11° CONGRESSO NAZIONALE

ICAR

Italian Conference on
AIDS and Antiviral Research

5-7 GIUGNO 2019

UNIVERSITÀ DEGLI STUDI
DI MILANO

Presidenza del Congresso
Antonella Castagna
Antonella d'Arminio Monforte
Massimo Puoti
Giuliano Rizzardini

Coordinatore Abstract
Franco Maggiolo

ABSTRACT BOOK

Challenges in HCV elimination

OC 1 SCREENING STRATEGIES FOR HEPATITIS C VIRUS ELIMINATION IN ITALY

*L.A. Kondili[1], M.G. Quaranta[1], A. Marcellusi[2], A. Craxi[3], M. Puoti[4], I. Gamkrelidze[5], S. Blach[5], H. Razavi[5], F.S. Mennini[2], and PITER Collaborating Group**

[1]Istituto Superiore di Sanità, Rome, Italy, [2]University of Rome Tor Vergata, Rome, Italy, [3]University of Palermo, Palermo, Italy, [4]Niguarda Hospital, Milan, Italy, [5]Center for Disease Analysis Foundation, Lafayette, United States, *available at www.progettopiter.it/rete.aspx

Background and Aim: Hepatitis C virus (HCV) elimination could be achieved in Italy but, cost-effective screening strategies are needed to make it a reality. HCV is more prevalent in the older Italian population, so our objective was to determine if birth cohort-based screening could be cost-effective in Italy.

Method: A Markov disease burden model was populated with Italian data to quantify the annual HCV-infected population by liver disease stage, sex, and age. An economic impact module was added to quantify medical costs (costs of screening, antiviral treatment, including assessment and monitoring, and liver-related complications) and health effects, denominated in quality-adjusted life years (QALYs), associated with HCV infection. Higher screening costs for high-risk groups required for HCV microelimination compared to the cost required for screening of general population are considered. Prevalence of undiagnosed, asymptomatic HCV infection estimated by the model considering the HCV prevalence in Italy and the number of treated patients was used to calculate the number of HCV antibody screens needed annually. The cost-effectiveness threshold was set at €25,000 as commonly accepted in the Italian guidelines. Modeled outcomes over 2018–31 were assessed under the status quo and as well as a scenario that met the World Health Organization's (WHO) targets for eliminating HCV by 2030.

The elimination scenario was assessed under four screening strategies: Universal screening; Screening the 1948–77 birth cohort; Screening the 1958–77 birth cohort. Graduated birth cohort screening (screening the birth cohort 1968–87 beginning in 2020 to identify young populations at risk for transmitting HCV, and expanding to the birth cohort 1948–67 beginning in 2023 to identify older populations before their disease advances.

Results: The graduated screening scenario was the least costly, with €6.0 billion in total medical costs by 2031. This was €107.4 million less than screening in the 1948–77 birth cohort, €109.1 million less than screening in the 1958–77 birth cohort, and €467.1 million less than universal screening. Relative to the status quo, graduated screening would gain 143,929 QALYs by 2031, compared to 142,244, 128,384, and 144,759 QALYs for the 1948–77 birth cohort, the 1958–77 birth cohort, and universal screening, respectively. Graduated screening would see a reduction of 89.3% in prevalent HCV-infected cases over 2018–31, compared to 89.0%, 89.7%, and 88.7% for the 1948–77 birth cohort, the 1958–77 birth cohort, and universal screening, respectively. Relative to the status quo, graduated screening yielded the lowest ICER of €3,552 per QALY.

Conclusion: In Italy, implementing graduated screening, beginning with the 1968–87 birth cohort in 2020, followed by the screening of the 1948–67 birth cohort from 2023 was the most cost-effective option, and showed the second largest reductions in overall disease burden by 2031.

Challenges in HCV elimination

OC 2 PREVALENCE OF HBV, HCV AND HIV VIRUS INFECTIONS IN A COHORT OF MIGRANTS IN SOUTHERN ITALY

C. Monari[1,2], L.Onorato[2,3,4], L. Alessio[1,3,4], G. Di Caprio[2,3,4], L. Surace[5], M. Starace[2], C. Sagnelli[2,3,6], L. Gualdieri[7], M. Pisaturo[2,3,4], G. Scotto[8], S. Curto[9], M. Macera[2,3,4], N. Coppola[1,2]

[1]Infectious Diseases Unit, AORN Sant'Anna and San Sebastiano, Caserta, [2]Department of Mental Health and Public Medicine, Section of Infectious Diseases, University of Campania Luigi Vanvitelli, Naples, [3]Medical Center, Caserta, [4]Medical Center, "Abraham's Tent", Caserta, [5]Medical Center Lamezia Terme – Catanzaro Lido – Soverato, [6]Medical Center, "Charity Nuns", Naples, [7]ASL Napoli 1, Ascalesi Hospital, Naples, [8]Infectious Diseases Unit, Foggia, [9]Medical Center, Potenza

Background: In the last decades the migratory influx from countries with intermediate-high HBV, HCV and HIV prevalence has become an issue for hosting western countries. Data about prevalence of these infections in migrants usually come from little cohorts. Aim: to verify HBV, HCV and HIV prevalence among migrants in southern Italy.

Material and methods: A multicenter prospective study was performed in 7 first-level clinical centers in southern Italy (Naples, Caserta, Potenza, Foggia and Lamezia Terme). In the period January 2012-June 2018 a screening program for HBV, HCV and HIV infections was offered free of charge to all migrants referring to these centers. Subjects with positivity for HBsAg, antiHCV or antiHIV were addressed to Infectious Diseases Units for further investigations.

Results: We observed 3839 migrants mostly coming from western Africa (59.9%) and Indo-Pakistan area (15.1%). 3224 subjects were males (86%), mean age was 28 years (±10 SD) (Tab1). 381 (9.9%) were positive for HBsAg, 136 (3.5%) for antiHCV and 62 (1.6%) for antiHIV. Among HBsAg negative subjects, 1448 (37.7%) were antiHBc positive. Moreover, 28 subjects (0.7%) had more than one infection: 9 HBsAg+/antiHCV+, 9 HBsAg+/antiHIV+, 8 antiHIV+/antiHCV+ and 2 HBsAg+/antiHCV+/antiHIV+ (Tab1).

Compared to females, males were younger ($p<0.01$) and mostly came from western Africa. A higher rate of ongoing (p 0.02) and previous ($p<0.001$) HBV infection was observed in males, whereas a higher prevalence of HIV infection was described in females ($p=0.01$). Migrants from western Africa showed a higher rate of HBsAg positivity (12.9%, $p<0.0001$), of HBsAg-/HBcAb+ status ($p<0.0001$) and antiHIV positivity ($p=0.004$). We found no significant difference in HCV prevalence according to sex or region of origin (Tab2).

On multivariate analysis, ongoing HBV infection was associated to provenance from western Africa (OR: 4.67, 95% CI: 1.70-12.80), eastern Europe (OR 3.44, 95% CI: 1.17-10.08) and male gender (OR:1.49, 95% CI: 1.04-2.14) (Tab 3a). All geographical areas (except for Asian countries other than Indo-Pakistan area), male gender and increasing age were all independently associated with an ongoing and past HBV infection (Tab 3b). HIV infection was associated to provenance from western Africa (OR 4.09, 95% CI: 1.26-13.29) and age (OR 1.04, 95% CI: 1.01-1.06) (Table 3d). Regarding HCV, we found an increased risk of infection among males (OR 1.84, 95% CI: 0.99-3.42), although not reaching the statistical significance (Table 3c). All subjects found positive for HBV, HCV or HIV serum markers were unaware of their serological condition.

Conclusions: Although subjects enrolled in this study may not be representative of the whole migrants population, the wide spread of HBV, HCV and HIV infections observed should be a warning for the Italian healthcare authorities to carry out appropriate and extensive screening policies, in order to prevent and reduce the risk of transmission of these infections.

Challenges in HCV elimination

OC 3 HCV TEST AND TREAT IN TWO MILAN PRISON INSTITUTIONS: AN EFFECTIVE STRATEGY TO ACHIEVE MICRO-ELIMINATION

R. Giuliani[1], T. Sebastiani[1], V. Casigliani[2], G. Arzilli[2], G. Scardina[2], E. Freo[1], L. Tavoschi[2], R. Ranieri[1]

[1]Infectious Diseases Service, Penitentiary Health System, San Paolo University Hospital, Milano, Italy, [2]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Background: People in prison represent a crucial high-risk population for HCV and other blood born infections control due the overrepresentation of people with a history of intravenous drug use, psychiatric patients and other vulnerable populations who have often reduced access to healthcare. With the advent of new direct antiviral agents (DAAs) HCV micro-elimination in prison setting became a feasible strategy. We studied the impact of an expanded HCV treatment program in Milan prisons between 2017 and 2018.

Methods: We conducted in 2017 and 2018 a cross-sectional evaluation of HCV treatment cascade in one detention prison, Opera (OP), and one pre-trial detention center, San Vittore (SV) in Milan. A dedicated protocol for HCV eligibility and care was applied. We collected data on demographic (sex, date of birth, origin country, drug addiction), HCV testing and treatment (HCV antibodies, HCV-RNA, previous therapies, treatment outcomes on all inmates present at 31st October 2017 and 2018. Data collection was closed on 31st December of each respective year.

Results: At 31st October 2366 inmates lived in the two facilities in 2017, 2369 in 2018, of the latter 1036 (43,7%) were already present in 2017 (28,7% in OP; 71,3% in SV). In 2017 and 2018 the majority were men (95.4%; 96,4%) with a median age of 41 years (IQR= 31-51) and were Italian nationals (57%; 61,9%). Prevalence of reported previous or current use of drugs remained high in the study period (46,5%; 44,2%).
Screening for HCV was offered to all inmates, reaching a coverage rate of 89% in both years, while HCV-RNA test coverage increased over time (90,6%; 99%). HCV sero-prevalence was stable (212, 10.1%; 194, 9,2%). Considering last available viremia at 31st December, in 2017 41 inmates (19,3%) were still viremic, with a difference between OP (16.1%) and SV (24,4%); in 2018 13 inmates (6,7%) had still positive HCV RNA, of which only one in OP (<1%). Regarding outcomes recorded at 31st December, 8 (3,8%) individuals had their eligibility process ongoing in 2017 and 3 (1,5%) in 2018, 30 (14,1%) individuals were on treatment in 2017 and 5 (2,6%) in 2018; 90 (42,4%) and 106 (54,6%) completed DAAs in prison, of which 38 (17,9%) and 76 (39,2%) achieved SVR respectively in 2017 and 2018. On 31st December 2017 and 2018, 151 (71,2%) and 179 (92,2%) patients were HCV-RNA negative, including 38 (17,9%) and 43 (22,2%) who had spontaneously cleared the infection. Inmates who were not initiated on DAAs decreased over time: 11 (5,2%) in 2017, 3 (1,5%) in 2018, mostly for psychiatric conditions.

Conclusion: Our study demonstrates the success of the HCV test and treat strategy to achieve HCV micro-elimination in a prison setting. These results show an increase of DAAs treatment coverage during 2017-2018 and consequently a significant drop of the pool of viremic individuals. However, high turnover of inmates in the pre-trial detention center remains a barrier for treatment initiation and elimination.

Challenges in HCV elimination

OC 4 EFFICACY AND TOLERABILITY OF DAAS IN HCV-MONOINFECTED AND HCV/HIV-COINFECTED PATIENTS WITH PSYCHIATRIC DISORDERS

N. de Gennaro, L. Diella, E. Milano, L. Monno, G. Angarano, M. Milella, A. Saracino

Clinica Malattie Infettive, Università di Bari

Background: Nowadays, few data are available regarding use of DAAs for chronic hepatitis C in psychiatric patients. This study seeks to evaluate outcome and safety of a DAAs-based antiviral therapy among HCV-monoinfected and HIV/HCV-coinfected patients with psychiatric comorbidities.

Material and methods: This retrospective, observational, single-centre study enrolled all consecutive HCV-infected patients (≥18 years old) presenting a documented psychiatric comorbidity, with or without HIV infection, who initiated DAAs-based regimen at our Center between 2015-2018. Patients were divided based on their psychiatric comorbidity, according to diagnostic criteria of DSM-V, into two groups: subjects treated with anxiolytic and/or antidepressant drugs (group A) and subjects on treatment with antipsychotics (group B). Week -12 sustained virological response (SVR-12) and adverse events (AEs) were evaluated.

Results: A total of 1,199 HCV-infected patients (1,081 HCV-monoinfected and 118 HIV/HCV-coinfected) initiated DAAs during the study period. Overall, 144/1199 subjects (12.0%) presented a psychiatric comorbidity, of whom 101 (70.1%) were on anxiolytic/antidepressant therapy (group A) and the remaining 43 (29.9%) were treated with antipsychotic drugs (group B). The clinical characteristics of patients at baseline are summarized in Table 1. Patients were 49.3% males with a mean age of 60 years (SD ±13.5), and 31.9% of them were cirrhotic; 125 (86.8%) were HCV-monoinfected and 19 (13.2%) were HIV/HCV-coinfected. Coinfected patients were mostly represented among subjects in treatment with antipsychotic drugs (p=0.030). The most frequently prescribed DAA-regimen was SOF+VEL±RBV (25.7% overall), especially in subjects in antipsychotic treatment (p<0.001). Twenty patients (13.8%) required a change of psychiatric drugs before DAAs-initiation. Overall, SVR -12 was achieved in 88.2% of subjects in intention-to-treat (ITT)-analysis. Lower SVR rates were observed in group B vs A (p=0.045) and in those changing psychiatric drugs before anti-HCV treatment vs others (p=0.015). In Table 2 the characteristics of the psychiatric disorder are detailed for both groups. The safety profile is described in Table 3. At least one AE occurred in 60 patients (41.6%). AEs were more frequently reported in group A compare to B (p=0.015). Serious AEs were uncommon (10, 6.9%), leading to 3 discontinuations. No death was reported.

Conclusions: The study points out the complexity of the anti-HCV treatment of patients with psychiatric comorbidity and suggests that slightly lower SVR rates can be expected in psychotic patients while adverse events are more frequently reported among anxious/depressive patients. A careful evaluation of the history and possible drug-drug interactions before starting therapy can have a remarkable impact on outcome, which was overall successful in our experience, thus encouraging a widespread use of DAAs also in such a "special population".

Challenges in HCV elimination

OC 5 ROAD TO HCV ELIMINATION IN HIV/HCV COINFECTED PATIENTS BY SCREENING AND UNIVERSAL ACCESS TO DAA: BASELINE DATA FROM THE FIRST SCREENING OF NOCO (NO COINFECTION) STUDY

A. d'Arminio Monforte[1], A. Tavelli[2], A. Cozzi-Lepri[3], S. Cicalini[4], A. Calcagno[5], R. Rossotti[6], E. Grilli[4], F. Bai[1], E. Quiros-Roldan[7], E. Girardi[8], A. Antinori[4], M. Puoti[6] for the NoCo Study of the Icona cohort

[1]ASST Santi Paolo e Carlo, University of Milan, Clinic of Infectious and Tropical Diseases, Dept of Health Sciences, Milan, Italy, [2]Icona Foundation, Milan, Italy, [3]Institute for Global Health, University College of London, London, UK, [4]Clinical Division of HIV/AIDS, INMI "L. Spallanzani" IRCCS, Rome, Italy, [5]Unit of Infectious Diseases, Department of Medical Siences, Amedeo di Savoia Hospital, University of Torino, Torino, Italy, [6]ASST Grande Ospedale Metropolitano Niguarda Division of Infectious Diseases, Milan Italy, [7]Department of Infectious and Tropical Diseases, University of Brescia, ASST Spedali Civili Hospital, Brescia, Italy, [8]Clinical Epidemiology Unit, INMI "L. Spallanzani" IRCCS, Rome, Italy

Background: The main objective of NoCo study is to evaluate the possibility of eliminating HCV in the HIV/HCV coinfected population in Italy over a 3-year period as result of increased HCV testing and extensive DAA treatment. The aim of this first analysis is to estimate the overall prevalence of active HCV infection in HIV pos patients in care in 2018.

Methods: This is a cross-sectional analysis using data from the first NoCo screening. Subjects included are those screened for HCV, independent of their previous HCV status, belonging to centers of the Icona network. The prevalence of HCV infection has been calculated as number of people with a positive HCV Ab divided by the number of people tested; the prevalence of active HCV as the fraction of participants with a positive HCV RNA among those who were antibody-positive. Prevalence of new HCV infections in those with negative HCV Ab before NoCo screening has also been calculated. Differences between HCV positive and negative were assessed using chi-square and non-parametric Kruskal-Wallis test. Predictors of new HCV infection were assessed using unadjusted and adjusted (for age, gender and mode of transmission) logistic regression.

Results: 5400 patients have been included so far [Figure1]. They represent approximately 10% of those estimated to be enrolled, so we cannot exclude a selection bias. Prior to study entry 1750 (32.4%) had known HCV infection, 3050 (56.5%) were HCV Ab negative and 600 (11.1%) had unknown HCV serology. At the first NoCo screening 1824 (33.8%) were HCV Ab positive and 3576 (66.2%) HCV Ab negative.

Demographic characteristics at first NoCo screening are shown in Table1. Compared to HCV Ab negative HCV Ab positive subjects were older, more frequently female, Italian, IVDU and with a longer history of HIV infection.

53 (8.8%) out of 600 participants with unknown HCV Ab status were found to be HCV Ab positive. 22 (0.7%) out of 3049 previously HCV Ab negative had an HCV seroconversion. The only independent predictor of HCV seroconversion was injection drug use (IDU) (AOR vs heterosexual=6.55, p=0.005) [Table2].

Only 469 subjects (25.7%) out of 1824 HCV Ab positive were HCV viremic, 55 (3.0%) were not tested for HCV RNA and 1300 (71%) were HCV RNA negative. A total of 1065 (58.4%) patients had already been treated with a DAA or IFN, 390 (21.4%) were never treated and 369 (20.3%) had unknown treatment status. 146/1065 (13.7%) of previously DAA- or IFN-treated patients vs. 323/759 (42.6%) of untreated and unknown treatment status patients were HCV RNA positive (p<0.01).

Conclusions: Surprisingly, 11% (600) of HIV positive individuals in care in 2018 have not been tested for HCV. IDUs are the group at highest risk of new HCV infection in Italy. Circulation of HCV among MSM appears lower than in other European countries. This result, together with the observation that almost 70% of HCV patients have already cleared the virus, the target of HCV coinfection elimination within 3 years, could be achievable.

This study is supported by a grant from Gilead International

Challenges in HCV elimination

OC 6 ANALYSIS OF BASELINE FACTORS ASSOCIATED WITH TREATMENT OUTCOME IN HCV-INFECTED PATIENTS STARTING A FIRST- LINE DAA-TREATMENT CONTAINING A NS5A INHIBITOR: PARTICULAR FOCUS ON NATURAL RESISTANCE

S. Barbaliscia[1], V.C. Di Maio[1], E. Teti[2], M. Aragri[1], S. Paolucci[3], C. Masetti[4], R. D'Ambrosio[5], E Degasperi[5], E. Polilli[6], V. Pace Palitti[7], G. Fiorentino[8], L. Foroghi[2], V. Cento[9], R. Scutari[1], B. Bruzzone[10], V. Calvaruso[11], N. Coppola[12], G.B. Gaeta[12], G. Morsica[13], T. Ruggiero[14], V. Ghisetti[14], A. Bertoli[1] , M. Milana[4], L.A. Nicolini[15], W. Gennari[16], S. Galli[17], C.F. Magni[18], V. Micheli[19], A. Lleo[20], A. Aghemo[20], R. Maserati[21], S Bonora[22], N. Iapadre[23], F. Morisco[24], M. Siciliano[25], V. Guarneri[26], B. Rossetti[27], M. Lichtner[28], V. Borghi[29], T. Pollicino[30], C. Caudai[31], L. Sarmati[2], M. Puoti[32], A. Pellicelli[33], S. Babudieri[34], G. Rizzardini[18], G. Taliani[35], G. Parruti[6], M. Zazzi[36], P. Lampertico[5], G. Raimondo[30], C. Pasquazzi[8], M. Angelico[4], F. Baldanti[3], M. Andreoni[2], C.F. Perno[37], A. Craxì[11], F. Ceccherini-Silberstein[1] on behalf of HCV Virology Italian Resistance Network (Vironet C)

[1]Department of Experimental Medicine, University of Rome "Tor Vergata", Rome,Italy, [2]Infectious Diseases Unit, University of Rome "Tor Vergata", Rome, Italy, [3]Molecular Virology Unit, Microbiology and Virology Departmentt, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [4]Hepatology Unit, University Hospital of Rome"TorVergata", Rome,Italy, [5]"A.M. e A. Migliavacca" Center for Liver Diseases, Division of Gastroenterology and Hepatology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy, [6]Infectious Diseases Unit, Pescara General Hospital, Pescara, Italy, [7]Hepatology Unit, Pescara General Hospital, Pescara, Italy, [8]Infectious Diseases Unit, Sant'Andrea Hospital–"Sapienza"University, Rome, Italy, [9]Residency program in Microbiology and Virology, Università degli Studi di Milano. Milan, Italy, [10]Hygiene Unit, IRCCSAOU San Martino-IST, Genoa, Italy, [11]Gastroenterology,"P. Giaccone" University Hospital, Palermo, Italy, [12]Infectious Diseases Unit, Department of Mental and Physical Health and Preventive Medicine, University of Campania L. Vanvitelli, Naples, Italy, [13]Division of Infectious Diseases, IRCCS, Ospedale San Raffaele, Milan, Italy, [14]Laboratory of Microbiology and Virology, "Amedeo di Savoia" Hospital, ASL, Città di Torino,Turin, Italy, [15]Infectious Diseases Unit, IRCCSAOU San Martino-IST, Genoa, Italy, [16]Microbiology and Virology Unit, University Hospital Policlinico of Modena, Modena, Italy, [17]Microbiology and Virology Unit, Sant'Orsola-Malpighi Hospital, Bologna; Italy, [18]1st Division of Infectious Diseases, ASST Fatebene fratelli Sacco, Milan,Italy, [19]Clinical Microbiology, Virology and Bioemergencies, ASST Fatebenefratelli Sacco, Milan, Italy, [20]Department of Internal Medicine, Humanitas Research Hospital, Rozzano, Milan, Italy, [21]Institute of Infectious Diseases, University of Pavia, Pavia, Italy, [22]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy, [23]Infectious Diseases Unit, S.Salvatore Hospital, L'Aquila, Italy, [24]Gastroenterology, «Federicoll» University, Naples, Italy, [25]Gastroenterology, Catholic University of Rome, Rome, Italy, [26]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy, [27]Infectious Diseases Unit, AOU Senese, Siena, Italy, [28]Infectious Diseases Unit,"Sapienza"University, Polo pontino, Latina, Italy, [29]Department of Biomedical Sciences, University of Modena School of Medicine,Italy, [30]Department of Internal Medicine, University Hospital of Messina, Messina, Italy, [31]Department of Medical Biotechnology, University of Siena, Siena, Italy, [32]Hospital Niguarda Ca'Granda, Milan, Italy, [33]Hepatology Unit, San Camillo Forlanini Hospital, Rome, Italy, [34]Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [35]Infectious and Tropical Diseases Unit, Department of Clinical Medicine, "La Sapienza" University of Rome, Rome, Italy, [36]Department of Medical Biotechnology, University of Siena, Siena, Italy, [37]Department of Oncology and Oncohematology, University of Milan, Milan, Italy

Background: We aimed to study the presence of natural resistance-associated-substitutions (RASs) and other pre-treatment risk-factors related to failure in HCV-infected (patients) pts, starting a first-line treatment with a NS5A inhibitor.

Methods: RASs in NS3/NS5A/NS5B (N=1862/1662/1344) were analysed in 2138 pts naïve to direct-acting-antivirals (DAA). Of them, 861 pts with a baseline (BL) NS5A-resistance-test and available outcome after a first-line NS5A-containing regimen recommended by the 2016-2018 EASL guidelines, were also analysed. HCV Sanger-sequencing was performed by home-made protocols in different Italian Vironet-C centers. Potential differences between the sustained-virological-response (SVR) and virological-failure (VF) groups were evaluated by Fisher's exact test. A multivariable logistic-regression analysis was performed to define risk-factors associated to treatment-response.

Results: Overall, 621/2138 (29.0%) pts showed at least one natural-RASs, particularly NS5A-RASs were observed in 17.9% pts. 816 pts (GT1a/b/g[267/229/2]-GT2a/c[88]-3a[161]-4a/d[69]) had an available outcome (761with a SVR and 55 with a VF) after the following recommended NS5A-containing regimen: daclatasvir/ledipasvir/velpatasvir(VEL)+sofosbuvir(SOF)+/-ribavirin(RBV) (N=128/137/198), 3D/2D (paritaprevir/ritonavir+ombitasvir±dasabuvir)+/-RBV (N=125/44), grazoprevir(GZR)+elbasvir(EBV)+/-ribavirin (RBV) (N=103), glecaprevir+pibrentasvir(G/P) (N=81). Analysing retrospectively the BL samples, a higher prevalence of natural NS5A-RASs was observed before treatment in VF-pts (34.5%) vs SVR-pts (17.9%; p=0.01). Notably, ≥2 risk-factors for failure were frequently observed at BL among pts who experienced a VF to a DAA treatment (69.1%) vs who achieved SVR (34.7%, p<0.001). By multivariable logistic-regression, BL HCV-RNA >800.000 IU/ml, presence of at least 1 natural RAS regimen-related and cirrhosis and were all negatively associated to SVR (see table). Restricting the multivariate analysis only with the new recommended-regimens (G/P; SOF/VEL; GZR/EBV) BL NS5A-RAS was still negatively associated to SVR (adjusted odd-ratios [95%C.I.]: 0.189[0.046-0.783], P=0.022). All 81 GT1/GT2/GT3 pts treated with G/P achieved SVR, with the exception of 3 failures (2GT1a and 1GT3a), interestingly the GT1a-relapse and GT3-breakthrough had at BL the NS5A-RAS L31M and A30K, respectively, both having HCV-RNA>800.000 IU/ml. Regarding SOF/VEL+/-RBV, all 198 GT1/GT2/GT3/GT4 treated pts achieved SVR with the exception of 3 relapser (1GT1a and 2GT3a), none showing BL-RASs regimen-related.

Conclusions: The presence of one or more specific pre-treatment risk factors, such as NS5A-RAS or RAS-regimen-related, HCV-RNA>800,000 IU/ml and cirrhosis was associated with virological failure for some specific regimens and genotypes. Further analyses are needed to confirm these observations, particularly for the new current regimens and in the context also of shorter treatment durations.

Immunological insights of HIV infection

OC 7 INTERLEUKIN 32: A NEW MARKER OF CHRONIC IMMUNE ACTIVATION IN HIV PATIENTS RECEIVING ANTIRETROVIRAL THERAPY

M. Statzu[1], L. Santinelli[1], C. Pinacchio[2], F. Frasca[1], C.M. Mastroianni[2], G. Antonelli[1], G. d'Ettorre[2], C. Scagnolari[1]

[1]Department of Molecular Medicine, Laboratory of Virology affiliated to Istituto Pasteur Italia - Fondazione Cenci Bolognetti, Sapienza University, Rome, Italy; [2]Department of Public Health and Infectious Diseases, Sapienza University, Rome, Italy

Background: Since residual immune activation status and abnormal cytokine profile are pathological hallmarks of well-treated HIV-1 infection and IL-32 is strongly related to the inflammatory cytokine network, we hypothesized that IL-32's action on IFN-γ and IFN-γ secreting T cell subsets may actively help sustain the immune activation and dysregulation recorded in patients living with HIV-1 achieving viral suppression. Therefore, we performed a comprehensive assessment of IL-32 gene expression in PBMC, CD4+ T cells, CD14+ monocytes and in the effector sites (lamina propria) of the gastrointestinal tract of HIV-1-infected subjects on long-term suppressive antiretroviral therapy. Moreover, since IFN-γ can induce IL-32 in vitro, we compared IL-32 expression levels to those of IFN-γ and gamma-interferon-inducible protein 16 (IFI16) and their correlation in the same HIV-1-infected patients. Lastly, we also examined the relationship between IL-32 levels, the expression levels of IFI16 and the frequencies of IFN-γ producing CD4+ and CD8+ T cell subpopulations in gut mucosa.
Methods: Transcript levels of IL-32, IFN-γ and IFI16 were evaluated in PBMC from 148 virologically suppressed HIV-1-infected patients and from 65 healthy individuals by Real Time RT-PCR assays. IL-32 and IFN-γ mRNA levels were also analyzed in CD4+ T cells, CD14+ monocytes and lamina propria lymphocytes (LPL) of the gut district in a subgroup of HIV-1-infected subjects. IFN-γ secreting CD4+ (Th1) and CD8+ (Tc1) T cell subset frequencies were evaluated in LPL by multiparametric flow cytometry.
Results: Gene expression results revealed that IL-32, IFN-γ and IFI16 levels in PBMC from HIV-1-positive patients were significantly elevated compared to those from healthy donors and correlated with each other. Dividing HIV -1-infected patients into 3 age groups (I group: 20-40 years old, II group: 40-60 years old, III group: 60-80 years old), we observed that HIV-1-positive patients aged 20-40 years had lower levels of IL-32 and IFN-γ than HIV-1 patients aged 40-80 years ($p<0.0001$ for all analysis). Both IL-32 and IFN-γ genes were also more strongly expressed in CD4+ T cells than in CD14+ monocytes. By contrast, IL-32 and IFI16 levels in LPL were comparable to those measured in PBMC, while IFN-γ levels were higher in PBMC than those in LPL. Negative correlations were found between IL-32 levels and the frequencies of Th1 and Tc1 subsets in gut mucosa.
Conclusions: Despite a decrease in inflammation and immune activation after drug intervention in the HIV-1-positive patients, IL-32 levels remain higher than those shown by healthy individuals and even the imbalance of IL -32, IFN-γ, IFI16, Th1 and Tc1 profiles persists.

Immunological insights of HIV infection

OC 8 EFFICIENT ANTI-HPV SPECIFIC T CELL RESPONSE AFTER VACCINATION IN HIV PATIENTS

M. Nasi[1], S. De Biasi[2], E. Bianchini[1], A. Neroni[3], M. Digaetano[4], D. Lo Tartaro[5], M. Pinti[2], L. Gibellini[1], D. Pavia[6], A. Bignardi[7], C. Mussini[1,4], A. Cossarizza[3]

[1]Department of Surgery, Medicine, Dentistry and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy, [2]Department of Life Sciences, University of Modena and Reggio Emilia, Modena, Italy, [3]Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy, [4]Infectious Diseases Clinics, Azienda Ospedaliero-Universitaria Policlinico di Modena, Modena, Italy, [5]Department of Biomedical, Metabolic and Neural Sciences; University of Modena and Reggio Emilia, Modena Italy, [6]Arcigay Modena "Mattew Shepard", Modena, Italy, [7]Arcigay - Associazione LGBTI Italiana, Bologna, Italy

Background: Persons living with HIV (PLWH) have a high risk of developing high-grade anal intraepithelial neoplasia or anal cancer. Most studies on HPV vaccination in HIV patients have only investigated the activity of the B cell compartment, measuring the antibody titre, while T-cell mediated immunity, which is crucial to control the viral infection, has received poor attention. Recently, it has been shown that young HIV+ patients treated with combined antiretroviral therapy can respond efficiently to HPV vaccine. However, no data are available on the quality of this response in terms of T cell polyfunctionality. For this purpose, we analysed the specific T cell response to HPV antigens in HIV+ patients before and after immunization, in order to determine the overall impact of the vaccine on T cell functions.

Material and methods: Gardasil 9 (VLP vaccine against different HPV strains, such as 16/18/6/11/31/31/33/45/52/58) was administered to a total of 39 subjects, of whom 19 were cART-treated HIV+ males (all MSM), <50 years old, with undetectable viremia and effective CD4 recovery, compared to 20 age-matched HIV negative MSM controls. Before starting vaccination and 2 months after the end of the vaccination cycle, mononuclear cells (PBMCs) were isolated from blood and cryopreserved. Thawed PBMCs were then stimulated with PepMix HPV16 or PepMix HPV18 (L1 protein of HPV16 or HPV18, respectively), or anti-CD3/CD28 (as positive control) and stained with LIVE DEAD AQUA, anti-CD3 PE-Cy5, CD4 AF700, -CD8, -CD45RA PE, -CD197 BV421. Cells were fixed and permeabilized by using BD Cytofix/Cytoperm kit. Then PBMC were stained with anti-IL-2 APC, -IFN-gamma FITC, -TNF-a BV605 and -IL-17 PE-Cy7 to detect the intracellular and simultaneous production of these 4 cytokines. A minimum of 2 million cells per sample were acquired by using an Attune NxT flow cytometer (Thermofisher), and data were analysed by using FlowJo 9.6 and SPICE.

Results: Preliminary data regarding 5 HIV+ patients and 5 healthy subjects showed that, before vaccination, HIV + patients had higher levels of CD4+ central memory T cells if compared to healthy donors. Percentages of CD4 + and CD8+ T cells producing different cytokines were similar between patients and healthy subjects before vaccination. The quality of L1-specific T cell response, in terms of polyfunctionality, was significantly different before and after vaccination. In particular, all subjects, either HIV+ or controls, displayed a higher production of IL-2, TNF-a and IL-17 both.

Conclusion: In the first subjects we have analyzed, it appears that, after vaccination, T helper cells specific for L1 proteins were skewed towards Th1 and Th17 phenotype. Given that Th17 cells are an important subset for immune-mediated protection at the mucosal ports of viral entry and are responsible of helping IgA production, we could speculate that HIV+ patients, similarly to controls, can develop an appropriate immune response to HPV.

Immunological insights of HIV infection

OC 9 INNATE IMMUNE AND EPIGENETIC MODULATORS REACTIVATE LATENT HIV-1 T CELL RESERVOIRS

E. Palermo[1], C. Acchioni[2], D. Di Carlo[3], A. Zevini[1], M. Muscolini[1], M. Ferrari[1], L. Castiello[1], S. Virtuoso[4], A. Borsetti[4], G. Antonelli3, O. Turriziani[3], M. Sgarbanti[2], J. Hiscott[1]

[1]Istituto Pasteur - Fondazione Cenci Bolognetti, Rome, [2]Department of Infectious, Parasitic and Immune-Mediated Diseases, Istituto Superiore di Sanità, Rome, [3]Department of Molecular Medicine, "Sapienza" University of Rome, Rome, [4]National HIV/AIDS Research Center, Istituto Superiore di Sanità, Rome

Background: The presence of T cell reservoirs in which HIV establishes latency by integrating into the host genome represents a major obstacle to a cure and has prompted the development of different strategies aimed at eradication of virus from latently infected cells. The "Shock and kill" strategy is one of the most pursued approaches directed towards the clearance of infection; although several Latency-Reversing Agents (LRAs) have shown promising reactivation activity, they have failed to eliminate the cellular reservoir. Here, we evaluated a novel immune-mediated approach to clear the HIV reservoir, based on the combination of innate immunity stimulation and epigenetic reprogramming.

Material and Methods: The latency reversal activity of the cyclic di-nucleotide cGAMP and the FDA-approved HDAC inhibitor Resminostat was assessed in the J-Lat 10.6 and ACH-2 models of latency in vitro; Jurkat E6.1 and CEM A301 cells were used as uninfected control to evaluate the ability of these compounds to induce selective killing of infected cells. The experimental conditions tested in vitro were first replicated in a primary model of HIV latency, the CD4+ T central memory (TCM) cells, obtained from healthy donors and infected with HIV-1 luciferase reporter virus, and finally in PBMCs obtained from HIV-positive ART-treated patients from Policlinico Umberto I University Hospital.

Results: We found that the STING agonist cGAMP is able to reactivate latent HIV-1 in vitro by triggering NF-κB signaling, however no significant differences were detected in cell death levels comparing HIV-harboring cells to uninfected controls. The combination of cGAMP and Resminostat resulted not only in a significant increase of HIV -1 reactivation, but also in the induction of selective apoptosis in HIV-infected cells in vitro. A reduction in HIV-harboring cells was also observed in TCM cells, upon stimulation with Resminostat and cGAMP that induced high levels of selective cell death following latency reversal. Finally, significant levels of cellular-associated HIV-RNA were found in PBMCs obtained from individuals on suppressive ART treated with Resminostat or cGAMP, although no synergistic effect was detected with the combination.

Conclusions: Despite the ability of several LRAs to reverse HIV-1 latency, no functional cure has been achieved so far. The limit of this approach could be attributable to the inefficacy of a single-LRA treatment, which is unable to induce the clearance of the reservoir following reactivation. Here we showed that a combination of two LRAs potentiates the latency reversal activity and induces apoptotic cell death in HIV-harboring cells. Collectively, these results represent a promising step towards HIV eradication by demonstrating the potential to exploit the immune system to reduce the viral reservoir and induce specific killing of HIV-infected cells.

Immunological insights of HIV infection

OC 10 PHENOTYPICAL RECOVERY OF THE T-CELL POOL FOLLOWING SWITCH TO DUAL INSTI-BASED CART

C. Tincati, D. Mondatore, A. Tavelli, L. Nekrasova, M. Sala, A. d'Arminio Monforte, G. Marchetti

Department of Health Sciences, Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, University of Milan, Italy

Background: Integrase strand transfer inhibitors (INSTIs) are often used in first and switch strategies as dual combination therapy, given their viral efficacy, high genetic barrier and tolerability. A gap in the literature exists, nonetheless, as to whether dual INSTI-based regimens have an impact on the profound immunological changes which persist in the course of suppressive cART. Aim of our study is to evaluate the kinetics of T-cell homeostasis parameters in subjects switching to dual INSTI-based therapy during viral undetectability.

Material and Methods: Retrospective study on HIV-infected subjects on virologically-suppressive NNRTI or PI-based cART who were switched to dual therapies containing INSTI.

T-cell homeostasis parameters were studied at 6 (T6) and 12 months (T12) after therapy switch in the course of stable viral suppression. Peripheral blood was stained with the fluorochrome-based antibodies to study T-cell naïve (CD45RA), memory (CD45R0), activated (CD38), and CD127-expressing subpopulations. Wilcoxon tests were used for statistics.

Results: We identified 45 subjects on suppressive cART switching to a dual INSTI-based therapy (Table 1). The majority of subjects were male and had an IVU/heterosexual epidemiology for HIV acquisition. Nadir CD4+ T-cell count was 234/uL (IQR 148-412) and approximately 25% had a previous AIDS diagnosis. At switch, the median time of viral suppression was 59 (IQR 25-85) months. Stable CD4+ T-cell counts and CD4/CD8+ ratio were detected following switch (CD4, at switch: 624/uL, 420-920; T6: 643/uL, 434-866 p=0.9; T12: 670/uL 506-1050, p=0.12; CD4/CD8 at switch: 0.7, 0.5-0.9; T6, 0.7, 05-1.0, p=0.18; T12, 0.8, 0.6-1.0 p=0.08). Of note however, following switch to a dual INSTI-based regimen, we found a significant increase of CD127-expressing CD4+ (at switch: 19%, 12-25; T6,22%, 16-30 p=0.0004; T12, 23%, 16-28, p=0.0002; Figure 1A) and CD8+ T-cells (at switch 25%, 19-32; T6; 27, 23-34, p=0.04; T12, 26%, 22-34, p=0.08; Figure 1B). Similarly, a significant expansion of naïve CD4+ T-cells was detected 12 months after the switch (at switch: 10%, 5-13; T6, 10%, 6-15 p=0.2; T12, 10%, 6-15 p=0.04; Figure 1C). No differences were detected in terms of activated and memory T-cell subpopulations.

Conclusions: Our results suggest that switching to a dual INSTI-based regimen in the course of viral suppression may favour immunological recovery of the T-cell pool, featuring the expansion of the CD127-expressing and naïve CD4+ T-cell subsets. Future studies need to confirm these preliminary findings which appear to support, from an immunologic standpoint, the use of dual INSTI-based regimens in the in the setting of toxicity-/optimization-driven cART modifications.

Immunological insights of HIV infection

OC 11 SEX-RELATED DIFFERENCES IN IMMUNE ACTIVATION MARKERS DURING HIV-1 INFECTION

L. Santinelli[1], C. Borrazzo[2], G.P. Innocenti[2], C. Pinacchio[2], M. Statzu[1], G. Ceccarelli[2], C. Scagnolari[1], G. Antonelli[1,3], C.M. Mastroianni[2], V. Vullo[2], G. d'Ettorre[2]

[1]Laboratory of Virology, Department of Molecular Medicine, Affiliated to Istituto Pasteur Italia - Cenci Bolognetti Foundation, Sapienza University of Rome, Rome, Italy, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy, [3]Microbiology and Virology Unit, Sapienza University Hospital, Rome, Italy

Background: Sex-related biological factors may affect disease progression during HIV-1 infection but gender-specific studies focused on immunological features, as peripheral and mucosal T-cell responses, remains an area of research largely neglected. Therefore, the aim of this study was to investigate whether the levels of immune activation measured in the Gut and Peripheral districts were influenced by the sex in a population of HIV-infected individuals treated with fully suppressive ART.

Material and Methods: Thirty HIV-infected individuals, undergoing long-term fully suppressive ART, were enrolled in this study. Peripheral Blood Mononuclear Cells (PBMCs) and Lamina Propria Lymphocytes (LPL) were freshly isolated from peripheral blood samples and gut biopsies collected by pancolonscopy, respectively. The expression of immune activation markers (CD38, HLADR) in naïve, central memory (CMEM) and effector memory (TEM) CD4 and CD8 T-cells was evaluated by multi-parametric flow cytometry and expressed by Mean Relative Difference (MRD) [the MRD is defined as (X1-X2) / X2, where X1 is the measure of the peripheral blood marker, while X2 is the measure of the marker referred to the GUT].

Results: Differences in the levels of immune activation between Gut and PBMC were observed in male (n=15) and female (n=15) HIV-1 infected patients, with higher values in the Gut compartment compared to PBMCs ($p<0.05$). For women, the MRDs are often below the 0 line, hence on average the immune activation marker has a higher value in the Gut than the Peripheral blood. For men, the MRDs are on average about equal to 0, thus the immune activation marker value is comparable between Gut and PBMC [mean value of the percentage differences: men (-0.52 ± 0.42 - statistically consistent with zero) and women (-1.7 ± 0.65)] (Figure 1). In addition, the relative difference between men and women were statistically significant for 17 of 24 immune activation markers considered (CD4 38+, CD4 NAÏVE CD38+, CD4 NAÏVE CD38+DR+, CD4 NAÏVE DR+, CD4 CMEM 38+DR+, CD4 CMEM DR+, CD4 TEM 38+, CD4 TEM DR+, CD8 38+, CD8 DR+, , CD8 NAÏVE CD38+, CD8 NAÏVE CD38+DR+, CD8 CMEM 38 +, CD8 CMEM DR+, CD8 TEM 38+, CD8 TEM 38+DR+, CD8 TEM DR +; Student t-test, $p<0.05$) (Figure 1).

Conclusions: A significant sex-based difference in the level of immune activation was observed in a population of HIV-infected male and female patients on long-term ART, which might contribute to the disease dimorphism. A more detailed characterization of these differences may support the introduction of sex-specific approaches in the clinical management of HIV-infected individuals.

Immunological insights of HIV infection

OC 12 STABLE MICROBIAL FUNCTION DESPITE SHIFTS IN THE FAECAL MICROBIOTA COMPOSITION ACCORDING TO THIRD-DRUG CLASS IN ANTIRETROVIRAL-NAIVE INDIVIDUALS INTRODUCING CART

G. Ancona[1], C. Tincati[1], E. Merlini[1], A. Calcagno[2], A. d'Arminio Monforte[1], G. Marchetti[1]

[1]Department of Health Sciences, Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, University of Milan, Italy, [2]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino

Background: Gut microbial dysbiosis (GMD) features HIV+ individuals, both naïve and cART-treated. Open questions still remain, however, as to whether diverse cART regimens impact the composition and function of the gut microbiome. Aim of the study was to assess whether differences exist in the faecal microbiota composition and function according to the third drug used in the course of cART.

Material and Methods: We have previously shown that GMD persists for more than two years following the introduction of suppressive cART (1). In a cohort of antiretroviral-naïve subjects (n=41) introducing cART and stratified according to the 3rd drug-class (Table 1), we measured in the course of follow-up (T0, T12, T24 months from cART introduction): i) faecal microbial composition (α-diversity comparisons and faecal relative abundance by Friedman test) and ii) bacterial metagenome prediction using PICRUSt software. Further, the estimate of unchanged drug proportion in faeces (gut persistence score, GPS) was calculated for all study subjects.

Results: NNRTI-based therapy was significantly associated to reduced richness α-diversity parameters at T12 (Observed: p=0.038; Chao1: p=0.006; Figure 1A), but not evenness indexes (Figure 1B). Furthermore, relative abundance analyses showed different profiles at both family and genus levels in subjects treated with NNRTI- and INSTI- based regimens over time: in particular, the former displayed a significant reduction of Coriobacteriaceae and Peptococcaceae and increases of the Veillonellaceae family (Figure 2A) while the latter showed decreases in the Peptococcaceae and increases in the Veillonellaceae family, as well as in the Allisonella genus (Figure 2B). Stable predicted metagenomic functions were found regardless of the third-drug class. A different GPS was shown across NNRTI-, INSTI- and PI-based regimens with higher GPS in INSTI- vs PI-regimens at T12 [8 (8-8) and 6 (6-7), respectively; p=0.008] and higher GPS in INSTI vs NNRTIs-regimens at T24 [8 (8-8) and 6 (5.25-8) respectively; p=0.011]. Of note, in NNRTI-treated subjects we also found a negative correlation between measures of evenness indexes (Shannon) and GPS (r=-0.51; p=0.017).

Conclusions: NNRTI- and INSTI-based regimens differentially affect the gut microbiota, possibly reflecting the diverse drug absorption through the gastrointestinal tract. Indeed, the use of NNRTI-containing regimens with a longer persistence in the gut seem linked to lowest bacteria α-diversity. Despite these findings, however, class-specific microbiome modifications are not related to a different predicted microbial function during cART, suggesting no substantial impact of antiretrovirals on gut microbial function, that need to be further detailed in ad hoc designed studies.

(1) CROI, 2017

Immunological insights of HIV infection

OC 13 NO ASSOCIATION BETWEEN PATTERNS OF 179-181TRIPEPTIDE OF THE V2 DOMAIN BINDING THE GUT-HOMING A4B7 INTEGRIN AND LEVELS OF BACTERIAL TRANSLOCATION MARKERS IN HIV-1 INFECTED PATIENTS NAÏVE TO ANTIRETROVIRALS

F. Balena, D.F. Bavaro, C. Fabrizio, A. Volpe, A. Lagioia, G. Angarano, L. Monno, A. Saracino

Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari Medical School, Bari, Italy

Introduction: Through the V2 domain, HIV-1 binds the α4β7 integrin, which assists the T-lymphocyte homing to the gut-associated lymphoid tissue, where HIV replication mostly occurs especially in early phases of infection. This triggers bacterial translocation, thus contributing to immune-activation in course of HIV infection. It is conceivable that the high variability of V2 region could influence the V2-α4β7 binding. Recent studies suggest that the V2 LDV/I 179-181tripeptide has the highest affinity for α4β7. Herein, we aimed to investigate whether various V2 179-181tripeptide are associated with different levels of lipopolysaccharide (LPS) and soluble CD14 (sCD14) as markers of microbial translocation/immune activation.

Methods: Blood samples were taken from naïve patients newly diagnosed with HIV infection. HIV-1 gp120 sequences were submitted to the HIV Gene Cutter tool (http:// www.hiv.lanl. gov/content/sequence/HIV/HIVTools.html), which clips predefined coding regions and the extracted V2 sequences were analyzed for the 179-181tripeptide composition. Plasma levels of LPS and sCD14 were quantified by commercially available kits (LPS BioAssay ELISA KIT; R&D Systems). Duration of HIV infection was estimated according to the frequency of ambiguous nucleotides in PR/RT sequences from standard HIV-1 genotyping: an ambiguity proportion ≤0.2% signifies a recent (< 1year) infection. Clinical and immuno-virologic data, were retrieved from our internal database. Descriptive statistics, univariable and multivariable association models were performed; a p value <0.05 was considered significant.

Results: A total of 174 naïve patients were enrolled, 85% males, with a median (q1, first-q3 third quartile) of 33 (27-43) years, harboring a subtype B HIV-1 strain in 71% of cases; a recent infection was estimated in 79 (45%) patients. Sexual intercourse was the most common (93%) risk factor for HIV acquisition (56% MSM); overall, 15% had AIDS at diagnosis (Table 1).

LDV179-181 mimotope was detected in 41% of patients, followed by LDI (27%). An Asp180 was found in 99% of cases. At univariable analysis, no association was found between the levels of LPS or sCD14 in LDV vs LDI vs other mimotopes (Figure 1). Moreover, median levels of LPS and sCD14 were not influenced by risk factor, duration of infection, CD4 cells count at diagnosis, or pVL. Multivariable analysis involving levels of LPS/sCD14 and duration of HIV infection, CD4 cells count, pVL at diagnosis, AIDS stage, and presence of LDV/I tripeptide at position 179-181, failed to identify any significant association.

Conclusions: We observed no association between the tripeptide composition and the extent of bacterial translocation/immune activation in HIV-1 infected patients, possibly due to the high conservation of Asp180.

A Healthy Brain in People Living with HIV

OC 14 COMPARATIVE NEUROPSYCHIATRIC TOXICITY PROFILE OF DOLUTEGRAVIR (DTG)-BASED VERSUS EFAVIRENZ (EFV)-BASED VERSUS OTHER RECOMMEND FIRST-LINE ANTIRETROVIRAL THERAPIES (ART): DATA FROM ICONA FOUNDATION STUDY COHORT

A. Mondi[1], A. Cozzi-Lepri[2], A. Cingolani[3], A. Tavelli[4], M. Puoti[5], V. Barocci[6], A. Londero[7], F. Bai[8], C. Pinnetti[1], P. Cinque[9], A. d'Arminio Monforte[8], A. Antinori[1] on behalf of the Icona Foundation Study Group

[1]HIV/AIDS Department, National Institute for Infectious Diseases "Lazzaro Spallanzani" IRCCS, Rome, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [3]Infectious Diseases Unit, Catholic University of Sacred Heart, Rome, Italy, [4]Icona Foundation, Milan, Italy, [5]Infectious Diseases Department, ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy, [6]Clinic of Infectious Diseases, Dept. of Biomedical Sciences and Public Health, Polytechnic University of Marche, Ancona, Italy, [7]Infectious Diseases Clinic, Department of Medicine University of Udine and Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy, [8]Clinic of Infectious and Tropical Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy, [9]Department of Infectious Diseases, San Raffaele Hospital, Vita-Salute University, Milan, Italy

Background: Both EFV and DTG have been associated with a higher risk of neuropsychiatric adverse events (NPAEs) compared to other antiretrovirals. Despite this, comparison of NPAEs risk between this two drugs in observational cohorts are lacking. The aim of the study was to compare the risk of neuropsychiatric toxicity among DTG-based, EFV-based regimens as well as other currently recommended first-line ART over a period in which all these treatment strategies have been used.

Materials and Methods: We included all ART-naive patients (pts), enrolled in the Icona cohort, who started a first-line recommended (as main or alternative) ART, according to EACS guidelines 2018, over the period January 2006-December 2018. Probabilities of both experiencing NPAEs (defined as occurrence of neuropsychiatric symptoms or start new treatment for neuropsychiatric disorders) either leading or not to treatment discontinuation (TD) and discontinuing third drug due to NPAEs (ignoring changes in the backbone) were estimated by Kaplan Meier analysis comparing pts starting EVF-based, DTG-based or other regimens. Predictors of TD due to NPAEs were identified by Cox regression analysis. A sensitivity analysis in pts starting ART from 2011 (year in which DTG was firstly available) was also performed.

Results: Overall, 7854 pts were included, of whom 1322 (17%) initiating a DTG-based regimen, 1542 (20%) an EFV-based regimen and 4990 (63%) a non-DTG non-EFV based ART. Compared to the other treatment groups, pts starting DTG were more likely to be non-Italian, MSM, class CDC C and to have abacavir/lamivudine as backbone [Table 1]. At univariable survival analysis, pts on an EFV-based ART, were more likely both to experience NPAEs (8.5% vs 5.2% for DTG and 3.2% for other at 2 year, log rank p<.001) and to stop third drug due to NPAEs (6.9% vs 2.4% for DTG and 0.3% for other at 2 year, log rank p<.001) [Fig. 1a,1b]. At multivariable analysis, after adjusting for key confounders, the third drug started was the only predictor of TD due to NPAEs and, particularly, starting DTG was associated with a lower risk of discontinuing treatment due to NPAEs compared to EFV (adjusted relative hazard [aRH] 6.84, p<.001) but with a higher risk compared to other ART (aRH 0.10, p<.001). This result was also confirmed restricting the analysis to pts starting ART after 2011 [Table 2]

Conclusions: In our analysis, we found a 2% risk of stopping DTG due to NPAEs by 2 year from initiating first-line DTG-based cART regimens. This estimated risk is lower than that observed in similar observational studies in Europe although higher than that recorded in the DTG-arm of phase-III randomized clinical trials. Our comparison also shows that this risk is higher than that experienced by people starting other EACS recommended first-line regimens but significantly lower than that seen for people starting EFV. Residual confounding by calendar year or other unmeasured factors cannot be ruled out.

This study is supported by a grant from ViiV HealthCare

A Healthy Brain in People Living with HIV

OC 15 NEUROCOGNITIVE IMPAIRMENT (NCI) IS NOT ASSOCIATED WITH INTEGRASE STRAND TRANSFER INHIBITORS (INSTIS) USE IN HIV POSITIVE PERSONS (PLWH)

A. Mondi, A.C. Brita, P. Lorenzini, A. Vergori, R. Gagliardini, V. Mazzotta, S. Cicalini, R. Bellagamba, A. Antinori, C. Pinnetti

HIV/AIDS Department, National Institute for Infectious Diseases "Lazzaro Spallanzani", IRCCS, Rome Italy

Background: Recent data have raised a warning about the frequency of neuropsychiatric adverse events during the treatment with INSTIs among PLWH, but the correlation with NCI has not been elucidated. Aim was to analyze the association of NCI with use of INSTIs as compared to other ART regimens among PLWH.

Materials and Methods: We included PLWH ART-treated for at least 3 months on the current regimen at the first neuropsychological assessment (NPA) between 2008 and 2018. Two different retrospective case-control studies (1:1) were designed comparing pts: i) with and without NCI ii) with and without HAND. Pts underwent NPA through a standardized battery of 12 tests on 5 different domains and were classified as having NCI or HIV associated neurocognitive disorders (HAND) according to Frascati's criteria. Matching criteria included age (<35, 35-45, 45-55, 55-65, >65yrs) and education (<8, 8-13, >13), conditional logistic models were fitted in order to identify the association with INSTIs.

Results: A total of 803 pts were selected, of whom 273 (34%) were impaired (100 NCI and 173 HAND: 128 (46.9%) ANI, 41 (15.0%) MND, 4 (1.5%) HAD). Main characteristics: male 80%; median age 47yrs; MSMs 43%; HCVAb+ 27.5%; HIVRNA <40 cp/mL 89.3%; median yrs of infection and education 19 (IQR 4-20) and o13 (IQR 8-13), respectively; median CD4 cell count nadir 251 (IQR 148-379) cell/mm3, current CD4 cell count 611 (IQR 443-782) cell/mm3. At NPA, 135 pts (16.8%) received a regimen containing INSTIs (70 raltegravir, RAL, 31 elvitegravir, EVG, 34 dolutegravir, DTG).

246 individuals with NCI were matched with 246 unimpaired controls (27 pts with NCI did not match). After adjusting for main confounders, no association between use of INSTIs and NCI was found (OR 1.00, 95%CI 0.55-1.81, p=0.991). None of single INSTIs was found to be associated with NCI compared to regimens including other third drugs excepted efavirenz (Table 1). The analysis carried on 173 cases with HAND matched with same controls, showed Higher But Not Significant Risk Of Hand Diagnosis For Dgv- And Ral-containing Regimen (table1).

Conclusions: Our data do not support an association between exposure to INSTIs and NCI. The potential increased risk of neuropsychiatric side effects observed in patients receiving INSTIs does not seem to be driven by impaired neurocognition.

A Healthy Brain in People Living with HIV

OC 16 CENTRAL NERVOUS SYSTEM EFFICACY OF DUAL VERSUS TRIPLE ANTIRETROVIRAL THERAPY IN A REAL-LIFE SETTING

M. Trunfio[1], D. Vai[2], E. Borgogno[1], V. Pirriatore[1], M.C. Tettoni[1], D. Imperiale[2], G. Di Perri[1], S. Bonora[1], A. Calcagno[1]

[1]Unit of Infectious Diseases, Amedeo di Savoia hospital, University of Torino, Torino, Italy, [2]Unit of Neurology, Maria Vittoria hospital, Torino, Italy

Background: Dual antiretroviral therapy (DT) represents a novel strategy to reduce drug-associated toxicity, pill burden and costs [1]. DT virological efficacy is slightly lower in certain patients' groups as compared to triple antiretroviral therapy (TT), with concerns about compartmentalized reservoirs, such as the central nervous system (CNS) [1]. Cerebrospinal fluid (CSF) viral escape (CSFE) [2,] and shift to proinflammatory profiles after switch to DT have been reported [3], but also neurocognitive improvement [4], so that more data on DT CNS efficacy are needed. We aimed to compare HIV-positive patients peripherally controlled on DT versus TT undergoing lumbar puncture (LP) in terms of CSF biomarkers.

Methods: Data on HIV-positive patients with plasma HIV-RNA <200 cp/mL on DT or TT undergoing brain magnetic resonance imaging (MRI) and lumbar puncture (LP) for clinical reasons between 2006-2018 were retrospectively included. CSF biomarkers were measured by immune-enzymatic, ELISA and immunoturbidimetric methods. Patients without confounding factors for HIV-associated neurocognitive disorders (HAND) underwent extensive neurocognitive assessment.

Results: 190 patients were enrolled: 26 (13.7%) on DT (57.7% INI+PI/r) and 164 (86.3%) on TT (42.7% PI-, 22.6% INI-, 18.9% NNRTI-based). No differences in demographic characteristics, viroimmunological efficacy nor clinical indications to LP were observed (Tab.1), but the length of HIV infection (p.01) and CPE score (p<.01). CSF HIV-RNA cp/ml did not differ between the two groups nor between the subgroups of DT and TT patients with low-level viremia (20 cp/ml<plasma HIV-RNA<200 cp/mL; Tab.1). CSFE was not significantly higher in DT (19.5% TT vs 30.8% DT, p.19). Similarly, HAND prevalence did not differ between TT vs DT (69.4% vs 72.7%, p.82), even if mild neurocognitive disorders and HIV-associated dementia were more frequent among DT patients with HAND (16% vs 50%, OR 5.4 [1.1-26.0], p.025; Tab.2). None of the age/schooling-adjusted and raw scores at the 18 neurocognitive tests differed between the neurocognitive tested subgroups, except for a higher prevalence of altered Corsi test score in DT (altered visuo-spatial short-term memory: 75% DT vs 38% TT, OR 4.9 [2.4-9.9], p.04). Finally, no differences in blood brain barrier and neuronal damage, intrathecal synthesis, CSF inflammation or CSF immune activation biomarkers were observed (Tab.3).

Discussion: Among patients with undetectable or low-level viremia requiring LP for clinical reasons, DT proved to be equally efficacious to TT in controlling CNS viral replication and equally safe in terms of CNS toxicity and of HIV-related neurodegenerative processes as suggested by the observed normality of several CSF biomarkers and neurocognitive domains. Longitudinal studies on larger sample sizes are needed to assess the possibility of more frequent CSFE and of more severe presentations of HAND among patients on DT.

A Healthy Brain in People Living with HIV

OC 17 MINI-ADDENBROOKE'S COGNITIVE EXAMINATION VERSUS INTERNATIONAL HIV-DEMENTIA SCALE FOR CURRENT HIV-ASSOCIATED NEUROCOGNITIVE DISORDERS

M. Trunfio[1], D. Vai[2], M. Milesi[1], A. Trentalange[1], S. Audagnotto[1], G. Orofino[3], D. Imperiale[2], S. Bonora[1], G. Di Perri[1], A. Calcagno[1]

[1]Unit of Infectious Diseases, Amedeo di Savoia hospital, Department of Medical Sciences, University of Turin, Turin, Italy, [2]Unit of Neurology, Maria Vittoria hospital, ASL Città di Torino, Turin, Italy, [3]Unit of infectious Diseases, Amedeo di Savoia hospital, Divisione A, Turin, Italy

Background: Aging and increased cardiovascular risk are major drivers for HIV-associated neurocognitive disorders (HAND) [1]. Accurate screenings for HAND are lacking, especially for asymptomatic neurocognitive impairment (ANI). Mini-Addenbrooke's Cognitive Examination (MACE) proved reliable accuracy in identifying mild cognitive impairment/dementia among HIV-negative patients with cardiovascular co-morbidities [2,3]. We evaluated diagnostic accuracy of MACE in detecting HAND and we compared it to the International HIV Dementia Scale (IHDS).

Methods: Consecutive HIV-positive adults tested for HAND (without clinical confounders) were prospectively enrolled. IHDS and MACE were administered: IHDS≤10 was deemed abnormal [4]; exploratory cutoffs were evaluated for MACE. Patients underwent full neurocognitive evaluation (NE) assessing 7 domains, all tests' scores were age/education-normalized and HAND was diagnosed according to Frascati's criteria. Diagnostic accuracy, inter-rater reliability and clinical utility analysis were performed.

Results: 145 patients were enrolled: 93.1% on cART, 78.6% male, 96.5% Caucasian, median age was 54 years (49-60), 88.3% with plasma HIV-RNA <20 cp/mL, median CD4+ T-cells count and nadir were 542 (402-810) and 208 (99-337) cells/uL, respectively. HAND was diagnosed in 86 patients (59.3%): 72 ANI, 13 mild neurocognitive impairment, 1 HIV-associated dementia. Diagnostic accuracy and clinical utility measures are shown in Tab.1. MACE at the exploratory cutoff ≤26 showed a better performance as a screening tool for HAND compared to IHDS, with higher performance accuracy. Altered IHDS and MACE score were associated with an odds ratio for HAND diagnosis of 6.5 and 17.3 ($p<.01$ both), respectively. IHDS and MACE AUROC were 0.75 (0.67-0.83; $p<.01$) and 0.86 (0.80-0.92; $p<.01$). Cohen's k coefficients for inter-rater agreement were: IHDS vs NE 0.42 (low), MACE vs NE 0.59 (moderate). MACE showed larger effect size than IHDS in distinguishing HAND vs non-HAND (Cohen's d: 1.4 vs 0.9), but lower for symptomatic vs asymptomatic HAND (Cohen's d: 1.0 and 1.8).

Conclusions: In HIV-positive patients aged above 50 a high prevalence of HAND was observed. MACE proved to be a more accurate and clinically useful screening test for HAND than the widely employed IHDS, especially for the nowadays prevailing asymptomatic forms. Considering the underlying contribution of cardiovascular disorders to HAND development, the quick and easy-to-perform MACE may reveal to be a better alternative to the currently only validated IHDS as a screening tool for HAND in an aging population.

A Healthy Brain in People Living with HIV

OC 18 NEUROPSYCHOLOGICAL PERFORMANCE IMPROVES IN FULLY VIROLOGICALLY SUPPRESSED HIV-POSITIVE INDIVIDUALS

A.C. Brita[1], B. Milanini[2], P. Lorenzini[1], A. Mondi[1], A. Vergori[1], S. Menichetti[1], R. Gagliardini[1], A. Giannetti[1], R. Bellagamba[1], S. Cicalini[1], A. Antinori[1], C. Pinnetti[1]

[1]HIV/AIDS Clinical Unit, INMI,Lazzaro Spallanzani, Rome, Italy, [2]Memory and Aging Center, Department of Neurology, University of California, San Francisco, California

Background: HIV can affect cognitive function; however, it is still debated if HIV-associated neurocognitive disorders (HAND) persist during effective cART. We aimed to characterize the neuropsychological change in a large sample of virologically suppressed HIV+ pts.

Methods: Single-centre, retrospective, longitudinal analysis of neurocognitive impairment (NCI) among HIV+ pts who achieved and maintained virologic suppression (<40 copies/mL), with two neuropsychological assessments (NPA) between 1996-2018. All participants underwent a standardized neuropsychological tapping 5 cognitive domains known to be affected in HIV at T0 and T1. Mood status and anxiety were assessed in a subgroup (n=96). HAND was classified according to Frascati criteria. The NPZ was derived by averaging of the individual z-scores on 8 tests (NPZ-8). Cognitive change was calculated as the difference between the two performances divided by the inter-NPA interval. A multivariable linear regression model was fitted to investigate clinical and demographic predictors of change over time.

Results: 394 pts included: male 82%; median age of 49y (IQR 42-55); heterosex 31%, MSMs 45%, IDUs 20%; HCV co-infection 27%; median yrs of infection and education 9 and 13, respectively; median time from T0 to T1 12m; CD4 nadir<200 cell/mm3 35% and median current CD4 603 cell/mm3. In all patients HIV-RNA was <40 cp/mL at both time points. At study entry, 56% were receiving 2NRTI+NNRTI, 24% NRTI+PI/b, 5% 2NRTI+INSTI and 15% other regimens. At T0, sixty-six (17%) and 94 pts (24%) were classified as NCI or HAND, respectively [62(16%) ANI, 31(8%) MND and 1(0.3%) HAD]. At follow-up, all participants performed better on NPZ-8 (0.09 vs 0.16, p<0.001), including those diagnosed with HAND (-0.34 vs -0.20, p=0.003) (Fig. 1). An overall improvement was observed on the domains of psychomotor speed (-0.30 vs -0.22, p=0.043) and executive functions (0.26 vs 0.34, p<0.001). The multivariable linear regression showed a significant negative association between male gender and HCV-coinfection with global cognitive change over time. No associations were found between depression and anxiety with cognitive change.

Conclusion: Neurocognitive performance improves in virologically well-controlled HIV+ pts over time. Adding a subsequent follow-up may help monitor the trajectory over time (decline vs fluctuation). Further studies on longitudinal assessment of global cognitive function are needed to better explore factors associated with change over time.

A Healthy Brain in People Living with HIV

OC 19 FRAILTY INDEX (FI) AND AGE PREDICT NEUROCOGNITIVE FUNCTIONING IN A REAL LIFE LARGE PROSPECTIVE HIV+ COHORT

G. Guaraldi[1], J. Milic[1], L. Cysique[2], A. Malagoli[1], M.G. Corni[1], E. Bardi[1], F. Carli[1], I. Franconi[1], C. Mussini[1], M. Bloch[3]

[1]Modena HIV Metabolic Clinic, University of Modena and Reggio Emilia, [2]Neuroscience Research Australia, School of Medical Sciences, Faculty of Medicine, The University of New South Wales, Sydney, NSW, Australia, [3]Holdsworth House Medical Practice, Sydney, NSW, Australia

Background: Frailty has been associated with neurocognitive impairment in cross-sectional studies. However, it is unclear whether frailty is predictive of neurocognitive function change (NFC) in aging HIV+ patients who are otherwise clinically stable. We aimed to evaluate in a large prospective HIV+ cohort, the association between baseline frailty and NFC at 12 months.

Methods: Consecutive HIV+ individuals ≥50yrs attending a single center were assessed for neurocognitive function (NF) at baseline and follow-up (1.07 years (IQR: 0.94-1.13)) using the computerised CogState battery. Each individual CogState raw score was transformed into z-score correcting for age and gender. A global NF performance score was defined as the mean of z-score by averaging individual task z-scores. Normal, mild and moderate/severe impairment was defined according to the global deficit score (GDS) method. NFC was defined as the delta between baseline and follow-up mean z-score. Frailty was determined using 67-Item frailty index (FI) generated by a standardised comprehensive geriatric assessment and excluding NF for the purpose of this analysis. In a multivariable linear regression model, we tested whether FI was predictive of NFC over the study period. The model included HIV parameters, and demographics.

Results: Of 482 evaluated patients, 76% were male, mean age was 57 (SDyears, median CD4=707 cells/uL and 98% were virologically suppressed. Baseline NF was described as normal in 400 (83.0%) patients, mildly impaired in 33 (6.9%) and moderate-severely impaired in 49 (10.1%). Follow up NF was normal in 399 (82.8%) patients, mildly impaired in 40 (8.3%) and moderate-severely impaired in 43 (8.9%). Table 1 details baseline and follow up NF. The simple speed task showed improvement while other task showed no statistically significant change. Individually 11/43 cases with moderate-severe NF at baseline obtained normal NF at follow-up, while the other remained impaired. Significant independent predictors of NFC were age (R=-0.009, SE=0.003, p=0.01), baseline NF performance (R=-0.25, SE=0.030, p<0.01) and FI (R=-0.44, SE=0.244, p=0.05). CDC HIV classification, nadir CD4 count and current CD4/CD8 ratio were not associated with NFC.

Conclusions: Age and frailty predict NFC at one year follow up in this clinically stable and virally suppressed HIV+ cohort. Frailty screening may be used as a prognostic tool for neurocognitive impairment.

A Healthy Brain in People Living with HIV

OC 20 CHANGES OVER TIME IN CLINICAL AND LABORATORY FEATURES AND CORRELATES OF SURVIVAL OF HIV-ASSOCIATED PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

I. Mainardi[1], A.G. Tarantino[2], R. Caccia[3], F. Turrini[3], F. Ferretti[1], A. Bestetti[1], A. Lazzarin[1], P. Cinque[1,3]

[1]Department of Infectious Diseases, San Raffaele Scientific Institute, Milano, [2]Department of Research, Manima, Assistance and Healthcare Organization, Milano, [3]Neurovirology Unit, Division of Immunology, Transplantation and Infectious Diseases, San Raffaele Scientific Institute, Milano

Background: Progressive multifocal leukoencephalopathy (PML) is a severe demyelinating disease caused by the polyomavirus JC (JCV) that affects individuals with a compromised immune system, including those with human immunodeficiency virus (HIV) infection. Being PML a rare disease, studies struggle at including large groups of patients. The aim of this study was to describe clinical and laboratory parameters over time, and analyse survival and its prognostic factors.

Material and methods: We reviewed 267 cases of PML in HIV-positive patients who were observed in or referred to our Department of Infectious Diseases between 1987 and 2019, and stratified the cases into four different time periods according to disease onset. We used Kruskall-Wallis test to compare variables between different time periods and log-rank test to assess survival, and analysed covariates by a Cox proportional hazard model to evaluate their impact on PML survival.

Results: Table I shows clinical and laboratory data according to the time period of PML onset. In more recent years, PML patients presented at a more advanced age and with higher CD4 cell counts; has higher CD4 cell counts and lower HIV-RNA level after three months; and a higher proportion of contrast-enhancing lesions and survival rate. By univariate analysis, longer survival was correlated to cART administration (p< .001), contrast-enhancement at magnetic resonance imaging (MRI) at any time during the disease (p< .001), CD4+ counts >200 cells/µL at onset (p= .009) and undetectable plasma HIV viremia at three-month follow-up (p= .007). There was no correlation with the other variables described in Table I. In cART-treated patients better survival was associated with undetectable plasma JCV-DNA (p= .020), undetectable plasma HIV at three-month follow-up (p= .035) and presence of contrast enhancement of MRI lesions at any time during PML (p= .043). A multivariate analysis model that included gender, CSF and plasma JCV-DNA level, CD4+ cell counts > or <200/µL, presence of brainstem lesions at first MRI, being cART naïve and the time period of PML onset, showed that, in PML patients undergoing cART, only plasma JCV-DNA level at PML onset remained associated with survival, with an increased hazard risk of 48% for each 1 Log increase of plasma JCV level (HR=1.49, CI=1.02 -2.18, p= .041).

Conclusion: Changes of PML features in cART treated patients seem to reflect a more efficient immune reconstitution in more recent years. Accordingly, PML mortality reduced throughout the years, although it remains unacceptably high. In cART-treated patients, only higher plasma JCV DNA level at onset of PML was independently associated with lower PML-survival.

New insights in HIV pathogenesis

OC 21 ANALITICAL TREATMENT INTERRUPTION DOES NOT ALTER SIZE BUT MIGHT CAUSE GENETIC DIVERSIFICATION OF THE HIV-1 PERIPHERAL RESERVOIR

C. Alteri[1], R. Scutari[2], L. Galli[3], M.C. Bellocchi[2], L. Carioti[2], V. Costabile[4], A. Poli[3], A. Galli[3], F. Ceccherini Silberstein[2], C.F. Perno[1], M.M. Santoro[2], A. Castagna[3,5], V. Spagnuolo[5]

[1]Department of Oncology and Hemato-oncology, University of Milan, Milan, Italy, [2]Department of Experimental Medicine, University of Rome Tor Vergata, [3]Infectious Diseases, San Raffaele Scientific Institute, Milan, Italy, [4]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [5]Università Vita-Salute San Raffaele, Milan, Italy

Background: The APACHE study shows that analytical ART interruption (ATI) with transient viremia did not alter the size of peripheral HIV-DNA in chronically HIV-1 infected patients with HIV-RNA<50 cps/mL for ≥10 years. Here, we investigate if ATI might impact on the genetic diversity of the HIV peripheral reservoir.

Methods: Five APACHE patients are analysed for total HIV-DNA (cps/10^6CD4+T), plasma HIV-RNA (cps/ml), C2-V3 sequences (HXB2 env nt: 805-1224, by Illumina MiSeq) at ATI, viral rebound (VR) and at achievement of undetectable viral load after ART resumption (post-ATI). These data are also obtained at three similar time-points for 5 combined-ART treated patients with HIV-RNA always <50cps/mL for ≥1 year (MODAT). To assess similarities between sampled virus populations, genealogical sorting indices (GSI, ranging from 0 [complete interspersion] to 1 [complete monophyly]), and prevalence of X4 species (FPR<10%) are defined. Wilcoxon signed-rank and Mann-Whitney tests are used to test changes in peripheral reservoir within and between APACHE and MODAT subjects, respectively.

Results: APACHE subjects experience VR after ATI at a median (IQR) time of 3 (3-5) weeks and, after ART resumption, achieve HIV-RNA<50 cps/ml in 13 (4.4-24) weeks. Median (IQR) total HIV-DNA and residual viremia are 982 (863-1114) cps/10^6CD4+T and 2 (2-5) cps/ml before AI, and 992 (553-1673) cps/10^6CD4 +T and 4 (3-9) cps/ml after ATI, with no significant change between the within-person pre- and post-ATI values (P=0.22 and 0.34). In MODAT, median (IQR) total HIV-DNA and residual viremia are 1037 (730-1750) cps/10^6CD4+T and 3 (2-7) copies/ml at I time-point, and 1104 (527-1598) cps/10^6CD4+T and 2 (0-5) cps/ml at III time-point, with again no significant change between the within-person values (P=0.34 and 0.10). No HIV-DNA and residual viremia differences are found at I and III time-point between APACHE and MODAT subjects (P>0.05).

By phylogenetic analyses (Figure1), C2-V3 DNA sequences at I, II and III time-points and C2-V3 RNA sequences at rebound tend to form separate clusters in 4/5 APACHE subjects (median [IQR] GSI: 0.68 [0.38-0.89], P<0.05). Only one APACHE subject has low viral diversity throughout the pre-ATI, rebound, and post-AI, making all sampled viruses closely related (GSI: 0.05 vs. 0.17 vs. 0.06, P>0.05). Differently, significant trend on monophyletic lineage is found only in 2/5 MODAT subjects (median [IQR] GSI: 0.62 [0.31-0.93], P<0.05).

Comparisons of X4-prevalence between I and III time-point show a trend of X4 enrichment at third time-point in APACHE sequences (delta-X4 median [IQR] X4 increase: +27 [2-30], P=0.08), but not in MODAT sequences (median [IQR] X4 increase: -3.7 [-62;4.14], P=0.50).

Conclusion: This proof of concept study indicates that, although transient viremia does not alter size of HIV-DNA and residual viremia from ATI to post-ATI, short treatment interruption might impact on genetic diversification of peripheral viral reservoir.

New insights in HIV pathogenesis

OC 22 HIV MEDIATED INSERTIONAL MUTAGENESIS INDUCES A VIRAL RESERVOIR IN T-REGULATORY CELLS

E. Bruzzesi[1,3], L. Rudilosso[2], P. Gallina[2], A. Calabria[2], S. Nozza[1], G. Tambussi[1], A. Castagna[1,3], E. Montini[2], D. Cesana[2]

[1]Department of Infectious Diseases, San Raffaele Scientific Institute, Italy, [2]San Raffaele Telethon Institute for Gene Therapy (SR-TIGET), San Raffaele Scientific Institute, Italy, [3]Faculty of Medicine and Surgery, Vita-Salute San Raffaele University, Milan

HIV reservoir is the most important barrier to viral eradication. Its maintenance is ensured by non-mutually exclusive mechanisms: low-level replication, latency and proliferating cells. It has been shown that HIV-1 insertions targeting BACH2 and STAT5B are enriched and persist for decades in hematopoietic cells of patients under Anti-Retroviral Therapy (ART), suggesting that insertional mutagenesis could provide a selective advantage to these cell clones, hence to viral persistence.

In preliminary studies, we specifically identified that chimeric mRNA transcripts containing viral HIV-1 sequences fused by splicing to the first protein-coding exon of STAT5B or BACH2 are present in the peripheral blood mononuclear cells (PBMC) of 30 out of 87 (34%) patients under ART. By performing droplet digital PCR, these chimeric mRNAs, putatively encoding for unaltered versions of BACH2 or STAT5B, were found to be specifically enriched (>10 fold, $p<0.001$) in T regulatory (Treg) cells in all patients tested (N=9) as the result of a selection mechanism triggered by promoter insertion, a phenomenon induced also by genotoxic lentiviral vector (LV). Given that HIV-1/STAT5B and HIV-1/BACH2 transcripts were specifically found in Treg cells collected over time, the HIV-mediated activation of these transcription factors should provide a long lasting selective advantage to Treg cells in HIV infected patients.

To functionally characterize the impact of the HIV-mediated deregulation of these transcription factors, we forced their expression in Treg cells purified from healthy donors. We found that LV-mediated expression of the wild type form of BACH2 and STAT5B did not alter Treg phenotype nor the function in vitro and significantly increased the proliferative capacity in competitive proliferation assays ($p<0.0001$). Moreover, their suppressive ability was confirmed in vivo, since co-injection in NSG mice of GFP- (N=4), BACH2- (N=7) and STAT5B (N=7) - transduced Treg cells with human allogenic PBMCs was able to prevent xenogeneic graft versus host disease in 75% of treated mice. Additionally, mice receiving STAT5B-over-expressing Treg cells showed a significantly reduced level of the overall human chimerisms ($p<0.001$) in blood when compared to mice treated with GFP-overexpressing Treg cells, suggesting for a superior activity of STAT5B-expressing cells in controlling the expansion of human PBMC.

Overall, these data provide novel compelling evidence that HIV-1 takes advantage of insertional mutagenesis to promote the expansion and persistence of Tregs through the activation of STAT5B and BACH2. By this mechanism HIV should favor the maintenance of a long-living and self-renewing cellular reservoir endowed with the ability to diminish the immune surveillance against infected cells. Hence, new targeted therapies aimed at interfering with BACH2 and STAT5B pathways could be exploited for the reduction of cellular reservoir and the eradication of the viral infection.

New insights in HIV pathogenesis

OC 23 HIGHLY ACTIVE ANTIRETROVIRAL THERAPY AND OSTEOGENIC DIFFERENTIATION: NEW HINTS INTO DRUG-INDUCED OSTEOPENIA

A. Cazzaniga, S. De Rose, V. Romeo, JAM Maier, S. Rusconi

[1]General Pathology Laboratory, DIBIC Luigi Sacco, University of Milan, [2]Infectious Diseases Unit, DIBIC Luigi Sacco, University of Milan

Background: Highly Active Antiretroviral Therapy (HAART) improves quality of life and survival. It is based on the administration of two or more compounds to have a multi-target effect against the virus as well as to reduce the risk of developing resistance. However, side effects occur in the long run, among which osteopenia, which eventually evolves in osteoporosis. For this reason, we studied the osteogenic differentiation of human mesenchymal stem cells (hMSC) treated with i) the protease inhibitors Darunavir (DRV) and Atazanavir (ATV), or ii) the integrase inhibitor Dolutegravir (DTG), in the presence or not of an osteogenic cocktail.
Material and methods: hMSC isolated from the bone marrow of healthy volunteers were cultured at 37°C in Dulbecco's Modified Eagle's Medium with 1000 mg/L glucose and containing 10% of fetal bovine serum (CM). Once they reached confluence, hMSC were exposed to CM or to a differentiation medium (OM) containing 10-8 M 1α,25-Dihydroxyvitamin D3, 10 mM β-glycerolphosphate and 0.05 mM ascorbic acid. ATV, DTG and DRV were added to the medium at a concentration of [2xIC90]. After 4, 7, 10, and 14 days, the RNA was extracted and reverse transcribed. The modulation of the main markers of osteogenic (RUNX2, COL1A1) and adipogenic differentiation (PPARγ) was investigated by Real Time PCR. Moreover, calcium deposition was evaluated by Alizarin Red Staining.
Results: hMSC did not show any toxicity at drug concentrations used: i.e. ATV [17.4 nM], DRV [4.1nM], and DTG [145nM]. RUNX2 and COL1A1 were overexpressed after 3 days of culture in OM in the presence or not of each drug. However, starting from day 7 of differentiation, ATV, DTG and DRV reduced RUNX2 and COL1A1 levels (Figure1), thus resulting in a diminished calcium phosphate deposition in the extracellular matrix (Figure 2). It is noteworthy that no modulation of the adipogenic differentiation marker PPARγ was observed (Figure 3).
Conclusion: When cells were treated with ATV, DTG or DRV in the presence of an osteogenic cocktail, the increase of RUNX2 and COL1A1 expression does not reach the threshold to obtain a full osteogenic phenotype. Importantly, no effects on the expression of PPARγ, the master regulator of adipogenesis, are detected. We conclude that HAART-induced osteopenia might be explained, in part, by the impairment of osteogenic differentiation of hMSC.

New insights in HIV pathogenesis

OC 24 AGING AND HEMATO-LYMPHOPOIESIS IN HIV INFECTION: ROLE OF PER2 IN THE REGULATION OF HEMATOPOIETIC PROGENITOR CELLS FUNCTIONS

V. Bordoni[1], E. Tartaglia[1], A. Sacchi[1], R. Casetti[1], E. Cimini[1], G. Grassi[1], O. Forini[1], A. Antinori[2], C. Agrati[1]

[1]Laboratorio di Immunologia Cellulare e Farmacologia, INMI-IRCCS L.Spallanzani, Roma, [2]Dipartimento Clinico INMI-IRCCS L.Spallanzani, Roma

Background: Chronic HIV infection apparently accelerates immune aging and is associated with abnormal hemato-lymphopoiesis, but the relationship among HIV-aging and HPC function is not well defined. In the context of aging it has been demonstrated in a murine model that Per2 (circadian rhythm gene) is a negative regulator of HPC survival and lineage potential. Whether Per2 induction in HPC during aging is involved in hematopoietic failure during HIV infection has not been investigated. The aim of this study was to analyze Per2 expression on circulating HPC during HIV infection and its relationship with HIV-associated aging.

Methods: Per2 expression in circulating HPC (CD34+ cells) was compared in 50 HIV infected patients under successful ART and in 25 healthy donors (HD). The level of cellular aging was assessed by measuring peripheral blood telomere length (TLR), telomerase activity, DNA repair enzyme ATM level and evaluating circulating properties of HPC.

Results: Our results showed that the relative TLR length and telomerase activity are significantly lower in HIV+ population than in HD: TLR length [median 1.4 2^-ΔΔCqTLR (IQR=0.9-1.6) vs median 1.7 2^-ΔΔCqTLR (IQR=1.2 -2), p=0.03)]; telomerase activity [median 28 CqTLR (IQR=28-30) vs median 26 CqTLR (IQR=26-28) p=0.007)]. The ATM signaling, known to regulate telomerase, is downregulated in HIV patients respect to HD (median 3.8% (IQR=3-6.5) vs median 11.2% (IQR=8.5-29), p=0.01 respectively), suggesting a dampen response to DNA damage. Since the downregulation of DNA damage response and telomere dysfunction impact HPC function, we verify the clonogenic potential of circulating HPC from HIV patients. We showed that the clonogenic potential of circulating HPC was significantly impaired in HIV+ patients with CD4 T cell count lower than 500/mmc compared to HD (median 20 colonies (IQR= 15-29) vs 27 colonies (IQR= 21-45), p<0.03). Interestingly, we found that the frequency of HPC expressing Per2 is higher in HIV+ patients than in HD (median 4.4% (IQR 2-12) vs median 3% (IQR= 0-5), p<0.006) and inversely related to telomerase activity (r2=0.6, p=0.0021). Finally, preliminary data showed that the negative regulator of Per2, the Sirt1 deacetilase is downregulated on circulating HPC from HIV patients, suggesting a dysregulation in the Per2/Sirt1 pathway.

Conclusion: These data suggest that in response to aging associated to HIV infection, HPC overexpressed Per2 that may affect the hemato-lymphopoiesis differentiation. These data support the rationale to explore the role of this regulator during aged-associated hemato-lymphopoiesis impairment in HIV infection, possibly providing a therapeutic target to restore lymphoid potential in the aged HPC compartment.

New insights in HIV pathogenesis

OC 25 DNA DAMAGE RESPONSE GENES: ANALYSIS OF MRNA EXPRESSION IN NAIVE AND ART-TREATED HIV POSITIVE PATIENTS

D. Di Carlo[1], F. Falasca[1], E. Panzini[2], I. Sciandra[1], T. Melengu[1], O. Turriziani[1], G. Antonelli[1]

[1]Department of Molecular Medicine "Sapienza" University of Rome, Rome, [2]University Hospital Policlinico Umberto I, Rome

Introduction: The understanding of molecular mechanisms that support human immunodeficiency virus replication allowed to develop therapeutic approaches that effectively control viral replication and dramatically improving the survival of HIV-infected patients. Nevertheless, many aspects of pathogenesis and persistence of infection are still unknown. During the last years, significant progresses have been made in the delineation of mechanisms underlying HIV-induced cell death. Among these, viral integration plays an important role together with pre- and post-integration processes. The induction of cell-killing triggered during viral integration involved the activation of DNA-dependent protein kinase (DNA-PK), a central integrator of the DNA damage response, which caused phosphorylation of p53 and histone H2AX. The aim of this study was to evaluate whether virological suppression could affect mRNA expression profile of genes involved in DNA damage response, by comparing cART-treated individuals with treatment-naïve patients and healthy donors.

Material and Methods: Seventy-five PBMC samples were obtained from HIV+ patients (35 treatment naïve and 40 cART-treated) and 30 sample from healthy donors (HD). All HIV-infected patients on cART had viral load (VL) <50 cps/mL. mRNA levels of FasR, XRCC1, LIG IIIα, Parp-1, DNA PKI, DNA PKII were determined by qPCR (Brilliant II Syber Green, Agilent Technologies) and normalized on β-actin; results were expressed as fold-change that was calculated by 2-ΔΔCt method. Differences between the different groups were analyzed for statistical significance using Mann-Whitney U and Kruskal-Wallis H tests.

Results: A significantly higher expression of mRNA levels of Parp-1, DNA PKII, LIG IIIα and FasR was detected in HIV infected individuals than in HD [Parp-1 1.8 ($p=0.001$), DNA PKII 16.7 ($p<0.001$), LIG III 3.1 ($p=0.006$), FasR 3.7 ($p=0.001$)]. Furthermore, splitting the infected population into two groups based on the viral load (naïve and cART-treated), a significant overexpression of DNA PKII and FasR mRNA levels was confirmed in both groups [naïve: DNA PKII 32 ($p<0.001$), FasR 17 ($p<0.001$); cART-treated: DNA PKII 13 ($p<0.001$), FasR 2.9 ($p=0.013$)] while an higher expression of Parp-1 and LIG IIIα was maintained only in cART-treated individuals [Parp-1 1.9 ($p<0.001$); LIG IIIα 2.8 ($p=0.004$)]. No significant differences in mRNA expression of DNA Pk I between treatment naïve patients, treated patients and healthy donors were detected.

Conclusion: Collectively, these results showed that the expression levels of some genes involved in the DNA damage response (Parp-1, DNA PKII, LIG IIIα and FasR) are higher in HIV+ patients than in healthy donors. Surprisingly, no significant differences between naïve and treated patients were observed. Although many mechanisms of post-transcriptional regulation have to be considered, these data suggest that a cellular damage persists despite suppression of viral replication.

New insights in HIV pathogenesis

OC 26 ENDOPLASMIC RETICULUM ASSOCIATED AMINOPEPTIDASES 2 (ERAP2) IS RELEASED IN THE SECRETOME OF ACTIVATED MDMS AND REDUCES IN VITRO HIV-1 INFECTION

I. Saulle[1], S.V. Ibba[1], E. Torretta[2], C. Vittori[1], C. Fenizia[3], F. Piancone[4], D. Minisci[5], E.M. Lori[1], D. Trabattoni[1], C. Gelfi[2], M. Clerici[3,4], M. Biasin[1]

[1]Department of Biomedical and Clinical Sciences L. Sacco, University of the study Milan, Milan, Italy, [2]Department of Biomedical Science for Health, University of the study Milan, Milan, Italy, [3]Department of Pathophysiology Medical-Surgery and Transplantation, University of the study of Milan, Milan, Italy, [4]Don C. Gnocchi Foundation ONLUS, IRCCS, Milan, Italy, [5]Department of Infectious Disease, ASST Fatebenefratelli Sacco, Milan, Italy

Background: Haplotype-specific alternative splicing of the endoplasmic reticulum (ER) aminopeptidase type 2 (ERAP2) gene results in either full-length (FL, haplotype A) or alternatively spliced (AS, haplotype B) mRNA. HapA/HapA homozygous (HomoA) subjects show a reduced susceptibility to HIV-1 infection, probably secondary to the modulation of the antigen processing/presenting machinery. ERAP1 was recently shown to be secreted from the plasma membrane in response to activation; we investigated whether ERAP2 can be released as well and if the secreted form of this enzyme retains its antiviral function.

Methods: Human monocyte derived macrophages (MDMs) were differentiated from peripheral blood mononuclear cells (PBMCs) isolated from 6 HomoA healthy controls and stimulated with IFNγ and LPS. ERAP2-FL secretion was evaluated by mass spectrometry. PBMCs from 14 HomoA and 16 HomoB were in vitro HIV-infected in the absence/presence of different doses (10, 100, 1000 ng/ml) of recombinant human ERAP2-FL (rhERAP2) protein; p24 viral antigen quantification was used to assess viral replication. IFNγ and CD69 mRNA expression, as well as the percentage of perforin -producing CD8+ T Lymphocytes were analyzed 3 and 7-days post in vitro HIV-1-infection respectively. MDMs from the same subjects were in vitro HIV-infected in the absence/presence of 100ng/ml rhERAP2.

Results: ERAP2 can be secreted from human MDMs in response to IFNγ and LPS stimulation. Addition of rhERAP2 to in vitro HIV-1-infected cells did not affect cell viability. As previously shown, HomoA subjects were less susceptible to in vitro HIV-1 infection ($p < 0.05$). Notably, the addition of rhERAP2 to cell cultures resulted in the reduction of viral replication in both PBMCs and MDMs from HomoA and HomoB individuals ($p < 0.05$ in all cases) with a peak effect observed using 100 ng/ml of the protein. In PBMCs, this protective effect was associated with an increase in IFNγ and CD69 mRNA expression and in the percentage of perforin-expressing CD107+CD8+ cells, mainly in HomoB subjects.

Conclusions: This is the first report providing evidence for the release of ERAP2 in the secretome of immunocompetent cells. Data herein also indicate that ERAP2-FL exerts its protective function against HIV-1 infection, even in HomoB subjects who do not genetically produce it. Presumably, this defensive extracellular feature is only partially dependent on CD8+ T cell activation as it was detected even in in vitro HIV-infected MDMs.

New insights in HIV pathogenesis

OC 27 INTERFERON-INDUCIBLE TRIM22 INTERACTS WITH HISTONE DEACETYLASE (HDAC)-1 TO MAINTAIN HIV-1 PROVIRAL LATENCY

E. Vicenzi[1], F. Turrini[1,2], G. Forlani[3], S. Ghezzi[1], R.S. Accolla[3], G. Poli[2,4]

[1]Unit of Viral Pathogens and Biosafety, Division of Immunology, Transplantation and Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [2]Vita-Salute San Raffaele University, School of Medicine, Milan, Italy, [3]Laboratories of General Pathology and Immunology "Giovanna Tosi", Department of Medicine and Surgery, University of Insubria, Varese, Italy, [4]AIDS Immunopathogenesis Unit, Division of Immunology, Transplantation and Infectious Diseases, San Raffaele Scientific Institute, Milano, Italy

The human immunodeficiency virus type-1 (HIV-1) establishes a state of latent infection in a small number of CD4 + T lymphocytes that represent a major obstacle to viral eradication. Latent HIV-1 infection arises when integrated proviral HIV DNA is transcriptionally silenced by host factors that act epigenetically at multiple levels. We have previously demonstrated that Tripartite Motif-containing protein 22 (TRIM22) inhibits HIV-1 transcription by impeding the binding of transcription factor Specificity protein 1 (Sp1) to the viral promoter in acutely infected cells. We next tested whether TRIM22 is also a relevant factor in maintaining a state of repressed HIV-1 expression in CD4+ T cell lines carrying latent HIV-1 proviruses. By simply knocking-down (KD) TRIM22 expression in the chronically infected ACH-2 cell line, but not in J-Lat 10.6 cells, we reversed HIV-1 quiescence to productive virus production, indicating that TRIM22 is a crucial factor in maintaining proviral latency in ACH-2 cells. Furthermore, TRIM22 KD potentiated HIV-1 expression in both ACH-2 and J-Lat10.6 cells upon cell stimulation with either tumor necrosis factor-a (TNF-a) or histone deacetylase inhibitors (HDACi). Immunoprecipitation experiments, indirect immunofluorescence and confocal microscopy demonstrated that TRIM22 interacts with HDAC-1 to promote a state of virus suppression. Thus, TRIM22 is a determinant of HIV-1 latency, at least in T cell lines, representing a potentially novel pharmacological target for strategies aiming at curtailing or silencing the pool of latently infected CD4+ T lymphocytes constituting the HIV-1 reservoir in individuals receiving combination antiretroviral therapy.

Let's PrEP now: Italian experiences

OC 28 PREP SERVICES IN ITALY: HOW MANY PEOPLE ACCESS THEM AND WHAT KIND OF SERVICES ARE OFFERED?

G.M. Corbelli[1], L. Badia[2], E. Barchi[3], F. Bonvicini[3], F. Caselli[4], B.M. Celesia[5], M. Cernuschi[6], A. Cingolani[7], M. Cordioli[8], G. Cuomo[9], I. Dal Conte[10], G. De Carli[11], A. Degli Antoni[12], F. Di Lorenzo[13], M. Errico[14], F.M. Fusco[15], S. Mattioli[1], V. Mazzotta[11], A. Muscatello[16], S. Nozza[17], T. Prestileo[13], A. Raimondi[10], R. Rossotti[18], A. Ruggieri[19], L. Sighinolfi[20], C. Stingone[21], S. Venturelli[22], V. Puro[11]

[1]Plus onlus/BLQ Checkpoint, Bologna, [2]Policlinico S. Orsola-Malpighi - Ambulatorio PrEP Bologna, [3]Arcispedale Santa Maria Nuova - Spazio Sessualità salute, Reggio Emilia, [4]Ospedale Infermi - UO Malattie Infettive, Rimini, [5]Università di Catania ARNAS Garibaldi - UOC Malattie Infettive, Catania, [6]Asa/Checkpoint Milano, [7]Fondazione Policlinico "A. Gemelli", IRCCS Roma, [8]AOUI Ospedale Policlinico "G.B. Rossi" - UOC Malattie Infettive e Tropicali, Verona, [9]Policlinico di Modena - Malattie Infettive - ambulatorio PrEP, Modena, [10]Ospedale Amedeo di Savoia - Ambulatorio IST, Torino, [11]INMI L. Spallanzani - Ambulatorio PrEP, Roma, [12]U.O.Malattie Infettive Azienda Ospedaliero-Universitaria - Ambulatorio PrEP, Parma, [13]A.R.N.A.S. Ospedale Civico - Malattie Infettive, Palermo, [14]Network Persone Sieropositive, Milano, [15]Ospedale Santa Maria Annunziata - SOC Malattie infettive, Bagno a Ripoli, [16]Fondazione IRCCS Ca' Granda - Osp. Maggiore Policlinico - Ambulatorio di Malattie Infettive, Milano, [17]Ospedale San Raffaele - Dipartimento di Malattie Infettive, Milano, [18]Ospedale Niguarda - SC Malattie Infettive, Milano, [19]Ospedale "Guglielmo da Saliceto" - UOC Malattie Infettive, Piacenza, [20]Azienda Ospedaliero-Universitaria - U.O. Malattie Infettive, Ferrara, [21]Policlinico di Tor Vergata - Ambulatorio di Malattie Infettive, Roma, [22]Ospedale di Bergamo – Ambulatorio PrEP

Background: Since March 2017, some clinical centres established specific services for pre-exposure prophylaxis (PrEP) users, but no official registry or monitoring has been adopted by national or local health authorities.
Material and methods: Plus, Italian network of LGBT living with HIV, disseminates information about how to access PrEP through a Facebook group and the website www.prepinfo.it providing a list of the centres offering services for PrEP users . A brief survey was proposed to these centres, including 2 additional centres not enlisted, regarding the number of PrEP users they served and basic information about the service itself.
Results: A total of 22 centres were included in the survey, 20 of which included in http://www.prepinfo.it/chi-ti-segue/ (see table 1): 16 are located in the North, 3 in Rome, 1 in Naples and 2 in Sicily. The first centre started offering services for PrEP users in March 2017, the most recent ones in March 2019. In this period, PrEP was started in 531 users who accessed the centres, all reporting sexual exposure: the vast majority (98%) were male, mostly (98%) men who have sex with men (MSM); 4 women and 6 transgender persons also accessed the services. Overall, 32 users (4%) stopped PrEP, only 4 of whom for side effects. Nine services (41%) provide users with a prescription within 7 days since the first visit, in 5 centres (24%) it takes 21-28 days, while in one centre it takes more than one month. In 15 centres (68%), prescriptions are provided for one month at the first visit and then every 3 months; in 6 centres (27%) a 3-month prescription is provided since the first visit. In 9 centres (43%), no ticket is due for follow-up tests (most of them using P01 as exemption code), while in all the others, users have to pay at least for some tests. All centres reported that their users buy the drug predominantly in local pharmacies.
Conclusions: This is to our knowledge the first attempt to monitor access to PrEP in Italy. Access seems to be still very difficult in large areas of our country, especially in Southern regions. Not unexpectedly, access concerns almost exclusively MSM, perhaps because PrEP recommendations are mainly focused on high risk MSM and information is disseminated mostly by gay organisations. PrEP discontinuation seems limited to a small proportion of users. Characteristics of services vary significantly. A national strategy for PrEP implementation would facilitate equal access in all Regions and could eventually translate into an epidemiological impact on the HIV epidemic in Italy. A more systematic data collection is needed in order to understand demographic and behavioural characteristics of users, as well as clinical outcomes in terms of diagnosis of sexually transmitted infections and tolerability.

Let's PrEP now: Italian experiences

OC 29 GETTING TOWARD A CHECKPOINT: EXPERIENCE OF A PREP SERVICE BY OUR ASSOCIATION

A. Bianchi[1], A. Tavelli[2], M. Lanza[1], D. Delelegn[1], V. Bertino[2], A. De Bona[2], E. Suardi[2], S. Negri[3], M. Bagnato[3], P.L. Vinti[1], A. Antonino[1], G. Fracca[1], M. Cernuschi[1]

[1]ASA. Associazione Solidarietà AIDS, Milan, Italy, [2]San Paolo Hospital, Milan, Italy, [3]Anlaids Sezione Lombardia, Milan, Italy

Background: TasP is a confirmed tool to get 90-90-90 target. Properly taken, PrEP is useful to reduce new Hiv infections. Since September 2017 to February 2019, ASA offers a service on appointment aimed to counteract PrEP, which is potentially able to increase Hiv and other STIs spread. An ID doctor and a psychologist receive whomever is looking for information about PrEP. During the first appointment, after a rapid Hiv test, the doctor informs them about medication, how to take it and how to care against other STIs, eventually by vaccination. HCV, syphilis, and - since February 2019 - Chlamydia and Gonococcus tests are also offered at the same time. The psychologist faces motivations leading to PrEP, sexual behavior (including chemsex), attitude towards Hiv, thoughts, fantasies and expectations regarding medication, giving opportunity to reflect over themselves. Both specialists stress that PrEP cannot substitute condoms. Mandatory condition to start taking PrEP is a preliminary month having only safe sex. A part of medical care during further appointments the psychologist assures attention to emotional aspects connected to PrEP.
Method: Self-administered questionnaires between September 2017 and February 2019 have been analyzed by descriptive statistics through STATA software. Here bio-psycho-social features are observed. Qualitative analysis on interviews with the psychologist have been conducted.
Results: 83 users (M 96%, >40 51.22%, homosexual 85,88%, graduated 42,35%, Italians 88,24%, using Chems 39%, previous STD and/or PEP 59%). During the first appointment we analyze: sexual habits; how and until when they will remain on PrEP; possible foreseen difficulties about having safe sex during the month preceding PrEP and about future adherence. Particular focus on Hiv fears and motivation to PrEP path. During the second appointment we talk about eventual difficulties of having safe sex. Following appointments are devoted to their own relationship with PrEP taking, changes in sexual life and eventually to share same path with other people.
Conclusions: As by preliminary analysis, the observed sample appears to be "tendentially" careful: from one hand that denies prejudice against PrEP, from the other hand it remains dangerous that only 34% is ever having safe sex. Among those lost along the path, nobody was doing safe sex constantly. Hiv fear, mostly about medical aspect only, is connected to stigma (41%) - even when U=U is widely confirmed - and to partial homosexuality's acceptance.19% of sample choose PrEP because of anxiety/hypochondria linked to their sexual life. Once taken the path, almost all the sample follows it easily and shows peculiar changes in sex emotional aspects. Progressing with the appointments, people increasingly use the opportunity to talk about themselves, their sexuality, identity and relationships. PrEP is confirmed as a valid tool for prevention, as well as for fight against stigma and for a better self-consciousness.

Let's PrEP now: Italian experiences

OC 30 PRE-EXPOSURE PROPHYLAXIS: VERY FIRST EPIDEMIOLOGICAL DATA AND CLINICAL OUTCOMES OF THE MODENA OUTPATIENT CLINIC USERS

A. Raimondi[1], G. Cuomo[1], C. Rogati[1], A. Bianchi[1], B. Beghetto[1], E. Roncaglia[1], G. Nardini[1], V. Borghi[1], G. Guaraldi[1], M. Coppini[2], C. Mussini[1]

[1]Clinica di Malattie Infettive, Azienda Ospedaliera-Universitaria di Modena - Modena, [2]Clinica Dermatologica, Università di Modena e Reggio Emilia - Modena

Background: pre-exposure prophylaxis (PrEP) with the association of tenofovir (TDF)/emtricitabine (FTC), administered to people with a high risk of HIV acquisition on a daily or on-demand regimen, is effective in preventing HIV infection. This study aims to investigate the epidemiology of users, the effectiveness and safety of PrEP, the prevalence of sexually transmitted infections (STIs) during PrEP and the appearance of any adverse side effects in PrEP users. As a secondary end-point, the study aims to assess the appropriateness of PrEP prescription in outpatient users.

Material and methods: an ongoing prospective observational study was started with recruitment of people who requested PrEP from July 2018 at the PrEP clinic in Modena. Epidemiological and clinical data available to March 2019 were collected during the first consultation and the further follow-up at one month and then every three months after the PrEP beginning. We performed serology for HIV, HAV, HBV, HCV, Treponema pallidum, blood test for renal function, pregnancy test for female users, and rectal, pharyngeal swabs plus urine samples for Chlamydia trachomatis and Neisseria gonorrhoeae PCR. The local ethics committee approved the study.

Results: 19 people were enrolled, underwent the basal check -up and obtained PrEP, for epidemiological characteristics see Table 1. Regarding indications for PrEP, 6 people (31.5%) reported an inconstant use of the condom, 8 (42%) had a previous sexually transmitted infection (STI), 2 (10%) were practicing chemsex, 1 (5%) had already been proposed a post-exposure prophylaxis (PEP), while 4 people did not report risk behavior. 15 (79%) of them started the intake according to the on-demand scheme and 4 (21%) according to the daily scheme. Since the beginning of the prescription, 3 users have reported side effects: one with self-limiting gastrointestinal symptoms, one with elevated drug-dependent transaminases, one person with increased creatinine who was the only one who had to stop PrEP due to acute renal failure. 2 people stopped on their own PrEP intake because no longer needed. As shown in Table 2 the most newly diagnosed STIs during the first test were N gonorrhoeae (all from rectal swab) and C trachomatis (2 from rectal and 1 from pharyngeal swab), whereas 2 people contracted syphilis during PrEP (one primary serologic infection, one with secondary rash disease). No HIV infection has occurred.

Conclusions: in our experience, the request of PrEP is limited to MSM only and one fifth of users would not need to take the prophylaxis. PrEP is effective in preventing new HIV infections but not other STIs, especially syphilis. With the beginning of PrEP it is possible to diagnose asymptomatic STIs such as rectal and pharyngeal gonorrhea and chlamydia. Considering the possible side effects, we recommend PrEP distribution under medical supervision.

Let's PrEP now: Italian experiences

OC 31 PRELIMINARY INTRODUCTION OF PRE-EXPOSURE PROPHYLAXIS (PREP) WITH EMTRICITABINE/TENOFOVIR DISOPROXIL (F/TDF) IN MSM POPULATION IN ROME

F. De Zottis[1], V. Mazzotta[1], G. De Carli[1], R. Bellagamba[1], A. Cingolani[2], S. Nappi[2], C. Stingone[3], M. Farinella[4], G.M. Corbelli[5], M. Andreoni[3], V. Puro[1], A. Antinori[1]

[1]Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani IRCCS, Roma, [2]Clinica Malattie Infettive, Fondazione Policlinico A. Gemelli IRCCS, Università Cattolica S. Cuore, Roma, [3]Clinica Malattie Infettive, Università di Roma Tor Vergata, Roma, [4]Circolo di Cultura Omosessuale Mario Mieli, Roma, [5]PLUS Onlus, Bologna

Background: F/TDF is currently the only drug approved for HIV PrEP as part of a comprehensive prevention strategy. Several studies confirmed its efficacy and safety, and most guidelines now recommend PrEP use in HIV high-risk people. Although PrEP is now an available preventive option in some European countries, its widespread use is currently limited in many others, including Italy, due to lack of awareness and to reimbursement and cost issues. In Italy, recent approval for F/TDF as generic is expected to enhance PrEP use.
Methods: We retrospectively collected data on PrEP use among high-risk HIV-negative adult men who have sex with men (MSM) or transgender women (TGW) who spontaneously accessed 3 centers for HIV care in Rome or were selected at local check point of MSM advocacy organizations. They were considered for PrEP if fulfilling one or more of the following within the last 3 months, according to national guidelines: a) >1 condomless anal intercourse; b) STIs treatment; c) chemsex use; d) use of post-exposure prophylaxis (PEP). Baseline screening prior to PrEP initiation included HIV, STIs, viral hepatitis, and renal function tests. At first visit, socio-demographics, sexual-recreational habits and medical history were recorded influencing daily or "on-demand" schedule prescription. The first control visit was performed 1 or 3 months later, according to the center PrEP program, and further controls every 3 months. All PrEP users bought generic F/TDF themselves in local pharmacies.
Results: From January 2018 to March 2019, 71 MSM were prescribed generic PrEP. No TGW accessed the program. Demographics and anamnestic data are summarized in Table 1. 58 persons (81.7%) fulfilled indications for PrEP; 11 referred past inconsistent use of condom or previous STI, 2 had blurred criteria; however PrEP was prescribed in the context of appropriate counseling respecting persons' strong willingness. 35 (49.3%) persons were prescribed daily F/TDF and 36 (50.7%) "on-demand" schedule; 3 changed schedule based on sexual habits. 32 (45%) reached time for a follow-up visit. Among those who tested for STIs at control visits, one case of syphilis and one of genital gonorrhea were diagnosed. All persons tested HIV negative at screening visit; none acquired HIV.
Conclusions: This initial experience suggests a still limited spread of PrEP among MSM community in Rome, indicating that awareness and use of PrEP in this population should be facilitated. Absence of TGW is probably related to the drug cost and lack of information network. The major drivers for prescription were inconsistent use of condom and previous STIs; chemsex use was reported in 24%. Both schedules were prescribed at a ratio of almost 1:1, based on individual preference. Implementations of communication tools and of a comprehensive PrEP program at national level, representing also an opportunity for other preventive measures, are urgently needed.

