search HCV and HIV infections, with HCV-RNA (genotype 3 a) 8600 UI/mL and HIV-RNA 12027 cp/mL: a new diagnosis of HIV(CDC B) and HCV coinfection was made.
Therefore we started a treatment with Vancomycin and Gentamycin.
Due to a clinical worsening it was necessary the sostitution of native tricuspidal valve with a mechanic HANCKOCK 29 mm valve.
On april 10, after clinical, laboratory (CRP 42 mg/L and procalcitonin 0,15 ng/mL) and radiological improvement, the patient was dismissed with the prescription of 12 days of oxacillin oral therapy in order to complete antibiotic therapy.
Actually the patient is followed at our Clinic of Infectious Disease in Chieti where he started ARV therapy, obtaining HIV virosuppression on july 5.
Conclusions: Septic pulmonary emboli in right-sided native valve infective endocarditis are rare finding that became most frequently in PWID and immunocompromised patients.
The management of this cases, according to their complexity , often require adding cardiosurgery procedures instead of antibiotics alone.

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Coinfections and Hepatitis

Bacterial and fungal infections in immunocompromised host

P 49 DIFFUSE MAC LYMPHADENITIS IN A HIV PATIENT UNDER ANTIMYCOBACTERIAL TREATMENT

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We report the case of a 60-years-old male who was diagnosed with advanced HIV infection (CD4 cell count: 20 cells/mm3; CD4 percentage: 6; viral load: 4 789 800 copies/mL) in May 2020, complicated by Pneumocystis Jiroveci Pneumonia (PJP). After completing treatment for PJP and starting antiretroviral therapy (ART), Mycobacterium Avium Complex (MAC) susceptible to macrolides and aminoglycosides was isolated from the broncho-alveolar lavage (BAL) performed during hospitalization. Therefore, in July 2020, antimycobacterial therapy with azithromycin (500 mg orally daily), ethambutol (15 mg/kg per day) and rifabutin (5 mg/kg per day) was introduced. Treatment was well tolerated and taken with excellent compliance.
In mid-September 2020, the patient presented with new left cervical lymphadenopathies, in absence of other symptoms. On clinical evaluation, the lymph nodes appeared hard, indolent and fixed to the underlying planes. At blood tests: CD4 cell count 88 cells/mm3; CD4 percentage 21; viral load 102 copies/mL. The ultrasonography of the neck showed multiple laterocervical lymphadenopathies of about 10-20 mm. A positron emission tomography (PET) with 18-fluorodeoxyglucose (FDG) demonstrated the presence of multiple and diffuse supradiaphragmatic and subdiaphragmatic lymphadenopathies, suggestive for lymphoproliferative disease. A left supraclavicular lymph biopsy was then performed, which showed numerous granulomas with focal necrosis and multinucleated giant cells, no malignant cells. The smear microscopy of the lymph node biopsy was negative, while the culture test was positive for MAC (susceptible to macrolides and aminoglycosides). Antimycobacterial treatment was continued unchanged and the lymphadenopathies gradually resolved. Chest high-resolution CT-scan, performed 6 months later, showed a marked improvement of the parenchymal involvement.
The case is interesting because of its atypical presentation. It might be interpreted as an episode of "paradoxical" immune reconstitution inflammatory syndrome (IRIS), although the clinical worsening was delayed (16 weeks after introduction of ART, while normally it occurs one to eight weeks after) and there was no evidence of systemic inflammatory condition. Otherwise, it could be defined as a disseminated MAC disease in severe immunosuppressed patient, but there was no pathogen isolation in blood samples and the patient did not refer systemic symptoms. Nevertheless, the most peculiar aspect of the case is the development of the systemic lymph node involvement during effective antimycobacterial and ART therapy.

Coinfections and Hepatitis

Bacterial and fungal infections in immunocompromised host

P 50 EVIDENCE OF PAEDIATRIC SEPSIS CAUSED BY A L.GARVIEAE CONTAMINATED PLATELET CONCENTRATE

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Background: Due to an increasing number of human clinical infections, L. garvieae has gained recognition as an emerging human pathogen, causing bacteraemia with infective endocarditis and septicaemia in adults. We describe three paediatric cases of transfusion-transmitted L. garvieae sepsis from platelet concentrate (PC) of the same donor.
Methods: The L. garvieae isolates and the donor's PC were retrospectively collected for whole-genome (WGS) sequencing and shot-gun metagenomics. Libraries were obtained by Illumina HiSeq (2×150 bp sequences). De novo assembly was performed to obtain a linear representation of the L. garvieae genome. Resistance genes, plasmids, virulence factors and phages were annotated using BLASTN e BLASTX and against specific databases. In order to define the identity of the isolated strains, a core SNP genome-based Maximum Likelihood tree was performed. A total of 21 publicly available L. garvieae sequences were retrieved in order to maximize genomic variability. The host-filtered microbial reads were taxonomically profiled using MetaPhlAn2 (v2.7.5).
Results: In September 2020, four paediatric onco-hematologic patients received a PC from the same donor (an healthy 59 year-old Italian female) at Bambino Gesù Children Hospital (OPBG). Three of four patients experienced L. garvieae sepsis one day after transfusion.
Thanks to WGS, an average genome size of 2.06 MB was obtained by the three OPBG isolates. All isolates shared a 99.9% of identity and were characterized by 440 SNPs, of which 43 were never described before. Plasmids pKL0018 (conferring resistance to tetracyclines and macrolides) and plG5 (involved in bacteriocin processing), and the temperate prophage Plg-Tb25 were detected in all three strains. By phylogenetic analysis, OPBG isolates clustered together (bootstrap 100%) in the subtree of human and cow L. garvieae strains (Figure 1).
By mapping donor's PC microbial reads (6.8% of total reads obtained by metagenomics) 4.85% belonged to Firmicutes, and 0.84% to Streptococcaceae (>97% identity with L. garvieae), confirming the L. garvieae infection from the PC transfusion.
Conclusions: These data showed for the first time a transfusion-associated sepsis due to transmission of L. garvieae in paediatric setting, and definitely confirm the importance to implement the screening of platelet components with new human defined pathogens to ensure the safety of blood supply.

Attach: https://www.icar2021.it/public/abstract/Attach_ABS_117.PNG

Coinfections and Hepatitis

Bacterial and fungal infections in immunocompromised host

P 51 AN ATYPICAL PULMONARY PATTERN IN A PATITENT WITH NEW HIV DIAGNOSIS

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Background: Infection with R. equi was initially described in animals and later in humans. It affects immunocompromised patients, especially those infected with HIV and in the majority of cases already suffering from AIDS, an increasingly rare condition nowadays thanks to the spread of HAART. Moreover, the detection of this pathogen raises interpretative doubts and it's often considered as contaminant. We present the case of a patient diagnosed with AIDS due to wasting syndrome and an atypical pulmonary pattern difficult to diagnose.
Material & methods: We reviewed all patient's medical records and compared our case to other published cases of R. equi infection in HIV-infected patients.
Presentation: The patient is a 51-year-old male from Colombia, who came to our attention in february 2021 for progressive deterioration of general conditions, up to cachectic state associated with widespread arthromyalgia, serotine fever and recent onset of dyspnea at rest. The positive HIV test was received the day after admission.
Chest CT scan was performed, showing a 21x14mm parenchymal cavitation in the right upper lobe. Suspecting tuberculous pneumonia, fibrobronchoscopy with BAL was performed, with negative PCR for BK and no acid-fast-bacilli detection.
Several problems were managed, including severe malnutrition, bedridden syndrome, systemic cytomegalovirosis with gastric involvement, severe left ventricular dysfunction.
However, the aetiology of the pulmonary pattern was unclear. During hospitalization, a set of blood cultures were positive for R. equi, which was subsequently confirmed on bronchial aspirate. Considering this microbiological isolate, the radiological picture of the lungs was attributed to this pathogen. We therefore started combination therapy with oral azithromycin and rifampicin.
There was a clear improvement in patient's conditions and he was discharged at the end of March 2021.
The patient was readmitted two months later for cardiogenic shock, but a repeated chest CT scan two months after starting antibiotic therapy showed an improvement in his lung cavitation. Therefore, given the clinical-radiological improvement and the achievement of immuno-virological compensation, treatment for rhodococcosis was suspended.
Conclusions: This clinical case represents one of the rare cases of pulmonary rhodococcosis. Although it presented with bacteraemic pneumonia with excavative evolution, typical features of R. equi infection in HIV patients, diagnosis and management were difficult. This because of interpretative doubts induced by R. equi positive cultures from blood or sputum, frequently regarded as a contaminant.
Duration of treatment is still debated, although there is agreement that it should be influenced by nature of lung lesions and immunological status of the patient. Prolonged treatment over several months may not be justified, especially in cases where the immunosuppressive condition that predisposed to infection has been controlled.

Coinfections and Hepatitis

Bacterial and fungal infections in immunocompromised host

P 52 HYSTOPLAMOSIS IN HIV. TWO CASE REPORTS FROM A NORTHERN ITALY HOSPITAL

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Background: Histoplasmosis is an endemic mycosis of the Americas that is usually asymptomatic, but it can result in severe illness in people with impaired immunity, including those HIV+, among whom the most frequent clinical presentation is disseminated disease.Symptoms are aspecific and may be indistinguishable from those of other diseases.
Materials and methods: we describe 2 cases of disseminated Histoplasmosis in HIV+ patients born in Ecuador, admitted to our ward in july 2020 and june 2021.
Results: 1) 56-old-man,living in Italy since 2010.He was admitted in ER in July 2020 for fever,severe diarrhoea, hypotenxion and significant weight loss.He was HIV+,but he had stopped ART 5 yrs before.Blood tests:WBC 2900/mmc, Hb 9,9 g/dl,CRP 10 mg/dl(<0.5),severe ipokalemia,PCT 2 ng/ml.CT scan:multiple enhanced superficial lymphnodes(LNs), both mediastinic and abdominal, thickening and parietal hyperemia of almost all colic segmentsCD4 count 2/mmc (1%), HIV-RNA 23,400 cp/ml.Quantiferon(QF pos;Leishmania,BK smear and PCR were negative.B-D-glucan was negative, galactomannan highly positive (4,066).PET:multiple LNs of pathological aspect above and below diaphragm and lung flogistic signal.A perigastric LN biopsy was performed;histology showed histiocytic granulomatous lymphadenitis with several macrophages with numerous fungal spores (Grocott and PAS positive;Fig 1);ZN negative.Liposomal amphotericin B was started (3 mg/Kg) with poor tolerability;a panfungal PCR on lymphnode was positive for H. capsulatum.In the following days patient condition worsened,with severe thrombocytopenia,severe anemia, until coma and exitus.
2) 34-years-old woman arrived in Italy 5 years ago.She was admitted in june 2021 for fever,abdominal pain,weight loss and bilateral laterocervical lymphadenopathy.Blood tests:lymphopenia (370/mmc),CRP 8.58 mg/dl.CT scan:multiple colliquated abdominal adenomegalies;thickening and parietal hyperemia of almost all colic segments.She resulted HIV+. CD4 count 6/mmc(2%),HIV-RNA at baseline 80,000 cp/ml.Cryptosporidium was detected on feces.PET:multiple pathological adenopathies above and below diaphragm.B-D-glucan and galattomannan were highly pos (respectively 200 and 4.7).A submandibular LN biopsy was performed;histology showed histiocytic granulomatous lymphadenitis with several macrophages with numerous fungal spores(Grocott and PAS positive),ZN negative. Panfungal PCR is ongoing.She started ART and liposomal Amphotericin B (5 mg/Kg) with good tolerability and with partial clinical improvement.
Discussion: Disseminated Histopalsmosis is relatively common opportunistic infection in AIDS patients from Americas.Due to the large South American community present in Italy (specially from Ecuador in Genoa) we hav to consider it in the differential diagnosis of AIDS presentation with diffused lymphoadenomegaly with/without lung involvement. Hystopathology and PCR are the mainstone of diagnosis.Prognosis is often poor specially if not suspected in early time.

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Coinfections and Hepatitis

HCV elimination

P 53 VILLA MARAINI POINT OF CARE TESTING: HCV ELIMINATION AMONG PEOPLE WHO USE DRUG IN ROME OUTSIDE THE HOSPITAL SETTING IS POSSIBLE

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Background: We evaluated in the key population of PWUD in the extra hospital setting of Villa Maraini Foundation: HCV seroprevalence, HCV active infections and re-infections, Linkage to Care (LtC)rates and the efficacy in terms of Sustained Virological Response (SVR).
Material and methods: The diagnostic-therapeutic algorithm included: voluntary based execution of a rapid HCV serological test using OraQuick® Rapid HCV Antibody Test on whole blood obtained by finger stick, after informed consent and an operator-guided questionnaire to investigate the main risk factors for HCV; in case of positivity, execution of HCV-RNA molecular rapid test; in case of diagnosis of HCV active infection, promptly LtC to the Infectious Diseases Clinic of Tor Vergata Polyclinic.
Results: 38% of PWID with positive serology had negative HCV-RNA, of these 40% had spontaneously cleared the virus, while 60% had obtained SVR thanks to treatment (7 patients with IFN-based regimens, 25 patients with DAAs); of 38% of PWID with positive serology we have no information about HCV-RNA as they did not want to perform the rapid molecular test; 24% of PWID with positive serology had active replication of HCV detected by rapid molecular test and among these 5 reinfections were highlighted. 17/34 patients with chronic active hepatitis were LtC and of these 10/17 received treatment and obtained SVR12. It also emerged that PWID were unaware of their serological and viraemic status respectively in 53% and 70.6%. 333 PWID (of which 23% intercepted at the street unit) performed HCV serological rapid test, and among these ones, 42% (141/331) was positive. All 141 subjects were promptly offered to perform the rapid HCV molecular test to confirm the presence of Hepatitis C and 64.5% (91/139) agreed it. Of these, 37.3% (34/91) were positive and therefore received confirmation of Hepatitis C. 50% of patients diagnosed in an out-of-hospital setting (17/34) actually went to hospital for access to treatment and 59% (10/17) received treatment with DAAs and obtained SVR12.
Conclusions: Rapid diagnostics (both serological and molecular) and the experience on the territory of Villa Maraini Foundation have been a winning formula in terms of diagnosis for out-of-care PWID and which would never have approached the hospital system mostly despite the lockdown and restrictions due to COVID19. To date, the most delicate and weak part in the cascade of care is the LtC, therefore the process of access to care must be remodeled through the decentralization of care.

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Coinfections and Hepatitis

HCV elimination

P 54 HCV DAAS TREATED PATIENTS: CASE SERIES 2015 - 2020 INFECTIOUS DISEASES UNIT VASTO HOSPITAL (ASL2 ABRUZZO)

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Background: Literature data showed the high efficacy of HCV direct acting antiviral agents (DAAs) in clinical trials.The aim of retrospective analysis of HCV DAAs treated case series is to assess if the same efficacy can be reached in real life conditions.
Methods: Retrospective analysis of HCV pts treated with DAAs at our Infectious Diseases Unit during the period 01/01/15–31/12/20 has been carried out.
Results: 186 HCV pts were treated in the period considered.The mean age was 58 yrs (range 26-87). Male pts were predominant (124-66%). Most pts were in two age groups (30–59 yrs and 60–79 yrs), coherently with Italian HCV epidemiology.
Pts were treated following AIFA indications that changed over time, extending criteria for access to therapy: in the early phase only pts with advanced fibrosis can be treated,while since 2017 pts with any fibrosis grade have access to therapy.
In our case series 33% (70) had cirrhosis (AIFA crit.1), 24% (45) had fibrosis F0-F1 (crit.8), 19% (37) had fibrosis F2 (crit.7),14% (26) had fibrosis F3 (crit.4), 2,1% (4) had severe extrahepatic manifestations (crit.3),1,1% (2) had renal insufficiency (crit.10) ,1,1% (2) were treated without fibrosis assessment for social issues (crit.12). Pts mean age was higher in the group with severe extrahepatic manifestations (69yrs) and lower in the group without fibrosis assessment (39yrs).
As reported in literature, genotype 1 is prevalent in Italy; in our case series genotype 1 predominance is confirmed(72 -38,7%),28 of which 1a and 44 1b, followed by genotype 2 (57-30,6%) and genotype 3 (46-24,8%), while genotype 4 is the least represented (11-5,9%).
Genotype 3 was associated with a higher percentage of cirrhosis (52%) in respect of other genotypes (1a-36%; 1b–25%; 2–35%; 4–45%).
Treatments prescribed in our Unit reflected guidelines evolution and progressive new DAAs approval.129 pts (69,3%) were naives; on the other hand,57 pts (30,6%) received previous treatment, 45 of which were null responder while 12 were relapser.Since 2017 has been prescribed almost exclusively 3 co-formulated drugs: Glecaprevir/Pibrentasvir, Sofosbuvir/Velpatasvir, Elbasvir/grazoprevir. 8 pts were co-infected with HIV; all of them achieved SVR. In 2 pts the antiretroviral treatment was modified for the presence of drug-drug interactions. Treatment was well tolerated and no adverse events occurred. DAAs therapy was completed by 178pts (96%), while only 8 pts discontinued therapy, 5 for voluntary suspension and 3 for adverse events (skin rash and pruritus). DAAs therapy efficacy was confirmed: in our case series only 4 pts didn't achieve a SVR. 2 of 4 pts that failed were re-treated: the first one that failed treatment with sofosbuvir Peg-IFN was re-treated with Daclatasvir sofosbuvir and ribavirin, the other one that failed Daclatasvir sofosbuvir ribavirin was re-treated with Vosevi: both achieved a SVR.
Conclusions: HCV DAAs treatment confirmed the high efficacy and the optimal safety profile even in real life conditions.

Coinfections and Hepatitis

Hepatitis epidemiology

P 55 HBV AND HCV SCREENING IN PATIENTS HOSPITALIZED FOR SARS-COV-2. PREVALENCE OF VIRAL HEPATITIS IN AN UNSELECTED, CONSECUTIVELY ENROLLED PATIENT POPULATION

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Background: The diagnosis of hepatitis C (HCV) and B (HBV) viral infection remains a challenge in asymptomatic chronic infection.
The World Health Organization (WHO) aims to eradicate chronic viral hepatitis within 2030, however, the prevalence of undiagnosed chronic viral hepatitis in the general population is unknown.
The aim of this study was to identify the seroprevalence of HCV and HBV at serological screening, in people hospitalized for SARS-CoV-2 infection.
Material and methods: This is a retrospective, single-center study conducted in internal medicine wards in a tertiary care hospital in Northern Italy, from 25th February 2020 to 31st January 2021. All people who were hospitalized for SARS-CoV-2 were considered eligible for the present research. Serology for HCV, HBsAg, HBcAb, and, when available, HCV-RNA and HBV-DNA were collected.
Results: During the study period, 1429 patients were admitted to our hospital for SARS-CoV-2 infection. Serologic test for HCV and/or for HBV were available for 382 (27%) patients. Among them, 238 (62%) were male, median age was 70 years (interval 21-103), 363 (95%) were Caucasian (360 Italian), 17 (4%) Latin-American and 2 (0.5%) were from Africa and Asia.
Among available data, 373/382 (98%) patients were screened for HCV serology, 372/382 (97%) patients for HBsAg and 320/382 (84%) were also screened for HBcAb.
HCV serology testing was positive in 14/373 (4%) patients, of whom 8/14 (57%) performed HCV-RNA. Among them, in 2 patients chronic HCV infection was diagnosed, with positive HCV-RNA, none of them started anti-HCV treatment at the moment of the study.
Among patients with previous HCV infection, 5/14 (36%) had also previous HBV infection, with positive HBcAb and negative HBsAg, and 2/14 (14%) had concomitant HIV infection, on treatment.
Similarly, among patients screened for HBV infection, 55/320 (17%) had previous HBV infection with positive HBcAb and negative HBsAg while in 2/372 (0.5%) patients, positive HBsAg was found: one had concomitant negative HBV-DNA and the other one was not tested for. Neither of them was on anti-HBV treatment nor had chronic HCV or HIV infection.
Overall, chronic HCV infection and chronic HBV infection were detected in 2/373 (0.5%) and 2/372 (0.5%) of the study population respectively.
Conclusions: The incidence of undiagnosed chronic HCV and HBV infection was low in our study population. However, serology test was performed in only 27% of patients admitted to our hospital during the first pandemic period and also HCV RNA and HBV DNA were not performed systematically in patients newly diagnosed as HCV or HBV infected, suggesting an underestimation of the problem.