Let's PrEP now: Italian experiences

OC 32 PRE-EXPOSURE PROPHYLAXIS: OVERALL PERCEPTION AND DISCOURAGING FACTORS AMONG A COHORT OF MSM – DATA FROM THE SEX-CHECK STUDY

A. Maccaro[1], L. Badia[1], V. Guardigni[1], P. Malosso[1], R. Pascale[1], S. Coladonato[1], B. Tazza[1], E. Rosselli Del Turco[1], G.M. Corbelli[2], G. Verucchi[1], P. Viale[1], S. Mattioli[2]

[1]Infectious Diseases Unit, Sant'Orsola-Malpighi Hospital, University of Bologna, [2]PLUS Onlus, Bologna

Background: Pre-Exposure Prophylaxis (PrEP) implementation in Italy is currently limited: first, many people among at-risk populations are not adequately aware of PrEP availability, safety, and efficacy; in addition, it is a non-reimbursable regimen, and access is not standardised nationally. In fact, no clear data exist about how access to PrEP is perceived by at-risk populations in Italy.

Material and methods: SEX-CHECK is a prospective, observational study aiming to evaluate at-risk behaviours, prevalence and incidence of STIs in a cohort of HIV-negative MSM and transgender women. It is held at BLQ Checkpoint, a peer-run, community-based service managed by PLUS Onlus (Bologna, Italy). As part of the protocol, we routinely ask every participant to answer, with the help of a peer counsellor, a questionnaire concerning his sexual habits; we also take note of his perception about his risk of HIV transmission and about PrEP, using a 1 to 10 score system. In this analysis, we included people who were not on PrEP at baseline nor decided to start in the following 3 months, despite being eligible for PrEP according to Italian Guidelines on HIV. Their answers were analysed to identify which factors could discourage them from starting PrEP.

Results: 16 out of the 77 people (21%) enrolled in SEX-CHECK, 15 cis-men and 1 trans-woman, were included in this analysis. Median age was 36 years (range 20-54). In the previous 6 months, 12 (75%) had sex with >10 partners. Inconsistent condom use was reported by 13 participants (81%). As for other risk factors, 2 (12%) received post-exposure prophylaxis, 3 (19%) were diagnosed with an STI in the previous 3 months, and 2 (12%) had chemsex, sharing straws and/or needles in 1 case (6%). 11 (69%) had high-risk behaviours, namely group sex, fisting, and/or sex toys sharing. Overall, 8 (50%) people considered their risk of contracting HIV infection as low (score 1-4), 6 (37%) as moderate (5-7), and 2 (12%) as high (8-10). Concerning their perception of PrEP, 10 participants (62%) thought they would benefit from it to a low to moderate degree; 12 (75%) expected to be moderately to highly exposed to considerable adverse effects, while 6 (37%) were moderately to highly worried they could be subject to social stigma. 11 (69%) would not spend the price of generic tenofovir/emtricitabine, stating it should be reimbursable.

Conclusions: Indecisiveness or reluctance to start PrEP does not seem to be uncommon in our cohort. Relevant discouraging factors seem to be an inadequate perception of at-risk situations and an excessive concern about adverse effects, leading people to an inaccurate "risk-benefit analysis"; fear of social stigma also seems to be worth noting. Educational interventions, such as those offered by community-run services, may be useful in regard to these aspects. Finally, an important role seems to be played by the non-reimbursable status of PrEP, about which debate is notoriously ongoing.

Let's PrEP now: Italian experiences

OC 33 PREP AND RISKY BEHAVIOUR: PRELIMINARY DATA FROM THE MILANO CHECKPOINT

M. Cernuschi, A. De Bona, D. Tesoro, E. Suardi, A. Tavelli, S. Negri, S. Bossolasco, A. Bianchi, A. Borrelli, D. Calzavara, D. Maineri, P. Vinti, L. Cosmaro, A. d'Arminio Monforte for the Milano Checkpoint association

ASST Santi Paolo e Carlo, Milano, Checkpoint Milano, Milano

Background: Milano Checkpoint is a new community-based association participating to the international Fast Track City Project set up on February 2019 thanks to the cooperation of five different associations (ASA, ANLAIDS, LILA, Arcigay, NPS), and the municipality of Milan. Activities include HIV and STI screening, counselling and monitoring for Pre-Exposure Prophylaxis (PrEP). Here we present data from the recent Checkpoint PrEP experience merged with previous activities of ASA Onlus. Aim of this analysis is to evaluate how PrEP usage affects risky behaviour and condom usage.

Material and methods: All subjects asking for PrEP included. HIV, and sexually transmitted infections (STI) (Syphilis, HCV, chlamydial and gonorrhoeal infections) were assessed on regular basis; all tests were free and voluntary. PrEP counselling and management were given by ID doctors, followed by a psychological interview. Data on sexual and risky behaviour were collected through anonymous risk-assessment questionnaires filled before each visit. Role of PrEP initiation on changes of risk-behaviors have been evaluated by paired t-test and McNemar test.

Results: In a 18-month period, 85 subjects accessed the service; none was found to be HIV positive. 22 subjects (25.9%) reported a STI in the previous 12 months: mostly HAV infection, syphilis and HPV-related conditions (36.4% each). Interestingly, 12 out of 85 subjects (14.1%) resorted to Post-Exposure Prophylaxis (PEP). 15/77 subjects (19.5%) used recreational drugs and 30/75 (40%) had sex after alcohol intake in the last 4 weeks.

A total of 46 subjects who started PrEP (FTC/TDF) underwent at least one visit after initiation; 18 of them chose the daily schedule (39%), while the remaining preferred an on demand schema. Data on condom, alcohol and substance usage as well as sexual activity after starting PrEP are reported in the 37 subjects with at least one baseline (pre PrEP) and one follow-up questionnaire.

A total of 22 subjects (59%) used condom regularly before PrEP, while 15 used it irregularly. At last visit after PrEP start, 9/22 (41%) of regular condom users became irregular, while 7/15 (47%) irregular users became regular. Overall starting PrEP did not affect the condom usage behaviour (p=0.804).

There were no significant differences either in the n of recreational drug users (7/37 before vs 8/37 on PrEP) or in that of alcohol users (16/37 vs 11/37) in the last 3 months. The n of partners did not significantly change (mean 9.2 SD 10 vs 8.7 SD 7.1; p=0.68); the n of unprotected sexual intercourses increased even if not significantly (mean 2.1 SD 4 vs 4.1 SD 5.7 p=0.07).

Conclusions: The Milano Checkpoint can be a powerful instrument to provide access to HIV and other STI testing for high-risk populations. Also, PrEP counselling and follow-up represents an additional tool among HIV prevention strategies. By our preliminary data PrEP usage does not clearly result in a higher risky behaviour.

Let's PrEP now: Italian experiences

OC 34 ASSESSMENT OF THE TROUGH CONCENTRATIONS OF TENOFOVIR IN HIV-NEGATIVE SUBJECTS ON PRE-EXPOSURE PROPHYLAXIS: A SINGLE CENTER, REAL-LIFE EXPERIENCE

D. Cattaneo[1], C. Gervasoni[1], S. Baldelli[1], P. Vinti[2], M. Fusi[1], D. Zagato[2], A. De Bona[3], E. Suardi[3], S. Bossolasco[4], M, Cernuschi[2,4]

[1]ASST Fatebenefratelli Sacco University Hospital, Milan, Italy, [2]Associazione Solidarietà AIDS (ASA) Onlus, Milan, Italy, [3]ASST Santi Paolo e Carlo, Milan, Italy; [4]IRCCS San Raffaele Scientific Institute, Milan, Italy

Background: Pre-exposure prophylaxis (PrEP) for HIV prevention has evolved significantly over the last years; clinical trials have indeed demonstrated the efficacy of oral PrEP and the field is scaling-up implementation. In most countries, branded and generic formulations of tenofovir disoproxil fumarate (TDF) are actually interchangeably used to address this task. Here, we measured tenofovir plasma trough concentrations in men who have sex with men (MSM) taking PrEP daily versus on demand and using different TDF formulations.

Methods: This retrospective, observational study considered all MSM subjects referring initially to the Associazione Solidarietà AIDS (ASA) Onlus and after to the Milano Check Point who performed a blood test for the measurement of tenofovir plasma concentrations. Tenofovir trough concentrations were directly measured or estimated taking into account the interval time between last dose intake and blood sampling. The derived data were stratified according to way of PrEP administration and type of TDF formulation.

Results: Forty MSM subjects were included in the present study (mean age 40±11 years, body weight 75±12kg). They had normal kidney (serum creatinine 0.9±0.1 mg/dL) and liver function (serum AST 27±7 IU/L) and started PrEP therapy 120±90 days before the assessment of tenofovir concentrations. A wide distribution in the estimated tenofovir trough concentrations was observed, with values ranging from 16 to 286 ng/mL (coefficient of variation 70%). No significant differences were found on tenofovir trough concentrations (105±62 vs. 110 ±59 ng/mL; p= 0.815) when comparing patients given PrEP daily (n=25) or on demand (n=15). Only 1 out of the 40 subjects was using the branded TDF formulation, whereas the remaining were on treatment with a generic formulation purchased at the community pharmacy (n=10, referred as TDF DOC), on a secure website (n=23, referred as Ricovir EM or Tenvir-EM), or purchased on unchecked websites (n=6; referred as generic online). A not significant trend for different tenofovir trough concentrations was observed when comparing the TDF generic formulations (127±73 vs. 118±65 vs. 88±49 vs. 70±10 ng/mL in subjects who were taking Tenvir-EM vs. Ricovir-EM vs. TDF DOC vs. generic online, respectively). Worthy of mention 25% of the enrolled subjects were concomitantly treated with other drugs, namely non-steroidal anti-inflammatory agents (n=3), benzodiazepines (n=2), antibiotics (n=1), duloxetine (n=1), dimethylfumarate (=1), metimazole (n=1) and hormonal products (n=1).

Conclusions: A wide inter-individual variability in the tenofovir trough concentrations was observed in HIV-negative MSM on PrEP. The type of drug administration (daily vs. on demand) did not significantly impact on tenofovir exposure. The possibility that the observed variability in tenofovir concentrations could have been significantly affected by the type of TDF formulation cannot be presently ruled out (the study is still ongoing).

Targetting 90-90-90

OC 35 THE UNAIDS 90-90-90 TARGET IS ACHIEVABLE: A FAST TRACK CITY EXPERIENCE

F. Maggiolo, L. Comi, R. Teocchi, E. Di Filippo, A.P. Callegaro, M. Rizzi
ASST Papa Giovanni XXIII, Bergamo

Background: Measuring progress towards the HIV care cascade allows to identify processes that should be improved to achieve UNAIDS 90-90-90 targets by 2020. This study assesses progress in the HIV care cascade among people living with HIV (PLWHIV) in a Province of Northern Italy.
Methods: We calculated the number of PLWHIV in our area using the eCDC HIV modelling tool (version 1.3.0) that simultaneously estimates the annual number of newly acquired HIV infections, the time between infection and diagnosis and the size of the undiagnosed population. Inputted data covered the period from 1984 to 2018. Data (year of diagnosis, AIDS diagnosis, CD4 at diagnosis, death, HIV-RNA blood level) on the diagnosed and treated populations were derived from the clinical database of the only Provincial Center authorized to treat HIV infection and cross-checked with the Regional administrative data-base. Virological response to cART was defined according to the last available HIV-RNA measure.
Results: At Jan 2019 patients actively followed at our Center were 2718. According to our calculation the total estimated number of PLWHIV was 3238, The prevalence of HIV infection in our area could therefore be estimated to be 300 cases for 100.000 inhabitants. Of the 3238 infected people 520 (16%) were unaware of their status or lost to follow-up. Over time, the proportion of undiagnosed subjects dropped drastically from 28% in 2000 to 6.9 % in 2019 (figure), but the time between infection and diagnosis was rather stable (mean 3.7 years). Patients aware of their HIV status and actively followed were 83.9% of all infected subjects. The number of diagnosed and alive subjects actively taking cART was 2572 (98.9%) of those in follow-up and 82.9% if compared to all PLWHIV. Finally, 94.8% of patients taking cART had their last viral load < 50 copies/ml. That brought to a final proportion of people living with HIV and virally suppressed of 78.5% [figure] above the 90-90 -90 goal.
Conclusions: To achieve the 90-90-90 targets a multi-faced approach including treatment, monitoring, care, PreP and PEP services is needed. All these services are currently offered to persons living in our Province. All services, but PreP drugs, are completely free of charge for any person living in Italy including illegal immigrants. We believe that the Italian model based on a socially-oriented healthcare system that provides free-care for all PLWHIV only in highly specialized Centers may help in achieving these goals. The Achilles heel in our setting still remains the proportion of PLWHIV who are unaware of their status mostly because they do not perceive they are at risk and do not seek for the test. The long and steady time elapsing between infection and diagnosis is an indicator of this situation. Efforts should be concentrated in improving the rate of diagnosed PLWHIV and to shorten the time between infection and diagnosis.

Targetting 90-90-90

OC 36 HIGH HIV PREVALENCE FOLLOWING SCREENING OF SUBJECTS WITH HIV INDICATOR CONDITIONS IN A HOSPITAL SETTING

C. Tincati[1], D. Barbanotti[1], T. Bini[1], A. Tavelli[1], M. Ravizza[2], A.M. Marconi[2], M. Cattaneo[3], D.A. Chiumello[4], A. Cerri[5], A. Priori[6], D. Ferrari[7], A. d'Arminio Monforte[1]

[1]Department of Health Sciences, Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, University of Milan, Italy, [2]Department of Health Sciences, Clinic of Gynecology and Obstetrics, ASST Santi Paolo e Carlo, University of Milan, Italy, [3]Department of Health Sciences, Clinic of Internal Medicine and Hematology, ASST Santi Paolo e Carlo, University of Milan, Italy, [4]Department of Health Sciences, Clinic of Anaesthesia and Intensive Care Medicine, ASST Santi Paolo e Carlo, University of Milan, Italy, [5]Department of Health Sciences, Clinic of Dermatology, ASST Santi Paolo e Carlo, University of Milan, Italy, [6]Department of Health Sciences, Clinic of Neurology, ASST Santi Paolo e Carlo, University of Milan, Italy, [7]Clinic of Oncology, ASST Santi Paolo e Carlo, San Paolo Hospital, Milan, Italy

Introduction: Approximately half of newly HIV diagnosed subjects are identified late in the course of infection (i. e. CD4+ T-cell count <350/uL at presentation) posing them at risk of developing AIDS and transmitting HIV. European recommendations suggest that all subjects presenting with medical conditions associated with a HIV prevalence >0.1% should be tested for HIV*. Aim of the present study is to verify the feasibility and the utility of offering HIV testing to individuals suffering from one or more HIV Indicator Conditions (HIV-IC) during hospital admittance.

Materials and Methods: We organized a screening campaign (HIV sCreening tEsts BEyond the taRGet, "Iceberg" project) to detect undiagnosed HIV infections at the ASST Santi Paolo e Carlo in Milan in subjects presenting with HIV-IC admitted in different hospital wards, from January to June 2019. All patients provided informed consent. Demographic and clinical characteristics were recorded for all subjects.

Results: In the course of the first three months of the project, 193 subjects suffering from a total of 206 HIV-IC were tested for HIV infection. Eleven of the 193 patients (5.7%) presented with two HIV indicator conditions and one subject (0.5%) with three (Table 1).

A total of 116/193 subjects (60.0%) were males, with median age of 39 (27-45) years. The majority (134, 69.4%) were Caucasian, with 117 (60.1%) Italians.

6 patients (3.1%) were diagnosed with HIV infection. 3/6 individuals presented with pneumonia, one resulting in P.jirovecii pneumonia (PJP, Pt 2) and another (Pt 3) resulting associated with HBV and HCV co-infections (Table 2). Of the remaining 3 HIV-infected subjects, one presented with dementia (Pt 4), one with gonorrhoea and syphilis (Pt 5) and one with a mononucleosis-like syndrome (Pt 6). 2/6 subjects were Italian, 3/6 were African and one was Latin American. Their median age was 37 (29–42) years. The median CD4 T-cell absolute count and percentage were 119 (16-609)/ul, and 5 (5-15) respectively (Table 2).

One patient (Pt 3) died during hospital stay because of severe complications of pneumonia and endocarditis despite minimal immunological impairment.

Conclusions: Up to 3% of the subjects we tested in a hospital setting because suffering from HIV indicator conditions resulted HIV positive, supporting the implementation of this screening strategy. Most subjects presented with low CD4+ T-cell counts and 30% with AIDS-defining events upon diagnosis, suggesting that this strategy may not serve as a useful tool for implementation of early HIV diagnosis. Nevertheless, opt-out strategy at least in case of several conditions might favour earlier HIV diagnosis to contain HIV epidemics.

*HIV in Europe. Guidance document: HIV Indicator Conditions: Guidance for implementing HIV testing in adults in health care settings.

Targetting 90-90-90

OC 37 TIME TO LINKAGE TO CARE (LTC) IN THE ICONA COHORT: 2010-2018

*P. Piselli[1], A. Tavelli[2], C. Cimaglia[1], G. Chiaradia[1], L. Rancilio[3], M. Oldrini[4], A. Cingolani[5], M.E. Quiros Roldan[6], V. Rizzo[7], S Rusconi[8], A. Caraglia[9], A. d'Arminio Monforte[10], E. Girardi[1] for the ICONA Foundation Study Group and for the Working Group of the project "Linkage to Care in HIV: a further piece to the analysis of continuum of care in HIV in Italy"**

[1]INMI L. Spallanzani IRCCS, Rome, [2]Icona Foundation, Milan, [3]Caritas Ambrosiana, Milan, [4]LILA, Milan, [5]Cattolica University, Rome, [6]University of Brescia, Brescia, [7]AORN dei Colli, PO D. Cotugno, Naples, [8]ASST FBF-Sacco, University of Milan, Milan, [9]Minister of Health, Rome, [10]ASST Santi Paolo e Carlo, University of Milan, Milan

Background and objectives: A timely linkage to care (LtC) after HIV diagnosis may benefit individual health and may reduce onward transmission of HIV. We determined the time from HIV diagnosis to LtC among persons with HIV (PWH) entering HIV care and enrolled in the ICONA cohort in 2010-2018. We also analysed determinants for a late LtC (>28 or >60 days) in the last three years (2016-2018) of enrolment.

Methods: We analysed time to LtC (defined as the time from HIV diagnosis to first CD4 or viremia determination or cART initiation, whichever came first) among persons enrolled in the ICONA cohort in 2010-2018. Limited to the last three years of enrolment, we performed a logistic regression analysis to investigate the association between late LtC (>28 or >60 days) and individual characteristics including gender, age (by 10 years of increase), being Italian, mode of HIV-transmission, education, job situation and AIDS diagnosis within 30 days from HIV diagnosis. In a sub analysis, AIDS cases diagnosed within 30 days from HIV diagnosis were not considered.

Results: 9143 patients were considered in the analysis (81% males and 67% Italians) of whom 48% were men-who-have-sex-with- men (MSM), 38% heterosexual contacts and 6.4% intravenous drug user (IDU); 7.2% had an AIDS diagnosis within 30 days from first positive HIV-test. Overall, median days to LtC was 16 days (IQR: 4-77), and it decreased significantly from 32 days (IQR: 6-276) in 2010-2011 to 11 days in the last three years (IQR: 3 -28; p<0001, Figure 1). This was particularly evident with an increasing number of CD4 at first determination. Among 2855 PWH enrolled 2016 onwards, factors significantly associated with time to LtC>28 days, were being IDU (OR=3.35 vs heterosexual) or lack of an AIDS diagnosis within 30 days from HIV diagnosis (OR=14.3) with a decreasing risk (-7%) for each 10-years of age of increase (Table 1). Similar results were observed when AIDS cases were not considered in the analysis. Finally, when considering a longer time LtC (>60 days), and excluding AIDS cases, significant determinants were: being female (OR=1.42), being IDU and be unemployed or with an occasional job (OR=1.56).

Conclusions: Among PWH entering in care in 2010-2018 progressive significant reduction in time to LtC was observed. Limiting the analysis to the last three years (2016-2018) major determinants of having a longer time to LtC were being a IDU or not having had an AIDS diagnosis. In some analysis female gender and unemployment were also associated with longer time to LtC.

[The project was partially funded by the Minister of Health (ref 4023/P.G.1).
*List of the associations involved in the project (in alphabetic order): Anlaids, Arcigay, Caritas, CICA, Circolo Mario Mieli, CNCA, Fondazione Villa Maraini, LILA, Nadir, NPS Italia, PLUS].

Targetting 90-90-90

OC 38 IS TIME FROM HIV DIAGNOSIS TO ART INITIATION PREDICTIVE OF VIROLOGICAL OUTCOME AND OF RETENTION IN CARE?

A. d'Arminio Monforte[1], A. Tavelli[2], A. Cozzi-Lepri[3], A. Castagna[4], S. Passerini[5], D. Francisci[6], A. Saracino[7], F. Maggiolo[8], G. Lapadula[9], E. Girardi[10], C.F. Perno[11], A. Antinori[12] for the Icona Foundation Study Group

[1]ASST Santi Paolo e Carlo, University of Milan, Clinic of Infectious and Tropical Diseases, Dept of Health Sciences, Milan, Italy, [2]Icona Foundation, Milan, Italy, [3]Institute for Global Health, University College of London, London, UK, [4]Division of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy, [5]III Division of Infectious Diseases, Luigi Sacco Hospital, ASST Fatebenefratelli Sacco, Milan, Italy, [6]Unit of Infectious Diseases, University of Perugia, Perugia, Italy, [7]Department of Infectious Diseases, Policlinic Hospital, University of Bari 'Aldo Moro', Bari, Italy, [8]Division of Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy, [9]Clinic of Infectious Diseases, ASST Monza San Gerardo Hospital, University Milano-Bicocca, Monza, Italy, [10]Clinical Epidemiology Unit, INMI "L. Spallanzani" IRCCS, Rome, Italy, [11]Haematology and Oncohematology Deparment, University of Milan, Milan, Italy, [12]Clinical Division of HIV/AIDS, INMI "L. Spallanzani" IRCCS, Rome, Italy

Background: Aim of this study is to evaluate the likehood of early ART initiation in Icona, and whether early ART start is associated to a better virological response and retention in care.

Methods: Patients from Icona cohort with first HIV diagnosis between January 2016 (universal ART initiation recommendation) and December 2017 are divided in 6 groups according to the time from first HIV pos test to ART initiation: <=7days (G1); 8-14 days(G2); 15-30 days(G3); 31-120 days(G4); 121-365 days (G5) and >365 days or no start (G6). Primary HIV infections and AIDS presenters are excluded. Time from HIV diagnosis to first visit at ID center (THIVID) has been calculated.

End points: Prevalence of early start (<=7 days from diagnosis); virological suppression at 12 weeks from ART start (12wVS); time to virological failure (VF: confirmed HIV-RNA >50copies/ml >6months from ART start); being in care and with virological suppression (HIV-RNA < 50 copies/ml) 1 year from ART start (cascade of care).

Statistics: logistic regression for predictors of being G1 and 12wVS; Kaplan-Meier curves and Cox model for time to VF and predictors. Follow-up accrued from the date of ART start to the date of VF or at last HIV-RNA (VL). Cascade of care is performed according to the 6 groups of ART start.

Results: A total of 1329 patients included: 85 (6.4%) belonging to G1, 116 (8.7%) to G2, 267 (20.1%) to G3, 639 (48.1%) to G4, 112 (8.4%) to G5 and 110 (8.3%) to G6. Differences in baseline demographic and clinical characteristics are shown in Table 1.

Independent predictors of early start are HIV RNA >100,000 copies/ml, CD4<350 cells/mmc, and shorter THIVID (Table 2).

Time to start ART is not associated with 12wVS; other predictors (calendar year, HIV-RNA, CD4 and ART-regimen) are shown in table 3.

The probability of VF by 1-year is 5.7% (1.9-16.5) in G1, 6.1% (2.6-14.0) in G2 and 3.3% (1.5-7.1) in G3, 3.1%(1.8-5.3) in G4 and 4.8% (1.5-14.0) in G5 (log rank=0.37) with no differences according to time of ART start by multivariate Cox model (table 4).

Figure 1 shows the cascade of care according to groups. 91% of patients on ART at 1-year show undetectable VL (89% of G1, 85% of G2, 94% of G3, 90% of G4, 94% of G5; p=0.12). Considering all the patients with HIV diagnosis, 69% of patients are in care with VS 1-year after starting ART (58 -72% G1, 86 -74% G2, 211 -79% G3, 481-76% G4, 77-69% G5; p=0.15) with no differences between groups.

Conclusions: Even if 83% of patients diagnosed in 2016-17 started ART within 4 months, only 6% started within 7 days and 65% started ART after 30 days from HIV diagnosis. Advanced HIV disease and shorter time from HIV diagnosis to the first visit are the main predictors of early start. Virological success is obtained in >90% of patients by 1 year from starting ART; in the Italian healthcare setting, timing of starting ART does not associate with differences neither in rate of virological response or shape of the cascade of care distribution.

The analysis of this study have been conducted thanks to the unconditional sponsorship of Gilead Sciences

Targetting 90-90-90

OC 39 CONTINUUM OF CARE AMONG NEW DIAGNOSED VS CHRONICALLY FOLLOWED HIV PATIENTS. RETENTION IN CARE ANALYSIS IN A SINGLE CENTER COHORT

A. Comelli[1], I. Izzo[2], F. Donato[3], A. Celotti[1], E. Focà[1], C. Pezzoli[2], F. Castelli[1], E. Quiros-Roldan[1]

[1]University Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili, Brescia, Italy, [2]Department of Infectious and Tropical Diseases, ASST Spedali Civili, Brescia, Italy, [3]Unit of Hygiene, Epidemiology and Public Health, University of Brescia, Brescia, Italy

Background: Despite the progress in HIV care, adherence to follow up remains critical. Public health institutions begin to consider retention in care as a new tool to fight against HIV pandemic, as embodied by the "90–90–90" strategy promoted by UNAIDS.Our aim was to explore how closely our center aligned with the "90–90–90" targets in new diagnosed HIV infections and in patients chronically followed. Moreover, we analysed the characteristics of LTFU patients, transferred and deceased patients excluded, in order to tailor targeted interventions aimed to improve retention in care.

Methods: An observational, retrospective study was conducted at the Outpatient HIV Clinic in Brescia, Northern Italy. We extracted all HIV-infected patients with at least one contact between January 2012 to April 2018 from the local database. Deceased patients (certified by the national mortality registry) and transferred ones (verified by the presence of a letter to or from the other HIV Clinic) were excluded.

We defined two cohorts of patients according to the year of HIV diagnosis: since 2011 ("new" cases) and before 2011 (chronically followed patients or "old" cases).

For each group we constructed a continuum of care with the following stages: 1) linkage to care, 2) prescription of cART and 3) viral suppression in patients on cART.

We collected medical records of all HIV-infected patients LTFU (lack of a contact for more than 12 months).

Results: Among the 3,822 patients extracted, "old" and "new" cases accounted for 81.1% (n=3,098) and 18.9% (n=724) respectively. 167 (3.4%) patients died and 868 (17.9%) moved to another HIV center.

The continuum of care among our HIV cohort shows a rate of 92% patients linked and retained in care, 98.4% of whom are currently on cART and 94.9% virologically suppressed. Among "new" cases, the corresponding rates are lower: 86.7%, 94.1% and 95.6% respectively.

Among chronically followed HIV patients, 6.7% (209/3,098) were LTFU in the study period. A significantly higher attrition among newly diagnosed patients: 13.3% (96/724).

The median interval between HIV diagnosis and last contact in "new cases" was 13 months. Only 73% had started cART and around 50% of them had a detectable HIV RNA at the last contact. Women and new diagnosed subjects represent a high percentage of LTFU patients in our cohort and, in comparison with LTFU patients with old diagnosis, LTFU among new cases were significantly younger, from foreign countries (mainly Africa) and heterosexuals.

Conclusions: The performance of our continuum of care is in accordance with the 90-90-90 strategy but it slightly differs between new HIV patients and the entire HIV cohort. Patients with recent HIV diagnosis, women, foreign people and people who do not reach HIV undetectability represent fragile populations with high LTFU rate and they need, particularly in the first year after linkage, a tailored counselling to improve retention in care and their adherence to HIV care program.

Targetting 90-90-90

OC 40 LOST TO FOLLOW UP: TEN YEARS CHALLENGE

M. Poliseno, D.F. Bavaro, F. Di Gennaro, G. De Vita, A. Saracino, L. Monno, G. Angarano, S. Lo Caputo

Infectious Diseases Department University of Bari , Bari, Italy

Introduction: Optimizing the "continuum of care" process and enhancing the retention in care are key points in HIV management. Therefore, becoming aware of the problem of loss to follow up, investigating its proportion and the underlining causes, has currently become a crucial challenge.
Aim of our study was to evaluate, in a large referral centre in Southern Italy, the rate of people lost to follow up (LFU) over a ten year gap (2008-2017), to assess clinical and epidemiological characteristics of patients out of care and to determine drivers associated to the disengagement from care.
Methods: Patients who failed retention between the 1st January 2008 and the 31st December 2017 were identified by analyzing the electronic healthcare record of the Clinic. People living with HIV (PLWHIV) were considered LFU if laboratory data and/or clinical visits were missing for more than 6 months. Demographics , last immune-virological data, co-infections, and last antiretroviral therapies (cART) were retrieved. Telephonic interviews were performed for those patients for whom no further information was available. Descriptive statistics and Chi Square test for trends were performed, as appropriate; a p value <0.05 was considered statistically significant.
Results: From 2008 to 2017, a median (q1, first-q3, third quartile) number of 1,030 (917–1,094) PLWHIV have been attending our Centre yearly; in the same period a total of 579 subjects were LFU. Over time, the rate of LFU compared to PLWHIV followed per year decreased from 6.9% to 4.7% (p for trend=0.255) (Figure 1). Features of LFU are shown in Table 1. LFU were mainly males (74%), Italians (82%), with a median (q1–q3) age of 44 (35–51) years; 43% of LFU had a hepatitis virus co-infection, while 35% had received an AIDS diagnosis. Overall, intravenous drugs use (IDU) represented the main transmission route (43%), although it decreased over the years (p for trend=0.05).
Among LFU, 31% had died 29% had moved to another centre, and 20% were definitively lost and could not be traced . 19% returned in care after a median (Q1–Q3) of 2 (2–3) years, 21% of whom for hospitalization. From 2008 to 2017, a substantial decrease of viremic subjects (from 65% to 29% respectively, p for trend <0.001), a significant increase of those on ART (from 65% to 95% respectively, p for trend <0.001), along with a decreasing trend of patients with AIDS (from 43% to 33% respectively, p for trend =0.239) was observed among LFU. Notably, overall deaths in LFU (p=0.09) and HIV-related deaths (p=0.068) remained stable.
Conclusions: The problem of LFU remains pivotal in HIV care, even if its rate has decreased over the years: compared to the past, patients fallen out of care are now mainly on cART with lower viral loads. A remarkable percentage of the LFU resulted to be definitively lost: higher attention should be focused on identifying PLWHIV at high risk of disengagement from care, and developing tailored retention reinforcement strategies.

Cancers and bacterial infections

OC 41 LATENT TUBERCULOSIS PREVALENCE AT HIV DIAGNOSIS: A MULTICENTER SIMIT STUDY

D. Goletti[1], A. Navarra[1], C. Cimaglia[1], E. Petruccioli[1], G. Cuzzi[1], A. Giannetti[1], V. Mazzotta[1], A. Spolti[2], C. Mastroianni[3], P. Pavone[3], M. Galli[4], F. Franzetti[4], E. Pontali[5], M. Lichtner[6], L. Sarmati[7], M. Compagno[7], D. Piacentini[8], V. Pirriatore[9], G. Lapadula[2], A. Gori[10], E. Tacconelli[8], E. Girardi[1], A. Antinori[1], A. Calcagno[9]

[1]INMI Lazzaro Spallanzani IRCCS, Rome, [2]Ospedale San Gerardo, Monza, [3]Policlinico Umberto I, Università Sapienza, Rome, [4]Ospedale Luigi Sacco Hospital - Polo Universitario, Milan, [5]Ospedali Galliera, Genoa, [6]Ospedale Santa Maria Goretti, Latina, [7]Policlinico Universitario Università Tor Vergata, [8]Università degli studi di Verona, Verona, [9]Università degli studi di Torino, Turin, [10]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan

Background: In 2017, WHO estimated 900,000 HIV-TB cases worldwide with 300,000 deaths from tuberculosis (TB) among HIV-infected people. WHO strongly recommends treatment for latent TB infection (LTBI) in people living with HIV. Italian guidelines recommend screening for LTBI in newly diagnosed patients with HIV. Tuberculin skin test (TST) and QuantiFERON (QFT)-based tests either QFT-Plus (QFT-P) or the previous version QFT-in tube (QFT-IT) which are based on IFNγ release, are assays globally used for LTBI detection.

Methods: To evaluate the prevalence of LTBI at the time of HIV diagnosis in a low TB endemic country. In a multicenter SIMIT-founded study we retrospectively enrolled subjects newly diagnosed with HIV from January 2016 to December 2017 (from 8 Italian public hospitals). Data are described as number (percentage) and median (interquartile ranges[IQR]).

Results: We included 768 patients; they were mostly male (79.9%), born in Italy (70.4%) and with a median age of 37 years. 153 subjects presented with AIDS (23 with active TB). Median CD4 count and plasma HIV RNA were 319 CD4 T-cells/mm3 (IQR:129-530) and 4.9 Log10 copies/ml (IQR: 4.2-5.4). Excluding patients with active TB, LTBI screening by TST was done only in 3 patients (0.4%); 1 of them was scored positive. Differently, QFT-IT or QFT-P was performed in 494 (out of 745, 66.3%) participants (offer of the test in the centers varied, range: 0-100). The QFT-P or QGT-IT was offered to the 77% of foreign- subjects (161/209) and to the 62% of Italian born individuals (333/537) (p<0.001).

By QFT, LTBI was diagnosed in 6.5% subjects (32/494), the majority (90.6%) had a risk factor for TB due to the origin from endemic country (29/32). TB preventive therapy was offered to 21 subjects (65.6%). Among them, 17 started the therapy and 9 completed it. Anergic results were observed in 17 patients (3.4%); 82.3% of them had CD4 T-cells <100/mm3, 5% between 100-200 CD4 T-cell count. We also stratified the results according to the CD4 T-cell number and the "uncertain range" of QFT results (IFNγ 0.2-0.7 IU/ml; Nemes AJRCCM 2017). Among those scored negative, the majority of patients with CD4 T-cells/mm3 <200, had a level of IFN-γ<0.2 IU/ml out of the uncertain range (QFT-IT: 99%; QFT-P TB1: 95%; QFT-P TB2 89%). Among those scored positive, the majority of patients with CD4 T-cells/mm3 ≥500, had a level of IFN-γ>0.7 IU/ml out of the uncertain range (QFT-IT: 80%; QFT-P TB1: 78%; QFT-P TB2 67%). In QFT-P assay, we found 5/17 discordant TB1- TB2- results (29%), mostly falling inside the uncertain range.

Conclusions: In this multicenter study we found that LTBI screening was mainly performed by QFT and performed in 66.3% of newly diagnosed HIV-infected patients, mostly born in TB endemic countries. LTBI was diagnosed in 6.5% and treatment offered only in 65.6% of them. A higher awareness of LTBI screening and preventive therapy offer need to be raised among the HIV units, as indicated by the Italian Guidelines.

Cancers and bacterial infections

OC 42 EVALUATION OF THE EFFECT OF HIV INFECTION ON QUANTIFERON PLUS RESULTS IN PATIENTS WITH ACTIVE TUBERCOLOSIS AND LATENT INFECTION

E. Petruccioli[1], T. Chiacchio[1], V. Vanini[1], G. Cuzzi[1], C. Cimaglia[2], A. Navarra[2], N. Riccardi[3,4], C. Pinnetti[5], V. Mazzotta[5], L.R. Codecasa[4,6], E. Girardi[2], A. Antinori[5], D. Goletti[1]

[1]Translational Research Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Epidemiology Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [3]Clinic of Infectious Diseases, Policlinico San Martino Hospital, University of Genoa, Genoa, Italy, [4] StopTB Italia Onlus, Milan, Italy, [5]Clinical Department, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [6]Regional Tb Refrence Centre-Villa Marelli Inst/Niguarda Hosp Milano

Background: In 2017, tuberculosis (TB) caused an estimated 300, 000 deaths among HIV-infected people (WHO 2018). Treatment for latent TB infection (LTBI) is strongly recommended in HIV-infected people. The QuantiFERON-TB-Plus (QFT-P), one of the IGRAs worldwide used to diagnose LTBI, measures IFNγ after M. tuberculosis-stimulation in TB1 and TB2 tubes containing peptides specific to elicit a CD4- or a CD4- CD8 response respectively. Aim of this study is to evaluate the effect of HIV-infection on QFT-P test in a low TB endemic country.

Methods: we prospectively enrolled 71 subjects with HIV-infection (27 with active TB: HIV-TB; 44 with LTBI: HIV-LTBI) and 277 individuals without HIV-infection (107 with LTBI and 170 with active TB disease). QFT-P has been performed for each enrolled patients.

Results: The sensitivity of QFT-P assay calculated in the active TB population was similar in HIV-infected and -uninfected subjects (78% in HIV-TB group and 80% in active TB patients without HIV). Comparing the levels of IFNγ response to QFT-P antigens, we observed a lower IFNγ level in HIV-LTBI compared to LTBI (TB1 stimulation: p=0.004; TB2 stimulation: p=0.003). Differently, the level on IFNγ in HIV-TB patients was similar to active TB patients without HIV. To note that each group reported similar level of IFNγ in response to TB1 or TB2 stimulation. We found that the majority of IFNγ values fell out of the uncertain range of 0.2-0.7 IU/mL (Nemes AJRCCM 2017) independently of HIV-status, both in active TB patients (HIV-TB: 63 %; TB: 66%, p>0.999) and LTBI subjects (HIV-LTBI: 75 %; LTBI: 88%, p=0.08). Interestingly, in the HIV-LTBI group we also observed a higher number of IFNγ results in the negative uncertain range (0.2-0.34 IU/mL), compared to LTBI subjects without HIV infection (HIV-LTBI: 23%; LTBI 4%; p= 0.0007). Surprisingly, we did not find any correlation between the CD4 count and the distribution of IFNγ results within the uncertain range in both HIV-LTBI and HIV-TB populations. Evaluating the ability to respond to TB1 and/or TB2, we did not find differences among groups. Moreover, independently of the HIV status, the number of discordant results (TB1- TB2- positive/negative) was similar in TB (HIV-TB: 7%; TB: 6%; p=0.8) and LTBI patients (HIV-LTBI: 9%; LTBI: 4%; p= 0.2). Interestingly, the majority of discordant results had IFNγ values falling in the uncertain range.

Conclusions: HIV infection did not have an impact on the accuracy of QFT-P score in patients with active TB and LTBI. The CD4 counts did not influence the distribution of IFN-γ values in HIV-infected patients. Notably, similar number of results within the uncertain zone was found among the HIV-infected and –uninfected subjects. This indicated that the HIV infection does not have any impact on the score associated to the "uncertain result". More studies are necessary to understand the effect of HIV-infection on the accuracy of QFT-P in the HIV-infected population.

Cancers and bacterial infections

OC 43 SYPHILIS REINFECTION IN HIV PATIENTS: THE EXPERIENCE OF A LARGE CLINICAL CENTER IN ROME

C. Picarelli[1], F. Lombardi[1], S. Belmonti[1], A. Ciccullo[1], A. Emiliozzi[1], D. Farinacci[1], D. Moschese[1], G. Baldin[1], S. Lamonica[1], A. Borghetti[1,2], A. Cingolani[1,2], S. Di Giambenedetto[1,2]

[1]Institute of Clinical Infectious Diseases, Catholic University of the Sacred Heart, Rome, Italy, [2]Fondazione Policlinico Universitario A.Gemelli, IRCSS, Rome, Italy

Background: Syphilis and other sexually transmitted infections (STIs) represent a growing concerning issue to cope with both in people living with HIV (PLWHIV) and in HIV seronegative patients worldwide.
This study is aimed to describe the epidemiology of laboratory confirmed cases of syphilis reinfections among HIV positive patients attending the Outpatient Service of our Clinic from 2000 to 2019, who had a homogeneous time of follow-up of at least ten years.
Materials and Methods: Standard review and descriptive analysis of data of all the HIV positive patients observed from 2000 to 2019 with a median time of follow-up of at least ten years with a first episode of treated syphilis infection who presented with a further episode of serologically documented syphilis infection (equal or more than 4-fold increase in RPR - Rapid Plasma Reagin - title at least 12 weeks after the completion of effective treatment for a previous syphilis episode that resulted in an equal or more than 4-fold decrease in RPR)
Results: Two hundred and twenty-four patients presented to our Clinic with a first diagnosis of serological syphilis; of them, one hundred and eighty-six had a homogeneous time of follow-up of at least ten years.114 (61.3%) were diagnosed with a reinfection. Median time of follow-up was 12.9 years (IQR 10.2 – 15.6). At first reinfection, the median age at was 37 years (IQT 31.5 – 42.8) and majority (n=108, 94.7%) were males; 81 (73.2%) were men reporting to have sex with men (MSM). 84.8% of the patients were Caucasian, 2.7% African and 13.4% were Hispanic. Median CD4 title at first reinfection was 491/mmc; moreover, in 57.9% of the cases it was lower than the previous determination available. HIV-RNA was undetectable for 61.4% of patients, while it was >50 cp/ml for 34.2% of patients (HIV-RNA determination was not available in 4.4% of patients); HIV-RNA determination was higher than the previous available determination in 21.9% of the cases, unmodified in 44.7% of the cases and lower than the previous determination available in 33.3%. 59.9% of the cases presented with a second reinfection, with a medium time of reinfection of 2.4 years (IQT 1.4 – 4.7); 36.8% had a third reinfection and 20.1% presented with four or more reinfections. Patients who did not present a reinfection had similar characteristics compared to those who presented a syphilis relapse. According to a logistic regression analysis, being Hispanic was the only variable slightly associated with an increased risk of relapse of syphilis (OR 3.211, 0.892 – 11.55, p=0.074).
Conclusion: Syphilis infections and reinfections are an increasing public health problem in PLWHIV. Further analysis are needed to identify the strategies to empower the consciousness of STIs in high risk groups and to implement appropriate preventive measures to avoid sexual transmission.

Cancers and bacterial infections

OC 44 PREDICTORS OF UREAPLASMA UREALYTICUM URINARY COLONIZATION IN HIV+ PREGNANT WOMEN: A PILOT STUDY

I. Franconi, C. Puzzolante, A. Bianchi, N. Riva, A. Raimondi, M. Digaetano, A. Santoro, V. Borghi, G. Guaraldi, C. Mussini

Infectious Diseases Unit, University of Modena and Reggio Emilia

Background: Prevalence of colonization by Ureaplasma urealyticum (U. urealyticum) of the genital tract of sexually active women ranges from 40 to 80%. Isolation of this bacterium from urinary tract of pregnant women has been associated with chorioamnionitis, spontaneous abortions or miscarriages and neonatal respiratory diseases. Our objective was to identify eventual HIV-related risk factors for U. urealyticum urinary tract colonization in HIV+ pregnant women.

Methods: This is a retrospective study of longitudinally recollected data of 83 HIV+ women attending the outpatient clinic of the Infectious Disease Unit at University of Modena and Reggio Emilia from January 2011 to September 2018. At first visit after pregnancy diagnosis all subjects were evaluated for HIV-viral load and CD4+ count. Urine samples were taken at first visit and monthly, if positive for bacterial growth a urine control was performed after treatment. Logistic regression analyses, age adjusted, were run to evaluate eventual predictors of U. urealyticum urinary tract colonization. Chi-square tests were performed to assess statistically significant differences in prevalence of colonization according to CD4+ count and detectable viremia.

Results: 83 pregnant HIV+ women were studied. 48 (57.8%) had a positive urine cultures for U. urealyticum, 37 (77%) of them were African. 46 (96%) of isolates acquired resistance to azithromycin at first urine culture after treatment. 26/33 (79%) of subjects with detectable viremia and CD4+ < 500 cell/mmc at beginning of pregnancy showed positive growth of U. urealyticum on urine samples. Pearson's Chi-square test showed a statistically significant difference in prevalence of urinary tract colonization by U. urealyticum between subjects with detectable and undetectable viral load (69.9 % vs 29.1%, $p < 0.05$) and CD4+ < or > 500 cell/mmc (74.4% vs 25.4%, $p < 0.05$), (Fig.1). Predictors of asymptomatic bacteriuria at multivariate logistic regression (age adjusted) analyses were: detectable viremia at beginning of pregnancy (HIV-VL > 40 copies/mL) [IC=1.391;8.871, p=0.008] and CD4+ < 500 cell/mmc [IC=1.526;9.857, p=0.004].

Conclusions: Our findings suggest that HIV-Viral load >40 copies/mL and T-cell CD4+ count < 500 cell/mmc at first visit after pregnancy diagnosis are associated with higher prevalence of U. urealyticum urinary tract colonization in HIV + women.

Keywords: Ureplasma urealyticum urinary colonization; Pregnancy; T-cell CD4 count; HIV-Viral Load

Cancers and bacterial infections

OC 45 CD4/CD8 RATIO PREDICTS THE ONSET OF VIRUS-RELATED CANCERS IN HIV-POSITIVE PATIENTS ON EFFECTIVE CART

E. Suardi[1], A. Cozzi Lepri[2], G. Madeddu[3], V. Spagnuolo[4], S. Vita[5], V. Manfrin[6], A. Bandera[7], A. Cingolani[8], A. Antinori[9], C. Mussini[10], G. Marchetti[1], A. d'Arminio Monforte[1], for the Icona Foundation Study Group

[1]Clinic of Infectious Diseases, San Paolo Hospital-ASST Santi Paolo e Carlo, University of Milano, Milano, Italy, [2]Institute for Global Health, University College of London, London, UK, [3]Department of Medical, Surgical and Experimental Sciences, Division of Infectious Diseases, University of Sassari, Sassari, Italy, [4]Division of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy, [5]Department of Public Health and Infectious Diseases, University Sapienza of Rome, [6]Department of Infectious and Tropical Diseases, St. Bortolo Hospital, Vicenza, Italy, [7]Infectious Diseases Unit, Departement of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy, [8]Institute of Clinical Infectious Diseases, Catholic University of Sacred Heart, Policlonico Gemelli, Rome, Italy, [9]Clinical Division of HIV/AIDS, INMI "L. Spallanzani" IRCCS, Rome, Italy, [10]Infectious Diseases Clinic, University of Modena and Reggio Emilia, Modena, Italy

Background: We assessed the role of CD4/CD8 in predicting virus-related and non-virus related cancers in a large cohort of patients on effective cART.

Methods: We included patients of the Icona cohort free from cancer at baseline, i.e. at time of first achievement of viral suppression (HIV-RNA<50 cp/ml) on cART.CD4/CD8 ratio was grouped as low (0-0.4), intermediate (0.4-1) and high (>1). The 0.4 cut-off was chosen as largely used in other cohorts as a prognostic marker for non-AIDS and AIDS-related events123.Virus-related cancers included non-Hodgkin and Hodgkin lymphoma (NHL, HL), Kaposi's sarcoma, hepatocellular carcinoma, HPV-related cancers. Non-virus related cancers included invasive cancers not listed above.Cox regression models were used to estimate the relationship between CD4/CD8 ratio and risk of cancer; time at risk accrued from baseline until the date of cancer diagnosis or last clinical visit. Multivariable models were adjusted for common causes of CD4/CD8 ratio and outcomes including CD4 nadir and current CD4 count and HIV-RNA (see Tables footnotes). Time-varying confounding was controlled using inverse probability of weighting. Because of the frequency of measurements in the cohort, the risk for the most recent value reflects that associated with the CD4/CD8 ratio measured on average 4 months prior to the event.

Results: 10,231 patients who achieved viral suppression were included. Over a median follow up of 50 (IQR:26,87) months, 117/10227 (1.1%) incident cases of virus-related cancer and 134/10494 (1.3%) of non virus-related cancer were observed. The most frequent virus-related and not virus-related cancers were NHL (30 cases, 25%) and HL (28 cases,24%) and lung cancer (35 cases, 26%) and breast cancer (15 cases, 11%) respectively. Patients' characteristics at baseline stratified by whether they develop cancer or not are described in Table 1. The CD4/CD8 ratio was not associated with the risk of non-virus related cancers, either at baseline or at most recent value(Table 2). In contrast, baseline CD4/CD8 ratio showed some association with the risk of virus-related cancers (HR0.59, 95%CI 0.37-0.94 for intermediate vs. low) and overall per one unit higher of CD4/CD8 ratio there was a risk reduction of 63%. The association between the most recent CD4/CD8 ratio and the risk of virus-related cancers was more consistent and stronger with low values (HR0.32, 95%CI 0.16-0.64 for high vs. low, HR0.48, 95%CI 0.28-0.81 for intermediate vs. low, Table3)from fitting the weighted Cox regression model.

Conclusions: There was some evidence that CD4/CD8 at the time of viral suppression was associated with a lower risk of virus-related cancers.The association was more consistent and stronger and independent of key confounders such as current CD4 count and HIV-RNA when considering the most recent value. This finding should be used to tailor virus related cancer screening and prevention strategies in high risk patients.

Cancers and bacterial infections

OC 46 PERSISTENCE OF high peripheral activated CD8+ T-CELLS AND not a low CD4/CD8 ratio predict hpv-related dysplasia iN CART-treated, HIV-iNFECTED subjects

C. Tincati[1], F. Bai[1], D. Mondatore[1], A. Vasile Baja[1], E. Suardi[1], M. Giovenzana[2], A. Pisani Ceretti[2], A. d'Arminio Monforte[1], G. Marchetti[1]

[1]Department of Health Sciences, Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, University of Milan, Italy, [2]Department of Health Sciences, Unit of Hepatobilyopancreatic and Digestive Surgery, ASST Santi Paolo e Carlo, University of Milan, Italy

Background: HPV-related dysplasia is a precursor of anal and cervical cancer. HIV-infected subjects are at increased risk of HPV-related disease progression, given their immune-depression and the impairment of HPV-specific immunity. A low CD4/CD8 T-cell ratio may mirror peripheral immune defects and has been linked to poor clinical outcome in HIV infection, yet, whether it associates with Squamous Intraepithelial Lesions (SIL) is currently unknown. Aim of this study was to investigate whether the CD4/CD8 T-cell ratio associates with SIL in HIV-positive subjects on effective cART.

Methods: We conducted a retrospective study on subjects enrolled in the San Paolo Infectious Diseases (SPID) cohort, who were on effective cART (HIV-RNA <50 copies/ml) and were screened for HPV-related dysplasia (anal/cervical PAP smears and HPV genotyping) in the period 01/2006-02/2019. SIL was defined as the presence of either ASCUS, Low SIL or High SIL. Demographic and viro-immunological parameters (CD4+ and CD8+ T-cell count, CD4/CD8 T-cell ratio, activated CD8+CD38+ percentages) at the time of the cytological evaluation were analyzed by Chi square, Mann Whitney test and multivariate logistic regression analysis.

Results: 419 cART-treated subjects were assessed for HPV-related dysplasia (Table 1). Cervical/anal SIL was reported in half of the patients (n=214, 51%). Individuals with SIL were more commonly males and MSM, presented a shorter time since HIV diagnosis and a shorter cART length and were more frequently treated with INSTI regimens; patients with SIL were also more frequently co-infected with T. pallidum (TPPA positivity), compared to subjects with normal anal/cervical cytology. Interestingly, activated CD38+CD8+ T-cell percentages, but not the CD4/CD8 T-cell ratio, were associated with SIL. HPV infection, in particular with multiple genotypes and High Risk (HR) genotypes, was confirmed associated with SIL (Table 1).

In multivariate analysis, the only factors independently associated with cervical/anal dysplasia were HPV infection and harbouring higher percentages of peripheral activated CD38+CD8+ T-cells (Table 2).

Conclusions: HPV infection is the major driver of dysplasia in the setting of HIV infection, underscoring the importance of vaccination in this context. While CD8+CD38+ resulted an independent predictor of dysplasia in virologically-effective cART-treated HIV-positive patients, the CD4/CD8 T-cell ratio was not associated with SIL, leading us to hypothesize that it may not fully capture the alterations of HPV-specific immunity in the setting of treated HIV infection.

Cancers and bacterial infections

OC 47 TWO-DRUGS REGIMENS DO NOT INCREASE THE RISK OF TUMOUR IN HIV+ PATIENTS

A. Borghetti[1], S. Bellino[2], F. Lombardi[3], D. Moschese[3], A. Ciccullo[3], N. Ciccarelli[4], G. Baldin[3], A. Dusina[3], A. Emiliozzi[3], S. Lamonica[3], S. Belmonti[3], A. Cingolani[3], P. Pezzotti[2], S. Di Giambenedetto[1,2]

[1]IRCCS Fondazione Policlinico Gemelli, Rome, Italy, [2]Department of Infectious Diseases,Istituto Superiore di Sanità, Rome,Italy, [3]Catholic University of Sacred Heart, Rome, Italy, [4]Dipartimento di Psicologia, Catholic University of Sacred Heart, Milano, Italy

Background: Currently-approved 2-drugs antiretroviral therapies (DT) are non-inferior to 3-drugs regimens (TT) in terms of plasma HIV-RNA suppression but concerns about immunological impairment have emerged, potentially leading to increased risk of cancer.

Material and methods: Patients followed at a single 3rd level center in Italy, starting a standard TT (2NRTIs+3rd agent) or a DT with proved non-inferior viral efficacy (i.e. 3TC or FTC+boosted PI, DRV/r+RAL and 3TC or RPV +DTG) between 2009 and 2018 were considered for the analysis; HBsAg-positive pts were excluded. Logistic regression model was used to estimate the probability to receive DT (propensity score, PS) according to confounding covariates. PS was then used to estimate the inverse probability weights (IPW), that were then stabilized using as numerator the probability of DT independently by individual covariates. Finally, marginal structural Cox regression models were used to evaluate the association of DT with the risk of developing a tumour.

Results: 1,107 patients, with a median follow-up time of 4.2 yrs, were evaluated; 69.2% were male, with a median age at study entry of 43 yrs. Overall 2,513 observations were recorded (479 with DT, 2,034 with TT). Groups differed for median baseline (BL) CD4 count (higher in DT arm), HIV-RNA (lower in DT arm) and cumulative exposure to antiretrovirals (longer with DT; see table 1).

Forty-three cases of tumour occurred, 8 with DT and 35 with TT, with no difference in incidence rates between groups. At a multivariate Cox model, DT was not associated with the risk of tumour (vs TT, HR 1.10; p=0.816); conversely, age (per 10-yrs increase, HR 1.61; p=0.002) and HIV risk factor (MSM vs heterosexual, HR 1.97; p=0.048) predicted risk of cancer after adjusting for nadir and BL CD4 count, CD4/CD8 ratio, therapeutic line and BL HIV-RNA. Marginal structural model using IPW (DT vs TT, HR 0.62; p=0.227) and stabilized IPW (DT vs TT, HR 0.63; p=0.251) confirmed no association of DT with risk of cancer. When restricting the analysis only to pts with BL HIV-RNA<50 cp/mL, DT still had no role in increasing risk of tumour, but at multivariate Cox regression an increased risk was seen with advanced age (per 10-yrs increase, HR 1.79; p=0.005) and longer ARV exposure (≥2 therapeutic lines vs ≤1, HR 4.65; p=0.017) after adjusting for confounders.

Conclusions: DT use did not increase the risk of tumours compared to TT in our cohort, but appropriately powered studies are needed to confirm these results.

ART and long-term safety issues

OC 48 OVERALL TOLERABILITY OF INTEGRASE INHIBITORS IN CLINICAL PRACTICE: RESULTS FROM A MULTICENTER ITALIAN COHORT

A. Ciccullo[1], G. Baldin[1], V. Borghi[2], G. Sterrantino[3], A. Latini[4], G. d'Ettorre[5], A. Lanari[6,7], M. Mazzitelli[8], A. De Vito[9], M. Colafigli[4], A. Capetti[10], L. Oreni[11], F. Lagi[3], S. Rusconi[11], S. Di Giambenedetto[1,12]

[1]Istituto di Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, Italy, [2]Azienda Ospedaliero Universitaria di Modena, Clinica Malattie Infettive e Tropicali, Modena, Italy, [3]Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze, Firenze, Italy, [4]Infectious Dermatology and Allergology Unit, IFO S. Gallicano Institute (IRCCS), Rome, Italy, [5]Department of Public Health and Infectious Diseases, Azienda Policlinico Umberto I, Rome, Italy, [6]Infectious Diseases Unit, AOU Senese, Siena, Italy, [7]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [8]Department of Medical and Surgical Sciences, Unit of Infectious and Tropical Diseases, Magna Graecia University, Catanzaro, Italy, [9]Department of Clinical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [10]Division of Infectious Diseases, Department of Infectious Diseases, Luigi Sacco University Hospital, Milan, Italy, [11]Infectious Diseases Unit, DIBIC Luigi Sacco, University of Milan, Milan, Italy, [12]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, UOC Malattie Infettive, Roma, Italy

Background: International guidelines currently recommend the use of Integrase inhibitors (INI)-based regimens as first line antiretroviral therapy (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 an INI. Censor was defined as death, suspension of the INI (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. Multi-variable models were adjusted for naïve status, calendar year and for significantly different variables between INIs at baseline.

Results: We enrolled 4343 pts from 9 centers; 3143 (72.4%) were males, with a median age of 49 ys (IQR 41 -55). Naïve pts were 733 (16.9%), of whom 168 (22.9%) AIDS-presenters. As to experienced pts, median time from HIV diagnosis was 16 ys (8-23); 2696 (76.2%) had a HIV-RNA≤50cp/mL at baseline (BL). Overall, 2282 pts (52.5%) started DTG, 1426 (32.8%) RAL and 635 (14.7%) EVG. During 10032 PYFU, we observed 1279 discontinuations (13 per 100PYFU); 448 of them (35%) due to simplification and 355 (28%) to toxicities (98 for CNS toxicity). Reasons of discontinuation were different between INIs [Table 1]. Estimated probability of maintaining DTG at 3 and 4 ys were 81.5% (SD ±1.0%) and 76.3% (SD ±2.4%), respectively; RAL 61.6% (SD ±1.4%) and 54.1% (SD ±1.4%); EVG 71.6% (SD ±2.4%) and 68.3% (SD ±3.0%) (Log-Rank between INIs p<0.001). At a multivariate analysis, being on a RAL-based ARV (vs DTG, aHR 2.9, 95%CI 2.3-3.6, p<0.001), a EVG-based ARV (vs DTG, aHR 1.3 95%CI 1.1-1.7, p=0.049) and a peak HIV-RNA>500k cp/mL (aHR 1.3, 95% CI 1.1-1.6, p=0.006) predicted INI discontinuation. Evaluating discontinuations due only to toxicities, we did not find a significant difference between INIs at Cox regression. A specific regression on discontinuation due to CNS toxicity, found that a previous INI exposure (aHR 1.9, 95%CI 1.1-3.3, p=0.017) was associated with the event, while being on RAL-based ARV (vs DTG, aHR 0.1, 95%CI 0.1-0.5, p=0.004) or on a EVG-based ARV (vs DTG, aHR 0.4, 95%CI 0.2-0.9, p=0.035) was inversely associated. Being on a EVG-based ARV (vs DTG, aHR 8.4, 95%CI 3.0-23.0, p<0.001) independently predicted discontinuation due to drug-drug interaction. Discontinuation due to simplification, meanwhile, were predicted by being on a RAL-based ARV (vs DTG, aHR 20.0, 95%CI 11.3 -35.2, p<0.001) or a EVG-based ARV (vs DTG, aHR 2.4, 95%CI 1.1-5.7, p=0.042).

Conclusions: Our data confirm the good tolerability of INIs in clinical practice. Differences emerge between the three drugs in reasons for discontinuation.

ART and long-term safety issues

OC 49 DOLUTEGRAVIR SAFETY IN A REAL-LIFE SETTING: RESULTS FROM THE SCOLTA COHORT

G. Madeddu[1], M.S. Mameli[1], N. Squillace[2], B. Menzaghi[3], R. Gulminetti[4], G.V. De Socio[5], A. Di Biagio[6], G.C. Orofino[7], G. Pellicanò[8], B. M. Celesia[9], L. Calza[10], C. Martinelli[11], S. Rusconi[12], A. Cascio[13], F. Vichi[14], G. Cenderello[15], L. Valsecchi[16], P. Maggi[17], G. Angioni[18], C. Dentone[19], K. Falasca[20], E. Ricci[21], P. Bonfanti[22], on Behalf of CISAI study group

[1]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, [2]Infectious Diseases Unit, Milano-Bicocca University, San Gerardo Hospital, Monza, [3]Infectious Diseases Unit, ASST della Valle Olona, Busto Arsizio, [4]Department of Medical Sciences and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo -University of Pavia, [5]Infectious Diseases Unit, Santa Maria Hospital, Perugia, [6]Infectious Diseases Clinic, Policlinico Hospital San Martino, Genova, [7]Division I of infectious and Tropical Diseases, ASL Città di Torino, [8]Department of Human Pathology of the Adult and the Developmental Age "G. Barresi", Unit of Infectious Diseases, University of Messina, [9]Unit of Infectious Diseases University of Catania ARNAS Garibaldi Catania, [10]Infectious Diseases Unit, S. Orsola Malpighi Hospital, Bologna, [11]SOD Malattie Infettive e Tropicali AOU Careggi, Florence, [12]Infectious Diseases Unit, DIBIC "Luigi Sacco", University of Milan, [13]Infectious Diseases Unit, Policlinico P. Giaccone Hospital, Palermo, [14]Infectious Diseases Unit, Santa Maria Annunziata Hospital, Usl centro, Florence, [15]Infectious Diseases Unit, Galliera Hospital, Genova, [16]Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Milano, [17]Infectious Diseases Clinic University of Campania "Luigi Vanvitelli", Neaples, Italy, [18]Infectious Diseases Unit, SS Trinità Hospital, Cagliari, [19]Infectious Diseases Unit, Sanremo Hospital, Sanremo, [20]Clinic of Infectious Diseases, Department of Medicine and Science of Aging, University "G. d'Annunzio" Chieti-Pescara, [21]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, [22]Infectious Diseases Unit, Ospedale A. Manzoni, Lecco

Background: Although Dolutegravir has proved safe in clinical trials, some observational studies have reported high rates of discontinuations due to adverse events mostly affecting the CNS. The aim of the present study was to evaluate the safety of DTG in a real life setting.

Materials and methods: Multicentre prospective cohort study performed in the context of SCOLTA (Surveillance Cohort Long-Term Toxicity Antiretrovirals).

Results: Out of 710 patients enrolled in DTG cohort, with at least 1 control visit, 75.1% were males, 92.4% Caucasian. Mean age was 47.8 (±11.4) years. Risk factor for HIV infection was sexual exposure in 472 patients (66.5%), intravenous drug use in 129 (18.2%), mother-to-child transmission/blood transfusion in 10 (1.4%), other/unknown in the remaining 99 patients (13.9%); 21.6% were coinfected with HCV. According to CDC classification, 331 patients (46.6%) were in stage A, 200 (28.2%) in B and 179 (25.2%) in C; 21.4% were naïve at antiretrovirals and 15.5% started DTG treatment with CD4<200 cells/mL.

After a median follow up of 22 months (interquartile range 15-25), toxicity-driven treatment interruption was observed in 65 subjects (9.2%): 19 (2.7%) CNS, 7 (1.0%) skin, 7 (1.0%) GI, 6 (0.9%) renal, 5 (0.7) muscle, 4 (0.6%) allergy, 3 (0.4%) abdominal pain, 3 (0.4%) liver, 2 (0.3%) erectile dysfunction, and 9 other or mixed reasons. More specifically, CNS-related discontinuation were due to headache in 4 patients, depression/anxiety in 4, psychomotor agitation in 4, sleeping alterations in 3, vertigo in 2, psychosis in 1 and neuropathy in 1.

Among adverse event-related interruptions, 36 (out of 710 pts, 5.1%) were reported in the first, 21 (out of 566, 3,7%) in the second and 7 (out of 277, 2.5%) in the third year of treatment. CNS symptoms-related interruptions showed a similar trend since 11 (out of 710 pts, 1.5%) were reported in the first, 7 (out of 566, 1.2%) in the second and 1 (out of 277, 0.4%) in the third year of treatment.

In a model including age, sex, naïve status, CDC stage, and regimen (any dual, TDF/FTC+DTG,3TC/ABC/DTG, others), we found that interruptions due to toxicity in general were related to age (HR by 1 year 1.04, 95% CI 1.02-1.07), sex (HR 1.71, 95% CI 1.02-2.87), naïve status (HR 2.38 95% CI 1.26-4.50) and stage C (HR 1.88, 95% CI 1.04-3.41). Considering only interruptions due to CNS events, naïve status and CDC stage C were still significantly associated (HR 3.65, 95% CI 1.23-10.80 and HR 4.37, 95% CI 1.26-15.14 respectively). No regimen type affected treatment discontinuation, after allowing for the aforementioned variables.

Conclusions: our data confirm also in a long follow up the tolerability of DTG in a real life setting. In particular, CNS toxicity-related interruptions were infrequent and mainly occurred during the first two years of treatment. Age, naive status and CDC stage C were significant predictors of discontinuation due to adverse events.

ART and long-term safety issues

OC 50 SCREENING FOR INDUCIBLE MYOCARDIAL ISCHEMIA IN ASYMPTOMATIC HIV SUBJECTS: FINAL RESULTS FROM CORDIS STUDY

V. Spagnuolo[1,2], L. Galli[2], A. Poli[2], C. Godino[3], N. Gianottii[2], S. Nozza[2], C. Muccini[1], E. Bruzzesi[1], A. Lazzarin[2], A. Margonato[1,3], A. Castagna[1,2]

[1]Faculty of Medicine and Surgery, Vita-Salute San Raffaele University, Milan, [2]Infectious Diseases Department, San Raffaele Scientific Institute, Milan, [3]Division of Clinical Cardiology, Cardiothoracovascular Department, San Raffaele Scientific Institute, Milan

Background: To assess prevalence rates and predictors of inducible myocardial ischemia (IMI), by use of ECG stress testing (EST), in people living with HIV (PLWH) with cardiovascular disease risk factors (CVDRF) and evaluate the association between IMI and carotid artery abnormalities.

Methods: Cross-sectional study on PLWH, men ≥50 years or post-menopausal women, with HIV-RNA <50 copies/mL and at least one of the following CVDRF: a familial history of coronary artery disease (CAD), smoking, hypertension, hypercholesterolemia and diabetes. PLWH included in the study underwent EST (according to Bruce treadmill protocol) since January 2016 until December 2018; ESTs were evaluated by a cardiologist for ECG changes indicative of IMI. Patients with a previous diagnosis of CAD or cardiac symptoms were excluded.

Bilateral carotid color-doppler ultrasonography (CDU) was also performed; results were classified as abnormal if a common carotid artery intima-media thickness (IMT) >1mm or ≥1 plaque (defined as an IMT>1.5 mm) or a stenosis (≥50% of the lumen) were present.

The 10-year ASCVD cardiovascular risk score was also calculated.

Logistic regression was applied to evaluate predictive factors of IMI.

Results: Overall 309 subjects were evaluated. IMI prevalence was 7.4% (23/309 subjects, 95%CI: 5.0% -11.0%). Subjects' characteristics are reported in Table1.

All subjects with IMI had an abnormal CDU compared with 66% of those without IMI (p= 0.008).

In subjects with abnormal CDU, IMI prevalence increased accordingly with the ASCVD risk score: 10.2% (95% CI=4.0%-22.2%), 16.9.% (95%CI=10.2%-26.5%), 19.7% (95%CI:11.8%-31.0%), 27.8% (95%CI=15.7% -44.1%) and 30.4% (95%CI=15.4%-51.1%) among subjects with ASCVD score ≤7.5%, >7.5%, >10%, >15% and >20% respectively; Cochrane-Armitage p for trend= 0.022.

After adjusting for years of HIV infection, nadir CD4+, body mass index, current CD4+ cell count, eGFR and triglycerides, IMI was associated with a higher ASCVD risk score (AOR for 1% increase=1.05; 95%CI=1.01 -1.11) and an abnormal CDU (AOR=7.88; 95%CI=2.47-35.36).

Conclusions: ECG stress test, a non-invasive and low-cost procedure, may be used as first-line screening for CAD in asymptomatic HIV-infected males with an abnormal CDU and an ASCVD risk score >7.5%.

ART and long-term safety issues

OC 51 LIPID PROFILE CHANGINGS AFTER SWITCHING FROM RILPIVIRINE/TENOFOVIR DISOPROXIL FUMARATE/EMTRICITABINE TO RILPIVIRINE/TENOFOVIR ALAFENAMIDE/EMTRICITABINE: DIFFERENT EFFECTS IN DIFFERENT PATIENTS POPULATIONS. RESULTS FROM A LARGE OBSERVATIONAL STUDY

L. Taramasso[1,2], A. Di Biagio[3], N. Riccardi[2,4], F. Briano[2], E. Di Filippo[5], L. Comi[5], S. Mora[6], M. Giacomini[6], A. Gori[7], F. Maggiolo[5]

[1]Infectious Diseases Unit, Department of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [2]Department of Health Sciences (DISSAL), University of Genoa, Genova, Italy, [3]Infectious Diseases Clinic, Policlinico San Martino Hospital, Genoa, Italy, [4]Infectious Diseases Department, San Raffaele Scientific Institute, Milan, Italy, [5]Infectious Disease Unit, ASST Papa Giovanni XXIII, Bergamo, Italy, [6]Department of Informatics Bioengineering, Robotics, and Systems Engineering (DIBRIS), University of Genova, Genoa, Italy, [7]Infectious Diseases Unit, Department of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy

Background: Tenofovir alafenamide (TAF) has similar efficacy compared to tenofovir disoproxil fumarate (TDF), but a less favorable effect on lipids. Aim of this study was to evaluate the impact on lipids of switching from rilpivirine (RPV)/ emtricitabine (FTC)/TDF to RPV/FTC/TAF in a large cohort of HIV-1 infected patients.

Material and methods: Retrospective study conducted in two Infectious Disease Centres in Northern Italy. All patients who switched from RPV/TDF/FTC to RPV/TAF/FTC were included. Change in lipid profile, renal function, and T-lymphocytes were evaluated at the switch and at first available follow up after the switch. Data at the two time points were compared through paired t-test, or paired samples Wilcoxon test, as appropriate. A linear regression model was used to evaluate correlations between baseline values of each variable and its change at follow up.

Results: 573 patients were considered, 99% with HIV-RNA <50 copies/ml, with mean age of 49.7 (±0.4) years and median 13.4 (6.9-22.5) years of HIV infection. After a median follow up of 12 (8-24) weeks, although mean CD4+ and CD8+ lymphocytes remained stable, (+ 8 cells/mmc and -5 cells/mmc, p= 0.4 and p= 0.6, respectively), mean CD4/CD8 ratio slightly increased (+ 0.02 p=0.001). In the same time frame the serum creatinine levels decreased from 0.96 (± 0.01) to 0.92 (± 0.01) mg/dl, p < 0.0001.

In patients with available data (431/573, 75%), mean total cholesterol (TC) changed from 173 ±1.7 to 188 ±1.8 mg/dl; mean HDL from 46 ±0.7 to 51± 0.7 mg/dl; mean LDL from 111 ±1.5 to 120 ±1.8 mg/dl; median triglycerides (TG) from 98 (75-147) to 110 (79-155) mg/dl, (p<0.0001 for all). Neither LDL/HDL nor TC/HDL ratio changed significantly. The variation in TC resulted inversely correlated to baseline TC value (R -0.252, 95% CI -0.27; -0.13, p <0.0001), as well as LDL change to LDL baseline value (R-0.238, 95%CI-0.26;-0.11, p<0.0001); HDL change to baseline HDL value (R-0.13, 95% CI-0.14;-0.02, p=0.009) and TG change at follow up to baseline TG levels (R-0.18, 95%CI -0.31;-0.10), Figure 1.

In patients with baseline diagnosis of hypercholesterolemia (TC>200 mg/dl, N=87), TC did not change, from 224±2.2 to 228±3.4 mg/dl (p=0.286), as well as LDL, from 150±2.5 to 151±3.2 mg/dl (p=0.751), while HDL increased from 51±1.6 to 55±1.7 mg/dl (p<0.0001) and both LDL/HDL and TC/HDL ratio decreased significantly, from 3.2±0.1 to 3.0±0.1 (p=0.014) and from 4.7±0.1 to 4.4±0.1 (p=0.004). In patients with baseline diagnosis of hypertriglyceridemia (TG>200 mg/dl, N= 50) TG levels did not change, from 238.5 (215 -310) to 212(163-292) mg/dl, p=0.088.

Conclusions: In this real life study, a slight increase in lipids was found after switching from RPV/FTC/TDF to RPV/FTC/TAF, but those results were not generalizable to people with hypercholesterolemia, in which lipids did not change and LDL/HDL and TC/HDL ratio decreased.

ART and long-term safety issues

OC 52 ADVANCED MACHINE LEARNING SYSTEMS IN HIV-1 INFECTED PATIENTS: A PROMISING TOOL TO PREDICT RENAL IMPAIRMENT

E. Grossi[1], L. Galli[2], A. Poli[2], S. Salpietro[2], L. Fumagalli[2], A. Castagna[2,3], A. Lazzarin[2]

[1]Centro Ricerche Semeion, Roma, Italy, [2]Clinic of Infectious Diseases, Istituto Scientifico San Raffaele, Milano, Italy, [3]Clinic of Infectious Diseases, Vita-Salute San Raffaele University, Milano, Italy

Background: In recent years, various studies highlighted the key role of renal impairment (RI) as a cause of morbidity and mortality in HIV-1 infected patients likely favored by the increased patients' longevity, concomitant comorbidities, ART toxicity, polypharmacy.
So far, no study has focused yet on the possibility to early detect people living with HIV (PLWH) that will develop a renal impairment after antiretroviral therapy (ART) start by use of potent mathematical models based on machine learning systems.
This possibility would be helpful in adopting strategies for prevention of RI.
Materials and Methods: We examined 1212 HIV-1 infected patients, followed at the Infectious Diseases Department of the San Raffaele Scientific Institute, who started ART between January 1998 and December 2014, with glomerular filtration rate (eGFR) determinations available both at the start of ART (baseline, BL) and ≥2 determinations over the 5 years after BL.
eGFR was calculated using the CKD Epidemiology Collaboration Equation (CKD-EPI). A diagnosis of renal impairment (RI) was defined by the occurrence of two consecutive eGFR determinations <60 mL/min/1.73m2 within 5 years of follow-up since BL.
Traditional and advanced machine learning algorithms were used to determine the most significant predictors of RI. The analysis considered as potential predictors 51 demographic, clinical and laboratory data measured at baseline. The contribute of ART is under investigation.
An evolutionary algorithm (TWIST system based on KNN algorithm) was used to split the dataset into optimal training and testing sets as well as to select features yielding the maximum amount of information. Then, machine learning systems with different learning laws were used to develop a predictive model based on a training testing crossover procedure.
Results: Overall, at BL, median age was 39 years (IQR=33-45), 84% men, with HIV diagnosis since 1.8 years (IQR=0.3-4.7), 27% HCV co-infected, median CD4+ 312 cells/μL (IQR=218-414), median HIV-RNA 4.73 log10copies/mL (IQR=4.20-5.18) and a median eGFR 109 mL/min/1.73m2 (IQR=97-117).
Over 5 years of follow-up, 23 patients developed RI. The machine learning systems employed (three-layers feed- forward back propagation and sine-net neural networks with 8 hidden nodes) obtained a mean global accuracy in predicting RI of 95.1% (95.7% sensitivity and 94.5% specificity) with an area under the curve (AUC) of 0.95 (Table 1, Figure 1).
A semantic connectivity map obtained with Auto-CM system, a fourth generation artificial neural network, explained the role of baseline variables in the predictive model, where higher age, lower nadir CD4+, presence of diabetes, use of aspirin and anti-hypertensive drugs resulted highly associated with renal impairment (Figure 2).
Conclusion: Machine-learning systems show a promising potential in predicting the 5-year renal impairment in HIV-1 infected patients starting from baseline clinical information and lab tests.

ART and long-term safety issues

OC 53 UNCOVERING EGFR PROFILES IN HIV-INFECTED PATIENTS: AN ALTERNATIVE STATISTICAL APPROACH

C. Brombin[1], C. Di Serio[1], L. Galli[2], A. Poli[2], L. Fumagalli[2], A. Castagna[1,2]

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

Background: The constant monitoring of renal function in HIV-infected patients is recommended by clinical guidelines to prevent kidney disease. While therapies have reduced cause-specific mortality in HIV patients, deaths due to other causes are increasing. More, some drugs for treating HIV have been shown to have nephrotoxic side effects. Estimated Glomerular Filtration Rate (eGFR) is used to index renal function. Several approaches have been proposed to model eGFR trajectories such as linear mixed effects models (LMEs) which include unobserved heterogeneity. However, these models do not allow for different susceptible strata, assuming an underlying homogeneous population.

Methods: To allow for possible differences in eGFR trajectories, we apply a novel modelling strategy based on latent class mixed effects models (LCMMs): this assumes the existence of possible unobserved sub-populations (namely, the latent classes), that can be heterogeneous and characterized by specific profiles over time. This approach is very flexible in modelling both quantitative and ordinal outcomes. The selection of the optimal number of latent classes is usually based on Bayesian information criterion (BIC). The implementation of LCMMs requires: (1) a structural latent model, where the latent process is represented as a function of time and other covariates and modelled according to a standard LME but without measurement errors; (2) a measurement model, which links the latent process to the outcome of interest. When heterogeneous population is assumed, a latent class-specific process can be defined and a multinomial logistic regression for the evaluation of latent class membership can be specified.

Results: The sample included 1854 HIV-infected patients (86.3% males, median [IQR] age 46 [39, 53]) with at least two EGFR determinations (median [IQR] of observations for patient 13 [7,23]). Median [IQR] EGFR at baseline was 110 [99, 118]. Baseline characteristics are reported in Table 1. The estimated LCMM for eGFR is reported in Table 2. Based on BIC, we choose a three latent classes model differing for baseline eGFR levels and for the evolution over time. At baseline, class 2 and 3 significantly differ from class 1 (p-value=0.0328 and p-value <0.0001). Moreover, eGFR significantly declined over time for patients in class 1 and class 2 (both p-values <0.0001), with larger decrease for class 2, while class3 remains stable. Overall, we found a significant and negative effect of CD4, of statins and INSTI, blood glucose levels, hypertension, total cholesterol and a significant and positive effect of HIVRNA, PI, NNRTI, triglycerides. This approach allows for further investigation in terms of class characterization for specific covariates.

Conclusions: The proposed approach allows to identify clusters of subjects with similar eGFR dynamics. This might suggest new insights since clinical information can be drawn once patients assigned to different classes have been characterized.

Resistance. Is it still a problem?

OC 54 DYNAMICS OF HIV-1 DRUG RESISTANCE OVER THE YEARS 1999-2017 IN ISOLATES FROM PERINATALLY INFECTED INDIVIDUALS FOLLOWED IN ITALY

D. Armenia[1,2], B Yagai[2], A. Bertoli[2], L. Palandri[3], H. Tchidjou Kuekou[4], F. Forbici[5], R. Gagliardini[5], M. Lichtner[6], M. Andreoni[7], A. Antinori[5], F. Ceccherini Silberstein[2], S. Bernardi[4], C.F. Perno[5,8], M.M. Santoro[2]

[1]UniCamillus, Saint Camillus International University of Health Sciences, [2]University of Rome "Tor Vergata", Rome, [3]University of Parma, Parma, [4]Children's Hospital Bambino Gesù, Rome, [5]National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, [6]La Sapienza University Polo Pontino, Latina, [7]University Hospital of Rome Tor Vergata, Rome, [8]University of Milan, Milan

Background: In developed settings, perinatally acquired HIV-1 infection has become a chronic disease of childhood with increasing numbers of adolescents surviving to adulthood. Perinatally infected individuals have been heavily pre-treated, and have a long history of antiretroviral treatment (ART), including sub-optimal regimens. This can increase the prevalence of drug-resistance, compromising the success of present and future treatment options. Thus, we aimed at evaluating the temporal trend of HIV-1 drug-resistance in perinatally infected individuals.

Materials & Methods: We included ART-experienced HIV-1 perinatally infected patients (pts) with at least one available plasma genotypic resistance test (GRT) for protease/reverse transcriptase and (when available) integrase, followed up in Central Italy from 1999 to 2017. The trends of resistance to NNRTIs, NRTIs, PIs and INIs, and resistance to 1, 2 and ≥3 classes were evaluated by using the Stanford mutations list 2018 according to the following time periods: 1999-2002, 2003-2015, 2006-2008, 2009-2011, 2012-2014, 2015-2017.

Results: We analyzed 554 plasma GRTs from 193 ART-experienced HIV-1 perinatally infected pts. Nearly half of the pts were born in Italy (47.2%) and were male (50.8%); 108 (55.6%) pts were infected with HIV-1 B; among non-B subtypes, the most prevalent were CRF02_AG (17.1%), F (13.5%) and C (5.7%). Pts were born in a median (IQR) year of 1993 (1989-1998); their median (IQR) age at first-line regimen was 2 (1-2) years, while their median (IQR) age at the moment of GRT was 17 (12-22) years. During their treatment history, around 63% of pts received a sub-optimal ART based on NRTI dual/monotherapy or unboosted-PI.

Overall, 69.3% of isolates showed resistance to any drug class; in particular, 35.0%, 58.7%, 45.8% 3.1% of isolates showed resistance to PIs, NRTIs, NNRTIs and INIs (N=184), respectively.

Resistance to any drug class dramatically decreased from 90% in 1999-2002 up to 44.2 % in 2015-2017, in conjunction with a remarkable increase of GRTs without resistance (from 10% to 55.8%, p<0.001, by Chi-squared test for trend) (Panel A). A significant decrease of resistance to 2 classes and ≥3 classes was observed from 1999-2002 to 2015-2017. By contrast, resistance to 1 class was almost stable up to 2014, but increased in 2015-2017.

Concerning the specific drug classes, the trends of resistance from 1999-2002 to 2015-2017 periods were as follows: PIs (from 53.3% to 11.5%, p<0.001), NRTIs (from 86.7% to 21.2%, p<0.001) and NNRTIs (from 45.0% to 28.8%, p=0.001). Resistance to INIs significantly increased from 0.7% in 2006-2008 to 5.8% in 2015 -2017 (p=0.018) (Figure, Panel B).

Conclusions: In HIV-1 perinatally infected individuals followed in Italy, a dramatic drop of drug-resistance has been achieved over time. However, drug-resistance to INIs is increasing and resistance to ≥3 classes remains a concern that deserves clinical attention in this fragile population.

Resistance. Is it still a problem?

OC 55 EVALUATION OF RESISTANCE PROFILE AND VIROLOGICAL RESPONSE IN DRUG-NAÏVE PATIENTS WHO START A FIRST-LINE REGIMEN CONTAINING AN INTEGRASE INHIBITOR

D. Armenia[1,2], S. Nozza[3], M.M. Santoro[2], M.R. Parisi[3], F. Maggiolo[4], E. Focà[5], C. Cerva[6], S. Rusconi[7], L. Gazzola[8], F. Ceccherini-Silberstein[2], C.F. Perno[9], A. Lazzarin[10], on behalf of the INIMAGE Study Group

[1]UniCamillus, Saint Camillus International University of Health Sciences, Rome, Italy, [2]University of Rome "Tor Vergata", Rome, Italy, [3]Clinic of Infectious Diseases, Istituto Scientifico San Raffaele, Milano, Italy, [4]Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy, [5]Division of Infectious Diseases, University of Brescia, Brescia, Italy, [6]Infectious Diseases Unit, University Hospital of Rome "Tor Vergata", Rome, Italy, [7]Infectious Diseases Unit, DIBIC "Luigi Sacco", University of Milan, Milan, Italy, [8]Clinic of Infectious Diseases, San Paolo Hospital, Milan, Italy, [9]University of Milan, Milan, Italy

Background: We evaluated the resistance profile and virological response in drug-naïve HIV-1 infected patients enrolled at the INIMAGE (INtegrase Inhibitors MAnagement by Genotype) study who started a first-line INI-based regimen.

Materials & Methods: The presence of major resistance mutations (MRMs) to PIs, NRTIs, NNRTIs and INIs according to the Stanford list was evaluated at baseline and at failure. Accessory resistance mutations (ARMs) to INIs were also evaluated. Kaplan-Meier curves were used to assess time and probability of virological success (VS, the first HIV-RNA <50 copies/mL after therapy start) after starting the INI-based regimen. Virological rebound (VR, the first value of HIV-RNA >50 copies/mL after VS) was also evaluated.

Results: Overall, 134 drug-naive patients were analyzed in median (min-max) year of 2016 (2014-2017); 87.3% of them were male, with a median (interquartile range, IQR) age of 38 (31-47) years. At baseline, 24.1% and 9.8% of patients had a HIV-RNA value of 100,000-500,000 and >500,000 copies/mL; median (IQR) CD4 count were 353 (173-547) cell/mm^3. 69.4% of patients was infected with HIV-1 B subtype. MRMs to PIs, NRTIs and NNRTIs was found in 0%, 8.9%, 12.9% of patients analysed, respectively. Concerning the INI-resistance, only one patient showed an MRM (R263K), while 8.3% of patients showed ARMs (T97A: N=5 [3.7%]; E157Q: N=2 [1.5%]; G163K: N=2 [1.5%]; G163R: N=1 [0.8%]; Q95K: N=1 [0.8%]). For 107 patients with an available HIV-RNA at follow-up, virological response was evaluated. The regimen mostly administered was DTG/ABC/3TC (39.3%), followed by DTG + TDF/FTC (30.8%), EVG/COBI/FTC/TDF (25.2%), RAL + TDF/FTC (3.7%). Only one patient was treated with a dual based regimen (DTG + DRV/COBI). After therapy start, the median time (95% Confidence Interval) of achieving VS was 13.0 (10.7-15.3) weeks. After 48 weeks of treatment, the probability of VS was 94% (standard error: 2.4%) (Figure 1, Panel A). After stratifying by INI administered, no significant differences were found neither for the probability of VS at week 48 nor for the median time of achieving VS (Figure 1, panel B). All the patients with INI mutations achieved VS. Only 3 patients experienced VR (two 24 weeks after VS; one after 12 weeks) at low level HIV-RNA (≤215 copies/mL). Genotypic resistance test was successful performed for one patient; no MRMs were found in protease, reverse transcriptase and integrase.

Conclusions: Our findings confirm that in drug-naïve patients, the presence of INI MRMs is still a rare phenomenon and does not have a clinical impact. Moreover, our results confirm that patients receiving an INI-based first-line cART achieve and maintain very high rates of virological suppression in real settings.

This work was supported with a grant from ViiV Healthcare Verona

Resistance. Is it still a problem?

OC 56 IMPACT OF PREVIOUS NRTIS RESISTANCE IN HIV POSITIVE PATIENTS SWITCHED TO DTG+2NRTIS UNDER VIROLOGICAL CONTROL

A. Giacomelli[1,2], A. Lai[1], M. Franzetti[3], F. Maggiolo[4], S. Di Giambenedetto[5], V. Borghi[6], D. Francisci[7], G. Magnani[8], M. Pecorari[9], L. Monno[10], I. Vicenti[11], L. Lepore[12], F. Lombardi[5], S. Paolucci[13], S. Rusconi[1,2] on behalf of ARCA collaborative group

[1]III Infectious Disease Unit, ASST-FBF-Sacco, Milan, Italy, [2]DIBIC L.Sacco, Univeristy of Milan, Milan, Italy, [3]UOC Infectious Disease Unit, ASST-Lecco, Lecco, Italy, [4]Department of Infectious Diseases, Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy, [5]Institute of Clinical Infectious Diseases, Catholic University of Sacred Heart, Policlinico Gemelli, Rome, Italy, [6]Infectious Diseases Clinic, Azienda Ospedaliero-Universitaria Policlinico, Modena, Italy, [7]Clinical Infectious Diseases, University of Perugia, Perugia, Italy, [8]Infectious Disease Unit, Reggio Emilia, Italy, [9]Unit of Microbiology and Virology, Modena University Hospital, Modena, Italy, [10]Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari, Italy, [11]Department of Medical Biotechnology, University of Siena, Viale Bracci 2, 53100, Siena, Italy, [12]Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari, Italy, [13]Molecular Virology Unit, Microbiology and Virology Department, Fondazione IRCCS Policlinico San Matteo , Pavia, Italy

Background: The accumulation of drug-resistance mutations on combined antiretroviral regimens (cART) backbone could affect the virological efficacy of the regimen. Our aim was to assess the impact of previous drug resistance to nucleoside reverse transcriptase inhibitors (NRTIs) on dolutegravir (DTG)+2NRTIs regimens in patients switched under virological control.

Material and methods: All HIV+ drug-experienced patients who started a regimen composed by DTG+2NRTIs [abacavir/lamivudine or tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF)/emtricitabine (FTC)] in the ARCA collaborative group with an HIV-RNA <50 cp/mL were included in the analysis. Patients with a previous virological failure (VF) to integrase inhibitors or with a previous DTG exposure were excluded from the analysis. The primary end-point was to assess the cumulative probability of VF (defined as 2 consecutive HIV-RNA >50 cp/mL or one HIV-RNA >1,000 cp/mL). The secondary end-point was to assess the impact of single and combined NRTIs mutation (based on Stanford list 2018) on VF of DTG+2NRTIs regimens. The cumulative risk of VF was assessed by Kaplan Meier curves and a multivariable Cox regression analysis was built to assess factors which were potentially related to VF.

Results: Five hundred and eighty-eight patients were included in the analysis of whom 423 (71.9%) were male, the median age was 51 (IQR 44-56) and 165 (28.1%) were treated with TDF or TAF/FTC. The median years on cART before the switch to DTG+2NRTIs were 8 (IQR 4-17) with a median time of viral suppression before the switch of 37 months (IQR 12-78). Patients with any previous NRTIs resistance were 148 (25.2%), M184V/I, K65R and more than 3 TAMs were present in 102 (17.3%), 6 (1%) and 77 (13.1%) patients, respectively. The median time of observation was 12 months (IQR 6-19). During the time of observation 259 (44%) discontinued DTG+2NRTIs for any reason (toxicity 20.8%, simplification 13.2%, VF 7.3%, other reasons 10.8%, not reported 47.9%). Nineteen patients experienced a VF with a median time to VF of 9 months (IQR 5-13). In univariate analysis no differences in the risk of virological failure was observed for patients with or without M184V/I, 3 or more TAMs, any NRTIs mutations, K65R and combining the single NRTIs mutations (Figure). In the multivariate model after correcting for age, gender, risk factors, immune-virological situation and years on cART no significant association was observed between NRTIs mutations and VF. Conversely, the duration of viral suppression before switch resulted associated with a lower risk of VF (for 1 month increase, aHR 0.98 95%CI 0.96-0.99; p=0.02).

Conclusions: According to our findings, previous NRTIs mutations appeared to have no impact on the risk of VF in patients under virological control who were switched to antiretroviral regimens based on DTG+2NRTIs. A longer interval on a controlled viremia decreased significantly the risk of VF.

Resistance. Is it still a problem?

OC 57 IMPACT OF RESISTANCE MUTATIONS ON VIROLOGICAL EFFICACY OF DTG-BASED MAINTENANCE TWO-DRUG REGIMENS: AN ARCA COHORT STUDY

R. Gagliardini[1], B. Rossetti[2], D. Redi[2,3], S. Modica[3], F. Montagnani[2,3], G. Zanelli[2,3], S. Di Giambenedetto[4], F. Lombardi[4], M. Pecorari[5], V. Borghi[6], A. Callegaro[7], V. Micheli[8], M. Annovazzi Lodi[9], A. De Luca[2,3], M. Zazzi[3]

[1]Lazzaro Spallanzani National Institute for Infectious Diseases IRCCS, Rome, Italy, [2]Infectious Diseases Unit, AOU Senese, Siena, Italy, [3]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [4]Clinic of Infectious Diseases, Catholic University of Sacred Heart, Rome, Italy, [5]Unit of Microbiology and Virology, Modena University Hospital, Modena, Italy, [6]Infectious Diseases Unit, Modena Hospital, Modena, Italy, [7]Microbiology and Virology Unit, ASST Papa Giovanni XXIII, Bergamo, Italy, [8]Unit of Clinical Microbiology and Virology, Luigi Sacco Hospital, ASST FBF-Sacco, Milan, Italy, [9]Virologia Molecolare, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Background: Two-drug regimens (2DR) are largely prescribed as maintenance therapy, nowadays mainly based on DTG. While many data have been reported about PI-based 2DR, the impact of resistance mutations and duration of virological suppression on DTG-based 2DR remains to be clarified. The aim of this study was to evaluate the impact of resistance mutations on virological outcome of DTG-based 2DR maintenance ART.

Material and methods: Virologically suppressed patients (pts) switching to DTG+3TC or DTG+RPV with pre-baseline (time of switch=baseline, BL) resistance genotype (at least PR/RT) were selected from the ARCA database. Primary endpoint was virological failure (VF: an HIV-RNA, VL, >200 cps/mL or 2 consecutive >50 cps/mL). The probability of VF was estimated by Kaplan-Meier analysis. Resistance to 2DR was defined as occurrence of at least Stanford HIVdb (v.8.5) low-level resistance (LLR) to at least one drug included in the current 2DR, based on cumulative genotype. CD4 changes were assessed using Student's t-test for paired samples. A secondary analysis comparing 2DR with DTG-based 3D regimens was also performed.

Results: A total of 318 2DR pts were analysed: 260 (82%) switching to DTG+3TC, 58 (18%) to DTG+RPV; 68% were males, median age was 51 (44-56) years, 12 (6-23) years of HIV infection, 5 (3-8) years of virological suppression, nadir CD4 231 (121-329), 5 (3-9) previous ARV lines, 59% previously exposed to INSTI, 11% with resistance to current 2DR. The integrase sequence was available in 14% of patients, none harbouring resistance to DTG. 20 VF were observed, of whom 4 (3/17 VF in DTG+3TC, 1/3 in DTG+RPV) in patients with at least LLR at BL (M184V+K219Q; D67N+K70R+K219Q; D67N+K70R+T215Y+219Q; E138A), in a median FU of 1.3 years (IQR 0.6-2). The 2-year estimated probability of VF was 8.7% (95% CI 4.4;13); 8.6% (4.1;13.1) in those without resistance and 9.7% (-4.4;23.8) in those with resistance (Log rank: p=ns, figure 1). No factor was significantly associated with VF at multivariate analysis, but in pts with <6 years of virological suppression, BL resistance was associated with a higher probability of VF (p=0.003). After 48 weeks, a statistically significant increase in CD4+ was detected (+56 cells/mmc, p<0.001), independently from baseline resistance. The 2-year estimated probability of VF in the reference 3DR group (n=564) was not different from that for the 2DR group: 8.8% (5.9;11.7) in the whole case file and 9.7% (6.6;12.8) in the presence of baseline resistance. Longer time of virological suppression was the only factor associated with a lower risk of VF in the 3DR dataset.

Conclusions: DTG-based 2DRs show high virological efficacy, even in the context of predicted incomplete activity, at least within a short-term follow-up. A longer duration of virological suppression seems to decrease the impact of resistance on virological outcome, however further studies are warranted to confirm this hypothesis and possibly define a clinically useful threshold.

Resistance. Is it still a problem?

OC 58 IN VITRO ANALYSIS OF DORAVIRINE ACTIVITY ON HIV-1 CLONES HARBORING MULTIPLE NNRTI RESISTANCE MUTATIONS

F. Saladini[1], F. Giammarino[1], A. Giannini[1], A. Boccuto[1], F. Dragoni[1], I. Vicenti[1], R.W. Shafer[2], M. Zazzi[1]

[1]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [2]Stanford University, Stanford, CA, USA

Background: Doravirine (DOR) is a novel once-daily NNRTI approved for the treatment of HIV-1 infection. During in vitro and clinical studies, DOR showed improved efficacy, pharmacokinetics and safety profile compared to efavirenz (EFV) and limited cross-resistance with rilpivirine (RPV) and etravirine (ETR). This study aimed to evaluate the in vitro antiviral activity of DOR in a panel of HIV-1 clones harboring combinations of major NNRTI RAMs.

Materials and methods: Viruses were generated from ten recombinant infectious clones with intermediate to high level resistance to RPV, ETR, EFV and nevirapine as determined with the Phenosense Assay, obtained from Stanford University through the AIDS Reagent Program. In vitro susceptibility to DOR was measured in duplicate by a TZM-bl cell based assay and fold-change (FC) values were calculated with respect to the IC50 value obtained with the wild-type NL4-3 strain. FC values were compared with predicted DOR activity by HIVdb and ANRS algorithms.

Results: Viruses harboring both DOR (labelled with an asterisk) and major NNRTI RAMs showed FC >100 in two cases (E138G/H221Y*/F227L*/M230L* and V106I*/Y181C/G190A/H221Y*), while a moderately decreased susceptibility was observed in two samples with mutations L100I/K103N/H221Y* and L100I/M230L* (FC 4.0 and 6.2, respectively). Three samples without DOR RAMs but including Y181C (K103N/Y181C, K101E/Y181C/G190A, K101E/E138K/Y181C) showed a considerably reduced susceptibility to DOR (FC 22.1, 31.8 and 14.2, respectively), while mutations K101P/K103N, K101E/Y181V and K101E/G190S present in three samples had a minimal impact, resulting in FC of 0.4, 2.8 and 3.1, respectively. Although biological or clinical FC cut-offs are still missing, HIVdb algorithm potentially underestimated DOR activity in 3 cases. Namely, (i) K103N/Y181C, (ii) V106I*/Y181C/G190A/H221Y* and (iii) K101E/E138K/Y181C had FC 22.1, >100 and 14.2, respectively, and were predicted as low-level resistance (i) and intermediate resistance (ii and iii). Similarly, ANRS underestimated DOR activity in samples (ii) and (iii), in addition to the sample with mutations K101E/Y181C/G190A (FC 31.8, all three samples considered as susceptible).

Conclusions: Although previous studies indicated that DOR retains full activity with clones harboring Y181C alone, these data suggest that DOR susceptibility can be affected by NNRTI cross-resistance in samples harboring Y181C plus one or more NNRTI mutations, even in the absence of specific DOR RAMs. Considering the complete activity on most single major NNRTI mutations, DOR resistance may thus result from the accumulation of multiple mutations, similarly to etravirine. In vivo studies are awaited to define the role of past NNRTI resistance patterns on clinical DOR activity as well as the possibility to use older NNRTIs on virus variants selected at DOR failure.

Resistance. Is it still a problem?

OC 59 PRETREATMENT HIV DRUG RESISTANCE AND TREATMENT FAILURE IN NON-ITALIAN HIV-1 INFECTED PATIENTS ENROLLED IN ARCA

D.F. Bavaro[1], D. Di Carlo[2], B. Rossetti[3], B. Bruzzone[4], I. Vicenti[5], E. Pontali[6], A. Zoncada[7], F. Lombardi[8], S. Di Giambenedetto[8], V. Borghi[9], M. Pecorari[10], P. Milini[11], P. Meraviglia[12], L. Monno[1], A. Saracino[1]

[1]Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari Medical School, Bari, Italy, [2]Pediatric Clinical Research Center "Romeo and Erica Invernizzi", University of Milan, Milan, Italy, [3]Infectious Diseases Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy, [4]Hygiene Unit, IRCCS AOU San Martino-IST , Genoa, Italy, [5]Dipartimento di Biotecnologie Mediche, Università di Siena, Siena, Italy, [6]Infectious Diseases Unit, Galliera Hospital, Genoa, [7]Infectious Diseases, Istituti Ospedalieri, Cremona, Italy, [8]Institute of Clinical Infectious Diseases, Catholic University of Sacred Heart, Policlinico Gemelli, Rome, Italy, [9]Clinica Malattie infettive, Azienda Ospedaliero Universitaria di Modena, [10]Polyclinic of Modena, Modena, Italy, [11]Infectious Diseases Unit, Macerata Hospital, Macerata, [12]1st Division of Infectious Diseases, ASST Fatebenefratelli-Sacco, Milan, Italy

Background: An increase in pretreatment drug resistance (PDR) to first-line antiretroviral therapy (ART) in low-income countries has been recently described. Herein we report the prevalence of PDR and risk of virologic failure (VF) over time among migrants to Italy enrolled in ARCA.

Methods: HIV-1 sequences from ART-naïve patients of non Italian nationality were retrieved from ARCA database from 1998 to 2017. PDR was defined by at least one mutation from the reference 2009 WHO surveillance list and the 2017 IAS list. Chi-squared or Fisher's Exact tests were used, as appropriate, to detect potential differences in PDR between B and non-B subtypes, and according to migrant origin. Differences in PDR prevalence over the years were evaluated by Chi-squared test for trend. Survival analysis (Kaplan-Meier curves and Cox Regression Model) was used to evaluate the probability and predictors of virological failure (the first of two consecutive viremia >200 copies/mL after at least 180 days of therapy) according to PDR.

Results: Protease/reverse transcriptase sequences from 1,155 patients, mainly migrants from Sub-Saharan Africa (SSA) (42%), followed by Latin America (LA) (25%) and Western Countries (WE) (21%), were included. Non-B strains were detected in 61.7% of cases, with an increasing trend in recent years (p=0.060). General features of subjects are showed in Table 1.

Overall, PDR was detected in 8.6% of sequences, with a significant difference between B and non-B strains (13.1% vs 5.8% respectively, p<0.001). 2.1% of patients carried a resistance mutation for protease inhibitors (PIs) (2.1% in B vs 2.3% in non-B respectively, p=0.893), 3.9% for nucleos(t)ide reverse transcriptase inhibitors (NRTI) (6.8% in B vs 2.1% in non-B respectively, p<0.001) and 4.3% for non-nucleos(t)ide reverse transcriptase inhibitors (NNRTI) (6.3% in B vs 3.1% in non B, respectively, p=0.013).

Over the years, PDR at diagnosis in B strains showed a slight decreasing trend only for PIs (p=0.086) (Figure 1A). Among non-B strains, PDR remained stable for all three drug classes (Figure 1B).

Median prevalence of PDR for all drug classes was significantly different if stratified for country of origin (11.1% for LA and Asia, 10.4% for WE, 8.8% North Africa and Middle East (NAME), 5.7% for SSA, respectively, p=0.042). Overall, prevalence of PDR over the years remained stable, while it decreased for PIs in LA (p=0.021), and for NRTI (p=0.020) among migrants from WE.

By Cox Regression Multivariate Model, having more than 1 class of PDR (p=0.015 vs. absence of PDR, see Figure 2), higher VL at diagnosis (p=0.008) and being migrants from SSA (p=0.001 vs. WE) were predictive of VF, while a recent calendar year of diagnosis (p<0.001) was protective for VF.

Conclusions: PDR appeared to be stable over the years in migrants to Italy enrolled in ARCA; however, it still remains an important cause of virologic failure together with VL at diagnosis.

Resistance. Is it still a problem?

OC 60 EVALUATION OF MULTIDRUG RESISTANCE OVER THE LAST TWO DECADES IN ART-EXPERIENCED HIV-1 INFECTED PATIENTS IN THE ARCA DATABASE

F. Lombardi[1], A. Giacomelli[2], D. Armenia[3,4], A. Lai[5], A. Dusina[1], A. Bezenchek[6], L. Timelli[6], F. Saladini[7], F. Vichi[8], P. Corsi[9], G. Colao[10], B. Bruzzone[11], A. Callegaro[12], A. Castagna[13,14], M.M. Santoro[4]

[1]Clinic of Infectious Diseases, Catholic University of Sacred Heart, Rome, [2]Infectious Diseases Unit, DIBIC Luigi Sacco, University of Milan, Milan, [3]UniCamillus, Saint Camillus International University of Health Sciences, Rome, [4]Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, [5]Department of Biomedical and Clinical Sciences L. Sacco, University of Milan, Milan, [6]IPRO - InformaPRO S.r.l., Rome, [7]Department of Medical Biotechnologies, University of Siena, Siena, [8]Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Firenze, [9]Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, [10]Laboratory of Virology, Careggi Hospital, Florence, [11]Hygiene Unit, Azienda Ospedaliera-Universitaria San Martino, Genoa, [12]Department of Laboratory Medicine, ASST Papa Giovanni XXIII, Bergamo, [13]Clinic of Infectious Diseases, Istituto Scientifico San Raffaele, Milano, [14]Clinic of Infectious Diseases, Vita-Salute San Raffaele University, Milano

Background: The therapeutic history of people living with HIV could be burdened by the development of multi-class drug resistance (MDR). Those subjects require more complex antiretroviral treatment (ART) and have an increased risk of clinical progression and death. Here we aimed to explore the prevalence and predictors of MDR-HIV in ART-experienced patients (pts).

Materials and methods: In this retrospective study we selected from the ARCA database all ART-experienced HIV -1 infected pts with at least one plasma genotypic resistance test (GRT) available, performed from 1998 to 2018. MDR-HIV was defined as a virus with at least one major resistance mutation (based on Stanford list 2018) in at least 3 different drug classes of the following 4 categories: NRTIs, NNRTIs, PIs and INSTIs.

Temporal trend of resistance in all isolates to any drug-class was evaluated by the Chi-square test for trend. The prevalence of pts harbouring an MDR-HIV and their demographic, therapeutic, clinical and viro-immunological characteristics were analyzed by taking into account cumulative GRTs. A multivariable multilevel logistic regression model was built to assess the independent factors associated with the cumulative MDR-HIV.

Results: We analysed 13807 isolates from 6244 ART-experienced pts. An overall decreasing of resistance (to 1, 2 e ≥3 drug classes) over two decades was observed (Figure); however, splitting the study period, this variation resulted significant in the first-time span 1998-2010 (p<0.001), while it remained stable from 2011 to 2018. In particular, MDR significantly decreased from 17% in 1998-2002 to 14% in 2008-2010 (p<0.001), and stayed nearly unchanged at around 9% over the period 2011-2018 (p=0.136).

By evaluating MDR in cumulative GRTs, 1294 (20.7%) pts included in the study harbored an MDR-HIV; of them, 72% were male, 92% carried an HIV-1 B subtype, 73% were Italian, 98% started ART before 2008. The median [IQR] age was 44 [39-50] years; sexual route was the main risk factor (52%), followed by intravenous drug use (IDU) (32%) and vertical transmission (3%); the median [IQR] number of ART regimens was 8 [5-12]. In the multivariable model, male gender (vs. female; adjusted Odds Ratio [95% Confidence Interval]: 1.47 [1.25 -1.73]), vertical transmission (vs. sexual: 3.97 [2.01-7.83]), number of previous PIs, NRTIs, NNRTIs, and INIs (per 1 increase: 1.59 [1.49-1.69], 1.14 [1.07-1.21], 1.72 [1.54-1.93], 1.39 [1.03-1.87], respectively), previous exposition to T20 (AOR 1.89, 1.34-2.68) were associated with an increased risk of MDR-HIV. Conversely, a Nadir CD4 >200 cells/mm^3 (vs. ≤200: 0.83 [0.81-0.97]) and starting ART from 2008 (vs. <2008: 0.54 [0.33 -0.88]) were associated with a lower risk of MDR-HIV.

Conclusions: An overall decreasing trend of MDR-HIV was observed. Nevertheless, after 2010, the prevalence of MDR is stable at around 9%, suggesting the need of continuous surveillance and accurate management of HIV -1 infected ART-experienced pts.

From naive to highly treated subjects. Efficacy of cART

OC 61 LOWER RESPONSE TO ANTIRETROVIRAL THERAPY (ART) AND PERSISTENTLY POOR SURVIVAL FOR AIDS PRESENTATION IN PEOPLE SEEN FOR CARE IN ITALY FROM 2009 TO 2018

A. Mondi[1], P. Lorenzini[1], A. Cozzi-Lepri[2], A. Cingolani[3], M. Farenga[4], S. Rusconi[5], G. Di Girolamo[6], A. Gori[7], M. Camici[1], C. Mussini[8], A. D' Arminio Monforte[9], A. Antinori[1] on behalf of the Icona Foundation Study Cohort

[1]HIV/AIDS Department, National Institute for Infectious Diseases "Lazzaro Spallanzani" IRCCS, Rome, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [3]Infectious Diseases Unit, Catholic University of Sacred Heart, Rome, Italy, [4]Infectious Diseases Unit A, Amedeo di Savoia Hospital, Torino, Italy, [5]Infectious Diseases Unit, ASST FBF-Sacco, DIBIC "L. Sacco", University of Milan, Milan, Italy, [6]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Roma, Italy, [7]Department of Pathophysiology and Transplantation, School of Medicine and Surgery, University of Milan, Milan, Italy; Infectious Diseases Unit, Departement of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [8]Infectious Diseases Clinic, AOU Policlinico of ModenaUniversity of Modena and Reggio Emilia, Modena, Italy, [9]Clinic of Infectious and Tropical Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy

Background: Despite the universal access to care, advanced HIV presentation (HIV diagnosis in patients [pts] with CD4<200 cell/mL or with an AIDS-defining event), is still an issue. The aim of this study was to evaluate characteristics of ART regimens, treatment outcomes and survival probability in advanced HIV presenters compared to the rest of ART-naive pts in a large Italian cohort.

Material and Methods: All consecutive ART-naive HIV+ pts, enrolled in Icona Foundation Study Cohort from January 2009 to December 2018, with HIV diagnosis within 3 months from enrolment, were included and divided into 3 groups: 1) pts with an AIDS diagnosis at or within 3 months from HIV diagnosis (AIDS presenters); 2) asymptomatic pts with CD4 count≤200 cell/mL at the enrolment (asympt CD4≤200); 3) asymptomatic pts with CD4 count>200 cell/mL at the enrolment (asympt CD4>200). Characteristics of ART regimens started were compared in the three groups by non-parametric tests. Probability of virological failure (VF) (2 consecutive HIV-RNA >200 cp/ml after 6 months of ART), treatment discontinuation (TD) for toxicity of any drug, as well as of survival, was estimated by Kaplan Meier curves in both the overall period and separately, analyzing two consecutive time periods (2009-2013; 2014-2018). Independent risks for the same outcomes were identified by fitting a Cox regression model.

Results: Overall, 7,001 pts were included: 959 AIDS presenters, 1,565 asympt CD4≤200 and 4,477 asympt CD4>200. ART was started in 6,440 (92%) pts of whom 95%, 97%, 90% in group 1, 2 and 3, respectively. Pts with advanced HIV presentation were more likely to start PI/b and less likely to initiate NNRTI as third drug. On the contrary, INSTI-based regimens were similarly distributed among the groups [Table 1]. By multivariable Cox regression, AIDS presenters were associated with a greater risk of virological failure and of discontinuing ART for toxicity compared to asympt CD4>200 pts [Table 2]. At survival analysis, AIDS presenters showed the lowest probability of overall survival among the three treatment groups [Fig.1a] and 4-year survival estimates for the three groups remained substantially stable over the two different consecutive time periods [Fig.1b, 1c]. After adjusting for the main confounders, both the groups with advanced HIV presentation were associated to a higher risk of death compared to asympt CD4>200. This data was confirmed also restricting the analysis to subgroup of pts starting ART [Table 2].

Conclusions: Among ART-naive individuals, AIDS presenters showed an increased risk of virological failure and more frequently discontinued ART due to toxicity. Patients presenting with advanced HIV disease, mainly AIDS presenters, remained at consistently higher risk of death, over the last 10 years. Public health strategies for emerging unknown infections and early treatment access are urgent to constrain the persistent mortality gap of this advanced vulnerable population.

From naive to highly treated subjects. Efficacy of cART

OC 62 VIROLOGICAL OUTCOMES OF FIRST LINE REGIMENS IN WOMEN LIVING WITH HIV FROM ICONA COHORT: COMPARISON WITH CLINICAL TRIALS DATA

C. Mussini[1], P. Lorenzini[2], A. Cingolani[3], M. Lichtner[4], S. Di Giambenedetto[3], A.M. Cattelan[5], E. Balletto[6], L. Sighinolfi[7], C. Abeli[8], M. Malena[9], G. d'Ettorre[4], A. d'Arminio Monforte[10]

[1]University of Modena and Reggio Emilia, [2]INMI L. Spallanzani, Rome, [3]S. Cuore Catholic University, Rome, [4] La Sapienza University, Rome, [5]Padova Hospital, [6]Clinic of Infectious diseases, University of Genoa, [7]Sant'Anna Hospital, Ferrara, [8]Busto Arsizio Hospital, [9]US Malattie Infettive, Azienda Scaligera, Verona, [10]University of Milan

Background: Women living with HIV (WLWH) are under-represented in RCT, and few studies are specifically designed. The aim of this analysis was to verify in a real-life setting the efficacy of newer cART regimens in WLWH and to compare the virological efficacy of regimens for whom WLWH-specific RCT are available (Waves and ARIA).

Methods: All cART naïve WLWH enrolled in Icona from January 2006 starting a ATV/r-, DTG-, EVG/c-, DRV/r or DRV/c -, RAL-, RPV-based regimens regardless of backbone and having at least 1 HIV RNA after 24 weeks from cART initiation were included in the analysis. Primary endpoint was occurrence of treatment failure (TF) (first of two consecutive plasma HIV RNA>200 c/mL after 24 weeks or discontinuation for any reason apart from simplification). Secondary endpoints were: 1) rate of treatment discontinuation or change of cART for any reason; 2) rate of treatment discontinuation or change of cART for toxicity; 3) occurrence of VF (HIV RNA >50 copies/mL at week 48 [Modified FDA Snapshot Algorithm]) for regimens mimicking available WLWH-RCT (EVG/c, DTG, ATV/r).

Incidence rate of single endpoint was calculated dividing the total number of events over the person years at risk. Cox regression analysis was used to estimate the hazard risk (HR) of the outcome according to different cART regimens, after adjusting for AIDS diagnosis, nationality, CD4 cell count, plasma HIV-RNA, HCV-Ab and NRTI backbone.

Results: 1084 WLWH were included (median FU: 1.9 yrs [IQR 0.9-3.2]). 258 WLWH (26%) started ATV/r, 166 (16%) DTG, 115 (11%) EVG/c, 219 (21%) DRV/r or DRV/c, 71 (7%) RAL, 219 (21%) RPV. Study population's characteristics according to third drug are reported in table 1. At multivariable regression, women on ATV/r showed higher risk of TF, after adjusting for main confounders; the only other factor independently associated to a higher risk of TF was AIDS (HR 1.55, 95%CI 1.12-2.16, p=0.009). Hazard risk of different outcomes for each third drug of the regimen are reported in figure 1. On the subgroup of 404 WLWH starting regimens mimicking available WLWH-RCT, the proportions of HIV RNA<50 using FDA snapshot were 50.7% in ATV/r (vs 81% in Waves and 71% in ARIA), 79.2% in EVG/c (vs 87% in Waves) and 74.7% in DTG (vs 82% in ARIA).

Conclusions: In a real world cohort of WLWH starting newer cART regimens, treatment failure is still an issue, particularly in women using PI/r based regimens. Results from clinical practice are not in agreement with those seen in randomized trials. These data suggest the need for focused intervention on adherence and vulnerability support in cART treated HIV infected women.

Supported by ViiV HealthCare

From naive to highly treated subjects. Efficacy of cART

OC 63 DETERMINANTS OF SWITCHING TO TAF-BASED CART OR DUAL COMBINATIONS (DT) FROM TDF-BASED REGIMENS IN A COHORT OF HIV-INFECTED INDIVIDUALS WITH CONTROLLED VIRAL LOAD≤50 COPIES/ML

A. Vergori[1], R. Gagliardini[1], N. Gianotti[2], A. Gori[3], M. Lichtner[4], A. Saracino[5], A. De Vito[6], A. Cascio[7], A. Di Biagio[8], A. d'Arminio Monforte[9], A. Antinori[1], A. Cozzi-Lepri[10]

[1]HIV/AIDS Unit, National Institute for Infectious Diseases, L. Spallanzani, IRCCS, Rome, Italy, [2]Infectious Diseases Department, San Raffaele Scientific Institute, IRCCS, Milan, Italy, [3]Department of Internal Medicine, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy; University of Milan, Milan, Italy, [4]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Polo Pontino, Latina, Italy, [5]Clinic of Infectious Diseases, University of Bari, Bari, Italy, [6]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Sassari, Sassari, Italy, [7]Department of Infectious Diseases, AOU Policlinico "P.Giaccone", University of Palermo, Palermo, Italy, [8]Infectious Diseases Clinic, Policlinico Hospital San Martino, Genova, Italy, [9]Clinic of Infectious and Tropical Diseases , ASST Santi Paolo e Carlo, University of Milan, Milan, Italy, [10]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK

Background: Switching to a TAF-based or to TDF-sparing (dual therapy, DT) regimens is safer than continuing to take TDF-containing regimens, particularly for bone/kidney health. The impact of new guidelines on ARV prescriptions and the determinants of switching to TAF-based vs. DT regimens have not been thoroughly investigated.

Material and methods: The analysis includes data from HIV-positive patients enrolled in the Icona Foundation Study cohort, with a stable VL≤50 copies/mL while on a TDF-based triple cART after January 1st 2016 (baseline). We investigated the probability of switching from TDF to DT or TAF-based combination antiretroviral therapy (cART). Comorbidities (diabetes, hypertension, dyslipidemia) were defined as: i) glucose >126 mg/dl; ii) reported information and/or use of blood pressure lowering drugs; iii) fasting total cholesterol >200 mg/dl, LDL >100 mg/dl, HDL <40 mg/dl for females or <50 mg/dl for males, triglycerides >150 mg/dl. Standard survival analysis of time to switch by means of Kaplan-Meier (KM) curves were used. Separate models were used for the endpoints of switching to DT or TAF-based cART. Cox regression models were used to identify independent predictors of time to switch towards each of the two strategies. A sensitivity analysis was also performed after exclusion of EVG/c. A competing risk KM analysis was also conducted to jointly model the two type of switches.

Results: A total of 1,420 participants were included, 21% female, with a median (IQR) age of 36 (30-42) years, CD4 count 522 (314-750) cells/mm3 (14% with < 200 cells/ mm3), CKD-EPI eGFR 99.1 (85.8-111.1) mL/min/1.73 m2, total cholesterol 166 (142-192) mg/dL, 86% acquired HIV through unprotected sex,33% of patients were of foreign origin, 6.5% had hepatitis B or C coinfection,12% had been diagnosed with AIDS before baseline. At baseline, the most commonly used anchor drugs besides FTC were RPV (27%), EVG (26%), DTG (20%) and DRV/r (13%). In the joint competing risk approach to analysis, by 2 years from baseline, the probability of switch to DT was 3.5% (95% CI 2.3-4.6) and 21% (95% CI 18.8-23.7) to TAF-based cART (Figure 1). A significant higher probability of switch to TAF-based regimen was found for those receiving INSTI at baseline (KM estimates: 50.2%; 95%CI 46%, 55% by 2 years, log-rank p<.0001), not confirmed after excluding people using EVG, in which a higher probability of switch was found for NNRTI (p<.0001).

For the DT endpoint, a higher probability of switch to PI/b (9.6%;95%CI 5%, 14%, p<0.001) was found.

Table 1 shows factors independently associated with the probability of switching stratified by switch type.

Conclusions: The use of PI/b regimen at baseline was associated with a higher risk of switching, regardless of the strategy. A baseline eGFR<60 predicted to switch to 2DC but not to TAF-based regimens. Switches towards TAF-based regimens appeared to be more frequent in more recent years, and significantly correlates also to currently receiving a INSTI regimen.

From naive to highly treated subjects. Efficacy of cART

OC 64 RESIDUAL VIREMIA IN HIV-INFECTED PATIENTS WHO CONTINUE A 2-DRUG REGIMEN WITH DOLUTEGRAVIR PLUS ONE REVERSE TRANSCRIPTASE INHIBITOR OR SWITCH TO ELVITEGRAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR ALAFENAMIDE: A RANDOMIZED STUDY (BE-ONE STUDY)

N. Gianotti[1], L. Galli[1], A. Poli[1], L. Della Torre[1], C. Vinci[1], E. Carini[1], A. Galli[1], S. Nozza[1], V. Spagnuolo[1,2], C. Muccini[1,2], A. Lazzarin[1], A. Castagna[1,2]

[1]IRCCS Ospedale San Raffaele, Milano, [2]Università Vita-Salute San Raffaele, Milano

Background: Aim of the study was to investigate residual viremia (RV) through 48 weeks in virologically suppressed, HIV-infected patients randomized to continue a 2-drug regimen (2DR) with dolutegravir (DTG) plus one reverse transcriptase inhibitor (RTI) or to switch to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF).

Methods: Randomized, single-center, open-label, 96-week superiority study (NCT03493568). Patients with HIVRNA <50 copies/mL for ≥6 months while receiving DTG plus one RTI for at least 3 months, were randomized 1:1 to continue the ongoing treatment or to switch to E/C/F/TAF. Documented resistance to NRTIs or InSTIs was an exclusion criterion.

Viral load was assessed by standard Abbott Real time PCR and RV was defined as any detectable HIV-RNA value below 50 copies/mL. Virologic failure (VF) was defined as a confirmed rebound in plasma HIV-RNA levels ≥50 copies/mL.

The primary endpoint was the proportion of subjects with no RV through 48 weeks of follow-up; the primary analysis was performed on the intent-to-treat (ITT) population including all randomized patients who received at least one dose of study treatment. Discontinuation for any reason other than virological rebound was not counted as failure, i.e. not considered to be suggestive of RV.

A sample size of 50 patients per arm was selected allowed to detect, with 80% power at an α of 0.05, a 25% increase in the primary endpoint in the E/C/F/TAF arm. However, a futility analysis performed at week 24 on 51 patients led to the termination of enrollment of further patients.

Results: Fifty-one patients were randomized; one patient withdrew consent at baseline (BL; figure 1). The BL characteristics of the 50 patients with follow-up data are detailed in Table 1. Forty-five (90%) were receiving lamivudine and 5 (10%) rilpivirine with DTG.

Six patients (3 in each arm) withdrew before or at week 48 (E/C/F/TAF arm: 1 due to weight gain, 1 due to diarrhea, 1 for VF; 2DR arm: 1 due to CNS toxicity, 1 withdrew consent, 1 for VF).

The proportion of subjects with no RV through 48 weeks of follow-up was 48% in the E/C/F/TAF arm and 76% in the 2DR arm (figure 2); difference (E/C/F/TAF – DTG) -28.0% (95% confidence interval: -57.8% to 1.8%; p=0.079).

VF occurred in 2 patients: 1 in the E/C/F/TAF arm (at week 24; genotypic resistance testing [GRT]: WT HIV for InSTIs, not available for NRTIs and protease inhibitors [HIV-RNA <200 copies/mL]; HIV-RNA returned <50 copies/mL without changing treatment), 1 in the 2DR arm (at week 4; GRT was not available due to very low level viremia [<100 copies/mL]; HIV-RNA returned <50 copies/mL without changing treatment).

Trends in immunological, inflammatory and immune activation markers are shown in Table 2.

Conclusions: Switch to E/C/F/TAF was not superior in suppressing RV compared to continuing a 2DR with DTG +1 RTI. The favorable trend in some inflammatory markers observed in the E/C/F/TAF arm deserves further study.

From naive to highly treated subjects. Efficacy of cART

OC 65 VIRAL POTENCY AND DURABILITY OF EMTRICITABINE/TENOFOVIR ALAFENAMIDE (F/TAF) BASED REGIMENS IN THE REAL LIFE SETTING

A. Antinori[1], A. Cozzi-Lepri[2], D. Moschese[3], S. Nozza[4], L. Comi[5], M. Santoro[6], L. Sarmati[7], C. Pinnetti[1], F. Ceccherini Silberstein[6], G. Marchetti[8], F. Maggiolo[5], A. d'Arminio Monforte[8] for the Icona Foundation Study Group

[1]Clinical Division of HIV/AIDS, INMI "L. Spallanzani" IRCCS, Rome, Italy, [2]Institute for Global Health, University College of London, London, UK, [3]Institute of Clinical Infectious Diseases, Catholic University of Sacred Heart, Policlinico Gemelli, Rome, Italy, [4]Division of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [5]Division of Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy, [6]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [7]Clinical Infectious Diseases, Fondazione Policlinico Tor Vergata, University of Rome Tor Vergata, Rome, Italy, [8]ASST Santi Paolo e Carlo, University of Milan, Clinic of Infectious and Tropical Diseases, Dept of Health Sciences, Milan, Italy

Background: F/TAF has been recently introduced in the antiretroviral setting based on randomized trials showing a comparable efficacy to that of F/tenofovir disoproxil fumarate (TDF) with greater kidney and bone safety. Nevertheless, information regarding TAF-based regimens in the real world setting is still lacking.

Material and methods: We included ART-naïve patients enrolled in the ICONA cohort who started TAF-based regimens as first line as well as those enrolled in a parallel cohort constructed ad hoc to include patients who were switched to a TAF-based regimen with a HIV RNA ≤50 copies/mL. All consecutive patients who started or were switched to an F/TAF-including regimen over 2015 to 2017 were included. Time to discontinuation for any cause, for toxicity or for treatment failure (TF) (confirmed HIV RNA >50 copies/mL after six months or discontinuation for any cause) were estimated by Kaplan-Meier curves. Cox regression models were used to identify independent predictors of the same outcomes, separately in the two groups.

Results: 2,137 patients were included; 381 ART-naïve starting an F/TAF regimen and 1,756 ART-experienced (ART-exp) who switched to an F/TAF regimen with stable viral suppression. Table 1 shows baseline characteristics of the enrolled population. The more frequently used combined regimens were E/C/F/TAF (41% naïve; 38% switched), DTG+F/TAF (30%; 7%), R/F/TAF (10%; 33%), D/C/F/TAF (10%; 7%). Among the ART-exp group, 1,288 had never previously failed ART while 468 had experienced virological failure to ≥1 regimen. Median duration of viral suppression at switching was 41 months (IQR 23, 72). In the ART-naïve group, the 1-year risk of discontinuing F/TAF was 8.1% (95% CI 5.1%-11.0%) for any causes and 2.5% (0.8%-4.3%) for toxicity, while the 1-year probability of TF was 10.4% (6.8%-13.9%). In the ART-exp group, the 1-year risks were estimated at 5.0% (95% CI 2.2%-7.7%), 0.6% (0.2%-1.0%) and 5.4% (3.5%-7.3%) for discontinuation for any cause, for toxicity and TF, respectively. In the ART-naïve group, by multivariable Cox regression, HCV coinfection was associated with an increased risk of discontinuation, and higher baseline VL with an increased risk of TF. In the ART-exp group, a more recent calendar year and a history of ART interruption due to toxicity were independently associated with a lower risk of TF, whereas a history of previous virologic failure was associated with higher risk (Table 2).

Conclusions: In our cohort, F/TAF-based regimens initiated for the first time demonstrated high efficacy and a low rate of discontinuation, both in the ART-naïve and in the ART-experienced population. Reduced risk of discontinuation or failure in more recent calendars year may coincide with a switch over time to F/TAF in combination with increasingly safer and more effective drugs. In the ART-experienced population, history of virologic failure and reasons for stopping previous regimens should be considered to identify people at higher risk of failing therapy.

This study is supported by a grant from Gilead International

From naive to highly treated subjects. Efficacy of cART

OC 66 BURDEN OF DISEASE IN PLWH HARBOURING A 4-CLASS DRUG RESISTANT VIRUS: DATA FROM PRESTIGIO REGISTRY

M.R. Parisi[1], A. Poli[1], M. Menozzi[3], M. Fiscon[4], E. Garlassi[5], D. Francisci[6], A. Di Biagio[7], G. Sterrantino[8], C. Fornabaio[9], A. Degli Antoni[10], G. Angarano[11], F.M. Fusco[12], A. D'Arminio Monforte[13], G.M. Corbelli[14], M.M. Santoro[15], M. Zazzi[16], A. Castagna[1,2] on behalf of the PRESTIGIO Study Group

[1]Clinic of Infectious Diseases, Istituto Scientifico San Raffaele, Milano, [2]Clinic of Infectious Diseases, Vita-Salute San Raffaele University, Milano, [3]Malattie Infettive, Policlinico di Modena, Modena, [4]UOS Malattie Infettive dell'Azienda Scaligera di Verona, Verona, [5]Malattie Infettive Arcispedale S.Maria Nuova-IRCSS, Reggio Emilia, [6]Clinica Malattie Infettive, Santa Maria della Misericordia, Perugia, [7]Clinica Malattie Infettive, Ospedale Policlinico San Martino, Genova, [8]Dipartimento di Medicina clinica e Sperimentale, Università degli studi di Firenze, Firenze, [9]ASST Cremona, Cremona, [10]Malattie Infettive ed Epatologia, Azienda Ospedaliero-Universitaria di Parma, Parma, [11]Università degli Studi di Bari "Aldo Moro", Malattie Infettive, Policlinico, Bari, [12]Ospedale Santa Maria Annunziata, Bagno a Ripoli, Firenze, [13]Clinic of Infectious Diseases, Dept of Health Sciences, ASST Santi Paolo e Carlo, Milano, [14]Plus Onlus, Bologna, [15]Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, [16]University of Siena, Siena, Italy

Background: Up to date, there are no data on survival and burden of disease in people living with HIV-1(PLWH, harbouring a 4-class drug resistant virus (NRTI, NNRTI, PI, INSTI). The aim of the study was to evaluate the survival and the incidence of AIDS and non-AIDS-related events in this fragile population.

Material and methods: Cohort study on PLWH, recorded in the PRESTIGIO Registry, with a documented 4-class drug resistant virus (i.e.: NRTI, NNRTI, PI, INSTI; if INSTI genotypic resistance test was not available, a documented viral failure to an INSTI-regimen was accepted as an inclusion criteria). The primary outcome was to evaluate the incidence rates of death, AIDS and non-AIDS-related clinical events occurred after MDR documentation(baseline, BL). The analysis was based on the data collected from BL until January, 2019. Disease progression was defined as the occurrence of at least one AIDS-related event (in PLWH without previous AIDS diagnosis) or death for any cause. Non-AIDS related events included: non-AIDS related malignancies, major adverse cardiovascular events(myocardial infarction, stroke), cirrhosis, chronic kidney disease, diabetes. Incidence rates (IR) were expressed per number of person-months of follow-up(PMFU) since BL and estimated by univariate Poisson regression. Time to disease progression, or the first incident AIDS or non-AIDS-related clinical event were estimated by Kaplan-Meier curves and compared by the log-rank test. In this analysis, for PLWH with multiple events, the first event was considered.

Results: Overall, 143 PLWH evaluated: median age was 49 years(IQR=43-53), 77% males. Patients'(pts) characteristics are reported in Table1.

During a median follow-up of 44 months (IQR=32-83), 15 PLWH had disease progression for an overall IR of 0.20/100PMFU (95%CI=0.11-0.31).

Twelve PLWH died [IR=0.16/100PMFU (95%CI=0.08-0.26)]: in 6(50%) pts death occurred after developing ≥1 AIDS-related event, in 2(17%) pts after ≥1 non-AIDS-related event, in 1(8%) patient after both AIDS- and non-AIDS-related events, in 3(25%) due to other causes (1 suicide, 1 bacterial pneumonia, 1 unknown).

Fifteen PLWH developed 17 incident AIDS-related events [IR=0.22/100PMFU (95%CI=0.13-0.34)]; the most frequent events were: tuberculosis(24%), esophageal candidiasis(12%) and NHL lymphoma(12%).

Eighteen PLWH developed 24 non-AIDS-related events [IR=0.31/100PMFU (95%CI=0.19-0.44)] were observed; the most frequent events were: chronic kidney disease(21%), myocardial infarction(13%), liver cancer(13%), anal cancer(13%). Fourteen pts had 1 single event, 2 pts had 2 events and 2 pts had 3 events.

No difference between the IR of AIDS and non-AIDS-related event(p=0.280).

Time to disease progression, first AIDS/non-AIDS-related event are shown in Figure1.

Conclusions: Among PLWH harbouring a 4-class drug resistant virus, the risk of mortality is still an issue, even in recent years, as well as the burden of disease due to both AIDS and non-AIDS related events.

From naive to highly treated subjects. Efficacy of cART

OC 67 VARIABLES RELATED TO BECOMING HEAVILY TREATED EXPERIENCED (HTE) PATIENTS IN A LARGE ITALIAN COHORT

S. Lo Caputo[1], A. Antinori[2], A. Tavelli[3], F. Ceccherini-Silberstein[4], C.F. Perno[5], A. Castagna[6], N. Bobbio[7], G. Parruti[8], R. Gagliardini[2], S. Bonora[9], A. d'Arminio Monforte[10], A. Cozzi Lepri[11] for the ICONA Foundation Study Group

[1]Clinic of Infectious Diseases, A.O.U.Policlinico, University of Bari, Bari, Italy, [2]National Institute for Infectious Diseases 'L. Spallanzani' IRCCS, Rome, Italy, [3]Icona Foundation Milan, Italy, [4]Department of Experimental Medicine and Surgery, University of Rome Tor Vergata, Rome, Italy, [5]Dept of Oncology and Oncohematology, University of Milan, Milan, Italy, [6]Department of Infectious Diseases, San Raffaele Scientific Institute, University Vita-Salute San Raffaele, Milan, Italy, [7]Department of Infectious Diseases, Galliera Hospital, Genoa, Italy, [8]Infectious Disease Unit "Santo Spirito Civil Hospital", Pescara, Italy, [2]National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy; [9]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy, [10]Clinic of Infectious and Tropical Diseases, Department of Health Sciences, University of Milan, ASST Santi Paolo e Carlo, Milan, Italy, [11]Institute for Global Health, University College London, London, UK

Background: We aim to analyse of the prevalence over time, immunological virological and clinical outcome of heavily treated experienced (HTE) patients in the Icona cohort.

Methods: We included all participants of Icona for with ≥1 clinical visit in 2008-2018. Four definitions of HTE were used. The date of HTE was defined at time in which one of the following events occured first: D1=to have used ≥4 anchor drugs (including the current one), having experienced virological failures (VF) to ≥2 drugs belonging to ≥3 classes; D2= to have used ≥3 anchor drugs of different classes (including the current one); D3=currently using either dolutegravir (DTG) bid or boosted Darunavir (b-DRV) bid or maraviroc (MVC) not as first line regimens; D4= to have previously experienced >5 therapy switches. A participant was defined as HTE if satisfied ≥1 definition. Patients' characteristics in Jan 2018 (index date) were compared in the HTE and non-HTE subjects by chi2 and Wilcoxon rank test. The prevalence of HTE over 2008-2018 was calculated by each separate definition and using the composite definition. The Kaplan-Meier method was used to estimate the incidence (with 95% CI) of VF>200 copies/mL and of a composite clinical endpoint including AIDS, non-AIDS defining conditions (NADC-START trial definition) and death. A multivariable Cox regression model was used to identify factors associated with faster progression to AIDS/NADC/death among the HTE population.

Results: A total of 1,243 out of 12,301 patients (10.1%) were defined as HTE in 2008-2018. This proportion is composed by the prevalence cumulated by 2008 (including all cases observed in 1997-2008) and by HTE incidence over the following years. The overall proportions were 0.2% for D1, 0.1% for D2, 0.7% for D3 and 6.5% for D4. Figure 1 shows the overlap of the different definitions for the aggregate 2008-2018 proportion. Compared to non-HTE, HTE pts were older (p=<.001), more frequently females (p=<.001), less frequently MSM (p=<.001), less frequently Italian (p=<.001), with lower CD4 nadir (p=<.001) and higher HIV RNA (p=<.001). A total of 28 HTE pts developed AIDS, 68 NADC and 6 died. The probability of various endpoints by 3, 5 and 8 years from HTE are shown in Table 1. Age was the only factor independently associated with the risk of faster progression to AIDS/NADC/death (Table 2).

Conclusions: Using a composite definition including a wide range of criteria signalling high previous treatment exposure, around 10% of HIV-positive subjects seen for care in Italy currently show potentials for having limited drug options even recently. HTE cumulated prevalence was high at 10% in 2008 but remained stable below 2% over the following years up to 2018. 13% of HTE people progressed to severe clinical outcomes by 8 years from entering the HTE group. It has still to be estimated how many of these patients are likely to necessitate new therapeutic options to further reduce their risk of morbidity and mortality.

Changing HIV epidemiology

OC 68 CHANGE OF PREVALENCE AND FACTORS ASSOCIATED WITH THE RISK OF AIDS PRESENTATION IN ITALY OVER LAST DECADE (2009-2018)

A. Antinori[1], A. Mondi[1], P. Lorenzini[1], A. Cozzi-Lepri[2], A. Cingolani[3], A. Latini[4], A. Saracino[5], A. Bandera[6], G. Marchetti[7], C. Mussini[8], E. Girardi[9], A. D'Arminio Monforte[7]

[1]HIV/AIDS Department, National Institute for Infectious Diseases "Lazzaro Spallanzani" IRCCS, Rome, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [3]Infectious Diseases Unit, Catholic University of Sacred Heart, Rome, Italy, [4]STI/HIV Unit, San Gallicano Dermatologic Institute IRCCS, Rome, Italy, [5]Division of Infectious Diseases, University of Bari, Policlinic Hospital, Bari, Italy, [6]Department of Pathophysiology and Transplantation, School of Medicine and Surgery, University of Milan, Milan, Italy; Infectious Diseases Unit, Departement of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [7]Clinic of Infectious and Tropical Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy, [8]Infectious Diseases Clinics, Azienda Ospedaliero-Universitaria Policlinico di Modena, University of Modena and Reggio Emilia, Modena, Italy, [9]Clinical Epidemiology Unit, National Institute for Infectious Diseases "Lazzaro Spallanzani", IRCCS, Rome, Italy

Background: Despite universal recommendations about early ART initiation, a consistent proportion of newly diagnosed HIV people continue to be diagnosed and to enter care late. In Europe, the annual proportion of patients presenting with AIDS between 2010 and 2013, accounted for 8-19% of all new HIV diagnoses, with a slight prevalence decline in the same period. Prevalence and factors associated with the risk of AIDS presentation over the last decade (2009-2018) in people seen for care at the main infectious disease clinical sites in Italy were investigated.

Material and methods: All consecutive individuals in the Icona Foundation Study cohort firstly HIV diagnosed from January 2009 to December 2018 with chronic infection over three months preceding their enrolment were selected and divided in three groups: a) ART-naïve patients with an AIDS defining event (AIDS presenters); b) ART-naïve asymptomatic patients with chronic HIV infection and a CD4 count <=200 cells/mm3 (asympt CD4<=200); c) ART-naïve asymptomatic patients with chronic HIV infection and a CD4 count >200 cells/mm3 (asympt CD4>200). Comparisons of categorical and continuous variables among groups were made using Chi-square and Kruskal Wallis test respectively. Multivariable logistic regression was fitted to identify factors associated with the risk of presentation with AIDS.

Results: A total of 7,001 naïve individuals were analyzed, 959 AIDS presenters (13.7%), 1,565 asympt CD4<200 (22.4%) and 4,477 asympt CD4>200 (64.0%). The main characteristics of the study population are reported in Table 1. AIDS presenters were more frequently older aged (44 yrs), not-Italian (27%), acquiring HIV by heterosexual transmission (55%), with primary education (8.7%), lower CD4 cell count (42 cells/mm3) and higher plasma VL (66% with >100.000 c/mL) (Table 1). Prevalence of AIDS presentation over time was 16.4% in the 2009-2010 period, 14.7% in 2011-2012, 13.4% in 2013-2014, 13.8% in 2015-2016 and 11.8% in 2017-2018 (chi-square for trend=0.003). From fitting a multivariable logistic regression, older age, heterosexual transmission, not-Italian origin, HBV coinfection, baseline HIV-RNA >100.000 copies/mL, lower educational level and occasional job (compared to employed) were all associated with a higher risk of AIDS presentation, whereas smoke habit, and more recent calendar years (2017-2018 vs 2009-2010) were associated with a lower risk (Table 2).

Conclusions: AIDS presentation still occurs in approximately 14% of newly HIV diagnosed individuals in Italy in the last decade, even though a slight reduction trend in the last years was observed. Older age, heterosexual route, non-Italian origin, low educational level and casual employment seems to identify a socio-demographic profile of HIV people who presents for care very late (at time of AIDS diagnosis). These are key informations for planning focused interventions to discover unknown infections.

Changing HIV epidemiology

OC 69 NON B SUBTYPES ARE THE MAJOR DRIVER OF HIV-1 TRANSMISSION DYNAMICS IN NORTH ITALY OVER THE YEARS 2012-2018

L. Colagrossi[1], M.C. Moioli[2], A. Nava[3], S. Carta[3], S. Chiappetta[2], V. Costabile[4], D. Motta[2], L. G. Chianura[2], R. Rossotti[2], D. Fanti[3], C.F. Perno[3,5], M. Puoti[2], C. Alteri[3,5]

[1]Residency in Microbiology and Virology, University of Milan, Milan, Italy, [2]Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [3]Chemical-clinical and Microbiological Analysis, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [4]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [5]Department of Oncology and Hemato-oncology, University of Milan, Milan, Italy

Background: To evaluate the dynamics and phylogenetic relationships of HIV-1 strains circulating in North Italy in the last years.

Material and Methods: HIV-1 pol sequences were obtained from 272 drug-naïve individuals (1 per patient) diagnosed for HIV-1 infection at Niguarda Hospital between 2012 and 2018. Phylogenetic trees were built using GTR model and 1000 bootstrap with maximum-likelihood method using PhyML. Transmission clusters (TCs) were defined by bootstrap >90% and genetic distance ≤0.02; TCs included large TCs (≥3 sequences, LTCs) and pairs (2 sequences). Factors associated with TCs were evaluated by uni-multivariable logistic regression analysis, using as confounders gender, age, subtype, risk factor, nationality, year of diagnosis, viral load and CD4 cell count at diagnosis, and transmitted drug resistance (evaluated by considering WHO-2009 list and bold IAS/Stanford 2018 mutations).

Results: Most patients were men (82.4%) and Italians (65.4%), with a median age of 39 (IQR:30-48) years. Heterosexual intercourses were the main route of transmission (46.7%), followed by men who have sex with men contact (MSM; 36.0%). Patients were infected mostly by B (64.3%), BF recombinant forms (11.0%) or CRF02_AG (8.1%) clades. Non-B subtypes, and particularly recombinant forms, were increasingly represented across years (from 26.9 to 44.1% and from 13.1 to 30.1%, respectively, p=0.011 and 0.006). Compared to patients infected by subtype B, patients harbouring non-B subtypes presented a lower proportion of MSM (17.5 vs 46.3%, p<0.001), of individual born in Italy (52.6 vs 72.6%, p=0.001), lower CD4 cell counts (median [IQR]: 307 [92-501] vs 389 [186-548] cells/mm3, p=0.037), and even if with a trend, higher viral loads, (median [IQR]: 5.1 [IQR: 4.1-5.5] vs 4.7 [4.1-5.5] log10 copies/mL, p=0.437).

Overall, 24.6% of individuals took part in TCs including 39 (58.2%) in small TCs and 28 (41.8%) patients in LTCs. Non-B subtypes were increasingly represented across LTCs (60.7% of non-B subtypes vs. 39.3% of B subtypes were involved in LTCs, p=0.004). LTC-individuals were more frequently MSM (p=0.003), and infected by CFR02_AG and CRF42_BF (p=0.016 and 0.010, respectively), than other patients. None of the identified LTCs carried transmitted drug resistance. By multivariate logistic regression, the HIV-1 infection by non-B subtype was the only factor significantly associated with higher probability to be in LTCs (odds ratio: 3.29 [1.37-7.93]). No other factors, including risk factors, were significantly associated with LTCs.

Conclusions: HIV-1 non-B diagnoses increased in North Italy over the years 2012-2018 and actively spreading among large TCs, participating to the epidemiological shift from B to non-B subtypes in North Italy. Overall our results highlight the epidemiological changes in HIV-1 infection occurred in Italy over the last years, thus suggesting the need for surveillance and intervention programs to identify and fight these local outbreaks.

Changing HIV epidemiology

OC 70 MULTICENTER PHYLOGENETIC ANALYSIS OF ACUTELY INFECTED INDIVIDUALS SHOWS THAT NON-B SUBTYPES ARE ASSOCIATED TO TRANSMISSION CLUSTERS IN ITALY

L. Fabeni[1], G. Bozzi[2], I. Abbate[3], G. Berno[3], A. Muscatello[2], L. Taramasso[2], M. Fabbiani[4], S. Nozza[5], G. Tambussi[5], S. Rusconi[6], E. Focà[7], C. Pinnetti[3], G. D'Ettorre[8], C. Mussini[9], V. Borghi[9], B.M. Celesia[10], G. Madeddu[11], A. Antinori[3], A. Gori[2], M.R. Capobianchi[3], A. Bandera[2] for the INACTION study group

[1]University of Rome "Tor Vergata", Rome, Italy, [2]IRCCS Ca Granda Ospedale Maggiore Policlinico - University of Milan, Milan, Italy, [3]National Institute for Infectious Diseases L. Spallanzani-IRCCS, Rome, Italy, [4]Infectious Diseases Unit, IRCCS San Matteo Hospital Foundation, University of Pavia, [5]Clinic of Infectious Diseases, San Raffaele Hospital, University Vita Salute, Milan, Italy, [6]Infectious Diseases Unit, Department of Biomedical and Clinical Sciences "Luigi Sacco" Hospital, University of Milan, Italy, [7]Division of Infectious and Tropical Diseases, University of Brescia, ASST Spedali Civili Hospital, Brescia, [8]Infectious Diseases Unit, Umberto I Hospital, La Sapienza University, Rome, Italy, [9]Clinic of Infectious Diseases, University of Modena and Reggio Emilia, Modena Hospital, Italy, [10]Unit of Infectious Diseases, Garibaldi Hospital, Catania, Italy,[11]Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Sassari

Background: Through a nation-wide, multicenter cohort study we aimed at characterizing factors associated with HIV-1 transmission in acutely infected individuals in Italy, using phylogenetic analysis in conjunction with clinical-epidemiological data to identify transmission clusters (TCs).

Materials and Methods: Phylogenetic analyses were performed on pol sequences from 165 HIV-1 acutely infected individuals diagnosed between 2008 and 2015 in 9 Centers within 7 Italian cities. Of these, 3 were Fiebig stage I, 17 were II, 22 were III, 47 were IV; 42 were V. For the remaining infections, Fiebig stage was unknown, but diagnosis was made on the basis of clinical data and/or a documented negative HIV-1 EIA test within the previous 6 months. Subtypes were identified by Neighbor Joining. TCs were identified by Maximum Likelihood tree (Mega 6, Generalised Time-Reversible (GTR) model, 1000 bootstrap support, genetic distance ≤ 0.2), and confirmed by Bayesian tree (Mr Bayes, Monte Carlo Markov Chain search run for 5x106 generations, posterior probability=1). Multivariable logistic regression was used to define factors associated with TCs, adjusted for year of diagnosis, gender, age, subtype, risk factor, viral load at diagnosis, CD4 cell count at diagnosis.

Results: Overall, the most prevalent variant was B (68.5%), followed by CRF02_AG (10.3%), CRF71_BF (7.9%), C (3.6%), CRF18_cpx (1.2%), and other variants (8.5%). Individuals were mainly male (86.7%), with a median (IQR) age of 44 (35-53) years; most of them were MSM (63.6%) and heterosexual (HE, 30.9%). Transmitted drug-resistance (TDR) to any drug class was 8.5%, mainly imputable to NNRTI resistance (5.5%). 15 TCs were identified (including 2-4 individuals), and involved 36 individuals (21.8%). Gender, age, year of diagnosis and risk factor did not show a significantly asymmetrical distribution in and out of TCs. The median (IQR) CD4 cell count (cell/mm3) and viremia (log10 cps/mL) at diagnosis [CD4: 431 (294-564) vs 476 (343 -632), p=0.21; viremia: 5.6 (4.6-6.1) vs. 5.8 (5.1-6.5), p=0.20] were similar without any significant difference between individuals in and those out of TCs. TCs were characterized by individuals infected with CRF02_AG (22.2% vs. 7.0% in vs out of clusters, p=0.01), CRF71_BF (19.4% vs 4.7%, p=0.01), and CRF18_cpx (5.6% vs. 0.0%, p=0.05). Multivariable logistic regression showed that harbouring a non-B subtype was a factor positively associated with TCs [AOR (95% CI): 2.4 (1.0–5.9); p=0.05].

Conclusions: Acutely infected individuals are a key population to characterize the current HIV-1 epidemic in Italy. Applying molecular epidemiology to a multicenter cohort, we showed that acutely infected individuals carrying non-B subtypes were overly represented in transmission networks across Italy, corroborating previous reports of increasing proportions in the general HIV population. This result should inform new intervention strategies to target the epidemic.

Changing HIV epidemiology

OC 71 HIGHER RATE OF VIROLOGIC FAILURE IN AFRICAN MIGRANTS COMPARED WITH NEWLY HIV-DIAGNOSED NATIVES AND FOREIGNERS FROM OTHER REGIONS

F. Lagi[1], S. Tekle Kiros[1], S. Di Giambenedetto[2], F. Lombardi[2], M. Pecorari[3], V. Borghi[4], L. Lepore[5], L. Monno[5], M. Setti[6], V. Micheli[7], P. Bagnarelli[8], E. Paolini[9], P. Cicconi[10], A. Bartoloni[1,11], G. Sterrantino[1]

[1]Department of Experimental and Clinical Medicine, University of Florence, Florence Italy, [2]Institute of Clinical Infectious Diseases, Catholic University of Sacred Heart, Policlinico Gemelli, Rome, Italy, [3]Microbiology and Virology Unit, Azienda Ospedaliero Universitaria di Modena, Modena, Italy, [4]Department of Infectious Diseases, Università di Modena, Modena, Italy, [5]Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari, Italy, [6]Clinic of Immunology and Internal Medicine, Ospedale Policlinico San Martino,Genoa,Italy, [7]Microbiology and Virology Laboratory, L. Sacco Hospital, Milano, Italy, [8]Virology Unit, Azienda Ospedaliera Universitaria Ospedali Riuniti di Ancona, Ancona, Italy, [9]Immuno-Ematology and Transfusion Medicine Service, Cremona Hospital, Cremona, Italy, [10]Infectious Diseases, San Paolo H. Milan, Italy, [11]Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, Italy

Introductions: The proportion of foreign individuals treated with combined antiretroviral therapy (cART) and virologically failed is precisely unknown, even though clinical trial data show that the prevalence of undetectable HIV RNA on treatment can reach 80-90%.
The study aims to compare the virologic failure rate and the associated factors in ART-naive foreigners versus naïve natives after the achievement of virologic suppression.
Methods: This is a retrospective observational cohort. All ART-naïve patients in the ARCA database since 2007 who achieved virologic suppression within 18 months of starting cART, with at least one baseline genotypic test and availability of nationality were enrolled. Personal data, ART regimens at the beginning and the end follow-up, viremia and CD4 data before cART, at the time of failure and the end of the follow-up, were included in the analysis. Categorical variables were analyzed with X2/Fisher's exact test, and continuous variables with Wilcoxon signed rank test. Kaplan-Meier method was used to assess the probability of virologic suppression and virologic failure. Mantel-Haenszel method to produce adjusted RR for each potential confounder in turn. Cox regression model was used for regression analysis.
Results: Of 2515 patients 466 (18.5 %) were foreigners, 208 (8.3%) from Africa, 118 from Latin America (4.7%), 111 (4.4%) from Europe (not Italy). Females were 605 (24.1%), the median age at entry was 37 years (IQR 30-45), subtype B 1788 (71.1), subtype non-B 235 (9.3), and circulating recombinant forms (CRFs) 492 (19.6%). 222 (8.6%) patients showed transmitted resistance: 82 (3.2%) for NRTI, 127 (5.1%) for NNRTI, 56 (2.2%) for PI. The maximum length of follow-up was 11 years, and 232 events were observed. Overall, the virologic failure rate after suppression was 2.13 x 100py [95% CI 1.87-2.42]. Strata specific rates were 5.69 [4.20-7.70] and 2.09 [1.40-3.12] for Africans and other foreigners, respectively. Time to achieve suppression was not different in the three groups (log-rank: p=0.7118). CD4 recovery between cART initiation and virologic suppression was lower for migrants from Africa (p=0.0172). After adjustment for current age, number of therapeutic lines, cART at the time of failure, nadir, zenith, AIDS events, route of transmission, HCV status, genotype and transmitted resistance mutations, the rate of virologic failure was 3.5 times higher in Africans compared to Italians [HR 3.6 95%CI 2.17-5.90]. No difference in failure rates was observed in other foreigners compared to Italians [HR 1.20 95% CI 0.76-1.8].
Conclusion: In our cohort, African subgroups of migrants showed higher virologic failure rates compared to natives and other foreigners. Despite free access to cART in Italy, African migrants probably face more barriers to access care due to exploitation, stigma, and discrimination.

New challenges of viral hepatitis

OC 72 THE USE OF ACCURATE VIROLOGICAL AND IMMUNOLOGICAL HEPATITIS B MARKERS CAN ALLOW AN EARLY DIAGNOSIS OF HBV REACTIVATION IN HBSAG-NEGATIVE/ANTI-HBC-POSITIVE PATIENTS WITH ONCOHEMATOLOGICAL DISEASES

R. Salpini[1], C. Cerva[2], M. Alkhatib[1], A. Battisti[1], L. Piermatteo[1], A. Sacco[1], V. Malagnino[2], W. Arcese[3], M. Cantonetti[3], F. Ceccherini-Silberstein[1], C. F. Perno[4], M. Andreoni[2], L. Sarmati[2], V. Svicher[1]

[1]Department of Experimental Medicine, Tor Vergata University, Rome, Italy, [2]Clinical Infectious Disease, Department of System Medicine, Tor Vergata University, Rome, Italy, [3]Department of Hematology, Stem Cell Transplant Unit, Tor Vergata University, Rome, Italy, [4]Department of Oncology and Haematooncology, University of Milan

Background: Prevention of HBV-reactivation (HBV-R) in patients undergoing immunosuppressive therapy is still challenging. The aim of this study is to investigate the role of HBV markers in predicting HBV-R in HBsAg-negative/anti-HBc-positive oncohematological patients.

Methods: HBV-R rate is assessed in 107 HBsAg-negative/anti-HBc-positive patients (47 receiving rituximab, 40 HSCT, 27 other chemotherapeutics). All patients received lamivudine-prophylaxis (median [IQR] duration: 29 [22-41] months) and were prospectively monitored every 3 months during and after prophylaxis completion. The role of HBV markers in predicting HBV-R was evaluated in 84 patients: 10 developing and 74 not developing HBV-R. Overall, 454 serum samples were tested for high-sensitive HBsAg, FujiRebio (HS-HBs; lower limit of quantification [LLOQ]: 5 mIU/ml, vs 50 mIU/ml of assays used in routine clinical practice), anti-HBs and HBV-DNA (LLOQ: 20 IU/ml, Roche). HBV-R is defined as serum HBV-DNA > 20 IU/ml along with hypertransaminasemia (Seto WK, 2016).

Results: At baseline, all patients are HBsAg-negative/anti-HBc-positive with undetectable HBV-DNA, 67.3% is anti-HBs positive [median (IQR): 152 (47-976) mIU/ml]. HBV-R occurs in 10/107 patients (5-year cumulative reactivation rate: 25.7%). Among them, 7/10 underwent hematopoietic stem cell transplantation and 3/10 received rituximab.

At HBV-R, median (IQR) HBV-DNA is 36 (20-522) IU/ml and ALT>ULN for 60% [median (IQR): 88 (60-763) U/L]. Among HBV-R cases, 5 develops HBV-R during and 5 after completing prophylaxis (median [IQR] months after prophylaxis completion: 3 [1-16]).

Focusing on the 84 patients, anti-HBs<100mIU/ml at baseline is the only virological marker correlated with a higher risk to develop HBV-R (22% of patients with anti-HBs<100mIU/ml vs 3% with anti-HBs>100mIU/ml experienced HBV-R, P=0.045). The on-monitoring analysis of virological markers shows that the positivity, confirmed in at least two different time-points, to HS-HBs (detection failed by routinely used HBsAg-assays) and/or to HBV-DNA (below LLOQ) is another risk factor for HBV-R (3/7 [42.9%] patients with HBV-R vs 2/74 [2.7%] patients without HBV-R are repeatedly positive to HBV-DNA and/or HS-HBs, P=0.004, OR [95%CI]: 27% [3.5-210.4]).

Conclusions: HBV-R frequently occurs in anti-HBc-positive/HBsAg-negative oncohematological patients with profound immunosuppression, suggesting the need to reconsider the potency and duration of prophylaxis in this setting of patients. A close monitoring based on an integrated use of accurate HBV-markers can help to detect minimal viral replication, allowing early HBV-R diagnosis.

New challenges of viral hepatitis

OC 73 THE INTEGRATION OF HEPATITIS B VIRUS IN RELEVANT REGIONS OF HUMAN GENOME OCCURS FREQUENTLY IN HBEAG NEGATIVE CHRONIC INFECTION DESPITE LIMITED LIVER DISEASE AND LOW-VIRAEMIA: IMPLICATIONS FOR AN ALTERED CELL METABOLISM

R. Salpini[1], L. Carioti[1], A. Battisti[1,2], L. Colagrossi[1,3], L. Piermatteo[1], M. Surdo[4], V. Cacciafesta[4], A. Nuccitelli[4], N. Hansi[2], F. Ceccherini-Silberstein[1], C.F. Perno[5], U.S. Gill[2], P.T.F. Kennedy[2], V. Svicher[1]

[1]"Tor Vergata" University of Rome, Department of Experimental Medicine and Surgery, Rome, Italy, [2]Barts Liver Centre, Blizard Institute, Barts and The London SMD, QMUL, London, United Kingdom, [3]Department of Microbiology and Virology, University of Milan, Milan, Italy, [4]GENOMA, Molecular Genetics Laboratory, Rome, Italy, [5]Department of Oncology and Haematooncology, University of Milan, Milan, Italy

Background: HBV integration in human genome was mainly described in HCC patients (pts), proving its role in oncogenesis. Few data are available on HBV integration in HBeAg-negative pts with a limited liver disease
Here, we aimed to analyze HBV intrahepatic reservoir and integration in HBeAg-negative pts with no/mild liver fibrosis.
Methods: Liver tissues from 40 HBeAg-negative pts were studied. Pts were classified as: group-1 (HBV-DNA<2,000IU/ml; n=8), group-2 (HBV-DNA 2,000-20,000IU/ml; n=14), group-3 (HBV-DNA>20,000IU/ml; n=18). cccDNA, intrahepatic total (it)-HBV-DNA were quantified by RT-PCR and pgRNA by digital-PCR. Exome Sequencing [Illumina, median(IQR) coverage: 115x (90x-140x)] was performed for 40/40 pts. HBV integration was identified by recognition of chimeric HBV-human sequences applying a bioinformatic pipeline based on Virus-Clip. The role of genes involved in HBV integration was analysed by GeneCards. The threshold of parameters predicting HBV integration was defined by AUROC.
Results: Group-1 and -2 show a comparable intrahepatic HBV reservoir. Conversely, compared to group-2, group-3 is characterized by higher median[IQR] cccDNA (2.6[2.3-2.7] vs 2.0[0.9-2.3]log copies/1000cells, P=0.01), it-HBV-DNA (3.9[3.5-4.4] vs 3.1[2.2-3.9]log copies/1000cells, p=0.005) and pgRNA (190[7-770] vs 3.3[1.5-12] copies/1000cells, p=0.02).
HBV integration is detected in 35% of pts, more frequently in group-3 than in -1 and -2 (55% vs 25% and 14.4%, p=0.03). Among the 17 integration events, 11 involves HBx region, followed by preCore-Core-(N=3) and Pol/S (N=3). Of note, we identified 2 long HBV integrants (354 and 1085 nt), both containing HBV-Enhancer-II, known to promote the expression of HBx protein, known for its transactivating properties. Accordingly, both pts had serum HBV-DNA >6 logIU/ml and increased ALT.
In 64.7%, HBV integration is observed within introns, mainly close to RNA splicing-site, at <100nt from exons (47.1%), regions critical for a proper mRNAs production. Notably, HBV integration often localizes in human genes, regulating cell proliferation and, thus, directly involved in carcinogenesis (NUP85, COL18A1, AGBL5, ANKRD52 and ELAC-2). Furthermore, HBV is found integrated in genes regulating lipid/drug metabolism (CYP2UI, LMF-1) or inflammatory/antiviral response (IFITM-1, NR3C1).
Finally, a higher amount of serum HBsAg is the only factor correlated with HBV integration (p<0.001): HBsAg>5,000IU/ml identifies HBV integration with the best diagnostic-accuracy (83.5%), 92% sensitivity and 73% specificity.
Conclusions: HBV integration occurs across all types of pts with HBeAg-negative disease, including low-viremic pts and with limited liver disease. The localization of HBV integration also suggests that these events are not restricted to carcinogenesis but may also be involved in genes regulating metabolism, inflammation and antiviral immunity.

New challenges of viral hepatitis

OC 74 DECLINE OF PREVALENCE OF RESISTANCE ASSOCIATED SUBSTITUTIONS TO NS3 AND NS5A INHIBITORS AT DAA-FAILURE IN HEPATITIS C VIRUS IN ITALY OVER THE YEARS 2015 TO 2018

D. Redi[1,2], B. Rossetti[1], V.C. Di Maio[3], M. Aragri[3], S. Paolucci[4], C. Masetti[5], L. Paglicci[1,2], B. Bruzzone[6], C. Minichini[7], F. Montagnani[1,2], V. Micheli[8], S. Landonio[9], E. Degasperi[10], G. Zanelli[1,2], R. Maserati[11], I. Maida[12], A.P. Callegaro[13], S. Barbaliscia[3], A. Bertoli[3], C. Paternoster[14], S. Marenco[15], F. Morisco[16], V. Calvaruso[17], G. Taliani[18], M. Puoti[19], G. Cenderello[20], A. De Santis[21], M. Lichtner[22], N. Coppola[7], R. Gulminetti[11], V. Cento[23], M. Rendina[24], E. Teti[25], G. Parruti[26], T. Ruggiero[27], V. Ghisetti[27], C. Pasquazzi[28], L.A. Nicolini[29], V. Vullo[30], A. Pellicelli[31], T. Prestileo[32], R. Cozzolongo[33], V. Sangiovanni[34] , M. Biolato[35], I. Lenci[5], A. Licata[36], A Ciaccio[37], V. Pace Palitti[38], A. Giorgini[39], G. Cariti[40], A. Ciancio[41], A. Aghemo[42], V. Borghi[43], P. Andreone[44], M. Brunetto[45], T. Pollicino[46], T. Santantonio[47], N. Cuomo[48], C. Caudai[49], S. Babudieri[12], P. Lampertico[10], G.B. Gaeta[7], G. Raimondo[46], M. Andreoni[25], G. Rizzardini[9], M. Angelico[5], C.F. Perno[50], A. Craxì[17], M. Zazzi[2], F. Ceccherini-Silberstein[3] on behalf of HCV Virology Italian Resistance Network (Vironet C)

[1]Infectious Diseases Unit, AOU Senese, Siena, Italy, [2]Department of Medical Biotechnology, University of Siena, Siena, Italy, [3]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [4]Molecular Virology Unit, Microbiology and Virology department, IRCCS Policlinic Foundation San Matteo, Pavia, Italy, [5]Hepatology Unit, University Hospital of Rome Tor Vergata, Rome, Italy, [6]Hygiene Unit, IRCCS AOU San Martino-IST, Genoa, Italy, [7]Infectious Diseases Unit, University of Campania L. Vanvitelli, Naples, Italy, [8]Clinical Microbiology, Virology and Bioemergencies Diagnosis, L. Sacco University Hospital, Milan, Italy, [9]Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Milan, Italy, [10]CRC "A.M. e A. Migliavacca" Center for Liver Diseases, Division of Gastroenterology and Hepatology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy, [11]Institute of Infectious Diseases, University of Pavia, Pavia, Italy, [12]Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [13]Department of Laboratory Medicine, ASST Papa Giovanni XXIII, Bergamo, Italy, [14]Infectious Disease Unit, Ospedale di Trento, Trento, Italy, [15]Division of Hepatology, University of Genoa-AOU IRCCS San Martino-IST, Genoa, Italy, [16]Department of Clinical Medicine and Surgery, University "Federico II" of Naples, Naples, Italy, [17]Gastroenterology, "P. Giaccone" University Hospital, Palermo, Italy, [18]Department of Clinical Medicine, Clinic of Tropical Medicine, Sapienza University of Rome, Rome, Italy, [19]Division of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [20]Infectious Diseases Unit, Ente Ospedaliero Galliera Hospital, Genoa, Italy, [21]Gastroenterology Unit, "La Sapienza" University of Rome, Rome, Italy, [22]Infectious Diseases Unit, Sapienza University, Polo Pontino, Latina, Italy, [23]Residency program in Microbiology and Virology, Università degli Studi di Milano, Milan, Italy, [24]Department of Emergency and Organ Transplantation, Section of Gastroenterology, University Hospital, Bari, Italy, [25]Infectious Diseases, University Hospital of Rome Tor Vergata, Rome, Italy, [26]Infectious Disease Unit, Pescara General Hospital, Pescara, Italy, [27]Laboratory of Microbiology and Virology, Amedeo di Savoia Hospital, ASL Città di Torino, Turin, Italy, [28]Infectious Diseases, Sant'Andrea Hospital – "La Sapienza", Rome, Italy, [29]Department of Health Sciences (DISSAL), University of Genoa, [30]Department of Public Health and Infectious Diseases, Sapienza University, Rome, [31]Hepatology Unit, San Camillo Forlanini Hospital, Rome, Italy, [32]Infectious Diseases Unit, ARNAS Civico-Di Cristina-Benefratelli, Palermo, Italy, [33]Division of Gastroenterology, National Institute of Gastroenterology S De Bellis, Castellana Grotte (Bari), Italy, [34]Hospital Cotugno, Naples, Italy, [35]Liver Transplant Medicine, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy, [36]Internal Medicine and Hepatology, Di.Bi.M.I.S, University of Palermo, Palermo, Italy, [37]Unit of Gastroenterology, Department of Medicine, Hospital San Gerardo, Monza, Italy, [38]Hepatology Unit, Pescara General Hospital, Pescara, Italy, [39]ASST Santi Paolo e Carlo, Milan, Italy, [40]Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, Italy, [41]Unit of Gastroenterology, University of Turin, Department of Medical Sciences, City of Health and Science of Molinette Turin Hospital, Turin, Italy, [42]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI), Italy, [43]Department of Biomedical Sciences, University of Modena School of Medicine, Modena, Italy, [44]Department of Medical and Surgical Sciences, Maternal-Infantile and Adult Sciences, University of Modena and Reggio Emilia, Modena, Italy, [45]Hepatology Unit, University Hospital of Pisa, Pisa, Italy, [46]Department of Internal Medicine, University Hospital of Messina, Messina, Italy, [47]Infectious Diseases Unit, University of Foggia, Foggia, Italy, [48]Microbiology and Virology, Azienda Ospedaliera Specialistica dei Colli Monaldi - Cotugno - C.T.O., Naples, Italy, [49]Microbiology and Virology Unit, Siena University Hospital, [50]Department of Oncology and Oncohematology, University of Milan, Milan, Italy

Background: A minority of patients fail to eliminate HCV and resistance-associated substitutions (RASs) are commonly detected at failure of interferon-free DAA regimens.

Material and methods: Within the Italian network VIRONET-C, the prevalence of NS3/NS5A/NS5B RASs was retrospectively evaluated in patients who failed an EASL recommended DAA-regimen in 2015-2018. NS3, NS5A and NS5B Sanger sequencing was performed using homemade protocols. The geno2pheno system was used to infer HCV-genotype/subtype and predict drug resistance. The changes in the prevalence of RASs over time were evaluated using the chi-square test for trend, predictors of RASs at failure were analysed by logistic regression.

Results: We included 386 real-life HCV pts failed to recommended DAA regimens: 92% (271/294) Italians, 75% (286/384) males, median age was 56 years (IQR 52-61); 106 (28%) were treatment-experienced: 91 (86%) with IFN-based treatments, 26 (25%) with DAA-based regimens. Metavir fibrosis stage was F4 in 76% (245/322), 65% (240/369) had clinical cirrhosis. Patients with HIV and HBV coinfection were 10% (33/317) and 8% (6/72), respectively. HCV genotype (G) was G1b in 122 pts (32%), G3a 103 (27%), G1a 97 (25%), G4d 30 (8%), G2c 19 (5%), G3h 5 (1.3%), G4a 4 (1%) and 1 (0.3%) each for G3g, G4n/o/v. DAA regimens were: LDV/SOF in 115 (30%), DCV/SOF in 103 (27%), 3D in 83 (21%), EBR/GRZ in 32 (8%), VEL/SOF in 29 (7%), GLE/PIB in 18 (5%) and 2D in 6 (2%); ribavirin was administered in 123 (32%). Antiviral treatment was completed by 352 pts (91%), while 34 (9%) discontinued prematurely. The NS5A fasta-sequence was available for all pts, NS5B for 361 (94%), NS3 for 365 (95%).

The prevalence of any RASs was 87%, namely 78/135 (58%) in NS3, 303/359 (85%) in NS5A, 114/286 (40%) in NS5B (Tab 1).

The prevalence of any RASs significantly declined from 2015 to 2018 (100%, 13/13 vs 81%, 101/125, p=0.01): NS5A RASs from 100%, 13/13 to 76%, 76/100 (p<0.001), NS3 RASs from 88%, 7/8 to 44%, 28/63 (p=0.02), while NS5B RASs remained stable.

Independent predictors of any RASs included liver cirrhosis/advanced fibrosis (AOR 3.72, CI 95% 1.51-9.17, p=0.004) and genotype (G2 vs G1a AOR 0.01, CI 95% 0.0-0.3, p<0.001; G3 vs G1a AOR 0.22, CI 95% 0.05 -0.98, p<0.047; G4 vs G1a AOR 0.13, CI 95% 0.03-0.63, p<0.011), with a modest effect scored for past treatment (AOR 3.45, CI 95% 1.00-11.92, p=0.05), after adjusting for DAA regimen and year of genotype.

Notably, full activity was predicted for GLE/PIB in 75.9% of cases and for at least two components of VEL/SOF/VOX in 59% of cases and no case with full-resistance to either regimen was found (Tab 2).

Conclusions: Despite decreasing prevalence over the years, RASs remain a common signature at virological failure of DAA treatment, particularly in patients with the highest grade of liver fibrosis. Their distribution may vary according to genotype, so the identification of RASs after failure could play a crucial role in optimizing retreatment strategies.

New challenges of viral hepatitis

OC 75 EVALUATION OF SELECTIVE PRESSURE ON TARGET REGIONS OF ANTI-HCV DIRECT ANTIVIRALS IN LIVER AND PLASMA COMPARTMENTS: APPLICATION OF MIXED EFFECTS MODEL OF EVOLUTION (MEME) ALGORITHM

S. Bagaglio[1], E. Messina[1], H. Hasson[1], C. Uberti-Foppa[2], G. Morsica[1]

[1]Division of Infectious Diseases, Ospedale San , Italy, [2]Vita-Salute University, Milan, Italy

Background: Compartimentalization of resistant variants to anti-HCV direct antivirals (DAAs) were poorly investigated in liver and plasma of HIV/HCV coinfected individuals. No data were available about different selective pressure on DAAs target regions at positions not associated with DAAs resistance in different compartments.

Aim: We aimed to evaluate selective pressure on target regions of anti-HCV direct antivirals in LT and plasma of HIV/HCV coinfected individuals in absence of drug pressure.

Methods: Twenty-eight HIV/HCV coinfected individuals (15 infected by genotype [GT] 1a, 6 by GT-3a and 7 by GT-4d), naïve to any anti-HCV treatment who performed liver biopsy for diagnostic purposes from 1995 to 2000 at Division of Infectious Diseases, Ospedale San Raffaele, were included in the study. Liver tissue (LT) and plasma samples (PS) were collected at time of liver biopsy. To analyze selective pressure on each codon of NS3 protease domain (aa 39-176) and NS5A domain 1 region (aa 12-105 target region) we applied data monkey tools to our data set. Specifically, we run Mixed Effects Model of Evolution (MEME) algorithm. MEME employs a mixed-effects maximum likelihood approach to test the hypothesis that individual sites have been subject to episodic positive or diversifying selection. A p value <0.05 was considered as statistically significant to detect selective pressure on each codon.

Results: The analysis of resistance profile of NS3 protease domain showed that 10/28 (35.7%) individuals harboured resistance associated substiutions (RASs) in LT and 9/28 (32%) in PS. All patients with RAS in NS3 domain were GT-1a. Concerning NS5a resistance profile, RASs were detected in10/28 (35%) LTs and in 6/28 (21%) PS: RASs were detected in 3 GT-1a and in 7 GT-4d LTs and in 6 GT-4d PS.

The application of MEME algorithm to detect selective pressure on NS3 protease domain showed that 16/138 (11%) codons were under pressure in LT, while in PS 9/138 (6%) sites resulted under selective pressure. In detail, codon 49 and codon 62 resulted under pressure in both compartments, while in LTs selective pressure was more frequently observed on C-terminal portion of NS3 protease domain (aa120-176) and on N-terminal portion (aa 49-72), excluding NS4a binding site, in PS. The analysis of NS5a domain1 showed that 6 (6%) codons were under selective pressure in LT, while in PS 2/94 (2%) sites resulted under selective pressure. In detail, codon 43 and codon 90 resulted under pressure in both compartments, while codons 13, 55, 56,78 were under pressure only in liver comparment.

Conclusions: Application of MEME algorithm allowed to detect different selective pressure in liver and plasma on NS3 protease region and NS5a domain1 considering not only RASs postitions but also other codons of each domain. The selective pressure seems to be more evident in LT and on NS3 domain, in particular at C-terminal portion. The NS5a domain1 resulted less sensitive to compartment selective pressure.

New challenges of viral hepatitis

OC 76 SPECIFIC NS5A POLYMORPHISMS CORRELATE WITH HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS INFECTED WITH HCV GENOTYPE 1B

M. Alkhatib[1], V.C. Di Maio[1], V. De Murtas[2], M. Aragri[1], R. Scutari[1], A. Sacco[1], E. Polilli[3], C. Masetti[4], E. Teti[5], S. Barbaliscia[1], A. Bertoli[1], V. Cento[6], V. Calvaruso[7], F. Morisco[8], V. Pace Palitti[9], C. Pasquazzi[10], P. Cacciatore[3], S. Francioso[4], F. Sozio[3], A. Pieri[3], S. Babudieri[2], C. Mussini[11], G. Parruti[3], V. Borghi[11], I. Lenci[4], A. Craxì[6], M. Andreoni[5], M. Angelico[4], I. Maida[2], A. Orro[12], L. Milanesi[12], M.M. Santoro[1], C. F. Perno[6], V. Svicher[1], F. Ceccherini-Silberstein[1], R. Salpini[1]

[1]Department of Experimental Medicine and Surgery, University of Rome "Tor Vergata", Rome, Italy, [2]Department of Clinical and Experimental Medicine, University of Sassari, Sassari, Italy, [3]Infectious Diseases Unit, Pescara General Hospital, Pescara, Italy, [4]Hepatology Unit, University Hospital of Rome "Tor Vergata", Rome, Italy, [5]Infectious Diseases Unit, University Hospital of Rome "Tor Vergata", Rome, Italy, [6]University of Milan, Milan, Italy, [7]Gastroenterology, "P. Giaccone" University Hospital, Palermo, Italy, [8]Gastroenterology, «Federico II» University, Naples, Italy, [9]Hepatology Unit, Pescara General Hospital, Pescara, Italy, [10]Infectious Diseases Unit, Sant'Andrea Hospital – "Sapienza" University, Rome, Italy, [11]Polyclinic of Modena, Modena, Italy, [12]Institute of Biomedical Technologies, National Research Council, Segrate, Milan, Italy

Background: Hepatocellular Carcinoma (HCC) generally rises after a stage of advanced liver fibrosis and cirrhosis with an incidence about 1-8% per year. The HCV protein, NS5A, is known to modulate viral fitness and to interact with different cellular proteins, including P53, thus inducing intracellular signaling pathways associated with cell proliferation. In this light, we explored the genetic variations in NS5A associated with HCC

Materials and Methods: This study includes 188 patients chronically infected with HCV genotype 1b, all cirrhotic and DAA-naïve: 34 diagnosed with HCC and 154 controls without HCC. NS5A domain-1 (amino acid: 1-183) sequences were obtained for all patients by Sanger method from plasma samples. Association of mutations with HCC was assessed by Fisher Exact test. Shannon Entropy (SE) was used to describe residues with significantly higher (P<0.05) variability (SE>0.2) in HCC compared to No-HCC

Results: HCC patients were characterized by comparable median (IQR) log serum HCV-RNA [5.6(5.3-6.1) vs 5.8 (5.3-6.1)IU/ml], ALT[65(37-86) vs 71(50-112)U/l], and significantly higher liver stiffness[28(20-33) vs 19(15-26) KPa, P<0.001] compared to No-HCC patients

By mutational analysis, four specific NS5A polymorphisms significantly correlated with HCC: S3T(8.8 vs 1.3%, P=0.01), T122M(8.8% vs 0.0%, P<0.001), M133I(20.6 vs 3.9%, P<0.001), and Q181E(11.8 vs 0.6%, P<0.001). Multivariate analysis confirmed that the present of at least one of the identified mutation is independently associated with the occurrence of HCC (adjusted OR 12.93, 95% CI 4.27-39.15; P<0.001), after correction for patients' demographics, gender, age, HCV-RNA, ALT, AST, and previous INF usage. Of note, HCC patients with > 1 of these mutations tend to have higher HCV-RNA levels respect to HCC patients without them [median (IQR): 5.7(5.4-6.2) vs. 5.3(4.4-5.6) log IU/ml, P=0.02], suggesting their role in enhancing viral replications and expression

By SE, other three residues were more variable in HCC: C13R/S (SE=0.264; P=0.03, located in highly conserved N-terminus NS5A domain), F127L/S (SE=0.225; P=0.03), and N137D/K (SE=0.264; P<0.001). Furthermore, an enrichment of additional mutations is observed at residue 181 (Q181E/G/H/P, SE=0.410; P=0.01). Notably, all the above-mentioned residues are localized in regions of NS5A domain-1 known to interact with cellular proteins as P53 (aa:1-149), involved in the apoptosis regulation, and/or with P85-PIK3 (aa:1-112), involved in Wnt/β-catenin signaling pathway regulating the cell growth

Conclusions: The association of specific NS5A polymorphisms with HCC provides a focus for further investigations aimed at elucidating the molecular basis of HCV-mediated oncogenesis. These viral signatures, if confirmed in a larger population, could play a crucial role as prognostic markers of HCC, especially in cirrhotic-HCV patients, helping to identify patients at higher HCC-risk, deserving more intense liver evaluation and/or early treatment

New challenges of viral hepatitis

OC 77 OCCURRENCE OF HIV VIROLOGICAL FAILURE IN HIV-1 POSITIVE PATIENTS DURING DIRECT ACTING ANTIVIRALS (DAAS) TREATMENT FOR HEPATITIS C VIRUS

G. Morsica[1], E. Messina[1], A. Castagna[1,2], S. Bagaglio[1], S. Salpietro[1], L. Della Torre[1], C. Uberti-Foppa[1,2], H. Hasson[1]

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

Background and aim: The introduction of DAAs for hepatitis C virus (HCV) in the last few years together with improvements in antiretroviral therapy (ART) for HIV infection, have led to the development of highly efficacious treatment strategies for HIV/HCV. Reactivation of HBV infection in HBsAg positive patients (pts) during DAAs treatment has been recently described, while the dynamic of HIV viremia remains poorly investigated in HIV/HCV infected pts under DAAs. Methods We retrospectively evaluated HIV load before and during DAAs treatment in 400 HIV/HCV coinfected pts from the CSLHIV cohort, who were treated with DAAs between years 2015-2018. These pts were under concomitant and stable ART and HIV load invariably undetectable for at least 6 months before starting DAAs.

Statistical analysis: The continuous variables are expressed as median values and interquartile ranges (IQRs), and the categorical variables as absolute counts. The data were analysed using Fisher's exact test (for frequencies), or the Mann-Whitney U test (for continuous variables); a p-value of <0.05 was considered statistically significant.

Results: Of 400 HIV positive pts, all with HIV-RNA < 50 copies/mL at DAAs initiation, 25 (6.25%) had a positive HIV viremia (> 50 copies/mL) during DAAs: 10 (2.5 %), had HIV blip (detectable HIV viremia not confirmed in a subsequent plasma sample), 15 (3.75%) had HIV virological failure (VF) assessed by HIV-RNA >50 copies/mL in two consecutive determinations. These 25 patients had a SVR to anti-HCV DAAs treatment; HCV-RNA became undetectable at week 4 of DAAs therapy in 6 HIV-blips pts and in 10 HIV-VF pts; at week 8 HCV-RNA became undetectable in 4 blips pts and 5 HIV-VF pts, P= 1.00. Characteristics of pts with HIV-RNA blip or VF are summarized in Table 1. The variables distinguishing pts with blip respect to those with VF were years of HIV-1 infection [median 18 (IQR 13-26) in blip pts. and median 31 (IQR-23-33) in VF pts, P=0.004] and duration of ART [median in blip pts 16 (IQR 4-19]; median in VF pts, 22 (IQR 18-24) P=0.006]. Additionally, pts with HIV-VF were older (median age 55 (IQR 52-57)] than those with HIV blips [median age 50 (IQR 48-54)], this result showing a trend towards significance, P=0.056. The other variables investigated were similarly distributed between HIV-VF pts and HIV-blips pts. Among 15 pts with HIV-VF, 9 changed ART regimen, while in 6 pts HIV-RNA returned to <50 copies/mL during or after DAAs without modifying ART. Resistance test was performed in 9/15 HIV pts at VF and 4/9 (44.4%) revealed resistance at least to one drug, while the other 5 pts had a HIV-wild type virus. Only one of these 15 patients referred no adherence to ART (this pt had no resistance).

Conclusions: We showed that HIV-VF may occur during DAAs treatment resulting in ART regimen change. We can form the hypothesis that HIV-VF was consequent to a reactivation of latently infected cells during DAAs treatment.

New challenges of viral hepatitis

OC 78 HIGH EFFICACY OF RESISTANCE-GUIDED RETREATMENT IN HCV INFECTED PATIENTS WHO PREVIOUSLY FAILED A NS5A INHIBITOR-CONTAINING REGIMEN: THE ITALIAN VIRONET C REAL LIFE EXPERIENCE

V.C. Di Maio[1], M. Aragri[1], C. Masetti[2], S. Paolucci[3], B. Bruzzone[4], E. Degasperi[5], S. Barbaliscia[1], T. Pollicino[6], C. Minichini[7], V. Calvaruso[8], M. Rendina[9], V. Cento[10], E. Teti[11], V. Micheli[12], V. Ghisetti[13], E. Polilli[14], V. Pace Palitti[15], S. Landonio[16], I. Lenci[2], S. Francioso[2], L. Donnarumma[17], L.A. Nicolini[18], A. Bertoli[1], M. Starace[7], C. Pasquazzi[19], A.P. Callegaro[20], F. Morisco[17], G. Cenderello[21], S. Marenco[22], R. Gulminetti[23], S. Novati[23], A. Scuteri[24], P. Andreone[25], S. Galli[26], A. Ciancio[27], V. Sangiovanni[28], N. Cuomo[29], A. Raddi[29], G. Morsica[30], H. Hamid[30], V. Borghi[31], I. Maida[32], M. Brunetto[33], P. Colombatto[33], R. Cozzolongo[34], A. De Santis[35], M. Lichtner[36], S. Babudieri[32], E. Biliotti[37], G. Taliani[37], T. Santantonio[38], M. Di Stefano[38], C. Paternoster[39], R. Ganga[40], M. Puoti[41], G. Rizzardini[16], A. Pellicelli[42], E. Milano[43], C. Mastroianni[44], A. Licata[45], F. Di Lorenzo[46], A. Giorgini[47], L. Sighinolfi[48], C. Dentone[49], A. Lleo[50], B. Rossetti[51], I. Beretta[52], P. Lampertico[5], G. Parruti[14], N. Coppola[7], M. Zazzi[53], G. Raimondo[6], M. Andreoni[11], A. Craxi[8], M. Angelico[2], C.F. Perno[54], F. Ceccherini-Silberstein[1] on behalf of HCV Virology Italian Resistance Network (Vironet C)

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Hepatology Unit, University Hospital of Rome Tor Vergata, Rome, Italy, [3]Molecular Virology Unit, Microbiology and Virology department, IRCCS Policlinic Foundation San Matteo, Pavia, Italy, [4]Hygiene Unit, IRCCS AOU San Martino-IST, Genoa, Italy, [5]CRC "A.M. e A. Migliavacca" Center for Liver Diseases, Division of Gastroenterology and Hepatology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy, [6]Department of Internal Medicine, University Hospital of Messina, Messina, Italy, [7]Infectious Diseases Unit, University of Campania L. Vanvitelli, Naples, Italy, [8]Gastroenterology, "P. Giaccone" University Hospital, Palermo, Italy, [9]Department of Emergency and Organ Transplantation, Section of Gastroenterology, University Hospital, Bari, Italy, [10]Residency program in Microbiology and Virology, Università degli Studi di Milano, Milan, Italy, [11]Infectious Diseases, University Hospital of Rome Tor Vergata, Rome, Italy, [12]Clinical Microbiology, Virology and Bioemergencies Diagnosis, L. Sacco University Hospital, Milan, Italy, [13]Laboratory of Microbiology and Virology, Amedeo di Savoia Hospital, ASL Città di Torino, Turin, Italy, [14]Infectious Disease Unit, Pescara General Hospital, Pescara, Italy, [15]Hepatology Unit, Pescara General Hospital, Pescara, Italy, [16]Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Milan, Italy, [17]Department of Clinical Medicine and Surgery, University "Federico II" of Naples, Naples, Italy, [18]Department of Health Sciences (DISSAL), University of Genoa,[19]Infectious Diseases, Sant'Andrea Hospital – "La Sapienza", Rome, Italy, [20]Department of Laboratory Medicine, ASST Papa Giovanni XXIII, Bergamo, Italy, [21]Infectious Diseases Unit, Ente Ospedaliero Galliera Hospital, Genoa, Italy, [22]Division of Hepatology, University of Genoa-AOU IRCCS San Martino-IST, Genoa, Italy, [23]Institute of Infectious Diseases, University of Pavia, Pavia, Italy, [24]Department of Medical and Surgical Sciences, DIMEC; Alma Mater Studiorum - University of Bologna, Bologna, Italy, [25]Department of Medical and Surgical Sciences, Maternal-Infantile and Adult Sciences, University of Modena and Reggio Emilia, Modena, Italy, [26]Microbiology Unit, Ospedale S.Orsola-Malpighi, Bologna, Italy, [27]Unit of Gastroenterology, University of Turin, Department of Medical Sciences, City of Health and Science of Molinette Turin Hospital, Turin, Italy, [28]Hospital Cotugno, Naples, Italy, [29]Microbiology and Virology, Azienda Ospedaliera Specialistica dei Colli Monaldi - Cotugno - C.T.O., Naples, Italy, [30]Division of Infectious Diseases, IRCCS, Ospedale San Raffaele, Milan, Italy; [31]Department of Biomedical Sciences, University of Modena School of Medicine, Modena, Italy, [32]Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [33]Hepatology Unit, University Hospital of Pisa, Pisa, Italy, [34]Division of Gastroenterology, National Institute of Gastroenterology S De Bellis, Castellana Grotte (Bari), Italy, [35]Gastroenterology Unit, "La Sapienza" University of Rome, Rome, Italy, [36]Infectious Diseases Unit, Sapienza University, Polo Pontino, Latina, Italy, [37]Department of Clinical Medicine, Clinic of Tropical Medicine, Sapienza University of Rome, Rome, Italy, [38]Infectious Diseases Unit, University of Foggia, Foggia, Italy, [39]Infectious Disease Unit, Ospedale di Trento, Trento, Italy, [40]Azienda Ospedaliera G. Brotzu-Cagliari, Cagliari, Italy, [41]Division of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [42]Hepatology Unit, San Camillo Forlanini Hospital, Rome, Italy, [43]Clinic of Infectious Diseases, University of Bari, Bari, Italy, [44]Department of Public Health and Infectious Diseases, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy, [45]Internal Medicine and Hepatology, Di.Bi.M.I.S, University of Palermo, Palermo, Italy, [46]Infectious Diseases Unit, ARNAS Civico-Di Cristina-Benefratelli, Palermo, Italy, [47]ASST Santi Paolo e Carlo, Milan, Italy, [48]Unit of Infectious Diseases, University Hospital of Ferrara, Ferrara, Italy, [49]Infectious Diseases Department, Sanremo Hospital, Sanremo, Italy, [50]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI), Italy, [51]Infectious Diseases Unit, AOU Senese, Siena, Italy, [52]Infectious Disease Unit, ASST Monza-San Gerardo Hospital, Monza, Italy, [53]Department of Medical Biotechnology, University of Siena, Siena, Italy, [54]Department of Oncology and Oncohematology, University of Milan, Milan, Italy

Background: At present, there is a limited documentation about the efficacy of retreatment in patients who previously failed a recommended NS5A-containing regimen in Italy.

Materials & Methods: Within the Italian network VIRONET-C, 444 NS5A-failing patients (pts) infected with different HCV-genotypes (GT) (GT1a/1b/2a-c/3a-b-g-h/4a-d-n-o-r-v=107/135/30/131/41) were analyzed. The retreatment of 125 failures was also investigated. Genotypic-resistance-test (GRT) was performed by Sanger-sequencing at the time of virologic failure.

Results: Failures following seven different NS5A-containing regimens were studied: 3D/2D (paritaprevir/ombitasvir±dasabuvir)±ribavirin (N=88/5), daclatasvir/ledipasvir/velpatasvir(VEL)+sofosbuvir (SOF)±ribavirin(RBV) (N=113/133/38), grazoprevir(GRZ)/elbasvir(EBV)±RBV (N=37), glecaprevir(G) /pibrentasvir(P) (N=30). Notably, 19.8% of NS5A-failing pts did not show any resistance-associated-substitutions (RAS), while 80.2% showed at least one NS5A-RAS, with multiclass-resistance in 36.5%. Considering new multi-genotypic regimens, 89.5% (34/38) SOF/VEL pts failed a 12w treatment, 41.5% (15/36) were cirrhotic and 61.0% (23/38) were infected with a non-1 GT (fig. 1A). Also in G/P failures, the majority of pts were infected with a non-1 GT (73%, 22/30) and failed an 8w regimen (96.7%, 29/30) while only 7.4% (2/27) were cirrhotic (fig. 1B). 52.9% of these failures showed at least one NS5A-RAS. To date, 125 NS5A-inhibitor failures started a retreatment with: SOF/VEL±RBV (N=30), SOF/VEL/voxilaprevir(VOX)±RBV (N=84), G/P±RBV (N=7), GRZ/EBV+SOF+RBV (N=3), GRZ/EBV+RBV (N=1). The majority were cirrhotic (49.6%) and relapsers (92.4%). The prevalence of NS5A-RAS before retreatment was 78.4% and multiclass-resistance 28.8%. Among pts completing post-retreatment follow-up, a sustained-viral-response at week 12 (SVR12) was observed in 76/87 (87.3%). SVR12 was 77.8% with SOF/VEL±RBV (N=27). Differently, SVR12 was 100% with G/P±RBV for 8/12/16 weeks (N=7), GRZ/EBV±SOF+RBV for 12/24 weeks (N=1/3) (fig 2).

Of 84 pts who started SOF/VEL/VOX±RBV retreatment for 12 weeks, 66/84 (78.6%) showed at least one baseline NS5A-RAS, 30/84 (35.7%) multiple-NS5A-RASs, and 27/84 (32.1%) multiclass-resistance. Among those with available outcome, 5/5 retreated with SOF/VEL/VOX+RBV achieved SVR12 (100%) vs 88.9% treated without RBV. Among the 5 virologic failures, 2 GRTs are available and the others are on-going. One GT1b infected patient non-responder, was without any RAS before and after failure. One GT1a relapse, confirmed at failure the same baseline NS5A-RASs Q30R+L31M, without any additional RASs in NS3/NS5B genes.

Conclusions: In this Italian real-life experience, NS5A-RASs were frequently detected in NS5A-failing pts, and multiclass-resistance was around 30%. Overall, SVR after GRT-guided retreatment was >90%, with the exception of the SOF/VEL retreatment. Our results show how HCV GRT after failure may be useful to optimize the retreatment strategies.

Social and PLWHIV related issues

OC 79 PROMOTING MIGRANT ACCESS TO SEXUAL AND REPRODUCTIVE HEALTH SERVICES FOR SEXUAL GENDER BASED VIOLENCE (SGBV) PREVENTION AND RESPONSE (PRO-ACCESS)

K. Ceesay, D. Di Dio, S.B. Dhiab, G. Floridia, M.C. Longo, M. Manuli, D. Matheson, G. Petrelli, S. Reale, S. Scalzo, A.A. Sleemankhel, M. G. Di Benedetto, F. Bellissimo and L. Nigro for the ProAccess/LILA Volunteer Group

Lega Italiana per la Lotta contro l'AIDS (LILA) - Catania

Background. Economic refugees and asylum seekers (People of Concern, PoCs) face sexual violence, murder, torture and religious persecution in their countries and during their attempt to reach Italy. The abuse and violence suffered, especially in Libya, are documented by CNN and Amnesty International reports. The number of women/girls and men/boys victims of trafficking and sexual exploitation has increased over the last years. PoCs continue to be victims even after reaching Europe. These events have led to an increase in SGVB, acquiring and spreading STIs and unwanted pregnancies.
Objectives: Pro-access is a programme, addressed to PoCs, to ensure and increase: i) diagnoses and treatment of STIs, HIV, HCV; ii) early identification and support of SGVB; iii) recovery and reduction of long-term consequences of SGBV; iv) empowerment of migrants.
Material and Methods: The target are PoCs in these areas: 1) houses/flats, "Sistema di protezione per richiedenti asilo e rifugiati" (SPRAR); 2) centri di accoglienza per richiedenti asilo (CARA); 3) other reception centres (centres for minors); 4) urban areas (refugees).
The activities are implemented by a team of doctors, psychologists, social workers, cultural mediators and outreach operators and are supported by LILA-volunteers.
Three visiting sessions are delivered at reception facilities. The first session imparts medical information, the second socio-psychological information, and the third verifies PoCs feedback, and tries to favor the emergence of psychological discomfort deriving possible SGBV. During the third session HIV and HCV tests are offered. A Drop-in Centre, low-threshold access, organized for PoCs, once a week, in LILA, offers: a) medical consultation (physician, infectivologist and gynecologist); b) psychological support; c) social services; d) HIV/HCV test; e) pregnancy test. Outreach activities are performed in key locations to meet PoCs and distribute IEC materials.
Results: All the results are reported in Table 1.
Conclusion: All activities were well received by PoCs, confirmed by their active participation and interest and desire for information, by the number of tests performed and by the number of PoCs followed at Drop-in. Our activities have confirmed that PoCs outside the reception system and resident within the reception system are at high risk of sexual exploitation, criminal activity and unregulated labor exploitation. We have perceived a need to address the increasing number of refugees and asylum seekers that are excluded from the reception system, or who have chosen to avoid the system. We recommend community-based approaches that would deliver services to their "door" through a mobile unit and peer-to-peer by training community leaders or champions.

*ProAccess/LILA Volunteer Group. J. Alieu, S. Bruno, G. Cacciatore, A. De Cristofaro, A. Leo, S. Maccarrone, M. Maresca, S. Timpanaro.
The program is fund by UNHCR.
The program is started in 2017 and is still ongoing.

Social and PLWHIV related issues

OC 80 IMMIGRATED HIV TRANSGENDERS IN ITALY: CLINICAL AND NEUROCOGNITIVE OUTCOME AND NEEDS

C. Atzori, P. Meraviglia, L. Valsecchi, G. Rizzardini, D. Minisci, N. Marazzi

Infectious Diseases Department, Luigi Sacco University Hospital, Milan, Italy

Background: South American immigrated HIV-positive transgender individuals (MtF) dwelling in Milan are a peculiar marginalized group poorly investigated in specific features, clinical and neuro-cognitive outcome and needs.

Methods: Cross sectional observational study of MtF subjects (CWS), on care for at least 1 year, based on socio demographic, therapy (including CPE) and laboratory data. Neuro-cognitive screening performed with 3 questions test followed by a battery of neuro psychological tests (Trail making A, B, A-B, Wais-R-Digit Span, Wais-R-Digit Symbol, Rey Auditory verbal, Lafayette grooved Pegboard) assessing concentration and speed of mental processing, mental flexibility, memory and fine motor functioning. Evaluation included for those who accepted, patient's self-administration of Cogiati test for gender identity and trans-sexuality and a questionnaire on perceived discrimination, economic outcome and specific needs. Statistical analysis was performed with Fischer exact test.

Results: data on 70 MtF transgenders HIV positive patients (pts) have been analyzed. Years of immigration 12 ±6.7, mean age 37±8.14 years, BMI 23±3.1 kg/m^2, self-perceived discrimination 14%. Years from HIV diagnosis 9.6±7, nadir CD4 318±214 cell/mmc, 45% had baseline HIV RNA>log 5. 97% pts completed full NPS test battery, 94% Cogiati questionnaire, showing a profile 3 (79%), and 4 (21%). NPS tests outcome was adjusted for age and school degree. HIV-RNA suppression was achieved in 84.8%. Mean ARV CPE rank was 7.11. Pathological outcome emerged in "3 questions test" in 53%, in Rey (62%), in Wais (69%), History of child abuse was reported in 53%. Additional factors for NPS impairment were: syphilis 67%, cocaine use 76%, alcohol abuse 61%, CNS medications 70%. Uni-variate analysis showed statistical correlation for neuro-cognitive impairment only for cocaine use, alcohol abuse, history of child abuse.

Conclusions: Neuro-cognitive defects despite of viral suppression and satisfactory CNS antiretroviral CPE rank suggest a complex multi-factorial pathogenesis. Reported previous abuse, psychiatric (anxiety, depression) and Sexual Transmitted Diseases (syphilis) co-morbidities, self-administered hormones and use of ricreative substance abuse may have significant impact on neuro cognitive outcome. MtF subjects in Milan declared low level of self perceived discrimination although scarce integration and self-clustering according to the nation of origin. Our data support the need for a better management of psychological and endocrinological care of this fragile and marginalized population.

Social and PLWHIV related issues

OC 81 DOES MATERIAL DEPRIVATION AFFECT LATE HIV PRESENTATION? ANALYSIS FROM DATA OF ITALIAN HIV-SURVEILLANCE SYSTEM, 2010-2016

M. Dorrucci[1], V. Regine[2], P. Pezzotti[1], L. Pugliese[2], B. Suligoi[2] and the Regional representatives of the Italian HIV Surveillance System[3]

[1]Dipartimento Malattie Infettive, Istituto Superiore di Sanità, Roma, [2]Centro Operativo AIDS, Istituto Superiore di Sanità, Roma, [3]Regional representatives of the Italian HIV Surveillance System. Abruzzo: M. Di Giacomo, L. Scancella; Basilicata: F. Locuratolo, G. Cauzillo; Calabria: A.D. Mignuoli, D.G. Chirico; Campania: G. Borgia; Emilia Romagna: E. Massimiliani; Friuli Venezia Giulia: T. Gallo, C. Braida; Lazio: V. Puro, P. Scognamiglio, A. Mammone; Liguria: G. Icardi, P.L. Lai; Lombardia: M. Gramegna, D. Cereda; Marche: F. Filippetti; Molise: A. Prozzo; Piemonte: C. Pasqualini; Provincia Autonoma di Bolzano: L. Pagani, R. Binazzi; Provincia Autonoma di Trento: P. Lanzafame, L. Collini, D. Bassetti; Puglia: M. Chironna, D. Loconsole; Sardegna: M.A. Palmas; Sicilia: G. Dardanoni; Toscana: F. Voller, M. Puglia, L. Pecori; Umbria: A. Tosti, R. Papili; Valle d'Aosta: M. Ruffier, M.G. Verardo, A. Catania; Veneto: F. Russo, F. Da Re

Background: to study the association between material deprivation and late HIV-presentation in Italy.
Material and methods: observational study using Italian HIV-surveillance data from 2010 to 2016 and the material deprivation rates estimated by provinces on the basis of European Union Statistics on Income and Living Conditions (EU-SILC) survey 2012, adapted from Ferrante et al. (1). In brief, the material deprivation rate is an indicator of poverty, calculated as the proportion of people living in households that are in a state of material deprivation. Multivariable multi-level (clustered in Italian provinces) logistic models were applied to assess the independent association between material deprivation rate and the late presentation diagnosis (i.e., CD4 ≤ 350 or AIDS at new diagnosis).
Results: we included 18,088 individuals diagnosed , aged > 15 years with known CD4 at HIV diagnosis. The majority were males (13,922, 77%), the median age was 39 years; 8,564 were heterosexuals (48%), 7,155 were MSM (40%), 912 IDU (5%); 4,586 (25%) were born abroad. Figure 1 shows the different distribution of the material deprivation by Italian province: higher deprivation rates were estimated in central or southern Italy (deprivation rate from 20% to 60%, i.e., from 4th to 5th quintiles). Overall, 10,058 (56%) individuals were classified as late presenters; figure 2 shows the distribution of late presenters by province: a slightly higher percentage of late presenters was observed in central and southern (58%) vs. northern Italy (55%).
Crude OR of late presentation for high (20%-60%) vs low deprivation (5%-19%) was equal to 1.13 (95% CI: 1.06-1.20) and adjusted OR (aOR) for high vs low deprivation was 1.18 (95% CI: 1.07-1.31); the other factors associated with late presentation were: older age (aOR for age > 40 vs ≤ 40 = 2.19; CI: 2.06-2.34); HIV-risk transmission categories (aOR for Heterosexuals vs MSM = 1.93; CI: 1.79-2.08; aOR for IDU vs MSM = 1.49 CI: 1.29-1.73); foreign nationality (aOR for foreigners vs Italians = 1.38: CI: 1.28-1.50); male gender (aOR for males vs females 1.29; CI: 1.18-1.40); year of diagnosis was not associated with late presentation (result not shown) .
Conclusions: delayed HIV diagnosis is common in Italy and the influence of the level of the deprivation in the Italian provinces seems marginal. Intervention campaigns aimed at promoting HIV testing and reducing the percentage of late presenters should primarily address older individuals, heterosexuals, IDU, foreigners, and males.

Reference

1. Ferrante MR, Fabrizi E, Pacei S. STIMA DELLA SERIE TEMPORALE 2007-2012 DEI PARAMETRI DI POVERTÀ E DEPRIVAZIONE PER I DISTRETTI SOCIOSANITARI E PER LE PROVINCE DELLA REGIONE EMILIA-ROMAGNA; http://statistica.regione.emilia-romagna.it/rc/indagine-reddito/stime-per-piccole-aree/pacei

Social and PLWHIV related issues

OC 82 EXERCISING WITH THE SUPPORT OF THE SMARTAPP: RESULTS ON PHYSICAL FITNESS, METABOLIC PROFILE AND PSYCHOLOGICAL PARAMETERS

M. Bonato[1,2], F. Turrini[3], V. De Zan[3], A. Meloni[1], R. Caccia[3], M. Plebani[1], E. Brambilla[1], A. Giordani[3], C. Vitobello[3], M. F. Piacentini[4], A. La Torre[1,2], G. Merati[1,5], L. Galli[3], P. Cinque[3]

[1]Università degli Studi di Milano, Milan, Italy, [2]IRCCS, Istituto Ortopedico Galeazzi, Milano, Italy, [3]IRCCS, San Raffaele Scientific Institute, Milan, Italy, [4]Foro Italico University of Rome, Rome, Italy, [5]IRCSS, Fondazione Don Carlo Gnocchi, Milan, Italy

Aim: Although physical activity is beneficial for health in people living with HIV (PLWH), adherence to exercise is low when not strictly supervised. It has been suggested that electronic devices could improve exercise adherence. Therefore, we designed a pilot study to assess improvements of physical fitness, metabolic and psychological parameters in PLWH exercising with the support of a smartphone application, compared to participants who exercised without the application.

Methods: This was a 16-week randomized, pilot study. PLWH were allocated to either an experimental group, which trained using a smartphone application (APP), or a control group, which trained following a hard copy program (No-APP). The program consisted of moderate physical activity three times/week including an initial coach-supervised period of 4 weeks, followed by 12 weeks where participants trained independently. At baseline (BL) and after 16-weeks (W16), participants were evaluated for cardiorespiratory fitness by peak oxygen consumption (VO2peak), body composition (body mass, body mass index-BMI, waist, hip circumferences, %fat mass-FM, and %fat free mass-FFM, by bioimpedentiometry), metabolic parameters (total-, HDL-, LDL-cholesterol, triglycerides), and Profile of Mood States (POMS; depression, fatigue, vigour, anger and tension). Intention-to-treat (ITT) analysis was used to assess differences in changes between groups, by Fisher's and Mann-Whitney tests. Changes between BL and W16 within groups were assessed by Wilcoxon signed rank test.

Results: Forty-eight cART treated participants were screened and 38 were eligible: 20 were allocated to the APP group and 18 to the No-APP group. Two APP and two No-APP participants were lost to follow-up. Median training adherence during the initial coach supervised period was 100% (IQR: 91-100%), with no differences between groups. During the autonomous training period (week 5-16), median adherence was 60% (IQR: 50 -80%) and 54% (IQR: 31-76%) in the APP (based on app records) and No-APP (self-reported) participants, respectively (p=0.517). However, ITT analysis showed a W16 improvement from BL of ≥15% of $\dot{V}$O2peak in 13/18 (72%) APP, but only in 3/16 (19%) No-APP participants (p=0.025). Significant W16 changes from BL were observed in APP, but not in No-APP participants, in $\dot{V}$O2peak, %FM, %FFM, total-, LDL-cholesterol, and triglycerides and significant change differences between groups in $\dot{V}$O2peak, %FM, %FFM, total-, LDL-cholesterol, and triglycerides. Analysis of POMS showed a significant improvement of vigour in APP and a significant worsening of depression and anger in the No-APP participants at W16 compared to BL. In addition, there were significant change differences in depression, vigour and anger between the two groups.

Conclusions: Exercising with a smartphone application may improve training adherence and therefore physical fitness, body composition, blood lipid profile and psychological outcomes in PLWH.

Social and PLWHIV related issues

OC 83 ANALYSIS OF EFFICACY, ADHERENCE AND QUALITY OF LIFE (QOL) OF EARLY PROACTIVE SWITCH TO ELVITEGRAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (E/C/T/TAF) IN PATIENTS WITH A PRIMARY HIV-1 INFECTION (ESTER STUDY)

M. Camici, A. Mondi, P. Lorenzini, S. Ottou, A. Vergori, M.M. Plazzi, R. Bellagamba, S. Cicalini, A. Antinori, C. Pinnetti

HIV/AIDS Clinical Unit, INMI Spallanzani, Rome

Background: It is still debated if optimization of antiretroviral therapy (ART) is feasible in order to improve adherence, tolerability and QoL in HIV positive patients (pts) starting ART during primary HIV infection (PHI) with stable virological suppression.

Material and methods: ESTER is a pilot 96 weeks (w) single arm, phase IV clinical trial enrolling HIV+ pts who started a 4-drug intensified ART with darunavir 800mg/boosted QD+ raltegravir 400 mg BID+ tenofovir/emtricitabine 300/200 mg QD during PHI and who reached virological suppression. Incuded pts were switched from first-line ART to once-daily single tablet regimen (STR) with E/C/F/TAF. Virological failure was defined as HIV-1 RNA test ≥ 40 cp/ml confirmed after 2w. Adherence was measured trough self reported questionnaire including VAS. The 30-item version Medical Outcome Study-HIV Health Survey MOS-HIV score was converted into continuous 0-100 summary scores for nine areas: general heath perceptions, physical, role, social and cognitive functioning, pain, mental health and health distress.

Results: 31 pts were enrolled, 96.8% were male, 83.9% MSM, median age was 34yrs (IQR 27-46), at baseline CD4 count 670 cells/mL (520-778).

Median CD4 cell count increased from BL to 24w and 48w and median CD4/CD8 ratio raised significantly from BL to 48w (Table 1). 1/31 (3.2%) treatment failure due to virological failure occurred (without drug resistance development and with resuppression without ART changes).

Reported pills assumption improved after switching to STR from 5/23 (21.7%) pts who declared to forget at least 1 pills every week to 2/23 (8.7%) pts at 24w and 2/18 (11.1%) at 48w (p=0.083, 0.180, respectively). Nonetheless, subjective perception of adherence did not change over time and was reported as a median value of 100% before and after the switch. The health perception of pts improved over time, passing from a mean value of 82.5% at BL, to 88% at 24w and 87.8% at 48w (p=0.173, p=0.283). QoL scores are reported in Table 2. Pain and physical functioning scores improved significantly from BL to w24. None of the MOS-HIV categories got worse.

Conclusions: Early proactive switch to E/C/T/F/TAF was associated to an improvement in adherence and quality of life scores in patients with PHI after switching from multiple pills regimen, even if small sample size of the interim analysis does not allow joining statistical significance to some of our outcomes.

Social and PLWHIV related issues

OC 84 ORGANIZATION AND ACTIVITY OF A VACCINATION SERVICE FOR HIV + PEOPLE: ASST-FBF-SACCO EXPERIENCE

P. Meraviglia[1], C. Gulisano[1], A. Ridolfo[1], M.V. Cossu[1], C. Negri[1], D. Minisci[1], L. Valsecchi[1], A. Capetti[1], L. Confalonieri[1], C. Boriello[2], M. Galli[1], G. Rizzardini[1]

[1]Department infection disease ASST-FBF-Sacco, Milan, [2]UOC vaccination ASST-FBF-Sacco, Milan

Background: Vaccinations represent a preventive strategy for health promotion in the HIV+ patients as recommended by all national and international guidelines. In 2017, the Lombardy Region adapted to the National Vaccine Prevention Plan (PNPV 2017-2019) of the Ministry of Health and at the same time provided that, in view of taking care of the patient with chronic pathologies, the vaccination service was made by ASST, while ATS had the role of governance.

Methods: Since 1/9/2018, the Department of Infectious Diseases (DMI) has activated a vaccination service with the following objectives: a) to promote access to vaccinations in HIV+ followed at DMI b) provide them with a complete certification of the vaccination status, c) assess the effectiveness and adverse events of the vaccinations. The following organization has been adopted: the service is active 3 days a week and is managed by a DMI medical-nursing team. The offer includes: anti-pneumococcal 13 and 23 valent vaccine (anti-Pneumo), anti-hepatitis A (anti-HAV) and B (anti-HBV), anti-papillomavirus (anti-HPV), anti-meningococcus B (anti-MenB) and ACWY (anti-MenACWY), anti-diphtheria/anti-tetanus (anti-DT), anti-diphtheria/antipertussis/anti-tetanus (anti-DTP), anti-Haemophilus (anti-HiB), anti-measles/pertussis/rubella (anti-MPR), and anti-chicken pox (anti-HVZ). These vaccines are supplied directly by AST.

DMI physicians set appointments according to the vaccination program discussed and agreed with their patients using a centralized electronic agenda. The same deliver to the patients an accompanying card with the recommended vaccines, CD4, date and time of the appointment, which they must give to the service. The vaccinating physician checks the patient's health status, obtains informed consent and records the vaccination in the regional computer program, releasing the certificate to the patient.

Results: On 03/27/2019 a vaccination program was offered to 876 patients: 774 were vaccinated, while 102 (11.6%) did not attend the scheduled vaccination session. The vaccinated people were 658 M and 116 F, median age of 46.9 ± 11.6 years (range, 21-85) and predominantly (86%) of Italian nationality; the median of CD4 was 717 ± 311 cells/mm3 (range 94-2476), only 11 cases <200. All vaccinates had undetectable HIVRNA.

228 anti-HAV vaccinations (421 anti HAV were done in 2018), 61 anti-HBV, 624 anti-Pneumo, 124 anti-MenB, 457 anti-MenACWY, 107 anti-HPV, 155 anti-HiB, 487 anti-DT and 4 anti-MPR were done. 12 patients (1.5%) presented side events to vaccination: 2 post-injection lipotimia, 3 local reactions in site of inoculation (anti-Pneumo 13) and in 7 cases fever and headache (5 anti-MenB, 2 anti MenACWY).

Conclusions: The vaccination service was favorably received by patients at our center and the recommended adherence rate was 88.%. Adverse events were rare and solved in a 2-3 days. Centralized registration provides practitioners with a useful tool to monitor the patient's vaccination status.

Social and PLWHIV related issues

OC 85 "AMARE CON SAPIENZA": AN INNOVATIVE DIGITAL PREVENTION CAMPAIGN TO INCREASE HIV NEW KNOWLEDGE AND TEST ACCESS IN A LARGE UNIVERSITY COMMUNITY

S. Vita[1], M. Lichtner[2], G. Morlino[3], L. Celani[2], M.A. Zingaropoli[2], V. Perri[2], S. Valeri[2], F. Cogliati Dezza[2], L. Santinelli[2], G. Masci[2], M. Falciano[2], A. Salotti[2], O. Turriziani[4], G. Antonelli[4], C.M. Mastroianni[2], V. Vullo[2]

[1]Infectious Disease Unit, SM Goretti Hospital Latina, [2]Department of Public Health and Infectious disease, Sapienza, University of Rome, [3]Snapback, Rome, [4]Department of Molecular Medicine, Sapienza, University of Rome

Background: The new knowledge, attitudes and practices regarding HIV/AIDS are cornerstones in the fight against the infection. The young adult audience makes massive use of digital media as social networks and chats, and this cannot be ignored for an effective information campaign.
The objective of this study is the evaluation of the effectiveness of digital methodologies to promote the prevention of HIV infection in the youth population.
Methods: The project included 3 phases. During the 1st one a cross sectional questionnaire was sent to university employees and students by email of Sapienza University. The questionnaire included 20 items focused on various methods of transmission and preventive measures including PreP, TASP and U=U concept and HIV test. The 2nd phase included the information campaign via social networks and digital ambient media installed in the university campus, both routing target people to the project website where they could get information about the infection and, importantly, actively contribute to the campaign playing quiz-games that, when correctively solved, animated a digital opera in the campus heart. The 3rd phase included the valuation of the campaign through the same questionnaire sent in the 1st phase, and counting the number of access to the nearby clinical center to perform HIV test, the access to the website and number visualization of social posts. Non-parametric tests were used for statistical analysis.
Results: A total of 5282 persons replied to the questionnaires. The questionnaire answers before the campaign showed that the 78.6% knew that an effective HIV lifelong therapy exists, but only 29.9% thought that a person under successful ART is not contagious. Moreover, 34.5% have heard about PrEP and just 24.7% knew PEP. The 68.3% of the population never did the test. Only 17.8% knows that the test is also available in pharmacy. Fig. 1 shows the informative campaign set up for 2 months.
Through the website and the social campaign were reached about 15.000 persons.
The questionnaire after the campaign showed an increase in knowledge regarding U=U concept, from 29.9 vs 49.4% ($p<0.001$) and a slight increase in PrEP from 34.5% to 37% (p=ns), and PEP knowledge from 24.7 to 39.5%($p<0.0001$). A decrease of rate of the population never did the test was observed from 68.3 to 57.7% ($p<0.0001$). A higher proportion knew that the test is available in pharmacy (17.8 vs 30.1%, $p<0.0001$).
Interestingly in the 2 months period of the campaign, an increase of 31% of the HIV tests and 22% of the new HIV diagnosis was registered in the closer clinical center comparing the same period of the previous year.
Conclusions: The digital ambient media approach used, even if short in time, was effective in improving the new knowledge of HIV prevention strategy and in the access to HIV test. A similar methodology should be used in other similar reality such us school, university or workplace to confirm and ameliorate these data.

Social Science and management of HIV beyond antiretroviral therapy

PD 1 EDUCATIONAL PROJECTS IN SCHOOLS: A RETROSPECTIVE ANALYSIS OF A 15-YEAR ACTIVITY

E. Mozzo[1], V. Ortolan[1], C. Novello[1], F. Batterman[2], N. Gatti[2], M. Crimaudo[2], C. Guaquinto[1]

[1]Fondazione Penta, Padova, [2]Associazione C.A.S.A., Padova

Background: Nowadays information about HIV/AIDS among young people is still insufficient. Education programs in schools are an important tool in order to reduce both the spreading of this infection and HIV-related stigma.

Material and methods: Since 2003 the C.A.S.A. (Condivisione, Accoglienza, Studio contro l'AIDS) association of Padova has promoted HIV educational meetings in various high schools in the Veneto Region. For each classroom, the first two hours consists of a medical doctor discussing the scientific aspects of infection; during the second part, an activist involves students in role-playing activities in order to discuss social aspects of HIV. An anonymous pre- and post-test are administered at the beginning and at the end of the meeting. Three answers for each of the 18 questions are possible: true, false and not known. Questionnaires collected from 2003 to 2017 among 16 years-old students were analyzed in order to highlight areas of major misinformation and to evaluate the efficacy of such educational program.

Results: A total of 3,808 pre and 3,562 post-tests were collected. Analysis of the pre-tests show that principal areas of misinformation are related to legal aspects, methods of transmission, HIV-testing and natural history of infection. With the question "Is it mandatory to reveal seropositive status?" 32.24% answered true, 21.95% false and 45.79% did not know the answer. Only 51.60% are aware that the HIV-test can be anonymous.

30.3% of respondents believed that mosquitoes transmit HIV; only 32.4% of people know that insects don't spread HIV-infection, whilst 37.26% haven't a precise idea.

Sharing of cutlery and toilet is believed to be at risk of HIV-transmission from 33.42% of interviewed; only 37.31% know it is not.

34.95% of students answered "don't know" in response to the question regarding the long interval that can pass between HIV infection and development of AIDS.

A significative difference in the percentage of correct answers among years was not noted.

As far as the post-test survey is concerned, our analysis shows that after the educational meeting 10% of students still gave a wrong answer to the item related to the possibility of HIV-transmission by sharing of toilet services or cutlery. This data can indicate that this incorrect information is deeply rooted in people, thus leading to an unjustified every-day fear of an HIV-infected person and stigmatisation of seropositive people.