Comorbidities

Cancers in HIV

P 56 CHARACTERISTICS OF A GROUP OF PLWH AND CANCER IN UMBRIA REGION

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Background: Cancers represent nowadays one of the main causes of morbidities and mortalities among people living with HIV (PLWH). The risk to develop neoplasms is higher in this special population compared to people without infection.
Aids Defining Cancers (ADC) have decreased in the last years due to early recognition of the infection and prompt beginning of antiretroviral treatment. Non Aids Defininig Cancers (NADC), instead, seem to increase probably because of the high frequency of co-infections and risk factors for neoplasms in this population, together with ageing. The virus itself through immune-suppression, immune-senescence and chronic flogosis may play a role in the risk of cancers.
Material and methods: Retrospective observational study on the population infected with HIV with diagnosis of cancer and at least one follow up visit at Infectious Diseases Outpatient Services of Santa Maria della Misericordia Hospital of Perugia from 2001 through 2020. Clinical, immunological and laboratory data were considered. Patients with insufficient data were excluded.
Results: Among the 170 patients which satisfied our inclusion criteria, the majority were men (67.6%), Italians (78.2%), infected through etherosexual intercourses (60.6%), alive at date (58.8%) and with an ADC (63.5%).
As for immune-virological assay, we found that patients with low level of CD4 and high viremia at diagnosis of HIV were diagnosed with cancer earlier than patients with better basal status.
In the whole population, KS was the most frequent cancer (31.2%), immediately followed by the others ADC and by NADC. Basal immune-virological assay was poorer in ADC.
Statistically, no variation of survival was seen according to sex, geographical origin, type of neoplasm, nadir of CD4 and zenit of HIV-RNA.
In the analyzed period, we saw a decrease of cases of ADC (except for KS) and an increase of NADC.
In particular, the cases of KS seen in the whole population raised from 26.2% before 2004 to 38.2% from 2010 through 2020. In the last decade 36 cases of KS were seen: they were mainly male (80.5%), Italians (77.7%), infected through sexual entercourses (58.3%). Basal immune-virological assay was poor and diagnosis of infection and tumor were simultaneously made in half of the cases.
Conclusions: A rapid commencement of antiretroviral therapy reduces opportunistic infections and diminishes chronic inflammatory state and the predisposition to cancer which is typical of PLWH.
NADC and KS seem to have increased in our population over the years. In particular KS was seen also in patients in good immunological conditions.
It is necessary to screen PLWH for principal tumours and treat risk factors for cancers.

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Comorbidities

Cancers in HIV

P 57 SUCCESSFUL MANAGEMENT OF PRIMARY CNS EVB-RELATED LYMPHOMA IN A LATE ADVANCED NAÏVE HIV

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Primary CNS lymphoma(PCNSL) is among the HIV-related lymphomas and its incidence is 2-6%in people living with HIV and 1000 times higher than in general population.Its clinical and radiological features mimic those of other diseases, which can be both oncological and infectious, including primary toxoplasma infection. Most of AIDS-associated PCNSL are high grade B cell lymphomas and EBV plays a dominant role in their development. Several analyses have tried to establish a cut off of EBV DNA loading in CSF as a diagnostic criterion, but histopathologic confirmation remains the necessary tool to get diagnosis. There are also debates about treatment: high-dose methotrexate, intrathecal rituximab, radiotherapy, or HAART alone. Some studies have demonstrated also valganciclovir's activity on EBV viral load.

Case Report: A 53-y.o. patient was admitted to our department in January after testing positive to HIV test, performed due to the presence of oral candida, purplish skin lesions, compatible with Kaposi's Sarcoma and right hemiparesis (at cerebral TC:hypodensity in left capsular nucleus with shaded hypodensity of the subcortical white matter in front-parietal ipsilateral).

Given the suspect of cerebral toxoplasmosis, therapy with cotrimoxazole and HAART were administered.Cerebral MRI showed an area, in the basalis nucleus, with a perilesional oedema and to a spinal tap which demonstrated high HIV-RNA and EBV-DNA load and a negative toxo PCR. He underwent serial MRI, which showed a slight but progressive size reduction. In the meantime, the patient recovered full motility and sensitivity functions.

Although PCR was negative, given the low molecular test sensitivity and the patient's clinical condition improvement, the diagnosis of toxoplasmosis was confirmed.

Spinal tap and MRI were repeated in March: EBV DNA load increased, as well as lesion size. Therefore, patient underwent a open biopsy by neuronavigation, showing a cerebral large B cell lymphoma.

The patient also presented Kaposi's sarcoma, which progressively worsened during hospitalization and in mid-February he even developed diffuse CMV infection; therefore doxorubicin and valganciclovir therapy was administered.

Considering the patient's comorbidities, ongoing chemotherapy and progressive response to HAART, decision was taken to not initiate any direct therapy to lymphoma.

Following the brain biopsy, the patient underwent a spinal tap which showed a reduction of CNS EBV DNA load and a cerebral MRI showed a reduction of lesion size. The patient's motility and autonomy improved progressively. He was discharged in April and nowadays he walks without auxilium.

Discussion: Our case suggests that a high EBV load could be a predictive marker for PCNSL and that it should be used to speed up the diagnostic process and to avoid intraoperative risks.

Moreover a therapeutic approach based on HAART and ganciclovir could be effective when EBV contribution to lymphoma's progression is predominant.

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Comorbidities

Cancers in HIV

P 58 EPIDEMIOLOGIC RESULTS FROM THE FIRST TWO YEARS OF ACTIVITY OF A NEWLY ESTABLISHED AMBULATORY FOR ANAL CANCER PREVENTION IN ROME

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Background: Preventive screening for anal cancer in HIV+ MSM and HIV+ persons with HPV-associated dysplasia is suggested by national and international HIV guidelines. High resolution anoscopy (HRA) represents the optimal exam to identify and treat anal cancer precursors; HPV DNA test and anal cytology take part to the process and give important additional information. In June 2019 we started a weekly ambulatory devoted to the prevention of anal cancer in HIV+ individuals. Here we report the results of the first two years of activity of the ambulatory.

Materials and methods: Screening for anal cancer is proposed to HIV+ MSM and subjects with cervical, vaginal, vulvar or penile intraepithelial neoplasia as part of clinical follow-up routine. Screening is performed through HPV DNA test, anal cytology and HRA, these exams are conducted during the same visit. Biopsies of suspected dysplasia are performed during HRA. Histology defined high grade squamous intraepithelial lesions (HSIL) are treated trough local ablation with an Infrared Coagulator (IRC). Individuals with low grade squamous intraepithelial lesions (LSIL) and high-risk subjects without anal dysplasia undergo periodic follow-up.

Results: 251 individuals have been screened to date. 11.2% of the ambulatory population is represented by women. 2.7% of the population is represented by male to female trans genders. 1 MSW performed the screening due to previous diagnosis of penile cancer. Mean age of the female population is 41.2 +/- 2.5 years; mean age of male subjects is 45.9 +/- 11 years. All participants were on stable and effective antiretroviral treatment. Mean T CD4 nadir was 412 +/- 60 cells/uL in women and 278 +/- 223 cells/uL in men. T CD4 count at the time of evaluation was 832 +/- 105 cells/uL in women and 726 +/- 298 cells/uL in men.

To date, 32.6% of the population underwent a follow-up visit subsequent to baseline screening, while 9.1% of subjects underwent at least 2 follow-up visits.

HPV DNA tested positive in 78.6% of women and 86.4% of males. High-risk genotypes were observed in 45.4% of HPV+ women and 56.3% of HPV+ men.

Anal cytology showed normal result in 91% of women and 34.6% of men, LSIL in 9% of women and 64.8% of men, HSIL in 0% of women and 0.6% of men.

HRA driven histology showed LSIL in 36.3% of women and 82% of men, HSIL was observed in 9% of women and 18% of men. Concordance rate between performed biopsies and dysplasia was 100% in women and 98.2% in men.

Recurrence of HSIL on the same area within 12 months from treatment was 16.6%.

Conclusions: Although the highest risk for anal cancer is traditionally observed in HIV+ MSM, prevalence of anal HPV infection and anal dysplasia is also high in HIV+ women and men with genital dysplasia. Histology proven HSIL of the anal canal were found in individuals with normal cytology or LSIL. Screening with HRA for the prevention of anal cancer should be part of routine follow-up of high-risk HIV+ individuals.

Comorbidities

Cancers in HIV

P 59 MALIGNANCIES IN HIV PATIENTS: A RETROSPECTIVE STUDY IN AN ITALIAN UNIVERSITY HOSPITAL AND SYSTEMATIC REVIEW OF LITERATURE

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Background: Highly active antiretroviral therapy (HAART) is changing the prevalence of malignancies in HIV patients, but still few studies have been carried out in Italy and in the world in this regard. The purpose of this paper is to describe and analyze the malignancies occurred in our cohort of PLWH, to compare our data with those of similar paper found through a systematic review of the literature of the last 20 years and to evaluate the epidemiological change of malignancies in HIV patients.
Methods: medical records from the Sicilian Reference Regional Centre for HIV/AIDS in Palermo, Italy, have been collected to perform a retrospective study from 1997 to 2019. Our data were compared with data from papers collected through computerized search on PubMed combining the terms ((malignancy[Title/Abstract]) OR (neoplasm[Title/Abstract]) OR (malignant[Title/Abstract]) OR (cancer[Title/Abstract])) AND (HIV) AND (prevalence) for the period between January 2000 and July 2020. An article was considered eligible for inclusion in the systematic review if it reported detailed data on prevalence of cancer in all HIV patients, both AIDS-defining cancers (ADC) and non-AIDS-defining cancers (NADC).
Results: a total of 789 HIV positive patients were included in the study, with 5607 person-year of follow up. Seventy-six cases of malignancy in ours PLWH were collected: 43 cases of ADC (56.6%) and 33 of NADC (43.4%). In particular, the diagnosed tumors were: Kaposi sarcoma (KS) (27 cases, 35.5%), non-Hodgkin lymphoma (NHL) (14 cases, 18.4%), head neck cancer (6 cases, 7.9%), bladder cancer (4 cases, 5.3%), Hodgkin lymphoma (HL) (4 cases, 5.3%), anal cancer (3 cases, 4%), cervical cancer (2 cases, 2.6%). Furthermore, in order to compare our data with data from other papers, 22 articles describing prevalence of malignancies in HIV patients, published between the years 2003 and 2020, were finally considered. Year of enrolment before 1993, male gender, older age at enrolment, intravenous drug use, low CD4 cell count, AIDS event, cancer occurrence and the absence of antiretroviral therapy were all associated independently with risk of death.
Conclusions: malignant cancers continue to be a significant cause of PLWH morbidity and mortality. Our retrospective study revealed a high percentage of NADC, apparently on the rise in recent years. There is a greater distribution of deaths over time in the case of NADC, on the other hand, in the case of ADC there is a greater number of deaths in the first years since the diagnosis of defining AIDS cancer. Progressive aging, the role of behavioural risks, such as smoking and alcohol intake and other viral co-infections could adversely affect the NADC epidemic. Choosing the appropriate primary prevention strategies through customized monitoring of these patients is fundamental and future studies will be needed in order to promptly administer specific intervention.

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Comorbidities

HIV and nervous system

P 60 EVOLUTION OF COGNITIVE PERFORMANCE OVER THE LAST TEN YEARS IN PEOPLE LIVING WITH HIV

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Background: After the introduction of combined antiretroviral therapy (cART) the prevalence of the most severe forms of HIV-associated Neurocognitive Disorders (HAND) in people living with HIV (PLWH) was significantly reduced. Principal last breakthroughs in cART can be identified in 3 moments: the introduction of the second generation protease inhibitors (PI) in 2007, first generation integrase inhibitors (INI) in 2011, and second generation INI in 2015.
Our aim was to compare global cognitive performance (GCP) in a HIV positive population among these 3 periods.
Method: We performed a retrospective, cross-sectional analysis of a monocenter dataset including 412 PLWH on cART who underwent a comprehensive neuropsychological assessment (NPA), exploring memory, attention, language, executive functions and fine motor abilities, during routine clinical care between November 2008 and September 2019. GCP was measured by transforming raw scores at each task into standardized Z-scores and averaging to calculate a composite total score.
We compared GCP among the 3 groups based on NPA date: 0 (2008-2010, n=227), 1 (2011-2014, n=99), 2 (2015 -2019, n=86). Factors associated to GPC were explored in the overall population.
Results: PLWH were 65.3% male with a median age of 48 yrs (IQR 42-55) and a median education of 13 yrs (IQR 8 -15). Median time from HIV diagnosis and first cART were 12 (IQR 4.8-18) and 9.6 (IQR 3.7-14) yrs, respectively. Overall 87.4% of PLWH showed HIV-RNA <50 copies/mL, with a median CD4 cell count of 162 cells/µL (IQR 55-273) at nadir and 576 cells/µL (IQR 421-757) at the time of NPA. Subjects belonging 3 groups significantly differed in several clinic and demographic characteristics (see Table 1).
GCP was significantly higher in group 2 when compared to group 0 [mean 0.40 (SD 0.91) vs -0.16 (SD 0.61); p<0.001] and to group 1 [mean 0.40 (SD 0.91) vs -0.27 (SD 0.91); p<0.001]. Furthermore, asymptomatic neurocognitive impairment (ANI) was significantly less frequent in group 2 than group 1 patients [10 (11.6%) vs 28 (28,3%); p= 0.005].
Higher GCP was associated to most recent NPA date (β 0.16; 95% CI 0.04/0.28 p=0.007), younger age (β -0.01; 95% CI 0.00/0.02; p=0.001), higher education (β 0.07; 95% CI 0.05/0.09; p<0.001), longer time from HIV diagnosis (β 0.01; 95% CI 0.00/0.02; p=0.015), lower plasma viremia (β -6.40; 95% CI 0.00/0.001; p<0.001) and higher CD4 cell count at nadir (β 0.001; 95% CI 0.00/0.001 p=0.004) after adjusting for INI use (β -0.04; 95% CI -0.26/0.18; p= 0.732).
Conclusion: In our population, GCP was significantly improved from 2015 onwards and then GCP improvement seemed to be driven also by clinical factors such as lower viremia and higher CD4 cell count at nadir.

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Comorbidities

HIV and nervous system

P 61 A WINNING PARASITE: HIGH PREVALENCE OF TOXOPLASMA GONDII-SEROPOSITIVITY IN PATIENTS WITH HIV INFECTION NAÏVE TO ANTIRETROVIRAL THERAPY

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Background: Toxoplasmosis is the most common opportunistic infection affecting the central nervous system in patients with AIDS and it usually develops from reactivation of a latent infection. The probability of suffering from it is estimated to be 30% among people living with HIV (PLHIV) with CD4 counts <100 cells/microL who are T. gondii-seropositive and are not receiving effective prophylaxis and antiretroviral therapy (ART).
The incidence of toxoplasmosis in PLHIV is associated with T. gondii-seroprevalence and it depends on geographical region, age, and nutritional habits.
A recent metanalysis, found that pooled prevalence of HIV and T. gondii co-infection is 26.3% in high-income countries. In Italy, T. gondii-seroprevalence in PLHIV is yet to be thoroughly described.
Our study aims to assess the prevalence of latent infection in patients diagnosed with HIV in our clinic in the last three years.
Material and methods: We retrospectively analyzed data from all ART-naïve PLHIV admitted to the HIV outpatient Clinic of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico from August 2018 to July 2021. At HIV diagnosis, demographic, epidemiological, laboratory test data were collected. Anti-T.gondii IgG antibodies were detected from sera samples collected at baseline by chemiluminescence. Data were analyzed with R version 4.0.3 using Fisher's Exact test and Mann-Whitney tests for categorical and continuous data, respectively.
Results: Fifty-one new diagnoses were analyzed. Patients were young with a median age of 39.0 years (IQR 31.5-47.0), males (45, 88.2%), Italian (35, 68.6%), male who have sex with men (MSM) (34, 69.4%), generally with no comorbidities (36, 70.6%). Overall, median HIV viral load was 5.1 (IQR 4.7 – 5.7) log10 copies/mL with a CD4+ count of 316.0 (IQR 144.5 – 529.0) cells/mm3 and a CD4/CD8 ratio of 0.3 (IQR 0.1 – 0.5).
At baseline, T. gondii-seroprevalence was 41.7% (20/48) with no statistical difference in any of the demographic, clinical and laboratory information investigated.
The prevalence of latent infection in our cohort is significantly higher compared to the pooled prevalence for western and central Europe and North America reported in literature (41.7% vs. 30.1%, p<0.0001).
During the study period, three patients developed toxoplasmosis: two with a cerebral localization and one during pregnancy.
Conclusions: In our outpatient unit, T. gondii-seroprevalence in newly diagnosed HIV ART-naïve patients was higher than the one described in literature for high-income countries.
A high seroprevalence might result in increased incidence of toxoplasmosis: this highlights the need to improve the diagnostic process and achieve adequate adherence to ART and prophylaxis.
Our findings, however, are limited by the small sample size and, to reflect the current Italian seroprevalence of T. gondii infection in PLHIV, need to be corroborated by larger and multicentric studies.

Comorbidities

Non infectious comorbidities in HIV

P 62 FACTORS ASSOCIATED WITH SIGNIFICANT WEIGHT GAIN IN HIV-1-INFECTED PATIENTS STARTING AN INITIAL ANTIRETROVIRAL THERAPY: A CASE-CONTROL STUDY

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Objectives: Weight gain is frequently observed among HIV-1-infected patients starting an initial combination antiretroviral therapy (cART), and has been associated with the use of integrase strand transfer inhibitors (INSTIs). Aim of our study is to assess risk factors associated with significant weight gain in cART-naïve HIV-1-infected persons.
Methods: A retrospective, case-control study was conducted to assess risk factors associated with significant weight gain (defined as an increase >5% of the baseline body weight) after 12 months of the initial cART.
Results: A total of 206 patients (171 men, mean age 44.4 years) were enrolled into the study: 84 subjects with significant weight gain (cases) and 122 with not significant weight gain (controls). The mean (+SD) weight gain after 12 months of initial cART was +3.55 (+1.62) Kg among cases and +1.46 (+0.77) Kg among controls. Factors associated with significant weight gain were female sex (OR 1.82; 95% CI, 1.31 to 2.38), age >60 years (OR 1.87; 95% CI, 1.38 to 2.41), CD4+ lymphocyte count <350 cells/mmc (OR 2.41; 95% CI, 1.73 to 3.08), males who have sex with males (MSM) risk category (OR 1.57; 95% CI, 1.11 to 2.08), current cART including INSTIs (OR 2.31; 95% CI, 1.67 to 2.89) or tenofovir alafenamide/emtricitabine (TAF/FTC) (OR 1.74; 95% CI, 1.21 to 2.12), vitamin D deficiency (OR 2.32; 95% CI, 1.69 to 2.95), elevated fasting insulin levels (OR 2.61; 95% CI, 1.92 to 3.38), and body mass index (BMI) >25 Kg/m2 (OR 2.18; 95% CI, 1.53 to 2.89). On the other hand, CD4+ lymphocyte count >600 cells/mmc and injecting drug use were associated with a lower risk of weight gain.
Conclusions: In our case-control study, a significant weight gain after cART initiation seems to be multifactorial, and associated with female sex, low CD4 cell count, vitamin D deficiency, fasting hyperinsulinemia, and use of INSTIs or TAF/FTC.