Conclusion: Results of this survey show a fair knowledge about HIV among young people. But if we bear in mind that this virus has been detected more than 30 years ago, it is simply not acceptable that someone still believes that mosquitoes or sharing of cutlery are implicated in HIV transmission. We must make an effort to implement educational events – especially among young people. In doing so we can spread real knowledge for the future, preventing not only new infections but also the stigma that surrounds seropositive people.

Social Science and management of HIV beyond antiretroviral therapy

PD 2 A SURVEY AS A CHANCE OF EDUCATION ON U=U IN PLWHIVA

G. Orofino[1], S. Patrucco[2], P. Altini[3], G.L. Cipero[2], A. Perziano[2], C. Owen[2], M. Gay[4]

[1]Ospedale Amedeo di Savoia, Torino, [2]Associazione Arcobaleno AIDS, Torino, [3]Dipartimento di Scienze della Sanità Pubblica e Pediatriche, Torino, [4]Ospedale SS.Antonio e Biagio e Cesare Arrigo, Alessandria

Background: Launched in 2016, the Undetectable=Untransmittable (U=U) campaign declares that a person living with HIV who has an undetectable viral load does not transmit HIV.
The slogan has been endorsed by more than 350 HIV organisations from 34 countries, including leading scientific and medical organisations such as IAS and UNAIDS.
Up to the end of December 2018, the scientific literature did not include any Italian research about U=U and its impact on a national basis.
The aim of this research is to examine the knowledge of the U=U slogan, its meaning and its possible effects on the ordinary lives of a group of people living with HIV+, treated at outpatients' clinics; the survey administration itself has been a chance to inform and educate patients about U=U, so all the respondents now are informed about this issue.
Material and methods: An anonymous questionnaire has been administered to outpatients treated in 2 regional clinics and 2 community centres in Piedmont region, from 15 January to 30 April 2019.
The questionnaire comprises 9 questions, both yes/no and open answers.
It starts with general data such as age, education, gender and sexual orientation, time on ART.
The first part consists of 4 items regarding general U=U knowledge.
The second part is about HIV transmission knowledge/perception: do you think that a HIV+ person, on ART and with constantly undetectable viral load, may infect another person through the three principal ways (sexual, parenteral, vertical)?
The third part includes items aimed at examining the person's effective knowledge of U=U and consequent effects on their behaviours.
The fourth and last part consists of items aiming to explore generalised opinions about other people, both HIV positive and negative.
All the respondents are Italians or Italian speakers.
Results: Up to 15 March, 191 questionnaires have been filled in. Mean age is 47 years, most respondents are high-school educated. Males are 146, females 44, transgender 1; heterosexual are 96, homosexual 77, bisexual 15. Meanly on ART for 10 years (6-month to 32-year span).
158 have never heard of U=U, while only 31 answered they had; about transmissibility in undetectable condition: through unprotected sexual intercourse 100 answered yes and 84 no; through parenteral way 134 answered yes and 47 no; through vertical way 85 answered yes and 86 no.
73 intend to discuss this issue with their physician, 43 do not.
Conclusions: Mid-term results show that U=U, both the slogan and its meaning, is mostly unknown by PLWHIVA in Italy. Should it be better adapted to the national context?
This survey confirms that informational/educational/awareness campaigns are needed by HIV+ people, who behave quite prudently (condom is widely used), but their awareness must be raised to allow them to choose their sexual behaviours more consciously.

Social Science and management of HIV beyond antiretroviral therapy

PD 3 TESTING MSM IN CRUISING VENUES

D. Zagato, A. Andolina, L. Beltrami, A. Bianchi, C. Ferrara, E. Garavaglia, V. La Monica, S. Lolli, L. Londei, F. Maddaloni, M. Manfredini, V. Nicotera, D. Pennisi, A. Pezzotti, M. Pierini, F. Poletti, F. Riili, C. Romero, J. Scalisi, P. Testoni, L. Valpreda, P. Vinti, A. Ünlü, M. Zoia, M. Cernuschi

ASA Associazione Solidarietà AIDS, Milan

Background: Asa Onlus has administered HIV rapid finger-prick tests,in anonymously and free of charge,from April 2018 to March 2019, in MSM cruising venues in order to screen high risk populations.The setting inside the venues is prepared following a standard with one welcoming area and one testing area.The test is carried out by a medical doctor in a space appropriate to protect privacy, who also gives the results.In case of reactive result,and if expressly requested, the doctor plans an appointment in a hospital in Milan for the confirmation HIV blood test.Before the test is carried out,there is an informational interview with an HIV specialist counselor in accordance with legislation.

Methodology: Self-administred questionnaires have been analyzed.Psycho-socio-cultural characteristics of the sample have been detected,and correlated to risk behaviours.Descriptive statistics and interactions between variables have been analyzed through the software STATA.Aim of the study:Describe the sample in order to evaluate risk and harm reduction interventions and early detection of new infections,with particular regard to use of chems or other drugs during sex,to sexual behaviours related to HIV status of the sexual partner,to U=U concept, and to follow-up of reactive results.

Results: 587 male users,Age 31-40 28,29%,High School 43,95 %,MSM 97,34%,Already tested within 1 year 90,28 %,Using Chems&drugs 19.93%,Knowledge of PrEP 67,80%, Group sex in venues 57%, Did not know partner health status 67,7 %,Ejaculation In Mouth 38,33%.Out of 587,10 turned to be reactive(8 in follow up)

Conclusions: In the general sample and in comparison with the last study,more people accepted having sex with people with HIV on treatment.A 5% increase of individuals who took the test within 1 year and a 3,9% decrease of those whom have nerve tested before was observed.The trend of having non protected sex with partner whose HIV status is unknown or is assumed negative supposing a lower risk persists. This data is significant also in the sample using chems.1 out 5 using chems tends not to properly protect during chemsex.Moreover,the trend of not knowing the HIV status of the partner persists.The low number of people using ghb and alcohol(8 people) suggests that a correct information of substance interactions is working.303 only out 528 never had ejaculation in mouth.3 reactive results out of 10 come from urban centers which do not have the same screening offer as Milan.The management of sending people to treatment has adequately worked thanks to the counselors who have also followed the people after the communication of the result.Regarding individuals with positive results even taking PrEP,despite not having feedback on the diagnosis, have admitted taking PrEP on demand, but not having enough notions on drug-taking methods.This data shows that more facilities for consultation on drug-taking methods and follow up should be implemented.

Social Science and management of HIV beyond antiretroviral therapy

PD 4 NOT ONLY MSM: WOMEN AND HIV TEST IN A COMMUNITY-BASED SITE

A. Bianchi, F.M. Esposito, A. Antonino, G. Fracca, M. Lanza, F. Rossi, J.G. Scalisi, R. Repossi, P. Testoni, D. Zagato, M. Cernuschi
ASA, Associazione Solidarietà AIDS Onlus, Milan, Italy

Background: ASA-Associazione Solidarietà Aids since 1985 is an association active in Hiv-Aids prevention and supporting PLWHIV,particularly focused on MSM. Since 2012,once a month,ASA provides in its premises a Rapid Hiv Test,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 infectious disease doc who returns the result. Being the test's result positive a psychologist can assist the person,following their explicit request.Who results Hiv+ is directed to the confirmation test,eventually lead in hospital by the same Rapid Hiv Test doc.The aim is to facilitate the retention in care.The test is part of the association's prevention/early detection programs.Since October 2016 ASA carries out the Rapid Hiv Test also in MSM bars and cruising points.
Methodology: self-administered questionnaires for the period April2018-February2019 have been analyzed. Psycho-socio-cultural characteristics of the sample have been detected,and correlated to risk behaviors. Descriptive statistics and interactions among variables have been analyzed through STATA software.
Aim of the study: to describe the sample for preventive intervention's evaluation and new infections early detection.327 users(M 67,28%, age range 26-30 and older, heterosexuals 54,94%,graduated 41,23%,Hiv already tested 61,16%,students or employees 58%,Italians 89,54%,using Chems 9,8%,n. of partners:3 and more).Out of 327,1 woman and 1 man turned to be positive.A second woman found positive never came back for confirmation test. Here some variables that have been crossed:-Gender(G)by: Age(A),Use of Condom By Partner Type(CPT),Use of Condom by Sex Activities(CSA),Use of Chems(UOC);-N. of partner by:A,G, SexualOrientation(SO),SexUnderDrug&Alcohol,CPT,CSA,UOC;-SO by:CPT,CSA,UOC;-Sex Under D&A by G by:CPT,CSA.
Conclusions: Since we test people in gay bars and cruising points,less MSM are undergoing to tests in our premises.As shown by preceding analysis,the sample is generally careful,regularly undergoing tests,and wearing condoms during casual penetrative intercourses,and seldom in oral sex.A new aspect:only a minimal part of men declares to use condom with every kind of partner(although less than who never use condom).Generally,women declaring to never use condom are 3 times more than men.This difference is enhanced during sex under drugs. Both M&W having casual sex under D&A increased to 1/3 this year vs ¼ last year.34.84% only used condom. M&W equally used chems.MSM are more involved in chems than heterosexuals.Seen the data complexity,to achieve 90-90-90 target we consider useful to follow offering:tests to MSM in bars and venues(where chemsex can occur),PrEP service,chemsex psychotherapeutic group,and inside premises test,particularly aimed to reach women who often neglect the risk.
ASA was supported by ViivHealthcare

Social Science and management of HIV beyond antiretroviral therapy

PD 5 CLINICAL RESEARCH INTEGRATED WITH NARRATIVE-BASED RESEARCH TO UNDERSTAND LIVING AND MANAGING HIV: TMC114FD1HTX4011 - DIAMANTE STUDY

A. Antinori[1], A. Vergori[1], M. Camici[1], V. Esposito[2], M.A. Carleo[2], P. Rosario[2], M. Andreoni[3], V. Malagnino[3], L. Campogiani[3], A. Cascio[4], M. Trizzino[4], G. Mazzola[4], D. Ripamonti[5], D. Valenti[5], E. Manzillo[6], T. Pizzella[6], L. Aprea[6], E. Focà[7], A. Celotti[7], A. Cappuccio[8], L. Reale[8], A. Uglietti[9], D. Mancusi[9], R. Termini[9]

[1]HIV/AIDS Unit, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [2]General Infectious Diseases Unit, Department of Infectious Disease and Infectious Emergencies, Cotugno Hospital, Naples, Italy, [3]Infectious Diseases Clinic, Foundation Policlinico Tor Vergata University Hospital, Rome, Italy, [4]Infectious Diseases Clinic, AOU Policlinico "P.Giaccone", Palermo - Italy, [5]Infectious Diseases Clinic, Papa Giovanni XXIII Hospital, Bergamo - Italy, [6]UOS Infectious Disease and Infectious Emergencies, Azienda Ospedaliera dei Colli, Naples, Italy, [7]Tropical and Infectious Diseases Clinic, ASST Spedali Civili di Brescia, University of Brescia, Brescia - Italy, [8]ISTUD Foundation, Milan, Italy, [9]Janssen-Cilag SpA, Cologno Monzese, Italy

Background: Despite the successful reduction in the morbidity and mortality in the HAART era, living with HIV (LWH) is still difficult with regards to the associated psychological burden. Narrative-based research is an interdisciplinary method based on the collection of patients' written narratives to gain insight on how a person lives his illness.

Material and Methods: The DIAMANTE study started in June 2018 involving 20 centers throughout Italy. This retrospective and prospective, non-interventional study collects data on LWH patients treated with D/C/F/TAF, on therapy effectiveness, and Patient Reported Outcomes (PROs). The study aims to enroll 250 LWH patients, subdivided in 3 groups based on their treatment history. Patients will be observed for 48 weeks after the study enrollment. PROs will be registered by the administration of HIV-Treatment Satisfaction Questionnaires together with the completion of narrative plots at enrollment and at last study visit. Researchers analyze the narratives according to Grounded Theory methodology with the support of the NVivo 10 software.

Results: Since end of February 2019, 138 LWH patients were enrolled in the study, of whom 49 already completed their narrative plots at the first visit. Sociodemographic data are reported in table 1. Narrative showed that patients felt mostly fear and anguish at HIV diagnosis and just 17% expressed confusion. Nevertheless, 73% of LWH patients felt reassured after the first visit thanks to the optimal relationship with clinicians described in 90% of narratives. Therapy is depicted as a doom only in 12% of the narratives; indeed 84% described as relief and protection the moment of the first prescription. HIV infection doesn't impact on daily activities of patients, nevertheless, just 62% coped with the disease. Furthermore, 20% of patients developed new interests and started taking better care of themselves after the diagnosis. The main difficulties arise from the stigma associated with HIV depicted in 86% of experiences. This stigma influenced particularly relationship with friends and colleagues respectively in 92% and 89% of cases: patients decided to keep the secret with people around them because they fear about prejudice and isolation. Nevertheless, when the secret was shared with relatives, partners and close friends, patients surprisingly felt supported and loved. Moreover, 24% of narratives described the fear of infecting people around them while 20% the worry of not finding a partner or having a family. Regarding their future, patients hope in a cure (35%), the end of stigma (12%), having a family (14%) and serenity (23%) while just 16% described fear

Conclusions: For the first time, a clinical study includes patients' narratives as PROs, pointing out as HIV impacts on patients' lives despite the HAART (i.e. poor symptoms and/or limitations on daily activities). Narratives correlated with clinical data will highlight new information for HIV management and prevention

Social Science and management of HIV beyond antiretroviral therapy

PD 6 "INTEGRATED PROTECTION FOR PEOPLE LIVING WITH HIV IN ANGOLA" (PIPSA) A "TEST/TREAT/ PREVENT HIV PROGRAM". PRELIMINARY DATA

*L. Verzotti[1,2], T. Baldoni[1,2], S. Guedes[1], E. Braganha de Nascimento[1], J.C.G. Da Costa[3], T. Chilumbo[4], S.V. Loa[5], G. Pellizzer[6], Nigro[1,6] for PIPSA Activists**

[1]Protecção integral para o Paciente Seropositivo Angola (PIPSA), Luanda, Angola, [2]Unione Medico Missionaria Italiana (UMMI), Verona, Italia, [3]Repartição Municipal de Saúde do Municipio de Kilamba Kiaxi, Luanda, Angola, [4]Direcção Provincial da Saúde de Luanda, Luanda, Angola, [5]Hospital Divina Providência; [6]Medici con l'Africa-Cuamm, Padova, Italia

Introduction. Antiretroviral therapy reduces the risk of serious illness among people living with HIV and when adhered to consistently can reduce the HIV viral load to such a low level that can prevent HIV transmission. We implemented a "Test/Treat/ Prevent HIV Program" (PIPSA) addressed to general population in nine health centers of Kilamba Kiaxi, a district of Luanda, to provide HIV information, to increase HIV counseling and testing, to help those who tested positives to start antiretroviral therapy, and adhere to treatment.

Methods and materials. We recruited and trained 10 activist for testing. Activists walk-in to clinics and use a peer-driven intervention to inform the daily client of the clinics and of the out-patient clinics on HIV prevention and on the importance of being tested; than the activists test the clients who accept to be tested and accompany and support those who tested positives in starting TARV. As a final point the activists through home care inform on the importance of starting TARV, adhering and retaining in care.

Result. PIPSA testing started 26st of November 2018 and is still ongoing.

The project is carried out in Luanda at Divina Providencia Hospital (HDP) and in eight out-patient clinics, three belonging to the municipality e five to HDP.

HIV rapid test is performed utilizing Determine and Unigold tests.

From October 2018 to February 2019, 17699 people, 71% F and 29% M, have been informed about the HIV virus and its routes of transmission. Of these 4010, 23%, agreed to be tested and were counseled and tested, 75% F and 25% M; females tested were 24% of the total, males 19%.

Of those tested 144 (3.6%) were positives, 29% M and 71% F; the positive rate was 3.4% for females and 4.3% for males. 16% of those tested positive have initiated TARV, 35% are receiving home based care to be accompanied to treatment and 49% refused to be treated.

Conclusion. Our preliminary data show that the HIV prevalence found in our sample seems higher than that of the country (3.6% vs 2.0%), this could be due to the fact that people tested are people who are attending an out-patient clinic, so not all of them are healthy. Only 23% of people informed accepted to be tested and most of them were females (75%). Only 25% of people tested positive have accepted and initiated TARV within two weeks from testing.

Furthermore our project indicate that a "Test/Treat/ Prevent HIV Program" involving peer operators (activists) is well accepted by people, in fact: most of the people have understood the importance of finding HIV infection on time. There is a need improve support and accompaniment of those who tested positives in starting TARV.

PIPSA is funded by Agenzia Italiana per la Cooperazione allo Sviluppo (AICS) and will last three years.

*PIPSA Activists: J. Bengui, M. Cardoso, U. Fernandes, M. Fundumuka, B. Gaspar, P. Kalandula, T. Mambo, C. Salvador, R. Salvador, J. Vemba.

Social Science and management of HIV beyond antiretroviral therapy

PD 7 RETENTION IN HAART AMONG YOUTH ACCESSING SAAJ (SERVIÇOS AMIGOS DOS ADOLESCENTES E JOVENS) IN BEIRA, MOZAMBIQUE

C. Vitali[1], G. Prennusci[2], E. Namarime[3], D. Pizzol[4], G. Putoto[5], L. Praticò[6]

[1]University of Pavia, Pavia, [2]University of Pavia, Pavia, [3]Doctors with Africa CUAMM, Beira, [4]Doctors with Africa CUAMM, Padova, [5]Doctors with Africa CUAMM, Padova, [6]Doctors with Africa CUAMM, Padova

Background: The extensive use of HAART improved health condition of HIV+ people and reduced transmission even in high prevalence settings like Sub-Saharan Africa where the transmission rate is still very high, especially in vulnerable categories. The study investigated determinants of retention in HAART among HIV+ youth in Beira, Mozambique, where the HIV prevalence rate is 16.3%. The research is based on field work carried out during March-June 2018 in 5 youth services (SAAJs, Serviços Amigos dos Adolescentes e Jovens). The SAAJs provide medical and psychological assistance, including HIV testing, counselling and treatment to youth aged 10 to 24 years, as part of a national program of the Health Ministry supported by Italian NGO Doctors with Africa-CUAMM.

Material and methods: The study was based on 18 focus group discussions with youth and activists from 3 community-based organizations, as well as 8 informant interviews with health practitioners from the SAAJs, activists and NGO coordinators. A retrospective analysis of patient records data and a prospective follow up on retention to treatment over a period of 9 months were performed. Further data on determinants of retention were extracted from the activist organizations' records of patients who had abandoned HAART.

Results: The quantitative data indicated that retention in HAART is indeed a serious issue, with about 25% of patients dropping out every month and only about 5% returning (see table n.1). Focus groups and interviews confirmed that patients often drop out in the initial phase of treatment because of side effects, as well as logistical difficulties in reaching the centres or frequent moves. Activist records confirmed that patients do not pick up their drugs at the SAAJ (29% forgot the appointment date, 16% were sick) or refuse to continue because of side effects (12%) (see chart n.1). The youth focus group discussions, on the other hand, shed light on deeper socio-cultural factors affecting retention, namely stigma and discrimination in the family and community. Most of the patients spoke of the fear of being seen by family members or neighbours while going to the SAAJ. Young women in particular seldom reveal their HIV status to family members (especially fathers and partners), and are thus at greater risk of abandoning treatment. Encouragingly, however, pregnant women are more likely to access the SAAJ; 80% of SAAJ accesses are women, 10% of whom are pregnant.

Conclusions: While Mozambique took the bold step of offering free HAART and runs sexual and reproductive health programs for adolescents, retention rate is still too low. This study offers insights into interventions that can help increase adherence by addressing not just access to centres and side effects but also discrimination. In particular, HIV+ activists who seek out patients who abandon treatment can play an important role in sensitizing families and communities, overcoming stigma, and increasing retention.

Social Science and management of HIV beyond antiretroviral therapy

PD 8 IMPLEMENTATION OF HIV PATIENTS CARE THROUGH PERSONALIZED EXERCISE PROGRAM

P. Vassalini, E.N. Cavallari, L. Santinelli, C. Borrazzo, L. Celani, G.P. Innocenti, G. Ceccarelli, G. Tancredi, C. Mastroianni, V. Vullo, G. d'Ettorre

Sapienza University of Rome, Rome

Background: Complementary interventions to antiretroviral therapy aimed to reduce residual immune activation play an important role in long term management of HIV infected individuals. Althoug exercise is generally considered a beneficial practice, attention should be payed when considering HIV patients because training can affect the immune system, causing immune suppression and pro-inflammatory effects depending on its intensity and frequency. Personalized exercise programs could exert a beneficial role on patients' immune activation, minimizing the risks associated with an exessive training.

Methods: Sedentary HIV infected individuals on effective antiretroviral treatment were randomized to start a 12 weeks personalized program of combined aerobic and resistance exercise or to keep their usual habits (sedentary status was defined through metabolic holter and a validated survey). Participants in the interventional group underwent blood sampling, bioimpedentiometry, ECG stress test and cardiopulmonary exercise testing (CPET) at baseline (T0) and at the completion of the program (T1). Subjects in the control group underwent blood sampling at T0 and after 12 weeks. Exercise was prescribed by a Sports Medicine specialist on the basis of the results of the baseline evaluation and a wrist heart rate monitor was provided to every participant in the interventional group with the indication to exercise between 60-81% of maximal heart rate.

Results: 102 subjects were randomized into the exercise group (n=72) and a control group (n=30). At T0, similar levels of immune activation were observed between the two groups. At T1, subjects in the interventional group showed decreased levels of activated CD4 and CD8 T cells in respect to baseline (Table 1) and lower levels when compared to controls. After exercise, participants showed improvement in stress test maximal heart rate (p=0.04), test duration (p=0.012) and walked distance (p=0.013), while the analysis of respiratory gas consumption with CPET showed improved results althoug without significant differences. Participants' body composition was similar at T1 and T0, on the other hand body cell mass (fat-free component of cells within muscle) increased after training (p=0.026). No adverse events were observed during the study.

Conclusions: In our population, personalized exercise training was safe and promoted a reduction of participants' immune activation. Further studies are needed to evaluate the long term effectcs on HIV co-morbidities.

Social Science and management of HIV beyond antiretroviral therapy

PD 9 IN-HOSPITAL VACCINATION PROGRAM FOR HIV POSITIVE PATIENTS: WHO ARE THE UNVACCINATED INDIVIDUALS

D. Barbanotti, L. Gazzola, A. De Bona, G. Ancona, F. Bai, S. Cianciola, K. Reister, P. Tognetti, C. Tincati, G. Marchetti, T. Bini, A. d'Arminio Monforte

Department of Health Sciences, Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, University of Milan, Italy

Background: Despite high efficacy of antiretroviral therapy, HIV population remains at risk of acquiring infections. Active immunization represents an effective tool to prevent many infectious diseases, with in-hospital vaccination being a promising strategy to increase patients' compliance. Aim of this study is to describe factors associated to undergoing vaccination program and of being already exposed to HAV and HBV hepatitis viruses.
Methods: A vaccination schedule program for HIV patients has activated at our out-patients clinic. According to international and Italian guidelines, vaccine offer included PCV13, MenACYW135, MenB, influenza virus, HAV, HBV (in HBsAg/Ab neg) and, for high risk patients younger than 45 years of age, HPV-9. All patients in care were offered to access vaccine schedules, according to the availability of different vaccines in the study period. All subjects signed informed consent for each administration.
Demographical and immunovirological characteristics of vaccinated patients were compared with unvaccinated HIV population in charge at our unit. Last visit before first access to program for vaccinated group and last values available for unvaccinated group were considered. Factors associated with access to vaccine program and to HAV/HBV immunization were evaluated by uni- and multivariate logistic regression analysis (including age, sex, nationality, HCV and risk factors for HIV).
Results: From December 2017 to January 2019, 379 consecutive HIV patients entered the vaccination schedule program and received at least one vaccine dose (Figure 1).
Patient entering the program were younger, more frequently male, MSM, Italian; all were on ART, with higher CD4 count as compared to patients not attending vaccination program (Table 1).
Multivariate logistic regression analysis showed that being older (aOR for each year more: aOR 0.9 [IC95% 0.9 -0.99], p=0.002) and non-Italian were factors associated with a lower probability to access the vaccination program (OR vs Italian pts 0.6 [IC95% 0.5-0.9]p=0.002), while being MSM was associated with higher probability (OR vs other risk factors 2.1[IC95%1.5-2.8] p>0.0001).
166/286 (58%) patients were HAVAb pos; factors associated with HAV positivity were being older and non-Italian; 84/307 (27.4%) were HBsAb pos/HBcAb neg (immunized). Younger age was associated with higher probability of HBV immunization; 108/327 were HBcAb pos: being older, male, non-Italian and HCV positive were risk factors associated with previous/ongoing HBV exposure (Table 2).
Conclusions: Vaccine schedules proposed to HIV-pos subjects in charge at our out-patient unit are unattended by more fragile populations, such as elderly, non-Italian, IDU and females, less conscious of their health issues. Moreover, non-Italian and older subjects are more frequently exposed to HAV/HBV, while young and Italians, have been more frequently vaccinated for HBV. Campaigns focused to high risk individuals should be promptly implemented

Social Science and management of HIV beyond antiretroviral therapy

PD 10 NON-OCCUPATIONAL POST-EXPOSURE PROPHYLAXIS: HOW EVERYDAY CLINICAL PRACTICE COMPLIES WITH GUIDELINES RECOMMENDATION?

R. Rossotti, M. Cantone, L.G. Chianura, M.C. Moioli, S. Chiappetta, F. Crippa, M. Merli, D. Motta, C. Orcese, A. Pazzi, G. Travi, B.P. Vigo, M. Puoti

Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan

Background: Non-occupational Post-Exposure Prophylaxis (nPEP) is an effective way to prevent HIV infection after unsafe behaviors. National and International Guidelines provide tools to decide when nPEP is recommended, but general indications are not always applicable in everyday clinical practice: some important information is often missing; the setting of prescription could be chaotic and without adequate privacy; the exposed client might be under the effect of recreational substances or an excessive anxious state. As a consequence, each physician could have different approaches for the case evaluation and nPEP prescription. Aims of present study: assess nPEP prescriptions in our Hospital and if they comply with what is recommended by Guidelines.

Methods: All the subjects who have been evaluated in the Emergency Room for nPEP prescription from 2013 to 2018 were retrospectively enrolled. Demographic, behavioral and clinical characteristics were collected. Relevant features (type of contact, serostatus of source partner, presence of additional risk factors) were used to build models that were compared with what recommended by SIMIT, EACS, BHIVA and DHHS Guidelines. Descriptive statistics and kappa test were used.

Results: 212 clients were analyzed: 94.3% were sexual and 5.7% non-sexual exposures. They were mainly men (91.5%) and Italian (81.1%) with a median age of 31 years (IQR 26-37). MSM were the majority (60.8%) and receptive anal intercourse was the most common way of exposure (32.1%); condom was not used in 53.3% of cases, while the source was a known HIV-positive individual in 39.6% of cases. 12.3% of subjects used nPEP more than once. nPEP was prescribed in 77.4% of contacts: no HIV transmission was observed.

The combination FTC/TDF+RAL, recommended as first line regimen by most Guidelines, was used in 67.0% of individuals: 2.9% used a backbone and 13.6% a third drug listed as alternative; 4.4% used drugs not recommended for nPEP prescription.

Reassessing each case according to what recommended by the Guidelines, SIMIT and EACS would have prescribed nPEP in a higher number of cases (82.1% and 91.5%, respectively), while BHIVA and DHHS would have confirmed less prescriptions (56.1% and 62.7%, respectively). The concordance was generally low (ranging from 58.0 to 76.4%) with an inter-rater agreement poor (when compared with SIMIT, EACS and BHIVA) or fair (when compared with DHHS). Moreover, concordance was low also when comparing the Guidelines between them (Figure 1).

Conclusions: Prescription of nPEP generally complies with recommended in terms of selected drugs. The prescription approach is intermediate when compared with what modeled from the Guidelines statements, but concordance is generally low. Nevertheless, each Guideline relies on different attitudes, thus great diversity in prescription policies is observed. A more conserved approach to nPEP is warranted.

Clinical HIV and Epidemiology

PD 11 DOLUTEGRAVIR-BASED ANTIRETROVIRAL REGIMENS FOR HIV LIVER TRANSPLANT PATIENTS IN REAL LIFE

D. Cattaneo, S. Sollima, P. Meraviglia, L. Milazzo, D. Minisci, M. Fusi, C. Gervasoni

ASST Fatebenefratelli Sacco University Hospital, Milano

Background: Liver transplantation is now considered a safe procedure in selected HIV-infected patients. Moreover, potential concerns related to drug-drug interactions between immunosuppressive agents and HAART have been overcome by the availability of booster-free, integrase inhibitor-based regimens. Only a few, scanty data are available on the use of dolutegravir in real life transplant settings.

Methods: The database of our Infective Diseases Clinics was investigated in search for liver transplant recipients on calcineurin inhibitor (CNI)-based maintenance immunosuppression being concomitantly treated with dolutegravir with at least one year of follow-up after dolutegravir introduction.

Results: Ten HIV-positive, liver transplant recipients were identified (9 men, 1 woman, mean age 57±3 years), being transplanted from 5.8±3.2 years. The immunosuppressive therapy consisted of tacrolimus (n=4) or cyclosporine (n=6), eventually combined with everolimus (n=2). After the transplant, as antiretroviral regimens the patients were being treated with TDF/FTC (n=7) combined with raltegravir (n=5), dolutegravir (n=1) or unboosted fosamprenavir (n=1); the remaining 3 patients were given ABC/3TC/raltegravir, raltegravir/atazanavir/ritonavir or raltegravir/darunavir/ritonavir, respectively. At 4.6±3.5 years post-transplant, all the patients were shifted to dolutegravir combined with TAF/FTC (n=6), ABC/3TC (n=1), darunavir/cobicistat (n=1) or unboosted atazanavir (n=1). At 1 year after the switch, 5 out of the 10 patients returned to their previous antiretroviral regimens for safety concerns. Specifically, one patient experienced increment in serum transaminases (+100%) associated with variable and unpredictable tacrolimus trough concentrations; one patient experienced increased serum creatinine concentrations (+125%) associated with variable and unpredictable cyclosporine trough concentrations; two patients experienced increased serum creatinine concentrations (40-60% increments); the last patient experienced repeated episodes of nausea/vomiting. Clinical conditions and laboratory examinations improved in all the patients after returning to the initial HAART.

Conclusions: Here, we have shown that the switch to dolutegravir was poorly tolerated, with half of the patients requiring switch back to their previous antiretroviral regimens. It should be recognized, however, that the safety concerns cannot be univocally ascribed to dolutegravir, but eventually also to cobicistat or CNI toxicity. We hypothesized that the observed significant fluctuation in the CNI concentrations might be ascribed to unanticipated effects of dolutegravir on ABC transport proteins.

The management of HIV-infected liver transplant recipients in clinical practice is a complex mission, aiming at balance the possibility to simplify antiretroviral regimens with the need to guarantee optimal immunosuppression and finest treatment tolerability. Such task requires a multidisciplinary approach.

Clinical HIV and Epidemiology

PD 12 HIGH INCIDENCE AND PREVALENCE OF SYPHILIS AMONG HIV-INFECTED MSM IN THAILAND

C. Muccini[1,2], S. Pinyakorn[3,4], C.J Kolsteeg[5], E. Kroon[2], C. Sacdalan[2], P. Prueksakaew[2], P. Phanuphak[2], J. Ananworanich[2,3,4], N. Phanuphak[2], D. Colby[2]

[1]Vita-Salute San Raffaele University, Milan, Italy, [2]SEARCH, The Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [3]U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, USA, [4]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, USA, [5]Utrecht University, Utrecht, The Netherlands

Background: Syphilis is a common sexually transmitted infection among men who have sex with men (MSM). It has been reported to increase HIV viral load (VL) and decrease CD4+ cell counts among HIV-infected persons. We report on syphilis prevalence and incidence in a cohort of HIV-infected individuals in Thailand and evaluate VL, CD4+, CD4+/CD8+ ratio pre and post-syphilis infection.

Methods: Syphilis diagnosis was analyzed during 2009-2018 in participants enrolled in the RV254/SEARCH010 cohort of acute HIV infection (AHI) in Bangkok, Thailand. VDRL was performed at baseline and every 24-48 weeks on all participants and when clinically indicated. Positive results are confirmed with RPR titer and TPHA. CD4+ and CD8+ testing, VL testing and clinical evaluation are performed every 12 weeks.

Results: Among 579 participants with AHI median age was 26 (IQR 22-31) years at enrollment, 97.4% were male and 94% were MSM (Table 1). Syphilis prevalence at baseline was 14.3% (n=83), rising from 4.4% in 2010 to 20% in 2017 and declining to 14.3% in 2018 (Chi-square test for trend p=0.003) (Figure 1).

Overall incidence (per 100 person-years) was 10.2%, increasing from 3.1 in 2010 to 16.5 in 2015 and remaining in the range 11-14% through 2018 (Chi-square for trend p=0.03) (Figure 2).

Cumulatively, 39.2% of the cohort had at least one episode of syphilis and 30.9% had reinfection during follow-up.

On multivariable analysis, participants with syphilis were more likely to be MSM (HR 3.68, 95% CI 1.16-11.62), use methamphetamine (HR 2.31, 95% CI 1.51-3.54) and have hepatitis C coinfection (HR 2.63, 95% CI 1.59 -4.34). Syphilis was not associated with age, being a student, alcohol use, drug injection, or hepatitis B.

Among 155 participants with 222 episodes of syphilis and who had VL <50 copies/mL pre-syphilis diagnosis, and data available before syphilis, at syphilis diagnosis and after treatment, 6 participants had VL >50 copies/mL at syphilis diagnosis, increasing to 9 after treatment (p=0.03, pre vs. post syphilis). Median (IQR) detectable VL (log10copies/mL) were 3.8 (1.9-5.2) and 2.6 (2.2-4.1), respectively.

Median (IQR) CD4+ counts (cells/mm3) were higher before syphilis at 663 (532-813) vs. 624 (501-774) at syphilis diagnosis (p=0.07), rising to 660 (547-826) post syphilis treatment (p=0.001, at syphilis diagnosis vs. post syphilis). Median (IQR) CD8+ counts (cells/mm3) were 607 (460-837) at syphilis diagnosis, a decline from 639 (491-840) pre-syphilis (p=0.42), and rebounded to 679 (527-870) post-syphilis treatment (p=0.0007, at syphilis diagnosis vs. post syphilis). CD4+/CD8+ ratio was stable at three time points [1.02 (0.78-1.38) vs. 1.04 (0.80-1.39), p=0.28 vs. 1.00 (0.77-1.31), p=0.03].

Conclusions: Syphilis incidence and prevalence are high among HIV-infected MSM in Bangkok. Syphilis appears to have a minimal effect on HIV VL among participants on antiretroviral therapy with viral suppression but is associated with a transient and modest decline in CD4+ count.

Clinical HIV and Epidemiology

PD 13 IS HIV SORTED? SURVEY – RESULTS HIGHLIGHTS FOR ITALY

B. Audoin[1], R. Caldera[2], M. Carlevari[2], S. Head[3], C. Zocchetti[2], J. M. Zuniga[4]

[1]International Association of Providers of AIDS Care (IAPAC), Paris, [2]Gilead Sciences srl, Milan, [3]Gilead Sciences Europe Ltd, Stockley Park, Uxbridge, [4]International Association of Providers of AIDS Care (IAPAC), Washington DC

Background: Fast-Track Cities is an initiative that aims to assist multiple stakeholders to accelerate and scale-up urban AIDS responses to reach the 90-90-90 treatment targets. The Is HIV Sorted? survey was commissioned by the International Association of Providers of AIDS Care (IAPAC) and Gilead Sciences. The survey aimed to provide insights into the general publics' awareness, perceptions, knowledge, and attitudes towards HIV and people living with HIV (PLHIV).

Material and methods: The survey included over 24,000 respondents (HIV-negative adults) from12 European countries (Italy, Ireland, Russia, Austria, France, Germany, Netherlands, Romania, Spain, Switzerland, Ukraine, and the United Kingdom). The Italian data (n=2,035) have been extrapolated.

Results: While there is low awareness about the means by which HIV is transmitted, respondents were generally open to HIV testing. However, 60% had never been tested for HIV. 72% would take an HIV test after engaging in unprotected sex with a new partner, the second highest of all countries surveyed. 87% do not believe they are at risk of acquiring HIV, yet over a quarter (27%) believe that HIV can be acquired by sharing a toothbrush with a PLHIV, and 11% believe you can get HIV from kissing a PLHIV. 16% think the term 'undetectable' means a person is free of HIV symptoms, and 52% of all respondents believe that PLHIV can still transmit the virus if their HIV treatment is having the 'best effect possible'.

34% agree HIV stigma is a thing of the past, and people have neutral attitudes towards PLHIV. However, 36% would not feel comfortable working with a PLHIV, and 10% of all respondents would not feel comfortable at all, which is the highest of all countries surveyed in Western Europe. Those who work in a hospital are most open to working with PLHIV (18%), while those in a school/college are most averse (44%). Over half (52%) of all respondents think PLHIV should not be allowed to work as health professionals and 50% think PLHIV should not be able to work in a hospital or care home.

Although HIV treatment has been dramatically simplified in recent years, only 13% of respondents think that PLHIV need to take 3 pills, 3 times a day (on average) to manage their HIV. This is the most encouraging response from all countries surveyed.

Conclusions: HIV-stigma is a major barrier to testing, which is the first key step to achieving the 90-90-90 treatment targets. A lack of HIV literacy among the general public not only contributes to HIV-related stigma, but also affects how the general public approaches HIV testing and prevention in their own lives. These survey data are valuable to initiatives such as Fast-Track Cities, enabling local stakeholders to work towards eliminating misperceptions about HIV, strengthen primary HIV prevention efforts, and make use of the tools we have to treat and prevent HIV.

Self-described

1 The Antiretroviral Therapy Cohort Collaboration. Survival of HIV positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. The Lancet. http:// dx.doi.org/10.1016/S2352-3018(17)30066-8 Available at: https://www.thelancet.com/journals/lancet/article/PIIS2352-3018(17)30066-8/fulltext [last accessed November 2018]

2 International Association of Providers of AIDS Care. About Fast Track-Cities. Available at: https://www.fast-trackcities.org/about [last accessed November 2018]

3 Opinium. Is HIV sorted survey (sample: 24,212). June–July 2018. Survey commissioned by the International Association of Providers of AIDS Care (IAPAC) and Gilead Sciences

Clinical HIV and Epidemiology

PD 14 IMPACT OF HIV SELF-TEST (HIVST) IMPLEMENTATION ON NEW HIV DIAGNOSES IN ITALY

G. Chiradia[1], A. Navarra[1], S. Pittalis[1], G. De Carli[2], N. Orchi[2], V. Puro[2], E. Girardi[1]

[1]Clinical Epidemiology Unit - National Institute for Infectious Diseases "L. Spallanzani" - IRCCS, Rome, [2]AIDS Reference Center- National Institute for Infectious Diseases "L. Spallanzani" - IRCCS, Rome

Background: Different studies highlighted the acceptability of HIV self-test (ST) both in general and key populations. Since December 1st 2016, blood-based self-test is also available in Italy, purchased over-the-counter through Italian pharmacies, for adults (>18 yrs). However, little is known about the impact of this HIV testing strategy for new HIV diagnoses and the relative contribution of HIVST in favouring access to HIV testing in our country.

The aim of the study was to estimate the contribution of availability of self-testing in favouring HIV diagnoses in Italy. Moreover, we compared epidemiological and clinical characteristics of newly ST diagnosed persons with those of facility-based conventional testing (CT) HIV diagnoses.

Methods: We conducted a prospective study in the largest public HIV counselling and testing centre in Rome. We analysed data collected in the context of an ongoing regional, multi-centre observational study on adults newly diagnosed with HIV infection, focusing on those attending the centre for voluntary HIV testing (excluding persons tested for pregnancy, blood donation or surgery) from Oct. 2017 to Sept. 2018. We performed Fisher's exact test to compare characteristics of individuals newly diagnosed through ST with those diagnosed through CT during the same period, and investigated knowledge, attitudes and practices (KAP) on ST.

Results: During the study period, out of 147 persons newly diagnosed with HIV infection, 14 (9.5%) had a first positive result with HIVST. Twelve (85.7%) were men-who-have-sex-with-men (MSM), only 2 (14.3%) were foreigners, 2 (14.3%) were first-time testers and the median first CD4 cell count was 535 cells/mmc. Compared with CT-diagnosed individuals, persons newly diagnosed through ST were more frequently MSM (74.6% vs 58.7%), born in Italy (85.7% vs 62.4%), younger (31 vs 36 yrs) and had higher median CD4 cell counts (535 vs 396 cells/mmc), though none of these differences reached statistical significance.

Forty-nine persons (10 diagnosed through ST and 39 through CT) answered the KAP questionnaire.

Among 10 ST-diagnosed, 70% found it easy to perform, and 50% thought that it reduced anxiety of waiting for test results.

Of 39 CT-diagnosed, 25 (64.1%) were aware of ST and one performed it once; of these, 72% believed that HIV test should be performed by a healthcare worker, 36% that the ST result was not reliable, 48% that it reduced anxiety of waiting for test results and 56% that ST is easy to perform.

Conclusions: Based on this preliminary observation, we hypothesize that availability of over-the-counter HIVST may favourably impact access to testing, and possibly increase the likelihood of an earlier HIV diagnosis. The majority of interviewed persons deemed that ST was easy to perform and one third that the result was not reliable; reduced time to obtain test results was considered important. Anyway, a non-negligible percentage of interviewed persons were unaware of self-testing availability.

Clinical HIV and Epidemiology

PD 15 "TEST AND TREAT": STATE OF THE ART. DATA FROM AN ITALIAN MULTICENTER COHORT

G. Baldin[1], A. Ciccullo[1], S. Rusconi[2], V. Borghi[3], A. Giacometti[4], S.T. Kiros[5], M. Colafigli[6], A. Lanari[7,8], L. Celani[9], A. De Vito[10], A. Giacomelli[2], C. Mussini[3], G. Sterrantino[5], S. Di Giambenedetto[1,11]

[1]Istituto di Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, Italy, [2]Infectious Diseases Unit, DIBIC Luigi Sacco, University of Milan, Milan, Italy, [3]Azienda Ospedaliero Universitaria di Modena, Clinica Malattie Infettive e Tropicali, Modena, Italy, [4]Clinic of Infectious Diseases, Dept. of Biomedical Sciences and Public Health, Polytechnic University of Marche, Ancona, Italy, [5]Division of Tropical and Infectious Diseases, 'Careggi' Hospital, Florence, Italy, [6]Infectious Dermatology and Allergology Unit, IFO S. Gallicano Institute (IRCCS), Rome, Italy, [7]Infectious Diseases Unit, AOU Senese, Siena, Italy, [8]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [9]Department of Public Health and Infectious Diseases, Azienda Policlinico Umberto I, Rome, Italy, [10]Department of Clinical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [11]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, UOC Malattie Infettive, Roma, Italy

Introduction: Test and treat (T&T) strategies are quickly gaining attention from clinicians, thanks to the availability of new drugs with improved virologically efficacy and high genetic barrier. Moreover, in low-income countries, T&T has a central role in the "treatment as prevention" approach. Data on T&T strategies in Italy are still lacking. Our aim is to describe clinicians' approach toward new HIV infections.

Material and Methods: We analyzed a multicenter cohort of HIV-1 infected patients (pts) diagnosed in 2018. We registered information about the dates of first positive HIV-1 test (including also self-test), first visit after the diagnosis, first blood tests for viro-immunological assessment (including genotypic resistance test), and antiretroviral therapy (ARV) initiation. We recognized 3 groups of pts: the "one-day treatment" (1DT) group, in which pts started ARV in the same day of the first blood sample; the "fast treatment" (FT) group, including pts that started ARV within 7 days and "standard of care" (SOC) in which therapy was started after 7 days. We excluded from the analysis pts with concomitant diagnosis of tuberculosis. We used chi-square test and Kruskal-Wallis test to compare categorical and continuous variables, respectively, between groups.

Results: We enrolled 188 pts from 9 Italian clinical centers, with a median age of 39 years (InterQuantile Range [IQR] 33-49); 154 (82.8%) were males, 133 (79.6%) were Italians and 36 (20.6%) were AIDS presenters. Median CD4+ cells count was 285 (IQR 120-498) cells/mmc and peak HIV-RNA was 5.29 (4.57-5.79) log copies/mL. As to ARV regimens, 113 pts started a triple therapy with tenofovir/emtricitabine plus an integrase inhibitor (78 with dolutegravir, 19 with elvitegravir and 16 with raltegravir), 32 with abacavir/lamivudine/dolutegravir, 21 with tenofovir/emtricitabine plus boosted darunavir, 11 with tenofovir/emtricitabine plus rilpivirine. Two pts started a dual therapy with lamivudine and dolutegravir. Median times from HIV diagnosis to the first visit and ARV initiation were 6 days (IQR 1-12) and 14 (IQR 7-27), respectively. Median time from the first visit and ARV initiation was 7 days (IQR 1-14). At ARV initiation, genotypic resistance test was available in 42.3% of pts, HIV-RNA determination in 85.8% of pts and CD4+ cells count in 91.5% of pts. Regarding the above described classification, 40 (21.3%) pts belonged in the 1DT group, 52 (27.7%) in the FT group and 96 (51.0%) in the SOC group. We registered statistically significant differences in CD4+ cells count ($p=0.030$), HIV-RNA ($p=0.025$), ARV regimen ($p<0.001$) and AIDS events at diagnosis ($p=0.017$) between the three groups.

Conclusions: Our data provide a snapshot of the Italian reality on the use of T&T strategies in clinical practice. In our cohort, the preferred approach is a more cautious one, with the clinicians preferring to start ARV after results from biochemistry and viro-immunological parameters.

Clinical HIV and Epidemiology

PD 16 TRACING THE FIRST HIV-1 EPIDEMICS IN THE MILAN AREA

A. Lai[1], A. Bergna[1], G. Zehender[1], A. Giacomelli[1], M. Ciccozzi[2], C. Balotta[1], M. Galli[1]

[1]Department of Biomedical and Clinical Sciences "Luigi Sacco", University of Milan, Milan, Italy, [2]Unit of Clinical Pathology and Microbiology, University Campus Bio-Medico of Rome, Rome, Italy

Background: Based on molecular phylogenetic analyses of early strains,the introduction of HIV-1 in Europe dates back to the early 1980s mainly through homosexual contacts from the USA or heterosexual contacts with subjects from Central Africa.The first cases of HIV in Europe have been identified in the UK among MSM,all carrying B subtype.In our country the first evidences of HIV-1 infections were reported in Milan area among IDUs.The aim of this study was to investigate the origin and the dynamics of first HIV cases in metropolitan area of Milan to understand future trends of the epidemics in term of intermixing among risk categories.
Methods: We analyzed 106 pol sequences collected between 1997 and 2002 at 'L. Sacco' Hospital of Milan from patients who have first HIV-positive test ranging from 1982 to 1999.The transmission networks were identified by MrBayes.Dated phylogeny was performed using Beast program considering two separate datasets, the first including IDUs(n=44) and the second involving subjects with sexual risk(n=53).The population grow was studied with the exponential model that fitted better than the others.
Results: Male were 70.7%(n=75);IDUs,HEs,MSM,bisexual and unknown risk were 41.5%(n=44),34% (n=36),13.2%(n=14),4.7%(n=5)and 6.6%(n=7),respectively.Only two patients carried non B subtypes and were excluded from the analyses.Based on tree topology 30 patients(28.8%) grouped into 9 significant epidemiological networks that included 2 to 9 sequences.No differences were observed in the distribution of risk categories inside or outside clusters;males were significantly more present in clusters than females(36.5%vs.10%, p=.007).For IDUs the dated phylogeny showed that the root of the tree dated back 33 years (95% HPD:4.7 -71.6) and the median tMRCA of significant clusters was 27 years (95% HPD:3.4-60.6) before 1999, corresponding to year 1972.For sexual transmission dated phylogeny showed a tMRCA of 58 years for the root (95% HPD:10-166.3),the median tMRCA of significant clusters was 35 years (95% HPD:5.4-145.8) before 2002,corresponding to year 1967.The estimated mean grow rate for IDUs was 1.2 (range:0.02-2.57) resulting in an estimated R0=12.8 considering a mean infectious period of 10 years and doubling time of the epidemics of 7 months. Differently,these parameters were 0.5(range:0.0014-1.15),R0=6 and 15 months of doubling time for sexual transmissions.The Bayesian Skyline plot showed that cases of sexual transmission exponentially grew from the beginning until 1980 when they reached a plateau;the IDUs started their exponential grow until reaching the plateau in 1990.
Conclusions: Our study indicated an early introduction of the virus at the end of 70s,ten years before the identification of first cases.We observed initial multiple penetration events related to sexual modalities of infection followed by the spread among IDUs,characterized by a highest R0 and doubling time of infection that explains their role in fueling the epidemic.

Clinical HIV and Epidemiology

PD 17 PHILOGENETIC ANALYSIS OF HIV-1 IN FOREIGN PATIENTS FOLLOWED AT SAN MARTINO HOSPITAL, GENOA

B. Bruzzone[2], A. Lai[4], L. Magnasco[3], P. Caligiuri[1], S. Varesano[1], N. Nigro[2], A. Di Biagio[3]

[1]Hygiene Unit, Department of Health Sciences, University of Genoa, IRCCS San Martino - IST, Genoa, Italy, [2]Hygiene Unit, IRCCS San Martino - IST, Genoa, Italy, [3]Infectious Diseases, Department of Internal Medicine, University of Genoa, IRCCS San Martino - IST, Genoa, Italy, [4]Department of Biomedical and Clinical Sciences, University of Milan, Milan Italy

Background: HIV epidemics in Europe underwent profound changes in the last twenty years, mainly because of the growing impact of migration. Although subtype B is still predominant in Western countries, there has been increasing circulation of non-B subtype strains. The aim of this study is to define through phylogeny the epidemiological features and transmission clusters among foreign patients in the area of Genoa .

Methods: We analysed pol sequences of patients diagnosed with HIV from January 2014 to June 2018 at the Infectious Diseases Clinic in San Martino Hospital, Genoa. Sequences were obtained using Viroseq HIV-1 Genotiping System V.2 (Abbott Molecular Inc., Des Plaines, IL) and were aligned with reference sequences from the Los Alamos National Laboratory website using Bioedit program. The evolutionary model was chosen as the best-fitting nucleotide substitution model, according to the hierarchical likelihood ratio test implemented in the Model Test software. The statistical robustness and reliability of the branching order in phylogenetic tree was confirmed with Maximum Likelihood approach using 1,000 replicates of bootstrap analysis. The recombination pattern was characterized using SimPlot and SplitsTree. Networks of epidemiological events were identified using Bayesian approach implemented in MrBayes program.

Results: 52 pateints were enrolled. Origin countries were South America, Africa, Eastern Europe and South East Asia in 45.3% (n=24), 30.2% (n=16), 20.7% (n=11) and 1.8% (n=1) respectively. Sexual intercourse was the only route of transmission; HEs and MSM accounted for 86.5% (n=45) and 13.5% (n=7), respectively; all MSM but one were South Americans. Globally, males were 60.4% (n=32) and resulted more prevalent among Eastern Europeans (n=9, 81.8%) and South Americans (n=16, 66.7%) compared to Africans (n=6, 37.5%). The mean age of patients was 36 years (range: 21-60 years). Forty-eight sequences were unequivocally assigned to a pure subtype or a known CRF, as a clade of monophyletic origin was identified by the phylogenetic analysis. Nearly half of the analysed viruses (n=24) harboured a non-B variant: 12 CRF02_AG, 5 URF, 2 A1, 2 C, 2 CRF06_cpx, 1 CRF60_BC, 1 F1. All CRFs and URFs but five were identified in African patients. Among B strains, 5 epidemiological clusters were identified composed of 2 to 4 patients (3 of them represented stable couples). Among subjects carrying CRF02_AG, two clusters were found involving a couple and 5 patients. (Fig.1)

Conclusions: Two major epidemiological patterns were identified: one constituted by B subtypes and belonging to South American, Eastern European and South East Asian patients and one by non-B subtypes, mainly CRF02_AG, belonging to African patients. The introduction of different subtypes in populations at risk may give rise to future epidemic waves of unpredictable epidemiological outcome, highlighting the importance to continue molecular and epidemiological surveillance.

Clinical HIV and Epidemiology

PD 18 FACTORS ASSOCIATED WITH BEING ON TREATMENT WITH A DRV-BASED REGIMEN AMONG ADULTS WITH HIV-1 INFECTION IN REAL LIFE

L. Galli[1], A. Castagna[1,2], A. Poli[1], S. Bossolasco[1], G. Gaiera[1], M. Guffanti[1], M. Maillard[1], A. Andolina[2], A. Lazzarin[1], R. Termini[3], M. Palma[3], D. Mancusi[3]

[1]Clinic of Infectious Diseases, Istituto Scientifico San Raffaele, Milano, Italy, [2]Clinic of Infectious Diseases, Vita-Salute San Raffaele University, Milano, Italy, [3]Janssen-Cilag SpA, Medical Affairs, Infectious Diseases; Cologno Monzese, Milano, Italy

Background: Darunavir (DRV) represents an effective option in the management of HIV1-infected patients (pts) among different treatment stages, from first-line to salvage therapies, including treatment simplification. Differences in treatment outcomes may occurr as antiretroviral (ART) regimens are selected based on patients' characteristics. Insight on characteristics of patients treated with boosted DRV (bDRV) with either ritonavir (DRV/r) or cobicistat (DRV/c) in real life, can be informative on effectiveness and tolerability that may help in tailoring ART.

Methods: Retrospective analysis on HIV1-infected adult pts, being treated with an antiretroviral regimen including bDRV, followed at the San Raffaele Hospital, and recorded in the CSLHIV Cohort. The analyses used data, extracted in aggregated and anonymized form. The analysis evaluated pts' characteristics at time of start of DRV-based regimen (baseline, BL) and changes in laboratory parameters since BL up to freezing date. Results were described by median (IQR) or frequency (%). Characteristics were compared according to dosage by use of chi-square and Wilcoxon rank-sum test, as appropriate.

Results: Overall, among 711 pts being treated with a DRV-based regimen, 86% of them was prescribed with a DRV-based regimen at a daily dose of 800 mg QD; 77% of pts treated with DRV 800 mg QD used cobicistat as a booster and 40% contained F/TAF as a backbone. Main pts' characteristics are described in Table 1.

During 1528 person-years of follow-up (PYFU) [median follow-up: 1.7 years (0.9-2.7)], 36 virological failures occurred (2 consecutive HIV-RNA>50cps/mL) for an overall incidence rate of 2.36/100-PYFU (95%CI: 1.59 -3.13). None of the 36 patients modified the ongoing ART: 29/36 spontaneously re-suppressed while 7/36 had HIV-RNA >50 copies/mL.

Pts treated with a daily dose of 800 mg QD as compared to those treated with 600 mg BID showed significant differences with regard to many demographic and clinical characteristics, with the former being older, with lower CD4 nadir, with more frequent AIDS diagnosis, diabetes and hypertension; among the changes in laboratory parameters, of note a smaller increase in triglycerides [0 (-22/-28) vs 5 (-22/-68), p=0.058] during follow-up in patients treated with 800 mg QD.

When comparing pts treated with DRV/c 800/150 mg QD as compared to those treated with DRV/r 800/100 mg QD, a smaller decrease in eGFR [-2 (-10/-3) vs -6 (-16/-2), p=0.011], a smaller increase in ALT [-2 (-11/-3) vs -5 (-16/-2), p=0.033] and in FIB-4 [0.01 (-0.12/-0.27) vs 0.13 (-0.07/-0.32), p=0.013] were observed during the treatment with the DRV-based regimen. Furthermore, pts treated with DRV/c 800/150 mg QD tended to have also a more favorable trend with regard to HOMA-IR [0 (0-0) vs 0.01 (-0.18/-0.87), p=0.09].

Conclusions: These results confirm the effectiveness and safety of bDRV in clinical practice; tailoring the bDRV regimen may differently impact safety and especially the metabolic findings.

Clinical HIV and Epidemiology

PD 19 INFLUENCE OF SEXUALLY TRANSMITTED INFECTIONS ON SEMINAL HIV LEVELS AMONG PATIENTS ON ART: PRELIMINARY DATA OF A CASE-CONTROL STUDY

C. Stingone[1], R. Scutari[2], E. Teti[1], L. Piermatteo[2], V. Malagnino[1], M. Brugneti[2], M. Compagno[1], A. Bertoli[2], V. Svicher[2], C. Cerva[1], M. Santoro[2], C.F. Perno[3], C. Alteri[3], L. Sarmati[1], M. Andreoni[1], F. Ceccherini Silberstein[2]

[1]Clinical Infectious Diseases, Department of System Medicine, Tor Vergata University, Rome, Italy, [2]Department of Experimental Medicine, Tor Vergata University, Rome, Italy, [3]Department of Oncology and Haemoto-oncology, University of Milan, Italy

Background: In the context of an undetectable peripheral HIV-RNA, semen HIV-RNA and HIV-DNA can be detected after 6 months of ART (Du, 2016), but no risk of HIV transmission is even reported (PARTNER study). However, sexually transmitted infections (STI) are known to increase the HIV shedding in semen of ART naïve patients, and their role in influencing the HIV seminal compartment despite peripheral undetectable HIV-RNA is still unclear.

Material and methods: This preliminary study includes 19 HIV-1 patients (pts) with undetectable plasma HIV-RNA (<20 cps/ml) for at least 1 year. At the enrolment, 9 are STI positive (cases; 7 syphilis, 2 Mycoplasma spp urethitis, 1 C. trachomatis infection), while 10 (controls) are STI negative. Pts are analysed for total HIV-DNA (detection limit 32 cps/106CD4+cells) and residual viremia (detection limit 2 cps/ml) in both, blood and seminal compartment by home-made protocols using ddPCR. Blood and semen specimens from cases are retrieved at baseline and after STI treatment.

Results: Pts are mainly MSM (89.5%) and HIV-1 infected by B subtype (73.7%), with a median (Interquartile-range, IQR) age of 35 (29-44) years. Median (IQR) CD4+ and CD8+ cell counts are 772 (576-1042) and 704 (626-927) cells/mm3, respectively. All pts are on successful combined NRTI-based regimen (median [IQR] time of undetectability: 172 [104-270] weeks; third drug: 10 INSTI; 4 NNRTI; 5 PI). No differences are found for these parameters between case and control groups. Peripheral total HIV-DNA is detectable in 17 pts (89.5%), with a median (IQR) value of 1157 (305-3433) cps/106CD4+cells. Differently, seminal total HIV-DNA is detectable only in 2 pts (10.5%, 1 case and 1 control), in both cases with a quantification <32 cps/106CD4 +cells. Peripheral and seminal HIV-RNA are detectable in 11 (57.9%) and 9 (47.4%) pts, respectively. The HIV-RNA quantification in both compartments never exceeds the 20cp/ml (median [IQR]: 2.7 [<2.0-3.5] in peripheral plasma vs. 5.5 [3.5-8.5] in seminal plasma) (Table 1). Again, no differences are found when HIV-DNA and HIV-RNA values in peripheral and seminal compartments are compared between cases and controls (P>0.50). However, 5 out of 19 pts (26.3%) show a seminal HIV-RNA positivity despite the peripheral HIV-RNA negativity. This discordance is more frequently observed in STI pts (4/9, 44.4%) respect to controls (1/10, 10.0%) (even if with a trend, P=0.14).

Six STI cases are analyzed at enrolment and after antibiotic treatment. Among these, 2 (33.3%) maintain undetectable seminal HIV-RNA, 3 (50.0%) show a reduction (-3.4, -2.3, and -12.2 respectively), and only one (16.7%) experiences a seminal HIV-RNA increase to 12.1 cps/ml.

Conclusions: These preliminary data show that successful combined antiretroviral treatment avoids the presence of HIV-DNA in the seminal cells in the majority of pts, maintaining HIV-RNA in seminal compartment at non-relevant levels, despite sexually transmitted coinfections.

HIV co-morbidities

PD 20 SEXUALLY TRANSMITTED INFECTIONS KNOWLEDGE IN HIGH RISK POPULATIONS

S. Giaché[1], L. Cotte[2], C. Chidiac[2]

[1]Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy, [2]Infectious Diseases Department, Hospices Civils de Lyon, Hôpital de la Croix-Rousse, Lyon, France

Background: Education regarding sexually transmitted infections (STIs) is important to reduce STIs incidence and pathogens circulation, especially in high-risk populations. We conducted a prospective study about STI knowledge in high risk populations attending Lyon's University Hospital.

Materials and Methods: HIV-infected patients (HIV+) and PrEP-users (PrEP) attending regular visit and people attending the STI clinic in the Infectious Diseases Department of Croix-Rousse Hospital, Lyon, France, were consecutively recruited between June and July 2018. Demographic data, sexual orientation, number of partners, condom use and history of STI were collected. Patients were asked to answer a questionnaire regarding the modes of transmission of HIV, HAV, HBV, HCV, syphilis (TP), gonorrhea (NG), chlamydia (CT) and HPV, the clinical features of these STIs, their treatment, the possibility of reinfection and the availably of vaccines. A composite score of STI knowledge was calculated, ranging from -13 to +13.

Results: 756 patients were enrolled (HIV+ 144, PrEP 103, STI clinic 509). Most patients were male (69%), of median age 32 years. 43% were men having sex with men (MSM). 25% of patients reported >5 partners in the past 6 months, 38% reported systematic condom use, 19% reported chemsex use and 41% reported a previous STI. Almost all patients (99%) answered questions regarding HIV modes of transmission, while answers for other STI ranged from 62% (NG) to 80% (TP). Knowledge regarding the modes of transmission for each STI are reported in table. Misconceptions regarding transmission were reported by 18%, 56%, 15%, 42%, 15%, 6%, 9% and 22% of patients for HIV, HAV, HBV, HCV, TP, NG, CT and HPV respectively. Only 48% of patients recognized that most STIs are asymptomatic, while 80% recognized the risk of transmission from asymptomatic patients and 84% the risk of reinfection.

PrEP patients answered more frequently and had a better knowledge than other patients, regardless the STI. These differences were observed even when restricting the analysis to MSM (HIV+ 84, PrEP 103, STI clinic 142). Overall, the median (IQR) composite STI score was 3 (1-5). Among MSM, the score was 7 (5-9) for PrEP, 3 (1-5) for HIV+ and 3 (1-6) for STI clinic.

Conclusions: STI transmission knowledge appears satisfactory for HIV but poorer for other STI in these high-risk populations. The risk of transmission from asymptomatic patients was largely unknown. PrEP-users MSM had better knowledge than other risk-groups.

HIV co-morbidities

PD 21 BIOIMPEDANCE VECTORIAL ANALYSIS (BIVA) USEFULNESS IN EVALUATING BODY COMPOSITION CHANGES IN HIV-1 INFECTED PATIENTS IN COURSE OF ART

D.F. Bavaro, P. Laghetti, R. Lattanzio, S. Lo Caputo, L. Monno, G. Angarano, A. Saracino

Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari Medical School, Bari, Italy

Background: Metabolic comorbidities are a major concern in people living with HIV (PLWHIV), hence the evaluation of nutritional status and body composition can offer important clues in this setting, especially in light of recent reports on weight gain in course of modern antiretroviral therapy (ART). Aim of the study was to assess which factors can impact the body composition of PLWHIV as assessed by bioimpedance vectorial analysis (BIVA).

Methods: A cohort of PLWHIV, all ART treated, attending our clinic from July to December 2018 underwent BIVA (BIA 101 New Edition, Akern, Florence, Italy) (50 Hz). Free fat mass (FFM), skeletal muscle mass (SMM), fat mass (FM), and basal metabolism (BM) were obtained. Clinical, ART, and immuno-virologic features of patients were retrieved from the internal database. The correlation among BIVA-derived parameters and PLWHIV characteristics was assessed by univariate and multivariate analyses.

Results: A total of 103 subjects [71% males, median (q1, first - q3, third quartile) age of 49 (43 - 75) years], all on ART from a median (q1-q3) of 8 (2 - 18) years, were included; 18% had a detectable HIV-RNA (median 30 cp/ml, q1-q3: 26 - 78); median (q1-q3) CD4 count was 633 (IQR 475-849) cell/mmc. A total of 20% PLWHA had a previous AIDS diagnosis and 35% presented at least one metabolic comorbidity, mainly dyslipidemia (24%), heart diseases (13%), or diabetes (7%) (Table 1).

Overall, by univariate analysis, patients with a previous AIDS diagnosis presented a lower FFM (p=0.03) and BM (p=0.003); the latter was also associated with CD4 nadir (p=0.02) and current absolute CD4 number (p=0.02). Moreover, a longer duration of HIV infection and of ART use correlated with lower FFM (p=0.004 and p=0.01, respectively), lower SMM (p=0.001 and p<0.001, respectively), and lower BM (p=0.003 and p=0.01, respectively). In addition, the presence of at least one metabolic comorbidity was related with lower SMM (p=0.02) and lower BM (p=0.01), along with higher FM (p=0.01).

The multivariable analysis confirmed on one hand the association between higher FM and presence of comorbidities (p=0.03), on the other hand the association between lower FFM and BM with previous AIDS diagnosis (p=0.02 and p=0.002, respectively) and ART duration (p=0.01, and p=0.02, respectively). Finally, a lower SMM was correlated with a longer ART duration (p=0.002).

Conclusions: Clinical stage, duration of ART and metabolic comorbidities affect body composition of PLWHIV in different ways, predisposing to fat mass increase and lean mass loss. BIVA could represent a simple, non invasive and reliable method for monitoring body composition changes and weight gain during ART.

HIV co-morbidities

PD 22 CHANGES IN BONE MINERAL DENSITY SWITCHING FROM TENOFOVIR DISOPROXIL FUMARATE: A COMPARISON BETWEEN LAMIVUDINE PLUS DOLUTEGRAVIR VERSUS FTC/TAF PLUS AN INTEGRASE INHIBITOR

A. Ciccullo[1], A.P. Lassandro[1], G. Baldin[1], A. Emiliozzi[1], D. Moschese[1], C. Picarelli[1], A. Dusina[1], D. Farinacci[1], S. Belmonti[1], F. Lombardi[1], A. Borghetti[2], A. Pontecorvi[3,4], S. Di Giambenedetto[1,2]

[1]Institute of Infectious Diseases, Catholic University of the Sacred Heart, Rome, Italy, [2]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, UOC Malattie Infettive, Rome, Italy, [3]Department of Endocrinology, Università Cattolica del Sacro Cuore, Rome, Italy, [4]Endocrinology Unit, Fondazione Policlinico Universitario "A. Gemelli' - IRCCS, Rome, Italy

Background: Bone toxicity is a well-known side effects of several antiviral agents, including tenofovir disoproxile fumarate (TDF) and protease inhibitors (PI). We aimed to compare the effects on bone mineral density (BMD) of a dual therapy (DT) with lamivudine (3TC) plus dolutegravir (DTG) versus a triple therapy (TT) with emtricitabine/tenofovir alafenamide fumarate (FTC/TAF) plus an integrase inhibitor (INI).

Materials and methods: We analyzed a cohort of HIV-1 infected, virologically suppressed patients on an INI-based TT with a TDF-containing backbone. Patients were either switched to 3TC+DTG (DT group) or switched from FTC/TDF to FTC/TAF while maintaining the same INI (TAF group). All patients performed dual-energy x-ray absorptiometry (DEXA) at time of switch (baseline, BL) and at week 48 of follow-up; areal BMD (g/cm2) was measured at the lumbar spine (L2 – L4) and at the femoral neck. Changes at 48 weeks were compared using parametric and non-parametric tests, as appropriate; we assessed predictors of changes by linear regression. Multivariable models were adjusted for Body Mass Index (BMI), HCV-coinfection, bisphosphonate use and smoking status whether or not significant at univariable analyses.

Results: We enrolled 40 patients, 14 in the DT group and 26 in the TAF group; twenty-four (60%) were males, with a median age of 55 years (Interquartile Range [IQR] 48-64), a median time from HIV diagnosis of 16 years (IQR 4-19) and a median time of TDF-exposure of 63 months (IQR 25-108). At baseline, 31 patients (77.5% of our population) presented a pathologic BMD value: eleven patients (27.5%) were diagnosed with osteoporosis at BL (5 in the DT group and 6 in the TAF group), while 20 (50%, 6 in DT and 14 in TAF) presented osteopenia. Full patients' characteristics are shown in table 1. There were no statistically significant differences between groups at baseline.

After 48 weeks of follow-up, patients in the DT group presented a significant improvement in spine BMD (+0.02 g/cm2, 95% Confidence Interval [95%CI] 0.01 to 0.03, p=0.017), as well as in spine T-score (+0.1, 95%CI 0.03 to 0.17, p=0.017) and spine Z-score (+0.05, 95%CI 0.01 to 0.09, p=0.017). At a multivariate analysis, no predictors of change were found. In this group we also registered an improvement in femur BMD, but it was not significant (+0.005 gr/cm2, p=0.065). In the TAF group, we recorded non-significant changes in spine BMD (-0.004 gr/cm2, p=0.854), spine T-score (-0.004, p=1.000) and femur BMD (+0.01 gr/cm2, p=0.197) after 48 weeks. Changes in spine BMD (p=0.031), spine T-score (p=0.012) and spine T-score (p=0.014) were significantly different between groups.

Conclusions: Our data show a greater improvement in spine BMD in patients switched to 3TC+DTG compared with patients on a TAF-containing triple therapy after 48 weeks of follow-up.

HIV co-morbidities

PD 23 ANNEXIN A1 PLASMA LEVELS AND CARDIOVASCULAR RISK SCORE IN HIV POSITIVE PATIENTS

C. Ucciferri[1], F. Vignale[1], E. Costantini[2], M. Pontolillo[1], C. D'Angelo[2], M. Reale[2], J. Vecchiet[1], K. Falasca[1]

[1]Clinic of Infectious Diseases, Department of Medicine and Science of Aging, University "G. d'Annunzio" Chieti-Pescara, Chieti, [2]Unit of Immunodiagnostic and Molecular Pathology, Department of Medical, Oral and Biotechnological Sciences, University "G. d'Annunzio", Chieti- Pescara, Italy

Background: The vascular endothelium plays a pivotal role in the pathogenesis of atherosclerosis and its clinical manifestations of the cardiovascular disease (CVD), myocardial infarction, heart failure, stroke, and peripheral artery disease. Experimental and clinical studies in general population suggest AnxA1 has a play an inhibitory role in innate forms of inappropriate inflammation. HIV-1 disease progression is paradoxically characterized by systemic chronic immune activation and gut mucosal immune dysfunction, which is not fully defined. AnxA1, an inflammation modulator, is a potential link between systemic inflammation and immune dysfunction during the simian immunodeficiency virus (SIV) infection.
The aim of this study was evaluated to correlation between AnxA1 plasma levels and cardiovascular risk scores in patients with HIV infection and viro-immunological stable.
Material and Methods: We enrolled 74 HIV-positive outpatients at the Infectious Diseases Clinics of Chieti. All patients was in cART and was virologically suppressed. Demographic and anamnestic data were collected, blood and immunological parameters were measured in addition to the Cystatin C, PCR, microalbuminuria and AnxA1 were analyzed. Different CV Risk scores by Framingham, ASCVD, DAD and PROCAM risk scores were calculated.
Results: We found AnxA1 levels 15.04+/-12.16 ng/ml. We had a negative association between AnxV1 level and Framingham score (r=-0.22 e p=0.05), ASCVD (r=-0.23 e p=0.04), DAD score (r=-0.24 e p=0.03), and PROCAM score (r=-0.30 e p=0.008). Also the anxA1 was associated to cardiovascular risk score, in fact we found a negative correlation between AnxA1 and Framingham score (r=-0.40 e p=0.001), ASCVD (r=-0.48 e p=0.001), DAD score (r=-0.39 e p=0.001), and PROCAM score (r=-0.49 e p=0.001). Therefore an association between AnxA1 and cystatin C (r=-0.41 and p=0.001) and microalbuminuria (r=-0.55 and p=0.001) was found.
Conclusions: Our work shows that exist a correlation between the AnxA1 and the results obtained from the cardiovascular risk scores HIV correlated. Indeed low levels annexins were significantly correlated with high risk CVD, highlighting how the inflammatory process participates in the pathogenesis of cardiovascular damage in the HIV-positive population. AnxA1 could be an easy marker to highlight the cardiovascular risk in the population

HIV co-morbidities

PD 24 PLASMA FIBRINOGEN IS ASSOCIATED WITH HIGHER INFLAMMATION AND SUBCLINICAL ATHEROSCLEROSIS IN HIV-1-INFECTED PATIENTS ON COMBINATION ANTIRETROVIRAL THERAPY

L. Calza[1], V. Colangeli[1], M. Borderi[1], A. Borioni[1], F. Volpato[1], I. Bon[2], M.C. Re[2], P. Viale[1]

Department of Medical and Surgical Sciences, [1]Clinics of Infectious Diseases, [2]Unit of Microbiology, S.Orsola Hospital, University of Bologna

Background: HIV infection is associated with faster progression of atherosclerotic disease and increased cardiovascular disease risk. Plasma fibrinogen is an inflammatory marker associated with atherosclerosis in the general population, but clinical data about fibrinogen and atherosclerosis in HIV-positive people are still limited.
Patients and methods: A cross-sectional study was performed to investigate correlation between plasma concentration of fibrinogen and presence of subclinical atherosclerosis in HIV-infected patients on stable cART, with age>40 years, and with a measurement of plasma fibrinogen and a carotid ultrasonography performed in the last 6 months. According to fibrinogen concentration <400 or >400 mg/dL, patients were divided into two groups: low fibrinogen (LF) and high fibrinogen (HF), respectively.
Results: On the whole, 264 patients were enrolled: 148 in the LF group and 116 in the HF group. Overall, 85.2% were men, 90.5% Caucasian, 13.3% were at CDC stage C, the mean age was 48.6 years (range, 40 -79), the mean CD4 T lymphocyte count was 517 cells/mm3, 249 (94.3%) had plasma HIV RNA <20 copies/mL, 54.9% were smoker, 38.6% had hypertension, and 59.1% had total cholesterol >200 mg/dL. Baseline characteristics of patients were comparable in both groups. In HF group there was a significantly higher prevalence of subclinical atherosclerosis than in LF group (65.5% vs 39.9%; p=0.028), and mean intima-media thickness (IMT) values in external carotid artery and carotid bifurcation were also significantly higher in HF group than in LF group. Mean interleukin-6 (IL-6) concentration was significantly higher in HF group than in LF group (3.45 vs 2.18 pg/mL; p<0.001), while high sensitivity C-reactive protein and tumor necrosis factor-α levels were comparable in both groups. Multiple logistic regression analysis showed that plasma fibrinogen was an independent risk factor for the presence of subclinical atherosclerosis and carotid plaques (odds ratio [OR] =2.68, 95% CI 1.79-3.44, p=0.008), and high fibrinogen concentration was associated with high IL-6 concentration. Receiver operating characteristic (ROC) curve analysis showed that the optimal cut-off value of fibrinogen for predicting the presence of subclinical atherosclerosis was 485 mg/dL (area under curve [AUC] =0.69, 95% CI 0.58-0.81, p=0.004). No significant association was reported between fibrinogen levels and current antiretroviral regimens.
Conclusions: In our study, plasma fibrinogen was independently associated with the presence of subclinical atherosclerosis and higher levels of IL-6, so it could be considered a predictor of the atherosclerosis progression rate among HIV-infected subjects independently of traditional cardiovascular risk factors.

HIV co-morbidities

PD 25 IMPACT OF CHEMOTHERAPY RELATIVE DOSE INTENSITY (RDI) IN TREATMENT OF HIV-ASSOCIATED LYMPHOMA (HIV-L)

V. Mazzotta, P. Lorenzini, C. Pinnetti, M. Bibas, A. Giannetti, A. Plazzi, A. Mondi, R. Gagliardini, A. Vergori, E. Grilli, S. Cicalini, F. Baldini, A. Grisetti, L. Alba, A. Antinori

National Institute of infectious Disease Lazzaro Spallanzani, Rome

Background: Despite reduced incidence by ART, HIV-L still represents a major cause of morbidity and mortality. Response to chemotherapy and survival of HIV-L may be influenced by conservative approach of lymphoma treatment due to toxicity or drug-drug interaction with ARVs. Higher RDI has been related to a better outcome, but few data were reported in HIV-L. Aim of our study was to estimate prevalence and factor associated to RDI in HIV-L and to investigate the impact of RDI on survival.

Methods: Single centre retrospective study on HIV patients (pts) with HIV-L (NHL and HL) between 2001 to 2018. Pts with Primary Central Nervous System and T-Cell Lymphoma were excluded. Demographic, clinical and therapeutic variables were collected, and International Prognostic Index score (IPIs) and RDI (=total delivered dose over the target) for doxorubicin (D) and cyclophosphamide (C) were calculated. Multivariable Cox and logistic regression were fitted to estimate OR and factors associated with survival and RDI <100% (rRDI).

Results: 165 pts included: 87% male, median age 46y, heterosexual 42%, MSM 30%, IDU 24%; 125 (73,5%) NHL and 45 (26.5%) HL. At diagnosis, in 40% HIV RNA was under detection limit and median CD4 was 195 cells/mm3. 73(42.9%) were ART naive at HIV-L diagnosis. IPIs shows: low, intermediate and high risk in 79 (46.5%), 74(43.5%) and 17(10%), respectively. A rRDI were delivered in 32 (18.8%) (C 12%, D 16%).

The overall 3-years probability of death was 41% [95%CI 33.7-49.4]: 46% [95%CI 36.9-55.8] for NHL and 30% [95%CI 18.4-45.5] for HL. By multivariable analysis only a high IPIs (OR 3.61, 95%CI 1.65-7.9, p=0.001) and changing ART before or during CT (OR 2.29, 95%CI 1.19-4.39, p=0.013) were associated to an increased mortality. rRDI was not associated to increased risk of death. Factors associated with more frequent rRDI were older age, IDU, and less recent years of diagnosis. No significant differences were found as regarding type and class of antiretroviral regimens or HIV-L histotypes (Tab. 1).

Conclusions: Prevalence of RDI reduction seems to be negligible in HIV population with HIV-L. Increased risk by ageing confirmed data from general population, whereas association with IDU may reflect more frequent comorbidities and drug interactions. Reduction of RDI decreased in the more recent calendar years, possibly due to a shift from a conservative to a curative approach in HIV population, even though RDI did not seem to influence survival of patients with HIV-L.

HIV co-morbidities

PD 26 EFFECT OF ALPHAFETOPROTEIN ON SURVIVAL IN HIV-INFECTED PATIENTS WITH HEPATOCELLULAR CARCINOMA

E. Messina[1,2], L. Galli[1], G. Morsica[1], H. Hasson[1], S. Bagaglio[1], S. Salpietro[1], A. Lazzarin[1], A. Castagna[1,2], C. Uberti Foppa[1,2]

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

Background: The prognostic relevance of high alpha-fetoprotein (AFP) levels has been scarcely reported although it is advised to test levels >200 or >400 ng/mL as prognostic factors of poor outcome. The association between AFP and prognosis of HCC has not been evaluated yet among people living with HIV (PLWH).

Methods: PLWH with a HCC diagnosis, between Nov 1999 and May 2018, with cirrhosis (Metavir F4), from the CSLHIV cohort were included. PLWH were eligible if they had available an AFP value at diagnosis of HCC. HCC staging and treatment allocation were based on BCLC modified system, (EASL 2018). HCC treatment was differentiated in curative (surgical resection, radiofrequency ablation and transplant) and non-curative (chemo or radioembolisation, systemic therapies, best supportive care).

Follow-up accrued from BL to the last available clinical visit/loss to follow-up/death.

The receiver operating characteristics (ROC) curve analysis was applied to determine the optimal cut-off of BL AFP predicting death.

In the analysis, the AFP cut-offs of 200 or 400 ng/mL, were also evaluated, as recommended in international guidelines.

The Kaplan-Meier method was used to estimate cumulative probability of death. Factors associated with the risk of death were identified using multivariate Cox proportional hazards regression models including: HCC calendar year, age, gender, HCV, HBV, years of ART, BCLC, number of nodules, HCC treatment strategy, BL AFP (alternatively stratified according to the optimal cut-off or 200 or 400 ng/ml), BL CD4+ T cell count and BL HIV-RNA.

Results: Fifty-three PLWH included: 85% male, median age 53 years (IQR=48-56), median BL CD4+ was 392 cells/μL (IQR=222-598), 81% with HIV-RNA<50 copies/mL; 18 (35%) in BCLC 0/A; 21 (41%) BCLC B/C; 12 (23%) BCLC D. Ten (20%) patients underwent transplant.

After a median follow-up of 20 months (IQR=8-42), 32 (60.4%) PLWH died. The ROC curve analysis estimated the value of 28.8 ng/mL as the optimal cut-off for the occurrence of death (Table1); BL AFP was ≥28.8 ng/mL in 32 (63%) pts, >200 ng/mL in14 (28%) and >400 ng/mL in11 (22%).

High AFP serum levels at diagnosis (≥28.8 ng/mL) were significantly associated with lower pseudo-cholinesterase (p=0.016), higher prevalence of a multinodular tumor (p=0.020).

By 3-years from HCC diagnosis, the cumulative probability of death was 28.9% (95%CI=13.2%-56.3%) versus 75.6% (95%CI=59.0%-89.3%) for BL AFP<28.8 and ≥28.8 ng/mL; 48.9% (95%CI=33.2%-67.2%) versus 85.0% (95%CI=62.2%-97.5%) for BL AFP≤200 and >200 ng/mL; 50.3% (95%CI=35.1%-67.7%) versus 90.9% (95%CI=66.7%-99.5%) for BL AFP≤400 and >400 ng/mL (Figure 1).

At multivariable analysis, BL AFP was independently associated with increased risk of death after a diagnosis of HCC (Table2).

Discussion: Our analysis shows that, in HIV-1 infected people with HCC, high AFP serum levels is a negative predictive marker for death independently of tumor stage at the time of diagnosis.

HIV co-morbidities

PD 27 THE UCSD PERFORMANCE-BASED SKILLS ASSESSMENT IS ASSOCIATED TO COGNITIVE PERFORMANCE IN HIV POSITIVE POPULATION WITH VERY GOOD IMMUNOLOGICAL CONDITION

V. Delle Donne[1], N. Ciccarelli[2], A. Borghetti[4], F. Lombardi[4], A. Dusina[4], D. Farinacci[4], A. Emiliozzi[4], E. Visconti[4], E. Tamburrini[1,4], M. Fabbiani[3], S. Di Giambenedetto[1,4]

[1]Università Cattolica del Sacro Cuore, Roma Italia, Istituto di Clinica Malattie Infettive, [2]Dipartimento di Psicologia, Università Cattolica di Milano, [3]U.O. Malattie Infettive e Tropicali, Fondazione IRCCS Policlinico San Matteo, Pavia, [4]Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma Italia, UOC malattie infettive

Background: HIV-infected patients frequently show everyday functioning (EF) impairment that have a multifactorial nature and can be associated to neurocognitive diseases. Usually, EF is measured by IADL scale, but this tool has shown low sensitivity in patients with no overt dementia. Our aim was to better explore EF and its association with cognitive functioning in the context of HIV infection by administering a new multi-domain and ecological assessment tool.

Material and methods: We performed a cross-sectional single cohort study by consecutively enrolling during routine visits 70 HIV+ subjects on antiretroviral therapy (ART) and 23 age-and-education matched healthy controls (HC) with MMSE≥27. Exclusion criteria were: age<18 years, active/past central nervous system opportunistic infections, history of neurological disorders, active psychiatric disorders, alcoholism or drug abuse and difficulties with Italian language.

Each patient underwent a comprehensive neuropsychological assessment (NPA), exploring memory, attention, language, executive functions and fine motor abilities. Global performance was measured by transforming raw scores at each task into standardized Z-scores and averaging to calculate a composite total score. To measure EF, IADL scale was administered; moreover, both groups underwent the UCSD Performance-Based Skills Assessment-Brief Version (UPSA-B), assessing financial and communication skills.

EF was compared in HIV+ vs HC and factors associated to EF in the HIV+ population were explored.

Results: HIV+ patients were 81% male with a median age of 54 yrs (IQR 48-60) and a median education of 13 yrs (IQR 11-17). Median time from HIV diagnosis and first ART was 13 (IQR 4-22) and 12 (IQR 4-19) yrs, respectively. Overall, 11% of HIV+ subjects were past injecting drug users, 6% HCV coinfected, 29% with past AIDS-defining events and 93% showed HIV-RNA <50 copies/mL, with a median CD4 cell count of 90 cells/µL (IQR 11-267) at nadir and 636 cells/µL (IQR 389-844) at the time of NPA. Median adherence to ART was 95% (IQR 85-100) on a 0-100 VAS scale.

All patients were cognitive asymptomatic and, on NPA, the total mean Z-score was 0.34 (SD 0.62). While IADL score was at ceiling, the mean UPSA-B total score was significantly worse in HIV+ group when compared to HC [mean 81 (SD 9.3) vs 89 (SD. 6.2); p<0.001].

In HIV+ patients, at multivariate linear regression analysis higher total cognitive z-score was associated to better performance at UPSA-B (β 7.79; 95% CI 4.65-10.92; p<0.001), after adjusting for education (β 0.21; 95% CI -0.33/0.75; p=0.441) and adherence (β 0.078; 95% CI -0.42/0.20; p=0.198).

Conclusion: UPSA-B seemed to better discriminate EF impairment than IADL in HIV+ patients and it was associated with cognitive functions, also in the absence of symptomatic cognitive impairment.

On these bases, UPSA-B seems a promising tool to measure EF functioning in the context of HIV infection with a very good immunological condition.

HIV co-morbidities

PD 28 RESTING EEG-LORETA AND CSF BIOMARKERS IN PATIENTS WITH HAND

V. Pirriatore[1], G. Noce[2], A. Barco[1], G. Stroffolini[1], S. Orlando[3], D. Vai[3], A. Bianco[3], M. Trunfio[1], D. Imperiale[3], S. Bonora[1], G. Di Perri[1], C. Babiloni[4,5], A. Calcagno[1]

[1]Unit of Infectious Diseases, Amedeo di Savoia hospital, Department of Medical Sciences, University of Torino, Torino, [2]IRCCS SDN, Naples, Italy, [3]Unit of Neurology, Ospedale Maria Vittoria, ASL "Città di Torino", [4]Department of Physiology and Pharmacology, University of Rome "La Sapienza", Rome, [5]IRCCS S. Raffaele Pisana and Cassino, Rome and Cassino, Italy

Background: HIV-associated neurocognitive disorders (HAND) are still diagnosed in people living with HIV (PLWH) successfully treated with combination antiretroviral therapy (cART). Previous evidence has shown that brain function can be fruitfully probed in patients estimating cortical sources of resting state EEG (rsEEG) rhythms. Aim of the study was to test whether rsEEG markers are related to specific cognitive domains and cerebrospinal fluid (CSF) biomarkers in a novel cohort of HIV-positive patients with HAND.

Methods: Patients diagnosed with HAND according to the Frascati's criteria, without significant comorbidities and with plasma HIV RNA<50 copies/mL were enrolled in a pilot study. Statistical analysis compared rsEEG (LORETA freeware) source estimates with scores of 10 neuropsychological tests and CSF biomarkers including tTau, pTau, βAmiloid42, neopterin, S100β, CSF-serum albumin ratio [CSAR], and CSF IgG synthesis (thresholds validated in HIV-negative subjects). Data are described with median values (IQR) and analysed through non-parametric tests.

Results: 32 patients were included: 22 (70%) were male, with median age and BMI of 57 years (49-63) and 24.2 Kg/m2 (23.5-25.0), respectively. Current and nadir CD4+ cell count were 600 (427-745) and 369 (153 -443) cells/μL; 11 (5-13) years of virological suppression were recorded. All but two patients (6.2%, MND) were diagnosed with ANI. 24 subjects (75.0 %) were treated with triple-therapies, 8 (25.0 %) with dual regimens; integrase inhibitors were commonly used (in 15 individuals, 46.9 %). Abnormal tTau, pTau, βA42, neopterin and S100β were observed in 6.2%, 18.7%, 6.2%, 21.9% and 6.2% individuals, respectively.

Occipital delta source activity (<4 Hz) was associated with longer executive functions (Trail making B), and worse score in Hamilton Anxiety Scale (HAM-A) and Auditive-visual function (p values <0.05, rho >0.5). Lower global alpha2 and alpha3 source activity (8-12 Hz) were strongly associated with higher CSF βA42 (p values 0.019 and 0.025, and rho values -0.618 and 0.596 respectively).

Conclusions: rsEEG source activity at delta and alpha rhythms may reflect brain dysfunction in HIV patients with HAND and were specifically related to executive functions, often altered in cognitively impaired individuals. The association of alpha source activity in patients with CSF β-amyloid protein warrant further studies for using rsEEG in the assessment of potential neurotoxicity and in the long-term follow up of ageing PLWH.

HIV co-morbidities

PD 29 AGING WITH HIV OR GETTING INFECTED AT OLDER AGE DEFINE TWO DISTINCT GROUPS OF AGED HIV PATIENTS

F. Maggiolo, L. Comi, R. Teocchi, E. Di Filippo, A.P. Callegaro, M. Rizzi

ASST Papa Giovanni XXIII, Bergamo

Background: PLWHIV are living longer and the HIV population is aging, with a life-expectancy approaching that of the general population. This phenomenon has been accompanied by an increasing number of patients diagnosed at older ages. We tried to respond to the question is if older patients with HIV are all the same irrespective of when they acquired infection

Methods: This was a cross-sectional, observational study conducted in a single center at the end of 2018. All HIV + patients aged >60 years were included. Socio-demographic data, HIV infection characteristics (mode of transmission, duration of infection, plasma HIV RNA and CD4 count at presentation), were obtained from the medical DB. All chronic non-communicable co-morbidities (NCC) and all chronic co-medications were recorded. The duration of infection was defined as the time elapsed from the year of diagnosis to the year of analysis and patients were divided in those with more (+10) and those with less (-10) than 10 years FU. A multivariable linear regression model was used to analyze data.

Results: We extracted data of 370 patients; 262 in the +10 group and 108 in the -10. The groups did not differ for gender (females 14.9 vs 18.5%), mean age (66.9 vs 67 years), baseline mean CD4 counts (236 vs 249 cells/mcL) and proportion of AIDS presenters (29.3 vs 29.6%). In the +10 group there was a greater proportion of IVDU (15.6 vs 0.9%) and the groups significantly differed for mean FU (19.1 vs 5.1 years) (P<0.0001). The mean number of chronic NCCs was 1.97 in the +10 and 1.56 in the -10 group (P=0.01) (figure). in the +10 group we counted up to 7 chronic NCCs for a single patient, while this number did not exceed 4 in the -10 group, furthermore, 15.6 % of subjects in the +10 group did not have any NCCs and this value raised to 22.2% in the -10 group. In a multivariable linear regression model only the patients' group (P=0.013) and age (P<0.0001) were significantly associated with the per-patient number of NCCs. The most common NCCs were hypertension, cardiovascular diseases, dyslipidemia, gastro-intestinal diseases and diabetes (figure). Beside NCCs, patients in the +10 group showed a significantly higher prevalence (17.9%) of positivity for HCV compared to patients in the -10 group (4.6%) (P = 0.0001), while for HBV there was only a trend (9.9 vs 3.7; P = 0.058). To treat Chronic NCCs patients took a mean of 2.6 pills in the +10 group and of 2.3 pills in the -10 group (P=NS). The most frequently used drugs included: cardiovascular agents (41.1%); vitamins (26.56%); metabolic agents (26.2), gastro-intestinal agents (26.2) and ASA (17.6%).

Conclusions: Within older patients with HIV we must distinguish those with a long infection history who aged with HIV from those who acquired the infection at older age, as the time of infection, along with age, are the main drivers of associated chronic NCCs and significantly influence the presence of co-morbidities and the need for poly-pharmacy.

Viral Hepatitis

PD 30 NO CHANGES IN LONGITUDINAL EVALUATION OF NEUROCOGNITIVE PERFORMANCE (NPA) IN ANTIRETROVIRAL-TREATED HIV/HCV CO-INFECTED PATIENTS RECEIVING DIRECTLY-ACTING ANTIVIRALS (DAAS)

S. Cicalini, A.C. Brita, P. Lorenzini, A. Vergori, E. Grilli, S. Menichetti, R. Gagliardini, A. Giannetti, A. Antinori, C. Pinnetti

National Institute for Infectious Diseases Lazzaro Spallanzani, IRCCS, Rome

Background: HCV co-infection may play a role in the genesis of neurocognitive impairment (NCI) in HIV-infected population, even though current literature shows conflicting results. It was supposed that NCI could be improved by successful HCV treatment, especially after the advent of new drugs DAAs. The VACS Index is a composite marker of disease severity and has also been linked to concurrent risk for NCI. We evaluated changes of the NPA and VACS in HIV/HCV co-infected patients (pts) receiving DAAs.

Materials and Methods: This longitudinal, single-centre, prospective study, included all consecutive antiretroviral-treated HIV/HCV co-infected pts, starting DAAs from Jan 2015 to December 2018. The NPA was carried out, before (T0) and after DAAs treatment (T1), through a standardized and comprehensive battery of 13 tests on 5 different domains. HIV-associated neurocognitive disorders (HAND) were classified by Frascati's criteria. Sustained virological response was evaluated at week 12 (SVR12) after the end of DAAs treatment (EOT). VACS Index was calculated at baseline and after DAAs. As appropriate, paired Wilcoxon and Mc Nemar's tests were used for statistical comparisons of NCI and VACS in overall population, in the subgroup with SVR12 and in the two strata with different level of fibrosis.

Results : We included 139 patients, with NPA performed at T0 and a median (IQR) of 2.8 (3-6) months after EOT: 75% were males with a median age of 54 (50-57) years, 74% of pts were intravenous drug users and reported median education level of 12 (8-13) years. The median CD4+ nadir was 230 (132-361) cell/mm3 and CD4+at T0 608 (412-820) cell/mm3, HIV-RNA was undetectable (< 40 cp/mL) in 129 pts (93%). HCV genotypes (GT) were 1a in 43%, 1b in 11% and 3 in 23%. Overall, 57% had an advanced liver disease (F3-F4). Pts were prescribed sofosbuvir/velpatasvir in 31.2%; sofosbuvir/ledipasvir in 18.1%; ABT-333+ABT -450/r/ABT-267+o-RBV in 14.5% glecaprevir/pibrentasvir in 5.1%; elbasvir/grazoprevir in 3.6%; other in 27.5%. SVR12 was achieved in 95%. At T0, NCI was detected in 43 cases (31%). However, because of the high frequency of potentially confounding factors, HAND classification could be applied to only 18 cases: 15 ANI, 2 MND and 1 HAD. When comparing NPA at T0 and T1, the frequency of NCI remained stable in the whole study population (31% versus 40%), in the subgroup with SVR12 pts (33% versus 29%), in pts with F0-F2 (25% versus 18%) and with F3-F4 (36% versus 37%). (Table 1).No significant changes over time in median values of VACS index were observed after DAAs, even after stratification of pts according to SVR12 and level of fibrosis.

Conclusions: Anti-HCV therapy with DAA does not seem to influence neurocognitive changes in this large number of HIV/HCV co-infected patients. These data mean against a major contribution of HCV on HAND pathogenesis. Further studies are needed to better investigate exact mechanisms of HCV on NCI development in HIV/HCV coinfected patients.

Viral Hepatitis

PD 31 IMMUNE INFLAMMATION MARKERS IN HCV INFECTED SUBJECTS WITH LOW LIVER FIBROSIS UNDERGOING DAA TREATMENT

B. Kertusha, C. Mascia, P. Nijhawan, I. Pozzetto, L. Fondaco, A. Carraro, R. Marocco, S. Vita, C. Mastroianni, M. Lichtner

Sapienza Università di Roma, Dipartimento di Malattie Infettive e Sanità Pubblica, Latina

Background and aims: Increased levels of chemokine interferon-gamma (IFN-γ)-inducible protein-10 (CXCL10) , soluble CD163 (sCD163) and soluble CD14 (sCD14) have been reported in HCV infected patients, with different extent depending on fibrosis stage. The aim of this study was to monitor the effect of HCV eradication by DAA on immune inflammatory stage in a cohort of low fibrosis subjects.

Methods: sCD163, sCD14 and CXCL10 were longitudinally measured by ELISA kit (RD system) in plasma samples from 77 subjects, 46 HCV infected subjects, 19 Low Fibrosis (LF), F0-F2 and 28 High fibrosis (HF), F3-F4, undergoing DAA therapy and 31 age and sex matched healthy donors (HD). Different time points were analyzed. Liver fibrosis was measured using Fibroscan. Non parametric tests were used for statistics. Friedman ANOVA with Dunn's Test, Mann-Whitney Test, Wilcoxon Test and Spearman correlation Test were used for statistical analysis.

Results: CXCL10 plasma levels were higher than HD at baseline only in HF pts ($p<0.0001$) and decrease significantly at different time points ($p>0.001$) after DAA treatment, reaching values similar to HD. No change was observed in LF group. Differently, sCD163 values were higher in both HF and LF patients at baseline comparing HD ($p<0.0001$ for both). They decreased significantly ($p<0.04$ and $p<0.01$) at SVR12 and 48, but remained high in both populations of LF and HF when compared to HD ($p<0.01$). Moreover, sCD14 was higher in LF and HF compared to HD with higher levels in LF. No differences were observed after DAA treatment.

Conclusions: These results indicate that HCV infected subjects with a low liver fibrosis with an apparent asymptomatic feature present a monocyte-related inflammatory milieu that could contribute to the HCV extra-hepatic diseases. DAA treatment is able to highly reduce these markers even if a complete normalization seems to be lacking.

Viral Hepatitis

PD 32 VIROLOGICAL PATTERNS OF HCV-PATIENTS WITH FAILURE TO THE LAST GENERATION PAN-GENOTYPIC DIRECT-ACTING ANTIVIRALS

M. Starace[1], M. Pisaturo[1], C. Minichini[1], S. De Pascalis[1], M. Macera[1], L. Occhiello[1], A. Di Fraia[1], L. Alessio[2], V. Messina[2], E. Claar[3], T. Ascione[4], A. Marrone[5], G. Brancaccio[6], I. Gentile[7], G. D'Adamo[8], G.B. Gaeta[1], N. Coppola[1] HCV infection Campania group (CampC)

[1]Infectious Diseases Unit, Department of Mental and Physical Health and Preventive Medicine, University L. Vanvitelli, Naples, Italy, [2]Infectious Diseases Unit, AO Caserta, Caserta, Italy, [3]Internal Medicine Unit, Evangelical Hospital Villa Betania Naples, Italy, [4]IX Interventional Ultrasound Unit for Infectious Diseases, AORN dei Colli, P.O. Cotugno, Naples, Italy, [5]Internal Medicine, University of Campania L. Vanvitelli, [6]Department of Molecular Medicine University of Padua, [7]Infectious Diseases Unit, University Federico II, Naples, Italy, [8]Internal Medicine Unit, P.O. Umberto I Nocera Inferiore

Background: Despite the excellent efficacy, direct-acting antivirals (DAA)-regimens are associated with failure in about 5% of cases.
Aims. To characterize the virological patterns and the resistant-associated substitutions (RASs) in the patients with failure to the last generation pan-genotypic DAA.
Methods: All the 63 consecutive HCV patients naive (pts) with failure to IFN-free regimen observed at the laboratory of infectious diseases of University of Campania, Naples from January 2018 to February 2019 were enrolled. All the pts had been treated with the last DAA regimens, that is Sofosbuvir(SOF) +Velpatasvir (VEL), Glecaprevir (GLE)+Pibrentasvir(PIB),
Grazoprevir(GZR)+Elbasvir(EBR) according to HCV genotype, international guidelines and local availability. Sanger sequencing of NS3 (for genotypes 1 and 4), NS5A and NS5B (for all genotypes) was performed at failure by home-made protocols.
Results: Table 1 shows demographic, virological and clinical characteristics of the patients enrolled and type of treatment. Patients enrollerd were mainly males (60%) with median age of 67.5 years (range 42-81). HCV RNA, IU/ml median value was 2.27E+06 (range: 9.08E+00-1.10E+07), 33.3% of patients had a diagnosis of cirrhosis. 5 patients were HCV genotype 1a, 41 1b, 5 2a/2c, 9 3a/3h and 3 were genotype 4.
According to therapeutic outcome, 90.5% were relapse, 4.7% were breakthrough and 4.7% were non-responder. Among the 63 patients failed at the last generation pan-genotypic DAA, 19 (30.1%) were been treated with SOF+VEL, 11 (17.4%) with GLE + PIB and 33 (52.4%) with GZR+ EBR. The duration of DAA had a median of 12 weeks (range 8-24), the timing of resistence test at the end of treatment had a median of 5 months (range 1-19). Figure 1 shows RASs distribution according to DAA therapy. The NS5A-RASs were more frequent in SOF+VEL (17/19, 89.5%) and in GZR+ EBR (32/33, 97%) than in GLE + PIB (2/11, 18.2%) failed patients (p=0,002 and 0,000 respectively). Moreover NS3-RAS were more often detected in patients with failure to GZR + EBR (10/33, 30.3%) compared to GLE + PIB (1/11, 9.1%) (p= 0,002) and SOF+VEL (2/19, 5.3%) (not statistically significant). While the NS5B-RAS were infrequent. Figure 2 shows patients with two or more RASs on HCV regions according to DAA-regimen. According to SOF+VEL 36.4% pts showed at least 2 RASs in two HCV region including NS5A and 70.3% pts showed at least 2 RASs only in NS5A region. Considering GZR+ EBR 27.3% pts showed at least 2 RASs in two HCV region including NS5A and 88% pts showed at least 2 RASs only in NS5A region.(p=0.00)
Conclusions: Patients with failure to last generation pan-genotypic direct-acting antivirals frequently show mutations above all in the NS5A region, in particular in patients experienced SOF+VEL and GZR+ EBR compared to patients experienced GLE + PIB failure. In our opinion the lower frequency of RASs in patients treated with GLE + PIB is probably due to the short lasting of the last cited therapy.

Viral Hepatitis

PD 33 THE PRESENCE OF SPECIFIC MUTATIONS IN HBSAG C-TERMINUS CORRELATES WITH LOWER HBSAG LEVELS IN VIVO, INTERFERE WITH HBSAG RELEASE IN VITRO AND ALTER HBSAG STRUCTURE IN HBEAG-NEGATIVE CHRONIC HBV GENOTYPE D INFECTION

L. Piermatteo[1], A. Battisti[2], L. Carioti[1], D. Di Carlo[3], O.E. Anastasiou[4], U.S. Gill[2], L. Colagrossi[5], A. Bertoli[1], M. Aragri[1], L. Fabeni[1], A. Iuvara[6], V. Malagnino[7], C. Cerva[7], M. Lichtner[8], C.M. Mastroianni[8], G.M. De Sanctis[9], M. Paoloni[10], M. Marignani[11], C. Pasquazzi[11], N. Iapadre[12], T. Mari[13], G. Parruti[14], J. Vecchiet[15], L. Sarmati[7], M. Andreoni[7], M. Angelico[16], S. Grelli[1,6], P. Kennedy[2], J. Verheyen[3], F. Ceccherini Silberstein[1], C.F. Perno[17], V. Svicher[1], R. Salpini[1]

[1]"Tor Vergata" University of Rome, Experimental Medicine, Rome, Italy, [2]Barts Liver Centre, Blizard Institute, Barts and The London SMD, QMUL, London, United Kingdom, [3]University of Milan, Paediatric Clinical Research Center 'Romeo and Enrica Invernizzi', Milan, Italy, [4]Institute of Virology, University-Hospital, University Duisburg-Essen, Essen, Germany, [5]University of Milan, Microbiology and virology, Milan, Italy, [6]Tor Vergata University Hospital, Microbiology and Virology Unit, Rome, Italy, [7]Tor Vergata University Hospital, Infectious Desease Unit, Rome, Italy, [8]"Sapienza" University, Public Health and Infectious Disease, Rome, Italy, [9]"Umberto I" University Hospital, Rome, Italy, [10]"S.S. Filippo e Nicola" Hospital, Infectious Disease Unit, Avezzano, Italy, [11]"S.Andrea Hospital", Department of Gastroenterology, Rome, Italy, [12]"San Salvatore Hospital", L' Aquila, Italy, [13]"Nuovo Regina Margherita" Hospital, Rome, Italy, [14]Pescara General Hospital, Infectious Disease Unit, Pescara, Italy, [15]University "G. d'Annunzio" Chieti-Pescara, Clinic of Infectious Diseases, Department of Medicine and Science of Aging, Chieti, Italy, [16]Tor Vergata University Hospital, Hepatology Unit, Rome, Italy, [17]University of Milan, Oncology and Haemato-oncology, Milan, Italy

Background: This study is aimed at evaluating HBsAg levels in different HBV genotypes in HBeAg-negative (eAg-) individuals with chronic HBV infection, and the correlation of specific mutations in HBsAg C-terminus (critical for a proper HBsAg-release) with HBsAg levels in vivo, their impact on HBsAg-secretion in vitro and on structural stability in silico.

Methods: HBsAg levels were investigated in 323 drug-naïve eAg- patients infected with HBV genotype D (N=228), A (N=65) and E(N=30).

In 228 genotype-D infected patients, association of mutations in HBsAg C-terminus with HBsAg<1000 IU/mL (N=130) is assessed by Fisher's Exact test. Impact of mutations on HBsAg-secretion is analyzed by transfecting HepG2 cells with plasmids encoding WT- and mutated-HBsAg, linked to a streptavidin-tag (StrepTag). The StrepTagged-HBsAg amount in supernatants is quantified by an ELISA targeting StrepTag, not affected by HBsAg-antigenicity and thus, capable to identify defects in HBsAg-secretion. HBsAg-structures and their stability are predicted by I-Tasser..

Results: HBV genotype D is characterized by HBsAg levels lower than genotypes A and E (2,016[520-6,173] IU/ml, 6,416[3,140-14,587]IU/ml, 9,937[4,566-16,032]IU/ml, respectively P<0.001). Results confirmed by ANOVA multivariable analysis (P<0.0001 for genotype D vs A, P=0.02 for genotype D vs E). In genotype D, specific HBsAg C-terminus mutations (V190A, S204N, Y206C, Y206F and S210N) significantly correlated with HBsAg<1,000IU/ml (P from <0.001 to 0.04).

These mutations lie on divergent pathways involving other mutations in HBsAg C-terminus: V190A with F220L (Phi=0.41, P=0.003), S204N with L205P (Phi=0.36, P=0.005), Y206F with S210R (Phi=0.47, P<0.001) and S210N with F220L (Phi=0.40, P=0.006). By multivariable analysis, the presence of >1 of these pairs of mutations was independently associated with HBsAg <1,000IU/ml after correction for patient's demographics, serum HBV-DNA and ALT (O.R.[95%CI]:14.75 [1.83-118.79], P=0.011). Notably, patients with these pairs of mutations are characterized by HBsAg levels 1log lower than patients without them (P=0.003-0.02).

Similarly, in vitro, all the above-mentioned pairs of mutations determine a significant decrease (up to 90%) in the amount of extracellular HBsAg compared to wt (P values ranging from 0.022 to <0.001).

Finally, by structural analysis, these pairs of mutations determine a relevant reduction in the stability of HBsAg C-terminus and a profound rearrangement of this domain.

Conclusions: HBsAg levels in HBV genotype D are significantly lower than in genotype A and E in eAg- chronic infection. In genotype D, specific clusters of mutations in HBsAg C-terminus correlate with lower HBsAg levels in vivo, have a detrimental effect on HBsAg-secretion by altering HBsAg structure and in turn its stability. The detection of these mutations can be useful for the clinical interpretation of HBsAg levels in HBV genotype D infection.

Viral Hepatitis

PD 34 TACKLING THE UNDIAGNOSED FRACTION: EVIDENCE-BASED PUBLIC HEALTH GUIDANCE FOR INTEGRATED HBV, HCV AND HIV TESTING IN THE EU/EEA

A.K. Sullivan[1,2], L. Combs[3], L. Tavoschi[4,5], S. Croxford[2], S. Desai[2], L. Mason[6], M. Hoekstra[7], V. Delpech[2], S. Finne Jakobsen[3], A.J. Amato-Gauci[4], D. Raben[3]

[1]Chelsea and Westminster Hospital NHS Foundation Trust, United Kingdom, [2]Public Health England, United Kingdom, [3]University of Copenhagen, Denmark, [4]European Centre for Disease Prevention and Control, Sweden, [5]University of Pisa, Italy, [6]Pallas health research and consultancy, The Netherlands, [7]Freelance consultant

Background: Reducing the undiagnosed fraction for HBV, HCV and HIV is a global and regional priority. In 2015 ECDC set off to develop the first European integrated HBV, HCV and HIV testing guidance based on latest evidence from the EU/EEA, the 2010 ECDC HIV testing guidance and expert opinion. The resulting guidance aims to support countries in their efforts to increase the coverage and uptake of HBV, HCV and HIV testing, while encouraging integration of testing interventions.

Methods: Systematic reviews of the scientific literature in the EU/EEA from 2010-2017 were undertaken to retrieve evidence on HBV/HCV/HIV testing initiatives. Grey literature published since 2008 for HBV/HCV and 2010 for HIV was also reviewed. Quantitative (e.g. testing uptake rates, positivity rates) and qualitative (e.g. acceptability) outcomes were extracted. Evidence was summarised by setting, type of intervention and target population into decision making tables with proposed recommendations. These were presented to a panel of European experts and recommendations were agreed employing a consensus-building approach. Good-practice examples as case studies for HBV/HCV/HIV testing in the EU/EEA were also identified among the evidence and via two open calls and were graded by the expert panel for inclusion in the guidance.