Comorbidities

Non infectious comorbidities in HIV

P 63 LOW VITAMIN D CONCENTRATION IS ASSOCIATED WITH HYPERCOAGULABLE STATE HIV-1-INFECTED PATIENTS ON COMBINATION ANTIRETROVIRAL THERAPY

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Background: Vitamin D insufficiency may lead to secondary hyperparathyroidism (HPT) and is often associated with abnormal coagulation tests and prothrombotic effect in general population, but data among HIV-infected patients are lacking still today.
Patients and methods: A cross-sectional study was performed to investigate correlation between serum level of 25 (OH) vitamin D and presence of hypercoagulable state in adult HIV-infected patients on stable antiretroviral therapy and with age>40 years. Vitamin D insufficiency was defined as serum level <30 ng/mL, and hypercoagulable state as the presence of plasma D-dimer >500 ng/mL or von Willebrand activity >160% or fibrinogen >440 mg/dL.
Results: On the whole, 214 patients were enrolled: 85% were men, 94% Caucasian, and the mean age was 48.3 years (range, 40-75). The mean CD4 T lymphocyte count was 522 cells/mm3, 191 (89%) had plasma HIV RNA <20 copies/mL, 58% were smoker, 18% had hypertension, 7% had diabetes mellitus, 6% had coronary artery disease, 5% had peripheral vascular disease. The mean serum concentration of vitamin D was 35.2 ng/mL, 102 (47.7%) patients had a vitamin D insufficiency, and hypercoagulable state was reported in 58 (27.1%) subjects. The mean vitamin D concentration was significantly lower among patients with hypercoagulable state than among those with normal coagulation markers (15.2 vs 36.5 ng/mL, p<0.001). In the multivariate linear regression analysis adjusted by confounding factors, vitamin D insufficiency was significantly associated with hypercoagulable state (OR 2.89, 95% CI 1.92-3.75, p<0.001), increased D-dimer (OR 2.41, 95% CI 1.58-3.12, p<0.001), increased fibrinogen (OR 1.97, 95% CI 1.32-2.54, p=0.023), hypertension (OR 1.86, 95% CI 1.28-2.71, p=0.037), and smoking (OR 1.66, 95% CI 1.19-2.26).
Conclusions: In our study, HIV-infected patients with vitamin D insufficiency had a significantly higher risk of hypercoagulable state than those with adequate levels, suggesting a central role of vitamin D in the pathogenesis of coagulation disorders also in HIV-positive people.

Comorbidities

Non infectious comorbidities in HIV

P 64 COGNITIVE PROFILE AND FUNCTIONAL PERFORMANCE IN OLDER PEOPLE LIVING WITH HIV: A COHORT STUDY

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Background: As the introduction of ART has deeply revolutionized the life expectancy of people living with HIV since the 90s, PLWH must deal with new challenges: aging with HIV appears to bring a higher risk of comorbid conditions in addition to usual geriatric syndromes and functional impairments. Frailty seems to affect adults with HIV at younger ages, and these populations tend to have higher rates of social isolation and loneliness usually at higher risk of neurocognitive decline.

Material and methods: PLWH over 64 years old were enrolled from the Outpatient Infectious Diseases clinic of Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome and were compared with historical geriatric cohorts without HIV infection paired by age and clinical characteristics. The patients were evaluated during 4 meetings (1 phone interview and 3 visits); SARC-F, Q9-SunFrail, FRAIL questionnaires were offered as well as performance tests (ADL, IADL, SPPB, TUG, Hand grip), DEXA, MOC, BMI, Mental Deterioration Battery, EKG, blood tests. Further referrals were offered according to the initial findings (osteoporosis and motor disorders assessment, neuroimaging). Data were studied by variance analyses and χ^2 test.

Results: From September 2020 to May 2021, data about 179 patients (52 PLWH) were collected. General characteristics of enrolled patients are reported in Figure 1a. As shown in Figure 1b, PLWH showed a higher degree of frailty and sarcopenia: the proportion of PLWH with SARC-F> 4 were higher than controls (p=0.008), as well as FRAIL questionnaire ≥ 3 was more common in PLWH than controls (p=0.004): these differences were confirmed even in the analysis stratified by sex. As reported by Q9-Sunfrail questionnaire results, risk of frailty resulting from polypharmacy, memory loss, solitude and lack of emotional support was higher in PLWH than controls (Figure 1c). Most participants had SPPB results compatible with frail subject (3-9 points) while time UP and GO test results were within the normal range (minimum 6.4 seconds to maximum 11 seconds) as well as for hand grip evaluation (even if the results were below average in half subjects). Neuropsychological assessment (MDB) pointed to a deficit in memory and attention-concentration impairment in PLWH alongside less severe language and executive functions deficits (Figure 1d).

Conclusions: These results showed how older PLWH are more at risk of frailty and disability than the same population without HIV infection. Frailty determinants in older PLWH seem to be related to mild neurocognitive impairment and to lack of social support. Prevention interventions to minimize frailty and disability in this population are highly recommended and further studies are needed to better address this topic.

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Comorbidities

Non infectious comorbidities in HIV

P 65 WEIGHT CHANGES IN OVERWEIGHT AND OBESE PEOPLE LIVING WITH HIV. RETROSPECTIVE ANALYSIS OF 10-YEARS OF FOLLOW UP

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Background: The increase in life expectancy of people living with HIV (PHIV) has led to an increase in the prevalence of metabolic comorbidities in recent years, in particular overweight and obesity, the causes of which are currently being researched. The aim of this study is to evaluate the annual weight gain of overweight and obese PHIV and which clinical and therapeutic factors are associated with greater weight gain.
Materials and methods: Retrospective cohort study conducted in the period March 2011-March 2021. PHIV with BMI ≥25 kg/m² (overweight) or ≥30 kg/m² (obese) were included. The association among annual weight gain and clinical and pharmacological variables was tested with a linear regression model.
Results: One hundred and sixty-four PHIV, 73% male, were included in the study. Median age at the time of enrollment was 53.5 (±10.34) years, BMI 29.7 (±4.35) kg/m² with 34% of obese PHIV and 66% of overweight PHIV in the cohort. Almost all (96%) had HIV-RNA <50 copies/mL, with mean CD4+ T lymphocytes 640 (IQR 457.50-914.50) cells/mm3.
Weight gain was found in 84.5% PHIV. The average weight gain was 1.30 kg/year (±1.70); +0.91 (±1.20) kg/year in overweight and +2.05 (±2.21) kg/year in obese PHIV. At the univariate analysis, a greater weight increase was associated to higher HIV viremia copy/years (VCY, β+0.30, 95%CI +0.12; +0.36, p<0.001), while an inverse correlation was found with the cumulative exposure to protease inhibitors (PI, β-0.15, 95%CI -0.08; 0.00, p=0.08) or non-nucleoside reverse transcriptase inhibitors (NNRTI, β -0.18, 95%CI -0.011; -0.001, p=0.021), older age (β -0.23, 95%CI -0.07; -0.01, p=0.003) and total years of HIV infection (β -0.31, 95%CI -0.08; -0.03, p<0.001). No correlation was found between cumulative or current exposure to integrase inhibitors (INI) and weight change during the study period. After adjusting for the main confounders, the years of HIV infection remained the only factor significantly correlated to the weight trend over the years, (β -0.32, 95%CI -0.08; -0.03, p<0.001) with an inverse correlation between years of infection and weight gain (Table).
Conclusions: Among overweight and obese PHIV, 84.5% increased their weight over a 10-year follow up. The extent of weight increase was inversely proportional to the years of HIV infection. Our findings suggest a steeper increase of global weight soon after the diagnosis of HIV infection, consistently with a "return to health" phenomenon, and a slower but continue increase over the next years, during a prolonged follow up of 10 years, independently by the cumulative time spent on PI, NNRTI and INI drugs.

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Comorbidities

Non infectious comorbidities in HIV

P 66 MANAGEMENT OF POLYPHARMACY IN PEOPLE LIVING WITH HIV: A 5-YEAR EXPERIENCE OF A MULTIDISCIPLINARY OUTPATIENT CLINIC

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Background: The availability of potent antiretrovirals has transformed HIV infection into a chronic disease. However, there are continuing challenges in managing HIV infection, particularly in older patients, who often experience age-related comorbidities resulting in complex polypharmacy and an increased risk for drug-drug interactions. For these reasons, in 2016 we set up an outpatient clinic for the management of polypharmacy in PLWH (Gestione Ambulatoriale Politerapie [GAP]). We here describe the results of our 5-year experience.
Material and methods: The database of GAP, with nearly 1000 PLWH on active follow-up, was retrospectively investigated to search for those with at least two recorded visits from September 2016 to June 2021. Data on patients' demographic characteristics, antiretroviral regimens and number of co-medications were also collected.
Results: 556 PLWH were included in the GAP database. They were mostly men (70%), with mean age of 55±11 years and a mean follow-up of 19±11 years after the diagnosis of HIV. Overall, the enrolled patients were given 4.2±2.7 drugs (from 1 to 17 drugs) 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); a trend for more drugs in males than females was also observed (4.3±2.8 vs. 3.8±2.6; p=0.048).
71% of PLWH were on triple antiretroviral regimens (21% TAF/FTC/RPV, 17% ABC/3TC/DOLU, 14% TAF/FTC/BIC); among the PLWH on dual antiretroviral therapies (29%) the most prescribed regimens were 3TC/DOLU (22%), DOLU/DRV/c (15%) and DOLU/RPV (14%). PLWH on dual therapies (29% females) were significantly older (58±9 vs. 54±11 years; p<0.001), had a longer history of HIV (21±9 vs. 18±11; p=0.003) 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.
39% of PLWH switched their antiretroviral therapies at the second GAP visit: in 32% of cases the switch resulted in a transition from triple to dual therapy. A significant reduction in the PLWH on booster-based antiretroviral regimens was observed moving from the first to the second GAP visit (53% vs. 23%; p<0.0001). Main reasons for the change in the antiretroviral regimens were treatment simplification (56%), drug toxicity (18%) or treatment failure (7%); in 20% of cases the reason was unspecified.
Discussion: The high prevalence of polypharmacy in PLWH, especially in the elderly, highlights the need for ongoing education on prescribing principles and the optimal management of individual patients. A multidisciplinary approach involving physicians and clinical pharmacologists could help achieve this goal. Simplified antiretroviral regimens (i.e. dual, booster-free) might be considered in the context of comorbidities and polypharmacy in older PLWH.

Comorbidities

Non infectious comorbidities in HIV

P 67 METABOLIC IMPACT OF SWITCHING FROM E/C/F/TAF TO B/F/TAF IN HIV-1 INFECTED PATIENTS

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Background: The management of the metabolic disease and weight gain in patients living with HIV (PLWH) is becoming increasingly important, particularly in those treated with antiretroviral therapy (ART) including integrase strand transfer inhibitors (INSTIs). To date, the role of cobicistat and the metabolic impact of different INSTIs is not clear. The aim of our study was to evaluate the variation of bio-humoral parameters and body composition, as performed by bioimpedance vectorial analysis (BIVA), in patients switching from E/c/F/TAF to B/F/TAF.
Material and methods: Starting from December 2019, all HIV-infected subjects who underwent a treatment shift from E/c/F/TAF to B/F/TAF and willing to participate to the study after informed consent, were enrolled and submitted to BIVA (BIA 101 New Edition, Akern, Florence, Italy)(50Hz) at baseline (T0), 6 (T6) and 12 months (T12) after therapy change. At any timepoint, fat mass (FM), fat free mass (FFM), skeletal muscle mass (SMM) and basal metabolism (BM) were assessed. Moreover, weight and plasmatic lipid concentrations (triglycerides, HDL and LDL cholesterol) were measured at each timepoint. Clinical and immuno-virologic features of all patients were retrieved from the internal database. Descriptive statistics and univariate association models were performed; a p value <0.05 was considered statistically significant.
Results: Overall, 34 HIV-infected patients (27 males) have been enrolled to date, with median age (q1, first-q3, third quartile) of 55 (47-60) years; a median (q1-q3) of 746 (585-920) CD4 cells/mmc was reported at baseline. Major recorded comorbidities were dyslipidemia (44%) and mild kidney impairment (21%) (Table 1). At time of writing, follow-up data were available for 24 individuals at T6 and for 22 at T12; data are shown in Table 2. At T12, a weight gain was observed with a median 0.8 kg increase from T0 (p=0.712). By BIVA, a median increase of FM (2.00 Kg/m; p=0.985) was recorded, while a trend towards a decrease of FFM (-1.9 Kg/m; p=0.985) was noticed, both not reaching statistically significance. Moreover, a significant decrease in both total cholesterol [median -13.5mg/dL; p=0.026] and LDL-cholesterol [median -23 mg/dL; p=0.044] was observed.
Conclusions: Based on the results of the bioimpedance analysis, our study suggests not significant changes of the body composition, while a decrease of total and LDL-cholesterol concentrations was observed 12 months after switching from E/c/F/TAF to B/F/TAF. A wider sample and a longer follow-up is warranted

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Pathogenesis and Immunology

COVID-19 pathogenesis

P 68 COVID-19 PNEUMONIA WITH MIGRATORY PATTERN IN AGAMMAGLOBULINEMIC PATIENTS: A REPORT OF TWO CASES

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Background: X-linked agammaglobulinemia (XLA) is a primary immunodeficiency characterized by marked reduction of serum immunoglobulins and by early-onset infections. Coronavirus Diseases-2019 (COVID-19) in immunocompromised patients presents clinical and radiological peculiarities which have not yet been completely understood. We report two cases of migrant COVID-19 pneumonia in XLA patients.

Case reports: Both patients are young men affected by XLA. The first was a 26-year-old student who underwent intravenous immunoglobulin injections every three weeks. He was hospitalized in April 2020. The other one, a 41-year-old butcher, suffered from chronical sinusitis treated with oral antibiotics. He was admitted in December 2020. Both presented with high fever in the absence of respiratory symptoms. Baseline CT scan showed ground glass opacities (GGOs) compatible with interstitial pneumonia. SARS-CoV-2 was amplified on RT-PCR from nasopharyngeal swab and bronchoalveolar lavage, respectively. Treatment with intravenous antibiotics, enoxaparin, remdesivir, and for one of them intravenous dexamethasone was initiated. No oxygen supply was needed. Due to the persistence of fever despite treatment, radiological follow-up was performed after approximately 15 days. Interestingly, in both patients a peculiar and specific radiological evolution was observed: a gradual resolution of the previous opacifications and consolidations together with the appearance of new infiltrates in different lung areas. Microbiological tests confirmed that none of them had cleared the virus. No other pathogens were isolated. In both patients, the virus was eventually cleared with high-dose immunoglobulins in the first case and a combination of anti-inflammatory drugs and intravenous anakinra.

Conclusion: Chest CT has a potential role in the diagnosis, detection of complications and prognostication of COVID-19. Little is known about COVID-19 in immunocompromised patients. We reported two cases of patients affected by XLA with SARS-CoV-2 infection and peculiar CT findings. Both presented with extensive bilateral GGOs which underwent complete resolution; however, follow-up CT showed new pulmonary opacities in different areas of both lungs with a migratory pattern. Their radiological findings appear compatible with the persistence of an initial pneumonia which however never seems to progress to more advanced stages of disease as observed in immunocompetent patients. On the other hand, COVID-19 should be included in the differential diagnosis of migratory pulmonary opacities along with organizing pneumonia (OP). Confirmed radiologically and histologically, OP, as an active and sometimes aberrant lung repair process, may represent the evolution of COVID-19 in patients with immunological disorders. Further studies are required to determine whether these findings could be considered recurrent radiological manifestations of SARS-CoV-2 infection in primary immunodeficient patients.

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Pathogenesis and Immunology

COVID-19 pathogenesis

P 69 MASS CYTOMETRY REVEALS REDUCTION OF CIRCULATING CD4 T FOLLICULAR HELPER AND CD4 T CELL EXHAUSTION IN AGED COVID-19 PATIENTS

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Aim: One the major death risks in COVID-19 patients is increasing age, but scanty data exist on the immunological differences between young and aged patients with severe or critical COVID-19. Therefore, there is an urgent need to identify key players driving protective or pathogenic immune responses in aged COVID-19 patients.

Methods: We studied peripheral blood mononuclear cells (PBMC) from 10 healthy donors (HDs) and 17 COVID-19 patients with severe symptoms who were divided in <60 years old (CUN, n=7) and >70 years old (COV, n=10). We optimized a mass-cytometry (CyTOF) panel containing Maxpar® Direct™ Immune Profiling Assay™(Fluidigm), a dry 30-marker antibody panel (viability marker Cell-ID™ Intercalator-103Rh included) plus the addition of 6 drop-in catalog antibodies (Fluidigm) and 2 custom-conjugated mAbs, for a total of 38 markers. The markers used were: CD3, CD19, CD45, CD4, CD20, CD45RA, CD8, CD25, CD45RO, CD11c, CD27, CD56, CD14, CD28, CD57, CD16, CD38, CD66b, CCR7, CXCR3, CXCR5, HLA-DR, IgD, TCRγδ, CD123, CD127, CD161, CD294, CCR4, CCR6, CXCR1, PDL1, CD80, CD40, CD24, PD1-1, CD11b/MAC, CD21, IgM. High-dimensional analysis was performed in viable CD45+ cells using Cytometry dATa anALYSis Tools v1.14 (CATALYST). Proliferation assay was performed on PBMC using CFSE on after 16h in vitro stimulation with CD3/CD28 and IL-2.

Results: Among myeloid and lymphoid compartments we could identify 28 cell clusters. COVID-19 patients showed an increase of activated transitional memory (TM) CD8 T cells, and a decrease in CD8 naïve T cells and mucosal associated invariant T cells (MAIT). We also observed a decrease in memory B cells and a huge increase in plasmablasts. In myeloid compartment, COVID-19 patients presented a substantial reduction of myeloid and plasmacytoid dendritic cells (DC) and an increase of low-density neutrophils (LDN). COV patients showed a decrease vs. CUN of both central memory (CM) CD4 T cell, CD8 naïve T cells and memory B cells, and an increased level of both mature CD57+ natural killer and plasmablasts. In COV vs. CUN, central memory CD4 T cells and B cells showed a decrease and increase, respectively, in their proliferation index and percentage of dividing cells. No differences were reported within CD8 compartment in COV vs. CUN patients. Within CD4 T cells, we observed that COV patients presented higher level of activated CM cells and activated TM expressing PD-1. COV patients displayed a reduction of non-activated TM and circulating follicular T cell (cTfh). Assessing the surface PD-1 expression on both CD4 and CD8 T cells revealed that CD4 CM, TM and cTfh of COV patients expressed higher level of this exhaustion marker. We did not observe any alteration in PD-1 expression among CD8 T cells.

Conclusions: Despite a high similarity of the immunological landscape among COV and CUN patients, elderly patients with severe SARS-CoV-2 infection are characterized by reduced cTfh and an exhausted CD4 T cell compartment.