Results: The evidence included 108 papers on HBV/HCV, 368 on HIV and 92 case studies mostly reporting studies from the UK and countries in Western Europe, including five and ten from Italy, respectively. A lack of shared threshold and heterogeneity in outcomes definition across studies limited the possibility for quantitative analysis. To improve the utility of the new guidance, a setting-based approach was adopted with focus on risk groups. A total of 43 recommendations were developed; covering primary healthcare, hospitals, other healthcare settings and community settings. New to the guidance are optimal testing frequency for at-risk groups, latest evidence for self-testing/self-sampling and partner notification, and inclusion of 15 case studies.

Conclusions: Systematic reviews enhanced by expert panel consensus can produce effective novel guidelines where evidence is lacking in specific topic areas and regions. An integrated HBV/HCV/HIV approach and the diversification of testing opportunities can help countries address all three infections more effectively and efficiently. The evidence-based guidance should encourage improved coverage and uptake in the EU/EEA, yet more research would be beneficial to address current gaps in the evidence such as effectiveness and model of care delivery for self-testing/self-sampling and partner notification.

Viral Hepatitis

PD 35 EFFICACY AND SAFETY OF VELPATASVIR PLUS SOFOSBUVIR REGIMEN IN HCV CHRONIC PATIENTS WITHOUT ADVANCED LIVER DISEASE NAIVE TO PREVIOUS DAA THERAPY: A META-ANALYSIS

M. Pisaturo, A. Russo, L. Onorato, N. Coppola

Department of Mental Health and Public Medicine – Infectious Diseases Unit. University of Campania Luigi Vanvitelli

Background: systematic data on treatment with sofosbuvir (SOF) and velpatasvir (VLP) for 12 weeks in anti-HCV/HCV RNA positive subjects without cirrhosis and advanced fibrosis and naïve to previous Interferon free regimen are scanty so a meta-analysis has been conducted to evaluate the efficacy of VLP plus SOF combination in these patients.

Methods: A systematic review and meta-analysis was conducted using MEDLINE, Google Scholar and Web of Science. All studies included had to fulfill the following criteria: (a) original data from randomized or non-randomized trials; (b) evaluation of efficacy of SOF plus VLP for 12 weeks in subjects without cirrhosis or advanced fibrosis, naïve to previous DAA therapy (c) identified fibrosis by liver histology (F0-F3 score for patients without cirrhosis and F0-F2 for those without advanced fibrosis) or Fibroscan (Transient Elastography-TE <12.5Pa for patients without cirrhosis and TE <9.5 for those without advanced fibrosis) or FIB-4 (score<3.25 for patients without cirrhosis and <1.45 for those without advanced fibrosis) or APRI (score <1 for patients without cirrhosis and <0.70 for those without advanced fibrosis) or Fibro-test (score <0.75 for patients without cirrhosis and <0.58 for those without advanced fibrosis) (d) report the primary outcomes clearly defined as Sustained Virological Response 12 (SVR), (f) written in English language, and (g) published online and indexed up to February 2019.

Results: A total of 1,103 potentially relevant articles were identified from the search of electronic databases. Of these, 1,072 articles were excluded after the first screening based on the title and abstracts, 31 were considered potentially valuable and full texts were retrieved for detailed evaluation. After further evaluation and manual search of the bibliography references of the relevant publications, a total of 16 articles met the inclusion criteria and were included in this meta-analysis. Table 1 shows characteristic of studies included in the meta analysis.

The prevalence of SVR with the double regimen of SOF and VLP was 96% (95% CI 0.96-0.97%) considering all the 4,907 subjects without cirrhosis included in the 16 selected studies (Table2, figure1). In 4 studies enrolling 1,371 subjects without advanced liver fibrosis the prevalence of SVR was also high [96% (95% CI 0.94 -0.97%)](Table2, figure2).

The prevalence of SVR was similar considering the 9 clinical studies and the 7 real-world studies (98%, CI 95%: 97-99% and 96%; CI 95%: 95-96%, respectively). (Table 2, Figure 1) Evaluating the data for the different HCV genotype, the SVR is high, ranging to 95-100%, also in HCV genotypes difficult to treat such as genotypes 1, 3 and 6 with a prevalence of SVR of 99%, 95% and 100%, respectively (Table 2).

Conclusion: Sofosbuvir plus velpatasvir therapeutic regimen was highly effective in HCV patients without advanced liver disease naïve to previous DAA regimen independently of the different HCV genotypes.

Viral Hepatitis

PD 36 ACCEPTABILITY AND EFFECTIVENESS OF A PRAGMATIC COMPREHENSIVE PROJECT OF LINKAGE TO CARE FROM ADDICTION SERVICES TO INFECTIOUS DISEASES UNIT IN HCV PEOPLE WHO INJECT DRUGS

A. Soria[1], E. Colella[1], E. Chiesa[2], A. Cardia[3], M. Bramani Araldi[4], D. Leto[3], G. Scaffidi[4], S. Mancastroppa[2], C. De Ferrari[3], A. Caruso[4], S. Marangon[2], M. Pecoraro[5], P. Columpsi[1], B. Tinghino[5], G. Galimberti[2], G. Migliorino[1], G. Lapadula[1]

[1]Unit of Infectious Diseases, San Gerardo Hospital, ASST Monza, [2]Addiction service (SERD) of Monza, ASST Monza, [3]Addiction service (SERD) of Limbiate, ASST Monza, [4]Addiction service (SERD) of Carate Brianza, ASST Vimercate, [5]Service of Alcohol disorders and new addictions (NOA) of Seregno, ASST Vimercate

Background: The WHO goal of HCV eradication by 2030 passes through strategic actions in target populations, specifically addressing people who inject or injected drugs (PWID).
Italian addiction services (SERD) offer opioid substitution treatment (OST) along with a multidisciplinary follow-up and represent a privileged setting for screening and treatment of HCV in attending PWID.
However, though screening for HCV-Antibody (HCVAb) is part of the laboratory package offered to all PWID at addiction service entrance, many users are still not linked to care in HCV treatment centers.
Methods: Since July 2018 we set up a pragmatic project of systematic fast-track referral of all HCVAb positive patients from SERD to Infectious Diseases (ID) Unit for treatment with direct acting antivirals (DAA).
Referral was arranged through direct contact (by phone or e-mail) with medical staff in a dedicated fast-track slot. At first appointment, comprehensive medical assessment, laboratory exams and arrangement for Fibroscan and abdomen ultrasound were organized, in order to reduce time wasting and risk of dispersion. An appointment for treatment initiation was arranged within 3 months. Here we present the cascade of care of the first 9 months of the project.
Results: Overall, in the addiction services of Monza-Brianza province, 1458 PWID are followed-up; of these, 532 (36.5%) are receiving OST with methadone or buprenorphine, and 186 (12.8%) are active injecting drug users. Test for HCV (HCV-Ab) was available for 480 subjects (90.2% of those in OST, but 32.9% of all users), and was positive in 238 out of 480 (49.6%) individuals. After excluding 32 subjects (13.4%) with negative HCV RNA (either for spontaneous HCV clearance or because of previous successful treatment with interferon/ribavirin), 69 out of 206 (33.5%) HCVAb positive patients have been referred to ID so far (median time between first contact and first appointment: 13 days): 11/69 (15.9%) did not show up at the first appointment, 15/69 (21.7%) had undetectable HCV RNA at screening. Treatment-by-second-appointment was started in 30/43 (69.8%) PWID after a median of 83.5 days from the first appointment. The remaining 13 subjects still have forthcoming scheduled second appointment. There were no discontinuations in patients on DAA, and 21 subjects had already completed treatment. Figure 1 shows the cascade of care.
Conclusions: Although preliminary, our results show that linkage to care for HCV treatment in a territorial defined population of PWID is feasible and effective. The main gaps in the cascade of care are the proportion of non-screened PWID attending the addiction services, and, to a lesser extent, the proportion of subjects who are referred but do not present at the first appointment. Conversely, once enrolled in ID service, PWID have shown a strong adherence to care. Removing barriers to access to HCV treatment centers by facilitating linkage to care could speed up the pace of HCV elimination in PWID.

Viral Hepatitis

PD 37 DAAS BASED TREATMENT FOR HIV/HCV COINFECTED PATIENTS: VIROLOGICAL AND METABOLIC OUTCOMES IN A REAL-LIFE STUDY

L. Onorato[1,6], L. Alessio[1], V. Sangiovanni[2], F. Borrelli[3], E. Manzillo[4], V. Esposito[5], F. Simeone[1], S. Martini[6], N. Capoluongo[2], S. Leone[7], G. Di Filippo[3], M. D'Abbraccio[5], L. Aprea[4], A. Salomone Megna[8], E. Milano[9], A. Saracino[9], N. Coppola[1,6]

[1]Infectious Diseases Unit, AORN Sant'Anna e San Sebastiano, Caserta, [2]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, [3]Infectious Diseases Unit, University Federico II, Naples, [4]IX Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, [5]Department of Infectious Disease and Infectious Emergencies, General Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, [6]Department of Mental Health and Preventive Medicine, Section of Infectious Diseases, University of Campania "L. Vanvitelli", Naples, [7]Infectious Diseases Unit, A.O S.G. Moscati, Avellino, [8]Infectious Diseases Unit, A. O G. Rummo, Benevento,[9]Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari.

Background and aims: Coinfection with HCV is common in HIV seropositive subjects. It is well known that both viruses can alter glucose tolerance, lipids metabolism and renal function. However, data from real-life studies evaluating the virological outcome of regimens based on all-oral direct acting antiviral agents (DAAs) and its impact on extra-hepatic manifestations of HCV in people living with HIV (PLWHIV) are missing. The aim of this study was to identify the factors associated with the viral response and to evaluate the effect on metabolic parameters of the treatment with DAAs in a cohort of HIV/HCV coinfected patients.

Methods: We conducted a multicentre retrospective cohort study enrolling all HIV/HCV coinfected patients treated with DAAs in one of the nine participating centres (8 in Campania, 1 in Apulia), for which HCV-RNA loads at 12 weeks after EOT were available. The primary outcome evaluated was the SVR12 rate; the epidemiological, clinical and virological characteristics associated with the viral response were analysed. Furthermore, viro-immunological, clinical and biochemical parameters were collected at baseline and compared to those acquired at EOT and at 12 and 24 weeks after.

Results: During the study period, 243 HCV-RNA-positive PLWHIV treated with DAAs, with a median post-treatment follow-up of 48 weeks (range 12-144) were enrolled. The mean age of patients was 51.3 (+7.7) years; 77.4% were males; 63.1% were injection drug users. At the enrolment the mean CD4+ cell count was 629.9 (+322.4) and 91.3% of patients had a HIV-RNA load <50 cps/mL; 39.3% were infected with HCV genotype 1a and 32.5% with genotype 3. A cirrhosis was present in 36.6% of subjects; 17 (7.0%), 110 (45%) and 116 (47.7%) were treated with first, second and third generation DAAs, respectively. The SVR12 was registered in 233 (95.9%) patients; no difference in sex and age distribution, risk factors, virological and immunological features, cardiovascular, metabolic, renal or psychiatric comorbidities, stage of liver disease and treatment received was observed between SVR and non-SVR patients. From baseline to the end of follow-up, we observed a significant increase in total cholesterol (from 159.3+41 to 173.5+41.6 mg/dl, p<0.001) and LDL cholesterol (from 91.9+34 to 105.9+33.5, p=0.001). No significant difference was observed for the creatinine clearance and for the fasting blood glucose levels.

Conclusions: The treatment with DAAs led to a high SVR12 rate in our cohort of HIV/HCV coinfected subjects, irrespective of epidemiological, clinical or virological characteristics. The increase in blood cholesterol level, already described after the treatment of HCV monoinfected subjects, was confirmed in our patients, while no improvement was registered in renal function and glucose tolerance. However, further data on larger samples with longer follow-up are needed to evaluate the effect of HCV eradication on metabolic outcomes in this setting.

Viral Hepatitis

PD 38 SERIOUS LIVER EVENTS AND LIVER-RELATED DEATHS IN HIV/HCV CO-INFECTED PATIENTS WITH DIABETES: DATA FROM THE ICONA FOUNDATION COHORT STUDY

S. Leone[1], P. Lorenzini[2], A. Cozzi-Lepri[3], G. Orofino[4], D. Bernacchia[5], A. Castagna[6], M. Menozzi[7], G. Guaraldi[7], G. Madeddu[8], A. Di Biagio[9], A. Gori[10], A. d'Arminio Monforte[11], for the ICONA Foundation Cohort Study

[1]Division of Infectious Diseases, Department of Internal Medicine, San Giuseppe Moscati Hospital, Avellino, Italy, [2]National Institute for Infectious Diseases L. Spallanzani, Rome, Italy, [3]Institute for Global Health, University College London, London, UK, [4]Infectious Diseases Unit A, Amedeo di Savoia Hospital, Turin, Italy, [5]Infectious Diseases Unit, ASST Fatebenefratelli-Sacco, DIBIC 'L. Sacco', University of Milan, Milan, Italy, [6]Infectious Diseases Department, IRCCS San Raffaele Scientific Institute & Vita-Salute University, Milan, Italy, [7]Clinic of Infectious Diseases, University of Modena and Reggio Emilia, Modena, Italy, [8]Infectious Diseases Unit, Department of Clinical and Experimental Medicine, University of Sassari, Sassari, Italy, [9]Infectious Diseases Unit, Policlinico San Martino Hospital, Genoa, Italy, [10]Infectious Diseases Unit, Department of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy and Department of Pathophysiology and Transplantation, School of Medicine and Surgery, University of Milan, Milan, Italy, [11]Clinic of Infectious and Tropical Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy

Background: Combination antiretroviral therapy has significantly reduced the mortality and morbidity among HIV-infected patients. The improvement in AIDS-related survival rates resulted in an increase of non-HIV-related deaths, including liver-related deaths. HCV infection seems to be associated with an increased incidence rate of diabetes, which itself plays a major role in the acceleration of liver disease and in the increased probability of liver-related complications. The aim of our study was firstly, to investigate the association between HCV infection and diabetes, and, secondly, to determine the risk factors of serious liver events (SLE) and liver-related deaths (LRD) and fibrosis progression among HIV/HCV co-infected patients.

Material and Methods: Patients free from SLE at baseline, enrolled up to December 2018 were included if they had at least one follow up visit. A cross-sectional analysis was performed to investigate the association between diabetes and HCV infection, by means of multivariable logistic regression. A further longitudinal analysis was performed in the population of HIV/HCV co-infected with FIB-4 index <3.25 at baseline, using the following endpoints: A) first event between SLE and LRD; B) liver fibrosis progression defined as the first of two consecutive FIB-4>3.25; C) first event between SLE, LRD and liver fibrosis progression. Diabetes diagnosis was used as time-dependent covariate.

Results: Data from 15,571 HIV patients were analysed: 2,944 (18.9%) were HCV-Ab positive and 739 (4.7%) presented a diagnosis of diabetes at their last follow-up. Viremic HCV co-infected patients had 3-fold risk (aOR 3.35 [95%CI 2.38-4.71]) of diabetes onset than HCV uninfected patients. On HIV/HCV co-infected population, 85 SLEs/LRDs occurred over 20,410 PYFU, for an IR of 4.2/1000 PYFU (95%CI 3.4-5.2). Diabetic patients had 3-fold risk of pooled SLE and LRD than patients without diabetes (IR 12.1/1000 [95%CI 5.8-25.4] and IR 3.9/1000 [95%CI 3.2-4.9], respectively; aIRR 3.06 [95%CI 1.30-7.19]). Furthermore, viremic HCV infection was independently associated with higher risk of SLE/LRD (aIRR 3.35 [95%CI 1.14-9.83]). Other factors independently associated with higher risk of SLE/LRD were the following: female gender, HBV co-infection, AIDS diagnosis, and higher FIB-4 at baseline. Multivariable analysis showed that HBV co-infection, AIDS diagnosis, viremic HCV co-infection, higher FIB-4 at baseline, and every day alcohol use were independently associated with liver fibrosis progression. Diabetes was not associated with risk of liver fibrosis progression (aIRR 0.94 [95% CI 0.51-1.75]) (Table 1).

Conclusions: Diabetic HIV/HCV co-infected patients had an increased risk of SLE and LRD compared to who did not have diabetes. These results warrant further investigations to better characterize the role of diabetes as an independent prognostic factor for liver-related complications among HIV/HCV co-infected patients.

Virology, Immunology and Basic science

PD 39 PRE-EXISTING PSYCHIATRIC COMORBIDITIES PREDICT DOLUTEGRAVIR DISCONTINUATION IN PEOPLE LIVING WITH HIV

M. Milesi[1], A. Borghetti[2], J. Cusato[1], C. Alcantarini[1], S. Bonora[1], A. Ciccullo[3], A. D'Avolio[1], G. Di Perri[1], S. Di Giambenedetto[2,3], A. Calcagno[1]

[1]Unit of Infectious Diseases, Amedeo di Savoia hospital, Department of Medical Sciences, University of Torino, Torino, [2] IRCSS, Fondazione Policlinico Gemelli, Rome, [3]Institute of Clinical Infectious Diseases, Catholic University of Sacred Heart, Rome, Italy

Background: Dolutegravir(DTG) is an integrase inhibitor(INSTI) that is listed among the preferred regimens in treatment guidelines for people living with HIV (PLWH).In some, but not all,cohorts a high rate of discontinuation for neuropsychological(NP) adverse effects was reported.Among the factors associated with this event the concomitant use of abacavir(ABC),female gender and older age were identified;additionally DTG exposure was reported to be higher in patients with NP symptoms.Several psychological symptoms were more common in patients carrying less common variants in SLC22A2 gene(encoding for OCT-2).Aim of this study was to identify risk factors for DTG discontinuation in two large Italian cohorts.

Methods: DOLU_OCT2 is a pharmacogenetic study enrolling patients that had received at least one dose of DTG.Ethics approval was obtained from each Institution's Ethics Committee. After signing a written informed consent patients'blood was withdrawn and genomic DNA was extracted using a QIAamp whole Blood Mini Kit (Qiagen,Valencia,CA, USA)according to the manufacturer's instructions. SLC22A2 808(rs316019) C>A polymorphism genotyping was conducted by real-time PCR-based allelic discrimination with the use of standard methods (LightCycler 96,Roche, Monza, Italy).Kaplan-Meier curves with log-rank analysis and Cox proportional hazard models were used.

Results: We enrolled 561 patients; 395 were male(70.4%) of median age and body mass index of 51 years(43 -57) and 23.9 Kg/m2(21.4-26.8).Chronic hepatitis was observed in 133(HCV), 32(HBV) and 25(HCV/HBV) patients. ABC was administered to 160 individuals (28.5%). Pre-existing psychiatric comorbidities were reported in 86(15.3%,mostly mood disorders and substance abuse)patients.Less common variants in SLC22A2 were observed in 90(CA alleles) and 9(AA alelles) subjects.After a median follow up of 27 months(18-37) DTG was discontinued in 105 subjects[18.7%,after a median of 7 months(1.5-17.2)].The most common reasons were NP adverse events(63, 11.2%),simplification(10, 1.8%)and gastrointestinal disturbances(9, 1.6%).Discontinuation rates for any reason(27.9 vs. 17.1%, p=0.022) and for NP symptoms(22.1vs.9.3%, p=0.001) were more common in patients with pre-existing psychiatric comorbidities. In patients without psychiatric comorbidities discontinuations for any reason(22.8vs.15.9%, p=0.07) but not for NP symptoms (7.6 vs.9.6%, p=0.15) were more common in patients with less common variants in SLC22A2. Gender,ABC (and other antiretrovirals) co-administration and age were not predictive of DTG discontinuation.

Conclusions: In these two cohorts DTG discontinuations were not uncommon and neuropsychiatric symptoms were the reason in 11.2% study participants. Pre-existing psychiatric disorders were the most relevant risk factor for discontinuation; in those without psychiatric comorbidities we observed a trend to a higher incidence of discontinuation in individuals presenting less common variants in OCT-2 encoding gene.

Virology, Immunology and Basic science

PD 40 GLECAPREVIR/PIBRENTASVIR PHARMACOKINETICS WHEN CO-ADMINISTERED WITH ANTIRETROVIRAL DRUGS IN A COHORT OF HCV/HIV PATIENTS

V. Pirriatore[1], L. Marinaro[1], R. Angilletta[1], A. Palazzo[1], A. Barco[1], C. Alcantarini[1], N. Forni[1], C. Montrucchio[2], M. Ferrara[1], A. Lazzaro[1], M. Tettoni[1], A. De Nicolò[3], A. D'Avolio[3], A. Calcagno[1], G. Di Perri[1], S. Bonora[1]

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy, [2]Unit of Infectious Diseases, Cardinal Massaia Hospital, Asti, Italy, [3]Interdepartmental Center for Clinical and Experimental Pharmacology (CIFACS), University of Torino, Torino, Italy

Background: Glecaprevir/pibrentasvir (Gl/Pib), a pangenotipic HCV treatment with excellent efficacy, is affected by potential drug-drug interaction when co-administered with CYP3A4 P-gp, BRCP, OATP1B1, 1B3 inducers or inhibitors. Available data don't recommend darunavir/r (DRV/r) due to increased risk of ALT elevations. Same recommendation is provided for darunavir/cobicistat (DRV/C), although no data are available with this combination. No concerns have been raised with Gl/Pib administered with elvitegravir/cobicistat (EVG/C) since Gl exposures remained within safety limits. Aim of our study was to describe Gl/Pib pharmacokinetics when co-administered with antiretroviral drugs (ARVs) in a real-life cohort of HIV/HCV patients.
Materials and methods: HIV/HCV co-infected patients treated with Gl/Pib receiving antiretroviral therapy (ARV) were enrolled. Gl/Pib plasmatic levels (Gl-pl and Pib-pl) (22±2 hours after last intake) were measured using UHPLC-MS/MS FDA and EMA validated method. Stiffness and steatosis were measured through transient elastography with ultrasound based controlled attenuation parameter (CAP). Non-parametric tests were applied as required. Data are reported as medians (IQR) and numbers (percentages).
Results: 62 determinations were collected from 30 patients (pt): BL characteristics are reported in table 1. 3 pts were treated with DRV/r or DRV/C for resistance issues. Median Gl-pl and Pib-pl were 16 ng/ml (7,2;43,5) and 11 ng/ml (7,75;22,2) respectively. A significant difference was observed between those receiving DRV/r and/or DRV/C, EVG/C, dolutegravir (DTG) and/or rilpivirine (RPV): Gl-pl 42 (15;42), 42 (17,2;77), 10 (5;12), p=0,049, respectively. No difference was observed between Pib-pl with different ARV (p=0,178). 1 female with DRV/C and metavir score 2 showed high GL-pl (896 ng/mL) and bilirubin increase with itchy rash during treatment. DRV/C was switched to raltegravir with symptoms regression and bilirubin normalisation. In 2 pt treated with EVG/C Gl AUC was 14773 and 13242 ng*h / ml; Cmax and Ctrough were 1913, 62 and 1971, 7 ng/mL respectively. 1 with DRV/C had Gl AUC 13772 ng*h /mL; Cmax and Ctrough were 1502 and 42 ng/mL respectively. All had metavir score 1. A positive correlation was observed between Pib-pl and CAP (p=0,048, rho=0,370). No difference in Gl-pl or Pib-pl with different metavir score (p=0,392, p= 0,897) and gender (p=0,482, p= 0,529) was reported.
Discussion: Gl and Pib plasmatic concentrations administered with different ARV regimens resulted comparable to literature values with higher Gl exposures with boosting agents. Intensive dose/time analysis in 2 patients with EVG/C and 1 with DRV/C, however, showed Gl exposures remaining within safety limits (3-fold increase compared to Gl-pl alone in non cirrotic patients). Our results support safe Gl/Pib co-administration with EVG/C and selectively in low metavir score patients when DRV/C have to be administered for therapeutic options' shortage.

Virology, Immunology and Basic science

PD 41 ANALYSIS OF MIRNAS IN TREATED HIV-1 PATIENTS WITH DIFFERENT LEVELS OF VIRAL SUPPRESSION

F. Falasca[1], D. Di Carlo[1], L. Mazzuti[1], M. Calabretto[1], L. Celani[2], G. D'Ettorre[2], I. Mezzaroma[3], G. Antonelli[1], O. Turriziani[1]

[1]Department of Molecular Medicine, [2]Department of Public Health and Infectious Diseases, [3]Department of Translational and Precision Medicine; Sapienza University of Rome

Background: Optimal virological suppression remains often an ideal goal since some patients may show persistent plasma residual viremia. Studies have shown that not only viral characteristics and pharmacokinetics, but also factors closely related to host could be associated to a disease control.
It has been demonstrated that some miRNA such as miR-150, miR-33a-5p, miR-223, miR-382 promote HIV-1 latency in resting CD4+ T cells and miR-324-5p, miR-34a and miR-132 interfere with viral replication at different stages of viral infection.
The aim of the study was to investigate if treated HIV-1 positive patients with different levels of viral suppression showed different miRNAs profile.
Methods: To evaluate cellular expression of miR-33a-5p, miR-34a, miR-132, miR-150, miR-223 miR-324-5p and miR-382 RT-Taqman assay was performed. Levels of miRNA were measured in PBMC from 56 antiretroviral therapy (ART) treated patients grouped in TND group (28 patients with a sustained undetectable viremia for at least 3 years) and LLV group (28 patients with at least 3 values of low-level viremia (LLV) between 37 -200 copies /ml). Twenty-three cellular samples from healthy donor (HD) were used as a control group. Kruskal Wallis test was used to evaluate differences in miRNA levels expression (log (2-ΔCt)) between groups. A regression model for logistic ordinal dependent variables (gender, age, therapy regimen, duration of therapy, stage of disease, years of infection) was built to identify factors associated with different miRNA expression levels calculated as fold changes and stratified according to the quartiles. Moreover, Pearson's correlation between miRNA fold changes value and clinical parameters was performed.
Results: Overall, cellular levels of miR-33a-5p, miR-34a, miR-150, and miR-324-5p were significantly higher in HIV infected patients compared to HD (tab1). When stratified according to viremia, both TND and LLV group showed significantly higher levels of miR-33a-5p, miR-34a, miR-150 than HD. In addition, a significantly higher expression of mir324-5p was found in TND group than HD (tab1).
Regression analysis showed that miRNA 34a and 324_5p expression levels included in the fourth quartile (fold change range: 1.37-2.96 p= 0.027 and 1.22-2.57 p=0.0045, respectively) were significantly associated with years of HIV-1 infection.
Furthermore, a positive correlation between CD4+ cell count and miRNA levels, except for miR-223, was found in patients with undetectable viral load.
Conclusions: These data suggest that expression pattern of some miRNA is altered in HIV infected population. Although, no difference of miRNA expression levels between patients with maximal viral suppression and patients with low level viremia was detected, analysis of other transcripts belonging to non-coding RNA, such as long ncRNA, siRNA and snoRNA, is needed to better understand the role of these molecules in maintaining maximal viral suppression.

Virology, Immunology and Basic science

PD 42 PREVALENCE OF RESISTANCE MUTATIONS IN A LARGE COHORT OF PERINATALLY HIV-1 INFECTED PATIENTS

R. Ungaro[1], L. Taramasso[1,2], B. Bruzzone[3], I. Vicenti[4], L. Galli[5], V. Borghi[6], D. Francisci[7], M. Pecorari[8], A. Zoncada[9], A.P. Callegaro[10], E. Paolini[11], L. Monno[12], S. Bonora[13], A. Di Biagio[14]

[1]University of Genoa, Department of Health Sciences (DISSAL), Genova, [2]Infectious Diseases Unit, Department of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, [3]Hygiene Unit, Policlinico San Martino Hospital, Genova, [4]Department of Medical Biotechnology, University of Siena, Siena, [5]Department of Health Sciences, University of Florence, Pediatric Infectious Diseases Division, Anna Meyer Children's University Hospital, Firenze, [6]Department of Infectious Diseases, University of Modena, Modena, [7]Infectious Diseases Clinic, Department of Medicine, University of Perugia, Perugia, [8]Microbiology and Virology Unit, Azienda Ospedaliera Universitaria di Modena, Modena, [9]Clinic of Infectious Diseases, Cremona Hospital, Cremona, [10]Microbiology and Virology Unit, ASST Papa Giovanni XXIII, Bergamo, [11]Unit of Immunohematology and Transfusional Medicine, Cremona Hospital, Cremona, [12]Infectious Diseases Unit, Bari Hospital, Bari, [13]Infectious Diseases Unit, Amedeo di Savoia Hospital, University of Turin, Torino, [14]Infectious Diseases Unit, Policlinico San Martino Hospital, Genova

Background: Currently, about 700 patients with perinatal HIV-1 infection (PHIV) are followed in Italy. The increased life expectancy of HIV-infected people poses the challenge of providing these young patients, often harbouring multiple drug resistant viruses, a treatment strategy remaining effective and tolerated for several decades. The few studies describing the prevalence of HIV drug resistance within PHIV, agree in reporting a high prevalence of drug resistance mutations (DRMs) decreasing sensitivity to different antiretrovirals. Data concerning the Italian PHIV population are lacking. Aim of this study was to assess the prevalence of DRMs in an Italian cohort of patients with PHIV, in order to define their remaining therapeutic options.

Material and Methods: We retrospectively analysed HIV-1 pol sequences of patients with PHIV, obtained from the Italian Antiviral Response Cohort Analysis (ARCA) database. DRMs were interpreted using the Stanford HIVDB resistance interpretation algorithm. An evaluation of susceptibility was conducted for every drug of the different antiretroviral classes; we defined limited therapeutic options (LTO) as the residual susceptibility to ≤ 1 antiretroviral class. Correlation between LTO and demographic, clinical and laboratory variables was investigated through a binary logistic regression model using LTO as a dependent variable.

Results : The profiles of a total of 94 patients with PHIV were retrieved from ARCA database. At the last available follow up point, 56/94 patients (60%) had HIV-RNA loads ≤ 50 copies/mL. Fourteen out of 94 patients (15%) had no DRMs. At least one major DRM to nucleos(t)ide reverse transcriptase inhibitors (N(t)RTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), protease inhibitors (PI) and integrase strand transfer inhibitors (INSTIs) was found in 74 (79%), 61 (65%), 33 (35%) and 7 (7%) patients, respectively. The most common DRMs are shown in Figure 1: of note, resistance to doravirine, cabotegravir and bictegravir was found respectively in 40%, 3% and 3% of patients. Dual class resistance was seen in 39/94 (41%) patients. Patients with LTO were 25/94 (27%): 19/94 (20%) had triple-class drug resistance, marked by concomitant DRMs to N (t)RTI, NNRTI and PI, and 6/94 (6%) patients harboured DRMs to all four classes. At multivariable model, LTO correlated with previous exposure to >10 therapeutic lines (p=0.049) and with HIV-RNA >50 copies/mL at last available follow up point (p=0.032).

Conclusions: The present study highlighted how patients with PHIV have high prevalence of DRMs and LTO in Italy, thus calling not only for new therapies, but also for new strategies to preserve drug susceptibility towards the upcoming new drug classes. Vertically infected patients bear the burden of years of suboptimal therapies plus possible drug resistance transmitted by their mother, and seeking for a tailored strategy to offer them a future in well-being is an urgent challenge to be faced.

Virology, Immunology and Basic science

PD 43 SOME HIV-1 GP120 POLYMORPHISMS COULD BE INVOLVED IN RESISTANCE TO FOSTEMSAVIR

L. Fabeni[1], B. Yagai[1], G. Berno[2], L. Carioti[1], R. Salpini[1], V. Svicher[1], C.F. Perno[3], M.M. Santoro[1], F. Ceccherini-Silberstein[1]

[1]Department of Experimental Medicine and Surgery, University of Rome "Tor Vergata", Rome, Italy, [2]Virology Unit, INMI L. Spallanzani, IRCCS, Rome Italy, [3]Department of Oncology and Hemato-Oncology, University of Milan, University of Milan, Milan, Italy

Background: Fostemsavir (FTV) is a member of a new drug class currently under investigation for highly drug-experienced HIV-1 infected patients. This antiretroviral is an attachment inhibitor that binds HIV-1 gp120, by blocking HIV attachment to host CD4+ T-cells. To date, mutations at seven positions (L116, A204, S375, M426, M434, S475 and V506) of gp120 are known to reduce FTV susceptibility both in vitro and in vivo. In this study, we evaluated the natural prevalence of such FTV-resistance mutations and their potential association with other HIV-1 gp120 polymorphisms.

Material and methods: The study was conducted on 1,997 HIV-1 gp120 sequences of B subtype obtained from plasma samples of individuals naïve to FTV from Los Alamos HIV Database. Prevalence of mutations at the FTV associated positions was evaluated in overall population and stratified according to HIV-1 tropism (Geno2Pheno algorithm, FPR=10%). A covariation analysis was performed to evaluate potential association between the FTV-resistance mutations and other gp120 polymorphisms present with a prevalence ≥5%. An average linkage hierarchical agglomerative clustering was also performed, analysing FTV-resistance mutations associated with each mutation alongside all the 511 gp120 amino acid positions.

Results: The following FTV mutations were detected: L116Q (0.05%), S375H (0.6%), S375M (1.4%), S375T (17.7%), M426L (7.6%), M434I (4.2%), M475I (1.7%). Among other natural polymorphisms at FTV resistance positions, only the mutation M426R was found with a prevalence >5% (16.3%). Generally, no specific association between viral tropism and FTV mutations prevalence was found, with the exception for S375M (R5 vs. X4: 0.7% vs. 3.9%, p=0.009) and S375T (16.6% vs. 22.1%, p=0.03). By the covariation analysis, specific gp120 mutations were positively correlated with FTV-resistance positions (Table). In particular, S375T correlated with I371V; S375M correlated with the three mutations L134W, I154V, and I323T; and M475I correlated with K322A. Finally, the polymorphism M426R strongly correlated with the mutations G167N, K192T, and S195N. The involvement of divergent pathways of gp120 mutations potentially associated with FTV-resistance has been confirmed by the existence of two distinct clusters and two pairs of mutations (bootstrap ≥0.98). Of note, all FTV mutations and polymorphisms present in the clusters are localized in class I/II–restricted T-cell epitopes and antibody epitopes, suggesting a potential role in HIV escape from immune response.

Conclusions: Despite the high variability of gp120, FTV-resistance mutations are found with a low prevalence in sequences from FTV-naïve individuals infected with HIV-1 B subtype. The potential contribution of some of these mutations with other specific gp120 polymorphisms to the development of a synergistic effect of resistance to FTV may have viro-immunological implications, thus deserving further in-depth in vitro and structural investigation.

Virology, Immunology and Basic science

PD 44 MYCOBACTERIUM TUBERCULOSIS COMPLEX GENETIC VARIATION AND MACROPHAGE POLARIZATION STATUS INFLUENCE PHAGOLYSOSOMAL ACIDIFICATION DURING INFECTION

M. Chiacchiaretta[1], N. Bresciani[1], A. Agresti[2], S. Zambrano[2,4], D. Mazza[3], F. Cugnata[4], C. Tassan Din[5], D.M. Cirillo[1], P. Miotto[1]

[1]Emerging Bacterial Pathogens Unit, Division of Immunology, Transplantation and Infectious Diseases, IRCCS Ospedale San Raffaele, Milano, Italy, [2]Chromatin Dynamics Unit, San Raffaele University and Scientific Institute, Milano, Italy, [3]Cancer Imaging Unit, Experimental Imaging Center, IRCCS Ospedale San Raffaele, Milano, Italy, [4]Vita-Salute San Raffaele University, Milano, Italy, [5]Infectious Diseases Clinical Department, Division of Immunology, Transplantation and Infectious Diseases, IRCCS Ospedale San Raffaele, Milano, Italy

Tuberculosis (TB) is the most common opportunistic infection in people living with HIV. Both M. tuberculosis (Mtb) and HIV pathogens are able to modulate macrophage (mφ) polarization, and this cellular mechanism might influence the synergism between TB and HIV. Since one of the main features of Mtb is its ability to block the phagolysosome maturation, we compared the acidification of phagolysosomes in M1 and M2 THP-1 derived mφ -like cells during in vitro infection with clinical isolates. As the role of bacterial genotype (lineage) in the Mtb infection is underestimated, we also considered different genetic background.

Clinical isolates and laboratory strains were engineered to express the fluorescent protein dsRed (EAI –L1, Beijing –L2, Haarlem, H37Rv, H37Ra, CDC1551 –L4, Africanum –L6). Strains were used for THP-1 derived macrophage (mφ)-like cells polarized toward M1 or M2 phenotype. Confocal microscopy was used to analyze the phagolysosomal acidification (LysoSensor Green) associated with the different strains at 4 h and 24 h post-infection. Image acquisition was carried out on a Leica TCS SP5 confocal microscope (63x, 1.40 NA immersion oil obj.; 0.89 µm x 7 stacks). Images were processed with ImageJ software to perform single-cell analysis and compare infected cells vs non-infected cells. For the analysis Mtb isolates were grouped by phylogeny (ancient: L1, L6; modern: L2, L4) and virulence (increased: Beijing, CDC1551; reduced: Africanum, EAI, H37Ra). The Mann-Whitney tests with Bonferroni correction were used to test differences between groups (reference strain: H37Rv).

Overall 6078 (3032 M1; 3046 M2) mφs were considered for the analysis of lysosomal acidification. Infection induced a statistically relevant increase of the number of lysosomes per cell compared to non-infected cells in both M1 and M2 macrophages ($P < 0.05$). More virulent strains were associated with higher acidification in both non-infected and infected M2 mφs (p-val <0.05), whereas acidification in M1 was induced only in infected mφs. No correlation was found between bacillary load and phagolysosomal acidification. Modern lineages were associated with higher bacterial burden.

Our data provide evidence that virulence features drive lysosomal acidification, while higher bacterial burden is associated with modern lineages. Virulent strains showed an association with lysosomal acidification also in surrounding, non-infected mφs, but only in M2 phenotype, suggesting a role for the microenvironment at infection site. Our single-cell approach highlights the role played in the infection by (i) the mφ's activation status and (ii) the isolate's features.

Virology, Immunology and Basic science

PD 45 PLASMA AND INTRACELLULAR PHARMACOKINETICS OF COBICISTAT IN THE CLINICAL SETTING

M. Ferrara, A. Trentalange, C. Alcantarini, A. Lazzaro, N. Forni, A. Ianniello, V. Avataneo, A. D'Avolio, A. Calcagno, G. Di Perri, S. Bonora

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

Background: Cobicistat (COBI) has replaced ritonavir as a booster for PIs and INIs.
No data are available on COBI pharmacokinetics (PK) according to different companion drugs and to intracellular(IC) accumulation. Aim of our study was to evaluate COBI plasma and intracellular (IC) exposure when taken with Atazanavir (ATV) or Darunavir (DRV), in the clinical setting.
Material and Methods: Patients (pts) were enrolled in our observational study (22 treated with ATV, 29 with DRV). Plasma and IC samples were collected as Ctrough (median 2 for patient). Moreover 9 pts administered with ATV/c and 9 pts with DRV/c once daily, were included in our study and underwent to intensive PK analysis. COBI and PIs plasma concentration were measured at the end of dosing interval and 2, 4, 8, 12 hours after drug intake and COBI and PIs plasma and IC Ctrough concentration were measured by means of UHPLC-MSMS validate method. Non-compartmental pharmacokinetic parameters were calculated and expressed as geometric mean (CI95%). Concentrations were expressed as ng/ml. Descriptive analysis were expressed as geometric mean (CI95%) and results analyzed by Mann-Whitney and by Spearman's test, as appropriate.
Results: 51 pts were 72% male, median age 53 (IQR 49,5; 56,5) and BMI 24,9 (IQR 22,0; 26,5).
COBI area under the curve (AUC), Cmax and Cmin when dosed with DRV resulted to be 3710,0 (2259,4 -5160,6) ng/h*mL, 541,0 (366,7-715,2) ng/mL and 11,3 (7,6-15,0) ng/mL, respectively. When dosed with ATV, COBI parameters resulted to be 11446,4 (8562,5-14330,4) ng/h*mL, 1273,6 (1108,7-1438,6) ng/mL and 60,3 (-16,8-137,4) ng/mL, respectively. All COBI PK parameters were significantly higher when dosed with ATV as compared with DRV (AUC p<0,001, Cmax p<0,001 and Cmin p=0,003).
Dosed with ATV, COBI plasma and IC Ctrough resulted to be 47,7 (-78,9,0; 174,5) ng/mL, and 103,7 (-2,6; 210,0) ng/mL, respectively, and COBI ratio IC/plasma was 2,170 (0,899; 3,441); Dosed with DRV, COBI plasma and IC Ctrough were 14,4 (5,4; 23,4) ng/mL, and 54,6 (21,8; 87,5) ng/mL, respectively, and COBI ratio IC/plasma observed was 3,786 (2,407; 5,166). Difference of COBI IC ratio between ATV and RV was not significant (p=0,106).
No correlation was found between gender, age and BMI and COBI, plasma and IC concentration, and ratio IC/plasma. Plasma and IC COBI concentrations showed to be significantly correlated (p=0,011).
Discussion and Conclusion: This is the first evaluation of COBI plasma and IC PK in the clinical setting. As it was previously showed for RTV, COBI plasma exposure showed to be higher, by two-fold, when dosed with ATV/c as compared to DRV/c. Moreover, cellular accumulation ratio (IC to plasma ratio) of COBI, ranging from 2.17 to 3.7, was shown to be lower than reported for RTV (up to 9). These data could contribute to explain the differences of tolerability previously observed between RTV and COBI (e.g. lower lipids increase).

Virology, Immunology and Basic science

PD 46 CHRONIC INFECTIONS BALANCE INFLAMMAGING: IMMUNITY OF CENTENARIANS WITH HIV OR HCV

G. Guaraldi[1], G. Dolci[1], S. De Biasi[1], D. Lo Tartaro[1], M. Nasi[1], J. Milic[1], C. Vaccari[1], H. Santos[2], I. Pintassilgo[2], C. Martins[2], C. Mussini[1], A. Cossarizza[1]

[1]University of Modena and Reggio Emilia, Modena, Italy, [2]Hospital Garcia de Orta, Lisbon, Portugal

Background: HIV and HCV are major drivers of inflammation at all ages, but the immunological features in extremely old individuals (like centenarians) with such chronic infections have been never described. To explore relationships between chronic infection and inflammaging, we characterized main immune cell subsets of two centenarians living with HIV or HCV, compared to 10 healthy centenarians without these infections.
Methods: We enrolled a 100-years old HIV positive male (Case A; CD4=560cells/µL (34%) with CD4/CD8=0.97, HIV RNA undetectable, CMV IgG+) who has been infected for 25 years in collaboration with the Hospital Garcia de Orta and NOVA Medical School of Lisbon, Portugal and a 100-years old HCV positive female (Case B; HCV G1b RNA=1,100,000; CMV IgG-) living in Modena, Italy. Peripheral blood mononuclear cells (PBMC) were stained with a large panel of fluorescent monoclonal antibodies (mAbs); monocytes were defined as total (CD14+,HLA-DR+), classical (CD14+,CD16-), intermediate (CD14+,CD16+) and non-classical (CD14dim,CD16+). NK cells were defined as CD16+CD56+; T cells were quantified using DURACLONE IM T (Beckman Coulter, BC) with the addition of other mAbs for the identification of senescent (CD57+), exhausted (PD-1+), activated (HLA-DR+). Naive (N), central memory (CM), effector memory (EM) and terminally differentiated EM (EMRA) were quantified among CD4+ and CD8 T+ cells. Analyses were performed on a 12 color acoustic focusing flow cytometer (Attune NxT, ThermoFisher) and a 21 color Cytoflex LX (BC).
Results: Table 1 shows the pictures (consent was provided) and data from Case A and Case B compared to ten well characterized healthy centenarians (controls, described in Nasi et al. Aging Cell, 2006). The most surprising features were the well preserved amount of naive cells among CD4 and CD8+ T cells, and the low degree of T cell activation and exhaustion, especially among CD4+ T cells. HCV infection seems to induce greater modifications in CD4+ T cells subsets that, conversely, were similar between Case A and controls.
Conclusions: Innate and adaptive immune cells were apparently well preserved in centenarians with HIV or HCV. Age-related immune decline was not exacerbated by these chronic infections. In these exceptional cases, chronic infections seem to counterbalance inflammation. Thus, the question arises concerning the paradoxical role of a virus causing immunosuppression, like HIV, that seems to control the proinflammatory status and immune activation typical of extremely old individuals.

Virology, Immunology and Basic science

PD 47 MARAVIROC AS A LATENCY REVERSING AGENT IN CELL LINE MODELS

I. Vicenti[1], F. Dragoni[1], M. Monti[2,4], A. Giannini[1], A. Ciabattini[1], B. Rossetti[3], A. De Luca[1,3], D. Medaglini[1], E. Montomoli[2,4], M. Zazzi[1]

[1]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [2]Department of Molecular and Developmental Medicine, University of Siena, Siena, Italy, [3]Infectious Diseases Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy, [4]VisMederi srl, Siena, Italy

Background: Silently HIV-1 infected cells escape antiretrovirals and immune attack playing a key role in virus persistence. The combination of compounds reversing HIV-1 latency and antiretroviral drugs blocking virus replication is being evaluated as a virus eradication strategy. Recent studies suggested that maraviroc (MVC), an anti-HIV-1 CCR5 antagonist, may exert an HIV-1 latency reversal effect. This study aimed at defining MVC mediated induction of HIV-1 in 3 in vitro cell line models of latency

Materials and Methods: HIV-1 promoter activation was evaluated in TZM-bl cells expressing luciferase under the control of HIV-1 LTR. Induction of extracellular and cell-associated HIV-1 RNA (CAR) was evaluated by real time PCR in U1/HIV-1 and ACH-2, two HIV-1 latently infected lymphoblastoid cell lines expressing different amounts of CCR5 and inducible to produce virus upon stimulation with transcription activators. NF-kβ induction was evaluated in all nuclear extracts by the NF-kB (p65) Transcription Factor Assay Kit. Expression of CCR5 was assessed by flow cytometric analysis. Cell lines were treated with 4-fold dilutions of MVC (80-0.31 μM) for 24 hours. Phytohemagglutinin (PHA, 10 μg/ml) and Ionomycin (ION, 1 μg/ml) in combination with Phorbol-myristate-acetate (PMA, 50 ng/ml) were used as control latency reversal agents (LRA). Induction was expressed as fold-activation (FA) with respect to untreated cells. MVC cytotoxicity was measured by the Cell Titer-Glo viability assay

Results: Cell surface CCR5 was detectable in 40% of TZM-bl, 94% of U1/HIV-1 and 5% of ACH-2 cells. MVC was not cytotoxic in the tested range (160-0.31 μM). No LTR activation was observed in TZM-bl cells at any MVC concentration tested (0.93±0.07 FA), nor with PHA (1.04±0.06 FA), with respect to ION+PMA (4.51 ±0.15 FA). HIV-1 CAR was weakly induced in U1/HIV-1 cells at different MVC concentrations (80-1.25 μM FA) with values (1.28±0.08 FA) comparable to PHA (1.30±0.37 FA), but considerably lower than ION+PMA (317.53±120.32 FA). HIV-1 CAR was not induced in ACH-2 cells at any MVC concentration tested (0.81±0.13 FA). In U1/HIV-1 cells, extracellular HIV-1 RNA FA was 3.11±0.92, 1.35±0.50, 1.90±0.46 at 80, 20 and 5 μM MVC, respectively, higher than PHA (0.83±0.19 FA) but lower than ION+PMA (1768.03±1055.31 FA). With ACH-2 cells, extracellular HIV-1 RNA was induced with 80 μM (3.97±0.32) and 20 μM (1.77±0.41 FA) MVC. No activation was observed with PHA (1.11±0.08 FA) and lower MVC concentrations (0.75±0.29 FA). NF-kB expression was not upregulated at any MVC concentration in either U1-HIV-1 (0.74±0.16 FA), ACH-2 (0.76 ±0.37 FA) or TZM-bl (1.11±0.05 FA) cells

Conclusions: Based on this and previous studies, MVC appears to act as a weak LRA in some cell line models. While further investigation could unveil the reasons for such differential effects, ex-vivo studies of patient derived latently infected CD4 cells are required to define a possible role of MVC as clinically relevant LRA

Virology, Immunology and Basic science

PD 48 ROLE OF BOOSTED VS UNBOOSTED PROTEASE INHIBITORS ON DOLUTEGRAVIR PLASMA AND INTRACELLULAR PHARMACOKINETIC IN DUAL THERAPY CLINICAL SETTING

M. Ferrara, L. Marinaro, C. Alcantarini, A. Barco, M. Milesi, M.C. Tettoni, A. Ianniello, A. De Nicolò, A. D'Avolio, A. Calcagno, G. Di Perri,

S. Bonora

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

Background: Dolutegravir (DTG) 50 mg qd plus atazanavir/ritonavir (ATV/r) 300/100 or darunavir/ritonavir (DRV/r) 800/100 mg has been scarcely described as possible NRTI-sparing dual regimen. While ATV has been reported to increase DTG plasma concentrations both dosed with ritonavir (RTV) and unboosted, DRV is reported to reduce DTG exposure. Since intracellular (IC) DTG concentrations in clinical setting have not been described aim of our study was to evaluate plasma and IC DTG pharmacokinetic (PK) when switching from RTV to Cobicistat (COBI), and to compare DTG PK when dosed with unboosted ATV 400 mg (uATV) to evaluate the role of boosters on plasma and IC DTG exposure.

Methods: Patients (pts) administered with DTG 50 mg plus ATV/r switching to Atazanavir/cobicistat (ATV/c) qd were included. As comparison plasma and IC DTG PK data from pts treated with DTG and uATV were considered. Plasma and IC DTG concentration were measured by means of UHPLC-MSMS validated method at the end of dosing interval (T0), 2 (T2) and 4 hours (T4) after drug intake. Non-compartmental PK parameters were calculated and reported as ng/ml and expressed as geometric mean (CI95%). Plasma and IC DTGCtrough sparse samples were collected from pts treated with DTG/r and DTG/c (plus ATV or DRV) and compared to data of DTG dosed with uATV.

Results: Eight patients underwent intensive PK analysis, 5 were male, age and BMI were 52 years (47-60) and 27 Kg/m2 (23-32). Dosed with ATV/r, DTG AUCss, Cmin, and Cmax were 55590,4 ng/mL*h (14244,0 -96936,9), 1108,4 ng/mL (193,1-2023,8) and 3637,4 ng/mL (953,4-6321,3), respectively. After switching to ATV/c, DTG AUCss, Cmin, and Cmax were 138809,33 ng/mL*h (108437,9-169180,7), 2772,7 ng/mL (1634,8-3910,7) and 8519,2 ng/mL (6622,1-10416,3), respectively. DTG AUCss, Cmin, and Cmax PK dosed with uATV resulted 55590,4 ng*h/mL (14244.0-96936.9), 1916,4 ng/mL (1151,1-2681,8) and 4317,1 ng/mL (2900,5-5733,9). Median IC, IC/plasma ratio of intensive PK analysis, plasma and IC DTG Ctrough data are reported in Table 1. Intensive PK analysis showed a 150% increase inDTG AUCss after switch from ATV/r to ATV/c (p=0,011), and 73% increase in plasma DTGCtrough after switch to COBI (p=0,008). DTGtrough IC concentration showed 7%, 26% and 18% accumulation within cells when dosed with uATV, RTV and COBI, respectively, showing a higher IC/plasma ratio with RTV(p=0,005) and COBI (p=0,019) than with unboosted PI.

Conclusions: This is the first evaluation of DTG plasma and IC concentration in the setting of dual therapy based on DTG and boosted PI vs unboosted PI in intensive PK analysis and Ctrough data. Comparing different booster plus ATV, DTG plasma 24 hrs exposure resulted higher plus COBI, as well as Ctrough plasma concentration. Moreover, IC DTG accumulation was significantly higher when dosed with boosted PI (with both RTV and COBI). Long-term clinical evaluation to better evaluate the role of boosting agents on DTG plasma and IC PK are warranted.

HIV therapy and management

PD 49 DURABILITY AND EFFICACY OF DOLUTEGRAVIR-BASED 2 DRUG REGIMENS IN VIROLOGICALLY SUPPRESSED PATIENTS: A REAL LIFE CLINICAL SETTING

V. Micheli[1], D. Rizzelli[1], D. Mileto[1], A. Mancon[1], F. Romeri[1], A. Giacomelli[2], M.V. Cossu[3], L. Oreni[2], A.F. Capetti[3], S. Rusconi[2], M.R. Gismondo[1]

[1]Laboratory of Clinical Microbiology, Virology and Bioemergencies, ASST Fatebenefratelli-Sacco, L. Sacco University Hospital, Milan, Italy, [2]Infectious Diseases Clinic, DIBIC Luigi Sacco, University of Milano, Milano, Italy, [3]1st Division of Infectious Diseases, ASST Fatebenefratelli-Sacco, L. Sacco University Hospital, Milan, Italy

Background: Two-drug regimens (2DR) are largely used for therapy switch in virologically suppressed patients; in this regard, Dolutegravir (DTG) represents the main choice as anchor-drug.
The aim was to assess efficacy and durability of 4 different DTG-based 2DR in HIV-1 virologically suppressed experienced patients in clinical practice.
Material and methods: Inclusion criteria were: baseline (BL) HIV-RNA (VL) <200 cp/mL; switch to DTG plus 3TC, RPV, DRV±r/c or ATV±r/c for at least 24 weeks; availability of ≥2 determinations of VL and CD4. The primary endpoint was the evaluation of virological outcome at last follow-up (FUP), also according to historical genotype when available (ARCA DB). Patients were categorized as: Not Detected (ND, all VLs <37 UND cp/mL); Detected (D, at least one VL<37 D cp/mL); Quantified (Q, at least one 37<VL<200); Blip (VL>200 cp/mL between two <37 cp/mL); Virological Failure (VF, 2 consecutive VL>200 cp/mL); Low Level Viremia (LLV, persistent 37<VL<200 cp/mL). Resistance has been evaluated using Stanford HIVdb and HIV subtype was obtained by means of REGA HIV-1 Subtyping. Pre-switch data were also evaluated.
Results: A total of 301 2DR patients (pts) were included: 59 switching to DTG+3TC, 73 to DTG+ATV, 71 to DTG +DRV and 98 to DTG+RPV; the main reasons for switch were simplification (46%) and toxicity (25%). Males were 66.4%, median age was 52 (47-56) years, years of HIV infection 18.2 (11.2-24), years of pre-switch therapy exposure 16.2 (9-19.9), FUP 28.2 months (20.7-35.9) with 7 points (5-8). At switch VL were ND, D and Q for 181 (60%), 89 (30%) and 31 (10%) pts respectively, while median CD4 was 673 (492-895) cell/mm3. Viral subtype was available for 143 pts: 117 were B and 26 non-B. The analysis was performed on 301 pts at month 6, 291 pts at month 12 (10 pts changed drug regimen between month 6 and 9) and 252 pts at month 24 (20 pts changed drug regimen between month 12 and 24 and 19 pts did not reach 24 months of FUP). In regards to VL trend, a decrease of patient with Q VL was observed at each FUP, also stratifying the patients in the 4 different 2DR groups. During the study period 5 (1.6%) pts experienced a blip, 7 (2.3%) LLV and 5 (1.6%) a viral rebound with or without drug resistance mutations. According to the historical genotype, pts presenting the worst resistance profile were treated with DTG+DRV, while pts with a more favourable one with DTG+3TC; all pts of the latter group are still successfully treated despite the presence of M184V in two. Six out of 7 pts with LLV presented the same condition in the period before the switch.
Conclusions: The 4 DTG-based 2DR showed high viro-immunological efficacy as switch strategy in drug-experienced patients. The choice of 2DR was based on genetic barrier, the degree of pre-treatment of the pts and the previous virological failures. The evaluation of historical genotype confirms the strategy chosen by clinicians and reinforces its added value in clinical practice.

HIV therapy and management

PD 50 IMPROVEMENT OF CD4/CD8 RATIO IN EXPERIENCED PATIENTS SWITCHING TO DOLUTEGRAVIR BASED DUAL THERAPIES

L. Taramasso[1,2], A. Di Biagio[3], E. Ricci[2], N. Squillace[4], R. Gulminetti[5], G.V. De Socio[6], B. Menzaghi[7], G.C. Orofino[8], G. Madeddu[9], G. Pellicanò[10], B.M. Celesia[11], A. Bandera[12], A. Gori[12], P. Bonfanti[13] on behalf of CISAI study group

[1]Department of Health Sciences (DISSAL), University of Genova, Genova, Italy, [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [3]Infectious Diseases Unit, Policlinico Hospital San Martino, Genova, Italy, [4]Infectious Diseases Unit ASST-MONZA, San Gerardo Hospital-University of Milano-Bicocca, Monza, [5]Department of Medical Sciences and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo -University of Pavia, [6]Department of Internal Medicine 2, Infectious Diseases Unit, Perugia "Santa Maria della Misericordia" General Hospital, [7]Unit of Infectious Diseases, ASST della Valle Olona – Busto Arsizio (VA), [8]Division I of Infectious and Tropical Diseases, ASL Città di Torino, [9]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, [10]Department of Human Pathology of the Adult and the Developmental Age "G. Barresi", Unit of Infectious Diseases, University of Messina, Messina, Italy, [11]Unit of Infectious Diseases University of Catania ARNAS Garibaldi Catania, [12]University of Milan, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [13]Unit of Infectious Diseases, A. Manzoni Hospital, Lecco

Background: Previous cohort studies reported a CD8 T-cell increase and a reduction of CD4/CD8 ratio in patients living with HIV (PLWHIV) and in treatment with dual therapies. Data are still lacking on dual therapies containing new drugs such as dolutegravir (DTG). Aim of the present work is to evaluate CD4/CD8 dynamics in patients in DTG based dual therapies (DTG-DUAL) and compare them with patients in DTG containing triple therapies.

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-DUAL were included and subsequently compared with patients in treatment with tenofovir/emtricitabine (TDF/FTC) + DTG and with abacavir/lamivudine (ABC/3TD)/DTG. At least 1 follow up visit was requested for study entry.

Results: 319 patients were enrolled, 91 in DTG-DUAL, 52 in TDF/FTC+DTG and 242 in ABC/3TC/DTG. Patients of the three groups had similar demographic characteristics and baseline labs values, except for HDL cholesterol in TDF/FTC+DTG group (mean 43± standard deviation 14 mg/dl, vs. 51±15 in DTG-DUAL and 51±18 in ABC/3TC) and for cumulative years in antiretroviral treatment in patients in ABC/3TC/DTG [median 9.0 (interquartile range 4.0-16.0) years vs. 12.2 (3.4-18.1) in TDF/FTC+DTG and 12.2 (6.8-18.3) in DTG-DUAL].

Mean CD4/CD8 ratio at baseline was 0.92 ±0.59 in DTG-DUAL, 0.72 ±0.47 in TDF/FTC+DTG and 0.81±0.50 in ABC/3TC/DTG. At one year follow up CD4/CD8 ratio increased significantly in all groups but DTG-DUAL: +0.05 (95% confidence interval -0.02, 0.13) in DTG-DUAL (p=0.21), 0.10 (95% CI 0.04, 0.16) in TDF/FTC +TDG (p=0.002) and 0.09 (95% CI 0.05, 0.14) in ABC/3TC/DTG (p<0.0001). The rise of CD4/CD8 ratio was driven by a significant increase in CD4 T cells/mm3 (+101, 95% CI 73, 128, p<0.0001), while CD8 T cell number remained stable through all groups (33 cells/mm3, 95% CI -1, 67, p=0.06). No differences were found among the three treatment groups.

Despite low sample size, we subsequently split the DTG-DUAL on the basis of drug combinations: DTG+3TC (22 patients), DTG+ darunavir (DRV, 21 patients), DTG + rilpivirine (RPV, 31 patients), DTG + atazanavir (ATV, 8 patients). As shown in the Table, CD4/CD8 ratio raised significantly only in pts on DTG+3TC.

Comparison between groups of therapy, after adjustment for baseline values of CD4/CD8 ratio, HDL cholesterol and years of previous antiretroviral therapy, as compared to ABC/3TC/DTG, revealed CD4/CD8 ratio change from baseline was only significant in subjects on DTG+3TC.

Conclusions: PLWHIV that are switched to DTG-DUAL therapies experience a significant improvement of CD4/CD8 ratio, also in patients with a long history of ART. Controlled studies with longer follow up will clarify the clinical impact of DTG-DUAL.

HIV therapy and management

PD 51 SIMPLIFICATION TO HIGH-GENETIC-BARRIER 2DR IN PLWH HARBOURING 4-CLASS DRUG-RESISTANT HIV-1 ENROLLED IN THE PRESTIGIO REGISTRY

D. Canetti[1,2], L. Galli[1], N. Gianotti[1], A. Celotti[3], L. Calza[4], R. Gagliardini[5], S. Rusconi[6], S. Modica[7,8], G. Cenderello[9], M. Ferrara[10], M. Santoro[11], M. Zazzi[8], A. Castagna[1,2] on behalf of the PRESTIGIO Study Group

[1]Clinic of Infectious Diseases, IRCCS San Raffaele, Milano, Italy, [2]Clinic of Infectious Diseases, Vita-Salute San Raffaele University, Milano, Italy, [3]Università degli Studi di Brescia, Spedali Civili di Brescia, Brescia, Italy, [4]Unit of Infectious Diseases, Policlinico Sant'Orsola-Malpighi, Bologna, Italy, [5]National Institute for Infectious Diseases L. Spallanzani, IRCCS, Roma, Italy, [6]Sacco Hospital, Infectious Diseases, University of Milan, Milano, Italy, [7]Infectious Diseases Unit, AOU Senese, Siena, Italy, [8]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [9]Infectious Diseases Department, Galliera Hospital, Genova, Italy, [10]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy, [11]Department of Experimental Medicine and Surgery, University of Rome Tor Vergata, Rome, Italy

Background: two-drug regimens (2DRs) proved effective and safe in treatment-naïve and virologically suppressed people living with HIV (PLWH) harbouring wild-type HIV, while limited information is available about their efficacy in drug-resistant HIV infections. The aim of this study was to describe the virological outcome of 2DRs in patients with HIV variants resistant to four drug-classes, including nucleoside reverse transcriptase inhibitors (NRTIs), non-NRTIs (NNRTIs), protease inhibitors (PIs), and integrase strand transfer inhibitors (InSTIs).

Material and methods: we included adult PLWH harbouring a documented 4-class drug-resistance to NRTIs, NNRTIs, PIs, InSTIs (if resistance tests not available, a documented viral failure to an InSTI was accepted), with HIV-1 RNA < 50 copies/mL at the start of the 2DR, after documented evidence of 4-class drug-resistance. All the patients were recorded in the national prospective PRESTIGIO Registry. Baseline (BL) was the date of the start of the 2DR. Follow-up accrued from the BL to viral failure (VF) or treatment failure (TF), lost to follow-up, death or data freezing (January 31, 2019), whichever occurred first. VF was defined as HIV-RNA > 50 copies/mL in two consecutive determinations or a single determination > 50 copies/mL followed by ART modification or a single determination > 1000 copies/mL. TF was defined as VF and/or any modification of the 2DR.

The incidence rates (IR) of VF or TF were calculated by use of univariable Poisson regression models and expressed as person-months of follow-up (PMFU).

Results: ten patients satisfied the inclusion criteria: details are described in Table 1.

Seven (70%) patients were treated with dolutegravir (DTG) plus darunavir/ritonavir (DRV/r); one patient (10%) each was treated with DTG plus rilpivirine (RPV), DTG plus maraviroc (MVC) or DRV/r plus etravirine (ETR), as illustrated in Table 2.

In all patients, DTG was administered at 50 mg bid; DRV/r was administered at 600/100 mg bid in 7 cases (88%), 800 mg bid plus 100 mg qd in one case (12%). Baseline Genotypic Susceptibility Score (GSS) was 2 in three patients (30%) and ≤1 in seven (70%); the patient who experienced VF had a GSS of 0 (Table 2).

During a median follow-up of 16.5 months (3.5 – 25.7), two TFs occurred for the following reasons: one VF (VL =16031 copies/mL) and one discontinuation because of potential drug interactions with direct-acting anti-HCV drugs; both events led to a more complex regimen. The IR of VF was 0.58 per 100-PMFU (95%CI: 0.002 – 2.28) and the IR of TF was 1.15 per 100-PMFU (95%CI: 0.11 – 3.31).

Conclusions: in virologically suppressed PLWH harbouring a documented 4-class drug-resistance, a high-genetic-barrier 2DR, dosed according to antiretroviral susceptibility profile, may represent a therapeutic strategy that deserves to be further explored.

HIV therapy and management

PD 52 A DUCTILE DUAL THERAPY WITH ENHANCED GENETIC BARRIER FOR MULTI-EXPERIENCED PATIENTS

F. Maggiolo, L. Comi, E. Di Filippo, D. Valenti, A.P. Callegaro, M. Rizzi
ASST Papa Giovanni XXIII, Bergamo

Background: Multi-experienced patients with harbored resistance mutations are usually excluded when less-drug regimens are considered. We explored the possibility to use a dual ARV therapy with enhanced genotypic barrier in these patients.
Methods: This was a cross-sectional, observational study conducted in a single center at the beginning of 2019. All HIV+ patients treated with dolutegravir (DTG) plus darunavir/cobi (DRV/c) were included. Socio-demographic data, HIV infection characteristics (mode of transmission, duration of infection, plasma HIV RNA and CD4 count), were obtained from the medical DB. The day DTG+DRV/c was started was considered the baseline point, while the last available datum was used to compute the outcome. The duration of infection was defined as the time elapsed from the year of diagnosis and the year DTG+DRV/c was started. All historical genotypes were considered to define resistance. Wilcoxon test was used for inferential analysis.
Results: 73 patients received DTG+DRV/c for a median of 17 months (IQR 15 months). Their median age was 52.4 years (IQR 9 years) and 30.1% were females. The median time from infection was 21.7 years (IQR 13 years) and, at diagnosis, 65.8% of them had a CD4 count < 200 cells/mcL. When DTG+DRV/c was introduced 50/73 of them presented at least 1 and up to 6 different non-communicable chronic disease (NCCs) most commonly constituted by dyslipidemia, cardiovascular, neoplastic, neurologic or psychiatric diseases. Furthermore, 11% where HCV-RNA positive, 4 % HBV positive (on entecavir) and 7% cirrhotic. Before DTG +DRV/c introduction they had been treated with a median of 7 (IQR 5) different regimens being 100% experienced for NRTI and NNRTI, 94.5% for PI, 84.9% for INI and 15.1% for entry inhibitors. At baseline 84.9% of patients were resistant to at least one NRTI, 68.5% to at least one NNRTI, 17.8 to PIs and 9.6% to INI or entry inhibitors. The most common resistance conferring mutations were 184V/I (71.2% of cases), TAMs (60.3%), 103N (39.7%), 181C (28.8%) and 65R (11%). In 6/7 patients with INI resistance DTG was used at the dose of 50 mg BID. At baseline 63% of patients had a viral load < 50 copies/ml; 8.9% between 50 and 200 and 28.1% > 200 copies/ml; at the end of follow-up the same figures were 91.4%, 5.7% and 2.8%; the 2 patients with a persistent viremia > 200 copies/ml had an adherence rate < 40% (figure). No new mutations were selected during DTG+DRV/c therapy. From an immunological standpoint, CD4 counts raised from a median of 558 (IQR 425) cells/mcL to a median of 641 (IQR 799) cells/mcL (P < 0.0001) (figure).
Conclusions: Therapy simplicity is relevant in patients with limited treatment options, too. In these subjects a high genetic barrier is mandatory to overcame hystorical resistance and to avoid further selection of mutations. Simplicity may favor adherence and management of concomitant NCCs enhancing the virologic response in these difficult-to-treat subjects.

HIV therapy and management

PD 53 PREDICTORS OF INCOMPLETE VIROLOGIC RESPONSE AND VIROLOGICAL FAILURE IN PATIENTS WITH ACUTE HIV INFECTION. RESULTS OF ITALIAN NETWORK OF ACUTE HIV INFECTION (INACTION) COHORT

L. Taramasso[1], M. Fabbiani[2], G. Bozzi[1], A. Muscatello[1], S. Nozza[3], I. De Benedetto[4], M. Ripa[3], R. Dell'Acqua[3], A. Antinori[5], C. Pinnetti[5], A. Calcagno[4], M. Ferrara[4], E. Focà[6], E. Quiros-Roldan[6], D. Ripamonti[7], M. Campus[8], B.M. Celesia[9], C. Torti[10], L. Cosco[11], A. Di Biagio[12], S. Rusconi[13], G. Marchetti[14], C. Mussini[15], R. Gulminetti[2], A. Cingolani[16], G. d'Ettorre[17], N. Geremia[18], G. Madeddu[18], A. Franco[19], G. Orofino[20], N. Squillace[21], A. Gori[1,22], G. Tambussi[3], A. Bandera[22] on behalf of INACTION study group

[1]Infectious Diseases Unit, Department of Internal Medicine, Fondazione IRCCS Ca' Granda, Policlinico Maggiore Hospital, Milan, Italy, [2]Infectious Diseases Unit, IRCCS San Matteo Hospital Foundation, University of Pavia, [3]Clinic of Infectious Diseases, San Raffaele Hospital, University Vita Salute, Milan, Italy, [4]Department of Medical Sciences, Unit of Infectious Diseases, University of Turin, Amedeo di Savoia Hospital, Turin, Italy, [5]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [6]Division of Infectious and Tropical Diseases, University of Brescia, ASST Spedali Civili Hospital, Brescia, Italy, [7]Infectious Disease Unit, ASST Papa Giovanni XXIII, Bergamo, Italy, [8]Infectious Diseases Unit, SS Trinità Hospital, ASSL Cagliari, Italy, [9]Unit of Infectious Diseases, Garibaldi Hospital, Catania, Italy, [10]Unit of Infectious Diseases, Department of Medical and Surgical Sciences, University "Magna Graecia", Catanzaro, Italy, [11]Infectious Diseases Unit, "Pugliese-Ciaccio" Hospital, Catanzaro, Italy, [12]Department of Infectious Diseases, IRCCS AOU San Martino IST, (DISSAL), University of Genoa, Genoa, Italy, [13]Infectious Diseases Unit, Department of Biomedical and Clinical Sciences "Luigi Sacco" Hospital, University of Milan, Italy, [14]Clinic of Infectious Diseases, Department of Health Sciences, University of Milan, ASST Santi Paolo e Carlo, Milan, Italy, [15]Clinic of Infectious Diseases, University of Modena and Reggio Emilia, Modena Hospital, Italy, [16]Institute of Clinical Infectious Diseases, Agostino Gemelli Hospital, Catholic University of Sacred Heart, Rome, Italy, [17]Infectious Diseases Unit, Umberto I Hospital, La Sapienza University, Rome, Italy,[18]Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Sassari, Italy, [19]Infectious Diseases Unit, ASP Siracusa, Italy, [20]Unit of Infectious Diseases, Divisione A, Amedeo di Savoia Hospital, Turin, Italy, [21]Infectious Diseases Unit, Department of Internal Medicine, ASST San Gerardo, Monza, Italy, [22]Infectious Diseases Unit, Department of Internal Medicine, Fondazione IRCCS Ca' Granda, Policlinico Maggiore Hospital, School of Medicine and Surgery, University of Milan, Italy

Background: Treating patients early after acute HIV infection (AHI) promotes the achievement of optimal virological and immunological control. However, little is known on patients who experience virological failure after AHI. Aim of the present study was to identify risk factors for suboptimal response (SR) to antiretroviral therapy (ART) after HAI and to investigate if ART regimens that are currently indicated in first-line treatment, according to Italian guidelines, could be protective towards SR.

Material and methods: Observational, retrospective, multicenter study. Patients diagnosed with AHI (Fiebig stages I-V) during 2008-2014 from 20 Italian centers have been analyzed. Subjects were followed from baseline (date of HAI diagnosis) to the last available follow-up. SR was defined as detectable HIV-RNA after 48 weeks of ART, viral rebound to >50 copies/mm3 after achievement of undetectable viremia, or an increasing HIV-RNA load despite ART use. Cox regression analysis was used to calculate the hazard ratios (HR) and 95% confidence intervals (95%CI) for SR. A sensitivity analysis was also performed to find HR for virological failure (VF), defined as HIV-RNA > 200 copies/mm3 after 24 weeks of ART or single HIV-RNA >1000 copies/ml after at least one previous HIV-RNA <50 copies/mm3. In this analysis, only patients with > 24 weeks follow up were included.

Results: Overall, 263 patients were enrolled, 227 (86%) males and with median age of 38 (30-46) years. Risk factor for HIV acquisition was heterosexual or homo/bisexual intercourse in 77 (29%) and 152 (58%) cases, while a minority of patients declared intravenous drug use, 9 (3%). During a median follow-up of 13.0 months (IQR 5.7-31.1), 38 (14.4%) patients showed SR, with an incidence of 0.7 per 100 person-months of follow-up (PMFU). At multivariable Cox regression analysis, two factors showed to be protective against SR: first ART counseled by current guidelines (aHR 0.3, 95%CI 0.14-0.84, p=0.019) and having a high CD4/CD8 ratio at first clinical presentation (aHR 0.15, 95% CI 0.04-0.62 for each point increase, p=0.009). Patients who presented with CNS symptoms had higher risk of SR (aHR 4.7, 95%CI 1.56-14.17, p 0.006). The correlation of CD4/CD8 ratio and that of CNS symptoms with SR were also confirmed restricting the analysis only to subjects (N=194) that were treated with ART within 3 months after the diagnosis of HAI.

On the other side, the use of a backbone other than tenofofovir/emtricitabine or abacavir/lamivudine was the only significant risk factor for VF (aHR 3.88, 95%CI 1.24-12.14, p=0.020).

Conclusions: In this large observational multicentre study, the use of the therapy counselled by current guidelines and higher baseline CD4/CD8 ratio resulted protective against SR in patients with HAI. Patients treated with backbones other than tenofofovir/emtricitabine and abacavir/lamivudine were at higher risk of VF after HAI.

HIV therapy and management

PD 54 TRENDS OF TRANSMITTED RESISTANCE MUTATIONS TO FOUR DRUG CLASSES AND HIV-SUBTYPES AMONG SUBJECTS RECENTLY DIAGNOSED AS HIV INFECTED OVER 2004-2019

M. Basso[1], B. Parisatto[1], C. Stagni[1], R. Scaggiante[2], M. Cruciani[3], R. Ferretto[4], V. Manfrin[5], E. Francavilla[6], S. Panese[7], F. Dal Bello[1], M. Andreoni[8], G. Palù[1], S. G. Parisi[1]

[1]Department of Molecular Medicine, University of Padova, Italy, [2]Infectious Diseases, Padova Hospital, Italy, [3]Center of Diffusive Diseases, Verona, Italy, [4]Clinical Infectious Diseases, Hospital of Santorso, Italy, [5]Infectious Diseases, Vicenza Hospital, Italy, [6]Infectious Diseases, Belluno Hospital, Italy, [7]Infectious Diseases Unit, dell'Angelo Hospital, Venezia, Italy, [8]Clinical Infectious Diseases, Tor Vergata University, Rome, Italy

Background: to evaluate circulation of drug resistance mutations (DRMs) and sub-types (ST) among subjects recently diagnosed as HIV infected (pts), over sixteen years, comparing previously reported trends with the most recent one, updated to 2019.
Material and Methods: on plasma from 2912 pts diagnosed from July 2004 to March 2019 in Veneto. protease (PR), reverse transcriptase (RT) and more recently Integrase (In) were analyzed for DRMs, susceptibility profile (Stanford db) and ST. Potential low level resistances were excluded. Chi-square test was applied. Infections acquired in the previous 12 months were defined as recent (R).
Results: in 5 periods (2004/06, 07/09, 10/12, 13/16, 17-19) 334, 796, 752, 750 and 280 pts were recruited; non-B-ST were 21.9, 29.3, 33, 32.7 and 48.9% (33.5% Italians in 17-19), respectively. Age, CD4 and % were analysed. A significant increase of non-B-ST ($p<0.0001$ for trend) and of the percentage of Italians with non-B strains ($p = 0.03$) was observed. Resistance to PR or to multiple classes declined but non-nucleoside RT inhibitors (NNRTI), as DRMs were found also recently in the latter periods (table 1). E138A alone, not included in the previous evaluations, increased from 2.3 to 1.8, to 3.2, to 3.6, to 4.7% in 2017-19. 157Q (12 pts) and 163K (3 pts), 260I (1 pt) and 263KN (1 pt) and no primary TDRM to In-Inhibitors (InIn) were found in 469 B-Type-Pts enrolled in 2014-19; 12,6% out of 469 had other major TDRM for RT/PI. In 227 non-B pts, 11,5% with other TDRMs, only a 143C and a 66I were found, while many accessory InIn-TDRMs were detected: 68IV (1 pt), 74IM (46 pts), 97A (25 pts), 119R (2 pts), 121 CFSY (1 pt), 138K (1 pt), 153F (1 pt), 157Q (8 pts), 223 (1 pt), 260I (5 pts), 263K (1 pt). In the 11 years period from 2009 to 2019, in the same area, at least 112 InIn failed and potentially transmitters patients were found to have InIn DRMs.
Conclusions: An increase of non-B strains and a slight increase of TDRMs among B-ST were observed. The persistent circulation of NNRTI-DRMs, the virtual absence of major In-DRMs but a circulation of many IN-polymorphisms have implications on the screening of In-DRMs at baseline and on the selection of the first-line HAART

HIV therapy and management

PD 55 PRESENCE OF V72I, G123S AND R127K INTEGRASE INHIBITORS POLYMORPHISMS COULD REDUCE CART EFFECTIVENESS

A. Celotti[1], F. Gargiulo[2], M. Properzi[1], M.A. De Francesco[2], E. Quiros-Roldan[1], I. Izzo[1], M.C. Pezzoli[1], A. Caruso[2], F. Castelli[1], E. Focà[1]

[1]Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, [2]Institute of Microbiology, Department of Molecular and Translational Medicine, University of Brescia and ASST Spedali Civili Hospital, Brescia

Background: Aim of this study was to assess the effectiveness of cART regimens at 24 and 48 weeks (W) in patients with Integrase Inhibitors (INI) accessory mutations and polymorphisms receiving INI-based regimens.
Materials and methods: We enrolled all cART-naïve or INI-naïve HIV-infected patients, with an available baseline INI genotypic resistances test between 2011 and 2016, before starting an INI-based regimen. Integrase sequences were analyzed using the Stanford University HIV Drug Resistance Database genotypic resistance algorithm (HIVdb Program, version 6.3.0). Outcome of the study was virological response at 24 and 48W of follow up (FU) according to snapshot analysis. We defined virological failure as two consecutive HIV-RNA > 50 copies/ml, or one > 1000 copies/ml. Patients were divided in those presenting accessory mutations to INI (Group 1), and patients with only polymorphisms or wild type (Group 2). Patients presenting polymorphisms correlated to virological failure were added to Group 1 and the sample was re-analyzed. Categorical and continuous variables were calculated as appropriate. A P value of <0.05 was considered statistically significant.
Results: We enrolled 83 patients; baseline characteristics of the sample and distribution of accessory mutations and polymorphisms are summarized in Table 1. 81 patients reached 24W of FU: 2/20 (10%) showed virological failure in the Group 1, compared to 4/61 (6.5%) patients in the Group 2, without significative differences. 17 patients of the Group 1 and 49 of the Group 2 reached 48 weeks of follow up, with respectively 0 (0%) and 2 (4%) virological failure, without significative differences. Interestingly, patients with polymorphisms G123S and R127K had higher risk of failure at 24W (respectively, relative risk - RR - 36, IQR 2.1-613, p=0,01; RR 36, IQR 2.1-613, p=0,01) and patients with V72I had an higher risk of failure both at 24W (RR 6.52, IQR 1.29-32.9, p=0,02) and 48W (RR 21.1, IQR 1.07-414, p=0.04). Hence, adding patients with V72I, G123S and R127K to Group 1, at 24W we found virological failure in 6/38 (15,7%) patients of Group 1 and 0/43 (0%) of Group 2 (p=0,008).
Conclusions: To date, the real clinical impact of polymorphisms or accessory substitutions on cART effectiveness is still unknown. However, our study showed that the presence of V72I, G123S and R127K polymorphisms could play a role in reducing INI effectiveness.

HIV therapy and management

PD 56 TREND OF ESTIMATED GLOMERULAR FILTRATION RATE IN A LARGE COHORT OF HIV MOTHER-TO-CHILD INFECTED PATIENTS, AN OBSERVATIONAL MULTICENTER STUDY FROM 2010 TO 2018

G. Sarteschi[1,2], A. Celotti[3], M. Mirabella[1,2], A. Della Vecchia[1,2], S. Mora[4], M. Giacomini[4], E. Focà[3], A. Di Biagio[1]

[1]Infectious Diseases Unit, IRCCS Policlinico San Martino Hospital, Genoa, [2]Department of Health Sciences (DISSAL), University of Genoa, Genoa, [3]Infectious and Tropical Diseases Department, University of Brescia and ASST Spedali Civili Hospital, Brescia, [4]Department of Informatics Bioengineering, Robotics and Systems Engineering (DIBRIS), University of Genoa, Genoa

Background: People vertically infected with HIV (PVI-HIV) are a special population, due to exposition since birth to HIV and antiretroviral therapy (ART). Among ART, Tenofovir disoproxil fumarate (TDF) was widely used in recent years, but there are few data on safety in these patients; in particular, data about estimated glomerular filtration rate (eGFR) trend in this population. Aim of our study is to evaluate eGFR trend in a multicentre cohort of PVI-HIV exposed to TDF.

Material and methods: Observational retrospective multicentre study, performed from 2010 to 2018. We enrolled PVI-HIV in follow up in Genoa and Brescia. In Genoa, we collected data of creatinine (mg/dL), height, weight and ART from the MedInfo online platform enclosed in Ligurian HIV Network (www.reteligureHIV.it), in Brescia, from the electronic medical record NetCare. We calculated eGFR with the Cockroft-Gault equation in adult and the revised Schwartz equation in underage. We matched data with ART (TDF, tenofovir alafenamide [TAF], protease inhibitor [PI]). We divided patients in 3 groups according to baseline eGFR (mL/min) at 2010 (A: ≥120, B: 80-119, C: <80).

Results: We enrolled 72 patient, 12 of them were excluded for lacking data. The average time of observation was 8 years [range 4-9]. Thirty-five patients (58%) was female, average age 19 years [range 6-27]. 51 patients (85%) received TDF at least 1 year, 32 (53%) associated TDF+PI at least 1 year, 9 (15%) never assumed TDF, 32 (53%) switched to TAF in 2018. We observed an average eGFR reduction of 20.1 mL/min (2.23 mL/min/year) (Fig. 1), this reduction was greater in TDF+PI group (2.56 mL/min/year) while it was lower in those never exposed to TDF (1.66 mL/min/year). Interestingly, a slight eGFR increase emerged in TAF-exposed patients (2.4 mL/min) between 2017 and 2018, absent in the overall population. Among the eGFR groups, there was 26 patients (43%) in group A, 29 (48%) in group B and 5 (8%) in group C; we observed an eGFR reduction greater in group A (3.7 mL/min/year) and group B (1.24 mL/min/year) and a slight reduction in group C (0.4 mL/min/year).

Conclusions: Our study reveals a progressive eGFR reduction, as expected, in PVI-HIV and exposed to ART. Despite the long-term ART exposure is an interesting data the slight reduction of renal function in the worst eGFR group, even if on TDF-containing regimens. More data are needed to confirm the improvement observed after the TAF introduction; however, based on these data, we suggest a constant evaluation of eGFR in these setting.

HIV therapy and management

PD 57 VITAMIN D INSUFFICIENCY IS ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS IN HIV-1-INFECTED PATIENTS ON COMBINATION ANTIRETROVIRAL THERAPY

L. Calza[1], V. Colangeli[1], M. Borderi[1], B. Granozzi[1], P. Malosso[1], I. Bon[2], M.C. Re[2], P. Viale[1]

Department of Medical and Surgical Sciences, [1]Clinics of Infectious Diseases, [2]Unit of Microbiology, S.Orsola Hospital, University of Bologna

Background: Vitamin D insufficiency is a very frequent condition among HIV-infected patients on combination antiretroviral therapy (cART) and has been associated with faster progression of atherosclerosis and increased cardiovascular disease risk.

Patients and methods: A cross-sectional study was performed to investigate correlation between serum level of 25 (OH) vitamin D and presence of subclinical atherosclerosis in adult HIV-infected patients on stable cART, with age>40 years, and with ultrasonography of the extra-cranial carotid arteries performed in the last 6 months. Vitamin D insufficiency was defined as serum level <30 ng/mL, deficiency as serum level <10 ng/mL, subclinical atherosclerosis as a carotid intima-media thickness (IMT) >0.9 mm and carotid plaque as IMT >1.5 mm at any site. Patients with diabetes mellitus or previous diagnosis of coronary artery disease or cerebrovascular disease were excluded.

Results: On the whole, 188 patients were enrolled: 86.2% were men, 92.5% Caucasian, 8.5% were at CDC stage C, and the mean age was 49.6 years (range, 40-76). The mean CD4 T lymphocyte count was 567 cells/mm3, 176 (93.6%) had plasma HIV RNA <20 copies/mL, 51.1% were smoker, 29.2% had hypertension, 51.1% triglycerides >200 mg/dL, 44.7% LDL cholesterol >150 mg/dL, 28.7% BMI >28 Kg/m2, and the mean 10-year cardiovascular disease risk (by the 2013 ACC/AHA equation) was 8.2%. The mean serum concentration of vitamin D was 35.2 ng/mL, 84 (44.6%) patients had a vitamin D insufficiency and 29 (15.4%) a deficiency. Subclinical atherosclerosis was reported in 105 (55.8%) subjects and carotid plaques were present in 47 (25%). The mean vitamin D concentration was significantly lower among patients with subclinical atherosclerosis than among those without (18.2 vs 41.3 ng/mL, p<0.001). Moreover, the multivariate linear regression analysis adjusted by confounding factors showed an independent association between subclinical atherosclerosis and vitamin D insufficiency (p=0.018), age >60 years, smoking, hypertension, BMI >28 Kg/m2, LDL cholesterol >150 mg/dL, duration of HIV infection >10 years, nadir CD4 count <200 cells/mm3, and exposure to ritonavir-boosted protease inhibitors >5 years. No significant association was reported between atherosclerotic disease and current antiretroviral regimens.

Conclusions: In our study, vitamin D insufficiency is significantly associated with subclinical atherosclerosis, so its role in HIV-associated cardiovascular disease should be further evaluated as a possible target for intervention.

HIV therapy and management

PD 58 PREDICTING 2-DRUG ANTIRETROVIRAL REGIMEN EFFICACY BY GENOTYPIC SUSCEPTIBILITY SCORE: RESULTS FROM A COHORT STUDY

B. Rossetti[1], S. Modica[2], R. Gagliardini[3], D. Redi[1,2], F. Montagnani[1,2], G. Zanelli[1,2], S. Di Giambenedetto[4], F Lombardi[4], M. Pecorari[5], V. Borghi[6], P. Meraviglia[7], F. Maggiolo[8], V. Micheli[9], M. Zazzi[2], A. De Luca[1,2] on behalf of ARCA study group

[1]Infectious Diseases Unit, AOU Senese, Siena, Italy, [2]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [3]Lazzaro Spallanzani National Institute for Infectious Diseases IRCCS, Rome, Italy, [4]Clinic of Infectious Diseases, Catholic University of Sacred Heart, Rome, Italy, [5]Unit of Microbiology and Virology, Modena University Hospital, Modena, Italy, [6]Infectious Diseases Unit, Modena Hospital, Modena, Italy, [7]First Division of Infectious Diseases, ASST Fatebenefratelli-Sacco, Milan, Italy, [8]Infectious Diseases Unit, Bergamo Hospital, Bergamo, Italy, [9]Unit of Clinical Microbiology and Virology, ASST Fatebenefratelli-Sacco, Milan, Italy

Background: HIV drug resistance has a deleterious effect on the virological outcome of antiretroviral therapy (ART). The aim of the study was to evaluate the ability of genotypic susceptibility score (GSS) to predict virological outcome following an ART switch to a 2-drug regimen in virosuppressed HIV-1 infected patients.
Material and methods: From the ARCA database we selected HIV-1 infected patients virologically suppressed switching to 2-drug ART (2006-2018, time of switch=baseline), with pre-baseline resistance genotype and at least one HIV-1 RNA determination during follow up. Primary endopoint was virological failure (VF: an HIV-RNA, VL, ≥ 200 cps/mL or 2 consecutive ≥ 50 cps/mL). Survival analysis was used to investigate predictors of VF. The GSS predicted by the latest and the cumulative genotype (CGSS) was calculated using the Stanford hivdb (v.8.5) with respect to the 2-drug regimen started. CD4 changes from baseline at weeks 24, 48 and 96 were assessed using Student's t-test for paired samples.
Results: We included 773 patients: 522 (68%) were males, 186 (24%) heterosexuals, with median age of 50 years (IQR, 43-56), 10 years of HIV (5-20), 7 years of ART (4-15) and 5 (3-8) previous antiretroviral (ARV) lines. At baseline patients had been virologically suppressed for 6.4 years (2.5-14), allowing isolated blips. The median zenith VL was 4.9 log10 (4.4-5.5), CD4 cells count at nadir 222 (108-324) and at baseline 640 (477 -860). Median GSS was 2 (1.5-2), with GSS <2 in 213 (28%) pts, median CGSS was 2 (1-2), with CGSS <2 in 250 (33%). The previous ARV classes used were NRTI in 770 patients (99%), NNRTI in 416 (54%), boosted PI in 639 (83%) and INSTI in 218 (28%). Current ARV regimens included: PI+3TC in 455 pts (59%), of which 3TC + ATV unboosted or ATV/r or ATV/c in 181 (23%) and DRV/r or DRV/c in 274 (36%), DTG+3TC in 260 (34%) and DTG+RPV in 58 (7%). During a median observation time of 75 wks (IQR 37-120) the estimated probability of VF at 48 weeks was 6% (95% CI 5-7) among patients with GSS=2, 4% (3-5) among patients with GSS 1-1.99 and 11% (4-18) among those with GSS <1 (Log Rank p=0.21). According to CGSS, the estimated probability of VF at 48 weeks was 5% (95% CI 1-6) among patients with CGSS =2, 6% (4-8) among patients with CGSS 1 -1.99 and 8% (3-13) among those with CGSS <1 (Log Rank p=0.006) (Fig 1). Observed median changes of CD4+ counts from baseline were +24 cells/μL (IQR -67;+132) at 24 weeks, +49 cells/μL (IQR -31;+159) at 48 weeks and +74 cells/μL (IQR -30;+197) at 96 weeks (p<0.001 for all comparisons). At multivariate analysis, adjusting for years of ART, CD4 cell count at nadir and at baseline, CGSS strata, number of previous ARV lines, only longer time since last VL>50 cps/mL was associated with lower risk of VF (+ 1 year, aHR 0.89, 95% CI 0.82-0.98; p=0.01).
Conclusions: Despite an effect of CGSS, the duration of virosuppression was the only independent predictor of virological efficacy of switching to 2-drug regimens.

Bacterial and fungal infections in immunocompromised host

P 1 A RARE CASE OF DISSEMINATED FUSARIUM SPP INFECTION IN A PATIENT WITH RECURRENCE OF ACUTE MYELOID LEUKEMIA

S. Mazzanti, L. Brescini, V. Barocci, A. Polenta, M. Di Pietrantonio, P. Mantini, V. Iencinella, S. Castelletti, A. Giacometti

Clinica malattie infettive, Ospedali Riuniti di Ancona, Università Politecnica delle Marche

Fusarium is an emerging human opportunistic pathogen of growing importance. Particularly among immunosuppressed patients with an increased incidence of disseminated infections over the past two decades.
The clinical presentation of fusariosis depends on the immunity of the host and it can be localized, invasive or disseminated.
Came to our attenction a 63 year old woman with recurrence of acute myeloid leukemia taking second-line chemotherapy; she noted since one month erythematous cutaneous nodules that became ulcerated, crusted and necrotic.
At the time of presentation she had several diffuse lesions at different stages. Of note: small erythematous nodular lesions on the lower lip, the abdomen, scalp and the forehead; other larger spherical lesions with a necrotic core in the postero-lateral region of the thigh and the largest lesion on the middle finger of the left hand, which was complicated by dactylitis (see pictures).
There was no history of trauma and no clinically apparent onychomycosis, only a small continuous skin solution in the second interdigital space of the left foot.
From an ulcer swab and skin biopsy we cultured Fusarium spp.
We initiated antimicotic therapy with voriconazole, while monitoring its plasma levels to ensure it remained within therapeutic range. Other possibile systemic sites of involvement were excluded.
On day 14 of hospital admission, the patient complained of calf pain worse on mobilizing. On examination, a round hard mass was palpable. Ultrasound scan showed a 5 x 2.5 cm heterogenous hyperechoic mass suggestive of a hematoma in the organization phase. A few days later, she noted two other non-painful masses, one on the left shoulder and the other overlying the right temple.
Ultrasound scan and CT of the facial mass showed the same radiological characteristics as those of the leg lesion.
Two possible causes of the haematomas were identified: secondary to severe thrombocytopenia in the acute phase of leukaemia, or invasion of blood vessels by Fusarium.
After 35 days of treatment with voriconazole, she had clinically improved. The cutaneous lesions had healed and after receiving granulocyte colony stimulating factor, the haematologist advised that she was ready to resume chemotherapy.
In conclusion, Fusariosis is a severe infection with high mortality. Immunosuppression is the single most important risk factor and also increases the risk of hematogenous spread and systemic disease.
Patient management includes systemic antifungals, surgical debridment of the infected sites, removal of venous catheters in case of catheter-related fusariosis, and reversal of immunosuppression in the patient.
Vasculitis is a known, but extremely rare, complication of fusariosis.

Bacterial and fungal infections in immunocompromised host

P 2 PREVALENCE OF SYPHILIS IN HIV INFECTED INDIVIDUALS: A RETROSPECTIVE STUDY IN TERTIARY UNIVERSITY HOSPITAL

Z. Di Rosa[1], C. Rovelli[1], D. Lombardi[2], M.L. Balsamo[2], A. Rossi[2], D. Dalla Gasperina[1], P.A. Grossi[1]

[1]University of Insubria, [2]ASST-Sette Laghi Varese

Background: Co-infection of HIV and Syphilis has been frequently reported and is currently on the rise, especially in men who have sex with men (MSM).

Material and methods: A single center retrospective cohort study was performed to evaluate the seroprevalence and clinical presentation of new episodes of syphilis among HIV patients followed at a teaching hospital in Northern Italy. All patients were tested by FTA-AB, TPHA and RPR. Demographic, clinical and treatment data were collected. Staging of syphilis was categorized into primary and secondary syphilis. We considered as past syphilis the patients with negative RPR test and anamnestic history of luetic treatment.

Results: From January 1996 to December 2018, a total of 817 HIV positive patients (563 [68.9%] M; 254 [31%] F; mean age 51.5 yrs [range 19-89]; 84.7% Italian, 8.7% African) were followed at our center. One hundred and twelve (13.7%) of them resulted positive for FTA-AB test and TPHA; 34/112 (30.4%) resulted RPR negative and were considered as past syphilis, while 78/112 (69.6%) resulted RPR positive with a history of sexual risk and clinical evidence of ongoing infection; the overall prevalence of active syphilis was 9.5%. Among 78 HIV patients with diagnosis of syphilis, 75 (96.2%) were male and 53 (70.7%) of them were MSM, 14 (18.7%) heterosexual, 3 (4.0%) had a history of i.v. drug abuse and 5 (6.7%) with unknown HIV risk factor. The majority of patients were Italians (94.4%). Latent infection was diagnosed in 64/78 (82.1%) patients; primary and secondary syphilis in 14/78 (17.9%). Twenty-three patients received the diagnosis of syphilis concurrently with the diagnosis of HIV infection. The temporal trend of new diagnosis showed a significative increase in last ten years (7.7% 1996-2008 vs 13.7% 2009-2018, p = 0.006). All patients were in cART therapy, the CD4 T cell count was evaluated at the diagnosis of Syphilis with an average of 486 cell/µL (range 5-1433 cell/µL). All infected patients were treated with antibiotic administration (penicillin or third generation cephalosporins). During the study period, 12/78 (15.4%) patients showed luetic reinfection.

Conclusion: HIV/Syphilis co-infection is a growing medical condition. The infection is predominant in male, particularly in the MSM population. Counseling at diagnosis of HIV infection is fundamental, in particular for the patients with promiscuous sexual behavior. Probably HIV patients in cART therapy (specially MSM) consider themselves safe from HIV-infection, underestimating the risk to contract other sexually transmissible diseases.

Bacterial and fungal infections in immunocompromised host

P 3 EPIDEMIOLOGY AND OUTCOMES OF ANTIBIOTIC RESISTANT PATTERNS OF BLOODSTREAM INFECTIONS IN HIV-PATIENTS; A 14 YEAR SINGLE CENTER STUDY

E. Franceschini, A. Santoro, S. Zona, G. Orlando, M. Menozzi, A. Bedini, I. Franconi, M. Meschiari, M. Di Gaetano, G. Guaraldi, C. Mussini

Azienda Ospedaliero-Universitaria di Modena

Objectives: To investigate incidence and outcome of antibiotic resistance (AR) patterns in HIV-infected patients with bloodstream infections (BSIs).
Methods: Retrospective observational study including all positive blood isolates in HIV-infected patients admitted to Modena hospital, from January 2004 to June 2017. BSIs diagnosis criteria were: positive blood cultures. Skin contaminants and relapses within 14 days were excluded. Results were interpreted in accordance with CLSI criteria until 2009 and with EUCAST break points from 2010. 30-day and 90-day mortality were described. Logistic regression analyses including age, sex, CD4, HIV-VL, MDR bacteria were used for mortality associated factors.
Results: 369 positive blood isolates (239 patients), were analyzed. 159 men (66.5%), mean age 45 (SD 12.2); median CD4+ cell/uL 227 (IQR 85-433); 16% had a HIV-VL > 100.000 copies/µL, 57.0% of patients were virologically suppressed. The most-common pathogens were Coagulase-negative Staphylococci (39.9%), Enterobacteriaceae (23.58%), Non-fermenting gram negatives (10.6%), S. aureus (7.8%), Enterococcci (7.6%), and Streptococci (7.3%). 30-day and 90-day mortality rates were 9.6% (23 pts) and 16.8% (62 pts), respectively.
13 (5.4%) patients had an MDR bacteremia (34 isolates, 9.2%). The incidence of specific resistance patterns was analyzed during the study periods (figure 1). Prevalence of ESBL enterobacteriaceae increased significantly over time (p. 0.001). We found a non-significant decrease in quinolone and carbapenem resistance in the last period, since we started a hospital antimicrobial stewardship program.
30-day and 90-day mortality rates in patients with MDR bacteria were 23.0% (3 pts) and 30.8% (4 pts). In logistic regression analysis, detectable HIV-VL resulted a significant risk factor for mortality at 30- and 90-day (OR 6.6, p 0.005; OR 3.2, p 0.017, respectively). CD4 cell count < 200 cell/ µL resulted significant for 90-day mortality (OR 2.8, p 0.03).
Discussion: In this cohort of HIV-patients, MDR organisms represented 9.2% of BSI with a 30-day mortality of 23%. We did not find any impact of MDR on mortality, but we find an impact of HIV viro-immunological status on mortality (especially at 90-day) suggesting a more important role of HIV compared to BSI.

Bacterial and fungal infections in immunocompromised host

P 4 CHANGES IN THE PROPORTION OF AIDS-DEFINING EVENTS FROM 2000 TO 2018 IN ANTIRETROVIRAL-NAIVE HIV-POSITIVE PATIENTS

A. Dusina[1], A. Emiliozzi[1], A. Ciccullo[1], G. Baldin[1], D. Farinacci[1], D. Moschese[1], C. Picarelli[1], S. Belmonte[1], F. Lombardi[1], S. Lamonica[1], A. Borghetti[2],
S. Di Giambenedetto[1,2]

[1]Institute of Clinical Infectious Diseases, Catholic University of the Sacred Heart, Rome, Italy, [2]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, UOS Malattie Infettive, Rome, Italy

Background: Different studies have shown that antiretroviral therapy (ART) is effective in reducing the risk of developing AIDS-defining events.However,little is known about the impact of change in HIV management guidelines on the relative risk of specific AIDS events over time.We investigated if the relative proportion of specific AIDS-defining events compared to others changed over time in HIV-positive,ART-naïve pts.
Methods: In this monocentric retrospective study,we analyzed a cohort of HIV-positive ART-naive pts,ie pts not previously treated at AIDS diagnosis,who were diagnosed with at least one AIDS-defining illness (according to CDC classification system) from 30 days before to 1 year after HIV diagnosis.The study period ranged from 2000 to 2018 and was divided into 5 intervals (2000-2004; 2005-2008; 2009-2012; 2013-2015; 2016-2018), corresponding to changes in HIV treatment guidelines.Chi-square test for trends and multivariate logistic regressions were used to evaluate the impact of time periods over the proportion of selected AIDS events compared to others.
Results: We analyzed 390 pts.Their characteristics were:289 (74%) males,281 (72%) Italians,median age 41 yrs (interquartile range,IQR,19-70),median CD4 cell count and HIV-RNA at AIDS diagnosis respectively 53 cells/mm3 (0-597) and 5.2 log10 cp/mL (1.5-6.6),median time between HIV and AIDS event diagnosis 0 days (-18-246).A total of 564 AIDS events was recorded.The most common events during the whole time period were pneumocystosis (PCP) (124 cases,22%),esophageal candidiasis(77,14%) and CMV disease(66,12%).The probability of observing PCP,CMV disease or esophageal candidiasis increased significantly in these periods (chi-square for trend p=0.0003, 0.02, 0.009 respectively). A progressive risk reduction was instead highlighted for Non-Hodgkin Lymphomas (NHL) (p=0.05).At multivariate analysis,an increased risk of PCP compared to other AIDS-events was confirmed in more recent periods (versus 2000-2004, for 2013-2015 adjusted Odds Ratio [95% Confidence Interval]: 2.27 [1,1-4.73]; for 2016-2018 4.19 [1.89-8.93]), in all periods apart from the last one for esophageal candidiasis (versus 2000-2004, for 2005-2008 2.50 [1.17-5.36], for 2009-2012 3.21 [1.40-7.32]; for 2013-2015 2.16 [2.67-13.34]) and in the fourth interval for CMV disease (versus 2000 -2004, for 2013-2015 5.69 [2.52-12.88]). A higher CD4 cell count was protective against PCP (versus <50 cells/mm3, 50-100 cells/mm3 0.47 [0.23-0.93]; 100-200 cells/mm3 0.38 [0.17-0.86]; >200 cells/mm3 0.37 [0.03-0.38]) while African race was predictive (versus others, 2.13 [0.08-0.38]).
Discussion: Our study seemed to suggest that the effect of changes in HIV treatment guidelines had a different impact on the relative prevalence of some AIDS defining illness over time.Whether this is due to major efforts in diagnosis and prevention of tuberculosis and NHL or a direct effect of an earlier ART start with more potent combinations is still not known.

Bacterial and fungal infections in immunocompromised host

P 5 NON-TUBERCULOUS MYCOBACTERIA (NTM) AMONG HIV+: PRELIMINARY FINDINGS FROM A SYSTEMATIC REVIEW, 2008-2018

F.M. Fusco[1], A. Calcagno[2], A. Bandera[3], F. Bartalesi[4], A. Di Biagio[5], C. Fabbri[6], G. Gualano[7], D. Goletti[8], C. Pallotto[9], M. Trezzi[6], A. Gori[10] on behalf of the IRENE Network

[1]Infectious Diseases Unit 1, S. Maria Annunziata Hospital, USL Toscana Centro, Florence, [2]Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, [3]Infectious Diseases Unit, Departement of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, [4]Infectious and Tropical Diseases Unit, Careggi University Hospital, University of Florence, Florence, [5]Clinic of Infectious Diseases, San Martino Hospital, Genoa, [6]Infectious Diseases Unit 2, S. Jacopo Hospital, USL Toscana Centro, Pistoia, [7]Respiratory Infectious Diseases Unit, National Institute for Infectious Diseases "L. Spallanzani" IRCCS, Rome, [8]Translational Research Unit, National Institute for Infectious Diseases "L. Spallanzani" IRCCS, Rome, [9]Infectious Diseases Unit, S. Donato Hospital, Azienda USL Toscana Sud Est, Arezzo, [10]School of Medicine and Surgery, University of Milan; Infectious Diseases Unit, IRCCS Ca' Granda, Ospedale Maggiore Policlinico Foundation, Milan

Background: Nontuberculous mycobacteria (NTM) are important causes of disease in immunosuppressed hosts, and their relevance is increasing worldwide among immunocompetent patients, also. Pulmonary disease (NTM-PD) is the most common localization of NTM infection in the general population, with disseminated and extra-pulmonary infections being less common.
HIV infection is one of the most important risk factors for developing NTM infections and M. avium complex (MAC) disease has been identified as an important pathogen among AIDS patients since the beginning of HIV/AIDS epidemic. However, the use of ART is changing the clinical picture of persons living with HIV (PLWH), and few spotted data are available about current epidemiological and clinical characteristics of NTM in this population.
We performed a systematic review of literature about NTM among PLWH in the last 10 years (2008-2018), in order to summarize main epidemiological and clinical data in this population.
Methods: A systematic search of scientific literature has been performed on PubMed, using the following search terms: ((nontuberculous[Title/Abstract] AND mycobacteria[Title/Abstract]) OR (nontuberculous[Title/Abstract] AND mycobacterial[Title/Abstract])) AND (HIV[Title/Abstract] OR AIDS[Title/Abstract]) AND ("2008/12/18"[PDat] : "2018/12/15"[PDat]). Selection criteria is reported in figure 1.
Results: From 147 manuscripts, 28 full-text papers reporting original data were included in the final analysis accounting for 20,979 patients (table 1). Studies were very heterogeneous as for settings, study designs, study populations (AIDS and non-AIDS) and aims. Many studies included patients with NTM isolates, but the rate of NTM-associated disease was clearly reported in one study only: prevalence of NTM-PD was 4%, while prevalence of disseminated NTM diseases was 5% among patients with NTM isolates.
Overall prevalence of HIV+ serostatus among patients with pulmonary NTM isolates was 29.5% (range 1.5 -51.8%); HIV-positivity was significantly associated with NTM-PD (OR 3.86- 4.27) in two studies. One study reported a beneficial effect of ART on NTM-PD (0 vs. 2%). The prevalence of NTM isolates in HIV+ patients was reported by 4 studies and ranged from 1.6 to 33%. Both incidence and mortality have been recently reported as significantly decreased.
Conclusions: The status of HIV infection still represents a significant risk factor for NTM infection, even if the use of ART reduced both incidence and related mortality among PLWH. Special attention should be paid to patients with low CD4 count, where MAC infection still represents a clinical challenge. These preliminary results are generated from heterogenous studies, and some of them are characterized as being of low quality. Therefore, further studies are needed to understand the clinical impact of NTM infections among PLWH in different settings, different geographic areas, and according to the availability of ART.

Bacterial and fungal infections in immunocompromised host

P 6 CLINICAL PRESENTATION AND OUTCOME OF PNEUMOCOCCAL DISEASES ACCORDING TO HIV INFECTION: DATA FROM SAN PAOLO HOSPITAL, MILAN FROM 2015 TO 2018

F. Bai[1], F. Parolo[1], C. Tincati[1], E. Suardi[1], M. Allegrini[1], C. Biassoni[2], G. Ortisi[2], O. Viganò[1], C. Aldieri[1], A. Cona[1], T. Bini[1], G. Marchetti[1], A. d'Arminio Monforte[1]

[1]Clinic of Infectious Diseases, S. Paolo Hospital, ASST Santi Paolo e Carlo, University of Milan, Milan, [2]Department of Diagnostic Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan

Background: Patients living with HIV are usually known to be more susceptible to pneumococcal infections with a high rate of invasive disease, raising the issue of a possible worse clinical presentation and outcome in HIV-positive (HIV+) subjects as compared to HIV-negative (HIV-) ones.
We aimed to investigate the presentation and clinical outcome of pneumococcal diseases diagnosed at San Paolo Hospital, Milan, from 2015 to 2018, according to HIV infection.
Methods: We conducted a retrospective study on subjects diagnosed with pneumococcal diseases in the period 01/07/2015-30/06/2018. Pneumococcal disease was categorized as pneumonia, upper respiratory tract infection, invasive disease, meningitis or other. Microbiological investigation was performed on sputum, bronchoalveolar lavage fluid (BAL), cerebrospinal fluid (CSF), blood samples, other fluids or through urinary pneumococcal antigen.
Differences in demographics, outcome and susceptibility test of pneumococcal diseases according to HIV infection were analyzed by Chi-square and Mann Whitney test.
Results: During the study period, 355 subjects were diagnosed with pneumococcal diseases, mainly pneumonias (260, 73.2%), diagnosed by urinary antigen (279, 78.6%) (Table 1).
19/355 (5.3%) infections by Streptococcus pneumoniae were in HIV+ patients; they were mostly ex IDUs (10/19, 53%), 12/19 (63%) were on cART and 6/12 (50%) had detectable HIV-RNA at pneumococcal diagnosis. Current CD4 count was 451/mmc (198-809) and CD4/CD8 ratio was 0.48 (0.14-0.56). HIV- subjects were older and more commonly Italian, compared to HIV+ ones. No differences in hospital admission, length of hospital stay, Charlson score, site of disease (pneumonia versus others), antimicrobial resistance patterns and outcome were found between the two groups (Table 1). Pneumonias were more frequently diagnosed in the last calendar period (21% in 2015-16 and 79% in 2017-18); we observed a not significantly lower proportion of pneumonias in HIV+ patients in the last years compared to 2015-2016 (5/54, 9.3% in 2015 -16 and 8/206, 3.9% in 2017-18) (Table 2). 21 of 76 (27.6%) pneumococcal isolates (blood culture, sputum, BAL, pleural fluids, CSF and other) showed some degree of penicillin nonsensitivity (intermediate o resistant strains) without differences in proportion of penicillin resistance according to HIV infection (Table 1). 43/355 (11.8%) patients died (42, 12.5% HIV- and 1, 5.3% HIV+ subject) with higher mortality in older (>75 years) patients (Table 3); 4 (1.1%) HIV- patients had a 60-days relapse of pneumococcal disease.
Conclusions: Although the few cases of pneumococcal diseases in HIV+ patients did not allow us to draw definite conclusions, no evidence was found of a more severe presentation or a worse clinical outcome in people living with HIV compared to HIV- patients. Increase in vaccine coverage in HIV+ patients and older subjects is needed to further reduce the prevalence and mortality of pneumococcal diseases.

Basics in viral hepatitis

P 7 AMINO ACID SUBSTITUTIONS IN THE NS5A OF DIFFERENT HEPATITIS C GENOTYPES AND DIFFERENT FIBROSIS LEVELS OR HEPATOCELLULAR CARCINOMA

S. Paolucci[1], A. Piralla[1], F. Novazzi[1], A. Fratini[1], R. Maserati[2], R. Gulminetti[2], S. Novati[2], G. Barbarini[3], P. Sacchi[3], M. Mondelli[4], S. Mantovani[4], F. Baldanti[1,5]

[1]Molecular Virology Unit, Microbiology and Virology Department, Fondazione IRCCS Policlinico San Matteo, Pavia, [2]Institute of Infectious Diseases, University of Pavia, Pavia, [3]Division of Infectious and Tropical Diseases, Fondazione IRCCS Policlinico San Matteo, Pavia, [4]Division of Infectious Diseases and Immunology, Department of Medical Sciences and Infectious Diseases Fondazione IRCCS Policlinico San Matteo, Pavia, [5]Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia, Pavia

Background: Amino acid substitutions in the interferon sensitivity-determining region (ISDR) within the NS5A region have been related to the development of hepatocellular carcinoma (HCC) in patients infected with hepatitis C virus (HCV). In addition, ISDR is located within protein kinase R (PKR)-binding domain involved in a tumor suppressor function. Other studies reported that NS5A resistance-associated substitutions (RASs) were associated with advanced liver fibrosis. However, the relation between NS5A substitutions and liver disease progression is still unclear. The aim of this study was to investigate whether a relationship exists between ISDR variants and RASs, and their respective association with the liver fibrosis stage or HCC.

Methods: Three hundred seventy-six patients infected with HCV with genotypes 1a, 1b, 2c, 3a and 4d were included in the study: 355 were treated with direct antiviral agents (DAAs) while 21 HCC patients were untreated. HCV RNA was quantified and sequenced by Sanger method before treatment or at the time of HCC confirmation. Liver fibrosis stage was assessed by transient elastography and equalized to METAVIR scores. The number of ISDR amino acid variants was defined as three for cutoff values.

Results: Evaluation of variants in the HCV NS5A gene was performed in 334/376 patients including all HCC patients. In detail, 178/334 (53.3%) patients had low fibrosis values (F0-F2), 121/334 (36.2%) had high fibrosis values (F3-F4) and 35/334 (10.5%) had HCC (14 DAA treated and 21 untreated). ISDR substitutions ≥3 were higher among patients with advanced fibrosis (39.6%) and HCC (25.7%) vs patients with low fibrosis level (20.2%; p=0.0012). Patients with advanced fibrosis stage (F3-F4) had a greater proportion of presence of insertions/deletions (INS/DEL) in ISDR as compared to F0-F2 patients (p=0.0037). In particular, a higher correlation between patients with advanced fibrosis or HCC and high frequency of ≥3 variants in ISDR was observed in patients with genotype 2c (p< 0.001), 1a (p=0.02) and 1b (p=0.02). No significant difference was observed in HCV load levels among patients with <3 substitutions and different fibrosis levels. While among HCC patients, there was a trend for subjects with ≥3 variants in ISDR to have a lower HCV load at the baseline (p=0.06). Finally, no correlation was observed between RASs at the baseline of DAA treated patients and advanced fibrosis.

Conclusions: Presence of ≥3 variants or INS/DEL in ISDR was associated with liver fibrosis stage and HCC. This was predominantly observed in patients infected with genotype 2c, 1a and 1b. As has already been hypothesized for duplication of V3 domain in NS5A, ≥3 substitutions and INS/DEL in ISDR might alter the protein functionality. In addition, amino acid changes in ISDR might interfere with the binding and repression of PKR, thus determining a progression in the liver damage. In contrast, RASs were not associated with advanced liver fibrosis.

Basics in viral hepatitis

P 8 HCV GENETIC VARIABILITY IN PATIENTS WITH HCV-GENOTYPE 1-RELATED HEPATOCELLULAR CARCINOMA

A. Di Fraia[1], M. Pisaturo[1], C. Minichini[1], M. Starace[1], L. Occhiello[1], N. Farella[2], G. De Stefano[2], V. Iodice[2], N. Coppola[1,3]

[1]Department of Mental Health and Public Medicine, Division of Infectious Diseases, University of Campania, Luigi Vanvitelli, Naples, Italy [2]AORN dei Colli, Cotugno Hospital, Naples, Italy [3]AORN S. Anna S. Sebastiano, Caserta, Italy

Background: Recently some reports showed that amino acid substitution (aas) 70 and/or 91 in the CORE region of HCV genotype 1b are predictor of hepatocarcinogenesis. Aims: evaluate genetic variability of HCV in patients with HCC analyzing aas in NS3, NS5, Core HCV regions.
Methods: 18 patients with chronic HCV (CCH) genotype 1b infection were enrolled, 9 with hepatocellular carcinoma (HCC; Cases) and 9 showed CCH without HCC (Controls). All were naïve to DAAs. For the 9 Cases, a sample of neoplastic tissue (cancer), non-neoplastic liver tissue (non-cancerous) and a serum sample (S) were collected. For the 9 Controls, a sample of liver tissue was collected. Sanger sequencing of NS3, NS5A and CORE regions was performed by applying homemade protocols for all samples. The sequences were analyzed by comparison with reference sequences taken from the Los Alamos database and from other databases. The phylogenetic trees were created using the Mega 10 program. Mutations and quasi-species were identified by the seqscape program software (Applied Biosystems) with a tolerance> 20% for improper sequences.
Results: Table 1 shows patients characteristics. By phylogenetic analysis of the three HCV regions, in the Cases there are no differences between the viral populations in the 3 compartments (Figure 1a-c). Table 2 shows aas distribution in the Cases and in the Controls. Analyzing the CORE region, M91L was harboured in 4 (44,4%) Cases in all the 3 compartments and in only 1 (11,1%) Control. R70Q was identified in 6 (66,7%) Cases in all 3 compartments and in 5 of the 9 (55,6%) Controls. Analyzing NS3 region, S61T and I71V were identified in 3 Cases in all 3 compartments and in 2 and in 3 Controls respectively. Then 6 Cases harboured E32K, 7 Cases D121N and other 5 Cases harboured D112N in at least one of the 3 compartments, these aas were not present in the Controls. Moreover 2 aas conferring resistance to anti-NS3 inhibitors were identified, 3 Cases and 1 Control presented S122G and 1 Case showed D168E. No difference between Cases and Controls was observed in NS5A region. Aas that confer resistance to DAAs (Y93H, L31M) have been identified, Y93H have been identified in two Cases and in 1 Control, L31M in 1 Control.
Conclusions: there is not difference between HCV viral populations in the 3 compartments of patients with HCC. Aas M91L in CORE region, associated with HCC, were found in 44,4% of the Cases and in 11,1% of the controls. Amino acid substitutions E32K have been found in the NS3 region in 66,7% of the Cases, D121N in 77,8% and D112N in 55,6% but not in the controls. Aas conferring resistance to NS3 (S122G and D168E) and NS5A (Y93H and L31M) inhibitor have been also found both in Cases and Controls. In the literature there are few studies analyzing the genetic variability of HCV in cancer and in non-cancer tissue. In our opinion with the increase of the Cases we can better study this phenomenon and identify other aas associated to HCC.

Cancers in HIV

P 9 A RARE CASE OF METASTATIC GIST ON HIV PATIENT

I. Uccella, G. Scevola, P.L. Alo, M. Mella, K. Casinelli, V. Dell'Uomo, P. Fabrizi, C. Falco, G. Farinelli, M. Limodio, L. Sarracino, M. Sebastiani, E. Anzalone

Ospedale Fabrizio Spaziani, Frosinone

Background: Gastrointestinal stromal tumors (GiST) are non-epithelial tumors, with cellular variability, more frequently in immunocompetents.

Material and methods: We describe a case of HIV-naïve patient presenting metastatic stomach GIST. On December 2018, a 48 years-older Indian man was attended at Emergency Department of Frosinone for fever and abdominal pains. His clinical condition had deteriorated with weight loss and persistent abdominal pain. Previous history of others disorders was negative. Pathologic findings on blood included only low hepatic alteration and high ferritin dosage (2000mcg/L,nv 20-200 mcg/L). Quantiferon dosage resulted indeterminate. The 4th generation Architect HIV Ag/Ab Combo test(Abbott) resulted positive and CD4-T cell count was 35 cells/ul with HIV-1 RNA viral load in plasma of 377.000 copies/ml. No evidence for other viruses, fungi, or parasites was found. Antiviral treatment based on genotype was started. The chest-RX resulted negative and abdominal ultrasound documented enlarged lymph and splenomegaly, only. The TC scan documented gastric wall thickening, two bilateral nodular pulmonary lesions, multiple spleen and adrenal glands lesions and two hepatic lesions: one (< 1 cm) at VII segment, and the second at VI segment (30 mm). The upper GI tract endoscopy, documented non-erosive gastritis with an ulcerated polypoid lesion. Histopathology of the gastric lesion showed inflammatory picture, only. Colonoscopy was negative for lesions and inflammatory diseases. On the hypothesis of disseminated tuberculosis, specific therapy was started. On ultrasound echo-contrast (Sonovue), the major hepatic lesion exhibits peripheral enhanced rim, internal increased vascular components and fast "wash in" and "wash out", similar to a cancer lesion. The MRI abdomen with hepato-specific contrast (Primovist) confirmed the ultrasound nodular imaging, and added the information of internal fluid areas, resulted hypointense, excluding a primitive liver lesion, but with non-specific pattern .Definitive diagnosis was based on typical histopathology of the liver lesion that documented CD117-expressing spindle cells, vimentin positivity, HHV-8 PCR negative.

Results: In our case the GIST diagnosis on HIV patient with severe immunosuppression was really difficult, and the neoplastic hypothesis was suspected by contrast-enhanced ultrasound with indication for biopsy. Repeated Quantiferon test resulted negative and TBC therapy was stopped. The patient attending oncologist visit to start specific chemotherapy.

Conclusion: GIST and Kaposi's sarcoma both present diffuse intestinal lesions with spindle cells, and differential diagnosis is mandatory, because distinct treatment. The occurrence of GIST is coincidental in HIV, but differential diagnosis of this cancer with unusual metastatic presentation with specific HIV related diseases should be recognized by pathologists and clinicians.

Cancers in HIV

P 10 KAPOSI'S SARCOMA ONSET IN A STABLY SUPPRESSED HIV-1 INFECTED MSM ON PI-CONTAINING DUAL THERAPY

D. Moschese[1], G. Baldin[1], A. Ciccullo[1], A. Emiliozzi[1], C. Picarelli[1], A. Dusina[1], D. Farinacci[1], F. Lombardi[1], S. Belmonti[1], A. Borghetti[2], S. Di Giambenedetto[1,2]

[1]Università Cattolica del Sacro Cuore, Roma, [2]Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Roma

Background: Kaposi's Sarcoma (KS) is one of the most common malignancies occurring in patients living with HIV infection. Although KS etiology remains unclear, there is strong evidence of its association with Human Herpes Virus 8 (HHV8) infection.
Report: We report the case of a 61-years-old HIV-1 infected man, with no past AIDS-defining events and on stable combination antiretroviral therapy (cART) since 2009. Since 2010 he had suppressed HIV-RNA and complete immune restoration (Table 1). On October 2014, he underwent a simplification of the antiretroviral regimen with darunavir/ritonavir plus lamivudine, later switched to darunavir/cobicistat plus lamivudine on January 2017. On his last checkup at our clinic, he reported the onset of a violaceous indolent skin macular lesion on his right forearm. The patient did not report any symptom and the clinician proceeded with the excision of the lesion. The histology reported "Subcutaneous and cutaneous lozenge: dimensions 1.4 x 0.9 x 0.7 c, see of a nodular lesion, elevated, DM cm 0.6: Kaposi's Sarcoma (Vim+, CD34+, panCK-). Completely excised." Blood samples were also collected and tested for HHV-8 whose VL resulted positive with low viremia (125 copies/ml). At the same time HIV-RNA was still undetectable (<37 copies/ml) and the CD4 count was 830 cells/mmc with a CD4/CD8 ratio of 1.66. The patient was proposed with gastro-colonoscopy that he refused. An intensification of cART with tenofovir alafenamide plus emtricitabine and darunavir/cobicistat was prescribed by the clinician who also planned chemotherapy with liposomal doxorubicin in agreement with the hematology consultant.
Discussion: Since the introduction of cART, the prevalence of KS has dramatically declined, highlighting the importance of both immune reconstitution and viral load control. Although cART usually prevents the onset of KS, there may be cases where cART alone may be insufficient to avoid such disease. Particularly, several cases of KS have been reported in undetectable individuals on triple therapy with INIs, suggesting a poor control of HHV8 with this class of antiretrovirals.
Conclusion: To our knowledge, there are no reported cases of KS onset in undetectable patients on a PI-containing two-drug regimen, suggesting that darunavir alone may not be sufficient in controlling HHV-8 replication.

Cancers in HIV

P 11 THYROID NEOPLASIA IN A COHORT OF HIV-INFECTED PEOPLE OF NORTHERN ITALY

A. Chiesa, T. Della Giustina, M. Properzi, N. Gregori, F. Castelli, E. Quiros Roldan

Department of Infectious and Tropical Diseases, University of Brescia and Spedali Civili General Hospital, Brescia, Italy

Introduction: Although thyroid diseases have been widely associated with HIV infection, few data are available about thyroid cancer (TC) in this patients. This study aims to assess the prevalence, the associated factors, and the histological distribution of TC in a large cohort of HIV-infected.

Material and methods: A retrospective study was performed on the whole cohort of HIV-infected patients followed at the Infectious and Tropical Diseases department of Brescia's University in the period 2005-2017 to identify concomitant TC. A second-linkage between HIV-infected followed by our Department and all subjects who received in-hospital
services or a medical certificate with an ICD9-CM code for TC was made. Demographic, viral, immunological, and histological characteristics were collected. Factors associated with TC were explored by logistic regression analysis.

Results: Among the 6343 patients in care of our Department (8720.398 years/persons), 11 had TC (0.23% of the whole cohort). The proportion patients with TC were equally divided among genders (45% female), 18% had a history of drug addition, 90% had at least one comorbidity and 36% were co-infected with HCV. At the diagnosis of TC, the median age was 48.6 years, and a mean of 8.7 years (SD 9.88) were passed since the first finding of HIV positivity, an average of 5 years (SD 5.89) since the initiation of cART. At that time 64% of subjects had undetectable HIV viremia and a medium of 527 CD4 Tcells/mm3 (26.2%, CD4/CD8 0.7). Two patients had a history of AIDS-defining condition. Among TC patients CD4 T-cells nadir was of 174 cells/mm3 (13%) with CD4/CD8 of 0.17. Follicular carcinoma was found in 1 of the 11 patients (9%), papillary carcinoma was detected in 7 patients (63%), medullary histotype in 2 subjects (18%), while in one case typology of cancer the was not recorded (9%). All subjects underwent thyroidectomy. One with papillary carcinoma had metastatic disease and finally died; diagnosis was made when he was 47 years old, he had good immune-virological condition until the exitus. The rest of them were in good conditions and were treated with sodic levothyroxine. In the multivariate logistic regression analysis including age, gender, HCVAb, CD4 Tcell nadir and CD4 Tcell increase (for 10 years older), TC was only independently associated with age (for 10 years old increase) OR 1.68; 95%CI 1.05-2.66; p=0.028.

Conclusions: In Italian North-western regions, the prevalence of TC in general population is 160/100.000 with a higher frequency of papillary carcinoma followed by follicular and medullary histotype. TC seems to be a rare condition among non AIDS-defining tumours in HIV patients, with a lower prevalence than the one reported in general population. Interestingly, the distribution among histotypes of TC was different in HIV patients from general population, with medullary carcinoma more frequent than follicular one. In this cohort of HIV-infected people aging increased the risk of TC.

Cancers in HIV

P 12 ANALYSING THE NEED FOR ANAL PAP TESTING IN HIV-POSITIVE WOMEN FOR SCREENING OF ANAL SQUAMOUS CELL CARCINOMA

M. Digaetano[1], E. Bacca[1], A. Bonazza[1], C. Rogati[1], M. Menozzi[1], G. Cuomo[1], E. Franceschini[1], V. Borghi[1], C. Mussini[1,2]

[1]Infectious Diseases Clinic, Azienda Ospedaliero-Universitaria Policlinico di Modena, Modena, Italy, [2]Department of Surgery, Medicine, Dentistry and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy

Background: Squamous cell anal carcinoma (SCCA) is more common in women than in men (incidence rate of 1.5 per 100,000 in men and 2.0 per 100,000 in women) and is one of the most common non-AIDS-defining malignancy among people living with HIV (PLWH). Cervical and anal squamous cell malignancies share ethology and pathogenesis. Both are caused by high risk HPV (HRHPV) genotypes, mostly 16 and 18, and are preceded by several grades of dysplastic alteration called squamous cell intraepithelial lesions (SIL). These can be identified by cervical or anal Pap test and can be treated. We perform an analysis on all HIV+ women outpatients accessing Infectious disease clinic of Modena identifying how many women can be considered at risk and should perform a screening for SCCA.

Material and methods: A retrospective observational study on 467 women with HIV infection was conducted. Data were extracted from electronic and paper records: history of HPV-related diseases, clinical data on HIV infection and cervical and anal Pap tests. According to literature, women with a positive pap test in their lifetime for cervical intraepithelial neoplasia (CIN) or for HRHPV, with a history of HPV related carcinoma or intraepithelial neoplasia in other districts and with immunosuppressive therapies ongoing are considered at risk.

Results: Positive Pap tests were 42(9%): 22 CIN I, 7 CIN II, 13 CIN III. In 2 cases of negative Pap tests HRHPV research was available and in both was positive (genotypes 16 and 18). 22 women out of 467 presented lesions such as CIN I (11), CIN II (1), CIN III (10) in a previous Pap test.

15 women (10 with a negative Pap test, 5 with a CIN III) had a positive history of HPV-related malignant neoplasm (10 cervix, 3 anal, 2 vulvar, 1 tonsil). 3 patients had a history of vulvar and vaginal intraepithelial neoplasia (1 VIN and 2 VaIN). 14 women were on immunosuppressive therapy, only 8 of these had a Pap test available and 1 was positive for CIN I.

Considering once women presenting two or more risk factors, at least 92 (19,7%) women should perform anal Pap test.

Only 8 women of the whole sample performed anal Pap test, 4 cases of which were low grade SIL (in one case CIN I to the cervical sample, the other 3 negative) and 1 high grade SIL (whose cervical pap test was negative).

Conclusions: As evidenced by literature and by our own experience on HIV+ MSM males, the rate of at-risk women would increase significantly if genotypic identification of HRHPV was performed routinely. The resolution of the main limit of our study: the missing data (Pap tests were available in 342 (73,2%) women out of 467), would also certainly increase the proportion of women to be screened. Other risk factors such as smoking habits, number of sex partners, history of anal intercourse are weakly linked to SCCA and have been not investigated. It will certainly be necessary to collect data over time to determine the impact of screening on the morbidity and mortality of the SCCA.

Cancers in HIV

P 13 IMPACT OF ANTIRETROVIRAL THERAPY ON THE RISK OF RECURRENCE IN HIV-1 INFECTED PATIENTS WITH KAPOSI SARCOMA: A MULTICENTER COHORT EXPERIENCE

M. Colafigli[1], A. Ciccullo[2], A. Borghetti[2], I. Fanti[2], F. Melis[3], S. Modica[4,5], I. Uccella[6], A. Bonadies[7], V. Ferraresi[8], E. Anzalone[9], A. Pennica[10], B. Rossetti[5], G. Madeddu[3], R. Cauda[2], A. Cristaudo[1], S. Di Giambenedetto[2], A. Latini[1]

[1]Infectious Dermatology and Allergology, IFO San Gallicano, Rome, Italy, [2]Clinical Infectious Diseases, Catholic University of S. Heart, Rome, Italy, [3]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Italy, [4]Department of Medical Biotechnologies, Azienda Ospedaliera Universitaria Senese, Siena, Italy, [5]Infectious Diseases Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy, [6]UOC Malattie Infettive, Frosinone, Italy, [7]Plastic Surgery, IFO Regina Elena, Rome, Italy, [8]Clinical Oncology, IFO Regina Elena, Rome, Italy, [9]UOSD AIDS, Frosinone, Italy, [10]AOU S Andrea, Rome, Italy

Background: Kaposi Sarcoma (KS) remains a relevant malignancy in HIV-infected patients (pts), with non-standardized management; despite past suggestion that ritonavir-boosted PI (bPIs)-based regimens could be preferable, no combination AntiRetroviral Therapy (cART) regimen was ever demonstrated to outperform the others and the impact of new drugs, drug classes or paradigms was never evaluated. Aim of this work is to evaluate the incidence of recurrence episodes (RE) and the possible associations with the prescribed antiretroviral regimens.

Methods: We collected retrospectively data regarding HIV-infected pts with a diagnosis of KS last seen in 6 Italian Centers after 2013/01/01. The exposure to cART, chemotherapy (CT), electrochemotherapy (ECT) or α-interferon (α-IFN) were recorded. Baseline (BL) was set at the diagnosis of KS and follow-up (FU) was censored at the 1st RE or at the last observation or 2019/03/15. Pts with multiple RE were evaluated as 1 case for descriptive statistical analysis and for as many cases as the number of RE for the Kaplan-Meier (KM)-estimated survival free from RE. The incidence of RE was calculated as the number of events during the FU.

Results: A total of 104 cases of RE in 99 pts were included in the database for 945.34 patient-year FU (PYFU). Median (IQR) BL calendar year was 2010 (2004-2015). KS was diagnosed <3 months (Mo) later than HIV in 31%, <3 Mo earlier in 23%, >3 Mo later in 37% and >3 Mo earlier in 8% of pts; cART was started >3 Mo earlier than the SK diagnosis in 23% of pts, <3 Mo earlier in 12%, <3 Mo later in 59% and >3 Mo later in 6%. At BL, 44% of pts had ever been exposed to suboptimal 2NRTI-based ART, 64.7% were prescribed a standard (49.5% bPI-based, 9% 1st generation unboosted PI-based, 6.1% NNRTI-based and 9.1% INI-based) 1st line regimen, 9.1% a mega-cART and 9.1% a suboptimal ART. Twenty-six (27%) pts had visceral localizations. Thirty-three (34%) pts were treated with a median (IQR, range) of 6 (4-9; 2-52) cycles of CT for a median (IQR) time of 5.2 (2.6-12.6) Mo, 4 (4%) with ECT and 12 (12%) with α-IFN for a median (IQR) time of 14.2 (6.8-41.4) Mo. At censor, 22% were receiving a bPI-based, 14% a NNRTI-based and 28% an INI-based standard cART, 24% a Less Drug Regimen (LDR) (17% bPI-based, 7% DTG-based) and 12% a Mega-cART. Twelve RE were observed in 7 pts (3/7 had just 1, 3/7 had 2 and 1/7 had 3 RE) for an incidence of 1.27% PYFU with a median (IQR) time free from new episodes of 7.48 (3.19-14.05) years; the clinical details of the 12 cases with RE are shown in Fig.1. Two deaths were observed (1 sepsis, 1 unknown reason in a lost to FU patient) in pts with no RE. The overall KM-estimated survival free from RE at 5 years was 89.6% (SD 0.033), at 10 years 87.9% (SD 0.037).

Conclusions: In our experience KS RE were infrequent. Despite the increasing use of new antiretroviral drug classes and new treatment paradigms, no excess of RE was observed in patients receiving such cART regimens.

Cancers in HIV

P 14 FACTORS ASSOCIATED WITH HCC OCCURENCE/RECURRENCE IN A COHORT OF HIV/HCV PATIENTS TREATED WITH DAAS. PRELIMINARY DATA FROM THE REC-HIV STUDY

A. Toschi[1], L. Badia[1], S. Coladonato[1], B. Tazza[1], M.A. Ursitti[2], E. Salsi[3], D. Laccabue[3], R. Corsini[2], M. Massari[2], A.M. Degli Antoni[3], L. Sighinolfi[4], G. Verucchi[1], V. Guardigni[1]

[1]Sant'Orsola-Malpighi, Bologna, [2]Arcispedale S. Maria Nuova, Reggio Emilia, [3]Ospedale di Parma, Parma, [4]Arcispedale Sant'Anna, Ferrara

Background: Nowadays, with the implementation of DAAs-based treatment, the consequences on the natural history of HCV infection has become a main interest of research. Even if different studies proved a reduction in the occurrence of HCV-related events after the SVR, still little is known about this issue in co-infected HIV-HCV patients. With the improvement of cART and the decrease in mortality due to AIDS, liver disease is becoming one of the main causes of mortality and morbidity in HIV infected patients. The aim of our study was to determine the rate and the predictors of HCC in HIV-positive cirrhotic individuals treated with Interferon-free DAAs-regimens.
Material and Methods: We retrospectively studied all cirrhotic HIV patients treated with DAAs, from October 2014 to January 2017 at the Department of Infectious Diseases of four Italian hospitals. We measured the rate, characteristics and potential predictors for occurrence of HCC, performing non parametric statistical analysis to compare patients who developed HCC and those who did not.
Results: We included 141 HIV-HCV co-infected patients and observed our cohort from the day they started DAAs therapy (baseline), over a median of 30 months. 79% were male, with a median age of 52 years (IQR 49-55y). After a median of 13 months from the baseline, HCC occurred in 12 patients (8.5%), and 2 of them were recurrences, with a rate of HCC recurrence of 40%. Patients who developed HCC had a longer history of HCV infection (median of 25 years against 22 years in those free from cancer) and genotype 3 was more common (41.7% against 29.5%), although we didn't find a statistical significance in this results (p value respectively of 0.09 and 0.59). As expected, we detected a higher rate of HCC in patients with more severe cirrhosis (i.e. higher CP class, p value = 0.04). Furthermore, we observed that a lower CD4+ count at the baseline had a positive association with the development of HCC (p value=0.05), while a lower CD4+-nadir had a negative association (p value=0.02). In our cohort, 5 patients were not taking any ART during the period of observation (3,5%), of these, 2 developed HCC (p value=0.06).
Conclusions: We observed a rate of 8,5% of HCC following DAAs treatment in cirrhotic HIV-HCV coinfected patients.
This rate was significantly higher in those with a lower CD4-count at the baseline, showing that there could be a correlation between the immune system defect and the progression of the hepatic disease. Notably, in our cohort patients with a lower CD4-nadir tended to develop HCC less frequently. Since we know the cumulative HIV viral load relates with higher incidence of HCC, we could assume that, due to their poor immunological status, ART was started earlier in these patients, leading to lower cumulative HIV viral load. More data, as the cumulative HIV-viremia in years and the starting time of ART, and more in-depth statistical analysis would be needed in order to enhance these correlations.

Cancers in HIV

P 15 BURKITT LYMPHOMA IN HIV-INFECTED PATIENTS: TREATMENT AND SURVIVAL IN THE MODERN ART ERA

G. Bozzi[1], L. Verga[2], M. Rossi[2], C. Gambacorti Passerini[2], D. Dalu[3], C. Fasola[3], I. De Benedetto[2,9], F. Crippa[4,8], E. Suardi[4], C. Zeroli[5], P. Vitiello[2,5], M. Mena[6], O. Giglio[7], A. Gori[1], A. Bandera[1] on behalf of the Musthal Study Group

[1]IRCCS Ca Granda Ospedale Maggiore Policlinico - University of Milan, Milan, Italy, [2]ASST Monza, San Gerardo Hospital, Monza, Italy, [3]ASST FBF-Sacco, Luigi Sacco Hospital, Milan, Italy, [4]San Paolo Hospital - University of Milan, Milan, Italy, [5]Ospedale di Circolo di Busto Arsizio, Italy, [6]Ospedale civile di Legnano, Legnano, Italy, [7]ASST Lariana, Sant'Anna Hospital, Como, Italy, [8]Niguarda Hospital, Milan, Italy, [9]Università degli Studi di Torino, Turin, Italy

Introduction: Combined antiretroviral therapy (ART) greatly reduces, but does not thwart completely, the risk of developing HIV-related non-Hodgkin lymphomas (NHL). Burkitt lymphoma (BL) accounts for up to 20% of HIV-related NHL with an increasing incidence in the last years and a less important association with immune suppression, maybe due to a partial effect of EBV in the pathogenesis of this hystotype (60–70% of HIV-related BL EBV-negative). Here, we aim at describing the BL population in our multicenter cohort of HIV-related NHL.
Methods: Multicenter observational cohort study including HIV+ pts from 6 Italian centers, receiving biopsy-proven NHL diagnosis since 2003. Data on HIV infection and lymphoma characteristics, chemo-immune treatment and outcome were recorded. Overall survival (OS) estimates by Kaplan Meyer and predictors of OS by Chi-square, Fisher's exact, and Cox regression were performed.
Results: Overall, 127 HIV-NHL were included in our cohort (86.6% males, medians: age 48 years, CD4+ at diagnosis 186/mmc). Among them, 86 (68%) had systemic DLBCL, 18 (14%) Burkitt, 11 (9%) plasmablastic, 6 (5%) primary CNS, 6 (5%) other histotypes. BL patients showed a median age at diagnosis of 45 years [IQR 41 - 50] and a median time from HIV diagnosis of 1 year [0 – 5]. As of route of HIV transmission, patients were MSM (38.9%), heterosexual (22.2%), IV drug users (16.7%) or unknown (22.2%). Median CD4 T cell count at BL diagnosis was 152/mcL [52-190] with 50% of patients showing <200/mcL CD4 cells at diagnosis and only 16.7% patients with a CD4 nadir higher than 200/mcL. Median HIV RNA levels at BL diagnosis were 4.6 log10cps/mL [1.6-5.2]. 33.3% patients were on ART at diagnosis, and all were suppressed. However, half of them experienced mild loss of viremia control after BL diagnosis and treatment. As of lymphoma baseline characteristics, 66.7% patients had Ann Arbor stage 3 or 4 lymphoma; 11.1% had CNS involvement. IPI score was distributed as follows: 0-1 (22.2%), 2 (5.6%), 3 (33.3%), 4 (33.3%), unknown (5.6%). In our casistic, 8/18 (44.4%) BL patients were treated with GMALL and 5/18 (27.7%) used intensified regimens; the other CT schemes used were R-DA-EPOCH (3 pts) and CODOX-M (1). One patient died before starting CT. At 24 months from diagnosis, cumulative risk of death for BL patients was 50%, while patients with DLBCL, plasmablastic lymphoma and primary CNS showed a cumulative risk of death of 37.2%, 45.5% and 33.3%, respectively. 75% deaths were due to NHL, all occurred within 24 months.
Conclusions: BL is known to develop in relatively young HIV patients and/or with relatively high CD4 T-cell counts, i.e. > 200 cells/mcL. This was just partly the case in our cohort. Despite common use of intensified regimens, we observed higher mortality for BL in comparison to DLBCL cases in our cohort. Large multicenter cohorts can help clarify epidemiology and outcomes of BL in the modern ART era and help define future management strategies.

Cancers in HIV

P 16 HPV GENOTYPING IS AS IMPORTANT AS CYTOLOGY IN ANAL SQUAMOUS CELL CARCINOMA EARLY DIAGNOSIS

M. Digaetano[1], C. Rogati[1], F. Spatafora[2], R.P. Iachetta[3], R.D. Villani[3], A. Farinetti[2], M. Menozzi[1], S. Tagliazucchi[4], M. Pecorari[4], R. Gelmini[2], C. Mussini[1,2]

[1]Infectious Diseases Clinic, Azienda Ospedaliero-Universitaria Policlinico di Modena, Modena, Italy, [2]Department of Surgery, Medicine, Dentistry and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy, [3]Nuovo Ospedale Civile di Sassuolo (Modena), Pelvic Floor Center, Department of Proctology, [4]Unit of Microbiology and Virology, Polyclinic University Hospital, Modena, Italy

Background: The prevalence of anal squamous cell carcinoma (SCCA) in the general population is about 1/100,000 but raises to 131/100,000 in MSM HIV+ subjects. Co-infection by human papillomavirus (HPV), persisting at the level of the anal mucosa, can lead to cytological changes that can evolve into squamous cell intraepithelial lesions from low to high grade of dysplasia (LSIL and HSIL). Aim of this research is to identify the best method of screening for precancerous lesions.

Methods: This prospective single centre study involved HIV+ MSM who underwent an anal cancer screening program using the anal Pap test, HPV genotyping and, in case of positive cytology or high-risk HPV genotype detection, high resolution anoscopy (HRA).

Results: 182 Pap tests were performed: 73 (40,1%) were positive for HPV related lesions, 64 (87,7%) low grade squamous intra-epithelial lesions (LSIL) and 6 (8,2%) atypical squamous cells of undetermined significance (ASCUS), high grade lesions (HSIL) were found in 3 patients (4,1%). 129 of 182 screened (70,9%) performed also HPV genotyping: 4 resulted negative, 11 low risk HPV genotype carriers (LRHPV), 13 probable high-risk HPV carriers (pHRHPV), 101 high risk HPV (HRHPV) genotype carriers. HPV16 was found in 30 patients (18,3%) and it was the most frequently identified high risk genotype followed by HPV 52 (27 patients, 20,9%) and HPV 51 (21 patients, 16,3%). HPV18 was found in 17 patients (13,2%). Only 35 HRHPV carriers (34,7%) had a positive Pap test. A total of 133 screened (73,1%) had the indication for HRA (67 positive Pap tests plus 66 HRHPV with negative cytology). Among 42 HRAs performed until today (39 in Pap test + and 3 in HRHPV carriers with Pap test negative), 21 (50%) showed LSIL and 8 HSIL (19%). 2 HSILs were found in HRHPV carriers with negative Pap test, 6 in Pap test positive. HRA confirmed cytology in 23 cases, showed a worsening in 7 cases and a lower grade lesion in 11 cases. 3 cases of clinical progression were detected at control, 1 with HRHPV but negative cytology became LSIL, 1 LSIL became HSIL and 1 carcinoma in situ was found in a patient treated for HSIL four months before.

Conclusions: HPV-related dysplasia is common among HIV+ MSM and is likely to evolve in a short period of time especially in the presence of high-risk genotypes. We recommend the association of HPV genotyping with cytology as first level of screening and HRA for treatment and follow up of lesions as this bundle allows to identify lesions in subjects with a negative Pap test.

Gender issues

P 17 PHYSICIAN GENDER DIFFERENCES IN HIV INFECTION CHRONIC MANAGEMENT

N. Gregori, A. Piazzoli, M. Properzi, A.C. Chiesa, C. Pezzoli, C. Carriero, D. Coletto, F. Castelli, M.E. Quiros Roldan

Department of Infectious Diseases and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy

Objectives: The primary aim of this study is to compare male and female clinical attitude in management of HIV patients, evaluating differences through continuum of care endpoints raccomended in the latest SIMIT guidelines. The secondary aim is to investigate the influence of doctor's job experience lenght and time frame of clinical control visit on HIV infection management quality.

Design and methods: This was a cross sectional study in 95 HIV patients (72.63% male, 27.37% female) in clinical follow up at Infectious Diseases oupatients' departments of ASST Spedali Civili of Brescia. The periodic control visits were performed by 8 infectious diseases practitioners (5 female doctors, 3 of them with less than 10 years of clinical experience and 2 with a 10 or more -year clinical experience, and 3 male doctors with a 10 or more-year clinical experience). The period of data collection last from March to July 2018. Quality of HIV patient management was evaluated according to 2017 SIMIT essential measures of HIV infection care, included counseling activities for HAART adherence, renal function and diet, based on annual control of virological, renal and metabolic markers, and prevention activities (screenings for cancers and bone toxicity and co- infections markers assay, as hepatitis and LUE). Each one of these dicotomic dependant variables was analysed in relation to independant variables (physician gender, years of carreer experience and time frame of clinical visit) using simple and multiple logistic regression models. For each variable OR, IC 95% and p-value were calculated.

Results: There was no evidence of impact of physician gender nor clinical experience lenght or time frame of visits on measures targeted to control alterated HIV viremia and blood values of glucidic methabolism and renal function. However, male physicians (OR: 0.31; IC: 0.12-0.74; p:0.01) and those with more than 10 year-experience (OR: 0.33; IC: 0.14-0.77; p:0.012) were less likely to pay attention to HAART adherence counseling in case of altered HIV viremia (>37 copies/mL). Regarding prevention measures, whereas prescription of MOC-DEXA was not influenced by any independant variable, oncologic screenings were more prescribed by female physicians (OR: 2.00; IC 0.00-0.17; p:0.002) and doctors with at least 10 years of work experience (OR: 7.01; IC: 1.68-36.73; p:0.012). Differently, physicians with less than 10 years-experience prescribed serological co-infections markers screening (hepatitis and LUE) during follow up more than their more experienced colleagues (OR: 0.23; IC: 0.05-0.91; p: 0.048).

Conclusion: Outpatients' department activities of our Infectious Diseases Clinic comply with 2017 SIMIT guidelines for the HIV infection chronic management, regardless the physician gender or years of work experience or time frame work. Anyway, the field of prevention is influenced by physician gender and clinical experience length.

Gender issues

P 18 IS SEXUAL HEALTH AN ISSUE TO BE ADDRESSED IN HIV-1 INFECTED AND UNINFECTED WOMEN?

R. Marocco, S. Vita, A. Carraro, B. Kertusha, I. Pozzetto, L. Fondaco, L. Ansaldo, M. D'Achille, G. Masci, C.M. Mastroianni, M. Lichtner
Infectious Disease Unit, Sapienza University, Latina, Italy

Background: Sexual function has been recognised as a crucial component of health. In fact, experience of female sexual dysfunction (FSD) is generally associated with poor quality of life. FSD is considered a public health problem affecting more than 40% of the world population of woman. Prevalence and factors associated with sexual dysfunction in HIV positive women are poorly know.
The aim of this pilot study was to describe the prevalence of FSD and Generalized anxiety disorder (GAD) in a cohort of HIV positive women.
Methods: 42 clinically stable, receiving effective ART, HIV women and 21 healthy female subjects were invited to participate in a FSD and GAD evaluations with self-administered respectively Female Sexual Function Index (FSFI) exploring desire, arousal, lubrication, orgasm, pain and satisfaction and GAD Test. An FSFI score 26.55 is classified as FSD and Z index 58,7 is classified with moderate/severe anxiety symptoms. Moreover, the subgroup of 22 HIV women in a fertile age were compared with 21 female healthy donors (HD). Sex hormones (oestradiol, progesterone, testosterone) were determined using CLIA kit. Non parametric Mann-Whitney test, Chi square test and Spearman coefficient correlation were used.
Results: In the HIV group, overall, 24 (57%) reported FSD and 18 women (43%) had a FSFI score< or=10. Considering different areas of FSFI, orgasmic function was associated with CD4+T cell (p=0,04, r=0,31). Regarding GAD, 17% of women presented a generalized anxiety disorder. Z-index was associated with orgasm domains (p=0,01; r=-0,35) and CD4+ T cells (p=0,02; r=-0,34). Comparing childbearing with menopause women, FSD was higher in the latter group as aspect (p=0,0005). When we compare young subjects with uninfected female controls (table1), a higher proportion of subjects with FSD was found (p=0.02).
Characteristics of 22 HIV women and 21 HD are listed in table 1Considering the different areas of FSFI, significant differences between the two groups in sexual desire, arousal and pain were found (respectively p=0.001, p=0.02, p=0.04). Interestingly, a positive correlation between level of testosterone and FSFI score only HIV+ women was found (p=0,02; r= 0,74).
Regarding GAD, a larger number of HIV women presented a generalized anxiety disorder (p=0.05), even if no differences in Z-index score was found in the two groups.
Conclusion: Our pilot study shows that FSD are detected in more than half of HIV infected women on stable ART in both fertile age and menopause and seems to be related to testosterone levels. The comparison with uninfected women underlying a persistent gap in the life quality of HIV young women that should be bridged.

Gender issues

P 19 VAGINAL IMMUNITY AND HPV INFECTION IN HIV INFECTED WOMEN UNDERGOING SUCCESSFUL ART

A. Carraro, S. Vita, R. Marocco, B. Kertusha, I. Pozzetto, L. Fondaco, L. Ansaldo, M. D'Achille, G. Masci, C.M. Mastroianni, M. Lichtner
Infectious Disease Unit, Sapienza University, Latina, Italy

Background: HIV women have an higher risk for HPV infection than healthy women, overall for high-risk HPV infection, with a subsequent higher risk to cause cervical intraepithelial lesions.
Particularly, a relation has been reported between low CD4+ counts and high risk HPV infection. In literature data are insufficient about the HPV prevalence in HIV women with undetectable viral load and high CD4 counts and data about HPV distribution related with NK linphocytes and inflammatory cytokines in the cervical-vaginal mucose.
Material and methods: 17 clinically stable, receiving effective ART, HIV women and 19 healthy female subjects were examinated. We analyzed on blood samples lymphocyte subpopulation and on vaginal liquid proinflammatory cytokines (IL-1beta, IL-6, IL-8), and HPV DNA with cervical swab. Futhermore Pap test is been performed in each woman. Non parametric Mann-Whitney test, Chi square test and Spearman coefficient correlation were used.
Results: HPV showed a prevalence of HPV reaching 70% of cases while healthy women 47% (p=ns). Instead, high risk HPV strain prevalence is about similar between two populations (1% and 35%)
No relation is reported between HPV prevalence and CD4+ count. The absolute NK cell number in HIV infected is lower than in healthy women (p=0.005) as well as the percentage level (p=0.001). However the HPV prevalence, both low (LR) and high risk (HR), is not related to NK level in both populations. Although not significant a lower NK count in HPV HR HIV positive women compare to (p=0.07) HD HPV LR positive.
In HIV women a lower IL 6 and IL 8 levels in the VL than in HD was found.
Looking at subpopulation "HIV+/HPV+", "HIV-/HPV+", "HIV+/HPV-" e "HIV-/HPV-", it's been observed that there is a progressive increase of IL 1beta and IL 6, with a statistical difference between IL 6 level in HIV+/HPV+ and HIV-/HPV- subpopulations. IL 8 value is higher in not HIV subpopulation.
In the 5% of HD the PAP test was abnormal compare to 11.7% of HIV positive women.
Conclusions: The colonization of HPV is quite common in HIV positive and negative women. Our study points out that HPV infection is a local infection in fact there were no differences in the group of HPV positive women compared to negative ones in terms of vaginal and even plasma cytokine levels. Almost all of our population had a negative pap smear, it would be interesting to explore the presence of local and plasma inflammatory changes in presence of pap test anomalies.

HCV elimination

P 20 The barriers for HCV treatment in Italian Drug Dependence Services (SerDs): data from the SCUDO Project

F.A. Nava, P. Fasciani, L. Cammarata, A. Lucchini, A. Manfredi, M. Riglietta, G. Taglianti, P. Trotta

Italian Society of Addiction Medicine (FeDerSerD), Milan, Italy

Background: In Europe the epidemiological data suggest that the 67% of people who inject drugs (PWIDs) are HCV positive, corresponding to about 3 million (Nelson et al., 2011). The evidence has shown that drug users may be one of the most important infection reservoir and that the direct antiviral agents (DAAs) are effective and well-tolerated also in addicts. For the above reasons each HCV elimination plan should include the PWIDs as a priority therapeutic target.

In Italy the prevalence of HCV is very high, overall in drug users (Nava et al., 2018). The data suggest that about 60% of people treated in the Italian Drug Addiction Centers (so called Ser.D.s) may be HCV positive, corresponding to about 90,000 (Nava et al., 2018). Most of them are not yet treated since there are several barriers that limits their access to DAAs (Nava et al., 2018).

Method: In order to promote the access to HCV treatment in drug users the Italian Society of Addiction Medicine (FeDerSerD) promoted a survey (the SCUDO Project) in 5 Italian Ser.D.s (Milan, Florence, Bergamo, Chieti, Novara) aimed to evaluate at the 31 December 2017 the prevalence HCV infection, the percentage of the patients treated with DAAs, and the barriers that may limit the HCV treatment.

Results: At the 31 December 2017 the patients screened were 1.634, corresponding to the 30% of patients that are in charge in the 5 Ser.D.s participating in the study. Of the patients screened 21% (n = 342) were resulted HCV antibodies positive. Of them 58% (n = 197) were RNA positive (some of positive antibodies patients were not tested for RNA). Of all diagnosed patients 80% (n = 157) were referred for treatment and only the 30% (n = 49) were treated with DAAs.

The major limits able to reduce the treatment were the lacking of use of rapid tests for screening and the fact that not all HCV patients were referred for the treatment (in the 100% of the cases), followed by the inability to treat for HCV the patients inside the Ser.D.s. (in the 80% of the cases).

Conclusion: Our survey shows how several barriers may acts in the Ser.D.s limiting the HCV treatment. Structured and integrated procedures able to screen all drug users and to treat all HCV positive patients on site should be promoted, transforming the Ser.D.s as "point of care" able to eliminate every referral barrier.

References:

Nava F.A., 2018. For a program of eradication of hepatitis C in the population at risk (drug users and convicts). Acta Biomed., 89 (Suppl. 10): 33-41.

Nelson P.K. et al., 2011. Global epidemiology of hepatitis C in people who inject drugs: results of systematic reviews. Lancet, 378: 571-583.

HCV elimination

P 21 ELIMINATION OF HEPATITIS C VIRUS IN key POPULATION: experience from two prisons IN ROME

S. Lardo, S. Rosati, G. Iannicelli, P. Magrini, M. Zaccarelli

INMI L. Spallanzani- IRCCS, Rome

Background: Hepatitis C is a major public health problem in prison. Ten million people are currently estimated to be in prison and approximately 30 million persons enter and leave prisons every year. In January 2017, 6211 people had cross through Lazio prisons. Italian Prisoners represent a community of people, particularly exposed to HCV infection both by high prevalence of HCV and transmission risk. Every year ≥30000 HCV positive individuals pass through Italian prisons and prevalence of HCV infection observed ranged between 22.4% and 38.0%. A care pathway for assessment, diagnosis and treatment should be established in all prisons, integrated within managed clinical networks.
The aim of the analysis is to describe our initial experience in managing HCV treatment in prison in Rome.
Material and Methods: HCV patients observed and treated with DAA as "Infectious Disease Consultants of CC Rebibbia and IP Regina Coeli Prison" between January 2016 and February 2019 were included.
We analyzed demographic, clinical (evidence of cirrhosis) and virological features (HCV genotype, HCV-RNA, HIV coinfection), DAA regimen prescribed and treatment outcome.
Results: Overall, 133 patients started DAA and were included. Of them, 77 (57.9%) were from Regina Coeli, 51 (38.4%) from Rebibbia and 4 (3.0%) from other prisons. The general characteristics of patients are reported in table 1. Of note, 90.2% were males, 17.1 non-Italian birth, 32.3% HIV coinfected and 14.3% had evidence of cirrhosis. 1a genotype was the more likely represented (47.3%) followed by 3 (27.8%). Sofosbuvir-Velpatasvir was the most likely DAA regimen used (63.9%). Seventy-seven patients already completed DAA therapy (54 are still in treatment): 47 achieved SVR12 (2 failed therapy due to interruption for personal decision). Of 23 patients without SVR evaluation, 7 patients cannot have been evaluated (lost in follow-up) for end of detention or transferred in other prison. Thus, the proportion of SVR12 are 47/47 (100%) if completed therapy (on-treatment) and 47/49 (95.9%) including patients who failed by interruption (int-to-treat).
Conclusions: The concepts of "control", "elimination" and "eradication" have long been the subject of numerous debates. HCV treatment for key populations such as prisoners could become an important HCV prevention intervention, especially in the IFN-free DAA era. Our experience demonstrated that treating HCV patients with DAA in prison is possible and with results like other HCV patients. We also evidenced the problem of treatment and/or follow-up interruption due to end
of detention in prison that requires efforts to be managed. A dedicate route to manage patients after detention has been organized.

Keywords: HCV elimination, prison, Key population

HCV elimination

P 22 HCV AND PRISON: HIGH RATES OF TOLERABILITY, COMPLIANCE AND EFFICACY OF DIRECT ACTING ANTIVIRALS (DAA) TREATMENTS IN A REAL-LIFE POPULATION OF HCV INCARCERATED PATIENTS FROM TWO COMPLEX PRISON SETTINGS IN FLORENCE, ITALY

E. Salomoni[1], A. Gabbuti[1], P. Pierotti[1], F.M. Fusco[1], M.A. Di Pietro[2], P. Blanc[1]

[1]SOC Malattie Infettive 1, Ospedale S. Maria Annunziata, Bagno a Ripoli (FI), [2]SOC Malattie Infettive 2, Ospedale S. Jacopo, Pistoia

Background: The treatment of HCV incarcerated patients (pts) is nowadays a crucial target in the HCV elimination program, but it presents many issues, such as uncertain detention length with possible unexpected release and interruption of therapy, and the frequent association with drug abuse requiring psychotropic therapy, that leads to a risk of drug interactions and scarce compliance. Sollicciano and Gozzini prisons in Florence are the two most insidious settings of Tuscany Region, considering they have the highest rate of overcrowding (44.8% vs tuscan median 6.8%), foreigners (67% vs 48%), drug users (30% vs 15%) and HCV prevalence (10% vs 5.3%).

Material and methods: We enrolled all pts receiving DAA therapy in Sollicciano and Gozzini prisons in Florence from Jan 2017 to Mar 2019. We analyzed baseline HCV-related characteristics, the history of drug abuse and the features of concomitant psychotropic therapy. We monitored psychological conditions during treatment through periodical toxicological and/or psychiatric evaluations.

Results: Fifty-one pts received DAAs: 84.3% M, 23.5% foreigners, 5.8% coinfected with HIV; their median age was 44 (25-57) yrs, 84.3% had the first prescription in prison, 9.7% was already on-treatment at the arrival. The 92.1% was naïve to HCV therapy, one had a documented reinfection after a previous DAA course.

Fibrosis stage was F≥3 in 33.3%; 35.3% was infected with G1a, 7.8% G1b, 4% G2, 47% G3, 4% G4, one pt had a mixed G1b-3.

The 92.2% of pts had a drug abuse history: 62.7% was actively in charge to the service for drug addiction (SerD); the remaining 29.5% had been followed by SerD in the past and in the 40% of cases still assumed psychiatric therapy. Overall, the 74.5% of pts regularly received at least one psychotropic drug: 27.4% opioid substitution therapy, 70.6% benzodiazepines (55.5% assumed two or more types), 27.4% antipsychotics, 39.2% antidepressants, 29.4% antiepileptic/anticonvulsants. Prescribed DAAs were: 51% GLE/PIB, 31.4% SOF/VEL, 9.8% SOF/LDV, 3.9% SOF + DCV, 3.9% GZR/EBR; a switch in psychotropic therapy because of drug interactions was necessary only in 5.9%.

The 70.6% of pts has already completed therapy and 60.8% has reached the w12 after the end of treatment: of these, the 90.3% had a documented SVR, of the remaining 9.7% no data are available since pts left the Institute before the follow-up exams.

Periodical toxicological and/or psychiatric evaluations showed a satisfactory grade of compensation: only two cases of temporary refusal of therapy (retracted in the same day) were observed; 25.5% of pts asked for de-escalation of psychotropic therapy during treatment.

Conclusions: In a very difficult-to-treat population, such as HCV prisoners of Sollicciano and Gozzini Institutes in Florence, DAA therapy demonstrated not only a high efficacy, but even a great tolerability and a high level of compliance, showing how treating prisoners nowadays can be considered a concrete and safe target to reach.

HCV elimination

P 23 SUBGROUP ANALYSIS OF HCV INFECTED PATIENTS TREATED WITH DIRECTLY ACTING ANTIVIRALS IN REAL CLINICAL PRACTICE: DO AGE AND CIRRHOSIS HAVE AN IMPACT?

V. Scaglione, C. Costa, V. Pisani, E.M. Trecarichi, M. Mazzitelli, G. Greco, F. Serapide, R. Lionello, V. La Gamba, S.D. Similia, C. Torti

Unità Operativa di Malattie Infettive e Tropicali, Azienda Ospedaliera Universitaria "Mater Domini", Università degli Studi "Magna Graecia" di Catanzaro

Background: Randomized clinical trials, as well as experiences on the field, have demonstrated >95% sustained virological responses (SVR). However, subgroup analyses comparing patients by age and/or cirrhosis are lacking, especially as far as real clinical practice is concerned.

Objectives: To test whether older patients and those with cirrhosis display worse virological and clinical outcomes compared with younger patients and those without cirrhosis.

Material and methods: All patients treated with directly acting antivirals in our centre from 2014 to 2018 have been included, provided that ≥3 months have lasted from the end of therapy and closure of the data-base. Patients have been stratified by age (i.e., <65 vs. ≥65 years) and cirrhosis (i.e., liver stiffness >14,6 KPa or clinical/ultrasound cirrhosis vs. absence of these criteria). Rates of SVR have been assessed either at week 12 or 24 post-treatment. Inter and intra-group comparisons have been performed at single points and along the follow-up for significant laboratory parameters.

Results: 217 patients were treated (5 had started treatment too recently to be evaluated). 188/212 (88.7%) obtained SVR (4 patients after retreatments). 22 (10.4%) patients were lost to follow-up before week 12-24. Only 2 patients died before the end of treatment for liver decompensation. Considering only the first treatment episodes, observed data analysis (i.e., excluding patients lost to follow-up) showed the following rates of SVR: 97% (overall), 97% (older age group), 97% (age group <65 years), 94% (cirrhotics), 100% (non cirrhotics). By contrast, at the intention to treat analysis (i.e., patients lost were computed as failures), SVR percentages were significantly lower for patients <65 years of age (77%) and for non cirrhotics (85%). In patients achieving SVR, statistically significant differences at baseline were lost at the time of SVR between age groups for haemoglobin (p=0.03 at baseline compared with 0.3 at SVR), and improvements in creatinine, alpha-fetoprotein, APRI and FIB -4 were found similarly in both age groups. Statistically significant differences were maintained between cirrhotic and non cirrhotic patients for platelet counts, albumin, APRI and FIB-4 scores, although they improved in both groups.

Conclusions: High rates of SVR were obtained. However, younger patients and those without cirrhosis displayed a greater risk of loss to follow-up. This may have important implications: since those who are lost may transmit HCV in case SVR is not achieved, these subpopulations should receive appropriate counselling while treated. The importance of a proactive approach appeared to be supported by consideration of significant benefits obtained also in those with cirrhosis and by a tendency towards similar values of some parameters, such as haemoglobin, in younger and older patients after DAA, while they were significantly different at baseline probably because of aging and disease effects.

HCV elimination

P 24 HEPATITIS C MICRO-ELIMINATION PROJECT

P. Casella[1], A. Cruciata[2], A.M. Lupi[1], D. Contucci[1], M.S. Garofalo[1], T. Girolami[1], M. Rivano[2], A. Rugova[2], M. Santori[2], F. Tamburrini[2], E. Biliotti[2], B. Di Vico[3], G. Taliani[3]

[1]Azienda Sanitaria Locale Roma 1 (ASL Roma 1), Rome, Italy, [2]Sapienza University of Rome, Department of Translational and Precision Medicine, Rome, Italy, [3]Azienda Ospedaliero-Universitaria Policlinico Umberto I, Rome, Italy

Background: Chronic hepatitis C virus (CHC) infection is common in people with drug addiction. The treatment of HCV by means of direct acting antivirals (DAAs) in this population is crucial to achieve the WHO goal of HCV elimination, as this population carries a high risk of transmission. Unfortunately, these individuals have limited access to HCV diagnosis and treatment. Therefore, it is important to plan a joint integrated approach between the health care services for drug addiction (SerD) and the hospital for HCV therapy. The aim of the present study was to design and describe the results of a HCV micro-elimination project, whose goal was to realize a continuum of HCV screening, diagnosis and treatment among people with drug addiction attending SerD services located in Rome.

Materials and methods: A collaboration for the HCV micro-elimination involved SerD services, located in 6 Districts pertaining to 6 municipalities of Rome, and the Policlinico Umberto I Hospital. A pre-specified path had been established (Figure). We examined the prevalence of HCV antibodies (Ab) and HCV infection and the rate of linkage to care and DAA treatment.

Results: Between January and November 2018, 181 subjects with drug addiction attending SerD were screened for HCV-Ab. Among the 181 people screened (age 43.2 ± 10.2 yrs, 83.4% male, 53.6% from Italy, 57.5% with heroin addiction, 15.6% with alcohol addiction, 44% with a history of intravenous drug use, 61.5% receiving opioid agonist treatment), 44.2% (80/181) tested positive for HCV-Ab. HCV-Ab positive patients were more frequently males (92.5% vs 76.2%, p=0.003), foreigners (61.2% vs 34.6%, p<0.001) and, as expected, had more frequently a history of intravenous drug use (85% vs 9.5%, p<0.001). Among the 80 subjects testing positive for HCV-Ab, 76 subjects (95%) received a confirmatory HCV-RNA testing and 86.8% (66/76) showed a detectable viremia, with a mean HCVRNA of 6.1 ±0.8 Log10 UI/mL. Genotype 1 was the most prevalent (42.4%), followed by genotype 3 (39.4%) and 4 (7.6%). Among the 66 patients with CHC, 62 (93.9%) patients were linked to care and 25 (40.2%) initiated DAA therapy. No demographic, clinical or virological characteristics differed between patients engaged in care compared to those not engaged. The rate of retention in care was 100%.

Conclusions: In this study, we report the results of a HCV micro-elimination project to diagnose, link to care and engage in care patients with drug addiction and CHC with the goal of maximizing access to DAA treatment. The diagnosis rate was 95%, the linkage to care was 93.9%, while the treatment rate was 40.2%. These data indicate that the implementation of a network involving different specialists increases the efficiency of the diagnosis rate and linkage to care of patients with drug addiction, nevertheless efforts are still required to successfully engage patients in HCV care in the era of DAA therapy in order to maximize the individual and public health benefits.

HCV elimination

P 25 HCV POST-ERADICATION: A REAL-LIFE EXPERIENCE

R. Curetti[1], D. Bossi[1], F. Bai[1], M. Chiamenti[2], G. Marchetti[1], A. De Bona[1], A. d'Arminio Monforte[1]

[1]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Italy, [2]Department of Diagnostics and Public Health, University of Verona, Gianbattista Rossi Hospital, Verona VR, Italy

Background: Few previous studies report clinical impact of HCV elimination, particularly in patients living with HIV. Aim of our study is to evaluate virologic and clinical outcome of DAA treated patients.
Material and methods: In our retrospective study we included all the patients consecutively treated for HCV infection with DAAs at our out-patients clinic (March 2015-August 2018). Trends of liver markers and stiffness (APRI, FIB-4, transient elastography (TE)) before and after therapy, prevalence of sustained virologic response (HCV-RNA undetectable at 12 weeks after end of therapy, SVR12), and adverse effects (AE) during DAAs were collected.
We followed up patients who achieved SVR12 until 31/01/2019 (or last visit available) reporting clinical events liver-related (HCC, ascites decompensation, hepatic encephalopathy, onset of esophageal varices) or not, like death for any cause, new diagnoses of cancer, diabetes, hypertension, dyslipidemia or sexually transmitted infections. Chi-square and Mann Whitney test were used for statistics. Survival analysis by Kaplan Meier curves was used to estimate time to clinical events.
Results: 193 HCV+ patients were included in the study, 135 (70%) co-infected with HIV (Tab 1).
187 patients (96,9%) achieved SVR12; the lowest rate of SVR12 was observed in patients with genotype 3 (86%) (Fig 1).
6 (3%) patients failed to achieve SVR12. Of these, 2 were non adherent to therapy, one relapsed, 2 were diagnosed with HCC and 1 developed a cholangiocarcinoma in an 8-months follow-up.
81 patients (42%) had >=1 AE (grade 1-2); AE were significantly associated with ribavirin use (RBV 61, 75% vs no RBV 20, 25%, p<0,0001). Most frequent AE were asthenia (15,5%), anemia (13,5%), gastric pain (8,8%), headache (7,33%), nausea (4,7%).
We observed a significative improvement in liver stiffness (measured by APRI, FIB-4 and TE), both in HCV+ and HIV/HCV+ subjects at SVR12 (Fig 2).
In a median follow up of 29.2 months (IC95% 26.4-32,1) we registered 39 clinical events among the 187 (20.8%) subjects reaching SVR12. The 6-month probability of clinical events was 10% (IC95% 5,3-15) without differences after stratification by cirrhosis (Fig 3). Ten events (5.3%) were liver-related while 29 not (15.5%) Only 1 event (diabetes mellitus) occurred in HCV mono-infected patient. Dyslipidemia and syphilis were the most frequent non-liver related events (occurring in 5.9 and 3.8% of patients) (Tab 2).
Conclusions: In our cohort DAAs were confirmed to be effective and safe both in HCV+ and HIV/HCV+ subjects. Few failures occurred, mainly with genotype 3 infections. Given the significant improvement in liver stiffness and the low probability of liver related clinical events after SVR12, we can assume that HCV eradication could have a positive impact on the evolution of HCV-related liver disease at least in a 2 years period. The new diagnoses of syphilis occurring after HCV eradication should alert on the possible risk of HCV reinfection.

HCV elimination

P 26 IS THE ELIMINATION OF HCV INFECTION FEASABLE IN PEOPLE WHO INJECT DRUGS IN A ROMAN SUBURB?

C. Taibi[1], I. Luzzitelli[1], U. Visco Comandini[1], R. Lionetti[1], M.G. De Palo[1], P. Carabini[2], L. Rapisarda[2], A.R. Garbuglia[1], G. D'Offizi[1] and HEPP group

[1]INMI Lazzaro Spallanzani IRCCS, Rome, [2]Ser.D. ASL RM D, Rome

Background: Nowadays, in developed countries the HCV transmission is mainly through shared needle during illicit drug injection. Retention in care of people who inject drugs (PWID) is generally poor, but projects aiming to improve and facilitate access to treatment have shown success. At the moment, no data about HCV prevalence is available in the Lazio Region. Our aim was to evaluate the prevalence of HCV-infection in a PWID population and among viremic patients (pts), to assess fibrosis and to establish a "cascade of care" leading to Direct Antiviral Agents (DAAs) treatment and to sustained virological response (SVR).
Material and methods: About 1000 pts PWID in charge to "Addiction Services" (SerD) in Rome, particularly in Ostia, will be recruited in the same place where opioid agonist treatment is delivered.After signing a written consent, PWID were enrolled and submitted to capillary HCV Quick test.In case of positive results, pts were sent to our Infectious Diseases Center to perform HCV-RNA test.DAAs regimen was offered to all pts resulted viremic. Those who agreed to start DAAs, underwent blood tests, fibroscan, hepato-splenic ultrasound (US) and clinical consultation.DAAs were dispensed every 28 days.Pt at risk of reinfection were retested with HCV-RNA every 6 months.
Results: Between March 2018 and March 2019, 169 PWID underwent to the HCV Quick test: the prevalence of HCV antibodies was 47,9% (81/169).Pts were mostly male (81,7%) with a median age of 46 years.Among HCV-Ab positive pts, 69,1% (56/81) were tested for HCV-RNA; 8 (9,9%) did not show-up for blood-test, and 17 pts are still waiting to do it. Out of 57 HCV-RNA test, 40 (71,4%) were quantifiable, while 16 (28,6%) resulted negative.In 29 out of 40 viremic pts it was performed a complete diagnostic and clinical assessment before starting treatment.In the remaining 11 pts, assessment is still ongoing.At baseline, the median HCVRNA level was 5,8 log.The most frequent HCV genotype was 1a (n= 17/29; 58,6%), followed by genotype 3 (n= 8/29; 27,6%).Mild fibrosis (F1-F2) was present in 13 (44,8%) pts, while advanced fibrosis in 16 (n.11 F3 e n.5 F4) (Table 1).Twenty pts achieved End-of treatment and all pts that concluded follow up obtained a SVR12.1 pt presented HCC and underwent to an hepatic resection.
Conclusions: The data available at this moment confirms an important reservoir of HCV infection and of pts with high risk of progressive liver failure.Furthermore, many pts had a known HCV positivity, but they had never performed specific hepatologic visit.The preliminary results, regarding epidemiology and SVR, confirmed the reported literature and in real life data.This study demonstrated the importance of a close collaboration between SerDs and the Specialized center of Infectious diseases in terms of reduction of HCV incidence into a PWID.An effort should be done in order to improve follow-up adherence in this patient who might also have an advanced fibrosis or cirrhosis, even HCC.

HCV elimination

P 27 STRATEGIES TO IMPROVING THE CASCADE OF CARE FOR HEPATITIS C VIRUS-INFECTED PEOPLE WHO INJECT DRUGS: THE EXPERIENCE OF A SINGLE CENTER

E. Ciraci[1], S. Semeraro[1], S. De Fazio[2], F. Dambra[3], M. D'Ancona[4], A. Gaspari[5], P. Gatti[1]

[1]UO Medicina Interna, Ospedale di Ostuni, ASL BR, [2]SERD Mesagne, ASL BR, [3]SERD Fasano, ASL BR, [4]SERD Francavilla, ASL BR, [5]SERD Ostuni, ASL BR

Background and aims: The availability of simple and tolerable direct actin antiviral (DAA) therapies for HCV infection with cure rates >95% explains the ambitious goal of WHO to eliminate HCV as a major public health threat by 2030. Despite people who inject drugs (PWID) represent a priority population, given the high prevalence and incidence of HCV infection, previous studies have shown low rates of diagnosis and treatment in this population. Our aim is to test the effect of a complex intervention in SerD (Italian acronym for Addiction Services) on testing for HCV, referral to hepatology services and start HCV treatment.

Materials and methods: A prospective observational study was carried out, from February 2018 to February 2019, in the hepatology service of the Ostuni Hospital with the collaboration of the SerD working in the ASL BR territory. The interventions comprised periodical educational meeting with delegates of SerD, an easy route for HCV-positive PWID to engagement with therapy, the application of strategies for implementations of adherence such as flexible clinic hours for receiving treatment, testing or other services, positive patient-provider relationships, clinical staff familiar with PWID vs general staff, for current PWID, clinic policies that did not insist on complete sobriety, incentives to peer counseling. The tournout of the intervention year was compared with a baseline year (2016).

Results: A positive HCV-RNA was confirmed in 24 (20 males, median age = 48 years old) of 33 anti-HCV positive PWID observed in the intervention year (72,7%). 67% of patients received an OST (opioid substitution treatment). All patients started an antiviral therapy with sofosbuvir/velpatasvir (6 pts) or with glecaprevir/pibrentasvir (18 pts). No drop out was observed and all of the 16 pts that completed the post-treatment follow up had a SVR12.

In the hepatology service, during the intervention year, the treatment of the PWID patients was the 36% of the total treatment versus a 11% of prescriptions in the 2016.

Conclusions: The introduction of a complex intervention in SerD allowed an increased engagement of HCV-positive PWID with the tests and with the treatments. As expected, the treatment adherence and the efficacy was high also in this hard to treat population.

HCV elimination

P 28 FIRST ITALIAN EXPERIENCE OF THE XPERT HCV VIRAL LOAD FINGER-STICK: A USEFUL STREET-TOOL FOR VULNERABLE POPULATION

E. Teti[1,2], V. Malagnino[1], C. Cerva[1], L. Foroghi[1], L. Coppola[1], M. Compagno[1], L. Campogiani[1], G. De Simone[1], I. Spalliera[1], L. Ferrari[1], C. Stingone[1], D. Masci[2], B. Coladarce[2], P. Sammarco[2], G. Rodoquino[2], E. Rossi[2], L. Sarmati[1], M. Barra[2], M. Andreoni[1]

[1]Infectious Diseases Clinic, Tor Vergata University, Rome, Italy, [2]Villa Maraini Foundation, Rome, Italy

Background and Aims: From 2018 – 2020, the focus is to find the millions of people living with viral hepatitis unaware. Of the 325 million people currently living with viral hepatitis C, 300 million are unaware they have the disease. Without finding those "Missing Millions" (often among the vulnerable groups such as People Who Use Drugs and homeless) that are yet to be diagnosed and linking them to care, all other efforts will only have marginal success. A major challenge, then, is ensuring the vulnerable patients who need treatment are identified in the simplest and quickest way.

Method: PWUD and homeless have been HCV screened on the street during two big events in two weeks of November 2018 in Rome: the second World Day of the Poor organized by the Vatican and the European Testing Week on the Street Unit of Villa Maraini Foundation within the Needle Exchange Program. OraQuick HCV Ab rapid test as first step evaluation and the Xpert HCV Viral Load Finger-Stick for a confirmation diagnosis in 60 minutes were used. Users, guided by the medical staff, made a questionnaire to assess personal information and risk behaviours. In case of positive tests, the Infectious Diseases Clinic of Policlinico Tor Vergata in Rome took subjects in charge.

Results: 276 subjects performed the HCV rapid test (79% male, median age 40 y), 39.8% was PWUD, 68.1% foreigner (27.2% from Asia, 20.3% from Africa, 12.7% from Eastern Europe), 75.4% unemployed, 73.4% completed only compulsory education, 5.8% graduated and nine illiterates were present. Most of the tested subjects never performed an HCV test (197/276). HCV seroprevalence in this population was 10.8% (30/276): 90% male, median age 41 y, 83.3% PWUD, 23/30 were Italian, 19/20 unemployed; 8/30 were already treated with Direct Acting Antivirals (DAAs). 13.3% had a positive Mantoux test and one of them received an HIV diagnosis at the same time. HCV RNA was detected in 9/30 (30%) patients and 3 of them started DAAs. No reinfections were detected.

Conclusion: The Xpert HCV Viral Load test can detect active infection from a finger-stick sample, which represents an advance over antibody-based tests that only indicate past or previous exposure. This proved to be a particularly useful test in a difficult context because of the tested population (PWUD and homeless) and setting (Street Unit): it is a useful and quick tool in these populations to control the reinfections and to find new diagnoses coming out the hospital setting.

HCV elimination

P 29 HEPATITIS C MANAGEMENT AND TREATMENT AMONG PEOPLE WHO INJECT DRUGS IN ITALY: AN EXPLORATORY PILOT SURVEY

E. Teti[1], S. Babudieri[2], M. Barra[3], A. Di Biagio[4], G. Parruti[5], R. Ranieri[6], T. Santantonio[8], G. Taliani[8], L. Sarmati[1], M. Galli[9], M. Andreoni[1], SIMIT (Società Italiana Malattie Infettive e Tropicali)

[1]Infectious Diseases Clinic, Tor Vergata University, Rome, Italy, [2]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Sassari, Sassari, Italy, [3]Villa Maraini Foundation, Rome, Italy, [4]Infectious Diseases, Policlinico San Martino Hospital, Genoa, Italy, [5]Infectious Diseases Unit, Pescara General Hospital, Pescara, Italy, [6]Penitentiary Infectious Diseases Unit, A.O. Santi Paolo e Carlo, University of Milan, Milan, Italy, [7]Infectious Diseases, University of Foggia, Foggia, Italy, [8]Hepatology Unit, Department of Clinical Medicine, Sapienza University of Rome, Rome, Italy, [9]Institute of Tropical and Infectious Diseases, L. Sacco Hospital, University of Milan, Milan, Italy

Background: People Who Inject Drugs (PWID) play a crucial role in the goal of eradicating hepatitis C (WHO's 2016 Viral Hepatitis Strategy) and despite the high efficacy and tolerability of Direct Acting Antivirals, many drug users have to be treated and there are many barriers that slow down the process. An exploratory pilot survey was conducted to determine service providers' current condition and the barriers experienced by PWID in accessing HCV treatment.

Methods: In December 2018, 9 purposively selected clinical centres engaged in the treatment of hepatitis C in PWID completed a 27-item online survey addressing the current treatment situation in PWID hepatitis C treatment, related barriers and linkage to care. HCV-related data and reported findings were extracted by responding centre.

Results: The survey mainly involved central-northern clinical centres (71.4%), with less than 4 prescribers (71.4%) despite they are currently treating around 500-1000 patients for Hepatitis C (>50% current or former PWID). In most cases, they have the possibility to carry out the necessary checks (100% blood sample, 85.7% fibroscan and 43% ultrasound) in few visits (85.7%) to deliver drugs in about one month (71.4%). They all agree on the need for fast-track for PWID and therefore they are all engaged in dedicated projects. The commitment to eradication is, in most cases, based on personal efforts and initiatives relating to each center, which despite the few prescribers, the lack of institutional support (85.7%) and the impossibility to use simplification scores since prescription and drug delivery portals (AIFA and regional) still require a lot of information. While the centres questioned express the need for a simplification of the bureaucratic processes, on the other they scrupulously follow PWID with a complete baseline staging and blood samples in the salient timing (baseline, end of treatment, SVR12), 42.8% of them even with more visits. 43% is available to the opening of prescription to general physician and doctors who work in services for PWID. For 57.4% of the centres, linkage to care remains the most problematic moment, to follow equally the lack of a correct epidemiological estimate and the implementation of the harm reduction policies. Finally, most of the centres don't find particular barriers related to PWID's features, but analysing them individually the main ones are: the difficult social background, the reinfection risk and the patient's poor motivation-Fig.1.

Conclusions: The needs emerged from this survey are: to work on PWID de-stigmatization, to simplify the prescription/drug delivery portals in order to be able to use scores, to increase PWID social assistance network and institutions' support in HCV eradication programs. This pilot project outlined interesting aspects for which it is possible to hypothesize the extension of the survey to a larger sample to obtain a current picture of the management and treatment among PWID in Italy.

HCV elimination

P 30 LATE RELAPSER AND REINFECTION IN HCV PATIENTS TREATED WITH DIRECT-ACTING ANTIVIRAL (DAA) DRUGS: REAL-LIFE DATA

C. Minosse[1], C. Taibi[1], I. Luzzitelli[1], R. Lionetti[1], E. Grilli[1], M. Zaccarelli[1], A.R. Garbuglia[2], M.R. Capobianchi[2], A. Antinori[1], G. D'Offizi[1]

[1]Infectious Disease – Clinical Department National Institute for Infectious Diseases, INMI Lazzaro Spallanzani IRCCS, Rome, [2]Virology Unit, National Institute for Infectious Diseases, INMI Lazzaro Spallanzani IRCCS, Rome

Background: The introduction of DAA therapy led to evaluate the possibility of HCV elimination. The success of this treatment overcome 95%, however the possibility of a reinfection or reactivation of HCV after SVR remain a challenge.The goal of this study was to assess the incidence of HCV reinfections after SVR in HIV-coinfected and HCV monoinfected patients.

Material and Methods: HCV RNA recurrence was defined as quantifiable HCV RNA following 24 weeks (wk) after SVR. The presence of HCV RNA was assessed using a quantitative HCV RNA assay (Abbott Real time v2.0, LOD 12IU/ml). Population-based HCV RNA sequencing was performed on the first available HCV RNA sample following HCV RNA recurrence. Genetic distances were estimated by Kimura two parameter model and phylogenetic reconstruction was performed using the maximum likelihood method based on Kimura two parameter model with a discrete gamma distribution and 500 replicates in the bootstrap resampling analysis using sequences of NS5B conserved region. To determine genetic relatedness between HCV strains, phylogenetic tree were built. Mean follow-up after SVR was 48 months.

Results: 1650 HCV chronic patients were given DAA therapy interferon free against HCV; 96% of them reached SVR. In 3 patients HCV RNA was detected after 24 wk from SVR. The first patient was an active PWID, HIV-HCV genotype (GT) 1b coinfected cirrhotic. He was treated with Sofosbuvir/Lepidasvir for 24 weeks. During the follow-up, at SVR12, he showed a reinfection with genotype 1a (T1), that he cleared spontaneously. After one year, he presented a second reinfection with a different strain genotype 1a (T2). The sequences corresponding to T1 and T2 segregated with a significant bootstrap in different clusters, and the genetic distance were 0,01555. The second patient presented a HCV chronic hepatitis GT1a, fibrosis F2 with a non-Hodgkin Lymphoma in remission. He was treated with Ombitasvir/paritaprevir/ritonavir + Dasabuvir and ribavirin for 12 weeks. He achieved SVR24, but he relapsed after one year with the same strain of genotype 1a with RAS (NS3: S174N, NS5A: Q30R, NS5B: S556G). The estimate of evolutionary divergence sequences disclosed a close genetic distance (0,00686 number of base substitutions per site) between the strain present at the T1 and that harboured prior of the DAA treatment. This fact was considered as a highly suggestive of later relapse of HCV infection and not a reinfection. He was retreated with Sofosbuvir/velpatasvir and ribavirin for 12 weeks with a SVR48. A third patient is a male patient with hepatitis C chronic GT1a with moderate fibrosis (F2) treated with glecaprevir/pibrentasvir for 12 weeks. At end of treatment he revealed a sexual exposure with HCV infected patient. At SVR12 he presents a low level of viremia and after 12 weeks he showed a reinfection with genotype 1b.

Conclusion: These findings has implications for determining the monitoring after SVR achievement.

HCV elimination

P 31 EFFICACY OF DIRECT ACTING ANTIVIRALS FOR TREATMENT OF CRONIC HEPATITIS IN HIV-HCV CO-INFECTED PATIENTS. THE REAL LIFE EXPERIENCE IN A COHORT OF SARDINIAN PATIENTS

F. Pes[1], I. Maida[2], S. Onali[1], E. Dore[2], C. Balestrieri[3], M. Casale[1], F. Ortu[4], P. Piano[4], L. Peddis[1], A. Cola[3], L. Barca[3], L. Chessa[1,3]

[1]Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy, [2]Department of Clinical and Experimental Medicine, University of Sassari, Sassari, Italy, [3]Liver Unit, Department of Internal Medicine, University Hospital of Cagliari, Cagliari, Italy, [4]Immunology Unit, Department of Internal Medicine, University Hospital of Cagliari, Cagliari, Italy

Background: Hepatitis C virus infection is the most important cause of liver failure and the second mortality cause of death in cART HIV treated patients. Liver fibrosis and evolution in cirrhosis is most rapidly in co-infected patients than in monoinfected patients. DAAs therapy changes HCV treatment history, even among co-infected patients. In this study we reported a real-life efficacy of DAAs treatment in a cohort of Sardinian co-infected patients. The primary end point was sustained virologic response (undectable HCV RNA) 12 weeks after the end of therapy (SVR12).

Materials and Methods: We recruited 128 co-infected HIV-HCV patients, who started DAA therapy at 2 liver unit from january 2016 to june 2018. We used different drug combination (from two to six months duration), depending on HCV genotype, cART and hepatic disease severity, in according with international guidelines.

Results: Male 96 (75,00%), median age 54,0 years, prevalent genotypes 1a 38 (29,69%) and 3 37 (28,90%). 53/128 (41,40%) were cirrhotic patients. The most important risk factor was injective drug use, in 106 patients (82,82%). Thirty-two (25,39%) were receveing methadone and all were on antiretroviral therapy. Forty (31,25%) patients had a history of interferon-based treatment. About 128 patients who started DAAs treatment, all completed the 12 weeks follow up. Of those 124 (96,87%) have HCV-RNA not detectable at the control after 12 weeks from the end of therapy. Only 1 (0,78%) was non responder at the treatment, and 3 (2,34%) relapse at the end of therapy. The most common side effects included itch (9,37%), headache (7,81%) and fatigue (6,25%). No one of our patients had a discountinuation of therapy for an adverse reaction.

Conclusions: Our data confirm that DAAs therapy is in general highly effective and well tolerated even among coinfected HIV-HCV patients, without or with advanced liver disease.

HCV elimination

P 32 EXTRA-HOSPITAL HCV COUNSELLING, TESTING AND TREATMENT AMONG PEOPLE WHO INJECT DRUGS AND HOMELESS: RESULTS FROM THE STOP HCV PROJECT IN BOLOGNA

G.M. Corbelli[1], B. Granozzi[2], L. Badia[2], P. Malosso[2], D. Testi[2], A. Toschi[2], V. Guardigni[2], G. Verucchi[2], P. Viale[2], S. Pieralli[3]

[1]Plus onlus, Bologna, [2]Policlinico S. Orsola-Malpighi – Dipartimento di Malattie infettive, Bologna, [3]Open Group, Bologna

Background: Feasibility and successfulness of treatment of hepatitis C (HCV) in people who inject drugs (PWID) and homeless (HL) has been debated. Several studies suggest that HCV treatment programs can be successful in these groups, but few data are available for specific Italian populations. The aim of this project is to demonstrate that correct counselling and treatment with Direct Antiviral Agents (DAAs) in an extra-hospital setting can help eradication of HCV infection in these populations.

Material and Methods: Stop HCV is a pilot project for counselling, rapid screening and treatment for HCV with DAAs outside of the hospital conducted by Open Group in collaboration with Plus and the S.Orsola-Malpighi Hospital in Bologna, made possible through unrestricted grants from AbbVie and Gilead. Since February 2018, saliva HCV test (OraQuick® Rapid HCV Antibody by OraSure Technologies) was offered alongside peer-counselling on HCV infection risk and prevention by Open Group volunteers in services where PWID and HL people gather (shelters, services for PWIDs and on the street) in Bologna. In those with confirmed HCV infection, transient elastography (Fibroscan®) and liver echography were performed the same day at the Open Group premises and HCV treatment initiation in 2-3 weeks was proposed. They also received counselling on HCV treatment and re-infection risk. HCV treatment was monitored outside of the hospital.

Results: Until 15 March 2019, 500 people were tested for HCV in shelters (43%), streets (33%) and services (25%); two thirds were male, median age 34 years (range 18-71), 66% were Italian, 28% extra-EU. 62% lived in shelters, 13% on the street and only 25% had a home. 65% was unemployed. 88% had a health insurance card, 58% a co-payment exemption. 27 people had a reactive rapid HCV test result, all of them had an HCV RNA test and 17 had it positive: 15 (88%) were male, median age 41, 7 (41%) were active drug users, 9 (53%) on opioid substitution therapy (OST), 9 (53%) on alcohol abuse, 7 (41%) had a psychiatric co-morbidity, 13 (76%) were unemployed. Median liver stiffness was 6.5 (range 3.8-19.8), 9 (52%) had Metavir F1, two had cirrhosis. Eleven (65%) had genotype 1a. Between January and March 2019, 11 patients started treatment with Glecaprevir/Pibrentasvir for 8 weeks and 1 patient with cirrhosis started Sofosbuvir/Velpatasvir for 12 weeks. Three of them had HIV/HCV coinfection. They have stopped HIV therapy but, with a proper counselling, they resumed it. Baseline HCV viremia was available for 11 pts (median 5.75 log; range 3,71-6.36 log); adherence to HCV treatment was 100%.

Conclusions: Feasibility, acceptability and efficacy of HCV counselling, testing and treatment outside of the hospital among PWID and HL seems high in our cohort. These results support the continuation of the project and re-linkage to care for those lost to follow up.

HCV elimination

P 33 FACTORS LIMITING ACCESS TO HCV TREATMENT IN A CONVENTIONAL HOSPITAL SETTING: FOCUS ON VULNERABLE POPULATIONS

B. Tazza, L. Badia, L. Bussini, G. Fornaro, B. Granozzi, V. Guardigni, G. Verucchi, P. Viale

Infectious Disease Unit, Department of Medical and Surgical Sciences, S. Orsola-Malpighi Hospital, University of Bologna

Background: Since the introduction of direct-acting antivirals (DAAs) into clinical practice, there has been a revolution in treating hepatitis C; with a Sustained Virological Response (SVR) of more than 97%, eradication of HCV is theoretically possible. Anyway, a possible obstacle to achievement of this goal could be the retention in care of vulnerable populations.
Aim of this study was to assess risk factors associated with not initiating DAAs in a cohort of HCV-positive patients followed by a tertiary level outpatient clinic.
Methods: All HCV infected adults who attended at least one visit at our Unit from May 2017 (date of expansion of DAAs access to all patients with chronic hepatitis C) to August 2018, and who at that time were viremic and eligible for a first course of DAAs were included in this analysis
We excluded those who at the beginning of the observation period had already started DAAs and those who were detained or pregnant during the period of observation.
We collected data regarding HIV status, past or current drug use, past or current alcohol abuse, gender, nationality, psychiatric comorbidities, grade of fibrosis and planned time from the first visit to DAAs start.
Binary logistic regression was used to analyse the correlation between baseline characteristics and actual access to DAAs treatment in the observation period.
Results: 547 patients met the inclusion criteria (62,3% males, median age 52 , range 18-90). Among these, 41,1% were HIV positive, 46,6% had a history of drug use, 6,9% currently used drugs, 15,9% had a history of alcohol abuse, 6,9% current abused alcohol and 17,2% had psychiatric comorbidity.
448 patients (81.9%) started DAAs in the period of observation, after a median of 175 days (range 6-593) .
At univariate analysis, we observed that HIV status was positively associated with initiation of DAAs (p=0,017). Past and current drug use, psychiatric comorbidity, longer waiting time for treatment initiation were all negatively correlated with DAAs initiation (p=0,003; p<0,001; p=0,018; p =0,001 respectively). There was no significant association between DAAs initiation and past or current alcohol abuse, gender, nationality and grade of fibrosis.
In multivariate analysis, all variables that had a negative correlation with the outcome of starting DAAs remained independently associated: past drug use (p=0,031) current drug use (p=0,001) psychiatric comorbidity (p=0,045) and longer waiting times before initiating DAAs (p<0,001).
Conclusions: Not surprisingly, delaying the appointment for treatment initiation, leads to a higher likelihood of not starting treatment. Our data also confirm that patients with psychiatric comorbidity, ongoing or history of drug use are more prone to miss the chance to initiate DAAs treatment planned with a conventional approach.
Therefore, strategies are needed, in order to offer an expedited DAAs initiation and to enhance linkage to and retention in care in these populations.

HCV elimination

P 34 1-YEAR EXPERIENCE TREATING HEPATITIS C VIRUS IN TURIN

T. Lupia, L. Boglione, D. Piccioni, G. Cinnirella, G. Cariti, G. Di Perri

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

Background: The history of HCV infection therapy radically changed in the last decade, with the introduction of the first-generation direct acting antivirals (DAAs). Despite the excellent efficacy of DAAs, a minority of patients (4–5%) still fail to eradicate HCV, mainly related to poor adherence but also to relapse or viral breakthrough. The main causes of a failure of DAAs are the presence of advanced liver disease, suboptimal treatment and NS5A mutations

Material and methods: Adult HCV-RNA positive patients, admitted to Infectious Disease Unit in Turin from 1 January 2018 to 1 January 2019, were analysed to assess the efficacy of several IFN-free retreatment strategies chosen. Patients with major DDIs according to Hepatitis Drug Interactions Checker (University of Liverpool) were excluded. Demographic, immune-virological and treatment data were collected. HCV RNA was measured through real-time PCR methods (Taqman method, range of quantification 15 and 107 UI/mL). Mutations were ruled out in patients failed to a prior DAAs regimen. Screening for Human Immunedeficiency Virus (HIV) and Hepatitis B Virus (HBV) were measured by immune-enzymatic methods. Liver stiffness was evaluated using transient elastography (Fibroscan). Datas are expressed as median (interquartile ranges).

Results: 404 adult patients were included. In most part males 273 (67,6%) [51 years old, plasma HCV RNA 1.730.162 (466.452-9.740.000) UI/mL] while female were 131 (32,4%) [48 years old, plasma HCV RNA 1.730.162 (123.904-2.431.807) UI/mL]. Metavir was distributed as follows: F1 (122, 30,2%), F2 (83, 20,5%), F4 (F4, 19,3%), F0 (62, 15,3%), F3 (58, 14,3%). Median liver stiffness was 9.4 (3,3-75) kPa. Experienced subjects to IFN-based regimens were 83 (20.5%) while adults previously treated with a DAAs regimen were 4 (1%) [3 Sofosbuvir/Velpatasvir 12 weeks (no RBV), 1 Glecaprevir/Pibrentasvir 8 wks). Adults were all HIV-negative and HBsAg/HBV DNA was positive in 2 patients, that have not required antiviral prophylaxis/treatment for HBV co-infection. Anti-HBc serology alone was positive in 34 patients (8%). 404 (100%) had have a first line treatment according to their immune-virological and clinical features and have started DAAs regimens following HCV EASL guidelines: 159 Sofosbuvir/velpatasvir 12 wks (3% with RBV), 204 Glecaprevir/Pibrentasvir 8wks, 5 Glecaprevir/Pibrentasvir 12 wks, 34 Elbasvir/Grazoprevir 12 wks (without RBV). 2 patients died (GI bleeding and after myocardial necrosis, respectively). 1 patients decide to stop DAAs for GI intolerance. SVR 12 was by 401 patients (99%).Four patients underwent to a second-line treatment with Sofosbuvir/Velpatasvir/Voxilaprevir for 12 weeks (without RBV) and data were reported in table 1

Conclusions: 1% of patients did not reported SVR after first-line treatment. Nowadays patients with difficult to treat genotype 3, higher fibrosis, previous IFN-failure and development of Y93H mutation after prior-DAA need new strategies to reach HCV elimination

Hepatitis epidemiology

P 35 CHARACTERIZATION OF TRANSMISSION CLUSTERS IN CHRONIC HCV INFECTED INDIVIDUALS IN ITALY

*L. Fabeni[1], M. Aragri[1], E. Teti[2], C. Masetti[3], V. C. Di Maio[1], L. Foroghi[2], S. Barbaliscia[1], A. Bertoli[1], R. Salpini[1], Spalliera[2], K. Yu La Rosa[1], V. Cento[4], L. Ferrari[2], S. Francioso[3], G. Fiorentino[5], P. Begini[6], V. Pace Palitti[7], A. Pieri[8], F. Sozio[8], P. Paba[9], R. Marocco[10], B. Bruzzone[11], S. Paolucci[12]; E. Degasperi[13], V. Calvaruso[14], I. Maida[15], C. Furlan[16], M. Marignani[6], G. Taliani[16], V. Borghi[17], W. Gennari[18], S. Landonio[19], S. Babudieri[15], C.F. Magni[19], M. Lichtner[10], C. Pasquazzi[5], G. Parruti[8], L. Sarmati[2], A. Craxi[14], M. Angelico[3], C. F. Perno[20], M. Andreoni[2], F. Ceccherini-Silberstein[1]**

[1]Experimental Medicine and Surgery, University of Rome "Tor Vergata", Rome, Italy, [2]Infectious Diseases Unit, University Hospital of Rome "Tor Vergata", Rome, Italy, [3]Hepatology Unit, University Hospital of Rome "Tor Vergata", Rome, Italy, [4]Residency program in Microbiology and Virology, Università degli Studi di Milano. Milan, Italy, [5]Infectious Diseases Unit, Sant'Andrea Hospital – "Sapienza" University, Rome, Italy, [6]Digestive and Liver Diseases Department, Sant'Andrea Hospital, Sapienza University, Rome, Italy, [7]Hepatology Unit, Pescara General Hospital, Pescara, Italy, [8]Infectious Diseases Unit, Pescara General Hospital, Pescara, Italy, [9]Virology Unit, Policlinico Fondazione Tor Vergata, Rome, Italy, [10]Infectious Diseases Unit, Sapienza University, Polo Pontino, Latina, Italy, [11]Hygiene Unit, IRCCS AOU San Martino-IST, Genoa, Italy, [12]Molecular Virology Unit, Microbiology and Virology Department, IRCCS Policlinic Foundation San Matteo, Pavia, Italy, [13]"A.M. e A. Migliavacca", Center for Liver Diseases, Division of Gastroenterology and Hepatology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy, [14]Gastroenterology, "P. Giaccone" University Hospital, Palermo, Italy, [15]Medical, Surgical and Experimental Sciences, University of Sassari, Sassari , Italy, [16]Department of Tropical and Infectious Diseases, Policlinico Umberto I, Rome, Italy, [17]Department of Infectious Diseases, University of Modena, Modena, Italy, [18]Microbiology and Virology Unit, University Hospital Policlinico di Modena, Modena, Italy, [19]Divion of Infectious Diseases, ASST Fatebenefratelli Sacco, Milan, Italy, [20]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy, *On behalf of HCV Virology Italian Resistance Network (Foundation Vironet C)

Background: We evaluated the characteristics of hepatitis C virus transmission clusters between patients (pts) with chronic HCV infection followed in several clinical centers in Italy.

Methods: Sanger sequencing of NS3±NS5A±NS5B was performed by home-made protocols from plasma samples of 887 HCV infected pts. Phylogenetic analysis was performed on NS5A sequences. We defined transmission "clusters" (TC) and "pairs" (TP) as clades with n≥3 and n=2 sequences, respectively. Uni-multivariable logistic regression was used to define factors associated with TC/TP.

Results: Overall, most pts were males (74.7%), with a median (IQR) age of 55 (49-61). Drug use (DU) was the most prevalent risk factor (RF) (N=615, 69.3%), mainly in pts with genotype (GT) 1a (47.2%), and GT3a (34.3%). GT1a was the most prevalent (39.9%), followed by 3a (25.9%), 1b (20.0%), 4d (8.9%), 2a (4.2%), and others (1.1%). 12.3% was HIV co-infected and 33.7% was cirrhotic. Resistance to any drug class was 35.5% mainly due to NS3 Q80K (25.7%, mainly in GT1a), and NS5A Y93H (18.7%, mainly in GT1b, 3a). Pts involved in TC/TP were 70(7.9%), composed by 23TP (79.3%) and 6TC (20.7%) (3-5 sequences). 6TC and 15TP were composed only by DUs, mainly with GT1a(62.1%), 1b(17.2%), 3a(13.8%). Other 6TP had ≥1 DU pts involved (4GT1a and 2GT1b). The last 2TP were composed by pts with blood transfusion and parenteral RF (1b and 3aGTs). Interestingly, 26TP/TC involved pts from central Italy, 1TP from central-south Italy, 1 from central-north Italy, and 1 from north Italy. Pts in TP/TC in comparison to those out of TC/TP were younger [48(35 -56) vs 56(50-61), p<0.001], with GT1a (60.0% vs 38.2%, p=0.001), and HIV co-infected (20.0% vs 11.6%, p=0.04). Regarding RF, DUs and parenteral were both positively associated to be in TP/TC (85.7% vs 67.9%, p=0.002; 5.7% vs 1.8%, p=0.03, respectively).

Resistance to any drug class in TC/TP was 32.9% (10TP and 1TC). Within TPs, 5 involved both pts with the same resistance while other 5 showed resistance only in one pt out of the pair. The TC, composed by 5 pts, DAAs naïve, showed NS3 [Y56F (100%)], NS5A [L31M (100%)], and NS5B [S556G (20.0%)] resistance. Multivariable analysis showed that younger age, GT1a, and parenteral RF were all associated with TC/TP [OR (95% CI): 0.95(0.93-0.97) p<0.001; 1.91(1.12-3.28) p=0.02, 17.2(3.00-98.3) p=0.001, respectively], while DU was positively associated to TC/TP with a trend toward significance [2.99(0.90-10.0) p=0.07].

Conclusions: Even if our findings show an overall low circulation of HCV TC/TP between HCV chronic infected pts in Italy, we identified factors such as younger age, parenteral and DU RF, and GT1a as mostly associated with TC/TP. The identification of resistance in TC/TP may also alert the potential risk of resistance transmission. Further studies are needed to better understand the complex dynamics and phylogenetic relationship between HCV infected pts, particularly involving also sequences from acute infection.

Hepatitis epidemiology

P 36 HEPATITIS E SURVEILLANCE IN LIGURIA: MOLECULAR CHARACTERIZATION OF STRAINS DETECTED FROM 2017 TO 2019

G. Barisione[1], P. Canepa[1], G. Guarona[1], C. Arcuri[1], A. Orsi[1,2], G. Icardi[1,2], B. Bruzzone[2]

[1]Department of Health Sciences (DiSSal), University of Genoa, Italy, [2]Hygiene Unit, Polyclinic Hospital San Martino, Genoa, Italy

Background: HEV virus is probably the major cause of acute hepatitis in adults worldwide, infection is transmitted by the oro-faecal route and in developing countries is related to contaminated water consumption, with genotypes 1 and 2 the more frequently identified. In Europe, where an increasing number of cases was observed, HEV infection is considered a foodborne zoonosis transmitted by contaminated pork meat and is usually associated with genotype 3. In immunocompromised patients HEV genotype 3 infection is an emerging cause of acute and chronic hepatitis possibly associated with cirrhosis. In this study we describe distribution of HEV infection in Liguria where an ongoing laboratory surveillance was started from 2017.

Materials and Methods: A total of 370 stool and serum samples were collected from 291 patients with specific clinical symptoms between January 2017 and February 2019. HEV-RNA was extracted from any samples using MagCore HF16 Automated Nucleic Acid Extractor (RBC Bioscience Corp). Viral RNA was detected by the FTD Hepatitis E RNA (Fast track Diagnostics). Samples tested positive for HEV were analyzed to determine the degree of genetic variability by the amplification of ORF1 genomic regions. Subsequently, cDNA of the genomic target was purified and sequenced by 3130-Avant Genetic Analyzer (Life Technologies, NY, USA). Construction of phylogenetic trees was carried out by Mega Package, version 7.0 (Fig.1A). Serum samples fromHEV RNA positive patients were screened to verify the presence of HEV IgM and IgG specific antibodies by ELISA (HEV-Ab ULTRA Dia.Pro - Diagnostic Bioprobes s.r.l).

Results: HEV-RNA was detected in 10/291 (3,4%) patients, and anti HEV IgM and IgG ELISA assay gave positive results in 8/10 patients. Interestingly, two HEV RNA positive serum samples from immunocompromised patients resulted negative for IgG and IgM at the beginning of infection, although HEV-RNA remains positive in serum for several months. Seven viruses belonged to subtype 3c one to 3f and one to subtype 3b; a genotype 1a strain was found in a patient returning from endemic area. Molecular analysis of ORF1 region revealed the circulation of viral strains related to those isolated from swine and humans across European countries. One epidemic cluster of patients with household contacts infected by the same variant was identified (Fig.1). Demographics characteristics of HEV positive patients were reported in Table.1.

Discussion: Our data suggest an autochthonous circulation of HEV strains belonging to genotype 3, with a high prevalence of sub-genotype 3c, the most frequently detected in European countries. Phylogenetic analysis revealed as the majority of HEV confirmed cases were sporadic and homologues to those detected in Germany, France and the Netherlands. Due to the severity of HEV infection in immunocompromised patients, appear to be important a prompt, sensitive and accurate diagnosis to prevent the persistence and the relapse of infection.

Hepatitis epidemiology

P 37 EPIDEMIOLOGY OF HCV IN MAIN PRISON INSTITUTION IN FLORENCE, TUSCANY

A. Gabbuti, F.M. Fusco, P. Pierotti, E. Salomoni, P. Blanc

SOC Malattie Infettive 1, Osp. S. Maria Annunziata, USL Toscana Centro, Florence

Background: The availability of direct antiviral drugs (DAAs) has made it possible to implement strategies to reduce HCV infection, with the ultimate goal to eradicate the infection. Prevalence of HCV varies in different populations, based on at-risk behaviours. Prisoners is a well-recognized at-risk population, for the presence of various risk factors: frequent injecting drug use (IDU), origin from highly endemic countries, high-risk sexual practices, tattoos.

In order to estimate the current HCV burden within the main prison institution in Florence, Tuscany, we describe epidemiological data of HCV+ patients transited in the correctional facility "Nuovo Complesso Penitenziario Sollicciano" (NCP)

Material and methods: The NCP is a male and female medium security prison and jail, for remand and sentenced prisoners. Since 2010, within the organization of the internal Health Service, the Infectious Diseases Services has been constantly implemented. An entry screening panel for HAV, HBV, HCV, HIV, LUE is offered to all prisoners. We retrospectively collected data about prisoners who underwent to screening in the period from January 1, 2017 to September 15, 2018.

Results: In the study period, 2427 prisoners transited: 86,4% were male, 34% were from Africa, 32,3% from Italy, 12,8% from no-EU Europe, 11,4% from EU-Europe, 5% from Americas, 4,6% from Asia

A total of 295 prisoners (12.15%) resulted HCV-Ab+, of them 78 (26.4%) prisoners resulted HCV-rna<15; 186 (63.05%) HCV-rna>15; data is not available for the remaining 31 because of refusal of screening, transfer to another institute, release. Out of the 78 prisoners resulted HCV-rna<15, 54 (69%) were naïve to HCV therapy, 14 (18%) eradicated the infection after IFN-based treatment, 10 (13%) recently eradicated HCV after DAA therapy. Out of the 186 HCV-rna positive prisoners, 124 (66,7%) were naïve to HCV therapy, 60 (32,3%) were IFN-experienced, and 2 (1,1%) were re-infections in DAA-experienced persons. Among those HCV-rna positive, prevalent risk was IDU (72,6%); psychiatric patients were 7,9%. Genotypes are available for 203 prisoners, from anamnestic data or recent laboratory determination: genotype 1 is the most diffused (56,6% of patients - 1a 41,9%; 1b 10,3%, 1 with no further determination 3,9%), followed by genotypes 3, 4 and 2, present in 35%, 5,4% and 3%, respectively. In 31 patients, genotypes were not available for refusal, transfer or release. Fifteen HIV/HCV, 1 HBV/HCV, and 1 HIV/HBV/HCV co-infections were detected.

Conclusions: These data analyse the current magnitude of this disease in a special setting such as prison. Even in the DAA era, most of HCV-infected prisoners is viraemic, and need for a treatment. These data may contribute to design improvements in treatment strategies, and suggest that prison is an important location to detect, address and treat HCV infection in people who may be underserved when in freedom, for their difficulties to access into community treatment pathways

Hepatitis epidemiology

P 38 HEPATITIS C VIRUS GENOTYPE DISTRIBUTION PATTERN ACCORDING TO AGE IN ITALIAN AND IN NON-ITALIAN PATIENTS IN THE 2016-2018 PERIOD

M. Basso[1], D. Zago[1], I Pozzetto[2], M. Pacenti[3], G. Brancaccio[1], S. Ragolia[1], G. Palù[1], S.G. Parisi[1]

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

Background: Determination of the infecting HCV genotype is important for the therapeutic approach despite the availability of pan-genotypic drugs: clinical trials reported small differences in the SVR rates among genotypes. The aim of this study was to describe an update description of the HCV genotype (gen) distribution by age in Italians (ITs) and nonItalians (nonITs) patients tested from January 2016 to December 2018 in the Microbiology and Virology Unit of the Padova University Hospital.

Material and methods: All patients who had HCV gen testing requested from 01/01/16 to 31/12/18 were included in the study. Age classes were 4: less than 18 years, 18-39 years, 40-64 years, ≥65 years. When a patient had more than one test available, only the first one was included in the statistical analysis. HCV gen was determined with INNOLipa assay and with multiplex real-time PCR methods Mann-Whitney test, Chi-square test and Fisher exact test were applied as appropriate.

Results: 2390 subjects (2177 ITs and 213 nonITs) were typed: overall ITs were older than nonITs (median age 55 years, IQR 48-67 years vs 47 years IQR 36-57 years, IQR p<0.0001) and median age values were comparable in ITs (54 years in 2016 and 2018, 55 years in 2017) and nonITs (47 years in 2016, 2017 and 2018) Eleven patients (0.5% of the study population) aged <18 years: 5 patients were non-Italian, 9 subjects had gen 1 (Fig 1). Patients aged 18-39 years were 265 (11.1% of the study population): gen 1 is the more frequently detected in ITs and nonITs and no significant difference between ITs and nonITs in gen frequency was found (Fig 2). In patients aged 40-64 years (1464 pts, 61.3%) gen 1 is more frequent in nonITs, conversely gen 2 and gen 4 are more frequent in ITs (Fig 3). Gen 4 is the more detected in nonITs aged more than 65 years (647 pts, 27.1%): of note 28.1% of ITs were older than 80. Among ITs, gen 1, gen 3 and gen 4 are more frequently detected in pts aged 18-39 and 40-64 than in subjects older than 65 and gen 2 infection frequency increased parallel to age. In nonITs patients no significant difference in gen 1, gen 3 and gen 4 frequency between the 3 age groups was observed and pts aged more 65 years had a higher percentage of gen 2 infection with respect to younger pts. Gen 1b proportion increased significantly accordingly to patients age in ITs: 26.8% of gen 1 in subjects aged 18-39 years, 40.2% in patients aged 40-64 years and 95.8% in subjects ≥ 65 years (chi square for trend p<0.0001).

Conclusions: Both in ITs and in nonITs gen 3 is the only one that has a comparable frequency in patients older than 18 and gen 2 prevalence increased with age. This updated analysis confirmed that age class 40-64 included the highest number of ITs, as reported in previous surveys: possibly the burden of HCV disease is greater than expected.

Hepatitis epidemiology

P 39 HBV AND HDV INFECTION IN IMMIGRANTS LIVING IN SOUTH ITALY: EPIDEMIOLOGICAL AND VIROLOGICAL CHARACTERISTICS

M. Pisaturo[2,6], L. Onorato[2], C. Sagnelli[2,4], L. Alessio[1,4], C. Monari[1], L. Gualdieri[5], C. Minichini[2], G. Di Caprio[1], M. Starace[2], M. Caroprese[1], L. Occhiello[1], G. Scotto[6], M. Macera[2], E. Sagnelli[2], N. Coppola[1,2]

[1]UOC di Malattie Infetttive, AORN Sant'Anna e San Sebastiano, Caserta, [2]Sezione di Malattie Infettive, Dipartimento di Salute Mentale e Medicina Pubblica, Università della Campania Luigi Vanvitelli, Napoli, [3]Centro di Accoglienza "La tenda di Abramo", Caserta, [4]Centro Suore Missionarie della Carità, Napoli, [5]Centro per la Tutela della Salute degli Immigrati, Napoli, [6]Centro sociale ex canapificio Caserta, 7. UOC di Malattie Infettive, Foggia

Background: Over the last few decades in several European countries, there has been a progressive increase in migration flows from countries with a high prevalence of HBV, in particular Asia and Sub-Saharan Africa. However, in Italy the epidemiological data relating to HBV and HDV infection in the migrant population are scanty and fragmented. The objective of our study was to investigate the demographic and virological characteristics of HBV and HDV infection in a cohort of immigrants living in Southern Italy.

Methods: Between January 2012 and december 2018 we offered a screening for HBV to all the immigrants attending to one of the 5 first-level centers, 2 in Naples, 2 in Caserta and 1 in Foggia included in the study. Data for demographic characteristics, socioeconomic status and risk factors for acquisition of HBV infection were collected for all enrolled patients. All HBsAg positive subjects were screened for HDV. Serum HBV-DNA levels were determined by real-time PCR and the HBV genotype was evaluated in viremic subjects. For all HDV positive subjects was performed HDV RNA by real-time PCR.

Results: 3184 subjects were screened; the 243 (7.6%) HBsAg positive subjects had a median age of 26 (range 15-55) years and 277 (94%) were male; 214 (88%) came from Sub-Sahariana Africa, 3 (1.2%) from North Africa, 17 (7%) from Eastern Europe, 8 (3.2%) from Indo- Pakistan area, one from South America (table 1); 8 of 243 subjects (3.2%) were positive for HDVAb. Table 2 shows the demographic and serological characteristics of the 243 HBsAg positive patients enrolled and stratified according to the serum status for HDV.

By stratifying patients according to HDV serology we found that the HDVAb negative subjects lived in Italy for a longer period (p = 0.001) compared to HDVAb positive patients. At multivariate analysis by logistic regression (table 3), no variables independently associated with HDV Ab positivity were identified. We found no differences between HBV-DNA levels in the two groups. The HBV genotype was available for 90 samples in the group of HDV Ab negative patients; genotype A was present in 17% of cases, C in 3%, D in 12% and E in 69%. HBV genotype was not avaible for HDV Ab positive group. HDV-RNA was performed for all HDV Ab positive patients but only one patients (12.5%) was found HDV-RNA positive.