Pathogenesis and Immunology

COVID-19 pathogenesis

P 70 PATHOGENIC HERV-W ENVELOPE IN SWAB SAMPLES AND IN T LYMPHOCYTES IS ASSOCIATED WITH THE RESPIRATORY OUTCOME OF COVID-19 PATIENTS

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Background: The identification of early biomarkers for predicting Coronavirus Disease 2019 (COVID-19) progression and of new therapeutic intervention for patient management are needed, considering that no standard therapeutic approach has been established yet. As recent findings that the Human Endogenous Retrovirus-W Envelope (HERV-W ENV) is activated in response to infectious agents and leads to various immune-pathological effects, the present study aimed to evaluated HERVs involvement during severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Materials and Methods: Residuals of naso-oropharyngeal swabs samples were collected at "Tor Vergata" University Hospital of Rome and the expression of HERV-K and HERV-W ENV, pro-inflammatory mediators, and also SARS-CoV-2 infection-related genes Angiotensin-converting enzyme 2 receptor (ACE2) and Nucleocapsid gene (N) have been analyzed by RT-Real time PCR. Moreover, HERV-W ENV expression in blood samples of hospitalized COVID-19 patients was analysed by flow cytometry and quantitative RT-PCR, and correlated with clinical signs, inflammatory markers, cytokine expression, and disease progression.

Results: A significant increase of the HERV-K and HERV-W ENV activity in parallel with the higher expression of pro-inflammatory mediators and ACE-2 and N gene has been observed in SARS-CoV-2 positive compared to negative swab samples and higher levels have been found in hospitalized patients. Moreover, a positive correlation between HERV-W ENV and IL-6, IL-10, TNF-alpha expression has been found. HERV-W ENV has been found expressed, both as mRNA and protein, in blood samples from COVID-19 but not in HDs. Lymphocytes displayed the highest values among all leukocytes, and CD3+ T cells showed the highest percentage of HERV-W ENV positive cells and correlated with the T cell differentiation, exhaustion, and senescence markers. Moreover, the percentage of HERV-W ENV-positive CD4+ T cells significantly correlated with coagulopathy and biochemical parameters associated with COVID-19 severity. Interestingly, a significant increase in the percentage of HERV-W ENV-positive lymphocytes across groups with different pulmonary involvement was observed. Notably, HERV-W ENV expression in swabs and in blood samples reflects the respiratory outcome of patients during hospitalization.

Conclusion: The data suggest HERV-W ENV as potential early biomarkers of the disease severity and contributing factor in the development and progression of COVID-19 and candidate it as a new potential therapeutic target.

Pathogenesis and Immunology

COVID-19 pathogenesis

P 71 IMMUNOLOGICAL PARAMETERS AND MICROBIOLOGICAL FINDINGS IN MECHANICALLY VENTILATED COVID-19 PATIENTS WITH SUSPECTED VENTILATOR-ASSOCIATED PNEUMONIA

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Background: Ventilator-associated pneumonia (VAP) is the most common infection acquired in the intensive care unit (ICU). To date, there is no diagnostic gold standard for VAP, and its diagnosis is based on presumptive scores. In COVID -19 patients, the viral disease itself and its therapies influence the clinical, laboratory and radiologic features required to achieve VAP diagnosis. Here we describe circulating and respiratory immune parameters as well as microbiological findings of suspected VAP in COVID-19 patients.

Material and methods: Prospective, single-center cohort study conducted from January 2021 to July 2021 in the COVID-19 ICU of the Policlinico di Milano.

At VAP suspicion, patients underwent blood exams, endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL) as per clinical practice. VAP was diagnosed according to the Centers of Diseases Control and Prevention definitions, which include positive BAL ≥104 colony forming unit (CFU)/mL or ETA ≥105 CFU/mL.

Flow cytometry analysis on fresh peripheral blood (PB) and BAL samples was conducted for the following immunological variables: i) lymphocyte (Ly), monocyte (Mo) and neutrophil (N) subpopulations and activation status (PB and BAL), ii) oxidative burst in Mo and N (PB).

Results: Twenty-five episodes of suspected VAP in 18 patients were included. Based on ETA and/or BAL results, VAP (18/25, 72%) and NO VAP (7/25, 28%) episodes were identified. The two groups did not differ by demographic or clinical parameters (Table 1).

ETA and BAL tested positive in 64% (16/25) and 44% (11/25) of episodes, with polymicrobial isolates in 2 and 1 case, respectively. Pseudomonas aeruginosa was the most frequent pathogen, found in 33% of both sampling cultures (6/18 ETA and 4/12 BAL). Table 2 and Figure 1 report concordance between ETA and BAL and microbiological findings.

No differences in circulating Ly, Mo and N subpopulations and activation status were found between VAP and NO VAP episodes. In BAL, VAP episodes were characterized by a higher percentage of N and lower of Ly and Mo as compared to NO VAP (N: mean 79.2% (SD 14.7) vs 46.7% (31.5), p >0.05; Ly: 6.2% (7.3) vs 29.0% (28.2), p 0.016; Mo: 7.9% (8.1) vs 11.1 (5.8), p>0.05). VAP episodes presented lower oxidative burst in circulating Mo and N than NO VAP, albeit with statistical significance only for non-activated Mo (mean fluorescence intensity (MFI): 425 (305) vs 930 (636), p 0.028). Table 3 and Figures 2 and 3 summarize the main immunological findings.

Conclusions: Preliminary findings suggest a different distribution of immune cells in BAL but not in PB between VAP and non-bacterial cause of respiratory dysfunction in mechanically ventilated COVID-19 patients. The lower MFI of circulating immune cells in VAP episodes possibly represents functional exhaustion during pulmonary bacterial infection. Differences in ETA and BAL results underscore the difficulty to achieve an accurate etiological diagnosis of VAP in COVID-19.

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Pathogenesis and Immunology

COVID-19 pathogenesis

P 72 SARS-COV2 POSITIVITY AT OROPHARYNGEAL SWAB AFTER RECOVERY: PERSISTENCE OF INFECTION, REACTIVATION OR REINFECTION?

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Background: The presence of neutralizing anti SARS-CoV2 antibodies in subjects who have contracted the infection suggests protection against following reinfections. Nevertheless, Literature reports cases of subjects who, after clinical recovery and negative swabs, developed the infection again. Reinfection with different strains and cases of reactivation of a previous infection have been described. Aim of this study is to describe clinical and virological characteristics of patients (pts) with a positive RT-PCR oropharyngeal swab for SARS-Cov2 after clinical and virological recovery of a previous COVID19 diagnosis .
Material and methods: pts admitted to the Infectious Diseases Unit of the University Hospital Maggiore della Carità di Novara between March 2020 and June 2021, who had a positive RT-PCR oropharyngeal swab for SARS-Cov2 after clinical recovery and a negative swab from a previous COVID19 diagnosis were analyzed. Values are reported as numbers (%) and median (IQR).
Results: Twentyseven patients (18 males), median age of 75 years old (47-95) with a previous diagnosis of SARS-CoV-2 interstitial pneumonia (78%) or SARS-CoV2 infection (22%), have been re-admitted to our Unit with a positive RT-PCR after a negative one. At the second admission, only 8 (30%) of them showed respiratory failure and only 2 (7%) had COVID -19 related symptoms (Table 1). Among 23 pts who underwent chest CT scan only 2 (7%) had interstitial pneumonia, while 3 (11%) had radiological findings consistent with scars. Median time between the first negative swab and the following positive test was 83 days (IQR 32-402), while median time to achieve a second negative RT-PCR swab was 10 days (IQR 2 -34). Three pts (11%) died within 30 days from admission, but none of them had a COVID-19 related death. Fifteen pts (55%) had more than three comorbidities. Variants detection was possible only in two cases, the others had a too low viral load to be sequenced.
Conclusions: Reinfections after the first episode of COVID-19 is increased by the presence of viral variants other than the native Whuan strain. The high prevalence of asymptomatic SARS-CoV2 positive subjects after virological recovery with a chest CT scan not significant for SARS-CoV-2 interstitial pneumonia, could be explained by a well-controlled reinfection by the patient's immune system or a reactivation of the previous infection due to prolonged persistence of the virus within the respiratory system. In both situations, the immune system control may play a role in the rapid negativization after the second episode. In the hypothesis of reactivation, the virus could remain latent in reservoir with a viral load mainly below the detection threshold. Although a low viral load is less dangerous in terms of transmission, the hypothesis of reactivation could have repercussions on the persistence of the circulation of the virus in the population, starting from subjects recovered from SARS-CoV2 interstitial pneumonia.

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Pathogenesis and Immunology

HIV cure

P 73 AN IN VITRO MODEL OF REVERSIBLE PROVIRAL LATENCY IN PRIMARY HUMAN MONOCYTE-DERIVED MACROPHAGES POLARIZED BY PRO-INFLAMMATORY M1-CYTOKINES

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Background: Combined anti-retroviral Therapy (cART) blocks HIV-1 replication, allowing a substantial recovery of immune functions and a life expectancy almost equal to that of uninfected people of the same age. However, cART must be taken daily for the rest of a patient's life in that treatment interruption causes rebound of virus replication and progression of disease in the vast majority of the patients. This is largely due to the existence of one or more viral reservoir(s) of infected CD4+ T cells and myeloid cells, especially tissue resident macrophages (Mø), unaffected by cART in which the virus is in a state of proviral latency.

In this regard, the international research effort is currently focused on defining: (1) the detailed immunological and molecular features of the lymphoid and myeloid associated HIV reservoirs as well as factors that modulate their state of latency and viral expression; (2) strategies and tools of immune-pharmacological eradication of the virus reservoirs or their containment and definitive silencing.

Material and methods: Our study has been primarily centered on an in vitro model of Mø reservoir, i.e. monocyte-derived macrophages (MDM) stimulated or not with the pro-inflammatory cytokines TNF-α (Tumor Necrosis Factor-α) and IFN-γ (Interferon-γ), with the aim of polarizing them towards M1 cells. M1 polarization of MDM has been characterized by our group as condition associated with a strong inhibition of virus replication in comparison to control, unpolarized-MDM. We then published (F. Graziano et al., Sci Rep 2018) that restimulation of infected M1-MDM with M1 cytokines lead to a state of reversible proviral latency.

Results: We have recently validated these results by visual means (looking simultaneously at cells harboring HIV DNA and expressing or not viral transcripts) in a collaboration with Dr. Joshua Vasquez, San Francisco University, California, USA. We are currently investigating the potential role and differences in the signal elicited by interleukin-34 (IL-34) and Macrophage Colony Stimulating Factor (M-CSF) in MDM, two cytokines that bind the same M-CSF receptor (R). Signaling through M-CSFR induces a fundamental signal for monocyte differentiation and survival, microglia and myeloid dendritic cells such as Langerhans cells in the skin. In particular, we are studying whether co-stimulation of IL-34-differentiated or M-CSF-differentiated M1-MDM are still responsive in terms of M1-induced restriction. Preliminary evidence suggests that MDM differentiation in the presence of IL-34, but not of M-CSF, could synergize with M1 cytokines in driving HIV-1 infection in a state of proviral latency.

Conclusions: M1-MDM represent a reliable and versatile model to dissect out factors and signals controlling proviral latency and its reversion in primary macrophages.

Pathogenesis and Immunology

HIV cure

P 74 TRANSIENT INCREASE OF PLASMA HIV RNA AFTER COVID-19 VACCINATION WITH MRNA-1272

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The latent viral reservoir is the main obstacle preventing HIV eradication. Vaccines have been evaluated as possible agents for "shock and kill" strategies. Due to the SARS-CoV-2 pandemic, a constantly growing proportion of individuals have received various vaccines against COVID-19, including those employing a novel mRNA technology. Despite having shown good efficacy and safety in PLWHIV, the effect of such compounds on HIV latency has yet to be evaluated. Previous studies have found transient increases in HIV VL after standard vaccinations (mostly after 7-14 days). This is most likely explained with a generalized inflammatory response with cytokine production, able to activate bystander cells harboring latent HIV. Here, we report the case of a man living with HIV who, having previously achieved stable viral suppression, experienced loss of viral control after receiving a dose of COVID-19 vaccine.

The patient, a 65-year-old male, was diagnosed with HIV in March 2020. Baseline plasma HIV RNA (viral load, VL) was 5,780,000 cps/mL and CD4+ count was 44/μL (3.6%, CD4/CD8 0.1%). No coinfection was diagnosed. Antiretroviral treatment (ART) with tenofovir alafenamide/emtricitabine/bictegravir was started two weeks after diagnosis, and well tolerated. Three months after ART initiation, VL was below 200 copies/mL and CD4+ count was > 200/μL. Six months after initiation the patient achieved VL suppression (< 50 cps/mL), confirmed by several subsequent determinations. In April 2021 the patient, suppressed for more than 6 months, received the first dose of mRNA-1273 vaccine (Moderna Biotech), which was also well tolerated, through the Italian vaccination campaign. Twenty-eight days later, before receiving the second dose, his blood samples were acquired for his quarterly routine bloodwork. HIV VL was 1,790 cps/mL, the patient was asymptomatic and blood chemistry was normal. Counseling was arranged. Questioned, the patient reported optimal adherence. Potential drug-drug interactions were screened and ruled out. Adherence to ART was indirectly confirmed by therapeutic drug monitoring, showing tenofovir trough concentrations (21 ng/L) within the expected range for TAF (10-25 ng/mL). Two weeks after the increase (and the second vaccine dose), a new bloodwork was obtained and VL was suppressed again.

Of note, C-reactive protein quantification was negative in our case; however, we might have documented the descending phase of a curve, as VL determination was at 28 days. To the best of our knowledge, this is the first report of plasma HIV RNA increase after a mRNA COVID-19 vaccine in a patient with documented adherence, possibly reflecting induced transcription. In the context of mass vaccination, our observation might be of use to guide the clinical practice of other physicians observing unexplained VL increases in ARV-adherent PLWHIV. Further studies are needed to evaluate the impact of novel mRNA vaccines as components of future eradication strategies.

Pathogenesis and Immunology

HIV immunology and immune-based therapies

P 75 EVALUATION OF A4-INTEGRIN ON T-LYMPHOCYTES IN HIV+ PATIENTS UNDER EFFECTIVE ANTIRETROVIRAL TREATMENT AND CHRONIC IMMUNE ACTIVATION

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Background: Despite effective antiretroviral treatment (ART) persistent immune activation is still an unsolved issue in people living with HIV and microbial products have emerged as potential drivers of this immune activation. During T cell activation, the expression of integrins changes to promote the entry of T cells into non-lymphoid sites. The α4β7 integrin promotes homing of T cells to intestinal sites and the Gut Associated Lymphoid tissue (GALT) is a key location for the HIV reservoir.

The aim of this study was to explore the expression of the α4-integrin in immune cells of HIV+ subjects under ART and evaluate the induction of α4-integrin expression on T-lymphocytes by different stimuli recognized by Toll-like receptors (TLRs).

Materials and methods: HIV+ patients under ART since at least 2 years and with undetectable HIV-RNA on enrolment and a group of healthy donors (HDs) were included in the study. Flow cytometry was used to evaluate T-lymphocyte subsets, their activation state (CD38 and HLA-DR) and α4-integrin median fluorescence intensity (MFI).

An in vitro peripheral blood mononuclear cells (PBMCs) system was used to understand the contribution of TLRs stimulation in inducing of α4-integrin expression on T-lymphocytes (R-848 for TLR7/8, LPS for TLR4). PHA and unstimulated conditions were used as controls.

Results: Sixty HIV+ patients (male/female: 41/19) with a median (IQR) age of 42.5 (38-52), mean CD4 cell count: 620/µl and 30 HDs (male/female: 16/14) with a median (IQR) age of 39 (33-47) were enrolled. CD4 and CD8 immune activation and α4-integrin expression on CD4 were increased in HIV+ subjects compared to HDs (p=0.0001, p=0.0002, p=0.0018, p=0.0404 and p=0.010, respectively). α4-integrin expression on CD4 was directly related to CD4 immune activation in HIV+ patients (Spearman ρ=0.4 p=0.0012). In vitro experiments conducted on 15 HIV+ patients and 15 HDs showed no significant differences in the expression of alpha-4 on CD4+ and CD8+ lymphocytes and related subpopulations after stimulation with IFN, as well as with the other ligands for the TLRs.

Conclusion: In HIV+ patients, α4-integrin was directly related to CD4 immune activation levels. Despite ART treatment and HIV suppression, gut-homing α4β7 positive CD4 were decreased in HIV+ patients compared to HDs. Targeting α4-integrin could represent a strategy for controlling persistent immune activation, restoring circulating gut-homing α4β7 positive CD4 and potentially reducing their infection in intestinal mucosa, thus reducing non-AIDS related morbidities.

From the in vitro study it was not possible to identify a stimulus, among those used, capable of inducing alpha-4 expression on T lymphocytes.

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Pathogenesis and Immunology

HIV immunology and immune-based therapies

P 76 VIROLOGICALLY SUPPRESSED IMMUNOLOGICAL NON-RESPONDERS

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Introduction: Nowadays, thanks to the therapies at our disposal, people living with HIV-1, who properly use antiretroviral drugs, reach out to a persistent virological suppression and a subsequent recovery of CD4 lymphocyte count, up to almost normal range values in most cases. Therefore, morbidity and mortality HIV-1-related have been dramatically reduced. However, there is a significant percentage of patients that are defined "immunological non-responders", showing persistent non-detectable viremia, nevetheless low or even decreasing CD4 lymphocyte counts.
Clinical Case: We present the clinical case of S.M.S. (m, 27 years old), coming from Guinea, sent to our clinic from the STD centre in June 2017, after testing positive to HIV-1 Ab-Ag on 31th of May 2021, performed during screening tests for a suspected lymphogranuloma venereum. At baseline blood tests he showed 89 CD4 lymphocytes/mmc and opportunistic infections resulted negative. He started cART with ABC/FTC/DTG and antibiotic phophylaxis against Pneumocystis jiroveci on the 8th of August 2017. His medical history is negative for hematological diseases. CART and primary prophylaxis have always been well-tolerated and properly taken, as evidenced by the persistent virological suppression found at each blood test performed during these years (HIV RNA <20 copies/ml since November 2017, more or less once every three months). The amount of CD4 lymphocytes has been gradually reduced over these years, ranging from 89/mmc (3%) on the diagnosis, to 42/mmc (4%) in November 2017, to 20/mmc (1%) in May 2018, till 11/mmc (1%) in December 2018. Then, in the context of a persistently suppressed viremia, there has been a progressive, slow increase untill today – in May 2021 S.M.S. CD4 were 52/mmc (3%). In the meantime, it was introduces a prophylaxis with azithromycin, then suspended. We have also recently stopped prophylaxis with trimetoprim-sulfametoxazolo.
Conclusions: The mechanism of uncomplete or absent immunological response to cART in HIV-1- infected patients has not been understood yet, but it brings to a increased susceptibility to opportunistic diseases and tumors, favoured by permanently ineffective cellular immunity.

Pathogenesis and Immunology

HIV pathogenesis

P 77 THE PROGESTIN MEDROXYPROGESTERONE ACETATE AFFECTS HIV-1 PRODUCTION IN HUMAN LYMPHOID TISSUE EXPLANTS IN A DOSE-DEPENDENT AND GLUCOCORTICOID-LIKE FASHION

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Background: Progesterone-only injectables are the contraceptive of choice in resource-limited settings, including Sub-Saharan Africa. The progestin medroxyprogesterone acetate (MPA) binds the glucocorticoid receptor (GR) with higher affinity than cortisol thus extending its effects beyond progesterone receptor (PR) engagement. Administration of high doses of MPA has been associated with increased HIV-1 susceptibility in animal models posing some concerns on its use in HIV-endemic areas. However, due to limitations of in vitro cultures of isolated female genital mucosa (FGM) and blood cells, the net effect of MPA systemic administration on HIV-1 infection in humans remains poorly understood. Here we investigated the impact of MPA on HIV-1 replication and inflammatory responses in lymphoid tissue, which is the main site of virus pathogenesis.