None of the patients enrolled was aware of their HBV or HDV serostatus

Conclusions: In this study we found a high prevalence of HBV and HDV in a cohort of immigrants living in our geographical area. This data suggest the need to adopt a universal screening and vaccination strategy for HBV in this vulnerable category.

Hepatitis epidemiology

P 40 AN ESTIMATION OF THE PREVALENCE OF OCCULT HBV INFECTION IN WESTERN COUNTRIES: A META-ANALYSIS

A. Russo, M. Pisaturo, L. Onorato, P. Chiodini, N. Coppola

Department of Mental Health and Public Medicine – Infectious Diseases Unit. University of Campania Luigi Vanvitelli

Background: Occult HBV infection (OBI) is defined as the presence of HBV-DNA in the liver of HBsAg negative subjects with serum HBV-DNA <200 copies UI/mL (Taormina criteria). In the literature there are no data on the prevalence of occult HBV infection in the Western World. The aim of this meta-analysis is to evaluate the prevalence of OBI in Western countries.

Methods: A systematic review and meta-analysis was conducted using MEDLINE, Google Scholar and the Cochrane Library. All studies included had to fulfill the following inclusion criteria: (a) they investigated the prevalence of OBI (HBV DNA in liver tissue in HBsAg-negative subjects), (b) were carried out in western countries; (c) were available as a full text manuscript, (d) written in English, (e) published from January 1993 up to December 2018. The exclusion criteria were: (a) meta-analyses, letters, reviews, meeting abstracts, or editorial comments; (b) studies investigating HBsAg-positive patients; (c) those investigating OBI outside Western countries; (d) to avoid small sample bias in the random effects model, those enrolling less than 5 subjects.

Findings: Thirty-four studies, from a total of 7376, met the inclusion criteria, allowing a meta-analysis on 2,729 patients. The overall prevalence of OBI was 34% (95% CI=26-42%), 28% (CI 95%: 12-48%) in 329 subjects without chronic liver disease and 35% (95% CI 26-44%) in 2,400 patients with chronic liver disease. The prevalence of OBI was 51% (95% CI 40-62%) in the 823 anti-HBc-positive subjects, and 19% (95% CI 10-30%) in the 1,041 antiHBc-negative subjects. Evaluating the data from 17 studies, the prevalence of OBI was higher in the 641 anti-HBc-positive subjects than in the 1,041 anti-HBc-negative (prevalence ratio=2.29; 95% CI=1.61 -3.26, p<0.001).

Conclusions: Data of our meta-analysis showed a prevalence of OBI of 34% in paper published in Western Countries. The OBI prevalence was higher in patients with anti-HBc positive (51%) compared to patients with negative anti-HBc (19%), with total prevalence ratio of 2.29.

In conclusion according to our data, in HBsAg-negative subjects the prevalence of OBI was high and was associated with anti-HBc positivity, however the limits are given by the number of subjects enrolled, by the type of study and by the different molecular biology techniques used in the works.

Hepatitis epidemiology

P 41 LOW NUMBER OF HEV CASES IN HIV-1 INFECTED PATIENTS IN A ROMAN HOSPITAL: THE SEROPREVALENCE WAS ASSOCIATED WITH OTHER VIRAL HEPATITIS COINFECTION HISTORY

B. Yagai[1], C. Cerva[2], V. Malagnino[2], M. Ciotti[3], L. Piermatteo[1], D. Armenia[1,4], A. Giovinazzo[1], C. Stingone[2], T. Guenci[3], L. Foroghi[2], P.P. Paba[3], A. Bertoli[1], E. Teti[2], V. Svicher[1], L. Sarmati[2], M.M. Santoro[1], S. Grelli[1,3], M. Andreoni[2], F. Ceccherini-Silberstein[1]

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Infectious Diseases, University Hospital of Rome Tor Vergata, Rome, Italy, [3]Virology Unit, University Hospital of Rome Tor Vergata, Rome, Italy, [4]UniCamillus, Saint Camillus International University of Health Sciences, Rome, Italy

Background: Hepatitis E (HEV) infection is a public health issue, mainly in immunocompromised people. Few clinical data are published about HEV-infection in patients living with HIV/AIDS in Italy.
Materials & Methods: Within a Roman-hospital, a prospective enrolment of HIV-1 infected patients for studying HEV-seroprevalence is on-going. Sera are tested for HEV-IgG/IgM and HEV-RNA by real-time PCR.
Results: Up to date, we enrolled 197 HIV-1 infected individuals and analyzed 152 with complete patient's/clinical information and HEV-serological and virological results. The median (IQR) age of the analysed population was 46 (39-55) years; 73.7% were male and 82.9% were Italians; the most frequent HIV risk-factor was heterosexual (48.0%), followed by men-having-sex-with-men (38.8%), and drug abusing (10.5%). The prevalence of other viral-hepatitis was: anti-HAV (52/90, 57.8%), anti-HCV (20/134, 14.9%), HCV-RNA+ (4.5%), HBcAb (48/139, 34.5%), HBsAg+ (3.5%), and anti-HDV (0.7%).
Six out of 152 patients (3.9%) were HEV-IgG+, none of them showed HEV-IgM+ and HEV-RNA+. Of these, 83.3% were Italians. HEV-IgG+ patients tended to be older than those HEV-IgG- (56[49-58] vs. 45 [38-54] years, p=0.124) and a higher proportion of them were drug-abuser (anti-HEV+ vs. anti-HEV-: 33.3% vs 9.7%, P=0.121). Among 83 patients with complete viral hepatitis serology markers, all 4 HEV+ patients had a history of other viral hepatitis (all HBcAb+ and anti-HAV). In particular, HEV+ patients showed a significantly higher proportion of HBcAb+ (4/4, 100%) compared to HEV- (25/79, 31.6%, p=0.013). Moreover, in HEV+ patients a higher proportion of HBsAg+ were observed (HEV+ vs HEV-: 1/4, 25.0% vs. 2/79, 2.5%, p=0.139). Concerning previous HDV exposure, HEV+ patients showed a significantly higher proportion of anti-HDV+ (1/4, 25.0%) compared to those HEV- (0/79, 0%, p=0.048). Finally, even though not reaching statistical significance, 4/4 HEV-IgG+ were anti-HAV+ (100%) vs 41/79 of HEV-IgG- (51.9%, p=0.121) and HEV+ showed also a higher proportion of anti-HCV+ (1/4, 25.0%) compared to HEV-IgG- (7/79, 8.9%, p=0.339).
Conclusions: In this preliminary study, we observed a low HEV-seroprevalence in HIV-1 infected patients (<5%), unlike a recent publication that reported a seroprevalence of 12.3% in Lazio blood donors (Spada et al, 2018). The study shows that HEV-infection in HIV-1 infected individuals was frequently associated with other viral hepatitis coinfection history.

HIV and nervous system

P 42 PREVALENCE OF ALEXITHYMIA AMONG HIV-INFECTED PATIENTS ON COMBINATION ANTIRETROVIRAL THERAPY

A. Spinelli[1], L. Calza[1], G. Piazza[2], S. Vitale[2], L. Appolloni[2], G. Pensalfine[2], M. Morotti[2], C. Puggioli[2], V. Colangeli[1], M. Borderi[1], P. Viale[1]

Department of Medical and Surgical Sciences, [1]Unit of Infectious Diseases, [2]Hospital Pharmacy, S.Orsola-Malpighi Hospital, University of Bologna

Background: Alexithymia is a multidimensional trait characterized by impairments in the cognitive assimilation of feelings and emotions. It is often associated with HIV infection and may reflect effects of the virus on brain areas that are also important for multiple cognitive functions, such as the prefrontal and anterior cingulate cortices. Moreover, alexithymia seems to be associated with an increased cardiovascular disease risk both in HIV-infected and HIV-uninfected people.

Patients and methods: A cross-sectional study was performed to investigate prevalence of alexithymia and its potential correlation with HIV-related factors and exposure to specific antiretroviral agents. The alexithymia was diagnosed by the adiministration of the Toronto Alexithymia Scale-20 (TAS-20) questionnaire. The TAS-20 cutoff scoring used was: <50, non-alexithymia; 50-60, border line or possible alexithymia; >61, alexithymia.

Results: The study involved 429 HIV-infected patients attending our HIV outpatient clinic during the year 2018, on stable combination antiretroviral therapy (cART), and who were administered the TAS-20 questionnaire. Overall, 364 (84.8%) were men, the mean age was 49.9 years (range, 19-78), the mean CD4 T lymphocyte count was 716 cells/mm3, 34 (7.9%) had a previous AIDS diagnosis, and 389 (90.7%) had plasma HIV RNA <40 copies/mL. Alexithymia was diagnosed in 60 subjects (14%), while 258 (60.3%) did not present this condition and 110 (25.7%) were classified as border line patients. Virological and immunological parameters were comparable in patients with alexithymia and in those without this trait. With regard to current antiretroviral therapy, a significantly association was detected between alexithymia and current use of lamivudine or atazanavir: the percentage of patients who were taking lamivudine was significantly higher among subjects with alexithymia than among those without this impairment (50% vs 37.2%, p=0.028), such as the percentage of patients taking atazanavir (16.7% vs 9.3%, p=0.042). However, no significant correlations were reported with other concomitant antiretroviral drugs.

Conclusions: In our study, prevalence of alexithymia among HIV-positive patients on cART was significant (14%) and comparable to that reported in the general population. Current use of lamivudine or atazanavir was significantly more frequent among persons with this psychological impairment, but larger studies are needed in order to better investigate its association with exposure to specific antiretroviral drugs.

HIV and nervous system

P 43 EXAMPLE OF COMPREHENSIVE NEUROCOGNITIVE ASSESSMENT IN A HIV POPULATION IN NORTHERN ITALY

A. Parisini[1], C. Bolla[1], M. Gay[1], E. Mantia[1], E. Sarchi[1], F. Lanzieri Pignataro[1], E. Blasi Vacca[1], F. De Luca[2], A. Pepoli[2], G. Chichino[1]

[1]Division of Infectious Diseases, SS.Antonio e Biagio e Cesare Arrigo, Alessandria, Italy, [2]Unit of Psychology, SS.Antonio e Biagio e Cesare Arrigo, Alessandria, Italy

Background: HIV related neurocognitive disorders (HAND) have several risk factors, including low CD4 nadir (<200 cells/µl), age > 50 years, cardiovascular risk factors and previous efavirenz exposure. Early screening and identification of HAND in HIV is not commonly done and standardized in ID clinics. Hereafter we describe screening and management algorithm of HAND in use in our Center.

Materials and Methods: Consecutive HIV positive adults, with history of low nadir, previous/current efavirenz use, and reported concentration problems and memory loss, have been prospectively enrolled since May 2018. Patients with concomitant unbalanced psychiatric syndrome, current drug use, previous cerebrovascular damages, and foreigners with poor italian language understanding were excluded. Who met the aforementioned criteria were screened for HAND with MINI Addenbrooke's cognitive examination (MACE)2 -3and International HIV dementia scale (IHDS)4. All patients who obtained a score < 10 and <26 respectively, underwent complete neuropsychological examination of the following cognitive areas: memory, attention function, language, praxia/visual-spatial function and processing speed. Patients with a diagnosis of HIV-associated dementia (HAD) thus performed brain MRI and lumbar puncture to detect HIV and JC Virus in CSF. Patients with detectable HIV viral load and/or positive JCV PCR in the CNS and/or suggestive MRI of encephalopathy with white matter damage, changed cART for optimizing CNS penetration.

Results: 48 patients were enrolled: 100% on cART, 72.9% male, 93.7% caucasian, median age 50 years (28 -68), 89.5% with plasma HIV-RNA <20 cp/mL; median CD4+ T-cells count and nadir 541 (169-2.196) and 254 (5-1.250) cells/µL. Median year of diagnosis was 2004 (1986 – 2018), 13 patients had history of previous drug-abuse, 15 had mild and controlled psychiatric disorders, 11 were treated in past for latent syphilis (no history of neuro-syphilis), 5 have a known cerebral vasculopathy. Five patients had previous efavirenz use. MACE and IHDS median scores were 26 (11-30) and 10 (1-12), with altered results observed in 52% (cutoff≤26) and 33.3% (cutoff≤10), respectively. Six patient underwent a full neuro-psychological analysis. HAND was diagnosed in 1 patient (HAD). He underwent both MRI (T2 hyper and T1 hypointensity in superficial and periventricular supratentorial white matter) and lumbar puncture showing detectable HIV viral load (70 cp/ml), negative JCV and syphilis. cART regimen was changed from dolutegravir/abacavir/lamivudine to darunavir/cobicistat, tenofovir alafenamide/emtricitabine and maraviroc.

Conclusions: Neurocognitive disorders account roughly for 25% of the HIV patients, ranging from aymptomatic neurocognitive impairment (ANI) to HAD. It is fundamental to keep in mind that ageing in HIV patients connote also neurological damage. A specific pathway is needed to assess neurological status and improve neuro-penetration of cART, in case of HAND diagnosis.

HIV and nervous system

P 44 GUILLAIN-BARRÉ SYNDROME AS IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME IN A PRIMARY HIV INFECTION: A CASE REPORT

M. Cantone[1,2], S. Chiappetta[1], M. Merli[1], M.C. Moioli[1], D. Motta[1], C. Orcese[1], A. Pazzi[1], R. Rossotti[1], G. Travi[1], B.P. Vigo[1], M. Puoti[1]

[1]Infectious Disease Department ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [2]University Federico II, Naples, Italy

Background: Acute inflammatory demyelinating polyradiculoneuropathy subtype of Guillain-Barré Syndrome (GBS) is a potentially life-threatening disease that is rarely associated with HIV infection. It might occur anytime during the course of the infection, but it is more common when there is a high viral load with low CD4 count or during seroconversion. GBS is also known to be associated to the Immune Reconstitution Inflammatory Syndrome (IRIS).

Case presentation: We present a case of a 54 old man with an acute HIV infection without other comorbidity, who started therapy with Dolutegravir+Emtricitabine/Tenofovir alafenamide (at baseline HIV RNA 1.875.000 copies/mL; CD4 320/mmc, Fiebig stage III).

After four days of antiretrovirals he developed ascending and worsening dysesthesias of lower extremities with muscular weakness and postural instability. A lumbar puncture was performed with analysis of cerebrospinal fluid that demonstrated marked inflammation (10 cells/mm3, proteins 220 mg/dL, HIV RNA 2500 copies/mL). All other causes of radiculoneuropathy supported by infectious etiology were ruled out.

He received intravenous immunoglobulin with no clinical response. Indeed he developed dysphagia and cranial nerve impairment with bilateral palsy of facial nerve. When the viral load has been available showing a value of 17.000 copies/mL (a decay of 2 log10 in less than one week), high dose of intravenous Methylprednisolone, as conventional treatment of IRIS, was started. The patient rapidly improved motor function with total recovery of neurological impairment in few weeks.

Conclusions: So far, seven cases of GBS during HIV infection have been published. High dose steroid treatment is not usually recommended for GBS, but it may be an effective option when inflammatory demyelinating polyradiculopathy is associated with IRIS.

HIV and nervous system

P 45 PRELIMINARY DATA ON THE LINK BETWEEN ALEXITHYMIA AND NEUROCOGNITIVE DEFICIT IN HIV

A. Cappabianca, M. Vitale, S. Madonia, A.M. Spera, V. Fortunato, A. Masullo, R. Santoro

Unit of Infectious Diseases – University Hospital S. Giovanni di Dio e Ruggi D'Aragona, Salerno, Italy

Background: Many studies have investigated the role of HIV infection on the emotional regulation processes linked to the ability to establish social relation and some of these studies explore the role of alexithymia (1, 2, 3). Alexithymia is a deficit of emotional regulation characterized by difficulty in communicating feelings and emotion and in elaborating affective experience. It is associated with increased cardiovascular risk (4, 5), counted among the risk factors for the development of medical complications and poor adherence to therapy. Starting from the multiple links existing between the emotional and cognitive sphere and considering that the effects of the virus on CNS are not limited to the cognitive sphere, our study explores the relationship between alexithymia and neurocognitive deficit in HIV.

Material and methods: Our study involved 30 HIV+ patients recruited from the Unit of Infectious Diseases Department of Salerno's

Hospital. We used the 20-item Toronto Alexithimya Scale (TAS-20) (6, 7) to measure alexithymia, the Montreal Cognitive Assessment (MoCa) (8) to assess cognitive impairment and the Hospital Anxiety and Depression Scale (HADS) to assess anxiety and depression. We analyzed the data using SPSS.

Results: Subjects have an average age of 42, are mostly men (73%) with 12 years of education.

On average they have been infected with HIV for 6 years and have been following HAART therapy for 5 years. 73% of the subjects is virosopressed and the group has an average viral load of 22,626, an average value of 605 CD4 and 0.81 CD4/CD8. No subject has co-infection with HCV or drug addiction.

The scoring showed a mean of 25.22 for the MoCa, and of 46.80 for the TAS-20. Both of them are important scores considering the clinical cut-off scores: ≤26 for the MoCa and ≥51 for the TAS-20.

We found cognitive impairment in 40% of cases. Subjects with cognitive impairment show a mean of 54.33 ± 12.52 at the TAS-20, higher than subjects with no neurocognitive deficit, who show normal TAS-20 mean score (41.17 ± 10.51) ($p < 0.05$). We found not significative differences considering HADS mean scores (Table 1).

Conclusion: We found that subjects with cognitive impairment have a higher degree of Alexithymia than patients without cognitive impairment , with a statistically significant difference ($p < 0.05$). These results are in line with what the literature suggests and confirm its relevance of the effects of the virus on the processes of emotional regulation in the HIV + patient.

HIV and nervous system

P 46 SELF-REPORT TESTS AS SCREENING TOOL FOR HIV-ASSOCIATED NEUROCOGNITIVE DISORDERS

M. Allegrini[1], F. Bai[1], L. Borghi[2], I. Strada[2], E. Merlini, S. Cannizzo, G. Marchetti[1], A. d'Arminio Monforte[1]

[1]Clinic of Infectious Diseases, San Paolo Hospital, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy, [2]Clinical Psychology Unit, San Paolo Hospital, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy

Background: Three Questions Test (3QT) is proposed by European AIDS Clinical Society as first approach in HIV + patients (pts) complaining cognitive symptoms, but it showed poor screening performance for HIV-Associated Neurocognitive Disorders (HAND). Conversely, HAND is associated with an impaired Health-related Quality of Life (HQoL). We evaluated the performance of 3QT in combination with HQoL's assessment (SF-36 questionnaire) as screening tool (ST) of HAND.

Material and methods: Cross-sectional study (2014-2018); antiretroviral (ART)-naïve and ART-treated HIV+ pts completed self-report 3QT (Do you experience frequent memory loss? Do you feel that you are slower when reasoning, planning activities or solving problems? Do you have difficulties paying attention?; positive test if the answer is "yes" on ≥1 question) plus SF-36 (8 health domains, 35 items summarized in Mental Health Index [MHI] and Physical Health Index [PHI]) as ST and a neurocognitive battery as gold standard (10 tests, 7 cognitive domains; HAND by Frascati criteria). Hospital Anxiety/Depression Scale (HADS) was also used. Exclusion criteria: CNS opportunistic infections, major depression, psychiatric/neurologic conditions, alcohol or psychotropic drugs abuse, not Italian speaking. Impaired ST: ≥1 altered test among 3QT, PHI and MHI. Logistic regression analysis was used to evaluate factors associated with impaired ST.

Results: 376 HIV+ pts included (82% males; median age: 44, IQR 36-52 years; 60% on ART; median current and nadir CD4+ T-cells: 528, 366-693 - 332, 170-470; plasma HIV-RNA ≥40 cps/ml in 42%): 20% reported cognitive complains at the evaluation; 25% showed HAND (23% Asymptomatic Neurocognitive Impairment, 2% Mild Neurocognitive Disorders); 54% had abnormal ST. Even if HAND was associated with ST (OR 1,73, 95%CI 1,07-2,81, p=0,03), ST poorly performed as screening test of HAND (Sensitivity: 64%, IC95% 55-74, Specificity: 49%, IC95% 43-55, Positive and Negative Predictive Value: 29%, IC95% 23-35 and 80%, IC95% 74-87; the correct classification rate was 53%). Impaired ST was independently associated with being ART-naïve and symptoms of anxiety/depression by HADS (Table). ST showed poor performance also stratifying the analyses for cognitive complains.

Conclusions: Patients' self reports of cognitive symptoms were not associated with objectively measured cognitive function and are an inadequate screening tool for HAND; conversely, anxiety/depression symptoms are drivers of subjective cognitive complains in HIV+ pts.

HIV and nervous system

P 47 CLINICAL INFERENCES FOR THE ASSOCIATION BETWEEN MODE OF HIV ACQUISITION AND DIFFERENT PATTERNS OF NEUROCOGNITIVE IMPAIRMENT

M. Trunfio[1], D. Vai[2], G. De Zan[1], V. Pirriatore[1], F. Bai[3], G. Palazzo[1], C. Alcantarini[1], M.C. Tettoni[1], D. Imperiale[2], S. Bonora[1], G. Di Perri[1], A. Calcagno[1]

[1]Unit of Infectious Diseases, Amedeo di Savoia hospital, Department of Medical Sciences, University of Turin, Turin, Italy, [2]Unit of Neurology, Maria Vittoria hospital, ASL Città di Torino, Turin, Italy, [3]Unit of Infectious Diseases, Santi Paolo e Carlo hospital, University of Milano, Milano, Italy

Background: HIV-associated neurocognitive deficits (HAND) show complex phenotypes limiting therapeutic interventions. HIV acquisition routes (ARs) underlie multiple factors (gender, sex, substance abuse, comorbidities) variably affecting viroimmunological parameters and neurocognition. We sought to assess whether different ARs may affect HAND phenotype and consequently neurocognitive screening tests (NC-STs) accuracy.
Methods: Caucasian adult people living with HIV on cART were consecutively enrolled and divided into three groups according to ARs: males who have sex with males (MSM), previous intravenous drugs users (pIDU) and heterosexuals (HS). Patients presenting confounding factors for HAND were excluded. Patients underwent NC-STs (International HIV Dementia Scale [IHDS] and Mini Addenbrooke's Cognitive Examination [MACE]), depression/anxiety assessment and full neurocognitive evaluation, consisting of 16 tests covering 7 main cognitive domains; all tests' scores were age/education-normalized. HAND diagnosis was made according to Frascati's criteria. Data were analyzed through non-parametric tests.
Results: 212 patients were enrolled. Patients' characteristics are shown in Tab.1. While a trend was observed for lower processing speed/reaction time in MSM (Trail making test part A, p.05), HS presented lower scores at short-term memory (Digit span forward, p.03), and together with pIDU proved lower performance in attention/working memory (Digit Symbol test, p.04) and visuoconstruction (Rey Complex figure Copy test, p <.01), as shown in Tab.2. HS presented also higher odds of failing at visuo-spatial short-term working memory tasks (altered Corsi test: MSM 13.8%, pIDU 25.7%, HS 30.9%, p.04), while pIDU at memory tasks adjusted for possible attention/learning deficit (altered Free and Cued Selective reminding test: MSM 7.4%, pIDU 16.2%, HS 2.4%, p.03). MACE - IHDS AUROC were 0.91 - 0.75 in MSM (both p<.01), 0.86 - 0.84 in pIDU (both p<.01) and 0.76 (p.02) - 0.60 (p.37) in HS. Wide variability was also observed in diagnostic accuracy and clinical utility indexes of both the NC-STs between the groups, as shown in Tab.3. At logistic regression, only educational level and ARs influenced diagnostic concordance between MACE and NC battery results (ARs: MSM vs HS OR 8.9 [2.4-33.0], p<.01; pIDU vs HS OR 4.0 [1.2-13.5], p.02), while no effect by CD4 nadir, viral suppression, sex, age and hepatitis coinfection was observed.
Conclusions: HAND phenotypes may differ according to ARs, independently from other common recognised factors able to condition HAND development and severity. MACE and IHDS performed similarly in screening MSM and pIDU and poorly in HS, despite the high prevalence of HAND in this group. Given the complex pathogenesis, HAND phenotype need to be better characterized in order to perform adequate tailored screening and diagnostic strategies and eventually treatment interventions.

HIV cure and vaccines

P 48 ASSOCIATION BETWEEN UNDETECTABLE HIV-1 DNA AND HIV-1 POL IN CHRONIC HIV-1 INFECTION

C. Muccini[1], L. Galli[2], V. Spagnuolo[1,2], A. Poli[2], S. Rolla[3], F. Rinaldi[4], R. dell'Acqua[5], A. Mastrangelo[1], D. Canetti[2], A. Lazzarin[2], A. Castagna[1,2]

[1]Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [3]Laboratory of Microbiology and Virology, IRCCS San Raffaele Scientific Institute, Milan, Italy, [4]University of Florence Department of Experimental and Clinical Medicine, Florence, Italy, [5]University Hospital Policlinico, Bari, Italy

Background: Up to now, no data are available on the association between negative HIV-1 Pol protein and undetectable HIV-1 DNA in chronic HIV-1 infection.
The aim of the study was to evaluate if negative HIV-1 Pol was associated with undetectable HIV-1 DNA in adults with chronic HIV-1 infection, prolonged suppressive antiretroviral therapy (ART) and good immunological profile.
Materials and methods: Cross-sectional parent study of the APACHE trial (NCT03198325), conducted on subjects with chronic HIV-1 infection, HIV-1 RNA <50 copies/mL for ≥10 years, absence of plasma residual viremia for ≥5 years and CD4+ >500 cells/μL screened for HIV-1 DNA. HIV-1 DNA was amplified and quantified in peripheral blood mononuclear cells (PBMCs) by Real Time PCR (ABI Prism 7900). At HIV-1 DNA determination, HIV-1 serostatus was tested by HIV Blot 2.2 Western blot assay (MP Diagnostics) and HIV-1 co-receptor usage was determined from the V3 nucleotide sequence by using the geno2pheno algorithm on proviral DNA extracted from PBMC sample; patients with false positive rate (FPR) ≤20% were considered infected with non-R5 virus while an FPR >20% defined a R5 virus. Other patients' characteristics were reported as median (IQR) or frequency (%). Multivariate logistic regression was used to determine factors associated with undetectable HIV-1 DNA.
Results: Overall, 96 patients were evaluated: 78 (81%) and 18 (19%) patients with HIV-1 DNA ≥100 copies/106PBMCs and with HIV-1 DNA <100 copies/106PBMCs, respectively. At HIV-1 DNA determination, median age was 32.5 (25.3-38.9), 61 (64%) were male, with ART start 7.7 (1.9-38.3) months after HIV diagnosis, HIV-1 RNA <50 copies/mL for 11.7 (10.6-14.0) years, absence of plasma residual viremia for 6.9 (6.2-7.2) years and CD4+ 763 (605-922) cells/μL. Nadir CD4+ was 253 (167-339) cells/μL among patients with detectable HIV-1 DNA and 353 (212-434) cells/μL among those with undetectable HIV-1 DNA (p=0.055). Patients' characteristics are reported in Table 1.
The proportion of patients with undetectable HIV-1 DNA among those with negative HIV-1 Pol was 35% (9/26) and 13% (9/69) among those with positive HIV-1 Pol (p=0.036).
At multivariate analysis, higher nadir CD4+ [adjusted odds ratio (AOR) 1.35 (95% confidence interval, CI=1.03 -1.76), p=0.029], more years of HIV-1 RNA <50 copies/ml [AOR 2.98 (95%CI=1.25-7.10), p=0.014], a R5-tropic virus [AOR (R5 vs. non-R5) 0.20 (95%CI=0.04-0.96), p=0.044] and negative HIV-1 Pol [AOR 6.59 (95% CI=1.47-29.54), p=0.014] were associated with undetectable HIV-1 DNA, after adjusting for age at HIV diagnosis, gender, HIV-1 tropism, months between HIV diagnosis and ART start and ART duration.
Conclusions: In patients with chronic HIV-1 infection, prolonged suppressive ART, absence of plasma residual viremia for ≥5 years and good immunological profile, negative HIV-1 Pol was associated with undetectable HIV -1 DNA as well as higher nadir CD4+, more years of HIV-1 RNA <50 copies/ml and R5-tropic virus.

HIV cure and vaccines

P 49 EFFICACY AND SAFETY OF TWO AGENTS ANTIRETROVIRAL REGIMENS: OUR EXPERIENCE IN "REAL LIFE"

L. Massoli[1], C. Contini[2], M. Libanore[1], A. Trentini[3], E. Biagi[1], M. Di Nuzzo[1], D. Segala[1], L. Sighinolfi[1]

[1]O.U. of Infectious and Tropical Diseases and of the Migrants, University of Ferrara, Italy, [2]Full Professor of Infectious and Tropical Diseases, Department of Medical Sciences, University of Ferrara, Italy, [3]Section of Medical Biochemistry, Molecular Biology and Genetics, Department of Biomedical and Specialist Surgical Sciences, University of Ferrara, Ferrara, Italy

Background: Some two agents antiretroviral regimens have demonstrated comparable efficacy to three agents regimens for maintenance therapy. The aim of this retrospective study is evaluate efficacy and safety of two agents regimens (3TC+DTG or 3TC+boosted PI) after 48 weeks of switching from standard three agents regimens. The switch to two agents regimens was proposed for simplification or toxicity due to the previous treatment.

Material and methods: Inclusion criteria were: stable (at least 1 years) 3 drugs - cART, no previous resistance mutations to the drugs used and stable HIV-RNA < 50 copies/ml for at least 1 year . We evaluated quantitative HIV-RNA (VL), CD4 and CD8 cells count, CD4/CD8 ratio, total cholesterol and serum creatinine before and 48 weeks after switching. Wilkoxon test was used for statistic analysis.

Results: Seventy three (73) patients were included: twenty-five (34.2%) female, forty eight (65.8%) male with median age 54 years old and in stable cART for at least 1 year (mean 11, 5 years). Thirty-nine (54%) were switched to 3TC+DGV regimen, thirty-four (46%) to 3TC+ boosted PI (ATV/r or DRV/c). One patient was lost at the follow up.

At week 48th we didn't observe statistically significant changes of CD4/CD8 ratio, serum creatinine and cholesterol. 71/73 patients maintained HIV RNA undetectable: two patients showed viral blips (HIV RNA detectable < 100 copies/ml) for lack of adherence. Absolute CD4 counts significantly increased from baseline to 48 weeks (mean + 53 cells/μL; $p < 0.003$).

Conclusions: Agree with literature, two agents regimens have been effective for maintenance of suppressed VL and increase of CD4 cells count. With the limitations of our small sample, they also seem to be safe. No differences were found between the two different two-drug regimens.

Bibliography

1. Libre JM , Hung CC,Brinson C, et al. Phase III SWORD 1&2: switch to DTG+RPV maintains virologic suppression through 48 wks. Presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 13–16 February 2017, Seattle . Abstract 44LB

2. Pulido F, Ribera E, Lagarde M , et al. ; DUAL-GESIDA-8014-RIS-EST45 Study Group . Dual therapy with darunavir and ritonavir plus lamivudine vs triple therapy with darunavir and ritonavir plus tenofovir disoproxil fumarate and emtricitabine or abacavir and lamivudine for maintenance of human immunodeficiency virus type 1 viral suppression: randomized, open-label, non inferiority DUAL-GESIDA 8014-RIS-EST45 trial . Clin Infect Dis 2017; 65:2112–8.

3. Lamivudine/dolutegravir dual therapy in HIV-infected, virologically suppressed patients Franco Maggiolo1* , Roberto Gulminetti2, Layla Pagnucco2, Margherita Digaetano3, Simone Benatti1, Daniela Valenti1, Annapaola Callegaro4, Diego Ripamonti1 and Cristina Mussini3

HIV cure and vaccines

P 50 HOW ARE ORGANIZED HIV CLINICAL CENTERS FOR VACCINATIONS IN THEIR PATIENTS? RESULTS FROM A SURVEY IN THE CISAI NETWORK

G. Orofino[1], A. Cascio[2], G. De Socio[3], P. Bonfanti[4], R. Gulminetti[5], M.C. Moioli[6], N. Forni[7], N. Squillace[8], K. Falasca[9], S. Martini[10], B. Menzaghi[11], G. Pellicanò[12], E. Sarchi[13], M. Guastavigna[1], E. Ricci[14]

[1]Mal. Inf. e Trop. A, Torino, [2]Mal. Inf. Policlinico Palermo, [3]Mal. Inf. Perugia, [4]Mal. Inf. Lecco, [5]Mal. Inf. Policlinico Pavia, [6]Mal. Inf. Osp. Niguarda, Milano, [7]C. U. Mal. Inf. Torino, [8]Mal. Inf. Monza, [9]C.U. Mal. Inf. Chieti, [10]Univ. Napoli L. Vanvitelli, [11]Mal. Inf. Busto Arsizio, [12]Mal Inf. Policlinico Messina, [13]Mal Inf. Alessandria, [14]CISAI Group

Background: Vaccinations are historically highly recommended in HIV positive adults but the recent outbreak of HAV hepatitis has dramatically demonstrated as this issue has been largely disappointed. So, in the last two years, an important call for action for vaccinations has emerged in the clinical centers for HIV+ people. HIVAC – CISAI project is aimed to check the situation regarding vaccine in some Italian clinical HIV service, to verify the modality of vaccine hesitancy in the HIV population and to sustain and promote the attention on this important clinical endpoint, also to try to standardize the response and close some gaps due to different regional modality to access to vaccines.

Material and methods: In this initial part of the project (HIVAC - CISAI) a survey has been obtained form 13 centers, representing north (8), center (2) and south (3) of Italy, with a total of near 12000 patients in cure. The principal items of the questionnaire were: organization of the vaccine service, informations regarding some distinct vaccine type and schedule of the suggested/offered vaccinations.

Results: In 3/13 (23%) cases, patients are sent to local vaccine centers; 4/13 centers (30%) has an internal vaccine service and 5/13 (40%) offer both possibilities. Vaccinations suggested/offered: 100% vaccine against HBV and HAV; 11/13 (90%) flu vaccination; 11/13 (90%) anti-pneumococcal vaccination; 10/13 (81%) anti-meningococcal vaccination; 9/13 (72%) Hib vaccination; 6/13 (47%) offer anti-HPV vaccination to all the patients, 4/13 (31 %) only to MSM and women under 45 years old, 2/13 (15%) only to MSM; 1/13 (8%) anti-VZV vaccination; 4/13 (31%) anti-MMR (measles, mumps, rubella) vaccination; 3/13 (24%) anti-poliomyelitis vaccination; 1/13 (8%) promotes anti-Herpes Zoster Vaccination to all the patients, 2/13 only to patients with comorbilities; 5/13 (40%) Tdap (Adult Tetanus, Diphteria, Pertussis) vaccination; 5/13 (40%) Yellow Fever and 10/13 (81%) Typhoid Fever.

Conclusions: All clinical centers interviewed take great consideration for vaccinations in HIV+ people. There is a concordance in offering the principal vaccines and some discrepancies with other ones, particularly HPV and Herpes Zoster, due also to distinct health regional policies. The double offer (internal service and invoice to external territorial service) seems to be optimal, but only data on effective vaccine coverage and hesitancy will provide more evidence on the optimal strategy to cope with.

HIV cure and vaccines

P 51 EFFICACY AND SAFETY OF MVC-CONTAING REGIMEN IN TREATMENT-EXPERIENCED PATIENTS

L. Pagnucco[1,2], D. Devita[2], R. Gulminetti[1]

[1]Fondazione IRCCS Policlinico San Matteo, Dipartimento di Malattie Infettive, [2]Università degli Studi di Pavia

Background: MVC, in combination with other antiretroviral medicinal products, is indicated for treatment of patients with CCR5-tropic HIV-1 infection.
Material and methods: We conduceted a retrospective, cohort study in treatment-experienced patients with R5-tropic HIV-1 who started a dual therapy including MVC. The primary endpoint was to assess the efficacy of an antiretroviral regimen including MVC and boosted protease inibitors.
Follow-up accrued from the date of MVC initiation to the date of treatment failure or to the date of last available visit.
Results: We included 34 patients who were switched to a MVC-containing regimen (14 ATV/r and 20 DRV/r) for different reasons: 29 pts because of drug-drug interaction or intolerance of the previous therapy , 5 pts because of virological failure. Most of the patients had a long-lasting HIV-1 infection with a median time wirh HIV of 15.8 years and also a long time of exposure to ART (Median 13.9 years) and they had experienced a median of 4 therapeutic lines. Most of the patients were males (26) with a median age of 48.8 years.
The median follow-up time was 87 months, At week 24 all patients reached undetectable viral load (HIV-RNA<50 cp/mL). During follow-up 4 patients presented a viral blip (65cp/mL , 94cp/mL, 73cp/mL, 89cp/mL,) that returned negative at the following control without modifying the antiretroviral regimen.
4 patients discontinued MVC+PI/r due to viral failure and 2 because of side effects possibly due to PI/r. 1 pt died of lung cancer. Patient who had started this regimen due to the previous cART we detected a small increase in CD4+ count whereas in pts who started MVC+PI/r beacouse of a previous viral failure, we observed a more significant improvement of the immunological status with an increase mean CD4+ T cell count of 190/ul in the first year of treatment. Liver function tests (ALT, AST and GGT) and renal function test (creatinine) remained stable overtime. Any SAE was reported.
Conclusion: In this small cohort of treatment/experienced patients a dual MVC+PI/r regimen was well tolerated and showed a good virological response during long-term follow-up.

HIV epidemiology and retention in care

P 52 DIFFERENT DYNAMICS OF THE HIV EPIDEMICS IN PLWHIV OF ITALIAN OR NON-ITALIAN ORIGIN IN A PROVINCE OF NORTHERN ITALY

F. Maggiolo, L. Comi, R. Teocchi, E. Di Filippo, A.P. Callegaro, D. Valenti, M. Rizzi

ASST Papa Giovanni XXIII, Bergamo

Background: Linguistic and cultural barriers, difficult housing, uncertainty about labor are all variables that may influence access to care even in a socially based system like ours. These variables may especially apply to PLWHIV of non-Italian origin. We analyzed the dynamic of the HIV epidemics in PLWHIV of Italian and non-Italian origin.

Methods: Data (year of diagnosis, AIDS diagnosis, CD4 at diagnosis, deathl) and demographic characteristics on the diagnosed and treated populations were derived from the clinical database of the only Provincial Center authorized to treat HIV infection and cross-checked with the Regional administrative data-base. The number of PLWHIV in our area was calculated with the eCDC HIV modelling tool (version 1.3.0) that simultaneously estimates the annual number of newly acquired HIV infections, the time between infection and diagnosis and the size of the undiagnosed population. Inputted data covered the period from 1984 to 2018. Inferential analysis was performed with t-test or chi-square test.

Results: At December 2018 patients actively followed at our Center were 2742: 2046 of Italian origin and 336 (12.2%) of non-Italian origin. Non-Italian came from sub-Saharan Africa (51.5%), South America (19.9%), East Europe (16.7%), North Africa (6.8%) and Far East (5.1%). Compared to those of Italian origin PLWHIV of non-Italian origin presented a higher proportion of women (44.9% vs 23.2%; P<0.0001); were younger, with a median age at diagnosis of 33.8 years (IQR 13) compared to 38.3 years (IQR 16)(P=0.001) and with a shorter median follow up: 10.1 years (IQR 10) versus 11.0 years (IQR 11) (P<0.0001). Risk factors for HIV, were also differently distributed (P<0.0001): heterosexual intercourse 80.4 vs 43.7%; MSM 15.8 vs 25.6%; IVDU 3.0 vs 30.1%, MTCHT 0.9 vs 0.5%; transfusion 0 vs 0.1%. At baseline non-Italian PLWHIV had a lower median CD4 count of 248 (IQR 403) cells/mcL compared to a median of 306 (IQR 463) cells/mcL (P<0.0001) in Italian PLWHIV. An higher proportion 24.7% vs 20.1% (P=0.05) of PLWHIV of non-Italian origin were AIDS presenters, too. Most relevant, the number of undiagnosed infections peaked in Italian PLWHIV in 1987 and in non-Italian in 2006 (figure). Since then the proportion of undiagnosed infections progressively decreased but are still higher 11.9% among non-Italian compared to Italian (7.2%) (figure).

Conclusions: We believe that the Italian model based on a socially-oriented healthcare system that provides free-care for all PLWHIV may limit discrimination. Nevertheless, in our experience, PLWHIV of non-Italian origin have a later access to cure and an higher rate of undiagnosed infections. Further efforts to reach this population should be warranted.

HIV epidemiology and retention in care

P 53 MOLECULAR EPIDEMIOLOGY OF HIV-1 INFECTION IN IMMIGRANT POPULATION IN NORTHER ITALY

C. Sagnelli[1], C. Uberti-Foppa[2], E. Cella[3], S. Bagaglio[2], V. Scolamacchia[3], H. Hasson[2], S. Salpietro[2], E. Messina[2], G. Morsica[2], S. Angeletti[4], M. Ciccozzi[3], A. Lazzarin[2], E. Sagnelli[1]

[1]Department of Mental Health and Public Medicine, Campania University Luigi Vanvitelli, Naples, Italy, [2]Department of Infectious Diseases, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy, [3]Medical Statistics and molecular Epidemiology Unit, Campus Bio-Medico University, Rome, Italy, [4]Laboratory clinical Science; Campus Bio-Medico University, Rome, Italy

Background: HIV-1 is characterized by a vast genetic diversity classified into distinct phylogenetic strains and recombinant forms.
Methods: We describe the HIV-1 molecular epidemiology and evolution of 129 consecutive HIV-1 positive migrants living in Milan (norther Italy). Polymerase gene sequences of 116 HIV-1 subtype-B positive patients were aligned with HIV-1 reference sequences (https://www.ncbi.nlm.nih.gov/) by using MAFFT alignment and edited by using Bioedit software. A Maximum Likelihood phylogenetic tree was performed by MEGA7 and was visualized by using FigTree v1.4.3.
Results: Of 129 migrants, 35 were born in Europe (28 in Eastern Europe), 70 in the Americas (67 in South America), 15 in Africa, and 9 in Asia; 76.4% were MSM. The serotype HIV-1-B prevailed (89.9%), followed by -C, -F1, -D, and -A. Compared with 116 HIV-B patients, the 13 with HIV-non-B showed lower Nadir of CD4+ cell/mmc (p=0,043), more frequently had sub Saharan origin (38.5 vs 1.72%, p=0.0001) and less frequently were MSM (40 vs. 74.5%, p=0.02). The Maximum Likelihood phylogenetic tree of the 116 HIV-1 subtype-B positive patients showed 13 statistically supported nodes (bootstrap>70%). Most of the sequences included in these nodes have been isolated from male patients from the Americas and the most common risk factor was MSM. The low number of HIV-1 non-B subtypes patients did not allow to perform this analysis.
Conclusions: These results suggest a shift of HIV-1 prevention projects' focus and a continuous monitoring of HIV -1 molecular epidemiology among entry populations. Prevention efforts based on HIV molecular epidemiology may improve public health surveillance setting.

HIV epidemiology and retention in care

P 54 HIV-1 RECOMBINANT FORMS IN MIGRANT POPULATION LIVING IN MILAN, NORTHER ITALY

C. Sagnelli[1], C. Uberti-Foppa[2], E. Cella[3], H. Hasson[2], S. Salpietro[2], E. Messina[2], S. Bagaglio[2], S. Angeletti[4], M. Ciccozzi[3], A. Lazzarin[2], E. Sagnelli[1]

[1]Dept. of Mental Health and Public Medicine, Campania University Luigi Vanvitelli, Naples, Italy, [2]Dept. of Infectious Diseases, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy, [3]Medical Statistics and Epidemiology, Campus Bio-Medico University, Rome, Italy, [4]Laboratory clinical Science; Campus Bio-Medico University, Rome, Italy

Background: Molecular epidemiology studies have shown an increasing prevalence of HIV non-B subtypes in HIV infected patients in Italy, from 0.3% in 1993 to 20% in recent few years, paralleled by an overtime increase of migrant population; in recent years such prevalence has reached 63.0% among HIV positive foreigners living in Italy. A similar increasing trend of circulating HIV recombinant forms (CRFs) has been described in Italy in the same period. We investigated the characteristics and evolution of HIV-1 in a migrant population living in Milan, norther Italy.

Methods: We enrolled 205 consecutive HIV-1 positive migrants living in Milan, naïve for antiretroviral therapy. Polymerase (POL) gene sequences of 205 HIV-1 recombinant form positive patients were aligned with HIV-1 reference sequences (https://www.ncbi.nlm.nih.gov/) by using MAFFT alignment and edited by using Bioedit software. A Maximum Likelihood phylogenetic tree was performed by MEGA7 and was visualized by using FigTree v1.4.3.

Results: Of the 205 migrants, 116(56.6%) showed serotype HIV-B, 13(6.3%), serotype HIV-non-B and 76 (37.1%) a HIV-1 recombinant form. Of the 76 HIV-1 recombinant cases, 80.3% were males and 60.6% M&M, the median age was 35.8 years and the immunological condition quite good (M±SD of CD4+ 373.8±246.8 cells/mm3; nadir CD4+ 331.2±231.6); 20 (26.3%) were born in Europe (13 in Eastern Europe), 42 (55.3%) in the Americas (39 in South America, of whom 19 in Brazil and 12 in Peru), 11 (14.5%) in Africa, and 3 (3.9%) in Asia,. The Maximum Likelihood phylogenetic tree of 76 HIV-1 recombinant form positive immigrants showed 14% BF-subtype sequences 2% A1B-subtype sequences, 6% CRF01/B-subtype sequences and CRF02/B-subtype sequences, 3% CD-subtype-sequences, 2% and a 6% were G-subtype sequences associated to an undetermined subtype form that requires further analysis. The phylogenetic analyses are still ongoing.

Conclusions: The continuing increase of complexity and genetic diversity of the global HIV-1 pandemic represent a great challenge for the monitoring of the infection. Molecular surveillance is needed to monitor the genetic evolution of HIV-1 epidemic, a practice of considerable utility in diagnostic accuracy and efficacy of antiretroviral treatment.

HIV epidemiology and retention in care

P 55 NEW HIV DIAGNOSES AMONG NON-ITALIANS, FROM 2010 TO 2017

V. Regine[1], L. Pugliese[1], B. Suligoi[1] and the Regional representatives of the National HIV Surveillance System[2]

[1]Centro Operativo AIDS, Istituto Superiore di Sanità, Roma, [2]Regional representatives of the National HIV Surveillance System
Abruzzo: M. Di Giacomo, L. Scancella; Basilicata: F. Locuratolo, G. Cauzillo; Calabria: A.D. Mignuoli, D.G. Chirico; Campania: G. Borgia; Emilia Romagna: E. Massimiliani; Friuli Venezia Giulia: T. Gallo, C. Braida; Lazio: V. Puro, P. Scognamiglio, A. Mammone; Liguria: G. Icardi, P.L. Lai; Lombardia: M. Gramegna, D. Cereda; Marche: F. Filippetti; Molise: A. Prozzo; Piemonte: C. Pasqualini; Provincia Autonoma di Bolzano: L. Pagani, R. Binazzi; Provincia Autonoma di Trento: P. Lanzafame, L. Collini, D. Bassetti; Puglia: M. Chironna, D. Loconsole; Sardegna: M.A. Palmas; Sicilia: G. Dardanoni; Toscana: F. Voller, M. Puglia, L. Pecori; Umbria: A. Tosti, R. Papili; Valle d'Aosta: M. Ruffier, M.G. Verardo, A. Catania; Veneto: F. Russo, F. Da Re

Background: Every year in Italy about 4000 new HIV diagnoses are reported and one third of them is among non-nationals. The aim of this study is to describe the trend and the characteristics of the new HIV diagnoses among non-Italians in Italy from 2010 to 2017.

Material and methods: Data from 2010 to 2017 were obtained from the Italian HIV surveillance system. Descriptive analysis was conducted on trends in new diagnoses by main characteristics.
Changes over time were investigated using the chi-squared test for trend.

Results: During the study period, the proportion of non-Italians among new HIV diagnoses increased over time, from 28.6% in 2010 to 34.4% in 2017. Overall, 9,021 new HIV diagnoses in non-Italians were reported, among them 58% were males and 42% females. Non-Italians had a median age of 33 years (IQR: 27-41) and 22% were aged <25 years. The number of new diagnoses among non-Italians < 25 years of age almost doubled between 2010 and 2017 (138 and 259, respectively).
The majority (44.0%) originated from Sub-Saharan African countries, 21.2% from Central and South America, 20.1% from Central and Eastern Europe, and 14.7% from other countries. The proportion of people originating from Sub-Saharan countries among new HIV diagnoses increased from 38% in 2010 to 55% in 2017 (p-value<0.05). Overall, heterosexuals accounted for 63.7% (36.0% females and 27.7% males), MSM for 20.0%, IDU for 2.4%. These proportions did not change over time. Differences were observed across geographical areas: among 3,972 Sub-Saharan Africans 60.0% were heterosexual women, among 1,811 people originating from Central and Eastern Europe 56.6% were PWID, and among 1,912 South Americans 57.1% were MSM.
Overall, the proportion of non-Italians diagnosed with a CD4 count <350 cells per mm3 (late presenters) was 58.3%. Out of them, one third had a concurrent AIDS diagnosis; this proportion remained stable over time (p-value > 0.05). The proportion of late presenters did not significantly differ by area of origin.
The most frequently reasons for HIV testing among men were symptoms (32.0%) and risk behaviors (31.3%), while among women were symptoms (29.0%) and screening during pregnancy (25.4%).

Conclusions: The proportion of new HIV diagnoses among non-Italians increased over time. A relevant increase was observed among individuals younger than 25 years and people originating from Sub-Saharan Africa. These results suggest the need to implement HIV testing interventions targeted at non-Italians, specifically at migrants that do not speak Italian or can be reluctant in engaging with public services. Moreover, prevention programs aimed at developing awareness on risk behaviors and increase testing should address most vulnerable groups, such as young people, women and individuals from Sub-Saharan Africa.

HIV epidemiology and retention in care

P 56 CAPACITY ASSESSMENT FOR PROVISION OF QUALITY SEXUAL REPRODUCTIVE HEALTH AND HIV-INTEGRATED SERVICES IN KARAMOJA, UGANDA

F. Di Gennaro[1], P. Lochoro[2], D. Pizzol[3], G. Putoto[3], W. Mazzucco[4], C. Marotta[4], J. Ictho[2], L. Monno[1], A. Saracino[1]

[1]Clinic of Infectious Diseases, University of Bari, Italy, [2]Doctors with Africa CUAMM, Kampala, Uganda, [3]Doctors With Africa Cuamm, Research Section Padua, Italy, [4]University of Palermo, Department of Science for Health Promotion and Mother to Child Care "G. D'Alessandro", Palermo, Italy

Background: Sexual and reproductive health (SRH) and Human Immunodeficiency Virus (HIV) are significant global health issues because of their respective associated morbidity and mortality. Uganda continues to bear a huge burden of HIV and AIDS with an estimated 1.3 million people living with HIV, among them 95,000 children.

Material and Methods: A cross-sectional health facility-based assessment was performed between November and December 2018 in Karamoja Region, northern Uganda. All the 126 health facilities in Karamoja, including 5 hospitals and 121 Health Centers (HC), covering 51 sub-counties of the 7 -districts were assessed. The dimensions explored by the study were the capacity of a) leadership and governance, b) human resource, c) service delivery, d) SRH and HIV service integration and e) users satisfaction and perceptions.

Results: Health unit management committees were present in 124 (98.4%) HCs and all the 5 (100.0%) hospitals had boards of governors. The 64% of the established health staffing positions were filled leaving an absolute gap of 704 units. As for service delivery capacity, on 5 domains assessed, the best performing was basic hygiene and safety measures in which 33% HCs scored "excellent" Presence of basic equipment were 29.4% of the facilities achieving the excellent score; while the availability of medicines at 27.8% and basic amenities at 26.2%. The least capacity was seen in laboratory services with only 6.3% of the facilities scoring excellent and 59.2% scoring poor.

The level of integration of SRH/HIV services was fairly good with the majority (55.56%) of health units providing SRH/HIV services in the same service site and the same provider offered on the same day (the "kiosk" model of integration). 19.84% of the health units reported no integration of SRH/HIV services.

Conclusions: HF in Karamoja have capacity gaps in a number of health system building blocks, many of these gaps can be addressed through improved planning and management in a supportive environment of good governance without additional resources. Given the high burden of disease caused by the sexual reproductive and maternal conditions, it makes a good return for countries to invest in improvements for these services

HIV epidemiology and retention in care

P 57 A RETENTION IN CARE PROGRAM IN HIV PATIENTS: WHO IS LOST AND FOUND IN 2018?

A. Raimondi[1], M. Digaetano[1], N. Riva[1], A. Bianchi[1], A. Bonazza[1], I. Franconi[1], C. Lucentini[1], E. Roncaglia[1], V. Borghi[1], G. Guaraldi[1], E. Girardi[2], A. d'Arminio Monforte[3], C. Mussini[1]

[1]Clinica di Malattie Infettive, Azienda Ospedaliera-Universitaria di Modena - Modena, [2]Unità di Epidemiologia Clinica, Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani - Roma, [3]Clinica di Malattie Infettive e Tropicali, Università degli Studi di Milano, ASST Santi Paolo e Carlo - Milano

Background: Retention in care is fundamental for the cascade of care. Our aims were to determine the proportion of patients lost to follow-up (LFU) between 2016-2018 and to establish their sociodemographic characteristics and the reasons for being lost.

Patients and methods: Once a year since 2016 we extracted from Clinic archives patients who didn't attend blood test and/or drug supply for at least 12 months, excluding dead. We recalled them to perform new test. A semi-structured questionnaire on reasons for being lost was proposed. Local ethical committee approved the study.

Results: Incidence of LFU was 3% in 2016 (48/1587), 3.5% in 2017 (56/1601), 3% in 2018 (51/1627); characteristics are shown in Table 1. 133 patients were lost for 155 times since 22 (16,5%) of them were lost twice.

55 times the patient (35%) moved to another city and clinic, 66 (43%) resulted unreachable, 27 (17%) accepted to perform the blood test, 4 (3%) refused, 3 persons were hospitalized for opportunistic diseases. 50% of unreachable were foreigners and 88% of them remained lost until today.

32 people answered the questionnaire: median age 44 (range 26-62), 50% African, 15 (47%) LFU more than once. Medical staff satisfied everyone, 81% raised problems with service (timetable, indications, distance, language barrier), 53% had problems with therapy (timetable, intake, pill burden, severe adverse effects), 78% raised stigma's issues on HIV status or sexual orientation, 41% felt uneasy about their perception of HIV condition.

Conclusions: LFU incidence was stable between 3-3,5% in 3 years, with an overall retention greater than 90% WHO's target. Those lost more than once outline a fragile sub-group that need dedicated program and a more careful investigation.

Reasons behind LFU are multifactorial, some depend on services, others rely on the personal experience of HIV; persistence of stigma in 2018 is unfortunately not surprising.

HIV epidemiology and retention in care

P 58 FIRST EXPLORATORY ANALYSIS OF QUALITY OF LIFE AMONG PEOPLE LIVING WITH HIV IN CALABRIA REGION

M. Mazzitelli[1], D. D'Elia[1], G. Greco[1], F. Serapide[1], C. Sorace[1], A. Vallone[2], G. Berardelli[3], G. Foti[4], C. Mangano[4], L. Cosco[5], P. Scerbo[5], A. Priamo[5], F. Bulla[5], N. Serrao[6], G. Guadagnino[7], A. Mastroianni[7], C. Torti[1]

[1]Unità Operativa di Malattie Infettive e Tropicali, Azienda Ospedaliera Universitaria "Mater Domini", Università degli Studi "Magna Graecia" di Catanzaro, [2]Unità Operativa di Malattie Infettive e Tropicali, Presidio Ospedaliero "G. Jazzolino" di Vibo Valentia, [3]Unità Operativa di Malattie Infettive, Polo Ospedaliero "Giovanni Paolo II", Lamezia Terme, [4]Unità Operativa di Malattie Infettive e Tropicali, Azienda Ospedaliera "Bianchi Melacrino Morelli" di Reggio Calabria, [5]Unità Operativa di Malattie Infettive e Tropicali, Azienda Ospedaliera "Pugliese-Ciaccio" di Catanzaro, [6]Unità Operativa di Malattie Infettive e Tropicali, Ospedale Civile "San Giovanni di Dio" di Crotone, [7]Unità Operativa di Malattie Infettive e Tropicali, Azienda Ospedaliera "Annunziata" di Cosenza

Background: Thanks to the introduction and the evolution of antiretroviral agents, HIV infection became a chronic disease. According to the most recent recommendations, reaching a good quality of life (QOL) in more than 90% patients who have a undetectable viremia has been set up as a main goal for people living with HIV (PLWH).

Objectives: Our objective was to evaluate the general QOL among PLWH and the factors that could have been associated with. A model was set up in order to assess adherence of practice to the current recommended goals (i.e. 90-90-90-90).

Materials and methods: In order to evaluate QOL, we used the WHOQOLHIV-BREF questionnaire, a tool approved and validated by the World Health Organization. Participation to the survey was proposed to all patients, older than 18 years, attending the Infectious and Tropical Diseases Units in Calabria (Catanzaro, Cosenza, Crotone, Lamezia Terme, Reggio Calabria and Vibo Valentia) for their routine clinical checks. Patients who were minor, not able to complete the questionnaire for lack of communications or affected by psychiatric disorders were excluded. For each patient, data regarding viro-immunological condition, comorbidities and life-style of patients were collected. As regard to the previous mentioned model, all data were calculated according to the prevalence of the HIV infection reported by the available literature.

Results: Between October 2018 and January 2019, participation to the study was offered to 481 patients, out of 577 who were in active follow-up in Calabria Region. One hundred and five patients refused to participate, and 67 were excluded. Three hundred and nine patients completed the questionnaire. Two hundred and fifteen (69.57%) were male. Mean age was of 49.1 years (standard deviation: 19.1). Overall, only 56.3% patients reported a good QOL. Among those, prevalent characteristics were age older than 50 years, living in a stable relationship, having no comorbidities. Among people who reported a bad QOL, lowest marks were registered in social and physical domains. No statistically significant difference for QOL was found considering virological suppression. According to data regarding prevalence of PLWH who are not still diagnosed, PLWH in Calabria region were estimated to be approximately 664 by adding those believed to be misdiagnosed to the 577 (about 85%) diagnosed and in care. Out of 309 patient (our sample), 305 (98.7%) patients were on antiretroviral treatment, among those 262 (86%) had a undetectable viremia and among those 147 (56%) reported a good QOL.

Discussion: Our preliminary data are the first that provide information about general QOL among PLWH in the Southern Italy. First, more active strategies to diagnose PLWH need to be set up. Secondly, adherence interventions on the importance of antiretroviral treatment are required. Third, targeted and further studies are necessary to establish which aspect influencing QOL can be amended.

HIV epidemiology and retention in care

P 59 EPIDEMIOLOGICAL TRENDS OF HIV INFECTIONS IN PROVINCE OF VITERBO: CONSIDERATIONS FOR THE FUTURE

G. Maffongelli[1], S. Aviani Barbacci[1], B. Koeler[1], S. Farinelli[1], R. Preziosi[1], F. Ferri[1], G. Sebastiani[1], D. Migliorini[1], L. Guastini[1], S. Dell'isola[2], E. Rastrelli[2], E. Liguori[2], A. Ialungo[2], R. Monarca[2], G. Starnini[2], L. Caterini[1]

[1]U.O.C. Infectious Diseases, Belcolle Hospital, Viterbo, Italy, [2]U.O.C.Medicina Protetta-Unit of Infectious Diseases, Belcolle Hospital, Viterbo, Italy

Background: The incidence of new diagnoses of HIV infection was high in the second half of the 1980s, reaching a peak in 1987, while since 2010 the incidence has slightly decreased.
The Department of Infectious Diseases of the Belcolle Hospital, the Belcolle AIDS Reference Center and Medicina Protetta Unit Of Infectious Diseases Belcolle, have been dealing with assisting patients with HIV infection in the province of Viterbo since 1985. In this abstract we report the epidemiological trend of HIV infection in our province from the 80s to the present day.
Material and methods: This is a retrospective epidemiological study, we show the trends of notified and treated patients with HIV infections in our department, dividing our experience into two times frames: between 1987 and 2001 and again between 2002 and 2017.
Results: From 1987 to December 2017, 1278 HIV-infected patients afferent to our services were diagnosed and subsequently treated. HIV infections have decreased from 777 cases during 1987-2001 to 501 cases in 2002 -2017, with an incidence of AIDS cases ranging from 34% (268/777) to 32% (163/501), although if we consider the last two years (2016/2017) this incidence is reduced up to 19% (19/74). Stratifying patients by risk factors during the first part of observation were recorded 524 patients (67%) in People who inject drugs (PWID), 45 (5%) in men who have sex with men (MSM)
and 122 (16%) heterosexuals, while during the second part we recorded 111 (22%) PWID, 160 (32%) MSM and 213 (41%) heterosexuals patients. Focusing on AIDS cases, the prevalence of AIDS in PWID remains very high, from 195 /524 (37%) in the first period to 57/111 (51%) during the second period. The risk factor of intra- venous drug users correlates with the development of AIDS events during both periods [yrs 1987-2001 OR 1.46, CI 95% 1.06-2.02, p value: 0.03/ yrs 2002-2017 OR 2.82, CI 95% 1.83 - 4.36, p value: <0.001].
Conclusions: Our data express the provincial reality of Viterbo and agree with the regional and Italian reality, which document a reduction in the absolute number of new HIV infections, with a substantial change in risk factors. In fact we have seen a reduction in the number of PWIDs, on the other hand there has been an increase in sexual risk. PWID however, represent a vulnerable population with social difficulties which result in difficulty in linkage to care and consequent high risk for AIDS events, despite antiretroviral treatments have been proven very effective. Therefore routes that are appropriate for the most vulnerable populations and that provide a better linkage to care are desiderable. The challenge in our future work is the HIV test education for all categories of individuals and the creation of personalized care pathways.

HIV epidemiology and retention in care

P 60 HIV INFECTION INDICATOR DISEASE-BASED ACTIVE CASE FINDING IN A UNIVERSITY HOSPITAL: RESULTS FROM THE SHOT PROJECT

M.S. Mameli[1], P. Bagella[1], A. De Vito[1], C. Fozza[2], A. Murtas[2], M.A. Montesu[3], G. Deligia[3], A.G. Fois[4], S. Negri[4], F. Filigheddu[5], N. Manzoni[6], C. Putzu[7], S. Babudieri[1], G. Madeddu[1]

[1]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Medicine, University of Sassari, [2]Unit of Hematology, Department of Medical, Surgical and Experimental Medicine, University of Sassari, [3]Unit of Dermatology, Department of Medical, Surgical and Experimental Medicine, University of Sassari, [4]Unit of Respiratory Diseases, Department of Medical, Surgical and Experimental Medicine, University of Sassari, [5]Unit of Internal Medicine, Department of Medical, Surgical and Experimental Medicine, University of Sassari, [6]Unit of Internal Medicine, University Hospital of Sassari, [7]Unit of Oncology, University Hospital of Sassari

Background: The SHOT project (Screening HIV Ospedale Territorio) is a prospective observational study started in 2017 with the purpose to implement HIV testing in hospitals.
Materials and methods: Patients were enrolled from Units of Infectious Diseases (ID), Hematology, Respiratory Diseases (RD), Dermatology and Internal Medicine of University of Sassari. Inclusion criteria were the presence of non-specific signs of infection and/or AIDS-defining comorbidities. Data were collected using dedicated forms for each Medical Specialization.
Results: We enrolled 280 patients, 188 males (67,2%) and 92 females (32,8%). Median age was 41 years old. The main reasons for screening were: fever (58) in ID and Internal Medicine; lymphadenopathy (25) in ID; non Hodgkin lymphoma (58) in Hematology, tuberculosis (7), community acquired pneumonia (7) in RD; sexually transmitted (27) diseases in Dermatology Unit. During 18 months, we diagnosed 10 new HIV infections with a prevalence in the study population of 3,5%. Five patients were diagnosed in RD Unit, three of them were males, aged 40 to 43 years, affected by Pneumocystis jiroveci pneumonia (PjP), while females were a 57 years old woman with a bilateral pleural effusion, the other one had an invasive pneumoccocal disease. A 29 years-old African woman with fever of unknown origin was diagnosed in ID. Two patients were tested and diagnosed in the Unit of Internal Medicine because of fever in a 72 years-old male, and because of diarrhea associated with a lymphadenopathy in a 66 years old man with an acute HIV infection. We also recruited one patient from critical care unit and another one from urology ward: the first one was hospitalized because of respiratory failure due to a PjP, the latter was a 73 years old man with a diagnosis of bladder cancer. In both cases HIV screeening proposal came from the Infectious Disease consultant. Five had a CD4 count <100/mm3, one <200/mm3, one <300/mm3, two >300/mm3 and one >900 mm3. Eight out of 10 patients had a viral load >100.000 cp/ml. Among AIDS presenters, CDC stage was C3 in four and C2 in one patient. All patients started promptly a combination antiretroviral regimen and obtained an undetectable HIV RNA. Nine out of 10 patients are currently on follow up in our outpatient clinic. The African young woman was lost to follow up almost a year ago.
Conclusions: The prevalence of HIV infections in the study population is surprisingly high considering the small number of individuals tested. Although most of patients were diagnosed with advanced stage, at least four of them would have been probably remained undiagnosed if not included in the study.
Therefore, proactive indicator disease guided HIV testing is a useful strategy to increase the number of HIV diagnosis in hospital settings.

HIV epidemiology and retention in care

P 61 CARE IS ALL YOU NEED: FACTORS ASSOCIATED WITH LOSS TO FOLLOW-UP IN A COHORT OF NEWLY DIAGNOSED HIV-POSITIVE PATIENTS

G. Ferraro, L. Badia, D. Testi, P. Malosso, B. Granozzi, G. Verucchi, P. Viale, L. Calza

Policlinico Sant'Orsola-Malpighi, Bologna

Background and aim: universal start of antiretroviral therapy (ART) is recommended after HIV diagnosis. Anyway, optimal timing of initiation and potential benefit of a very rapid initiation (such as same-day treatment) are still debated, especially in countries where retention in care is high.
Aim of our study was to investigate factors associated with loss to follow-up and potential correlation with timing of ART initiation in a cohort of patients recently diagnosed with HIV.
Materials and Methods: we retrospectively reviewed data from new HIV diagnosis from June 2016 to June 2018 by our Infectious Diseases Unit in Bologna. AIDS presenters, acute/primary HIV infections and pregnant women were excluded from this analysis; patients who refused to start an active ART after the diagnosis were excluded too. Logistic regression was used to analyze factors correlated with a loss to follow-up after 6 months from the diagnosis.
Results: We enrolled 100 patients. 19% were cis-women, 79% cis-men and 2% trans-women. 65% were italians, the percentage of MSM was 57%, while the median age at the diagnosis was 33 with a range of 18-69. 86% of patients were still in care 6 months after diagnosis; at univariate analysis a positive correlation between being retained in care after 6 months and the age at the time of the diagnosis (β=0.12, p=0.006) was found. On the other hand, being foreigner and the days from the test to the start of ART showed a negative correlation (β= -1.42, p=0.019 and β=-0.01, p=0.021 respectively). In the multivariate model, the only factor which resulted statistically significant with a positive correlation was the age at the time of the diagnosis of the HIV infection (β=0.09, p=0.04).
Conclusions: Young age seems a risk factor for loss to follow-up in our cohort, while time of ART initiation, gender, and ethnicity seem to play a minor role.
Strategies to improve retention in care in the younger population are needed to keep the rate of retention in care above 90%.

HIV immunology and immune-based therapies

P 62 SEROREVERSION FROM POSITIVE TO NEGATIVE WESTERN BLOT HIV-1 POL

F. Rinaldi[1], S. Rolla[2], L. Galli[3], A. Poli[3], C. Muccini[4], A. Mastrangelo[4], C. Tavano[2], A. Lazzarin[3], A. Castagna[3,4], A. Bartoloni[1,5]

[1]University of Florence, Department of Experimental and Clinical Medicine, Florence, Italy, [2]IRCCS San Raffaele Scientific Institute, Laboratory of Microbiology and Virology, Milan, Italy, [3]IRCCS San Raffaele Scientific Institute, Infectious Diseases, Milan, Italy, [4]Vita-Salute San Raffaele University, Infectious Diseases, Milan, Italy, [5]Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, Italy

Background: The aim of this study was to evaluate the proportion of seroreversion in HIV-1 Pol from positive to negative after a long exposure to antiretroviral therapy (ART).
Materials and methods: Retrospective analysis on HIV-1 chronic infected patients (pts) with a first positive western blot (WB) HIV-1 Pol and a second WB determination performed at least 6 months apart.
Immunological changes between the two WBs were calculated by mixed linear regression models.
Characteristics were described by median (IQR) or frequency (%). A multivariate logistic regression was performed to assess factors associated with the switch.
Results: Overall, 140 pts were included: 74% males; at first WB, the age was 42 (32-49) years, with CD4+ 444 (273-640) cells/µL, CD8+ 855 (583-1227) cells/µL, CD4+/CD8+ ratio 0.52 (0.28-0.82).
The time interval between the two WBs was 69 (26-175) months; at second WB, subjects had been infected with HIV since 14.7 (6.3-19.4) years, treated with ART for 12.0 (3.7-18.3) years, 127 (91%) pts had HIV-RNA <50 cps/mL.
Twenty-two (15.7%) pts had a seroreversion in HIV-1 Pol from positive to negative. At first WB, no differences were observed between pts with and without seroreversion (Table 1); at the second WB, pts who seroreverted had lower CD8+(p=0.043) and higher CD4+/CD8+ ratio (p=0.011) and a slightly significance in higher CD4+ (p=0.094) and a greater increase (slope) in CD4+/CD8+ ratio [with seroreversion: 0.07 (95%CI=0.04-0.09); without seroreversion: 0.04 (95%CI=0.02-0.05); p=0.092]. At least one HIV-RNA determination >1000 cps/mL occurred in 5 (22.7%) and 36 (30.8%) pts among those who seroreverted during the time interval between the two WBs and those who did not, respectively (p=0.612).
By multivariate analysis, the switch to a negative HIV-1 Pol was associated with greater recovery in CD4+/CD8+ ratio [AOR per 0.1-point per year higher=1.64 (95%CI=1.22-2.20), p=0.001] and the absence of viral load>1000cps/mL between the two WBs [AOR Yes vs No= 0.06 (95%CI=0.01-0.46), p=0.007] after adjustment for age, gender, months to ART start, years of ART and CD4+/CD8+ ratio at first WB.
Conclusions: A seroreversion in HIV-1 Pol was observed in 16% of pts with a long exposure to ART and it was associated with a greater immunological recovery and a lower occurrence of viral failure during ART.

HIV immunology and immune-based therapies

P 63 DIFFERENTIAL NKP44 EXPRESSION ON PDC OF HIC PATIENTS ASSOCIATES WITH CONSERVED IFNA PRODUCTION AND IS CORRELATED TO CD4-PROTECTIVE NKP44 EXPRESSION ON NK CELLS

F. Bozzano[1], F. Marras[2], I. Bonaccorsi[3], E. Pontali[4], L. Nicolini[5], A. Di Biagio[5], C. Dentone[6], G.C. Orofino[7], L. Moretta[1], G. Ferlazzo[8], A. De Maria[5,9,10]

[1]IRCCS Bambino Gesù Children's Hospital, Rome, Italy, [2]Istituto Giannina Gaslini,Genoa, Italy, [3]Laboratory of Immunology and Biotherapy, Department of Human Pathology, University of Messina, Messina, Italy, [4]S.C. Malattie Infettive, Ospedale Galliera, Genoa, Italy, [5]Clinica Malattie Infettive, Ospedale Policlinico San Martino Genova, Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy, [6]U.O.C. Malattie Infettive, Ospedale Sanremo, V.priv.Barabino 15, Sanremo (IM), Italy, [7]U.O.C. Malattie Infettive, Ospedale Amedeo di Savoia, Torino, Italy, [8]Dipartimento di Patologia Umana, University of Messina, Messina, Italy, [9]Center of Excellence for Biomedical Research (CEBR), University of Genova, Genova, Italy, [10]Department of Health Sciences, DISSAL, University of Genova, Genova, Italy

Background: HIV-1 infection is increasingly becoming under cART treatment a chronic disease with prevalent metabolic/cardiovascular morbidity. There is however active interest in controlling and purging the HIV-DNA reservoir. HIV-1 controllers (HIC) (Elite Controller,EC); Long-term non progressor,LTNP) represent a model of efficient virus containment. We have recently shown a specific involvement of Natural Killer cell (NK)-mediated innate mechanisms in the containment of HIV RNA and DNA. Plasmacytoid Dendritic Cells (pDCs) are among the first innate cells encountering HIV-1 upon mucosal challenge and are the main IFNa producers. They share with NK cells one receptor, NKp44, which is divergently regulated on NK cells of HIC vs. progressors. NKp44 has opposite function in NK cells and pDCs. We here studied NKp44-controlled pDC function in HIV and PP patients to understand its participation to the control of HIV-1

Materials and methods: PBMC from 12 HIC and 15 HIV-1-infected PP were obtained during different programs of follow-up for surveillance and treatment of HIV-1 infection. PBMC from Healthy donors (HD, n.15) were obtained from local blood bank. Flow cytometry and specific mAbs was used to analyse NKp44 induction on pDC and on NK cells. ELISA assay was performed to evaluate pDC IFNa production. IL6, IL8, TNF-a were evaluated in supernatants by Flowcytomix Human Th1/Th2 KIT (eBiosciences-Bender). Cells were cultured in vitro in the presence of IL-2 for NK cell activation, or of IL-3 pDC activation.

Results: We first analyzed by flow cytometry the expression of NKp44 and BDCA2 on pDC in PBMC from HD to verify activation. Group analysis of NKp44 expression after IL-3 activation confirmed a considerably lower induction on pDC in HIC patients compared to PP (p=0,014, U-test). NKp44 expression on NK cells and on pDC after activation, were correlated. In addition, dramatic reduction of IFNα production upon pDC NKp44-mediated triggering was observed in PP vs,HIC (4,33±0,43; 395,6±4 pg/ml PP vs HIC; p<0.01). The low level expression of NKp44 on HIC pDCs was still sufficient to inhibit the production of IL-6 and TNFa in HIV, while NKp44 crosslinking was unable to block pDC production of IL-6 and TNFa in PP.

Conclusions: The reduced NKp44 expression on pDC in HIC patients parallels its regulation on NK cells and underlies relevant functional consequences. This regulation of NKp44 expression avoids complete shut off of IFN-α production under stimulated conditions thus controlling virus replication, and at the same time is sufficient to inhibit proinflammatory and virus-inducing cytokines including TNFα and IL-6. PP patients on the contrary have a complete inhibition of IFN-α production but fail to block TNFα/IL-6 production. The peculiar regulation of NKp44 expression on pDC from HIC therefore provides a new synergistic mechanism providing innate support to CD8 +CTL and NK cell function in the control of HIV replication and of HIV reservoir size.

HIV immunology and immune-based therapies

P 64 LUCIFERASE IMMUNOPRECIPITATION SYSTEM (LIPS) ANTI-HIV ANTIBODY ASSAY DURING TREATMENT INTERRUPTION

A. Mastrangelo[1,3], P. Burbelo[2], L. Galli[4], A. Poli[4], C. Muccini[1], V. Spagnuolo[1,4], R. Caccia[3], F. Turrini[3], A. Bigoloni[4], A. Galli[4], A. Castagna[1,4], P. Cinque[3,4]

[1]Vita-Salute San Raffaele University, Milan, Italy, [2]Dental Clinical Research Core, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, Maryland, [3]Neurovirology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy, [4]Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy

Background: Currently available assays lack of specificity in determining the so-called "active" HIV reservoir. Luciferase immunoprecipitation system (LIPS) assay allows a reliable quantification of circulating antibodies. Previous reports have suggested that this assay could be a measure of HIV reservoir, due to the likely correlation between levels of anti-HIV antibodies and the antigen burden. Our aim is to investigate by LIPS, among patients who underwent analytic treatment interruption (ATI), the evolution of anti-HIV antibody response and its association with time and magnitude of viral rebound (TVR and MVR, respectively), and other viro-immunological parameters.

Materials and methods: This study evaluated 9 patients with chronic HIV-1 infection, who underwent ATI (APACHE study). Inclusion criteria were HIV-RNA<50 copies/mL for ≥10 years, no plasma residual viremia for ≥5 years, CD4+ >500 cells/μL, HIV DNA <100 cps/106 PBMC. Co-receptor R5 tropism was determined at inclusion on proviral DNA from V3 sequencing and Geno2pheno algorithm, and expressed as False Positive Rate (FPR).

We exploited LIPS assay to quantitatively detects antibodies against 7 HIV antigens (gp120, gp41, matrix [MA], protease [PR], integrase [INT], p24, retrotranscriptase [RT]). Antibodies were tested in plasma samples collected at baseline (BL), viral rebound (VR) and resuppression (RS). Wilcoxon signed rank test was used to test for significant changes in antibody level. Linear relationships were evaluated by Spearman correlation coefficients.

Results: Patients experienced VR a median of 21 days after TI (range: 14-56); all patients restarted cART and achieved HIV-RNA<50 copies/mL a median of 88 days after VR (range: 15-197). The median MVR was 4.84 log10cp/mL (IQR 3.47-6.47).

None of the antibodies showed significant changes between the different time points, except for a significant increase in anti-PR values at RS compared to BL (Table 1).

High BL values of anti-gp120 tended to be associated with longer TVR (r=0.6, p=0.068, Figure 1) and anti-RT and anti-p24 at RS were significantly associated with shorten TVR (p<0.05). Values of all the other antibodies at any time point were not associated with TVR. For none of the antibody at any given time-point was there an association with MVR, CD4+ T-cell count at BL, nadir CD4+, years of HIV infection or years on effective cART. Lower values of FPR, suggesting a R4-tropic virus, were associated with higher anti-INT, anti-RT and anti-MA levels at BL. Correlation matrix of anti-HIV antibody panel is shown in Figure 2.

Conclusions: Apart from a modest increase in anti-PR, we have found no differences in the anti-HIV antibodies landscape pre- and post-ATI. No consistent associations were observed with either TVR or MVR, except for a tendency to a longer viral suppression in patients with higher levels of anti-gp120 antibodies. The presence of a virus predicted as R4-tropic was associated to a heightened antibody response.

HIV immunology and immune-based therapies

P 65 ANALYSIS OF THE ROLE OF ΓC-CYTOKINES IN HIV LATENCY ESTABLISHMENT IN DIFFERENT T CELL SUBSETS

G.M. Butta[1], M.C. Crosti[1], M.M. Hernandez[2,5], V. Simon[2,3,4], R. De Francesco[1,6], L. Manganaro[1]

[1]INGM-Istituto Nazionale di Genetica Molecolare, Milan, Italy, [2]Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, New York, USA, [3]Global Health and Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai, New York, USA, [4]Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, USA, [5]The Graduate School of Biomedical Sciences, Icahn School of Medicine at Mount Sinai, New York, USA, [6]Department of Pharmacological and Biomolecular Sciences, Università degli Studi di Milano, Italy

Background: HIV integrates into the host genome to create a persistent viral reservoir. Stimulation of CD4 T lymphocytes with common γc-chain cytokines renders these cells more susceptible to HIV infection making them the key component of the reservoir itself.
Specifically, we and others observed that IL-15 and IL-7 stimulation relieve an early block to infection by inducing the phosphorylation/inactivation of the restriction factor SAMHD1 in a JAK dependent manner.
Our previous studies with high-resolution single cell immune profiling using Mass Cytometry by time of Flight (CyTOF) revealed that IL-15 stimulation altered the composition of CD4 T cell populations by increasing proliferation of memory CD4 T cells, including CD4 T stem memory cells (CD4 TSCM).
Among the different γc-chain cytokines, IL-15 is specifically up-regulated during primary HIV/SIV infection, when the reservoir is established. We hypothesize that γc-chain cytokines play a pivotal role during latency establishment by facilitating infection of specific CD4 T cell subsets.
Material and Methods: Peripheral blood mononuclear cells are isolated from buffy coats from anonymous healthy donors, CD4 T cells are purified using CD4 antibody-coated magnetic beads. CD4 T cells will be stimulated with equimolar amounts of IL-2, IL-15, IL-7.
CD4 T lymphocytes infection is carried out with the Second Generation Dual-Fluorescent HIV (HIV-GKO, a kind gift from Dr. Verdin) that carries csGFP under the control of the HIV LTR promoter and Kusabira Orange (mKO) under the control of the cellular promoter EF1α. Cells productively infected are characterized by expression of both csGFP and mKO, while latently infected cells express only mKO. Four days after infection, cells are stained with a panel of antibodies to differentiate the various T cells subsets.
Results: We observed that primary memory CD4 T cells, cultured in IL-2, IL-7 and IL-15, support latent and productive infection with HIV-GKO. IL-2 stimulated CD4 T cells displayed a higher percentage of LTR silent proviruses. However, analysis of HIV infection in the different memory T cell subsets pointed to IL-15 increasing the frequency of TSCM compared to central and/or effector memory T cells in both the latent and productive compartment.
Conclusions: Taken together, the cytokine milieu in which CD4 T cells reside influence the establishment of HIV persistence by facilitating the infection as well as the proliferation of infected T cells with stem cell properties, thus creating a self-renewing reservoir.

HIV immunology and immune-based therapies

P 66 CHARACTERIZATION OF HIV-1 SPECIFIC T-CELL RESPONSES IN AN ITALIAN COHORT OF HIV-1 NATURAL CONTROLLERS

D. De Battista[1], S. Heltai[1], F. Sironi[1], A. Riva[2], M. Tinelli[3], S. Nozza[1], G. Tambussi[1], S. Ghezzi[1], G. Poli[4], P. Lusso[5], M.S. Malnati[1]

[1]OSR Scientific Institute, Milan Italy, [2]L. Sacco Hospital, University of Milan, Italy, [3]Hospital of Lodi, Lodi Italy, [4]Vita-Salute San Raffaele University, School of Medicine, Milan, Italy, [5]NIAID-NIH, Bethesda MD USA

HIV-1 infection is associated with a progressive decrease of CD4 T-cell count associated with an increase in viral load. However, a small proportion of Natural Controllers (NC) maintain a high level of CD4 and a low viral load for several years in the absence of antiretroviral therapy. Our study characterized the HIV-1 specific CD8 T-cell response in three Italian cohorts with a different pace of disease progression. Immunodominant Gag- and Nef-specific responses as well as Tat-specific responses were investigated. Chronically HIV-infected patients under therapy (CHIwT) showed lower Gag- and Nef-specific responses compared to NCs and therapy-naïve (Naïve) patients ($p<0.05$). NCs showed a higher frequency of Tat responses (56.4%) than CHIwT (20%, $p<0.01$) and Naïve (16%, $p<0.01$), with a significant increase of Tat-specific IFN-γ-producing T cells (median 80, IQR 13-457, $p<0.05$), which correlated inversely with plasma viral load ($r=-0.3231$, $p=0.0346$). Fully differentiated Tat-specific CD8 T cells (expressing CD45RA) were higher in NCs (median 0.29% of total CD8, IQR 0.2-0.54%) than in Progressors (median 0.17%, IQR 0.11-0.38%, $p<0.01$), correlating inversely with viral load ($r=-0.4202$, $p=0.0208$). Interestingly, Tat-specific responses showed a peculiar pattern in NCs, with a high prevalence of two distinct functional subsets, CD45RA+ GzB+ IFN-γ+ MIP-1β+ CD8+ T cells (89%) and CD45RA+ GzB- IFN-γ+ MIP -1β+ CD8+ T cells (67%), that were absent in Progressors. In conclusion, robust Tat-specific T-cell responses with unique features are associated with the control of HIV-1 viremia in Italian NCs.

HIV pathogenesis

P 67 THE EFFECT OF SEMINAL PLASMA ON COLONIC MUCOSA AND ITS POSSIBLE ROLE IN HIV-1 TRANSMISSION

V. Iannone[1], S. Dispinseri[1], M. Cavarelli[2], C. Moog[3], C. Foglieni[4], U. Elmore[5], S. Nozza[6], M. Alfano[7], P. Viganò[8], G. Scarlatti[1]

[1]San Raffaele Scientific Institute, Division of Immunology, Transplantation, and Infectious Diseases, Viral evolution and transmission, [2]CEA, Center for immunology of Viral infections and Autoimmune diseases (ImVA) CEA/DRF/Universite Paris Saclay/JACOB/IDMIT INSERM U1184, Fontenay-aux-Roses, [3]U1109 INSERM/UDS Faculte de Medecine, Strasbourg FRANCE, [4]San Raffaele Scientific Institute, Cardiovascular Research area, Strategic research on heart failure, [5]San Raffaele Scientific Institute, Division of Experimental oncology, Gastrointestinal surgical oncology, [6]San Raffaele Scientific Institute, Infectious diseases Area, [7]San Raffaele Scientific Institute, Division of Experimental oncology - URI - Urological Research Institute, Bladder cancer, [8]San Raffaele Scientific Institute, Division of Genetics and Cell biology, Reproductive sciences Lab

Background: Sexual HIV-1 transmission occurs through the genital and intestinal mucosa. We described previously that in the colonic epithelium HIV attracts myeloid cells, which catch HIV. Human seminal plasma (HSP) rich in pro-migratory and pro-inflammatory factors is a source of virions in HIV-infected individuals. These may induce alterations of the colonic mucosa, activation of immune cells, and in turn affect HIV transmission. Here we study the role of HSP and HIV on epithelial integrity and Macrophage (Mc) and Dendritic cell (DC) migration in the mucosa.

Materials & Methods: Ex-vivo colorectal mucosal tissue cultures are apically treated with:HSP from HIV+, therapy naive individuals, from HIV negative, fertile individuals, and from randomly identified individuals, or with HIV culture supernatant. Structural epithelial integrity is evaluated with H&E staining. JAM-A, E-CAD, Mc and DC staining is analysed by confocal microscopy. 21 migratory/inflammatory factors are quantified by ELISA in HSP.

Results: HSP from the 3 groups and HIV did not affect the mucosal structure. JAM-A and E-CAD were evenly distributed regardless of the stimuli. DC migrated to the apical surface, while Mc did not. CXC and CC chemokines and Transforming growth factor Beta were elevated to different levels in all HSPs, while Interleukins were low.

Conclusion: HSP and HIV do not perturb the mucosal integrity, but selectively affect migration of immune cells. Further studies will clarify the role of the single HSP factors and of the immune cells in modulating HIV infection.

HIV pathogenesis

P 68 NATURAL HIV CONTROL IN A HIV/HCV CO-INFECTED PATIENT WITH A SEVERE LEUKOPENIA: A CASE REPORT

C. Agrati[1], V. Mazzotta[2], V. Bordoni[1], I. Abbate[3], A. Amendola[3], F. Forbici[3], E. Cimini[1], R. Casetti[1], MR Capobianchi[3], M. Bibas[2], A. Antinori[2]

[1]Laboratory of Cellular Immunology and Pharmacology, INMI "L. Spallanzani" - IRCCS, Rome, [2]Clinical Department, INMI "L. Spallanzani" - IRCCS, Rome, [3]Laboratory of Virology, INMI "L. Spallanzani" - IRCCS, Rome

Background: The majority of naïve HIV infected patients require antiretroviral treatment to control HIV replication; several co-factors, such as HCV co-infection and leukopenia are known to contribute in worsening HIV disease progression and clinical outcome. We here describe one HIV/HCV co-infected patient with a severe leukopenia, able to control HIV replication without any antiretroviral treatment. We aimed to define the hematopoietic progenitor cell features and viro-immunological properties in order to characterize his protective immune profile.

Materials and Methods: The frequency of CD34+Lin- hematopoietic progenitor cell subsets were analyzed by flow cytometry and their functional capabilities were tested by Colony-Forming Cell (CFC) Assays. CD4 and CD8 T cell profile was analyzed by polycromatic flow cytometry, and HIV specific response was quantified by polyfunctional analysis and ELISpot assay. HIV-RNA and HIV-DNA were analyzed by molecular assays.

Results: A caucasian 63-years old male was diagnosed for HIV (HIV-RNA undetectable and CD4 T cell count 191/mmc, 34%) and HCV active infection (HCV-RNA: 101027 cp/ml, genotype 1a) in May 2018. The patient refused antiretroviral treatment. In September 2018, the patient was admitted to hospital for bacterial pneumonia with fever, severe leukopenia (leukocytes: 900/mmc) and thrombocytopenia (Platelets: 33000/mmc). HIV-RNA persisted lower than 30 cp/ml. The severe leukopenia was associated with a general low growth capability of bone marrow derived hematopoietic progenitors and with a low frequency of multipotent lymphoid precursors, suggesting a possible impairment of leukocyte replenishment. T cells were few and dramatically skewed toward an effector profile, suggesting a strongly engaged immune system. Finally, a very high frequency of HIV-specific T cells (3.5 %) showing a polyfunctional profile was found: 70% of HIV specific T cells are able to simultaneously mediate 4 different functions (IFN-γ, TNF-α MIP-1β, CD107a).

Conclusion: We presented a case of one HIV/HCV co-infected patient with a severe leukopenia but able to control HIV replication in the absence of any antiretroviral therapy. Despite a low CD4 T cell count, his cell-mediated immune response is strongly skewed toward effector functions and showed a high frequency of HIV-specific CD8 T cells with polyfunctional profile. This report highlights the capability of specific immune response in controlling HIV replication even in the presence of co-morbidities.

HIV pathogenesis

P 69 SERUM MICROVESCICLES AS NEW INFLAMMATION MARKERS IN HIV INFECTION

A. Auricchio, K. Falasca, C. Ucciferri, M. Pontolillo, F. Vignale, J. Vecchiet
Clinics of Infectious Diseases, PO SS. Annunziata, "G. d'Annunzio" University, Chieti

Background: The Microvescicles (MVs) are extracellular vescicles released by human cells using pollulation. They are made of a cellular bilayer of phospholipids containing proteins and genetic material (mRNA ans miRNA). The MVs have several functions: intercellular communication in inflammation, immunodeficiency, tumor growth and viral infections. The MVs set the cell adhesion, the cellular stress protection and several coagulation factors. That's why the study of MVs' composition could be used as diagnostic, prognostic and therapeutic tool in HIV infection characterized by a chronic inflammation.
Aim of the study: The aim of the study is to survey the sieric levels of MVs derived from endothelium, platelets and leukocytes to define which of them are activated or inhibited analyzing the proteic arrangement. We want to clarify the role of MVs in inflammation and in particular the correlation between MVs and chronic inflammation.
Material and methods: HIV-positive patients were enrolled at the Infectious Diseases Clinics in Chieti. All the patients were under stable antiretroviral therapy, with undetectable serum virus for at least a year. We combined the patients with HIV-negative subjects with the same chatacteristics.
We used cytometry to relieve the total blood level of MVs and the different subtypes at the Citometry Unit of CeSI-MeT in Chieti. The blood was stored in Trucount Tubes containing EDTA. We used MitoTracker and DRAQ5 to take over tre presence of MVs.
Using a proteomic analysis we identified the activated and the inhibited MVs.
We took into consideration three subpopulations: MVs CD31+ from endothelium (EMVs), MVs CD45+ from leukocytes (LMVs) and MVs from platelets.
Discussion and Conclusion: This study highlights a significant increase in the level of the proteins of the acute phase of inflammation in the HIV+ patients. All the activated proteins have an important role in the inflammatory response to the infection. NF-kB, LIF and IRF2 stimulate the viral replication, while PPAR-a and OGA inhibit it.
The inhibited proteins have anti-inflammatory effects. The circulating levels of total MVs, EMVs and LMVs were lower than in the HIV-negative population. The levels of MVs derived from platelet were higher than the same MVs in the HIV-negative population. That's why HIV infection induces the production of mediators thad feed the chronic inflammation and the viral replication. These two effects are connected since the inflammation itself induces the viral replication using cytokines such as TNF-a and IL-1. The HIV infection can inhibit the MVs'proteins whit anti-inflammatory effects.

HIV pathogenesis

P 70 CMV VAGINAL SHEDDING IN A COHORT OF HIV WOMEN UNDER SOPPRESSIVE ART

S. Vita[1], P. Hawan[2], C. Mascia[2], A. Carraro[2], R. Marocco[1], B. Kertusha[2], L. Fondaco[2], I. Pozzetto[2], L. Ansaldo[2], G. Masci[2], M. D'Achille[1], V. S. Mercurio[1], M. Lichtner[1,2]

[1]S.M.Goretti Hospital, Latina, [2]Sapienza University of Rome, Rome

Background: Asymptomatic cytomegalovirus (CMV) replication occurs frequently in the genital tract of human immunodeficiency virus (HIV)–infected men but fewer data are available about the frequency of CMV shedding in the genital tract of HIV-infected women, or about factors affecting vaginal CMV shedding. Aim of the study was to evaluate the prevalence of CMV vaginal shedding in HIV-positive women in effective antiretroviral treatment and systemic and mucosal immuno-inflammatory status related to it.

Materials and Methods: The study population was enrolled at the UOC of Infectious Diseases of the Santa Maria Goretti Hospital in Latina between October 2018 and February 2019. 38 women, 17 of whom were infected with HIV on effective ART and suppressed viral load and 21 healthy subjects with similar age were recruited. Blood samples (BS), vaginal lavages (VL) were collected. We analyzed on BS: lymphocyte subpopulations, sexual hormone levels, CMV IgG level, CMV-DNA PCR. On VL we analyzed: CMV DNA PCR. Moreover on BS and VL IL-6, IL-1b, sCD163, sCD14, CXCL-10, IL-8 level were detected. Non-parametric tests were used for statistical analysis.

Results: The seroprevalence of CMV infection in HIV women was 100% while in HD 71% (p=0.01). The level of CMV IgG level was higher in HIV women than HD (p=0.003). Neither HIV women nor HD presented CMV vaginal shedding. Only one HD showed a presence of CMV DNA into the blood.

Plasma levels of cytokines and soluble proinflammatory factors, such as CXCL-10, sCD163, IL-6 and were significantly higher in HIV positive plasma (p=0.0004, p=0.001, p<0.001). Regarding VL a higher level of IL-6 and IL-8 was found in HD (p=0.0009, p=0.02).

In HIV women CMV IgG levels correlated with IL-1b in plasma (p=0.03), no other correlation with other parameters studied were found.

Conclusions: The prevalence of CMV was higher in HIV-infected women, and CMV IG levels were also found to be higher, although the viral shedding was absent. Moreover CMV IgG levels already related in literature to classical markers of monocytes-macrophage activation seem to be correlated even at IL-1b a cytokine involved into the recruitment of CMV-susceptible cells facilitating virus dissemination and it has been related as mediator at the aging process. A higher number of HIV women CMV positive and negative needed to confirm these data.

HIV prevention (PrEP and PEP)

P 71 ANLAIDS LAZIO AND THE EXPERIENCE IN THE FIELD OF BACHELOR DEGREE IN NURSERING

R. Galipò[1], S. Bartolucci[2], E. Farinola[1], P. Ferri[1], S. Ondedei[1], C. Salvatori[1], M. A. Pulimeno[2], M. Ghenzer[1]

[1]Anlaids Lazio, Roma, [2]Opi di Roma

Introduction: Health awareness between young people: this is one of the main goals of Anlaids Lazio, that for years has been promoting information campaigns with a particular eye for teens and young ones. Within the academic year 2018/19, it developed a prevention project dedicated to the students of the Bachelor Degree in Nursing within the Lazio region in cooperation with Opi Roma, in order to provide information and also training for young people about to become health workers. The project stems from the awareness that nurses are among those professionals whose operational potential is widely recognized in its technical, relational and educational nature. The main skills are in fact the prevention of diseases, assistance of the sick person as well as health education.

Method: The Project involves In/Formative meetings lasting about three hours for each year of attendance, led by a multidisciplinary team. Before carrying out the meetings, the students are given a pre-intervention questionnaire in order to understand what young people know about HIV infection and other STIs and about the transmission and prevention procedures. The collaboration with OPI, will then ensure the new graduates a constant training, through ECM courses targeted on the related topics.

Results: The initiative, still underway, is in its first year of implementation. There are 12 University Degree Courses taking part in the initiative, for a total of 778 participating students. Most students are under the age of 30. The data analyzed up to now have been around 400, in particular they shows that:

- 20% of students thinks that HIV is only found in the blood;
- 18% considered the oral-genital intercourse not at risk;
- 15% considered that vaginal secretions are not contagious;
- about 25% thinks that kisses are at risk for HIV infection;
- almost 15% considered it risky to embrace a person with HIV and that the same can be recognized from the physical appearance or that only homosexual people can be infected;
- over 30% have confused the person with AIDS with the person with HIV.

The students also made an important statement, almost everybody recognized the importance of protecting themselves from the infection with a correct use of the condoms, with a small percentage of exception (5%) who thinks that see the contraceptive pill a method of protection from the infection

Finally, many doubts have emerged about HPV infection and other STIs, some (such as chlamydia and gonorrhea) which are unknown to a percentage of 12% of students.

Conclusions: In conclusion we can affirm the importance of the educational process to protect health as an inseparable element in the formation of young people. Therefore such a project can be seen as a very important experience for the whole young population; the professional aspect becomes more and more essential as we can state that there is a huge lack of general information about such delicate issues within the sexuality sphere.

HIV prevention (PrEP and PEP)

P 72 EFFICACY, SAFETY AND RISK COMPENSATION IN SUBJECTS USING PREP IN MILAN: A CASE-CONTROL STUDY

R. Rossotti, M. Merli, L.G. Chianura, M.C. Moioli, M. Cantone, S. Chiappetta, F. Crippa, D. Motta, C. Orcese, A. Pazzi, G. Travi, B.P. Vigo, M. Puoti

Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan

Background: Emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) has been licensed in the US as pre-exposure prophylaxis (PrEP) since 2012. In Italy, its use expanded after patent expiration and the availability of generic drugs. Despite the proven high efficacy in preventing HIV infection, PrEP carries some concerns about toxicity and risk compensation with consequent increase in sexually transmitted infections (STIs). Aims of present study: compare safety and efficacy of FTC/TDF in PrEP users (cases) and in HIV infected patients (controls); compare incidence rates (IR) of STIs.

Methods: All subjects who started FTC/TDF as PrEP from 2018 with at least one month of follow up were included as Cases. Controls were HIV-positive subjects attending our Outpatient Department and who started cART from 2013 up to 2018. Controls were paired according to risk factor for HIV acquisition and age. Controls were matched 1:2:1 according to the backbone (2 FTC/TDF and 1 abacavir-based). Demographic and clinical features were collected. Descriptive statistics and non-parametric (Chi-squre and Mann-Whitney as appropriate) tests were used. IR for STIs per patient/year (PY) was calculated.

Results: 23 Cases and 69 Controls were included in the analysis; MSM were the 95.7%. Median age was 32 years (IQR 29-35), 21.7% was not Italian and 21.7% used pre-exposure prophylaxis at least once before PrEP. Controls were well balanced in terms of demographic, previous STI history and behavioral features (except cigarette smoking that was more common in Controls than in Cases, 50.7% versus 13.0%, p=0.003). Controls have a median CD4 count of 435 cell/mmc (IQR 214-575) with a median HIV RNA of 4.6 log10 cp/mL (IQR 3.8-5.3). Dolutegravir was the most common third drug (47.8%). No difference in terms of adverse events (AE) was observed (26.1% in Cases and 21.7% in Controls, p=0.667), while a tendency towards significance was observed for AE leading to drug discontinuation (0% in Cases and 15.9% in Controls, p=0.069).

No HIV infection was registered in Cases. Over the course of 5.92 PY on PrEP, the IR of STIs was 2.87 (95% CI 1.69-4.53) per PY; over the course of 165.45 PY on cART, the IR of STIs was 0.45 (95% CI 0.35-0.56) per PY, significantly lower than in Cases (p<0.0001). In Controls the most common STI was syphilis (40.6%), while in Cases was non-gonococcal proctitis (30.4%), p=0.025.

No differences in terms of HPV anal infection were observed (81.3% in Cases and 100% in Controls, p=0.578). Although low, middle and high risk HPV distribution was similar in the two groups (p=0.719), Controls had a higher diversity in genotypes (5 per each individual versus 2, p=0.002) and had a tendency to have major benefit from vaccination, that would be protective for 81.8% of Controls and 50.0% of Cases (p=0.093).

Conclusions: PrEP resulted well tolerated and effective, but the higher IR of STIs confirms the concerns about risk compensation issues.

HIV prevention (PrEP and PEP)

P 73 NO INCREASE IN PREVALENCE OF CHLAMYDIA TRACHOMATIS AND NEISSERIA GONORRHOEAE INFECTIONS AFTER 6 MONTHS OF FOLLOW UP IN A COHORT OF MSM WITH HIGH PREVALENCE OF RISK FACTORS FOR HIV ACQUISITION EVALUATED IN A PREP COMMUNITY-BASED SERVICE IN ITALY: PRELIMINARY DATA FROM THE SEX-CHECK STUDY

P. Malosso[1], L. Badia[1], B. Granozzi[1], R. Pascale[1], V. Guardigni[1], A. Maccaro[1], G. Fornaro[1], B. Tazza[1], P. Viale[1], G. Verucchi[1], G. Corbelli[2], S. Mattioli[2]

[1]Department of Medical and Surgical Science - Alma Mater Studiorum – University of Bologna, [2]PLUS Onlus, Bologna

Background: PrEP implementation in Italy is limited by the lack of data about prevalence and incidence of sexually transmitted infections (STIs) and risk factors for HIV in HIV-negative men who have sex with men (MSM) and transgender women (TGW). Community-based programs could be helpful to reach this population. Our purpose was to assess sexual behavior, risk factors, prevalence and incidence of STIs in a cohort of HIV-negative MSM with high risk sexual behavior, evaluated in a community-based service.
Methods: We recruited HIV-negative MSM and TGW with one or more risk factors for STIs and HIV. Enrolled individuals, at baseline and after 3, 6, 9 and 12 months, underwent screening tests for HIV, HCV, Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG), syphilis and filled in a survey about sexual habits with the help of a peer counsellor.
The study was conducted at the community-based, peer-lead "BLQ Checkpoint" managed by PLUS Onlus (Bologna), using rapid tests, giving results in about 90 minutes. We report data from baseline and those collected at the 6-months evaluation.
Results: Forty-four cis-men and one TGW were enrolled. Median age was 40. At baseline,19 individuals were on PrEP, 28.9% had a positive serology for syphilis and the prevalence of CT/NG was 20%. At the 6-months re-evaluation, individuals on PrEP were 26, and prevalence of CT/NG reduced to 15.5%.
In those on PrEP, at baseline, 100% had 10 or more partners in the last 6 months, 73.7% reported inconsistent condom use, 89.5% reported at least one high-risk sexual practice (sex toys sharing, group sex participation, fisting), 57.9% were chemsex users, 26.3% reported partners of unknown HIV-status. After 6 months the report of 10 or more partners in the last 6 months, inconsistent use of condom, high-risk sexual procedures, chemsex use reduced to 76.9%, 57.6%, 61.5% and 30.7% respectively. Four new case of syphilis were found. Prevalence of CT/NG at baseline was 26.3%, and after 6 months reduced to 15.3%. In those not on PrEP, at baseline, 53.8% had 10 or more partners in the last 6 months, 30.7% reported inconsistent condom use, 34.6% reported high-risk sexual practices and 7.6% practiced chemsex. After 6 months 57.8% had 10 or more partners, 10.5% reported inconsistent condom use, 63.1% reported at least one high risk sexual practice, and 44.4% chemsex users. One new case of syphilis was found. Prevalence of CT/NG at baseline and after 6 months was 15%. No active or previous HCV infections were found in both subgroups.
Conclusions: In our entire cohort the overall reduction in prevalence of CT and NG was all due to the decrease of infections in individuals on PrEP and this goes with a reduction in prevalence of high risk sexual behavior in this subgroup. Our data suggest that periodical peer-counselling and testing for STIs in a community-based setting, like "BLQ Checkpoint", could prevent the increase of NG and CT infections expected for "risk compensation" in PrEP users.

HIV virology

P 74 EVALUATION OF USEFULNESS OF INTEGRASE GENOTYPIC RESISTANCE TEST IN PBMCS IN HIV-1 INFECTED PATIENTS WITH LOW/UNDETECTABLE PLASMA VIRAL LOAD

D. Armenia[1,2], B. Yagai[2], V. Borghi[3], C. Gori[4], W. Gennari[3], G. Berno[4], R. Gagliardini[4], A. Vergori[4], A. Latini[5], C. Mussini[3], A. Antinori[4], F. Ceccherini-Silberstein[2], C.F. Perno[4,6], M.M. Santoro[2]

[1]UniCamillus, Saint Camillus International University of Health Sciences, Rome, Italy, [2]University of Rome "Tor Vergata", Rome, Italy, [3]University of Modena and Reggio Emilia, Modena, Italy, [4]National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [5]San Gallicano Dermatological Institute, IRCCS, Rome, Italy, [6]University of Milan, Milan, Italy

Background: Despite the increasing usage of integrase inhibitors (INIs) in clinical practice, few data about integrase resistance on peripheral blood mononuclear cells (PBMCs) are available. Thus, this study aims to explore INI-resistance detected in PBMCs in comparison to plasma compartment, as previous or contextual GRT.
Materials and Methods: Patients (pts) with low (<1000 copies/mL) or undetectable plasma HIV-RNA (<50 copies/mL) with an available integrase GRT on both PBMC and plasma compartments were included. INI major (MRM) and accessory (ARM) resistance mutations were evaluated according to the Stanford resistance list 2018. Mutations detected in PBMCs were compared to those detected in contextual and/or previous cumulative plasma GRTs. The presence of stop codons and/or APOBEC-associated substitutions was also considered.
Results: Among 150 pts included in the analysis, 51% had a plasma HIV-1 RNA <50 copies/mL at the moment of PBMC GRT, while in the remaining 49% of pts, the median (IQR) viremia was 124 (78-259) copies/mL. The majority of pts was infected with HIV-1 B subtype (73.9%) and was Italian (80.7%), showing median (IQR) viremia zenith and nadir CD4 count of 5.44 (4.95-5.75) log10 copies/mL and 163 (50-292) cells/mm3, respectively. One-hundred and two (67.9%) pts were previously exposed to an INI before PBMC GRT, while 82 (54.7%) were under an INI-based regimen at the moment of GRT.
Regarding INI-resistance, the proportion of pts with at least one MRM detected in PBMCs was lower (n=4, 2.7%) compared to that with MRMs in plasma GRTs (n=14, 10.0%; P=0.009, by Chi Squared test). Among 15 pts harboring INI-resistance in at least one compartment, 11 (61.1%), 3 (16.6%) and 1 (5.6%), showed resistance only in plasma, in both compartments or only in PBMCs, respectively. Concerning the specific INI-resistance mutations, the unique pt harboring resistance only in PBMCs previously failed a raltegravir-based regimen, and showed the E138K MRM together with several stop codons and APOBEC-associated substitutions. All the other three pts who showed resistance in PBMCs were previously exposed to INIs and showed the same mutations in plasma (1: G140S+Q148H; 2: Y143C/H; 3: N155H). No stop codons were found in these three cases.
Considering the INI-ARMs, the proportion of pts with at least one ARM was similar in both compartments (33.3% in PBMCs vs. 28.7% in plasma, P=0.454) and no difference in the median [IQR] number of ARMs detected per pt was observed (PBMCs: 0 [0-1] vs. plasma: 0 [0-1], P=0.684).
Conclusions: Major resistance to INI in pts with low/undetectable plasma HIV-1 RNA is low. Integrase GRT performed in PBMCs might be useful for pts without any previous therapeutic and/or resistance information, revealing with good reliability polymorphisms potentially associated with resistance. Further investigation, preferably through ultra-sensitive technology, are needed to clarify the clinical impact of INI-resistance present in PBMCs.

HIV virology

P 75 SANGER AND NGS METHOD IN COMPARISON

P. Caligiuri[2], L. Boatti[5], P. Canepa[2], N. Nigro[1], C. Arcuri[2], G. Guarona[2], S. Razeti[4], A. Di Biagio[3], M. Setti[3], B. Bruzzone[1]

[1]Hygiene Unit, Polyclinic Hospital San Martino, Genoa, Italy, [2]Hygiene Unit, Department of Health Sciences, University of Genoa, IRCCS San Martino - IST, Genoa, Italy, [3]Internal Medicine and Clinical Immunology Unit, IRCCS AOU San Martino-IST, Genoa, Italy, [4]Arrow Diagnostics Srl, Genoa, Italy, [5]SmartSeq Srl Spin-Off dell'Università del Piemonte Orientale, Alessandria, Italy

Background: HIV-1 genotypic resistance test (GRT) has been considered an important tool for monitoring HIV infection and is usually recommended by Italian guidelines for guiding antiretroviral therapy (ART) in naïve patients and in virologic failure with HIV-RNA >200 copies/ml. It is also suggested in patients with virologic failure at low level viremia (HIV-RNA 50-200 copies/ml). For these purposes, Sanger method has always been considered the gold standard, although it allows detection only of variants accounting for representing at least 20% of the viral population. Conversely, Next Generation Sequencing (NGS) allows to detect variants also accounting for representing 1% of the viral population, hence its use is suggested in naïve patients to detect and identify resistant variants not detectable with GRT. The aim of this study was to evaluate feasibility, reliability and possible role in clinical practice of the NGS HIV-1 Solution kit (Arrow Diagnostics Srl).