Material and Methods: We inoculated human tonsillar tissue explants with a HIV-1 CCR5- (BaL) and CXCR4- (LAI) variant and monitored the amount of p24gag and cytokines released in culture supernatant over time. We compared these readouts between untreated control explants and those treated with MPA at two different concentrations 10 and 100nM for different lengths of time (before infection vs throughout culture) to model peak concentration and kinetic observed in plasma of depot MPA (DMPA) users. To address the role of GR and PR engagement in the observed responses we also treated donor-matched explants with a selective GR agonist, dexamethasone (DEX) at 10nM, and progesterone (P4) at 100nM, in the presence or absence of an antagonist of both GR and PR, mifepristone (RU-486) at 1μM.

Results: Explant treatment with MPA reduced the replication of both HIV-1 strains BaL and LAI as well as the production of the pro-inflammatory cytokines IL-1β and IL-17A. The magnitude of such effect was proportional to MPA dose and length of treatment, and it was comparable with an anti-inflammatory response elicited by DEX via GR. Blockage of PR and GR with RU-486 abolished the observed changes in HIV-1 and cytokine production in both MPA- and DEX-treated explants, and increased IL-22 levels compared to untreated control. Although IL-22 expression was significantly reduced only by DEX, RU-486 treatment resulted in higher IL-22 levels in explants treated with MPA before infection whereas no difference was observed for longer treatment (throughout culture) with both MPA 10 and 100nM.

Conclusions: Our data suggest that MPA at doses that are compatible with peak concentrations observed in serum of DMPA users affects the immune responses in lymphoid tissue via GR with an immediate impact on local HIV-1 replication. The reduced IL-17A and IL-22 production may be indicative of a selective effect on T cell subsets targeted by HIV-1 thus explaining reduced virus production levels. Such mechanism may also underlie the local epithelial thinning observed in the FGM of DMPA users as well as in animal models and warrants further investigations.

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Pathogenesis and Immunology

HIV pathogenesis

P 78 THROMBOSPONDIN RECEPTOR PATHWAY CAN REGULATE HIV MUCOSAL TRANSMISSION IN SEMEN FROM HIV SEROPOSITIVE SUBJECTS

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Background: AIDS is mainly a sexually transmitted infection and the genital mucosa is thus the major site for initial host-HIV-1 contact. Semen, usually present during genital HIV-1 transmission, is a complex mixture of soluble factors with immunoregulatory functions, which could interfere with semen infectivity thus enhancing or inhibiting HIV-1 infection. Here, we present our preliminary data on the identification of soluble factors involved in the pathogenesis of genital HIV-1 transmission combining HIV specific functional assays and proteomic analysis.

Material and methods: Seminal fluid (SF) samples from 7 HIV-1 seropositive (HIV+ SF) and 10 healthy HIV seronegative (HIV- SF) individuals were evaluated for their capacity to interfere with HIV infection of TZM-bl by 3 recombinant viruses or HIV translocation across immunocompetent genital mucosal reconstruction. In parallel, SF proteome was analysed by mass spectrometry. Resulting identified proteins in SF with functional neutralizing or non-neutralizing activities were analysed differentially using DAVID and gprofiler software allowing the definition of specific signatures.

Results: Five out of 10 HIV- SF and five out of 7 HIV+ SF blocked HIV mucosal translocation whereas the remaining 5 HIV- and 2 HIV+ SF increased it, respectively. Among 7 HIV+ SF, 3 strongly increased HIV replication but had no effect on HIV translocation whereas 2 others increased translocation but had no or low effect on HIV neutralization. Importantly, 2 out of 7 HIV+ SF that inhibited both classical infection and mucosal translocation showed a very similar expression of protein pattern significantly different from the HIV+ SF with enhancing functional activities. Hence, in these HIV+ SF, 1549 proteins were identified, 67 were significantly differently expressed ($p<0.05$), with 21 upregulated and 46 downregulated in the 2 HIV blocking HIV+ SF when compared with the other five HIV+ SF, Furthermore, among the proteins specifically enriched in these HIV+ SF fluids, a unique set of 8 proteins were present in HIV+ SF with HIV neutralizing and translocation blockade activities. These 8 proteins define a unique biological pathway, namely the thrombospondin receptor pathway involving two proteins: CD47, an integrin acting as receptor for thrombospondin and F2, the thrombin factor II.

Conclusions: Thrombospondin receptor pathway has been already suggested to interact with gp120 and inhibit HIV infection in human saliva. Similarly, it could be a pathway involved in regulation of HIV infection at mucosa site.

Social science, Epidemiology and Prevention

Gender issues

P 79 SEX AND THE WOMEN: TEST IN A COMMUNITY-BASED SITE IN COVID-19 TIME

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Background: ASA-Associazione Solidarietà Aids-since 1985 is an association active in Hiv-Aids prevention and supporting PLWHIV,particularly focused on MSM population.Since 2012, once a month, ASA provides in its premises a Rapid Hiv Test, anonymous & free of charge, to encourage mass screening. A questionnaire and an informed consent form are handed out to the incoming people. Before the test is carried out, an Hiv specialist counselor conducts an informal interview in accordance with the law. The test is performed by an ID doctor who returns the result. Being the test's result positive, a psychologist can assist the person. Individuals that result Hiv+ are directed to the confirmation test, eventually lead in hospital by the same Rapid Hiv Test doc, to facilitate the retention in care. The test is part of the association's prevention/early detection programs.After a suspension from March to June,it has resumed regularly since July 2020,in compliance with Covid standards.
Methodology self-administered questionnaires(July 2020-June 2021)have been analyzed.Psycho-socio-cultural characteristics of the sample have been detected,and correlated to risk behaviors.Aim of the study:to describe the sample for preventive intervention's evaluation and new infections early detection.
Results: 136 users (M 70%;age range 31-40;homosexuals 44% and hetero 40%,graduated and over 41%;Hiv already tested 77%;employees 43% Italians 87%;using Chems 12%;no.of partner:3 & more).1 turned out to be positive.Here, some variables that have been crossed:
-Gender(G)by:Use of Condom By Partner Type(CPT),Use of Condom by Sex Activities(CSA),Use of Chems(UOC)
-Sexual Orientation by:CPT,CSA,UOC
-Sex Under D&A by G by:CPT,CSA
-UOC by Sex Under D&A
-Test already taken by STI
-STI by: CPT, CSA
Conclusions: As in the past,the sample is used to the test,uses condoms in casual and penetrative intercourses.30% of it has sex under drugs or alcohol.Only 29% of the users,however,have used condoms (previous analyses 40%). The women in the sample increased by 1/3;like the men,they tend to have more than 3 partners in a year,and they use Chem as much as men do (12%).Proportionally,women have more sex under D&A(47 vs. 23%):they probably use alcohol as a disinhibitor.In the sample,among those who have had STI,no one claims not to use a condom in any situation,and as many as 90% have been tested in the past.In the wake of these findings,we would like to keep offering the test to the general population(where,as these data show,risk behaviour is widespread,even among women)as a prevention tool and a promoter of virtuous circles.In accordance with the present Covid-19 standards,we will also resume bringing tests and information stands into MSM premises(and we will also start in hetero premises),as in the past they have proved to be an effective tool for raising awareness.The test is still,together with TasP,U=U and PreP,a key tool in pursuing the 90-90-90 target.ASA was supported by Viivhealthcare.

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Social science, Epidemiology and Prevention

Gender issues

P 80 UNEXPECTED WOMEN

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The realization of this project aims to train the operators of the Anti-Violence Center on how to welcome lesbian and bisexual women who could belong to the Centers, to enhance basic knowledge on the LGBTIQ + community in order to avoid behaviors deriving from a incorrect "ecological communication", to inform about the legal norms that these women carry with them.
A part of the training will be centered solely on the issue of HIV-positive.
We know that many of the operators are not aware of the serological condition that many women carry with them, also because the serological coming out of women in the LGBTIQ + community is subject to many misunderstandings; it also indirectly proposes a path of reflection on one's own emotional and relational behaviors. Related to sexual orientation and HIV status.
The training was specifically designed for the workers of the anti-violence centers and reception centers to bring out a critical thought: there is gender-based violence on the same gender that is often and deliberately not spoken of, with which due to lack of tools it is difficult relate; there is a female serological status hidden behind obsolete and dangerous prejudices and stereotypes.

Social science, Epidemiology and Prevention

HIV epidemiology and retention in care

P 81 IMMUNE RECOVERY IN NEW HIV DIAGNOSES IN OVER 50S

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The increase in new HIV diagnoses in over 50s has been a stable trend in Italy for several years.
Several factors contribute to making this segment of population increasingly susceptible to infection: poor perception of risk, screening campaigns not including this age group, the perception among healthcare providers that older people are asexual and therefore not at risk of HIV resulting as a barrier to test offer in this group. This is a significant public health concern as this group are disproportionately affected by late diagnosis.
In the Infectious Diseases Dept. of Cagliari we studied immuno-virological patterns of 50 patients who, since 2011, have been diagnosed with HIV infection at an age of over 50, comparing it with 50 patients who instead were diagnosed at an earlier age, representing our control-group.
The evaluation provided 3 yrs of follow-up. Three parameters were considered for the evaluation of immune recovery: the CD4 T lymphocyte count in percentage and in absolute terms, and the CD4/CD8 ratio, measured at 6-month intervals, for 36 consecutive months. This allowed a broader and more precise assessment of the immunological status of the naive patient along the early stages of treatment. For both patient cohorts, the impact of antiretroviral therapy was important for virological suppression and immune recovery. The mean values of parameters examined were analyzed and compared, showing statistically significant differences in all time intervals.
The results of our study indicate that age at diagnosis of HIV infection constitutes a negative prognostic parameter for the patient's immune recovery.
The CD4 absolute count sees a more marked recovery in Under50s compared to Over50s: both cohorts started from average values <350 cells/μL (313.3 cells/μL in Under50s, 207.8 cells/μL in Over 50s), the values at 36 months show a clear difference: 740.8 cells/μL against 505.9 cells/μL (p-value: 0.0002). The percentage of CD4s also showed a statistically significant difference between the two patient cohorts: for the Under50s from 17.68% to 31.04%, while for the Over50s from 12.34% to 24.21% (p-value at 36 months: 0.001), which could be linked to increased inflammatory dysregulation. In this sense, it was useful to compare the CD4/CD8 ratio: at 36 months of therapy, 0.92 for the Under50, 0.67 for the Over50 (p-value: 0.01).
Our study showed that age at diagnosis is of a primary importance prognostic factor: even though the effectiveness of therapy allowing rapid and effective control of viraemia, immune recovery is conditioned by immunosenescence, typical of old age. So, it is important, in future perspective, strengthen the prevention of infection for all age groups.

Social science, Epidemiology and Prevention

HIV epidemiology and retention in care

P 82 IS EXTERNA SERVICE STILL MEANINGFUL IN THE TIME OF COVID-19? REFLECTION

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Background: Since 2010, EXTERNA is a free of charge service offered - in partnership with ASA Milano - to PLWHIV undertaken by San Luigi ID Center (HSR), Milan concerning Linkage to care and Retention in care. EXTERNA, usually coaching in presence at ID outpatient clinic, was modified by limitations due to the emergency state, with San Luigi ID Center acting as an anti-COVID-19 prevention and therapy center, and by ATS (local health authority) rules. Outpatient clinic has been closed between March and Mai 2020, reopening its reduced activity below restrictive rules due to COVID -19, incentivizing telemedicine as preferable choice. The service born in collaboration between ASA Milano and San Luigi ID Center took a downturn. The importance to fight against isolation, to discover and to support the possible emotional impact due to HIV and COVID-19 fear, and the re-emerging anxiety of PLWHIV as fragile people led to a service reorganization, facing developing needs in a varied situation.

Methods: Since February 2021 EXTERNA offers online interviews on a secure platform for a half hour time, below spontaneous PLWHIV request, asked by mail or by phone, and scheduled at the same time than the ID outpatient visit.

Results: Requests have strongly decreased, and they were concerning either freshly diagnosticated infections or PLWHIV suffering of comorbidities. Counseling drove to psychotherapy demand. Direct contacts with PLWHIV confirmed that they prefer to conduct in presence better than online interviews.

Conclusions: Observing interviews contents, passed thoughts and imaginaries connected to HIV reappeared as the fear, share by the community, that the 4th 90 could get critical. To offer online continuity in PLWHIV support - when it was impossible in presence – has been a winning solution, counteracting isolation and repeating the importance to talk about HIV aspects, other than medical. Based on the few spontaneous counseling requests, the weight of doctor/patient relationship, the connection HIV/disease to ICAR20 QoL, and in presence interview – in the time of the pandemics - aimed to unveil topics and fragilities of PLWHIV, we focus our future activity on QoL, intercepting who is in struggle to ask for help, inquiring into possible subjective reasons, mobility, emotional impact due to copresence of HIV and COVID-19 viruses, re-emerging of death fear due to the two viruses association in PLWHIV/fragile subjects. ASA was supported by Viivhealthcare.

Social science, Epidemiology and Prevention

HIV prevention (PrEP and PEP)

P 83 CHANGE AND DECREASE OF PRE AND POST EXPOSURE ASSISTANCE ACTIVITIES (PREP AND PEP) CAUSED BY THE COVID-19 PANDEMIC

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Background: fast diffusion of SARS-CoV-2 infection all around the world heavily conditioned our lives and found local hospitals and health facilities mostly unprepared. Top priority was given to limiting the spreading of the disease, with little space for the care of all "NON-COVID19" diseases, including HIV infection. Here is discussed the change in activity in PEP and PrEP clinics, in a monothematic infectious diseases hospital, which has admitted COVID-19 cases only, between March and June 2020, and between September 2020 and May 2021.

Material and Methods: our hospital has offered an active Post Exposure Prophylaxis Service for more than 20 years, thanks to an Infectious Diseases ER active all year 24/7, which cares for a large range of patients from Naples and its province. We also offer a Pre Exposure Prophylaxis Service active since May 2019 for subjects who desire protection in addition to the condom use. Prophylaxis activities went under radical change in 2020 due to the high number of COVID -19 patients, who received prioritary care. To measure this change we considered the total number of exposed patients registered in 2020 and the total number of medical examinations for each one of them, compared to the average registered in 2017, 2018 and 2019 (Tab.). In regards to the PrEP ambulatory, we counted the number of drug prescriptions (EmtricitabineTenofovitDisoproxil) made in February 2020, and compared them to those made between March and December 2020. We also registered the number of new patients lost to follow-up in 2020.

Results: Regarding PEP, we find a decline in both the number of patients itself (reduction of the 29%) and in the number of examinations (reduction of the 48%). A contextual reduction of the examination/patient ratio (from an average of 2,92 to 2,11) was also found. The causes probably lay both in the fear of the infection and in administration difficulties operators found (physicians on call could not find the time and space to properly evaluate an Exposure case). For what concerns the PrEP clinic, from the data we can see a sharp fall in the number of prescriptions made after March 2020 (61% decrease) with a great number of patients lost to follow-up (21 on a total of 38 registered, equal to 55%). The reason comes from the hospital's decision to temporarily close the PrEP clinic, with the impossibility to draft new PrEP users. Efforts were focused on caring for patient already in therapy, using "online" prescription methods (via email, Whatsapp, etc.).

Conclusions: emergencies correlated to airborne infectious diseases further aggravate chronic logistics problems in our hospitals, which are not always easy to manage. The construction of clinics external to the main facilities, with sanitized corridors and enough room for social distancing, may allow the continuation of PEP and PrEP activities, guaranteeing an efficient healthcare system even in these difficult times.

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Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 84 THE EXPERIENCE OF THE ANLAIDS FORUM DURING THE SARS-COV-2 PANDEMIC

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Background: Since 2007 ANLAIDS Onlus offers an online forum where questions about HIV prevention or doubts concerning HIV transmission and diagnosis can be submitted. We wanted to understand if there is a relationship between the number of sexual intercourses at risk for HIV reported on the forum and the coronavirus pandemic period, characterized by severe social restrictions.
Material and Methods: During the 2020-2021 Sars-CoV-2 pandemic period (analyzed from February 2020 to February 2021) we received 447 posts; 70 have been discarded because the reported risk events certainly were not referred to the studied interval.
We classified the questions by distinguishing the type of sexual intercourse (same sex i.e. MSM; heterosexual i.e. HEs), the use of condoms or methods of protection if relevant, and therefore the associated HIV risk.
We attempted to relate the data from the ANLAIDS forum with "COVID-19 ISS open data" with two statistical experiments based on the linear regression and check if they can be connected and can answer these 2 questions:
question 1: Is it conceivable that an increase in daily coronavirus cases leads to a decrease in sexual acts reported on the forum?
question 2: Is the trend in the number of sexual intercourses reported on the forum inversely proportional to the number of coronavirus cases reported in Italy in a specific month?
Results: Overall, of the 377 posts in the analyzed period, 287 were related to sexual intercourses; 90 were linked to social situations not at risk for HIV; only 3 were related to potential occupational risk.
Regarding all posts associated with sexual events, 27.35% of cases were referable to MSM intercourses, while 72.65% of cases were related to HEs; 37.04% of the reports involved a concrete risk for HIV.
A real HIV risk for single sexual act was more likely among MSM (41.67%) than among HEs (35.66%). The risk most reported by MSM has been receptive oral sex with ingestion of seminal fluid while among the HEs has been unprotected insertive vaginal intercourse. Three subjects reported being diagnosed as HIV positive.
Regarding question 1 the set of data was valuable but it was not possible to forecast the trend of sexual acts according to the number of SARS-CoV-2 infections of the previous day ($p=0.05$, $r2=0.01$).
About question 2 a weak relation was found between the number of reports on sexual risk and the magnitude of the COVID-19 pandemic in the months subject to analysis ($p=0.17$, $r2=0.16$) suggesting that the increase of SARS-CoV-2 has led to a detectable decrease of sexual acts.
Conclusions: The sexual intercourses reported in the forum still demonstrates a great lack of information on how HIV is transmitted and a low awareness of the risk of contracting HIV.
During the COVID-19 pandemic, people continued to have sex despite restrictions on freedom of movement and meeting, even if a trend of limitation in sexual encounters was observed.

Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 85 INCREASED RISK OF HIV VIRAL BLIPS DURING COVID-19 PANDEMIC: A SINGLE CENTER RETROSPECTIVE STUDY

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Background: On March 8, 2020 the Italian government imposed restrictive community containment measures to limit the spreading of SARS-CoV-2. From then on, healthcare workers were working under critic conditions, leading to limitation in the access of outpatient care. This situation had a great impact in the management of chronic diseases including HIV. During lockdown the HIV Outpatient Clinic of Ospedale Maggiore della Carità was able to ensure antiretroviral therapy (ART) supply, nevertheless many patients (pts) refused to access the Infectious Diseases ward. Therefore, the aim of this study was to explore whether COVID-19 pandemic had a negative impact on HIV viremia in our cohort.
Material and Methods: all pts in stable ART for at least 6 months and usually highly adherent, in care at the HIV Outpatient Clinic of Ospedale Maggiore della Carità Novara, were included in this retrospective observational study. HIV viral load (VL) values in 2019 and 2020 were analysed. We compared viral blips (VB), defined as a single HIV viremia >50 copies/ml preceded and followed by an undetectable one, residual viremia (RV), defined as a HIV-RNA between 20 and 50 copies/ml and virological failure (VF). Pts that spontaneously declared suboptimal adherence at follow-up visits underwent a drug resistance test. Statistical analysis was performed using SPSS ®, paired samples were tested through McNemar's tests.
Results: 529 pts were included. In 2019 20 pts (3.7%) had a VB, 16 (3%) a RV and 9 (1.7%) a VF, while in 2020 we observed VB in 37 pts (6.9%), RV in 49 pts (9.2%) and 3 (0.56%) VF. Sixteen pts in 2019 and 15 in 2020 had a persistent low-level viremia between 50 and 200 copies/ml. The difference between VB reported in 2019 and 2020 was statistically significant (3% vs 6.9% p=0,017). We observed a statistically significant difference (3% vs 9.2% p<0,001) in RV between 2019 and 2020. No significant difference was observed in VF between 2019 and 2020.
In 2020,8 pts spontaneously reported suboptimal treatment adherence (i.e. every other day intake) due to difficulties in ART supplying, however they presented undetectable VL at follow-up visit. For the same reason 11 pts in 2020 completely interrupted ART. At the follow-up visit a drug resistance test was performed: no one showed any resistance mutations, allowing the restart of their previous ART. All of them showed an undetectable VL at the following visit.
Conclusions: restrictive measures imposed in 2020 by the SARS-CoV-2 pandemic had a significant impact on HIV outpatient care and consequently on HIV viremia. In our small cohort, an increase in VB and RV was observed, while VF was stable in 2019 and 2020. This worsening in treatment compliance was largely due to lockdown and difficulties to access to our facilities. Retention in care is one of the HIV treatment cornerstones; in difficult situation such as the outbreak of a new disease, outpatient care should be rethought to ensure ART and access to care.

Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 86 THE CHALLENGE OF LATE PRESENTERS PATIENTS WITH AIDS-DEFINING DISEASES DURING THE COVID-19 PANDEMIC

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Background: The impact of current SARS-CoV-2 pandemic on the healthcare services had serious consequences, especially for the most fragile populations such as HIV-positive subjects.. Disruption in HIV care delivery due to COVOD-19 containment could increase HIV-related morbidity and mortality.
Material and methods: In the period April to September 2020 we reported four cases of HIV-positive late presenters with an AIDS-defining life-threathenig condition that, due to the difficult access to the hospital during the pandemic, were characterized by a delayed HIV recognition and institution of correct treatment.
Results: The first two patients were and a Italian 53-year-old man and a 31-year-old homeless woman, who presented to us with dyspnoea and dry cough. In both patients chest CT-scan revealed extensive bilateral ground glass opacities with air space consolidation. In the first patient, who had not known risk factors for opportunistic infections, clinical suspicion was at first focused on SARS-CoV-2 infection but two consecutive throat/nasal swabs were negative for SARS-COV-2. HIV serology tested positive and T CD4 lymphocytes cell count was 54/mmc (4.2%). Clinical suspicion of PCP (Pneumocystis pneumonia) was done and treatment with trimetoprim-sulphametoxazole was begun, that determined a fast improvement and resolution of pneumonia. In the second patient PCP lead to acute respiratory failure and need of mechanical ventilation. The PCP treatment was also complicated by a severe skin and haematological side effects to trimetoprim-sulphametoxazole.
The case no. 3 was an 57-year-old woman who in the previous two months was followed at an Haematology outpatient service because of a severe pancytopenia that was attributed to an hydiopatic myelofibrosis. Her T lymphocites T CD4 cell count were 10 cells/mmc (3.4%) and a T CD4/T CD8 ratio of 0.04. The patient was diagnosed with concomitant pulmonary Mycobacterium avium infection, oesophageal candidiasis and CMV sepsis. A prolonged hospitalization was needed for treating such severe conditions and monitoring drug-induced side effects..
The case no. 4 was an 55-years-old man with dysartria, severe impairment to walk and a history of weight loss. When considering brain magnetic resonance imaging and positive serology for HIV, presumptive treatment for Toxoplasma gondii encephalitis was started. Nevertheless neurological conditions of the patient progressively worsened and he is died six weeks after hospital admission. Autoptical exhamination of the brain revealed an EBV-related Primary Central Nervous System Lymphoma.
Conclusions: The rate of HIV-positive late presenters subjects is still relevant. Our case series showed that AIDS-defining opportunistic diseases, with the delay of diagnosis in the pandemic era, can have a rapidly worsening clinical course such as we were used to see in the pre-HAART era.

Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 87 DECREASE IN NEW DIAGNOSIS OF HIV/AIDS IN THE TWO YEARS PERIOD 2019-2020: IMPACT OF COVID -19 PANDEMIC

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Background: the emergence of SARS-CoV-2 has caused a pandemic of unprecedented proportions with substantial impacts on population health. Brescia Provence was highly affected in terms of confirmed cases, hospitalized patients and death. Preparedness for and management of COVID-19 clearly became emergent public health priorities, and the impact on other important public health initiatives, such as expanded HIV screening and linkage to care, remain largely unknown. Our Infection Diseases Department, that provides HIV services for almost 4000 HIV-infected patients has worked hard to ensure access to HIV treatment and care during COVID-19. Keeping HIV prevention efforts moving forward during pandemic became difficult. Here, we present the new HIV diagnosis and describe the characteristics and circumstance of the new HIV cases during 2020 and compared with those of 2019.

Material and Methods: this is a Single-Center retrospective observational study. We selected among all patients with new diagnosis of HIV infection took in care at Department of Infectious and Tropical Diseases, Brescia Spedali Civili Hospital. We recorded all the demographical, clinical and viro-immunological data, including information about risk factors for HIV acquisition and the reasons why patients performed the HIV test. We compared the data of patients received in 2020 with those took in care in 2019 in order to observe any difference caused by COVID-19 pandemic in the access to care.

Results: the number of individuals receiving an HIV diagnosis declined by 31.2% during 2020 (77 patients in 2019 vs 53 patients in 2020). Although the proportion of HIV diagnoses among men remained predominant during both years, the proportion of all diagnosed HIV infections attributable to females increased from 13% to 26.4%. The percentage of diagnosed infections attributed to male-to-male sexual contact declined slightly during 2019–20, from 40% to 30% and median age at HIV diagnosis decreased of one decade (45 years old vs 36 years old). The proportion of patients with new HIV diagnosis from East Europe accounted for 17% of diagnoses in 2020 (only 5% in 2019). Diagnosis of HIV infection made during hospitalization were 11% and 22.6% of patients during 2019 and 2020 respectively. At the time of HIV infection diagnosis, 24.7% of patients during 2019 and 30.2% during 2020 presented with advanced HIV infection defined as presence of at least one AIDS-defining event. Pneumocystis pneumonia was the most frequent AIDS defining-condition in 2020.

Conclusion: We attended in our Center a decrease in new HIV diagnosis in 2020 compared to 2019. This important decrease was observed particularly during the two waves of COVID-19 pandemic. We express our concern that HIV new diagnoses will increase as a result of people's inability to get tested or treated in this period. More efforts are needed to improve local screening programs both during and after COVID-19 pandemic.

Attach: https://www.icar2021.it/public/abstract/Attach_ABS_183.jpg

Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 88 IMPACT OF COVID19 ON PEOPLE LIVING WITH HIV: AN ANALYSIS OF GAETANO MARTINO HOSPITAL IN MESSINA

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Background: COVID19 pandemic and the measures taken to prevent the spread of the virus, such as lockdown, had a great impact on the global population. Among the people who have suffered the most from the lockdown there are people with chronic diseases, who need continuous medical care or periodic checks. We decided to conduct a retrospective study to investigate how the COVID19 pandemic and lockdown have affected the people living with HIV (PLWH) treated at the Infectious Diseases of "Gaetano Martino" hospital in Messina.

Materials and Methods: The impact of COVID19-related distress was assessed on mental health (depression, anxiety, loneliness, aggression, restlessness), adherence to HIV treatment, drug, alcohol and cigarette use, sexual habits, availability of contraceptives, number of meals per day. The study was performed administering a questionnaire of 53 items, anonymously, to our patients. The data collected was processed with McNemar test and Chi-Squared test.

Results: The questionnaire was administered to 141 patients, 54 males and 15 females. 69 people agreed to participate, 34 refused, we weren't able to reach 38 people. The impact of COVID19 and the lockdown resulted in an increase of 23,4% in the use of drugs, mostly in males, an increase of 47% in alcohol consumption and in cigarettes use in 51,2% of people, paired with an increase in weight gain due to a greater frequency of meals and reduced physical activity. Notably, the increase in weight gain was significant mostly for male people, while females had a drop in weight, with a mean difference in time of about 10 Kg. As for mental health issues we observed an increase in anxiety and depression, there was a significant percentage of fear of getting COVID19, with no difference between male and female, we observed a greater percentage of fear to infect other people mainly in male people (14,8% for male people, 6,7% for females). We observed that mental issues such as anxiety and depression had a significant correlation in dropping therapy (correlation coefficient ρ 0.320). Also we observed an increase in unprotected sexual intercourse mostly in male people. Unexpectedly, there was no increase in sexually transmitted diseases (STIs) diagnosed after the pandemic. Notably 53% of people were convinced that antiretroviral therapy was protective for SARS-CoV2.

Conclusions: We can assess that the lockdown had a terrible impact on our seropositive people. As a result there was a significant drop in the continuity of antiretroviral therapy, and we observed that many people were less strict in their treatment.

It is important for these people to have a constant follow-up and a periodic check with their doctor, to assure the continuity in therapy and the contact with the healthcare figure. We believe that promoting telemedicine to keep in touch with the patients could be an effective strategy in order to avoid discontinuity in treatment.

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P 89 PREVALENCE OF COVID-19 AND/OR SARS-COV-2 INFECTION IN INDIVIDUALS WITH OPIOID USE DISORDER: FONDAZIONE VILLA MARAINI'S EXPERIENCE

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Background: Previous reports have suggested that the prevalence of COVID-19 might be lower in individuals with opioid use disorder (OUD) than in the general population. In this preliminary study, we explored the prevalence of COVID-19 and the seroprevalence of SARS-CoV-2 infection in a sample of clients of Fondazione Villa Maraini, an ONG affiliated to the International Red Cross-Red Crescent that provides free services to drug users in the metropolitan area of Rome (Lazio, Italy).

Methods: The work team consisted of a doctor, a psychologist, a socio-health worker and a group of Fondazione Villa Maraini volunteers. Appropriate personal protective equipment (PPE) and procedures were adopted during the study, according to the WHO's recommendations. The participants were enrolled among the clients of Fondazione Villa Maraini's services on April 19-26. Participants underwent a rapid test on capillary blood sample for detecting Sars-CoV-2 seroconversion (Panbio™ COVID-19 IgG/IgM rapid test device, Abbott). Positive subjects were screened for the presence of the viral infection through antigen rapid test (nasopharyngeal swab).

A pre-test consultation was carried out through a questionnaire concerning the personal medical and toxicological history and to the social and hygienic conditions experienced during the COVID-19 pandemic.

Results: One-hundred-fifty-five individuals (26 women) were enrolled in the study. The mean age (±SD) was 45.7±9.5 for men and 41.5±10.2 for women. The number of subjects with OUD was 151 (97.4%). Most of the participants received long term replacement treatment with methadone (86.5%) or buprenorphine (2.6%). Only 2.6% of the participants had been administered the vaccine at the time the study was conducted.

Only one participant among the people with OUD had been diagnosed with COVID-19, indicating a cumulative prevalence of 0.66%. The cumulative prevalence of COVID-19 in the general population of the Lazio region at the same date was 7%. The seroprevalence of SARS-CoV-2 infection in the OUD sample was 1.98% (including the single case of COVID-19 case and 2 asymptomatic cases). Seroprevalence data for the general population at the same date were not available. Based on the ratio between seroprevalence and cumulative COVID-19 cases in early months of 2021 in France [Hozé et al. 2021] we estimated a seroprevalence of >18% in the general population of the Lazio region.

Conclusion: These findings support the hypothesis that individuals with OUD are less vulnerable to COVID-19, despite the high prevalence of chronic comorbidities (47%). Follow-up studies including control groups are currently underway to further investigate the mechanisms responsible for this still unexplained phenomenon.

Hozé et al. Monitoring the proportion of the population infected by SARS-CoV-2 using age-stratified hospitalisation and serological data: a modelling study. Lancet Public Health. 2021 Jun;6(6):e408-e415. doi: 10.1016/S2468-2667(21)00064-5.

Social science, Epidemiology and Prevention

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P 90 EPIDEMIOLOGY AND CLINICAL FACTORS ASSOCIATED WITH DEATH IN COVID-19 PATIENTS MANAGED OUTSIDE THE INTENSIVE CARE UNITS

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Background: At the beginning of the COVID-19 pandemia, an institutional coronavirus registry (COVID-19 Network), was established at IRCCS Ospedale Maggiore Policlinico in Milan including some hospitals from Lombardy, Veneto, Abruzzo, and Emilia-Romagna, to answer present and future research questions.
Aim of this current analysis is to describe clinical and epidemiological characteristics of this cohort of patients (from March to 31st May 2020), and to identify risk factors associated to mortality.
Materials and Methods: The COVID-19 Network includes all consecutive adults (>18 years) with a positive RT-PCR result for SARS-CoV-2 admitted to included hospitals, excluding those admitted to intensive care units (ICU). Population characteristics were described by proportions, mean, standard deviation, median, interquartile range, depending on their distribution. Multivariate linear regression was performed to identify risk factors associated to outcome.
Results: 1018 patients (mean age 65+16) were enrolled, 368 (36.2%) were females. A major part of patients was admitted from emergency room (n=527; 52.4%). Two-hundred and twenty patients (21.6%) died in hospital after a median length of hospitalization of 15 days (IQR 4-13). Thirty-one patients (3.1%) needed to be transferred to ICU.
The most important causes of death were respiratory failure (n=179; 81.7%), shock (n=12; 5.5%) and heart failure (n=6; 2.7%). Mortality was attributed to SARS-CoV2 infection among 145 patients (66.5%). Five hundred fifty-three patients (55%) received low flow oxygen support at admission, while 230 (23%) were in non-invasive ventilation (C-PAP, NIV or HFNC). The most frequently comorbidities were diabetes (n= 186; 18.8%), dyslipidemia (n= 137; 13.9%), atrial fibrillation (n=96, 9.7%), cancer (n=74, 7.5%), dementia (n=71, 7.2%). Two hundred thirty-five patients (23.3%) were immunocompromised: hematologic neoplasm (3.7%), treated with chronic steroid (2.5%), chemotherapy or other immunosuppressors (2.4%).
On analysis fully adjusted for all comorbidities, risk factors associated to mortality were age older than 75 years (OR 1.07, CI 1.05-1.09), [OR for 75-84 years, 7.78 (2.26-26.8); for 85 or more OR 11.8 (3.27-42.5)], and number of comorbidities (OR 1.8; CI 1.15-2.80).
Comorbidities associated with worse outcome were heart failure (OR 2.51, IC 1.73-7.16), diabetes (OR 1.63; CI 1.04 -2.56), cancer (OR 3.43, IC 1.87-6.29) and dementia (OR 4.60, IC 2.48-8.52).
Considering respiratory support, patients who needed non-invasive ventilation had a significantly higher risk of in-hospital mortality (OR 4.31, 2.69-6.89), the need for low-flow oxygen support was not associated with risk of death (OR 0.84, 0.57-1.25).
Conclusions: During the first wave of SARS-CoV2 epidemic, mortality was 22%. This is in line with published data on similar patients' cohorts. Older age and previous comorbidities (more than one) are the most important risk factors associated with mortality.

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P 91 CLINICAL CHARACTERISTICS AND PREDICTORS OF DEATH AMONG HOSPITALIZED PATIENTS INFECTED WITH SARS-COV-2 IN SICILY, ITALY: A RETROSPECTIVE OBSERVATIONAL STUDY

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Background: since late December 2019, SARS–CoV-2 has spread worldwide, leading the WHO to declare a global pandemic. COVID-19 presents a highly variable spectrum of severity of illness. Most infected individuals exhibit a mild to moderate illness (81%); however, 14% have a serious disease and 5% develop a severe acute respiratory distress syndrome (ARDS) requiring intensive care support. Mortality rate of coronavirus disease 2019 (COVID-19) continues to rise across the world. Data regarding predictors of mortality in patients with COVID 19 are still scarce.

Methods: our multicentre retrospective observational study provides a complete description of the demographic and clinical characteristics, comorbidities and laboratory abnormalities in a population of 421 hospitalized patients recruited in eight ID units in Southern Italy (Sicily) and aims to identify the baseline characteristics predisposing COVID-19 patients to critical illness or death.

Results: in our study, older age, pre-existing comorbidities and some changes in laboratory markers at the time of admission were associated with a higher risk of mortality. Male sex, on the other hand, did not reach statistical significance.

Conclusions: symptoms like fatigue, older age, number of co-pathologies and use of CPAP were the most significant contributors in the clinical prognosis estimation. Further research is needed to better characterize the epidemiological features of COVID-19, to understand the related predictors of death and to develop new effective therapeutic strategies.

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P 92 RE-FRAMING COMMUNICATION: VISUAL METAPHORS IN COVID-19 ITALIAN INFORMATION CAMPAIGNS

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The COVID-19 pandemic has represented an unparalleled discursive phenomenon at a global level. Communication around COVID, and in particular the social and media communication campaigns through posters and videos, constitutes a particularly interesting body of analysis for investigating gender and group stereotypes. The study is even more interesting if we compare the COVID-19 communication campaigns with other communication social campaigns such as those around HIV, investigating the phenomena of social representation linked to diseases.
The aim of our study is to verify with what visual and linguistic tools the communication campaigns in Italy, both at a regional and at a national level, have dealt with COVID19 and most notably with what cognitive metaphors the disease has been interpreted in the national media space. Starting from well-known Sontag's essays (1978, 1989), and from more recent studies on cognitive metaphors and their framing function in public discourse, we will focus our attention on the conceptual metaphors underlying visual realisation of information campaigns on COVID19, in comparison with AIDS information campaigns.

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P 93 HEALTH AND WELLBEING AS PERCEIVED BY OLDER GAY MALES LIVING WITH HIV IN ENGLAND. A QUALITATIVE INVESTIGATION OF THE INTERSECTION BETWEEN SEXUAL ORIENTATION, HIV STATUS, AGE AND GEOGRAPHICAL LOCATION

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Due to the therapy now available, people living with HIV (PLWHIV) are living longer lives and their needs are unexplored. Additionally, there is a lack of research that has explicitly examined how the intersectionality of ageing with HIV and sexuality are linked with health and wellbeing in different environments. The aim of this study is to highlight how older gay males living with HIV experience and make sense of health and wellbeing in relation to their condition while living in their local area, considering the intersection of age, sexual orientation and HIV status.
The participants were 19 gay males aged 50 and over who have been living in England for more than 5 years and were diagnosed with HIV for longer than 2 years. Participants were living in one of the pre-determined areas divided into urban and rural. Participants were recruited through advertisements posted by HIV and LGBT charities and groups on social media. Interviews were conducted as videocalls on Skype between March 2020 and March 2021. Interviews were audio recorded and transcribed verbatim. Interviews were analysed using thematic analysis and participants were able to provide feedback to a draft of the analysis.
Considering the results, three main themes were identified from the analysis as follows: health as a holistic balance, person-centred needs and the impact of HIV on people's lives. These three themes are linked together through the common narrative of the personal journey of living with HIV that emerged from the interviews. Also drawn from the interviews was how OPLWHIV have multiple needs that are linked with their personal journey living with HIV. Participants highlighted how myths and misinformation were important fuel for ignorance and stigma and they can mislead the reality of scientific information while feeding into out-of-date knowledge and preconceptions. Stigma and discrimination can assume a kaleidoscope of forms and might be aimed at different characteristics of the person. For example, participants highlighted how they can be discriminated against for their age, for their HIV status and/or for their sexual orientation. Discrimination is particularly perceived within the gay community. Stigma and discrimination are also seen as impacting the personal journey of living with HIV for example affecting the process of disclosure of the HIV status.
There is a need to consider HIV in the context of the personal journey of OPLWHIV. Considering the main narrative that emerged, a lifespan approach should be taken when considering the needs of this population. Furthermore, participants highlighted how stigma and discrimination are still an issue affecting different characteristics of older people living with HIV and affecting the overall everyday life in OPLWHIV. More attention in needed to tackle discrimination and to address the needs of OPLWHIV.

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P 94 LOW-WAGE AGRICULTURAL MIGRANT WORKERS IN APULIAN GHETTOS, ITALY: GENERAL HEALTH CONDITIONS ASSESSMENT AND HIV SCREENING

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Introduction: There are about 500,000 migrant workers in Italy's agricultural sector, around half of its total workforce. Many of them live in Ghettos, shantytowns, isolated from city centres, without water or proper standards of hygiene, sanitation, or health services. Since 2015, Doctors with Africa-CUAMM have aimed to improve the health conditions of agricultural workers living in 3 Ghettos in Puglia by offering free-of-charge primary health care service in several settlements through a mobile clinic and a multidisciplinary team. In order to improve the quality of the service offered intercepting health needs, this study aimed to assess general health conditions and HIV prevalence.
Methods: Between June 2019 and February 2020, Doctors with Africa CUAMM in partnership with University of Bari-Infectious Diseases Clinic Bari, Anlaids and the apulian section of the Italian Society for Infectious and Tropical diseases - (SIMIT) performed a screening campaign for HIV–diabetes–hypertension, involving migrants living in 3 Apulian establishments: Ghetto Pista, "Sankara House" and "Arena House" (Fig.1). A standardized questionnaire was administered through a face-to-face interview, a medical examination was carried out and medical treatment was prescribed and issued when needed, also an HIV test were performed. A descriptive statistical analysis was performed. A logistic regression model was implemented as follows. Muscle and joint pain/fatigue was considered as dependent variable and each one of the available factors at the baseline evaluation as independent variables.
Results: Overall 321 migrants (n 298, 92% male, mean age 29 years) were enrolled in the study (50% from the Ghetto Pista, 42% in Sankara house and 8% in Arena house). At the medical screening 1 HIV test resulted positive. Hypertension was found in 12% of the migrants visited, tachycardia in 4%, diabetes in 2%, ipoxemia in 4% , TB symptoms in 17%, penil - vaginal secretions/ulcerations in 2%. Among others symptoms explored, muscle and joint pain/fatigue resulted to be the most frequent reported by 34% of the migrants, followed by cough (10%) and headache (8%). Significant predictors of muscle and joint pain/fatigue were: low BMI values (OR= 1.32; 95% CI 1.19–1.99), absence of education (OR= 1.85; 95% CI 1.02–2.95), being employed with a regular contract (OR= 2.64; 95% CI 2.39–2.83) and living in the ghettos since >12months (OR= 1.74; 95% CI 1.24–2.21). On the contrary, being female resulted to be a protective factor (OR= 0.59; 95% CI 0.46–0.87).
Conclusion: Our experience suggests that the health conditions of this population are mainly linked to the specific working activities in the agricultural fields, as well as to the hygiene, living conditions, and lack of social protection in their life and job. A multisectoral reflection on how to tackle the root causes of intervein to improve health conditions in such settings.

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Social and behavioural science, marginalized groups, community aspects and community surveys

P 95 THIRD YEAR OF MONO-SYMPTOMATIC THERAPEUTICAL GROUP FOR CHEMSEX USERS

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Chemsex is an ever-growing widespread phenomenon in the Milan MSM scene, as well as in many other towns and cities in Europe, and whilst, at some extent, counselling and information are available to manage the use reducing harm, a call for help has been rising from those who would like to quit. Chemsex is niche phenomenon, specific of the MSM community, even though it's now spreading, with different patterns and consequences, also to the heterosexual world, therefore public services are not yet ready to offer specific treatments.

In 2019 ASA founded the first Mono-symptomatic therapeutical group for Chemsex users in Italy to provide the community with a place of cure, free from stigma and medicalization. The group is hosted by a a professional psychotherapist and a volunteer.

It is a weekly semi-open group, composed of a varying number of participants, (generally between 5 and 8) aimed mainly but not exclusively to HIV+ population; it has been advertised on the association magazine and website, fliers in gay venues in the Milan area, in HIV clinics, and on apps, right now it is pretty much renowned inside the community and psychiatrists and by other medical workers who address users to it. The mono-symptomatic therapeutical group's method is rooted psychoanalytic tradition of group therapy as its used for other addictions such as eating disorders or gambling: through peer confrontation, where common experiences are shared, the participants are given the opportunity to create a bound. Chemsex use is often a "solution" to the impossibility to create meaningful, deep relationships, and the group is a specific tool used to introduce participants to new ways of perceiving unknown and unspeakable emotions, the "unthought known" to use C. Bollas words. Feelings of loneliness, of self deprecation, internalized homophobia, find a mirror in the experience of other participants and can finally be felt, described, understood... and worked on in order to move on to a more consistent and satisfied subjectivity.
During social distancing periods the group has met online, and this created a some problems as well as new opportunities, such as the participations of various members from different parts of the Country and even of the world (South America).

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P 96 A DELAYED FATAL DIAGNOSIS DUE TO STIGMA IN A HIV-POSITIVE WOMEN

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Background: Even 40 years after the beginning of the HIV epidemic, stigma, discrimination, and domestic violence are still faced by a remarkable proportion of WLHIV. It has been shown that domestic violence is an underrecognized barrier to women's ability to obtain regular medical care for HIV/AIDS. Thus can contribute to impair adherence both to treatment and care, causing clinical progression. Here in, we describe the case of an HIV women with the diagnosis of pericardial effusion and concurrent cardiac tamponade caused by a sternum fracture currently under legal investigation as potential cause of death. At hospital admission the patient did not report any domestic abuse and only with worsening of her clinical conditions, she disclosed the partner's aggression.
Case summary: A 50-year-old HIV woman with a history of IVDU showed up to the emergency department for headache, nausea, chest pain and fever. Urgent ECG and cardiology evaluation were performed, showing a typical pericarditis ST sopra-elevation pattern. A bedside echocardiography showed images consistent with minimal pericardial effusion. For this reason, an anti-inflammatory therapy with corticosteroid and colchicine was started. Blood cultures were performed and wide broad-spectrum antibiotic therapy with ceftriaxone and levofloxacin was started.
For the worsening of symptoms and occurrence of dyspnea, a new cardiac ultrasound was performed. It showed a severe pericardial effusion with cardiac tamponade. Moreover, vegetations on mitral and aortic valves were detected. Therefore, daptomycin was added. In the meantime, S. aureus grew on blood culture. A CT scan of chest/abdomen, performed to screen patient for possible embolization phenomena, accidentally showed an important sternum break. When patient was informed about these findings, she disclosed the domestic violence received by her partner. Because of her hemodynamic instability and further worsening of clinical conditions, the patient was immediately admitted to the intensive care unit, but unfortunately she died.
Discussion: Self-perceived stigma, especially among women and other vulnerable populations, is still widely represented in people with HIV and may have important implications also in the management of significant clinical events. Probably due to shame and fear feelings, the patient did not feel confident to disclose immediately an important event that would have allowed us to manage more properly her case from the beginning. Therefore, it is crucial not only to be focused on "pure clinical aspects", but also to apply an holistic approach, investigating psychological and social aspects. These efforts may not only lower the risk of psychological distress but has potential to alleviate the effect of stigma on HIV infected women, in order that they gain the ability to accomplish wellness, increase life span and improve quality of life.

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P 97 ARE CHANGING MODELS OF COMMUNICATION EASY IN THE 4TH DECADE?

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Nadir onlus

Background: The Covid 19 crisis has hit particularly PLWHIV continuum of care/ routine follow up. Clinical trials have shown several cases of viral rebounds in Spitali Generali Brescia and Policlinico Gemelli Rome. The lack of a creation of alternative tracks to allow vulnerable people with immunological damage or impairment to receive the continuum of care in most Italian Regions, has increased anxiety of PLWHIV about their own health status, frustration about the 4th ninety achieved along decades of efforts.
In the other hand COVID 19 has stressed the need to implement alternative models of communication with the clinician that can satisfy health aspects when the physical presence of the PLWHIV can be avoided.
Material and methods: PLWHIV so far have shown reluctancy to the new model of communication. Nadir has therefore elaborated a training project (Giornate di Nadir, October 2021) to facilitate the acceptation of the change in perspective. As a first step a questionnaire has been distributed in advance, (we expect online or in streaming aprox. 350 people of 35 different cities), to evaluate the level of knowledge and reluctancy in implementing the telemedicine, also considering territorial and personal difficulties, the time doctors can dedicate to his/her patient about side effects, AE, related and non-related pathologies to regain the 4th ninety people have lost. At G di N, presentations of different systems of telemedicine will be explained, with a focus on the DIGITAS system (Altems Univ,) and the Metabolic Clinic hybrid system (Modena Univ.).
The second questionnaire, distributed after the training should evaluate the first change of perception.
The last session of G di N is aimed at editing a consensus document to define a common standard of telemedicine acceptable by PLWHIV.
In the 4 months after G di N, technical assistance will be provided to territorial organizations to help more difficult to reach target populations.
The third questionnaire will be submitted 4 months after the end of G di N (end of February 2022) and it will underline how the local Groups, the clinicians and the administrations are implementing ethical recommendations to include telemedicine in different HIV settings.
Results: The first questionnaire will show a discrepancy among the perception of communication in distance HIV people have.The second will pinpoint the changes of actitude in different settings.The third will be aimed at understanding the results the territorial organizations will get to fulfill the need of a long term communication in distance using systems other than telephone, Wapp, SMS.
Conclusions: The study will give the answer on how training can change perception and prejudice of PLWHIV towards up to date systems.The interim results will be presented at ICAR 2021. The final results will be presented at ICAR 2022.

Virology and Pharmacology

HIV virology

P 98 ANALYSIS OF HIV QUASISPECIES AND MONITORING OF VIRAL REACTIVATIONS IN AN HIV D+/R+ KIDNEY-LIVER TRANSPLANTATION

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Background: HIV-positive individuals have a high incidence of end-stage renal disease and hepatocellular carcinoma (HCC) due to coinfection with HBV and HCV viruses. Kidney transplantation and orthotopic liver transplant are considered the best curative treatments for both end-stage renal disease and HCC. HIV infection is now a manageable chronic disease and people living with HIV (PLWH) are candidates to receive organ transplant as the general population. One of the major concerns about HIV D+/R+ transplants is the risk of donor-derived superinfection. Both kidney and liver may be reservoirs of HIV infection and may harbour variants able to super-infect transplant recipients (TR). Aim of the study was to in deep analyse PBMC-associated HIV quasispecies in a HIV D+/R+ kidney-liver transplantation, in order to verify HIV superinfection of the TR and possible other viral reactivations able to be of concern.

Material and methods: The study involved a 54 years old HIV infected deceased woman, donating kidney and liver to two HIV infected men, aged 49 and 61 years. The kidney recipient had end stage renal disease on hemodialysis and the liver recipient had an untreatable hepatocellular carcinoma inside Milan criteria. Standard viro-immunolological evaluations were performed at the moment of transplantation, and thereafter, including drug-resistance genotyping. HIV env V3 quasispecies in PBMC were evaluated in donor and recipients at transplantation and, in TR, at different time points during the follow-up, as well as the type and frequency of HIV integration sites in the host genomes.

Results: At the moment of transplantation, donor and recipients were all ART-HIV suppressed. After transplantation, no major changes in CD4 counts were observed in both TRs, who maintained a nearly suppressed HIV-1 viremia, but with evidence of peripheral replication as assessed also by the increase overtime of proviral integration sites in PBMC. HIV-1 DNA load in PBMC reached a transient peak after transplantation in the liver recipient, remaining stable in the kidney recipient. Drug-resistance genotype in both recipients did not show major changes during follow-up. CMV and EBV transient reactivations were observed only in the kidney recipient, not requiring specific treatment. The phylogenetic env tree showed no intermixed quasispecies among donor and TR during all the follow-up period. At the same time, HIV genetic heterogeneity did not increase overtime in the two TR, despite the occurrence of residual HIV replication and episodes of reactivation of herpetic viruses.

Conclusions: In the present study quasispecies analysis highlighted no evidence of HIV superinfection in our donor/recipients couple. In addiction, immunosuppressive treatment did not result in relevant viral reactivations during the follow-up of TR, confirming that HIV D+/R+ transplantation may be a safe and valuable therapeutic intervention for HIV infected people.

Virology and Pharmacology

HIV virology

P 99 SETTING UP OF A NOVEL ULTRASENSITIVE RT-QPCR ASSAY FOR EVALUATING THE HIV REVERSE TRANSCRIPTASE ACTIVITY

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Background: Detection of plasmatic HIV viral load (VL) by PCR remains the ultimate standard to confirm diagnosis of HIV-1 infection and to monitor the response to therapy. In some cases, however, such an assay could not provide complete information on the actual replication capacity of a circulating or latent virus. We have recently demonstrated the potentialities of a real-time RT quantitative PCR assay for the assessment of the plasmatic HIV-1 RT for the functional screening of the status of HIV-1 patients (Macchi et al., 2020). Unfortunately, however, preliminary results indicated that the assay should be properly for HIV-1 patients with low VL levels. Here we describe studies aimed to ameliorate the sensitivity of our assay.

Material and methods: The RNA template of the assay, previously extracted from I143J3 cells stably transfected with a vector for the US6 gene of HSV-1 coding for gD, was replaced in our novel assay with a synthetic RNA specific for gD (gD-synt-RNA). gD-synt-RNA was generated ad hoc in house by in vitro transcription from DNA of I143J3 cells. The transfecting vector contained the promoter for the RNA polymerase of T7 bacteriophage upstream from the sequence coding for gD. The promoter region was utilized to design the forward primer. An amount of 100 ng of the DNA template was used for an in vitro trascription reaction by means of a recombinant T7 RNA polymerase (MegaScript ®, Ambion). The potentialities of gD-synt-RNA for quantification of low levels of HIV RT, were evaluated using different conditions of the main variables involved in the RT-qPCR reaction, including different amounts of commercial HIV-RT, of synthetic RNA template and RT units, different mixes of the reaction buffer, and different dNTP concentrations. Results. The effectiveness of detection of very low amounts of commercial HIV-RT enzyme, were evaluated by dilution limit tests. **Results:** indicated that, using an input of 106 RNA molecules, 500 nM rt-primer and 0.1 mM dNTP, and different amounts of RT enzyme from 1x10-3 U to 1x10-9 U, the amplification curves obtained and the related Ct allowed to establish that a specific retro-transcripted cDNA could be detected even in the presence of 1x10-9 U of HIV-RT. **Conclusions:** The novel RT-qPCR assay, using gD-synt-RNA as a template, may be considered as a promising basis for an additional tool potentially capable of furnishing information on the functional virological status of HIV-1-infected patients.

Virology and Pharmacology

HIV virology

P 100 PERFORMANCE OF THE AD-SEQ HIV-1 SOLUTION A NEXT-GENERATION SEQUENCING COMMERCIAL KIT FOR HIV DRUG RESISTANCE ANALYSIS

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Introduction and aim: Sanger sequencing (SS) detects mutations present in at least 20% of the viral population. Recent studies have demonstrated that resistance related mutations that cannot be detected with SS may have unfavorable clinical consequences such as treatment failures. Next–generation sequencing (NGS) technologies have provided faster and more efficient results than the SS method. The sensitivity of NGS technologies allows the detection of minor variants with a frequency below 20%.
Objective of this work was to evaluate the performance of the AD-SEQ HIV-1 Solution assay based on next-generation sequencing for the analysis of HIV drug resistance mutations in protease (PR), reverse transcriptase (RT) and integrase (IN) gene regions.
Materials and Methods: Plasma samples (n=20) were obtained from 20 HIV-positive patients with different HIV-RNA viral load (from 43 to 4240000 copies/ml). Samples were analyzed using AD-SEQ HIV-1 Solution (AD-SEQ HIV-1, Arrows Diagnostics) assay, a next-generation sequencing for the identification of the drug resistance mutation in PR, RT and IN gene regions, with ISeq NGS technology.
Sanger sequencing (SS) was used to analyze resistance mutations in the PR and RT gene regions using the Viroseq HIV-1 Genotyping System and a home-brew protocol for integrase gene.
Results: Resistance mutations detected with NGS at frequencies above 20% were identical to the SS results. Drug resistance mutations (DRMs) were detected in 9 samples using Sanger sequencing and 15 samples using AD-SEQ HIV-1 (detection threshold: 5,0%). Overall , 67 major DRMs were detected; 40 were detected by both methods, 24 were detected by AD-SEQ-HIV-1 only and 3 were detected with SS only.
Conclusions: The AD-SEQ HIV-1 NGS based assay, for the analysis of HIV drug resistance mutation provided valid results for all the samples analyzed (also that with very low HIV-RNA viral load), it was accurate for detecting major DRMs and detected mutations at lower level compared with SS method.

Virology and Pharmacology

Pharmacology, pharmacogenomics and drug interactions

P 101 DOLUTEGRAVIR PLASMA AND INTRACELLULAR PHARMACOKINETICS ACCORDING TO DRUG COMPANION IN THE CLINICAL SETTING

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Background: Dolutegravir (DTG) is currently used in association with of different N(t)RTIs: as a third drug in the standard of care triple drug regimen (3DR) and as part of dual regimen (2DR) plus lamivudine (3TC). DTG pharmacokinetics (PK) has been suggested as a determinant of neuropsychiatric tolerability. Aim of our study was to evaluate DTG PK according to companion N(t)RTIs in the clinical setting.

Methods: Patients (pts) administered with DTG 50 mg plus abacavir/lamivudine (ABC/3TC), tenofovir alafanamide/emtricitabine (TAF/FTC), or 3TC were included, after informed consent given. Plasma and intracellular (IC) DTG concentration were measured by means of UHPLC-MSMS validated method at the end of dosing interval (24+/-4 hours after intake, (Ctrough)). Non-compartmental PK parameters were expressed as geometric mean (CI95%). Pts characteristics were compared by Mann-Whitney and Kruskal-Wallis test and correlation analyzed with Spearman's test.

Results: 80 pts were included in the study: 25 pts on TAF/FTC, 16 on ABC/3TC and 39 on 3TC. 85% of them were male, age and BMI were 49 years (41-58) and 22 Kg/m2 (19-25). Geometric mean DTG plasma Ctrough plus TAF/FTC, ABC/3TC and 3TC resulted to be respectively 869.1 (590.7-1147.5), 1772.2 (2139.0-1405.3) and 1590.7 (1301.4 -1880.1) ng/mL (p=0.001). IC Ctrough resulted to be 197.4 (133.2-261.7), 389.0 (170.8-607.2) and 398.5 (312.0 -485.0) ng/mL (p<0.001), respectively, and IC/plasma ratio 0.206 (0.160-0.253), 0.219 (0.156-0.282) and 0.250 (0.227-0.274) (p=0.211). Correlation between DTG plasma and IC Ctrough were significative and linear in all groups (0.785, p<0.001) and an overall borderline linear and significative correlation was observed between DTG plasma Ctrough and age (0.208, p=0.064). No difference by gender or correlation with BMI was reported.

Conclusions: DTG plasma and IC exposure resulted to be higher in 3TC-including regimens, with no difference when dosed alone (2DR) or plus ABC (3DR), and IC accumulation was lower in TAF-including regimens. Long-term clinical evaluation to better evaluate the role of 3TC on DTG PK are warranted.

Virology and Pharmacology

Pharmacology, pharmacogenomics and drug interactions

P 102 CYCLOSPORINE A INHIBITS VIRAL INFECTION AND RELEASE AS WELL AS CYTOKINE PRODUCTION IN LUNG CELLS BY THREE DIFFERENT SARS-COV-2 VARIANTS

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Background: In December 2019, SARS-CoV-2 spread worldwide causing the COVID-19 pandemic. Patients affected by this pathology are characterized by several different clinical manifestations, which all have in common the hyper-activation of the immune system, even low-severity cases. This is triggered by the so-called cytokine storm, and it is associated with progression of disease severity and COVID-19-related deaths. Despite several approaches having been tested, no specific therapeutic protocol has been approved.
Cyclosporine A (CsA), a well-known inhibitor of cyclophilins, interferes with viral infection and/or replication via sequestration of cyclophilin A (CyPA) from binding to viral accessory proteins of different viruses, i.e. VSV, HBV, HCV, VV, HIV-1, and SARS-CoV. Moreover, CsA is known to be a potent immunosuppressor known to prevent T cell activation via the formation of a tri-partite complex that includes CyPA and calcineurin.
We investigated the effects of CsA on SARS-CoV-2 infection in CaLu3 cells, a human pulmonary cell line; results showed that CsA hampers both viral infectivity and the production of proinflammatory cytokines by three different variants of SARS-CoV-2, suggesting a potential exploitation of this drug in the therapy of COVID-19.
Material and Methods: CaLu3 pulmonary cells were treated with 0.1, 1, or 10 μM CsA either before or after infection with SARS-CoV-2. The analyzed variants were EU, Alpha and Gamma. The cytotoxic effect of CsA was monitored by MTT assay. Samples were collected 48 hours post infection. Viral RNA was quantified by droplet digital PCR (ddPCR). Real-time PCR was employed to assess IL1a, IL6, IL8, TNFa, IFITM3 and CH25H mRNA expression. Protein concentration and localization was evaluated by western blot and immunofluorescence analysis. Finally, in order to quantify the resulting effective viral production, infectious virus particle titration was evaluated by TCID50.
Results: Our findings show that: i) CsA-treated cells, either before or after SARS-CoV-2 infection, express significantly lower levels of Spike protein, whereas the levels of expression of the entry receptors, ACE2 and CD147, were unaffected; ii) the RNA levels of nucleocapside were significantly decreased in cells treated with CsA treatment; iii) CsA treatment dampens the number of released infectious viral particles (evaluated by analyzing the levels of N1 RNA in the supernatant and by TCID50) in both experimental conditions; iv) CsA dampens the virus-induced synthesis of cytokines (i.e. IL6, IL8, IL1α and TNFα), type I IFN-modulated restriction factors (IFITM3) and cholesterol 25-hydroxylase. Similar results were obtained with all the three different variants.
Conclusions: Altogether, these results suggest that CsA is able to counteract in vitro viral replication and to dampen the subsequent induction of cytokines in a human pulmonary cell line model. Therefore, CsA might be considered for repositioning to timely treat severe COVID-19 patients.

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Virology and Pharmacology

SARS-CoV-2 virology

P 103 ANTIVIRAL ACTIVITY OF AMPHIBIAN SKIN PEPTIDES AGAINST HIV AND SARS-COV-2

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Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to the Coronaviride family and represents the causative agent of COVID-19. As of March 2020, due to the marked spread of the virus and the significant increase in cases, the WHO has declared the status of a global pandemic. Therefore, the research of new antiviral molecules is of paramount importance to reduce the spread of virus-induced diseases. An emerging class of therapeutic agents is represented by antimicrobial peptides (AMPs), known for their antiviral, antifungal, antiparasitic, antioxidant and antitumor activities. In particular we will focus our attention on the study of antimicrobial peptides deriving from the secretion glands of frog skin. The antiviral activity of temporins isolated from Rana temporaria was evaluated against Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) and Human Immunodeficiency Virus (HIV).

Materials and Methods: The synthesis of the peptides was carried out using the Fmoc chemical method in the solid phase, followed by purification by reverse-phase HPLC. To evaluate the cytotoxic activity of the compounds, the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was performed. Antiviral activity has been evaluated against several viruses, including HIV and SARS-CoV-2, via plaque assay and molecular testing.

Results: Different concentrations of the peptides were tested with HIV and SARS-CoV-2. For both viruses, considerable antiviral activity was observed in the virus pre-treatment, when the peptides were pre-incubated with viruses, and subsequently inoculated on the cells. These data were also confirmed by molecular assays (RT-PCR), evaluating the expression of viral genes.

Conclusions: Our results show that temporins affect the extracellular phases of the viral cycle, destroying the viral envelope and blocking the viral attack and entry phases. In conclusion, it is possible to evaluate the peptides deriving from the skin of amphibians as new possible antiviral agents.

Virology and Pharmacology

Vaccines

P 104 DEVELOPMENT OF SARS-COV-2 IGG ANTIBODIES IN AN ELDERLY POPULATION AFTER M-RNA VACCINATION: A REAL-LIFE EXPERIENCE

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Background: To reduce the spread of severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) required the development of effective and safe vaccines. The first vaccine approved was the BNT162b2 mRNA vaccine (Pfizer-BioNTech), followed by mRNA-1273 vaccine (Moderna). Phase II vaccine trials demonstrate an elevated antibodies development, but the participants mean age was 35.8 and 31.3 years, respectively. However, there are few studies about the safety and efficacy of the mRNA vaccine among elderly people.
Our study evaluates the development of SARS-CoV-2 IgG antibodies in elderly people living in retirement nursing homes.
Material and methods: We conducted a retroprospective enrolling 118 people living in two retirement nursing homes in Sassari. We collected data about comorbidities and previous SARS-CoV-2 infection. All patients received two doses of mRNA vaccine. We collected blood samples the day of the second dose administration and 30 days after. Data on adverse events after vaccinations were recorded.
The presence of antibodies was evaluated with LIAISON® SARS-CoV-2 TrimericS IgG by DiaSorin. We correlated the level of antibodies with clinical data. A positive response was defined as the development of IgG title >33.8 binding antibody unit (BAU)/mL. A high response was considered for IgG title >2080 BAU/mL.
Results: Median age of patients was 84.5 (IQR 78.0-88.3) years, of which 34 (28.8%) were males. After the first vaccine dose, subjects with a previous SARS-CoV-2 infection developed a higher antibody level (p-value <0.0001) than people who did not contract the infection. Among people with previous SARS-CoV-2 infection, all patients reached detectable antibodies after the first dose, and 68/82 (82.9%) patients reached an antibodies level above the maximum cut-off. After the second dose, nobody else in this group reached the same cut-off. Among people who did not have a previous infection, 18/36 (50%) did not develop antibodies after the first dose, and 2/36 (5.5%) after the second dose. The number of patients developing a high level of antibodies increased significantly after the second dose (p=0.013) (Figure 1). At the multivariate analysis, diabetes and chronic kidney disease (CKD) were associated with lower development of IgG at the second blood sample (Table 1).
Regarding reported adverse events (myalgia, asthenia, fever, discomfort), we have observed a higher prevalence among people with a previous SARS-CoV-2 infection compared to the population without previous SARS-CoV-2 infection, in particular after the second dose (p-value <0.006).
Conclusion: Our study shows that mRNA vaccine is associated with antibodies development in elderly population. However, high prevalence of adverse events has been reported in previously infected people, especially after the second dose. Thus, in consideration of risk-benefits, further studies are needed to assess if one dose regimen could be a suitable option for previously infected elderly people.

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Virology and Pharmacology

Vaccines

P 105 VACCINATION AGAINST SEXUALLY TRANSMITTED INFECTIONS IN A STI CLINIC

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Background: Vaccination against sexually transmitted infections (STIs) is a major objective for any STI Clinic. Immunization for HAV, HBV and HPV is free for subjects at high risk of infection; vaccinations against meningococcal (quadrivalent and/or B serotype) are strongly recommended under special conditions but they are not free for HIV-negative individuals and have an unfavorable tolerability profile since high grade fever, pain at the site of injection and headache are common side effects. Herein we describe our vaccination activity in HIV-positive patients, PrEP users and subjects attending the Clinic for STI screening.

Methods: This monocentric, retrospective analysis included all subjects attending our STI Clinic who were evaluated for vaccination from 2018 onwards. Descriptive statistics (median and interquartile range for continuous variables, absolute and relative values for categorical variables) were used. Mann Whitney U for continuous variables, Chi-square and Fisher's exact tests for categorical variables were applied.

Results: The analysis included 572 individuals: they were mainly males (84%), Italians (82%) and with a median age of 44 (IQR 36-53) years. The majority was HIV-infected (75%), the others were PrEP users (20%) and subjects attending STI screening (5%). HIV-positive and negative individuals had different demographic features and vaccine management, as shown in Table 1: HIV-uninfected subjects generally required more immunization courses. They received less anti-meningococcal vaccines but more immunizations against HAV, HBV, and HPV. Among Italians born after 1979, who underwent compulsory anti-HBV vaccination in their childhood, the need of a booster dose was higher in HIV-negative individuals (25% vs 7%, p=0.002). However, there is the suggestion that HIV-positive patients needed more commonly a full re-vaccination course (83% vs 39%, p=0.080) and not just a booster dose.

Conclusion: Vaccination activity was relevant but revealed different need among HIV-positive and negative subjects. PrEP users and subjects attending STI screening required less anti-meningococcal vaccination: tolerability and cost may be a barrier to prescribe these immunizations. HIV-positive patients were older and less eligible to HPV vaccination that is limited to people younger than 45 years. Of note, the need of an additional booster dose for HBV was higher among HIV-negative subjects; the reasons for this difference are not clear: it may be speculated that HIV-positive patients were vaccinated soon after they acquired the infection, so they did not need a further dose when they accessed the STI Clinic. Although the small sample size failed to achieve the statistical significance, PrEP users and subjects attending STI screening required less frequently the full re-vaccination course compared to HIV-positive individuals.

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Virology and Pharmacology

Vaccines

P 106 SERO-SURVEY ON LONG-TERM CARE FACILITY RESIDENTS REVEALS RISK FACTORS OF SUB-OPTIMAL ANTIBODY RESPONSE TO BNT162B2: IMPLICATIONS FOR BREAKTHROUGH PREVENTION

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Background: The impact of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) on hosts of Long-Term Care Facilities (LTCFs) has been dramatic at global scale as aging and comorbidities pose individuals at increased risk of severe disease and death.
Aim of this study was to investigate differences in antibody titers and factors related to humoral responses in hosts of the largest nurse facility in Milan.
Methods: We evaluated SARS-CoV-2 S-IgG antibodies titers using a commercially available test (Anti-SARS-CoV-2, Roche) in 478 residents and 649 health care workers two months after the complete vaccination with BNT162B2. Response to vaccination was classified as high, medium, low and null response by stratifying the level of anti-S IgG values in 4 strata: >1000, 101-1000, 1-100 and <1 BAU/mL, respectively. Associations among host-related factors and predictors of humoral response were investigated by standard statistical methods.
Results: By stratifying levels of humoral responses, we found that 62.1%, 21.6%, 12.1% and 4.2% of hosts had high, medium, low and null S-IgG titers, respectively. Hosts with previous COVID-19 and those with SARS-CoV-2 N-IgG positive serology showed higher levels of serological response (both $p<0.001$), while the administration of corticosteroid or cancer diminished all levels of specific antibodies ($p=0.019$ and $p=0.004$). Significant associations were observed between these parameters and the prevalence of suboptimal response ($p<0.001$, $p<0.001$, $p=0.028$ and $p=0.005$). Null response to vaccine was associated with previous COVID-19, nucleocapsid serology and corticosteroid usage ($p=0.005$, $p<0.001$ and $p=0.039$, respectively) but not with neoplastic comorbidity. Among subjects with a previous COVID-19 clinical diagnosis, we did not find any case of null response to vaccine, either in those with positive or negative nucleocapsid serology (0/125 and 0/7, respectively). Differently, among hosts without a documented previous diagnosis of COVID-19, null response to vaccine was lower in those with positive nucleocapsid serology compared to subjects with negative serology: 0.7% (1/143) vs. 10.6% (19/180), respectively ($p<0.001$).
Independent predictors of an increased risk of null response were advanced age, corticosteroid therapy and diabetes mellitus ($p=0.025$, $p=0.17$ and $p=0.037$). In contrast, previous diagnosis of COVID-19 resulted strongly associated with a reduced risk of null response to vaccination ($p<0.001$).
Conclusions: Besides previous COVID-19, age and some comorbidities, such as diabetes and cancer, and corticosteroid treatment influence humoral responses to SARS-CoV-2 in elderly individuals. SARS-CoV-2 specific antibodies in elderly individuals may deserve to be measured and a third dose of vaccine should be evaluated in some cases after mass vaccination, in order to prevent reinfection in LTCFs, despite the maintenance of barrier measures.

Virology and Pharmacology

Vaccines

P 107 A CASE OF MENINGITIS AND CEREBRAL VENOUS THROMBOSIS A WEEK AFTER BNT162B2

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Background: As Covid vaccine administrations increase, reports of side effects also increase [1,2,3,4,5,6,7,8,9], which in most cases are only transient. However, some more serious events such as deep venous thrombosis, pulmonary embolism and cerebral venous thrombosis have been reported, even after mRNA vaccines. Given the limited number of cases, it is still to be determined whether these effects are effectively correlated to the vaccine and how much genetic predispositions could influence the onset of these manifestations.

Material and methods: We report the case of F.Z., a 21 years old white male. He was admitted to the ER for persisting symptoms, at least four days, including bitemporal throbbing headache, fever with a body temperature of 38°C and arthralgia. He didn't present other symptoms that could help identify a source of infection. Neurological examination showed neck stiffness, positive Kernig's sign (both supine and sitting Kernig's sign), positive Lasegue sign (80 degrees), negative Brudzinski's sign. The general clinical examination showed insect bites.

Significant aspects in the patient's medical history were:

mononucleosis infections in 2020,

recent scout's trip with outside camping two weeks before, in which he noticed non itchy insect bites that lasted more than two week,

first dose administration of COVID19 vaccine (BNT162b2) one week before,

family history of thrombophilia (a grandmother with G20210A prothrombin heterozygous mutation).

At the admission we planned a cerebral CT scan that didn't show abnormalities, a lumbar puncture and blood samples for microbiological exams.

Results: The CSF was clear and with a slightly elevated opening pressure, and showed some inflammatory characteristics such as high wite blood cells 94/uL (almost all mononuclear cells), lactate and total proteins. We found positive serology for Toscana Virus, high level of D-dimer (2631 ug/L). Since the patient continued to suffer from headache after a week from the admission we decided to repeat the cerebral CT scan which showed a suspected venous thrombosis, confirmed by the MRI scan with gadolinium.

Conclusions: Pfizer vaccination is overall a safe procedure [10,11,12,13,14], but in some cases could trigger an excessive thrombotic reaction that could lead to severe thrombotic events [1,2,3,4,7,8,9]. Infections (in our experience from Toscana Virus) and thrombophilic predisposition (family history of thrombophilia) may be possible risk factors for an excessive thrombotic reaction in patients that underwent COVID19 vaccinations.

Virology and Pharmacology

Vaccines

P 108 ADHERENCE TO VACCINATION IN PEOPLE WITH HIV INFECTION IN S SARS-COV2 PANDEMIC ERA

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Background: HIV patients are at risk of more frequent and serious infectious diseases, thus vaccinations are very important and effective for this specific subgroup of the population. 6 years ago a strong implementation of vaccination policy started in our center, also due to a resurgence of HAV hepatitis. HIV patients show different response to vaccines and sometimes diminished protection. Aim of this survey is to explore vaccination hesitancy (confidence, complacency, convenience) in people with HIV infection during SARS-CoV2 pandemic.

Methods: During their routine medical examination at the Infectious Diseases Clinic in Turin 915 adult HIV + patients were prescribed appropriate vaccines. The vaccination panel includes, for all: anti-pneumococcus, anti-meningococcus B and C, anti-haemophilus influenzae, anti-hepatitis A, anti-hepatitis B, anti HPV; anti-Herpes Zoster and yellow fever only in selected cases. The patients were usually referred to the competent vaccination center. Some vaccines could also be carried out at our center to promote adherence in patients hesitant for convenience reasons. In the last months the patients were also informed about SARS-CoV2 vaccinations and motivated to adhere to the vaccination campaign.

Results: Preliminary data: 676 (74%) male patients, mean age 51 years and 602 (89%) Italian; 239 (26%) female patients, mean age 50 years and 167 (70%) Italian. All subjects were receiving antiretroviral therapy. Male group: 554 (82%) underwent at least one prescribed vaccination, 116 (17%) didn't undergo any vaccination, 6 (1%) refused ex ante vaccination. Female group: 179 (75%) underwent at least one prescribed vaccination, 46 (19%) didn't undergo any vaccination, 14 (6%) refused ex ante vaccination.

Conclusions: Results show high adherence to vaccination prescription, at least in the initiation phase, referring to ABC taxonomy for describing and defining adherence to medications1. More time is required to explore persistence and discontinuation due to length of vaccination schedule and to SARS-CoV2 pandemic. Having created a vaccination habit can have an important educational value for SARS-CoV2 vaccination campaign. Especially in SARS-CoV2 pandemic era, it is very important to support and improve attitudes towards vaccination in people with HIV, since precise vaccination coverage and vaccine hesitancy are not well established in this subgroup of patients. More hesitancy or "no-vax "attitude in female may be due to cultural (African women) or psychological (coping with condition of seropositivity) issues.

1Vrijens B, De Geest S, Hughes DA, et al. A new taxonomy for describing and defining adherence to medications. BrJClinPharmacol. 2012; 73(5): 691- 705

Virology and Pharmacology

Vaccines

P 109 ANTIBODY DEVELOPMENT AGAINST SARS-COV-2 FOLLOWING COMIRNATY VACCINE: COMPARISON BETWEEN HEALTHY AND FRAIL PATIENTS

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Background: At the end of 2019 a novel coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2) was identified causing a health, economic and social crisis, which brought WHO to declare the pandemic state in March 2020. SARS-CoV-2 is responsible for coronavirus disease 2019 (COVID-19). COVID-19 symptoms can range from general malaise, cough and fever to acute respiratory distress syndrome (ARDS). Despite all the preventive measures to limit the viral spread and due to the absence of an etiological therapy, vaccination is the most effective strategy to contrast SARS-CoV-2.

From December 2020 Italy started a vaccination campaign first involving healthcare workers, followed by some categories of patients with frailty.

The aim of this study was to evaluate the kinetic of antibody production after vaccination in frail patients and in healthy donors.

Material and methods: Fifty patients were enrolled in this study: 27 patients undergoing hemodialysis (median age=64), 23 HIV positive subjects (median age=62) and 36 healthcare workers (median age=45). All participants received Comirnaty vaccine (Pfizer-BioNtech). Sera samples were collected 3 weeks after the first dose and 1, 2 and 3 weeks after the second dose. A serum sample was also collected from the control group and hemodialysis group 1 week after the first dose and 3 months after the second dose. All samples were centrifuged for serum separation and later analyzed using the LIAISON® SARS-CoV-2 TrimericS IgG kit (DiaSorin S.p.A., Saluggia, Italy) an indirect chemiluminescence immunoassay (CLIA) technology for the detection of serum IgG antibodies to SARS-CoV-2 trimeric spike protein.

Results: One week after the first dose all the healthcare workers resulted negative to the antibody count, whereas antibodies against the spike protein were developed in 4 dialysis patients. Three weeks after the first dose, the antibody titer was significantly higher in the control group than in patients group as well as at 1, 2 and 3 weeks after the second dose ($p < 0,0001$). Three months after the second dose the healthcare workers group kept showing a higher antibody titer than the dialysis patients ($p = 0,0053$). Finally, the two groups of patients were compared: 3 weeks after the first dose and 2 weeks after the second dose the HIV patients showed a higher antibody titer ($p = 0,0041$; $p = 0,0156$), whereas 1 and 3 weeks after the second dose no significant difference was observed.

Conclusions: The control group seems to be more responsive to the vaccination, although its median age is significantly lower than the patients group. Although some aspects remain to be defined, this preliminary study suggests that patients undergoing hemodialysis are less responsive to the vaccination.

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