Material and methods: Ten samples belonging to 6 naïve and 4 ART experienced patients were tested. HIV-RNA was extracted from plasma samples using NucliSens EasyMAG system (BioMérieux, Boxtel, The Netherlands) and sequencing was obtained using Viroseq HIV-1 Genotyping System V.2 (Abbott Molecular Inc., Des Plaines, IL). Next Generation Sequencing (NGS) was performed by using Arrow for NGS HIV-1 Solution kit. Pol and Integrase sequences obtained with the two methods were analysed and the presence of drug resistance mutations was analysed by using the Stanford HIVDB resistance interpretation algorithm.

Results: HIV-RNA ranged from 118 to 2 x 106copies/ml. For all patients, Reverse-Transcriptase, Protease and Integrase sequences, both with Sanger and NGS method were obtained and analysed. Among the naïve patients, 5 carried a "wild type" virus for all 3 genes while 1 showed a virus harbouring the 138A and 179T mutations both by Sanger and by NGS (in 97,6% and 97,5% variants). All patients showed viruses with the 103N and 184V mutations when using NGS with a <20% cut-off; in 2 patients the virus showed also the 97A and 138A mutations with the same cut-off.

Among the ART experienced patients, Sanger and NGS showed the same mutations with frequency >20%. Interestingly, mutations present in historical genotypes were detected by NGS using a <20% cut-off.

Conclusions: Arrow for NGS HIV-1 solution demonstrated good reproducibility and accuracy allowing the detection of mutations associated to clinical resistance with prevalence < 20%. Our data are in agreement with previous studies reporting the presence of 184V and 103N minority variants in naïve patients. Detection of low frequency mutations possibly associated with virologic failure appears to be important in monitoring treatment outcome. NGS proved to be a cost effective and useful tool for the characterization of viral quasispecies to better define the trend of resistance transmission.

HIV virology

P 76 TEST REPETION IN LOW-LEVEL HIV VIREMIA

B. Bruzzone[1], G. Barisione[2], S. Varesano[2], M. Setti[3], A. Di Biagio[4], N. Nigro[1], F. Torretta[5], P. Strada[5], G. Ubezio[5]

[1]Hygiene Unit, Polyclinic Hospital San Martino, Genoa, Italy, [2]Hygiene Unit, Department of Health Sciences, Polyclinic Hospital San Martino, Genoa, Italy, [3]Internal Medicine and Clinical Immunology Unit, Polyclinic Hospital San Martino, Genoa, Italy, [4]Infectious Diseases, Department of Internal Medicine, University of Genoa, Polyclinic Hospital San Martino, Genoa, Italy, [5]Transfusional Service, Polyclinic Hospital San Martino, Genoa, Italy

Background: Consistently undetectable HIV viremia is the main target of Antiretroviral Therapy. HIV viremia expressed in copies/ml can be currently quantified by using any of at least 4 available commercial tests. All use real-time amplification and have analytical sensitivity at or slightly below 50 copies/ml. Good agreement in terms of sensitivity and reproducibility was observed among the different assays, whilst differences can be found in specificity, especially when testing non-B subtypes.
HIV-RNA values <50 copies/ml (residual viremia) have interested the scientific community in the search for both causes and prognostic significance. On the other hand, values >50 copies/ml define virologic failure, with both clinical and psychological impact.
In this study we evaluated if any <50 copies/ml HIV-RNA detectable value found in our routine represented a reliable assessment of viral load or a measurement error due to assay variability occurring when working in near-the-limit range of quantification.
Materials and Methods: From January to December 2018, 3951 consecutive samples have been tested for HIV-RNA by using VERSANT® HIV-1 RNA 1.5 Assay (kPCR) (Siemens HealthCare Diagnostics). All samples with a <50 copies/ml result, included those below the lower limit of quantification (LLOQ) of the assay (37 copies/ml) but over the lower limit of detection (LOD - 3 copies/ml), have been retested with the same test on a second aliquot stored at -20°C. Finally, the qualitative screening tri-NAT PROCLEIX ULTRIO® Elite assay (Grifols Diagnostic Solutions) was used on a third aliquot.
Results: Overall, 123/3951 (3.1%) samples were quantified from 4 to 50 copies/ml (mean 23). When retested by KPCR, 48/123 (39% - previous mean 16) resulted "target not detected (TND)" while 75/123 (61% - previous mean 28) were quantified from 4 to 108 copies/ml (mean 22).
In the qualitative assay, 13/48 (27%) and 70/75 (93%) resulted positive in the samples resulted TND and confirmed positive at the retest, respectively.
The 75 samples found positive both times in the quantitative test were then divided into 2 groups, depending on the detected value at the first test: below and over LLOQ. The mean copies/ml in the repeated test resulted 15 in the first group (50 samples), and 34 in the second (25), respectively.
In summary, when the first assay gave a result detectable below 37 copies/ml, the repeat test was found either negative (73%) or detectable with a mean value of 15 copies/ml, while when the first result was ≥37 copies the repeat was either negative in a very lower percentage (7%) or detectable with a mean value of 34 copies.
Conclusions: Test repetition in <50 detectable results in HIV quantification is a troublesome decision in many laboratories. In this study deriving from on the field experience seem to suggest that repetition of results <50 and >LLOQ is more likely to provide useful information, while if the result is >LOD and <LLOD can be reliably presumed as negative.

HIV virology

P 77 QUANTITATIVE DETECTION OF HIV1-PROVIRAL DNA WITH A FREEZE-DRIED READY-TO-USE PCR-BASED REAL TIME PCR ASSAY: PRELIMINARY CLINICAL OUTCOMES

L. Spinelli[1], V. Micheli[2], A. Mancon[2], M. Ballarini[1], L. Bavagnoli[1], G. Ferri[1], M.L. Incandela[1], D. Rigamonti[1], M. Gramegna[1]

[1]Sentinel CH. SpA, via Robert Koch 2, 20152 Milano, Italy, [2]ASST Fatebenefratelli Sacco – Microbiologia clinica, Virologia e Diagnostica Bioemergenze

Background: The introduction of highly active antiretroviral therapy (HAART) in late '90s has changed the history of HIV-1 infection, enabling viral replication suppression and CD4 cells recovery. However, HIV persists in host cells as proviral integrated DNA. Total HIV-DNA, in addition to HIV-RNA and CD4 count, seems to have a prognostic value as a marker of disease progression: high levels of HIV-1 DNA are associated with higher risk of viral rebound and blips and disease progression, while patients with low levels of HIV-DNA are more likely to achieve and maintain viral suppression. Standardized molecular methods for the quantification of HIV-DNA are in development based on molecular biology techniques for measurement of the two most significant forms of HIV -1 DNA, integrated and non-integrated. The aim of this work was to evaluate the performance of a new assay designed to detect and quantify HIV-DNA in human samples.

Material and methods: A novel quantitative Real-Time PCR based-assay was developed as a ready-to-use test with specific sets of primers and probes able to amplify two different conserved regions within HIV-1 genome. A third set was included for the internal control. These three sets were combined in a lyophilized ready-to-use mix and all the targets were co-amplified and detected using a Real-Time PCR instrument (CFX96, Bio-Rad). At first, the kit performances were tested with NIBSC PCR reference Kit / 95 Series (ARP956). Then, a total of 25 samples from HIV suppressed patients addressing to Sacco Hospital were tested: samples were selected on the basis of availability of a Genotypic Resistance Test (GRT), performed on whole blood to assess the presence of drug resistance mutations in proviral genome; three patients with failed GRT analysis were also included. PCR reactions were performed on nucleic acids extracted from whole blood.

Results: The new freeze-dried ready-to-use assay demonstrated robust and accurate target amplification, according to the data obtained with NIBSC PCR reference Kit and in the clinical practice. This detection kit proved to be specific for HIV-1. All tested samples were in accordance with clinical samples previously diagnosed as positive. The test showed an optimal linearity and a LoD lower than 10 copies/reaction.

Conclusions: The described Real-Time PCR assay proved its effectiveness for the detection and quantitation of HIV -1 Proviral DNA in samples. The preliminary study showed a high sensitivity and a specificity of 100%. The high-sensitivity and specificity of this assay, linearity and quantitation performances, associated with the ready-to-use and room temperature storage, would have a direct impact on the continuous and correct management of the affected patients.

HIV virology

P 78 THERAPEUTIC MANAGEMENT OF HIV POSITIVE PATIENT BY A NEW REAL TIME PCR DEVICE FOR VIRAL DNA QUANTIFICATION

A. Renesto[1], *A. Gani*[1], *N. Paccagnella*[1], *A. Dalla Pozza*[2], *N. Montesano Gesualdi*[1], *S. Mason*[1]

[1]AB ANALITICA srl, Padova, Italy, [2]University of Padova, Padova, Italy

Background: The quantification of the HIV DNA load in the peripheral blood mononuclear cells is considered an important and useful tool for therapeutic management of the patient.
Aim of this study: was the development of the new device REALQUALITY RQ-HIV DNA, based on Real time PCR technology, for the quantification of proviral HIV DNA. This assay is able to satisfy requirements of sensitivity and analytical specificity necessary for the use in the diagnostic field.
Materials and methods: Specific primer and probes were designed on LTR region of HIV genome by analyzing a multiple alignment of 3500 HIV sequences, registered in the reference database (http://www.hiv.lanl.gov). Analytical specificity of the assay was evaluated both in silico and in vitro with spiked samples containing specific LTR sequences of several subtypes. Analytical sensitivity was calculated by using serial dilutions of a plasmid containing HIV-1 target sequence (LTR region of subtype B). In addition, different concentrations of extracted DNA obtained from the cellular line 8e5 (NIH AIDS reagents program) were investigated. Diagnostic performance were preliminarily evaluated on a total of 40 clinical samples and on 2 External Quality Assessment (EQA) QCMD panels. An in house assay, targeting the pol gene, was used as reference method.
Results: Primers and probes were able to correctly identify HIV 1, group M, subtypes A, B, C, F, G, AE, AG, as demonstrated by results of both in silico and in vitro tests. Analytical sensitivity of the assay was defined as 10 copies/reaction on 106 cells. Preliminary diagnostic performance showed a high analytical sensitivity and specificity. Good correlation of the quantification data was observed between REALQUALITY RQ-HIV DNA kit and the reference method.
Conclusions: REALQUALITY RQ-HIV DNA showed a high analytical specificity, by identifying all the principal viral subtypes of HIV 1 group M. The analytical and clinical sensitivity of the new kit satisfied requirements necessary for monitoring the efficacy of treatment. REALQUALITY RQ-HIV DNA could be useful for therapeutic management of HIV-infected patients.

HIV virology

P 79 THE DUAL-TARGET APPROACH IN THE METHOD FOR HIV-1 RNA TESTING UNVEILS UNEXPECTED VIROLOGICAL PATTERNS, WITH POSSIBLE IMPACT ON CLINICAL MANAGEMENT

A. Amendola[1], F. Forbici[1], I. Abbate[1], C. Pinnetti[2], A. Antinori[2], M.R. Capobianchi[1]

[1]Laboratory of Virology, INMI L. Spallanzani, Rome, [2]Clinical Department, INMI L. Spallanzani, Rome

Background: Aptima HIV Quant Dx is a new totally automated diagnostic assay (Hologic) for HIV-1 RNA monitoring, based on dual-target detection (pol+LTR); the second target is used for viral load (VL) calculation when pol is not amplified (LTR-only). This method replaced the previous method RealTime HIV (Abbott), based on single-target detection (pol) since May 2018 at the Laboratory of Virology of INMI. Rough comparison of VL results obtained with the new method revealed some patients, historically fully suppressed, showing measurable LTR-only levels. This study was aimed at assessing the reproducibility of this phenomenon, its extent, possible biological significance and implications in therapy management.

Material and methods: Aptima HIV Quant Dx was used as routine HIV VL assay. RealTime HIV-1 was used for comparison. HIV-1 subtype, retrieved from GRT (ViroSeq HIV-1 Abbott), was available for 80% of LTR-quantified samples.

Results: During nine months of monitoring, 11,201 clinical samples have been tested: 94.35% were measured with pol target, 5.65% were LTR-only. Among the LTR-only, 15.80% were accurately quantified (mean: 455 copies/ml, range: 30-9182), 84.20% were detected not-quantified (DNQ: <30 copies/ml). Available LTR-only residual samples (n=114 either DNQ or quantified) were re-tested with RealTime (LOD: 40 copies/ml), resulting all but one either undetected or <40 copies/ml (Table), consistent with the fact that most of these patients with the previous assay had been considered virologically suppressed in the last 5-10 years. HIV subtype (available for 80% of patients) and therapeutic regimen did not seem to be associated with LTR-only detection.

For some LTR-only patients repeatedly >50 copies/ml, fulfilling the criteria for virological failure, pol-based GRT plasma testing was not successful, with lack of target sequence amplification; on the contrary, GRT was successfully performed on proviral DNA showing absence of major resistance mutations. In parallel, proviral DNA quantification performed in some patients resulted repeatedly LTR-only, indicated a well sized HIV reservoir.

Conclusions: Lack of reduction of HIV RNA <50 cp/ml, or confirmed rebound >50 cp/ml is a marker of virological failure. With Aptima dual target approach, a slight discrepancy with single-target method appear. This discrepancy is consistently observed for some patients, historically considered virologically suppressed, reaching up to 10,000 cp/ml HIV RNA. Circulating HIV RNA seems to lack the pol-region, as it is not detected by pol-targeting assay and could not be sequenced, while the proviral DNA seem not to be defective. Accurate monitoring of HIV dynamics in these patients is necessary to establish the relevance and the implication of this phenomenon by pathogenetic (i.e. infectivity of LTR-only virions, reservoir turnover, immune activation, ecc.) and clinical standpoint.

HIV virology

P 80 DEVELOPMENT OF A MODIFIED QUANTITATIVE COMMERCIAL ASSAY FOR EXTRACTION AND QUANTIFICATION OF HIV-1 PROVIRAL DNA

L. Di Sante[1], S. Belladonna[2], A. Corsi[1], P. Sestilli[3], R. Longo[4], S. Caucci[4], S. Menzo[4], A. Costantini[1], P. Bagnarelli[4]

[1]Department of Molecular and Clinical Sciences, Polytechnic University of Marche, Ancona, Italy, [2]Molecular Division, Abbott srl, Roma, Italy, [3]Virology Unit, Azienda Ospedaliera Ospedali Riuniti, Ancona, Italy, [4]Department of Biomedical Sciences and Public Health, Polytechnic University of Marche, Ancona, Italy

Background: Current cART allows successful long-term management of HIV-infected patients by greatly reducing HIV/AIDS-associated morbidity and mortality. Although in most patients cART efficiently suppresses viral replication to undetectable levels, proviral DNA persists in host cells, establishing a viral reservoir from which replication can resume in case of therapy interruption or failure. Since HIV-DNA determination could play a pivotal role in patient monitoring, the aim of this study is to develop an extraction and amplification protocol for HIV proviral DNA, by modifying a quantitative commercial assay designed for HIV-RNA.

Material and methods: HIV-1 proviral DNA was extracted on the Abbott m2000sp instrument, using an open mode protocol and the Abbott mSample Preparation SystemDNA Kit. The DNA internal control of the Abbott real-time HBV kit was added to the lysis buffer. The linear dynamic range of the assay was assessed by testing replicates (13 each) of pNL4-3 10-fold dilutions (101 to 104 cp/reaction, R2 = 0,9961). The Limits of Quantification and Detection (LOQ and LOD) were determined by probit analysis. Two calibrators, seronegative whole blood spiked with pNL4-3, at two different final concentrations (103 and 105 cp/ml) were extracted and amplified to generate a master calibration curve. A set of blood samples from a cohort of patients, mostly with undetectable plasma HIV-RNA and undergoing stable cART for at least 6 months, were analysed, negative and positive controls were included to validate each session. Human telomerase reverse transcriptase was used to assess the total number of cellular genomes to normalize results.

Results: The LOQ and the LOD (hit rate 95%) were respectively 54 and 12 cp/reaction, following extraction and amplification, and 10 and 5 cp/reaction after amplification only. The mean calibration curve slope and intercept were calculated to quantitatively determinate HIV-1 DNA from blood specimens and controls. Target amplification was achieved in 102 out of 116 samples (88%) and comparable Ct values (18 to 23) were always obtained for internal control, indicating absence of inhibition. DNA proviral loads varied widely among HIV-1 infected patients, possibly due to differences in infection history and disease progression.

Conclusions: Commercial DNA quantification assays are usually carried out extracting only patients' samples and the quantification is obtained interpolating their CTs over an external calibration curves in which calibrators are not processed as clinical samples (no extraction process required). The novelty of our assay relies on an automated, specific and sensitive quantification assay for HIV-1 proviral DNA that is validated throughout the entire process of extraction and amplification, thus avoiding the quantitation bias related to the use of external standards.

HIV virology

P 81 IMPACT OF ANALYTICAL TREATMENT INTERRUPTION ON REASSORTMENT OF HIV-1 DRUG RESISTANCE MUTATIONS IN PERIPHERAL RESERVOIR

R. Scutari[1], M.C. Bellocchi[1], V. Spagnuolo[2-3], S. Barbaliscia[1], L. Galli[2], A. Galli[2], A. Poli[2], L. Carioti[1], M.M. Santoro[1], C.F. Perno[4], C. Alteri[4], F. Ceccherini-Silberstein[1], A. Castagna[2-3]

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Infectious Diseases, San Raffaele Scientific Institute, Milan, Italy; [3]Università Vita-Salute San Raffaele, Milan, Italy, [4]Department of Oncology and Hemato-oncology, University of Milan, Milan, Italy

Background: Analytical antiretroviral treatment interruption (ATI) does not lead to expansion of the peripheral HIV reservoir. But, it is still unclear what impact short ATI and subsequent reinitiation of ART might have on archived major resistance mutations (MRMs).

Methods: Seven chronically HIV-1 infected patients with HIV-RNA<50cps/ml for ≥10 years, undergoing towards ATI (APACHE) were analysed for total HIV-DNA (cps/10^6CD4+T, by ddPCR) and pol sequences (HXB2 pol nt:170-1415, by Ilumina MiSeq) at ATI, viral rebound (VR) and at achievement of undetectable viral load after ART resumption (post-ATI). These parameters were also obtained at three similar time-points (I, II, III) in 7 combined-ART treated patients with HIV-RNA always <50cps/ml for ≥1year (MODAT). Intra-patient prevalence of MRMs (Stanford list 2018) was assessed at each time point. Wilcoxon signed-rank test and Mann-Whitney test were used to test changes in MRM prevalence within and between APACHE and MODAT subjects, respectively.

Results: APACHE subjects experience VR after ATI at a median(IQR) time of 4 (3-7) weeks and, after ART resumption, achieve HIV-RNA<50cps/ml in 24 (4-29) weeks. Median(IQR) total HIV-DNA is 982 (692-1286) cps/10^6CD4+T before ATI, and 992 (553-2183) cps/10^6CD4+T after ATI, with no significant change between the within-person pre- and post-AI values (P=0.13). No differences are found at first and third time point for HIV-DNA between APACHE and MODAT subjects (P=0.62 and 0.53). At baseline, 5/7 APACHE and 4/7 MODAT carry MRMs (Table 1) with a median[IQR] intra-patient prevalence of 38.1 [6.2-99.6] and 78.6 [49.9 -99.4], corresponding to a mutational load of 329 [95-687] and 453 [150-776] cps/10^6CD4+T, respectively. In APACHE, MRMs persist at plasma level in 2/7 individuals at ATI (28.6%, both with an intra-patient prevalence >99.0%), and in peripheral reservoir in 4/7 subjects (57.1%, with a median[IQR] intra-patient prevalence of 6.5 [0.6-99.7], corresponding to a mutational load of 109 [91-638] cps/10^6CD4+T). Post-ATI, HIV-DNA MRMs are found in 3/7 subjects (57.1%, with an intra-patient prevalence of 1.4%, 99.6%, and 99.8%, corresponding to a mutational load of 39, 860 and 511cps/10^6CD4+T, respectively). Comparing the MRMs in pre- and post-ATI HIV-DNA sequences, while MRMs characterized by a baseline intra-patient prevalence >60% remain stable over time, MRMs with a baseline intra-patient prevalence <60% significantly decrease from pre- to post-ATI (intra-patient prevalence: 7.2 [1.8-29.8] vs. 0.0 [0.0-0.6], P=0.01; mutational load, cps/10^6CD4+T: 88 [15-256] vs. 0 [0-1], P=0.003).

Comparing changes of MRM prevalence in MODAT patients, no differences are found between baseline and follow-up, even considering MRMs with a baseline intra-patient prevalence <60% (P=0.18).

Conclusion: This proof of concept study indicates that ATI is associated with rearrangement of peripheral archived MRMs, and in some cases may be associated with their complete reversal.

Issues on antiretroviral therapy

P 82 RETROSPECTIVE EVALUATION OF EFFECTIVENESS, PERSISTENCE IN TREATMENT AND SAFETY OF OLDER (≥50 YEARS OLD) HIV-INFECTED PATIENTS WHO STARTED WITH AN ANTIRETROVIRAL COMBINATION THERAPY INCLUDING DARUNAVIR/COBICISTAT (DRV/C)

A. Vergori[1], A. Giannetti[1], G. Passavanti[1], S. Cicalini[1], P. Lorenzini[1], R. Bellagamba[1], A. Antinori[1], C. Bottaro[2], R. Termini[2], A. Uglietti[2]

[1]HIV/AIDS Unit, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [2]Janssen-Cilag SpA, Cologno Monzese, Italy

Background: Effective combination antiretroviral therapy (cART) has improved survival in individuals with HIV, resulting in an increasing number of older-aged individuals living with HIV. Older patients with HIV may suffer from aging-related comorbidities that could complicate the management of HIV infection. Aim of this analysis was to evaluate effectiveness, safety and persistence on treatment of Darunavir/cobicistat (DRV/c)-based regimen in older-aged (≥50 years old) HIV-infected patients.

Materials and Methods: This is an observational, retrospective analysis of HIV experienced, virologically suppressed patients who switched to any triple DRV/c-based regimen (DRV/c/FTC/TAF; DRV/c+FTC/TDF; DRV/c +ABC/3TC) according to current clinical practice with at least 12 months of clinical observation.

The primary objective was treatment discontinuation for any cause excluding simplification. Secondary objectives were: to evaluate pure virological failure, safety and tolerability (renal function defined as estimated Glomerular Filtration Rate-eGFR and lipid profile) of DRV/c-based regimens. Time-to-event analysis was performed by Kaplan Meier method. Cox proportional hazards regression analysis was fitted to identify factors independently associated with treatment discontinuation. A sensitivity analysis on safety was performed considering previous TDF exposure.

Results: A total of 88 patients were included: 87.5% male with a median age of 56 years old (IQR, 54-59), a median of 21 years (10-28) from HIV diagnosis, median number of therapy lines 4 (2-7.25) and a median duration of cART of 11.9 years (7-17.8). Previous regimen consisted mainly of TDF/FTC plus PI/r (n. 51/88, 58%) and ABC/3TC/PI/r (19/88, 21.6%). During a median of 98 PYFU, 3/88 (3.4%) discontinuations for any causes other than simplification were found, 30/88 (34%) interruptions for simplification were observed with an IR of 30.7 x 100PYFU. Concerning pure virological failure, only 1 event was detected. No discontinuations for toxicity were observed. Cox regression analysis did not show any significant association for treatment discontinuation. After 12 months, no statistically significant differences in eGFR, total cholesterol, LDL, HDL, triglycerides were found (Table 1). After a stratification by TDF exposure, the comparisons between baseline and 12 months values did not show any difference.

Conclusions: This analysis showed that a higher proportion of male patients with age ≥50 years old, experienced > 2 lines of therapy, with a long time of HIV history and cART, started a regimen with DRV/c. These results support clinician's major concern towards a benefit of a higher genetic barrier in this fragile and difficult category of patients. As well, DRV/c-based regimen appear safe in older patients, with low impact on the safety and independently from the backbone previously used. Further investigations are needed to explore efficacy and safety according to gender and to the different combined partner drug.

Issues on antiretroviral therapy

P 83 3TC-DTG PREDICTS A REDUCED PROBABILITY OF HEPATIC STEATOSIS IN MONOINFECTED HIV+ PATIENTS

D. Moschese[1], A. Ciccullo[1], F. Taccari[1], A. Borghetti[2], E. Emiliozzi[1], D. Farinacci[1], A. Dusina[1], F. Lombardi[1], S. Belmonti[1], G. Baldin[1], S. Di Giambenedetto[1,2]

[1]Università Cattolica del Sacro Cuore, Roma, [2]Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Roma

Background: Liver steatosis is a common finding in patients receiving chronic therapy. HIV-infected patients also experience liver damage due to the activity of HIV itself, thus rising an increasing concern for developing nonalcoholic fatty liver disease (NAFLD) and its complications. In our study, we aimed to assess the prevalence of liver steatosis and its possible correlation with the therapeutic history of this population.
Methods: We started a screening program, performing abdomen ultrasound (US) on HIV-positive patients at our clinical center. US was performed by the same operator through the same GE device (V2); detection and grading of hepatic steatosis were based on the assessment of liver echogenicity. The grade of hepatic fibrosis was evaluated via Fib-4. About the patients (pts) analyzed, we collected baseline characteristics such as sex, age, nationality, risk factor, as well as HIV clinical history and liver function tests at the time of visit; those with a history of chronic hepatitis (viral or alcoholic) were excluded. We compared parameters through non-parametric tests and linear regression, as appropriate.
Results: We analyzed 60 pts: 45 (75%) were males, with a median age of 50.5 years (IQR 42.0–58.0), a median of 13.1 years from HIV diagnosis (IQR 6.2–20.0) and a median time from ARV initiation of 10.8 years (IQR 5.8–18.5). Full patients' characteristics are shown in table 1. Median hepatic right lobe length was 15cm (IQR 14-16) while median spleen diameter was 10.5cm (IQR 9.6-12.0); 14 pts (23.3%) had mild steatosis, 12 (20%) a moderate one while 3 pts (5%) presented severe steatosis. Being on a 2-drug regimen with 3TC+DTG was inversely associated with any grade of hepatic steatosis (vs other regimens, aHR 0.07, 95%CI 0.01-0.90, p=0.042). In patients with low-grade steatosis, a higher fib-4 value was predicted by years of suboptimal ARV (per 1 year more, +0.6, 95%CI 0.1-1.2, p=0.032), while it was negatively predicted by time of exposure to DTG (per one month more, -0.02, 95%CI -0.03 to -0.01, p=0.035); in patients with more severe steatosis, a higher fib-4 was exclusively predicted by a longer time of suboptimal therapy (+0.3, 95%CI 0.1-0.6, p=0.039).
Conclusion: Although NAFLD remains a common finding in HIV-infected patients receiving ART, those on DTG + 3TC seemed less likely to develop this condition, thus suggesting a safer metabolic profile of the 2-drug regimen when compared to standard cART.

Issues on antiretroviral therapy

P 84 SWITCH TO DOLUTEGRAVIR-BASED REGIMENS AND DECREASE IN SCD14 LEVELS IN HIV-1 INFECTED PATIENTS ON SUPPRESSIVE ART

S. Belmonti[1], F.Lombardi[1], A. Cingolani[1,2], E. Visconti[1,2], A. Borghetti[2], G. Baldin[1], A. Ciccullo[1], E. Tamburrini[1,2], R. Cauda[1,2], S. Di Giambenedetto[1,2]

[1]Università Cattolica del Sacro Cuore, Roma Italia, Istituto di Clinica Malattie Infettive, [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma Italia, UOC Malattie Infettive

Background: Biomarkers of chronic inflammation predict morbidity and mortality in HIV-1 infected patients even on fully suppressive ART; however, the effect of specific antiretrovirals on these biomarkers remains unclear.
We explored the impact of switching to a regimen containing Dolutegravir (DTG), on soluble markers of inflammation (interleukin-6; IL-6, c-reactive protein; CRP), monocyte activation (soluble CD14; sCD14) and altered coagulation (D-dimer) in virologically suppressed HIV-1 infected patients.
Methods: We retrospectively analyze integrase inhibitor naïve subjects, with HIV-1 RNA <50 copies/mL for > 6 months, who switched ART to a DTG-based regimen and maintained this regimen for ≥48 weeks. Plasma levels of IL-6, CRP, sCD14 and D-dimer were quantified by ELISA assay at time of DTG-based therapy initiation (baseline, BL) and after 48 weeks (W48). Results were log10 transformed and paired t-test was used to assess changes in biomarkers level from BL to W48. Regression analyses were used to explore the potential confounders measured at BL that could affect the changes in biomarkers level. Associations between the levels of the biomarkers were tested by Pearson's correlation.
Results: The study included 133 subjects: 69.2% males, mean age 49 yrs, mean CD4 662 cell/mm3, 60.2% on PI or NNRTI-based triple regimen and 39.8% on dual-therapy with lamivudine plus PI/r. At BL 37 patients (28%) simplified the three-drug to a two-drug regimen with lamivudine plus DTG, 43 patients (32%) switched from the original triple therapy to a DTG-based triple regimen and 53 patients (40%) switched the original dual therapy to lamivudine plus DTG. Interestingly, we found that at week 48 the sCD14 levels significantly decreased with a mean log10 change of –0.07 µg/mL (95%CIs -0.09;-0.04, p<0.001), whereas the variations observed for IL-6 (-0.03 pg/mL 95%CIs -0.12;0.06), CRP (-0.02 µg/mL 95%CIs -0.07;0.05) and D-dimer (-0.03 µg/mL 95%CIs -0.07;0.02) were not significant (all p values >0.5). By linear regression model, the change of sCD14 level was not affected by antiretrovirals switching strategies used at BL (from triple to triple dtg-based or triple to dual dtg-based or dual to dual dtg-based regimen) and was not associated with other covariates. Positive correlations were found between the change in sCD14 level and the variations of the other biomarkers (all p values <0.005). No difference in HIV-1 RNA and CD4 counts or variation in co-morbidities, BMI, concomitant medications, alcohol and smoking habits was found at W48 as compared to BL.
Conclusions: In HIV-1 infected patients with substained virological suppression, switching to DTG-based regimens might result in a lower stimulation of monocyte/macrophage activity as reflected by the decrease of plasma sCD14 levels in this setting. This finding could have important clinical implications because lower sCD14 levels have been associated with reduced morbidity and mortality in treated HIV-1 infection.

Issues on antiretroviral therapy

P 85 INTRODUCTION OF GENERICS MEDICINES INTO CLINICAL PRACTICE: PROBLEM OR RESOURCE?

C.B. Traversi[1], S. Bertini[1], A. Ferrero[1], D. Piccioni[1], E. Geninatti[2], E. Marrazzo[2], G. Cinnirella[1]

[1]Amedeo di Savoia Hospital Pharmacy, ASL City of Turin, [2]Pharmacovigilance Regional Centre of Piedmont, ASL City of Turin

Over the past two years, several generic medicines have been introduced into the clinical practice to treat Chronic Hepatitis B (HBV) and Human Immunodeficiency Virus (HIV) infections, such as entecavir, tenofovir and lamivudine for HBV, lamivudine, nevirapine, abacavir / lamivudine for HIV.
The first drug introduced as generic, over five years ago, was lamivudine, available since October 2016 at the pharmacy of the Amedeo di Savoia Hospital in Turin, for the treatment of HBV, and since May 2018 for HIV treatment. Generic Nevirapine was available later, in October 2017, while tenofovir, abacavir / lamivudine and entecavir only in 2018.
Therapeutic switch between branded medications and their corresponding generic showed reports of suspected adverse drug reactions (ADRs).
Considering the large number of patients that attend this hospital, we decided to:
- analyze suspected reports of ADRs recorded at our hospital,
- analyze reports of ADRs in the National Pharmacovigilance Network (RNF) in the period 2017-18, data obtained by Pharmacovigilance Regional Centre of Piedmont,
- evaluate our data and their impact on RNF to encourage and develop strategies to improve pharmacovigilance actions.

"Amedeo di Savoia" Hospital is the reference Hospital in Piedmont for HIV, HBV and HCV infection diagnosis and treatment. Approximately 5.000 patients are taken in care by the hospital.
In the period 2017-18, from RNF database analisys, we identified, at our hospital, only 9 reports of suspected adverse reactions related to generic medicines and exactly 3 to nevirapine, 2 to lamivudine, 2 to entecavir, 1 to abacavir / lamivudine and 1 to tenofovir. ADRs registrated are all not serious and involves gastrointestinal tract, skin and nervous system.
National reports of ADRs and percentual related to generic medicines are summarized in table 1.
The Regional suspected side effects reports are 12, described in table 2, all related to generic drugs, 83% of them registred by clinics of our hospital.
Our analisys shows that generic drugs are as efficacy and safety as branded drugs.
Despite under-reporting of ADRs, our investigation demonstrated that the problems occurs in a small number of patients compared to all patients treated. Therefore,it shouldn't be necessary the adoption of a strategy for generic drugs monitoring, but it's important to identify the best drug for every single patient.

Issues on antiretroviral therapy

P 86 EVALUATION OF ABACAVIR-RELATED ADVERSE REACTIONS IN A COHORT OF HIV POSITIVE PATIENTS NON-CARRYING HLA B*5701 ALLELE

G. Gardini, M. Properzi, A. Marchi, A. Chiesa, N. Gregori, F. Castelli, E. Quiros-Roldan

Department of Infectious and Tropical Diseases, University of Brescia and Spedali Civili General Hospital, Brescia, Italy

Introduction: Abacavir (ABC) is a nucleoside reverse transcriptase inhibitor (NRTI) widely used to treat HIV infection. ABC-hypersensitivity reaction (HSR) usually occurs within the first 6 weeks of therapy and is reversible after ABC discontinuation. Life-threatening and fatal reactions are rare and mostly occur in case of prolonged ABC therapy after HSR onset or ABC rechallenge. Carriage of human leukocyte antigen (HLA) B*5701 allele increases the risk of HSR, therefore since 2008 HIV treatment guidelines recommend HLA B*5701 screening before ABC administration, greatly reducing HSR rate. However, clinically suspected ABC-related HSR are described in HLA B*5701 negative patients. Aim of this study is to evaluate the relationship between HLA B*5701 pattern and ABC-related HSR, focusing on HSR prevalence in HLA B*5701 negative patients.

Materials and methods: All patients aged >18 years old with HIV infection and known HLA B*5701 pattern, followed at our Department since November 2018 were included. Patients were divided in two sub-groups according to HLA B*5701 pattern and antiretroviral regimen prescribed (containing or not ABC) as follows:

a) Group A: HLA B*5701 allele carriers treated with ABC (before HLA B*5701 testing was currently available)

b) Group B: HLA B*5701 allele non-carriers treated with ABC

We considered all adverse events (AEs) reported during ABC administration, differentiating between HSRs and non-HSRs, according to ABC HSR definition included in the ABC EU Summary of Product Characteristics and the U.S. Prescribing Information.

Results: 3144 patients were included: a total of 107 HSR (3.4%) were recorded. According to HLA B*5701 pattern, 171 patients (5.4%) resulted allele carriers and 2973 (94.6%) non-carriers. 18.7% (32/171) of carriers and 59.5% (1769/2973) of non-carriers were treated with an ABC-containing regimen.

In Group A, we observed 22/32 patients with a defined ABC-HSR (68.8%); HSR occurred mostly in males (n= 13, 59%), mean age at HSR diagnosis was 41.86 years (SD 11.38). The most frequent reactions were skin-rashes and gastrointestinal symptoms; mean time from first ABC-administration to HSRs was 33.95 days (SD: 49.02). On the other hand, ABC-related HSR occurred in 4.8% (85/1769) of HLAB*5701 negative patients (Group B). In this group the majority of patients were males (n= 55, 64.7%), mean age at HSR was 43.19 years (SD: 9.58). The most reported AEs after ABC initiation were gastrointestinal symptoms, followed by constitutional and cutaneous disorders. Mean time to HSR was 64.16 days (SD: 123.93).

Overall, no fatal reactions were described.

Conclusion: HLAB*5701 testing is mandatory before starting an ABC-containing regimen. However, a not negligible percentage of HLAB*5701 non-carriers may experience, even after years of ABC-based treatment, a HSR, promptly leading to drug interruption.

Issues on antiretroviral therapy

P 87 DOES RALTEGRAVIR 1200 MG ONCE DAILY ACTUALLY IMPROVE ADHERENCE OVER RALTEGRAVIR 400 MG TWICE DAILY? RESULTS FROM CLINICAL PRACTICE

A. Emiliozzi[1], A. Ciccullo[1], G. Baldin[1], A. Dusina[1], D. Farinacci[1], C. Picarelli[1], D. Moschese[1], S. Belmonte[1], F. Lombardi[1], S. Lamonica[1], A. Borghetti[2], S. Di Giambenedetto[1,2]

[1]Institute of Clinical Infectious Diseases, Catholic University of the Sacred Heart, Rome, Italy, [2]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, UOS Malattie Infettive, Rome, Italy

Background: After a decade from the introduction of raltegravir (RAL) 400 mg, a new formulation of RAL 1200 mg once daily was introduced, in order to improve the compliance to RAL-containing regimens. We investigated the efficacy and the tolerability of the new RAL formulation through patient-reported outcomes.

Material and methods: We enrolled all HIV-1 infected patients who started RAL 1200mg (as a first-line regimen or as part of a switch strategy) at our clinical center between May 2018 and December 2018. Through an adherence questionnaire, we collected patients' opinion on the ease of administration and the onset of side effects. Cox regression models were performed to estimate the predictors of RAL discontinuation. We also evaluated the changes in immunological, metabolic and renal function parameters at 12 weeks of follow-up using linear generalized models.

Results: 98 pts started RAL 1200mg: 63 were males (64.3%), with a median age of 55 yrs, a median time from HIV diagnosis of 17 yrs and a median time from ART initiation of 13 yrs. 89 pts (98%) started a regimen with 2 NRTIs (87 with FTC/TDF and 2 with ABC/3TC) while 9 started a dual regimen with a boosted PI; 69 pts (70.4%) came from a regimen containing RAL 400 and 8 pts were treatment-naive. Reasons of switching were: optimization (71, 78.9%), toxicity (10, 11.1%, of which 2 GI toxicity, 2 renal toxicity, 3 CNS toxicity, 3 dyslipidemia), drug-drug interaction (3, 3.3%), other reasons (6, 6.7%). During 29.9 Patient-Years of Follow-Up, we registered 7 treatment discontinuations (TD). One patient was stopped after 2 consecutive HIV-RNA determinations >40 cp/ml; 4 (4.1%) TD were due to simplification and 2 (2.0%) to GI toxicity. No predictors of TD were found through Cox regression analysis. At 12 wks of follow up, no significant changes in CD4+ cells count and CD4/CD8 ratio were recorded and no significant differences were observed in terms of total and LDL cholesterol, transaminases and CPK. Regarding the report of side effects collected through the questionnaire, 8 pts (8%) complained GI symptoms: 7 of these came from a well-tolerated RAL 400 based regimen. One patient referred insomnia, one patient naïve for RAL complained of headache and dizziness (regressed after switching to RAL 400) and 3 pts referred hair loss. Eventually, we noticed that, despite an accurate counselling, 8 pts (6 of which RAL-experienced) misunderstood the physician's indications about the dosage and took just one pill of RAL 600 mg per day. However, no virological failures were recorded among these patients.

Conclusion: Our study confirmed the efficacy of RAL 1200 mg, that in our cohort seemed to induce more side effects compared to the previous formulation, and warrants physicians to stress the correct method of administration of the new RAL 1200mg, in order to avoid an insufficient concentration of the drug. Further studies with a higher number of patients and longer follow up are needed to confirm this result.

Issues on antiretroviral therapy

P 88 THE HIV-1 INTEGRASE GENETIC BACKGROUND INFLUENCES THE RESISTANCE PATHWAYS THAT PATIENTS TREATED WITH RALTEGRAVIR SELECT IN VIVO

S. Caucci[1], E. Di Mercurio[1], M.L. Ferreri[1], K. Marinelli[1], L. Monno[2], P. Bagnarelli[1], S. Menzo[1]

[1]Department of Biomedical Sciences and Public Health, Polytechnic University of Marche, Ancona, Italy, [2]Department of Biomedical Sciences and Human Oncology, University of Bari, Bari, Italy

Background: The introduction of integrase inhibitors has represented an important step for antiretroviral therapy. Raltegravir was the first representative of a class of integrase strand transfer inhibitors (INSTIs), followed by elvitegravir and more recently dolutegravir and bictegravir, while cabotegravir is due to be approved soon. Resistance against these compounds in vivois mostly associated with 3 main mutation pathways: Y143C/R, Q148H/R/K orN155H. The molecular mechanisms that drive the selection of a specific pathway arestill poorly understood. The aim of this study was to investigate the influenceof the viral genetic background in the integrase gene on the selection of a specific resistance pathway.

Material and Methods: Seven patients treated with INSTIs whose viral isolates naturally developed drug resistance mutations (either N155H or Q148H/G140S) were enrolled in this study. Integrase genes were amplified from plasma samples and cloned into anHIV molecular clone (pNLmodΔintGFP) suitable for the phenotypic study of integrase sequences. Site directed mutagenesis was applied to these clones to reproduce the wildtype genotype and both the natural resistance pathway (observed in vivo) and the alternative pathway for each patient.After transfection of all clones in packaging cells, the supernatants were used to infect apermissive cell line. Fluorescent emission of the reporter GFP was measured during in vitro replication ofrecombinant viruses to calculate the replicative capacity (RC) and the 50% inhibitory concentration (IC50)of raltegravir and dolutegravir.

Results: The combination G140S/Q148H displayed in all clones a higher IC50 compared to N155H, for both raltegravir and dolutegravir. The RC of widtype clones was variable from patient to patient, and he introduction of resistance mutations greatly reducedit, albeit again with a high degree of variability, depending on the viral genetic context. The mutation Q148H determined the maximum loss of RC. However, in clones from patients where it was naturally selected by treatment, its association with the G140S secondary mutation allowed a higher recovery of RC compared to those from patients where either the Y143R or the N155H pathway was selected. The mutation N155H had generally less impact on RC, even less so in clones from patients where the N155H was naturally selected. The association of G140S/Q148H and N155H confers higher resistance to both inhibitors but at a high cost in replicative capacity, which explains its rarity in vivo.

Conclusions: The genetic background of HIV integrase gene at baseline is likely to have influenced the resistance mutational pathway naturally observed in these patients. In particular, despite the lower resistance conferred by N155H, this mutational pathway may be selected in patients with a peculiar viral genetic background, refractory to G140S/Q148H, as conferring a better overall replicative capacity at the drug concentrations obtained in vivo.

Issues on antiretroviral therapy

P 89 EVALUATION OF BONE HEALTH AND RENAL FUNCTION IN HIV-INFECTED YOUTHS TREATED WITH AN ANTIVIRAL REGIMEN CONTAINING DOLUTEGRAVIR

S. Mora[1], M. Ratti[2] , K. Maruca[1], E. Longoni[2], S. Lazzarin[2], A. Manzo[2], L. Paradiso[2], E. Albani[2], G.V. Zuccotti[3], V. Giacomet[2]

[1]Laboratory of Pediatric Endocrinology Division of Genetics and Cell Biology, IRCCS San Raffaele Scientific Institute, [2]Unit of Paediatric Infectious Disease, ASST FBF Sacco, University of Milan, [3]Clinic of Paediatrics, V Buzzi Hospital, ASST FBF Sacco, University of Milan

Background: Antiretroviral therapy, particularly TDF- and PI-based regimens, has been associated to renal dysfunction and impairment of bone health. Dolutegravir, a second-generation INSTI, has shown a favourable safety profile in adult population with an improvement in BMD, a lower increase in bone turnover markers and a substantial preservation of renal function. The aim of this study was to verify if these findings could be extended to younger HIV-infected patients.

Material and methods: Adolescents and young adults with HIV infection, and previously exposed to antiretroviral treatment were eligible for the study. Patients switched from PI- and NNRTI-based regimens to a Dolutegravir-containig regimen. Renal function, alkaline phosphatase (ALP), 25hydroxy-vitamin D (25OHD), and parathyroid hormone (PTH) were assessed before switching. Measurements were repeated after 12 months on new regimen. Bone mineral density (BMD) was measured on the lumbar spine and whole body by DXA at baseline and after 12 months.

Results: We enrolled 15 patients (10 girls) aged 16.9 (3.6) years at baseline. Their initial CD4 was 35.9 (9.7)% and 791 (290) n. After 12 months of new regimen, the CD4 percentage was 37.9 (6.7) and the count was 901 (345). Urinary function was unaltered during the observation period. Urinary calcium/creatinine ratio was 0.09 (0.08) and 0.06 (0.04) at baseline and 12 months, respectively. ALP activity did not change significantly, being 192.7 (161.5) and 144.0 (127.5) at baseline and at 12 months, respectively. Clinically irrelevant changes of 25OHD and PTH were recorded. Whole body BMD z-score at baseline was -0.5 (0.9), and -0.1 (0.9) after 12 months ($p = 0.016$). Initial BMD z-score of the lumbar spine was -0.8 (0.9), and final measurement was -0.9 (0.9).

Conclusions: Our data indicate that short-term antiretroviral treatment that includes Dolutegravir in the combined regimen does not impair renal function in young patients with HIV infection. Bone metabolism markers are not altered after 12 months of treatment. Moreover, such regimen does not impair bone mineral density, both in the whole skeleton and in the lumbar spine. The regimen containing Dolutegravir should be considered safe for renal and skeletal health in young patients.

Issues on antiretroviral therapy

P 90 CURRENT USE OF TAF/EMTRICITABINE + DARUNAVIR/COBI AS INITIAL THERAPY OR OPTIMIZATION STRATEGY IN 5 CENTRES IN TUSCANY: DEMOGRAPHICAL AND CLINICAL PROFILE OF 141 PATIENTS AND REASONS FOR CHOICE

F.M. Fusco[1], B. Rossetti[2], D. Messeri[3], F. Vichi[1], F. Lagi[4], G. Sterrantino[4], C. Spertilli Raffaelli[5], R. Cinelli[6], S. Sani[6], M. Di Pietro[3]

[1]SOC Malattie Infettive 1, Osp. S. Maria Annunziata, Firenze, [2]UOC Malattie Infettive, AOU Senese, Siena, [3]SOC Malattie Infettive 2, Osp. S.Jacopo, USL Toscana Centro, Pistoia, [4]Dipartimento Medicina Sperimentale e Clinica - Università di Firenze - Azienda Ospedaliero-Universitaria Careggi, Firenze, [5]Dipartimento di Biotecnologie Mediche, Università di Siena, Siena, [6]UO Malattie Infettive, Spedali Riuniti, Livorno

Background: According to last Italian Guidelines for the HIV management (1), darunavir(DRV)-based cART are recommended in naive patients in special conditions. Recently introduced DRV/COBI/FTC/TAF single tablet regimen (STR) can increase the patients' compliance and is recommended as optimization strategy.
The regimen including coformulated FTC/TAF + coformulated DRV/COBI is often used, for its capability to reduce long-term toxicity and for the reduced risk of resistance in case of failure, compared to NNRTI and INI other than DTG (2). In order to understand the reasons driving the physicians in the choice of this regimen, we conducted a preliminary retrospective observational study about clinical data of patients who started FTC/TAF +DRV/COBI, also in preparation of a prospective regional study on DRV/COBI/FTC/TAF use.
Material and methods: In 5 centres in Tuscany (2 in Florence and 1 in Siena, Pistoia and Livorno), an anonymous pre-formulated database has been used to collect selected variables among patients who started FTC/TAF +DRV/COBI in 2017-18. Data were derived from clinical records.
Results: A total of 141 patients started FTC/TAF+DRV/COBI in the study period.
Fifteen patients were naïve to therapy, their demographical and clinical characteristics are summarized in the table 1.
The remaining 126 patients switched to FTC/TAF+DRV/COBI. Of them, 55% had HIV-RNA <50 at the time of switch. In these patients a mean of 4 ART regimes have been previously used. Most of them (78%) was already taking a therapy including DRV. Detailed characteristics of these patients are summarized in the table 2. Due to short follow-up time, the virological outcomes of remaining patients is still under investigation.
Reasons for switching were mostly proactive switch (45%), and simplification (37%). Switches were done because of virological failure or toxicity of previous therapies in 14% and 4%, respectively.
During the study period only 5 patients stopped the treatment with FTC/TAF+DRV/COBI, in 4 cases for simplification to a STR regimen (3 to 3TC/ABC/DTG and one to FTC/TAF/EVG/COBI), in one case to a DTG/RPV dual therapy.
Conclusions: in real-life the association FTC/TAF+DRV/COBI is commonly used, especially among patients already using DRV, where the tolerability is already verified. Reasons for switching to FTC/TAF+DRV/COBI are similar as for other optimization strategies: mostly proactive switch (probably for the presence of TAF) and simplification in order to increase the compliance. This regimen is well tolerated, with few cases of interruption mostly due to a further simplification to a STR before DRV/COBI/FTC/TAF STR introduction. On the basis of these preliminary data, we believe that a prospective regional study aimed to investigate indications, tolerability, compliance, patients reported outcomes (PROs) and viro-immunological outcome of DRV/COBI/FTC/TAF STR is useful.

Issues on antiretroviral therapy

P 91 USE OF INTEGRASE-INHIBITORS AS PART OF DUAL OR TRIPLE REGIMENS IN THE ITALIAN MASTER COHORT BETWEEN 2009 AND 2017

F. Iannuzzi[7], S.N. Rich[10], E. Quiros Roldan[1], G. Paraninfo[1], G. Migliorino[7], F. Vichi[5], E. De Filippo[2], L. Sighinolfi[6], S. Lorenzotti[8], A. Saracino[4], N. Mazzini[9], R. Cauda[3], G. Carosi[9] for the Master cohort group

[1]University Division of Infectious and Tropical Diseases, University of Brescia, Brescia, [2]Infectious Diseases, Papa Giovanni XXIII Hospital, Bergamo, Italy; [3]Infectious Diseases, Policlinico A. Gemelli – Catholic University, Roma, Italy, [4]Infectious Diseases, Policlinico di Bari, Italy, [5]Infectious Diseases, S.M. Annunziata Hospital, Firenze, Italy, [6]Infectious Diseases, Nuovo Polo Ospedaliero di Cona, Ferrara, Italy, [7]Infectious Diseases, San Gerardo Hospital, Monza, Italy, [8]Infectious Diseases, Istituti Ospitalieri, Cremona, Italy, [9]M.I.S.I. Foundation, Brescia, Italy, [10]Department of Epidemiology, University of Florida, USA

Background: In the last 10 years the use of Integrase inhibitors (INI) as part of two-drugs (2D) or three-drugs (3D) regimens increased greatly due to their high efficacy and tolerability. Aim of the study was to describe the use of INI in a large Italian cohort

Material and methods: Patients in the MaSTER cohort initiating INI for the first time (INI-naïve) as part of a 2D or 3D regimen between 2009 and 2017 were selected. We described clinical and demographic characteristics overall and by calendar year of treatment initiation (2009-2011, 2012-2014 and 2015-2017). Moreover, we compared the characteristics of the patients initiating 2D or 3D regimen. Statistical analysis: chi-square, Welch's T-test, Wilcoxon rank sum test.

Results: Among 3422 patients previously INI-naive, 1001 (29%) initiated INI as a 2D regimen and 2421 (71%) as a 3D regimen (Table 1); 29% were female and the median age was 52 (IQR: 47-57) years. Most of treatment were initiated in latest years (67% between 2015 and 2017). Dolutegravir, raltegravir and elvitegravir was the first INI used by 46%, 40% and 14% of the patients, respectively. Among 2D regimens, the companion drug was a boosted PI in 65%, a single NRTI in 23% and a NNRTI in 12% of the cases. Compared to patients prescribed with a 3D regimen, patients prescribed with 2D were more likely to be older (>65 y.o., 11% vs 6%; p<0.001), Italian (92% vs 88%, p<0.001), renally impaired (eGFR <60, 14% vs 5%), previously diagnosed with AIDS (29% vs 25%, p<0.001) and with current CD4 count <350 cells/mm3 (26% vs 21%, P=0.003). By contrast, they were less likely to be co-infected with HCV (HCV-RNA positive 1% vs 2%, p=0.005) or HBV (HBsAg positive 4% vs 7%, p<0.001). No differences in terms of gender, HIV risk factors and history of cardiovascular events were found.

Prescribing attitudes changed across time: raltegravir, almost invariably used before 2015 (96% of all INI prescriptions in 2009-2014), was superseded by other INI in 2015-2017, when dolutegravir was prescribed in 67% of the cases (83% of 2D regimens and 63% of 3D regimens). In parallel, patients prescribed with INI became progressively older, more frequently non-Italian and with higher CD4+ counts (see Table 2). The proportion of 2D regimens decreased across time (from 49% in 2009-2011 to 21% in 2015-2017). Also, the companion drug in 2D regimen changed: boosted PI was the choice in 94% of cases in 2009-2011 but only in 38% of cases in 2015-2017, when the association of 1 NRTI + 1 INI represented 47% of 2D regimens (and 10% of all new INI prescription).

Conclusions: Use of 2D regimens including INI was widespread since 2009 and more frequent among older patients and among those with renal impairment. Prescribing attitudes of INI profoundly changed across time, reflecting the availability of newer drugs and the widespread use of INI in the general HIV-positive population.

The data analysis were carried out thanks to an unrestricted grant from ViiV Healthcare.

Management and treatment of viral hepatitis

P 92 CD4+ T- CELL COUNT AND CD4/CD8 RATIO TREND AFTER HCV ERADICATION IN HCV/HIV-COINFECTED SUBJECTS TREATED WITH DAAS: AN OBSERVATIONAL RETROSPECTIVE STUDY OVER A 4 YEAR PERIOD

M. Di Nuzzo, C. Contini, M. Libanore, D. Segala, L. Sighinolfi

Malattie Infettive, Ospedale Nuovo S. Anna, Ferrara

Background: Immune activation and inflammation due to HIV infection is currently considered the driving force of CD4+ T-cell depletion and of the functional impairment of the immune system. Hepatitis C virus (HCV) coinfection, has been suggested as contributing to immune activation. Since direct-acting antiviral agents (DAAs) has been introduced, HCV has been treated and eradicated in a large proportion of HIV/HCV-coinfected patients. However, the impact that HCV eradication has on immune activation and immune recovery is still unclear. We want to investigate CD4+, CD8+ T-cell count, and CD4/CD8 ratio trend in cirrhotic and not-cirrhotic HIV/HCV-coinfected patients after DAAs treatment and HCV eradication.

Materials and Methods: We retrospectively reviewed all HIV/HCV-coinfected patients treated with DAAs, from January 2015 to February 2019 at HIV Department in Ferrara. We recorded demographic data, HCV and HIV-related data at baseline and 24 weeks after treatment completion.

Subjects without a sustained virological response (SVR24: HCV RNA not detectable 24 weeks after treatment completion), with HIV RNA > 50 copies/ml at any time over the study period, or ART initiation < 6 months, were excluded. We considered cirrhotic those with liver stiffness >12.5 kPa (Metavir score: F4). Median and interquartile range (IQR) are presented for not-normally distributed continuous variables, numbers and percentages of cases for categorical variables. Mann-Whitney U test was used to compare not-normally distributed data, Wilcoxon signed ranked test to compare changes in continuous variables over time within a sample, two-way ANOVA test to compare changes over time between two samples. P value < 0.05 was considered statistically significant.

Results: We treated 108 HIV/HCV-coinfected patients (M:F= 2.6:1) over the study period, and 66 were eligible for the study [Figure 1]. Baseline characteristics of patients are shown in Table 1. CD4+ T-cell count was statistically different between cirrhotic and not cirrhotic subjects at baseline and at SVR24 [Table 1, 3]. At SVR24, CD4+ T- cell absolute count showed a significant increase ($p<0.05$) both in cirrhotic (5 cell/mmc, SD 30.8) and not-cirrhotic subjects (105 cell/mmc, SD 85.69) [Table 2]. The CD4+ T-cell count increase was larger among not-cirrhotic subjects ($p=0.0106$). CD4+ T-cell count percentage significantly increased only in not-cirrhotic subjects ($p=0.006$). CD4/CD8 ratio did not changed after achieving SVR24 in both groups.

Conclusions: Cirrhosis has probably an impact on CD4 T-cell count, being CD4+ T-cell count statistically different between cirrhotic and not cirrhotic subjects at baseline and at SVR24. Once achieved HCV eradication (SVR24), CD4+ T-cell count increased more in not cirrhotic subjects ($p=0.0106$), but CD4/CD8 ratio did not change. The role of HCV and cirrhosis on inflammation and immune activation requires further investigations.

Management and treatment of viral hepatitis

P 93 POSITIVE IMPACT OF DAA ON PATIENT-REPORTED OUTCOMES AND NEUROCOGNITIVE PERFORMANCES IN HCV MONO-INFECTED AND HIV/HCV CO-INFECTED PATIENTS

E. Pollastri[1], S. Odolini[1], S. Volpi[1], V. Cappa[2], S. Calza[2,3], A. Spinetti[1], S. Zaltron[1], P. Nasta[1], S. Compostella[1], G. Zuglian[1], C. Carriero[1], C. Chirico[1], F. Castelli[1], E. Focà[1]

[1]University department of Infectious and Tropical diseases, ASST Spedali Civili of Brescia, [2]Unit of Biostatistics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy, [3]Big&Open Data Innovation Laboratory (BODaI-Lab), University of Brescia, Brescia, Italy

Background and Aims: HCV chronic infection may worsen Patient-Reported Outcomes (PROs) including quality of life (QoL), fatigue and its functional repercussions on work productivity. HCV related neuroinflammation might also correlate with cognitive dysfunction compromising neurocognitive performances (NCP). We aimed to evaluate the impact of DAA both on PROs and on NCP.

Material and Methods: A perspective observational study on HCV mono-infected and HIV/HCV co-infected patients treated with DAA was conducted at the Clinic of Infectious and Tropical diseases of Brescia, ASST Spedali Civili, from October 2017 to June 2018. Data were collected at baseline (BL), end of treatment (EOT) and 12 weeks after EOT (SVR12). PROs were evaluated with the following questionnaires: Chronic Liver Disease Questionnaire (CLDQ), Fatigue Severity Scale (FSS), Visual Analogue Fatigue Scale (VAFS) and Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH). Montreal Cognitive Assessment (MOCA) test allowed evaluating NCP. Exclusion criteria were: HIV infection with lymphocytes CD4+ nadir <200 cell/µL or HIV related encephalopathy, current alcohol or drug abuse and severe psychiatric disorders. Population features were analysed to identify factors related to PROs and NCP. Statistical significance was considered with p-value <0.05.

Results: 76 patients (60.5% males) were included in the study: mean age was 60.7, 29 patients (38.1%) had advanced fibrosis, 6 patients (7.9%) were HIV/HCV co-infected, 18 patients (23.6%) were taking a polytherapy (≥ 5 drugs), ribavirin (RBV) was added in 10 cases (13.1%) (table 1). Improvements were registered in all questionnaires at SVR12, with significant changes in CLDQ, VAFS and MOCA (table 2). QoL was lower in women and elderly. RBV assumption temporary affects QoL and fatigue. Female sex, age and polytherapy were related to worse NCP. HIV/HCV co-infection and fibrosis did not affect the scores.

Conclusions: DAAs seem to be associated with improvement in PROs and NCP, regardless of fibrosis degree and HIV/HCV co-infection. These aspects must be always considered in real settings, particularly in specific populations including women, elderly or those assuming polytherapy. Further research is needed to analyse both long-term changes in PROs and NCP.

Management and treatment of viral hepatitis

P 94 THE HEALTH SAVING COSTS OF HCV TREATMENT OF DRUG USERS: EVIDENCE FROM THE REAL PRACTICE OF DRUG DEPENDENCE SERVICES (SERDS)

F.A. Nava, A. Chiesa, G. Strepparola, G. Pennisi, R. Vitali, L. Trevisi, A. Lucchini

FeDerSerD (Italian Society of Addiction Medicine), Milan, Italy

Background: The World Health Organization (WHO) has set up the elimination of hepatitis C virus (HCV) worldwide by 2030. This goal may be reached thanks to the introduction in the clinical practice of direct anti-viral drugs (DAAs) that are able to heal the disease reducing the public healthcare costs. In some countries such as Italy the access to HCV care of people who inject drugs (PWIDS) is yet largely unsatisfactory.

Aims: The main aims of this study were to evaluate in HCV positive patients attending the Drug Dependence Services (Ser.D.s) of the metropolitan area in Milan (Italy): 1) the efficacy and the effectiveness of patients' journey of the treated patients; 2) the public health costs and the economic benefits in term of health cost saved for each PWID treated.

Methods: We performed a retrospective study including 1,333 PWID took in charge by Ser.D.s in Milan of the area Marisana-Melegnano, over one year (January – December 2017). The data were collected using the electronic clinical database of the public health service of Martisana-Malegnano (ASST – Martisana Malegnano) able to register for each patient every medical benefits received during the year (including specialist, hospital admissions, diagnosis processes, etc.).

Results: In the cohort of the patients included the study we found 274 HCV-positive PWIDs, 65 ofwhich were treated. The mean of the health direct costs per each treated patient (excluding the cost of the drug) was € 1,418. The above costs may be further reduced of 12% if the patient is included in a more effective patients' journey, including harm reduction measures able to reduce the re-infection rates.

Conclusion: The study shows that the HCV treatment in PWID can significantly reduce over the years not only the individual health costs but also the health community costs. Moreover, our study shows that an integrated and effective patient's journey, together with harm reduction measures, can be further effective and cost saving for the health care system.

References

Nava F.A., 2018. For a program of eradication of hepatitis C in the population at risk (drug users and convicts). Acta Biomed., 89 (Suppl. 10): 33-41.

WHO, 2017. Global Hepatitis Report. http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/

Management and treatment of viral hepatitis

P 95 THE NORMAL ALT: ACHIEVEMENT OF TRANSAMINASES TRUE NORMAL VALUE IN A COHORT OF HIV/HCV CO-INFECTED SUBJECTS AFTER SVR

R. Rossotti, M. Merli, C. Baiguera, M. Cantone, T. Angelini Zucchetti, V. Picciotto, F. Bosca, M. Vinci, M. Puoti

Niguarda Hepatitis Center - Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan

Background: Laboratory ranges of normality are based on the features of the general population living in a certain area, but do not describe the real normality of a biochemistry parameter in a healthy individual. In 2002 Prati et al. defined the true normal value of ALT for people without HCV, in 2017 the American College of Gastroenterology set its threshold of normality. Not achieving a "true normal" ALT value is associated with a relative risk 8-times higher of liver-related death and with an increased risk of cardiovascular death. Aims of present study: describe the proportion of co-infected individuals who reach normal ALT values after SVR and assess predictive factors.

Methods: Co-infected subjects who underwent anti-HCV treatment and who achieved SVR from 2014 to 2018 were analyzed. Demographic, clinical, treatment and laboratory features were collected at baseline, at week 4, week 8, End of Treatment (EOT), SVR12, SVR24, SVR48, and then every year (up to 144 weeks after EOT). Descriptive statistics and non-parametric (Chi-squre and ANOVA as appropriate) tests were used; KM probability curves and Odd Ratio (OR) were calculated.

Results: 155 co-infected individuals, mainly men (79.4%), with a median age of 52 years were enrolled; 43.9% was cirrhotic, 41.9% was infected by genotype 1a. They were all receiving antiretrovirals with full HIV viral suppression; median CD4 cell count was 522 cell/mmc. ALT normality was achieved by 69.0% of subjects, while 8.4% did not normalize; a proportion of 21.9% showed a fluctuation of values over time. Normalization was reached after a median of 4 weeks of treatment. Diabetes was less common in those who normalize than in those who did not (6.5% versus 15.2%, p=0.037), as well as female gender (16.1% versus 34.8%, p=0.016) and liver cirrhosis (35.5% versus 63.0%, p=0.006). No other differences emerged between the groups besides a suggested higher HBsAg-positivity in those with continuing altered biochemistry (6.5% versus 2.2%, p=0.055).
Figure 1 shows the probability of achieving ALT normality.
After excluding from the analyses 14 individuals with normal baseline ALT values, no HIV-related factor was found to be related with a persisting altered parameter, while female sex (OR 2.77, 95%CI 1.22-6.30, p=0.013), cirrhosis (OR 3.10, 95%CI 1.49-6.46, p=0.002), stiffness above 14 kPa (OR 2.76, 95%CI 1.33-5.73, p=0.006), ribavirin use (OR 2.40, 95%CI 1.15-5.03, p=0.019) and alcohol use (OR 2.18, 95%CI 1.05-4.53, p=0.035) were associated with persisting altered transaminase.

Conclusions: The majority of co-infected subjects achieved normal ALT after SVR; as expected, cirrhotics maintain more often abnormal transaminase values. Behavioral and metabolic issues are associated with an ongoing liver damage. Gender differences need further investigation. Despite high SVR rate, our data suggest that liver disease might remain a relevant issue in HIV co-infected patients who continue to have altered liver biochemistry.

Management and treatment of viral hepatitis

P 96 THE USE OF INTRAHEPATIC PORTOSYSTEMIC SHUNT IN HIV POSITIVE PATIENTS: A RETROSPECTIVE MULTICENTRIC STUDY

A. Lombardi[1,3], R. Rossotti[4], A. Airoldi[8], F. Schepis[9], L. Turco[9], V. Zuccaro[1], M. Tran Minh[8], M. Colaneri[1,3], M. Sambo[1,3], M.G. Lupi[1,3], M.T. Giordani[10], P. Sacchi[1], M. Fabbiani[1], P. Quaretti[7], L. Scudeller[5], J. Rockstroh[6], M. Puoti[4], R. Bruno[1,2]

[1]Infectious Diseases Unit, IRCCS "San Matteo", Pavia, Italy, [2]Department of Medical, Surgical, Diagnostic and Paediatric Science, University of Pavia, Pavia, Italy, [3]Department of Internal Medicine and Therapeutics, University of Pavia, Italy, [4]ASST Grande Ospedale Metropolitano Niguarda, Infectious Diseases Department, Milano, Italy, [5]Clinical Epidemiology and Biostatistic Unit, Fondazione IRCCS "San Matteo", Pavia, Italy, [6]Bonn University Hospital, Bonn, Germany, [7]Interventional Radiology, Fondazione IRCCS Policlinico San Matteo Pavia, Pavia, Italy, [8]Department of Hepatology and Gastroenterology, ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy, [9]Department of Gastroenterology, Policlinico di Modena, Modena, Italy, [10]Infectious and Tropical Diseases Unit, Vicenza Hospital, Vicenza, Italy

Background: Chronic liver disease is a common finding in human immunodeficiency virus (HIV) infected subjects. In this population progression of liver disease occurs faster than in the non-infected subjects and liver-related death represents an important cause of non-AIDS-related death. Transjugular intrahepatic portosystemic shunt (TIPS) is a procedure used in advanced liver disease (ALD) to reduce portal hypertension and its related complications. However, few data are available about efficacy, safety and tolerability of this procedure in HIV-infected patients.

Methods: We retrospectively selected all HIV-infected patients with ALD who underwent to TIPS placement in 5 European Centres during the period 2009-2018. Patient's data were collected at baseline (time of TIPS placement) and during a two-year follow-up. The incidence of mortality and liver related complications were estimated by Kaplan-Meier analysis. The evolution of laboratory data after TIPS placement was evaluated through linear regression.

Results: Overall, the median model for end-stage liver disease (MELD) score at baseline was 14, chronic hepatitis C was the most frequent liver disease (61.5%), and variceal bleeding and refractory ascites were the indication to TIPS placement in 77.7% and 50% of patients, respectively. Of note, 33.3% of patients were exposed to dideoxynucleoside analogues (D-drugs) during their therapeutic history. TIPS placement led to a significant decrease of portosystemic pressure gradient (mean change -12.4 mmHg). A progressive increase in haemoglobin (mean change 2.49, p=0.025) and platelets (mean change 20500, p=0.019) values was also observed in the 2-year follow-up. TIPS placement did not change CD4+ cells count and HIV viral load. Two-year mortality was 29.5%, and in the same timeframe 83%, 78%, 61% and 27% of patients remained free of bleeding, spontaneous bacterial peritonitis, ascites and hepatic encephalopathy, respectively. (Fig. 1)

Conclusions: Overall, TIPS appears as a safe and effective procedure in HIV patients able to reduce the consequences of portal hypertension, especially those related to hypersplenism, although the risk of hepatic encephalopathy is higher than in the non-HIV patients. It is also important to note that the TIPS placement did not affect the efficacy of antiviral drugs.

Management and treatment of viral hepatitis

P 97 A LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY METHOD FOR SIMULTANEOUS DETERMINATION OF SIMEPREVIR, DACLATASVIR, SOFOSBUVIR, AND GS-331007 APPLIED TO A RETROSPECTIVE CLINICAL PHARMACOLOGICAL STUDY

D. Ferrari[1,2], S. Bagaglio[3], M. Raso[2], L. Galli[3], S. Premaschi[2], E. Messina[3], G. Morsica[3], M. Locatelli[2], C. Uberti-Foppa[3,4], H. Hasson[3]

[1]SCVSA Department, University of Parma, Parma, Italy, [2]Laboratory Medicine Service, San Raffaele Hospital, Milano, Italy, [3]Clinic of Infectious Diseases, San Raffaele Hospital, Milano, Italy, [4]Vita-Salute San Raffaele University, Milano, Italy

A highly sensitive liquid chromatography-tandem mass spectrometry (LC–MS/MS) method was developed and validated for simultaneous determination of daclatasvir (DCV), simeprevir (SMV), sofosbuvir (SOF), and its major metabolite GS-331007 in human plasma using stable-isotope-labeled (SIL) analogs as internal standards (IS) to minimize a possible matrix effect. Liquid-liquid extraction (LLE) of the analytes and IS from human plasma was performed using a commercial extraction kit requiring low sample volume (50 µl). The analytes were eluted under a gradient program with mobile phase A (water + 0.1% formic acid) and mobile phase B (methanol + 0.1% formic acid) at a flow-rate of 0.6 mL/min for 10 min. The detection was performed on a Qtrap 5500 triple quadrupole tandem-mass spectrometer using multiple reaction monitoring (MRM) mode via the positive electrospray ionization interface. The method was validated according to the European Medicine Agency (EMA) guidelines over the clinically relevant concentration range of 15.6-2,000 ng/mL. The high reproducibility, the low matrix effect associated with the use of SIL-IS, and the need of small sample amounts make this method particularly suited for high-throughput routine analysis. The proposed method was successfully applied to a retrospective clinical pharmacology study involving 67 HIV/HCV co-infected patients treated with a SOF-based therapy. DCV, SMV, SOF, and GS-331007 plasma levels were measured at week 4 of treatment and compared with the patients' clinical and laboratory characteristics. Higher GS-331007 plasma concentrations were observed in female patients compared to males, which can be explained by different anthropometric characteristics between genders. Importantly, patients with high plasma levels of GS-331007 also showed enhanced concentration of DCV and SMV probably due to a specific metabolic/pathological condition. Altogether, our findings indicate that the proposed method is a reliable and accurate new tool for high-throughput screening of large patient cohorts that could be readily used to optimize treatment modalities and reduce drug-related toxicities.

Management and treatment of viral hepatitis

P 98 SUCCESSFUL ONGOING RETREATMENT WITH GLECAPREVIR/PIBRENTASVIR+SOFOSBUVIR+RIBAVIRIN GUIDED BY RESISTANCE TEST IN A PATIENT WITH HCV GENOTYPE 3 WHO FAILED GLECAPREVIR/PIBRENTASVIR WITH BOTH NS3 AND NS5A RESISTANCE

*M. Aragri[1], C. Masetti[2], V. C. Di Maio[1], I. Lenci[2], M. Milana[2], A. Bertoli[1], K. Yu La Rosa[1], M. Ciotti[3], S. Grelli[3], C. F. Perno[4], M. Angelico[2], F. Ceccherini-Silberstein[1]**

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [2]Hepatology Unit, University Hospital of Rome Tor Vergata, Rome, Italy, [3]Virology unit, University Hospital of Rome Tor Vergata, Rome, Italy, [4]Department of Oncology and Oncohematology, University of Milan, Milan, Italy, *On behalf of HCV Virology Italian Resistance Network (Foundation Vironet C)

Background: HCV Genotype (GT) 3 is still one of the most challenging GT to treat. It has been described for this GT that baseline NS5A resistance-associated substitutions (RAS) can reduce the efficacy of direct-acting antivirals (DAA)-based regimens in patients with chronic HCV infection.
Methods: A 47-year-old man, HCV GT3a infected with advanced liver fibrosis, naïve to treatment, with high baseline HCV RNA (5.693.154 IU/ml, Abbott real time HCV-RNA assay) started glecaprevir+pibrentasvir (G/P) treatment for 16 weeks. Even if responded rapidly (at 22 days HCV-RNA = 90 IU/ml), showed a viral breakthrough at 6 weeks with an increase of HCV-RNA (1739 IU/ml). At this time point (and also at baseline and at follow-up), NS3-NS5A-NS5B genotypic resistance testing (GRT) was performed by home-made Sanger sequencing.
Results: GRT performed at week 6 and 8 revealed the same resistance pattern in both NS3 and NS5A (A156G NS3-RAS and A30K+Y93H NS5A-RAS). The retrospective GRT at baseline showed only the A30K NS5A-RAS. According to the recent MAGELLAN-3 data, where G/P+sofosbuvir+ribavirin for 12-16 weeks for retreatment after G/P failure showed 95% sustained virological response (SVR), in a context of multidisciplinary team including experienced treaters and virologists, at the G/P regimen was added first ribavirin and then sofosbuvir. After an overall ongoing retreatment with G/P+sofosbuvir+ribavirin for 8 weeks the patient achieved SVR12 (see figure).
Conclusions: This is the first case where ongoing retreatment with G/P+sofosbuvir+ribavirin showed SVR in a patient HCV infected with GT3 who failed glecaprevir/pibrentasvir with both NS3 and NS5A resistance. The presence of a high baseline HCV RNA and NS5A natural RAS before treatment in a context of a GT3 infection may have contributed to the therapeutic failure. In this case-report, HCV GRT and multidisciplinary team discussion was helpful to guide retreatment decision by intensifying the ongoing DAA-regimen, which led finally to the achievement of the SVR.

Management and treatment of viral hepatitis

P 99 REAL-WORLD EFFECTIVENESS AND SAFETY OF GLECAPREVIR/PIBRENTASVIR IN PATIENTS WITH CHRONIC HEPATITIS C: AN INTERIM ANALYSIS OF THE ITALIAN DATASET OF A MULTICOUNTRY POSTMARKETING OBSERVATIONAL STUDY

The MARS Study Group: A. Aghemo[1], A. Alberti[2], P. Andreone[3], M. Angelico[4], A. Antinori[5], M.R. Brunetto[6], L. Chessa[7], A. Ciancio[8], A. Craxi[9], G.B. Gaeta[10], M. Galli[11], A. Gasbarrini[12], A. Giorgini[13], P. Lampertico[14], M. Lichtner[15], M. Milella[16], F. Morisco[17], M. Persico[18], M. Pirisi[19], M. Puoti[20], G. Raimondo[21], G. Rizzardini[22], A. Romano[23], M. Russello[24], V. Sangiovanni[25], G. Serviddio[26], E. Villa[27], M. Vinci[28], A.L. Zignego[29], A. De Michina[30], G. Guida[30], A.S. Roscini[30]

[1]Istituto Clinico e di Ricerca Humanitas, Rozzano (MI),[2]Dipartimento di Medicina Molecolare Università di Padova, [3]Dipartimento di Scienze Mediche, Materno Infantili e dell'Adulto, Università di Modena e Reggio Emilia, [4]Dipartimento di Medicina - UOC di Epatologia, Fondazione PTV - Policlinico Tor Vergata, Roma, [5]Dipartimento Clinico UOC Immunodeficienze Virali, INMI Lazzaro Spallanzani IRCCS, Roma, [6]Dipartimento di Medicina clinica e sperimentale Università di Pisa - UO Epatologia, Azienda Ospedaliero - Universitaria Pisana, Pisa, [7]Medicina Interna e Malattie del Fegato, AOU Cagliari, Monserrato (CA), [8]Dipartimento di Scienze Mediche, SC GastroEpatologia U, A.O.U. Città della Salute e della Scienza di Torino, Università di Medicina, Torino, [9]Dipartimento Biomedico di Medicina Interna e Specialistica - Reparto di Gastroenterologia, Azienda Ospedaliera Universitaria Policlinico P. Giaccone, Palermo, [10]Dipartimento Salute Mentale e Fisica, UOC Malattie Infettive, Università degli Studi della Campania "Luigi Vanvitelli", Napoli, [11]Dip. Scienze Biomediche e Cliniche L.Sacco - UNIMI, III Divisione Malattie Infettive, ASST Fatebenefratelli Sacco, Milano, [12]UOC Medicina Interna, Malattie dell'Apparato digerente e del fegato, Fondazione Policlinico Universitario A. Gemelli, Roma, [13]Dipartimento di Malattie epatologiche, gastroenterologiche e metaboliche, Reparto U.O di Epatologia e Gastroenterologia, ASST Santi Paolo e Carlo, Milano, [14]Dipartimento di fisiopatologia medico chirurgica e dei trapianti /Dipartimento di Medicina, UOC Gastroenterologia ed Epatologia, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, [15]Dipartimento di Sanità Pubblica e Malattie Infettive, Sapienza Università di Roma, polo pontino, UOC Malattie Infettive, Ospedale SM Goretti, Latina, [16]DIMO - U.O.C. di Malattie Infettive, Azienda Universitaria Ospedaliera Consorziale-Policlinico Bari, Bari, [17]Dipartimento di Medicina Clinica e Chirurgica, UOC di Gastroenterologia ed Epatologia, Università Federico II, Napoli, [18]Dipartimento di Medicina Clinica Medica, Epatologica e Lungodegenza, AOU OO. RR. San Giovanni di Dio Ruggi e D'Aragona, Salerno, [19]Università del Piemonte Or. Medicina Traslazionale, SCDU Medicina Interna 1, AOU Maggiore della Carità di Novara, Novara, [20]Dipartimento Medico Polispecialistico, Malattie Infettive, ASST Grande Ospadale Metropolitano Niguarda, Milano, [21]Dipartimento di Medicina Clinica e Sperimentale, UOC di Epatologia Clinica e Biomolecolare, Università ed AOU di Messina, [22]Dipartimento Malattie Infettive, ASST Fatebenefratelli Sacco, Milano, [23]Dipartimento di Medicina (DIMED) UOC Clinica Medica 5°, A. O. Di Padova, Padova, [24]Dipartimento Medicina Interna, UOSD Epatologia, Azienda Ospedaliera di Rilievo Nazionale e di Alta Specializzazione Garibaldi - Presidio Ospedaliero Garibaldi-Nesima, Catania, [25]Dipartimento Malattie Infettive e urgenze infettivologiche, Reparto infezioni sistemiche dell'immunodepresso, A.O. Domenico Cotugno, Napoli, [26]Unità Universitaria di Epatologia, OORR Ospedali Riuniti - Università degli Studi di Foggia, [27]UC Gastroenterologia, Dipartimento di Specialità Mediche, Azienda Ospedaliera Universitaria di Modena, Modena, [28]Dipartimento Medico Polispecialistico, S.C. Epatologia e Gastroenterologia, ASST Grande Ospadale Metropolitano Niguarda, Milano, [29]Centro Interdipartimentale di Epatologia MASVE, Azienda Ospedaliero-Universitaria Careggi, Firenze, [30]Medical Department, AbbVie srl, Roma

Background: Data on the efficacy and safety of Glecaprevir/Pibrentasvir (G/P) for the treatment of HCV infection in clinical practice are still limited. The MARS study (Real World Evidence of the Effectiveness and Clinical Practice Use of G/P in Patients with Chronic Hepatitis C Genotypes 1-6), still ongoing, evaluates this therapeutic regimen in a large population of patients with chronic HCV infection from Italy, as part of a wide international study.

Materials and Methods: All HCV infected patients, consecutively treated with G/P, were enrolled in 29 Italian Centers from Jan to May 2018, with a follow-up until SVR12. The achievement of a sustained virological response (HCV-RNA absent in blood sampling of patients 12 weeks after therapy termination), and the presence of adverse events (AE) and/or serious adverse events (SAE) were the main endpoints of this prospective post-marketing study. This interim analysis reports data from the October 2018 data cut.

Results: 337 patients were enrolled in Italy. 322 had available data in the Electronic Data Capture system at the time of the data cut, 117 of them had completed the study. Baseline characteristics of the available population (N=314) where: mean age 57.6±13 years, 48.4% males, 99% white, mean BMI 24.4±3.6 (Table1).

The most frequent genotypes (GT) were GT 1 (n=180; 57.3%) and 2 (n=70; 22.3%). 31 patients (9.9%) had been infected with GT 3. METAVIR score was: F0-1 in 224 patients (71.3%), F2 in 9 (2.9%), F3 in 11 (3.5%); F4 in 18 (5.7%), missing data in 52 (16%). The majority of patients showed normal renal function (stage I, n=121, 38.5%) or slightly reduced (stage II; n=116, 36.9%); 13 subjects had stage III CKD (4.1%), 1 had stage IV and 1 stage V (0.3%).

Main coinfections were HIV (34, 10.8%) and HBV (19, 6.1%); 1 patient was on hemodialysis and 1 on peritoneal dialysis. Psychiatric disorders were present in 30 patients (9.3%).

The majority of patients (n=258; 82.2%) were naïve to any HCV treatment. The expected duration of G/P therapy was 8 weeks for 288 patients (91.7%), 12 weeks for 25 patients (8%) and 16 weeks for only 1 subject (0.3%). During the treatment period 7/265 subjects with available data showed total bilirubin ≥ 2xULN and increased from baseline, without a concomitant increase in ALT/AST.

22 (6.8%) patients reported any adverse event; 3/22 reported a SAE (0.9%), 1 of these SAE was fatal (with no reasonable possibility of being related to the drug) (Table2). One hepatic decompensation occurred.

The current ITT analysis provides SVR12 data for 117 patients, showing an overall SVR12 99.2% (116/117), as detailed in Fig1. The only patient not achieving SVR12 discontinued study treatment due to an adverse event (nausea/dizziness) after the first dose.

Conclusions: The MARS "real-life" study shows a high SVR12 rate, confirming the excellent efficacy and safety of the G/P combination as described in the registration trials, even in the 8 weeks strategy.

Management and treatment of viral hepatitis

P 100 Trieste experience in the treatment of Hepatitis C in people who inject drugs: the integrate management between addiction treatment service (SerD), liver clinic, and infective disease department

M. Giuffrè[1,2], A.C. Baez[3], A. Colombo[1,2], I.M. Crosato[4], F. Masutti[2], M. Santi[3], C. Stanic[3], R. Balestra[3], S.L. Crocè[1,2,5], R. Luzzati[1,4]

[1]Dipartimento Universitario Clinico di Scienze Mediche Chirurgiche e della Salute, Università degli Studi di Trieste, [2]Clinica Patologie del Fegato, Azienda Sanitaria Universitaria Integrata di Trieste, [3]Dipartimento delle Dipendenze, Azienda Sanitaria Universitaria Integrata di Trieste, [4]Malattie Infettive, Azienda Sanitaria Universitaria Integrata di Trieste, [5]Fondazione Italiana Fegato

Background: according to Italian Statistics, people who inject drugs (PWID) have high rates of Hepatitis C Virus (HCV) infection (30-60%). PWID have inadequate access to directly acting antivirals (DAA) due to (1) their mistrust towards the healthcare system and (2) the lack of coordination between medical specialists who play a pivotal role in the diagnosis and treatment of HCV infection. We aim to characterize the cascade of care in Trieste, to improve HCV treatment access and delivery for PWID.

Description of Model of Care: universal and free-of-charge infective screening is offered to PWID by SerD staff. Patients are introduced to counseling where HCV risk behaviors and harm reduction policies are carefully explained. HCV antibody detection represents the first-line of screening. Around 90% of HCV-antibody positive patients agree to further testing (HCV-RNA and genotype). Patients are further evaluated by abdominal ultrasound and liver elastography and then referred to: (1) the Infective Disease Department (adult and/or HIV-coinfected patients) or (2) the Liver Clinic (< 25 y.o. and/or patients with higher degree of liver fibrosis) – where the medical specialist prescribes DAA. Therapy administration and supervision are planned according to patients' compliance, socio-economic status, family support, and psychiatric comorbidities in order to avoid drop out and incorrect drug intake.

Effectiveness: between January 2015 and December 2018, 255 individuals were treated for HCV infection, and 19 of those presented with HCV/HIV co-infection. 45 patients were referred to the liver clinic, whereas 210 to the infective disease department. The most prevalent genotype were 3 (51%, subtype 3a in 61% of cases) and 1 (40%, subtype 1b in 57% of cases). 177 patients (69%) presented fibrosis F2 at the beginning of therapy, 30 (12%) with F3, and 29 (11%) with F4. 249 (97.6%) patients had a sustained viral response at 12 weeks (SVR12), while 2 were non-responders, 2 had relapsing infection, and 2 presented with reinfection. According to the data, the SerD saw a drastic increase in supervised treatment of HCV positive individuals (compared to the total HCV treated patients in the Trieste Area): from 7% in 2015-16 to 36% in 2017 and 86% in 2018.

Conclusion: our HCV care model demonstrated how addiction treatment service (SerD) is fundamental to deliver and monitor HCV treatment in PWID successfully. The goal of the system is to create a personalized and straightforward care process that appoints the complexity and vulnerability of the patient. Simplified, integrated and more flexible plans that promote the therapeutic relationship between the patients and the SerD medical and nursing personnel, allow (1) quicker access to treatment (2) increased adherence to therapy, and (3) changes in risk behaviors, thus reducing reinfection rate and progressively decreasing virus prevalence in the target population.

Management and treatment of viral hepatitis

P 101 WEIGHT GAIN, LIPID PROFILE AND BODY COMPOSITION CHANGES IN HIV/HCV-INFECTED PATIENTS TREATED WITH DIRECT ANTIVIRAL AGENTS

M.F. Mariani, D.F. Bavaro, P. Laghetti, S. Lo Caputo, L. Monno, G. Angarano, A. Saracino

Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari Medical School, Bari, Italy

Introduction: Changes in lipid distribution in HCV-infected patients successfully treated with Direct Antiviral Agents (DAAs) have been previously described, even if the clinical impact of these metabolic alterations is still controversial. Aim of our study was to evaluate the effects of HCV treatment on body composition in a group of HIV/HCV co-infected patients studied by bioimpedance vectorial analysis (BIVA).

Methods: Starting from November 2018, all HIV/HCV co-infected subjects eligible to a DAA treatment and willing to participate to the study after informed consent, were enrolled to undergo BIVA (BIA 101 New Edition, Akern, Florence, Italy) (50Hz) at baseline (T0), at the end of the anti-HCV treatment (EOT) and 6 months after therapy completion. 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. 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, 21 HIV-HCV infected patients starting DAAs have been enrolled to date. At time of writing, follow-up data at both baseline and EOT were available for 10 individuals, 7 males, with median age (q1, first-q3, third quartile) 55 (50-60) years, all on antiretroviral therapy with undetectable HIV-RNA, with a median (q1-q3) of 724 (600-996) CD4 cells/mmc at baseline. HCV genotype 1 was the most frequently observed (50%) followed by 2 (20%) and 4 (20%); one patient had liver cirrhosis. Major recorded comorbidities were hypertension (3 pts) and mild kidney impairment (3 pts) (Table 1).

At EOT, a weight gain was observed in 9/10 pts, with a median (q1-q3) 2.2 (1.1 - 2-7) kg increase from T0 (p<0.001). By BIVA, a significant post-DAAs median increase of FM (p<0.02) was recorded [2.35 (1.17 - 3.27) Kg/m], while a non significant trend towards a decrease of FFM [-0.15 (-0.55 - 0.82) Kg/m] and SMM [-0.4 (-0.67 - 0.32) Kg/m] was noticed. BIVA also evidenced a significant increment (p<0.001) of BM after HCV eradication [28.8 median (20.1 - 60.7) Kcal] (Table 2). Moreover, a significant increase (p=0.01) in LDL levels [median 23.5 (19.2 - 38) mg/dL] together with a no significant decrease of HDL [2 (-2.25 - 5.5) mg/dL] and no significant variation in TG levels [0 (-20.5 - 6) mg/dL] were observed (Table 3).

Conclusions: An expected increase of Cho-LDL concentrations was observed at the end of the DAA treatment, which was associated with weight gain. Based on the results of the bioimpedance analysis, our study suggests that the weight gain is, in turn, mainly driven by an increase of body fat mass. A wider sample and a long follow up of lipid profile and body composition changes after HCV eradication is warranted.

Management and treatment of viral hepatitis

P 102 DAA FAILURE IN HCV GENOTYPE NOT 1: VIROLOGICAL FEATURES AND EFFICACY OF RE-TREATMENT

L. Occhiello[1], M. Pisaturo[1], M. Starace[1], C. Minichini[1], A. Di Fraia[1], S. De Pascalis[2], M. Macera[2], V. Messina[3], V. Sangiovanni[4], E. Claar[5], D. Precone[6], G. Stornaiuolo[2], M. Stanzione[2], I. Gentile[8], G. Brancaccio[2], S. Martini[9], A. Masiello[10], A. Salomone Megna[11], C. Coppola[12], A. Federico[13], E. Sagnelli[1], M. Persico[14], A. Galeota Lanza[15], A. Marrone[16], G.B. Gaeta[2], N. Coppola[1,3]

[1]Laboratory for the identification of prognostic factors of response to the treatment against infectious diseases, University of Campania "L. Vanvitelli", Napoli, Italy, [2]Infectious Diseases and Viral Hepatitis, Department of Mental and Physical Health and Preventive Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [3]Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, Italy, [4]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [5]Internal Medicine Unit, Evangelical Hospital Villa Betania Naples, Italy, [6]Internal Medicine Unit A.O Sarno, Sarno (SA) Campania L. Vanvitelli, & Infectious and Transplant Medicine, AORN Ospedali dei Colli- Monaldi Hospital, Naples, Italy, [7]Gastroenterology Unit, AOU San Giovanni di Dio Ruggi d'Aragona, Salerno Italy, [8]Infectious Diseases Unit, University Federico II, Naples, Italy, [9]HIV Unit, University of Campania L. Vanvitelli, Naples, Italy, [10]Infectious Diseases Unit, A.O S.G. Moscati, Avellino Italy, [11]Infectious Diseases Unit, A. O G.Rummo, Benevento, [12]Hepatology Unit, Gragnano Hospital, Gragnano, [13]Internal Medicine and Hepatology Department of Clinical and Experimental Medicine, University of Campania "L. Vanvitelli", [14]Internal Medicine and Hepatology Unit, PO G. Da Procida-AOU- San Giovanni e Ruggi D'Aragona, University of Salerno, [15]Hepatology Unit, Cardarelli Hospital, Naples, Italy, [16]Department of Medical, Surgical, Neurological, Metabolic, and Geriatric Sciences, University of Campania "L. Vanvitelli*

Background: Direct-acting antivirals (DAA)-regimens are associated with failure in about 5% of cases. The failure was associated to the emergence of resistance associated substitutions (RASs) within the viral quasispecies. This real-life study characterized the virological patterns in genotype not-1 patients failing IFN-free regimens and evaluated the efficacy of re-treatment.

Methods: All the consecutive 75 HCV genotype not-1 patients with failure to IFN-free regimen observed at the laboratory of infectious diseases of University of Campania,Naples from October 2015 to December 2018 were enrolled. All the patients had been treated with DAA-regimens according to HCV genotype, international guidelines and local availability. Sanger sequencing of NS3, NS5A and NS5B was performed at failure by home-made protocols.

Results: Table 1 shows demographic, virological and clinical characteristics of the patients enrolled and type of treatment. Patients were mainly males (80%) with median age of 58 years (range 31-86). 62,6% of patients had a diagnosis of cirrhosis, 26 patients were HCV genotype 2a/2c, 44 were genotype 3 and 5 were genotype 4.

The prevalence of RASs in NS5A region were more frequently detected in genotype 4 (80%) and genotype 3 (61,3 %) than in genotype 2a/2c (38,5%) with no statistical meaning. RAS in the NS5B region were identified only in genotype 3 (18,1%) and genotype 2a/2c (3,8%). Out of the 75 patients enrolled, 35 (46,6 %) patients were re-treated.

Table 2 shows the epidemiological, clinical and virological characteristics of the 35 retreated patients genotype not-1. According to therapeutic outcome, 84% were relapse, 4% were breakthrough and 12% were non-responder at retreatment.

The 18 patients re-treated with genotype 3 less frequently (77,7%) showed an SVR than the 11 patients with genotype 2a/2c (84,6%) with no statistical meaning.

In table 3 we analyze the SVR prevalence according to genotype, previous/latest DAAs regimen, RASs distribution and Resistance-Guided Therapy (RGT).

60% of patients with genotype 2a/2c, 50% with genotype 3 and 60% with genotype 4 without SVR show RASs.

According to therapeutic regimen, SVR was more frequent in patients HCV genotype 2a/2c treated with the latest DAAs regimen respect to previous generation DAAs (91% vs 9%, p=0.0001); also for patients with HCV genotype 3 treated with the latest generation DAAs (64,3% vs 35,7%, p=0.1306) SVR was more frequent. All HCV genotype 4 patient failed at retreatment.

Conclusions: The prevalence of RASs was high in our real-life population. Failed patients have at least one RASs in one HCV region. The latest DAA regimen more frequently obtained SVR despite previous regimen for HCV genotype 2a/2c and 3. HCV genotype 4 remains a difficult-to-treat genotype. Patients with RGT more frequently obtain SVR. NS3, NS5A and NS5B sequencing seems mandatory in the choice of re-treatment DAAs considering the not excellent prevalence of SVR in this subset.

Management and treatment of viral hepatitis

P 103 RETENTION IN CARE AMONG CHRONICALLY HBV-INFECTED PATIENTS: ONE MORE REASON TO TREAT

L. Magnasco[1], L. Di Nino[1], M. Mirabella[1], L.A. Nicolini[2]

[1]Department of Health's Science, University of Genoa, Genoa, Italy, [2]Infectious Diseases Unit, San Martino Policlinic Hospital, Genoa, Italy

Background: According to clinical guidelines not all chronically HBV-infected patients require immediate antiviral treatment (AT), but patients who are not treated should undergo careful follow-up.
Previous evidence shows a low linkage to care of chronically HBV-infected patients, but no definite factors that might predict retention in care have been identified.
The aim of our study was to identify predictors of low retention in care in a cohort of patients with chronic HBV-infection.
Material and methods: All adult patients with chronic HBV who underwent at least one outpatient visit at the Infectious Diseases Department (San Martino Policlinic Hospital, Genoa) during the period 2014-2018 were included. Demographic data, viral co-infections (HIV and HCV), type and timing of HBV treatment were evaluated and retrieved from electronical clinical records.
According to site procedures, patients with chronic HBV are usually evaluated every 6 months. Given the retrospective nature of the study, AT was prescribed according to caregiver decision. Patients missing appointments for scheduled visits or blood exams for more than 12 months were considered lost at follow up.
Retention in care was evaluated as a time-dependent variable. Kaplan Meyer (KM) analysis was used to assess factors associated with retention in care. Factors significantly associated with retention in care in the KM analysis were included in a Cox's regression model.
Results: Overall, 143 patients were enrolled in our cohort. Demographic and virological features of our patients are described in table 1. The average age at first outpatient visit was 41±14.66 years. Among the patients receiving HBV therapy, 86 (92.5%) were on AT with nucleos(t)id analogues and 7 (7.5%) with interferon + ribavirin.
The median duration of retention in care in our cohort was 2225±2760 days. Seventeen patients (11.9%) were lost at follow up.
At the KM analysis, both AT (of any kind) and HIV co-infection were significantly associated with retention in care (p<0,0001). After including both variables in a Cox's regression analysis, AT remained significantly associated with retention in care (p=0,041), while HIV co-infection did not (p=0,241).
Conclusions: In our experience, antiviral treatment administration was significantly associated with retention in care, independently from the presence of HIV co-infection. Although HBV treatment might be delayed in some cases, this data should be taken into account when dealing with patients at risk of loss at follow up.

Management and treatment of viral hepatitis

P 104 LIVER STIFFNESS VARIATION AFTER SVR ACHIEVEMENT IN A COHORT OF HIV/HCV CO-INFECTED SUBJECTS

R. Rossotti, C. Baiguera, M. Merli, M. Cantone, T. Angelini Zucchetti, V. Picciotto, F. Bosca, M. Vinci, M. Puoti

Niguarda Hepatitis Center, ASST Grande Ospedale Metropolitano, Niguarda, Milan

Background. Liver stiffness (LS) assessed with Fibroscan is an established non-invasive tool to evaluate hepatic fibrosis: it is used in clinical practice as indicative of histology stage and is also suggestive of the risk of portal hypertension (PHT). It is expected that LS decreases after SVR achievement, but only an improvement above 30% is considered to be clinically significant. Additionally, an improvement below 15% has been related to the risk of hepatocellular carcinoma (HCC) development. Several papers described major LS improvement in HCV mono-infected patients starting from higher values of fibrosis, but so far no data are available about co-infected individuals. Aims of present study: describe the proportion of co-infected individuals who significantly improve their baseline LS; describe variation of LS indicative of PHT; evaluate factors predictive of significant LS decrease; define if minor LS variations are related to increased risk of HCC or death.

Methods: Co-infected subjects who underwent anti-HCV treatment, achieved SVR from 2014 to 2018 and with a baseline and at least one follow up LS assessment were included. Demographic, clinical and laboratory features were collected. PHT was defined as probable with a LS≥21 kPa, undetermined with LS 13.6-20.9 kPa, absent if LS ≤13.5 kPa. Descriptive statistics and non-parametric (Chi-squre and ANOVA as appropriate) tests were used; Odd Ratios (OR) were calculated.

Results. 93 co-infected individuals, mainly men (80.6%), with a median age of 52 years were enrolled; 51.6% was cirrhotic, 34.4% was infected by genotype 1a and 32.3% by genotype 3. After SVR, 48.4% showed a LS improvement >30% (34.4% remained stable and 17.2% worsened). Figure 1 shows METAVIR stage and PHT variation. No baseline differences emerged between those who improved and those who did not beside a higher percentage of F4 fibrosis (68.9% versus 35.4%, p=0.0008) and ribavirin use (75.6% versus 52.1%, p=0.019).
The predictors of improvement >30% were baseline F4 fibrosis (OR 4.04, 95% CI 1.70-9.59, p=0.001), baseline MELD score >9 (OR 0.07, 95% CI 0.02-0.33, p=0.0002), ribavirin use (OR 2.84, 95% CI 1.17-6.89, p=0.019), a CD4 count above 500 cell/mmc (OR 14.35, 95% CI 3.88-53.0, p=<0.0001) and a previous HBV infection (OR 2.60, 95% CI 1.13-6.0, p=0.024).
No differences in terms of death, HCC or other sever hepatic events were observed between those who showed an improvement >15% and those who did not.

Conclusions: Despite high SVR rate, barely half of the co-infected subjects improved significantly LS value and the proportion of those at risk of PHT did not change. Only liver variables resulted predictive of LS reduction (as already described, the higher is baseline LS value, the higher is the reduction after SVR). Nevertheless, immune function seems to play a role since a better CD4 count resulted predictive of LS significant improvement.

Management and treatment of viral hepatitis

P 105 HCV CONTINUUM OF CARE IN REAL LIFE IN MAIN PRISON IN FLORENCE, TUSCANY, AND FACTORS DELAYING HCV TREATMENT

A. Gabbuti, F.M. Fusco, P. Pierotti, E. Salomoni, P. Blanc

SOC Malattie Infettive 1, Osp. S. Maria Annunziata, USL Toscana Centro, Florence

Background: Prisons are worldwide recognised as a high-risk environment for blood-borne viruses. HCV prevalence is up to 40 times greater in prisons vs. community, due to the presence of several risk factors, such as the injecting drug use (IDU), the presence of many prisoners coming from highly endemic countries, and unsafe sexual practices. The availability of direct acting antiviral (DAA) therapy is dramatically changing the HCV picture, but there are few real-life data evaluating its use within prisons, and few is known about the factors delaying the HCV Continuum of Care in this setting.

Material and methods: The "Nuovo Complesso Penitenziario Sollicciano" (NCP) is a male and female medium security prison and jail, for remand and sentenced prisoners. An entry screening panel for HAV, HBV, HCV, HIV, LUE is offered to all prisoners. We retrospectively collected data about HCV+ prisoners who underwent to screening in the period from January 1, 2017 to September 15, 2018, in between the changes on DAA indications by AIFA and Tuscany Region Authorities.

Results: In the study period, 2427 prisoners transited: 86,4% were male, 34% were from Africa, 32,3% from Italy, 12,8% from no-EU Europe, 11,4% from EU-Europe, 5% from Americas, 4,6% from Asia.

A total of 295 prisoners (12.15%) resulted HCV-Ab+, of them 186 prisoners (63.05%) resulted HCV-rna>15; 78 (26.4%) HCV-rna<15; data is not available for 31 because of refusal of screening, transfer to another institute, release. Among those HCV-rna positive, prevalent risk was IDU (72,6%). Genotypes are available for 203 prisoners, with genotype 1 being the most diffused (56,6%). Sixteen HIV/HCV co-infections were identified.

During the study period, 213 HCV+ patients performed a total of 329 entrances in NCP, of them 26 (12,2%) stayed less than 1 month, 76 (35,7%) stayed more than 28 days but less than 6 months, 111 (52,1%) stayed more than 6 months.

All HCV+ patients were sent to Infectious Diseases visit: the rate of missed visit is elevated, because of refusal, early release or for concomitant judicial activities (court hearing, or lawyer visit). All patients staying more than 2 months underwent to abdomen ultrasound inside NCP in few times. On the contrary, elastography, to be performed in the general hospital outside NCP, required a median waiting time of 4 months (median 120 days, min-max 13-274), contributing for 25% to non-beginning of DAA.

During the observation period 24 patients received complete DAA therapy, with SVR24 documented for 23 (one patient completed treatment, then lost to follow-up for release).

Conclusions: Despite the efforts, to date there have been few HCV treatments in NCP. Main organizational barriers are represented by rapid turn-over of prisoners, judicial activities constraints and delay in performing instrumental tests externally to NCP. It is necessary to specifically tailor the integrated care pathways in prisons, in order to increase the number of treatments.

Management and treatment of viral hepatitis

P 106 LIVER-RELATED CLINICAL EVENTS IN A COHORT OF CIRRHOTIC PATIENTS AFTER SUCCESSFUL HCV TREATMENT WITH DIRECT ACTING ANTIVIRALS

E. Colella[1], G. Lapadula[1], M. Fava[2], N. Squillace[1], P. Vitiello[1], M. Rossi[1], F. Sabbatini[1], P. Columpsi[1], G. Migliorino[1], A. Soria[1]

[1]Unit of Infectious Diseases, San Gerardo Hospital, ASST Monza, [2]University of Milano-Bicocca

Background: Despite a reduced risk of liver-related events (LE) in HCV cirrhotic patients (pts) after sustained virologic response (SVR) with direct-acting antivirals (DAA), monitoring is still recommended. Little is known on factors predicting the occurrence of LE after HCV cure.

Methods: All cirrhotic pts successfully treated with DAA from January 2015 to December 2018 have been observed from the end of treatment (EOT) to the date of LE, death, or last available follow-up. LE was defined as: hepatocellular carcinoma (HCC, recurrence or de-novo), ascites, variceal bleeding, encephalopathy, or spontaneous bacterial peritonitis.

Log-rank test was used in Kaplan-Meier failure estimates. Uni and multivariate Cox hazard regression models were performed to assess possible predictors of LE among demographic and clinical variables recorded at EOT .

Results: Among 235 cirrhotic pts who achieved SVR after DAA, 21 (8.9%) had a LE (10 HCC, 7 ascites, 4 encephalopathy), after a mean (SD) of 427 (396) days, as compared to 732 (399) days of follow-up of the remaining 214 pts (P=0.001). Pts experiencing a LE were more frequently in Child B vs A class (7/21, 33.3% vs 9/214, 4.2%, P<0.001), had a higher MELD score (MELD>10: 13/21, 61.9% vs 50/214, 23.4%, P<0.001), had more often failed previous DAA (6/21, 28.6% vs 6/214, 2.8%, P<0.001), had more frequently a history of HCC prior to DAA initiation (8/21, 38.1% vs 7/214, 3.3%, P<0.001), had a higher mean (SD) FIB-4 (7.6 [3.8] vs 5.6 [4.3], P=0.046). No differences were observed in age, gender, HCV genotype, HBV or HIV co-infection, previous interferon-based therapy, type of DAA, use of ribavirin. At survival analysis, Child B, MELD>10, platelets <75,000/mm3, FIB-4>5, previous DAA failure, and history of HCC before DAA were all associated with a shorter time to LE (Figure 1). At univariate Cox regression analysis, Child B (HR 10.9, 95%CI 4.3-27.3, P<0.001), MELD>10 (HR 6.7, 95%CI 2.7-16.6, P<0.001), platelets<75,000/mm3 (HR 4.4, 95%CI 1.8-10.4, P=0.001), FIB-4>5 (HR 3.7, 95%CI 1.3-10.1, P=0.011), previous DAA failure (HR 11.0, 95%CI 4.1-29.3, P<0.001), history of HCC prior to DAA initiation (HR 15.6, 95%CI 6.3-38.4, P<0.001) were all associated with an increased risk of LE. At multivariable analysis, after adjusting for age, gender, and HIV status, only a history of HCC (HR 10.2, 95%CI 2.6-39.1, P=0.001) and FIB-4>5 (HR 3.6, 95%CI 1.01-13.10, P=0.048) were associated with an increased risk of LE.

Conclusions: In the post-DAA era, HCV-cured cirrhotic pts with more advanced liver disease have an increased risk of developing LE, mandating continuous monitoring. Beyond expected variables related to a more advanced liver disease (Child B vs A, higher MELD score, lower platelets), and a history of HCC which is per se a risk factor for HCC recurrence, it is noteworthy the increased risk of LE in DAA-cured HCV cirrhotic pts with a history of previous DAA failure. Moreover, a FIB-4 score >5 was an independent predictor of LE.

Management and treatment of viral hepatitis

P 107 HIGH SVR12 RATES IN PATIENTS WHO PREMATURELY DISCONTINUED DIRECTLY ACTING ANTIVIRALS (DAA) REGIMENS: DATA FROM THE NAVIGATORE-LOMBARDIA NETWORK

M. Fabbiani[1], A. Lombardi[1], M. Colaneri[1], P. Del Poggio[2], G. Colloredo[2], R. D'Ambrosio[3], E. De Gasperi[3], M. Zuin[4], A. Giorgini[4], L. Pasulo[5], F. Maggiolo[6], F. Castelli[7], A. Pan[8], O. Spinelli[9], T. Re[10], A. Lleo[11], M. Rumi[12], C. Uberti Foppa[13], A. Soria[14], A. Aghemo[11], P. Lampertico[3], M. Puoti[15], G. Rizzardini[16], S. Fagiuoli[5], R. Bruno[1] for the NAVIGATORE-Lombardia Study Group

[1]U.O. Malattie Infettive e Tropicali, Fondazione IRCCS Policlinico San Matteo, Pavia, [2]Policlinico S. Marco, Zingonia, [3]Divisione di Gastroenterologia ed Epatologia, Fondazione IRCCS Ospedale Maggiore Policlinico, Milano, [4]Unità di Epatologia e Gastroenterologia, Ospedale San Paolo, Milano, [5]Unità di Gastroenterologia, ASST Papa Giovanni XXIII, Bergamo, [6]U.O. Malattie Infettive, ASST Papa Giovanni XXIII, Bergamo, [7]Dipartimento di Malattie Infettive, Spedali Civili, Brescia, [8]U.O. Malattie Infettive, Istituti Ospitalieri, Cremona, [9]UO Medicina Interna Cantù, ASST LARIANA Como, [10]U.O. Malattie Infettive, ASST Ovest Milanese, Legnano, [11]Medicina Interna ed Epatologia, Humanitas Research Hospital, Rozzano, [12]UO Epatologia, Ospedale San Giuseppe, Milano, [13]UO Malattie Infettive, Ospedale San Raffaele, Milano, [14]UO Malattie Infettive, Ospedale San Gerardo, ASST Monza, Monza, [15]UO Malattie Infettive, ASST Grande Ospedale Metropolitano Niguarda, Milano, [16]Dipartimento di Malattie Infettive, Ospedale Luigi Sacco, Milano

Background: High sustained virological response (SVR) rates are obtained in HCV-infected patients treated with directly acting antivirals (DAA) for 8-12 weeks. However, it is not known if reducing treatment duration could maintain high virological efficacy.

Methods: The NAVIGATORE-Lombardia Network database includes data on more than 17,000 patients treated with DAA in real-life setting in the Lombardy region (Italy) since December 2014. From this database, we selected patients treated with all interferon-free DAA regimens (with the exclusion of sofosbuvir+ribavirin combination) who (i) prematurely discontinued treatment before the pre-defined end of treatment (EOT) and (ii) had an available HCV-RNA collected at least 12 weeks after treatment interruption. SVR12 was defined as undetectable HCV-RNA 12weeks after the actual EOT. SVR12 rates were explored in the different treatment groups and according to treatment duration.

Results: Overall, 365 patients (58.4% males, median age 60.5 years, 14.5% HIV-coinfected, 1.9% HBsAg+) were included. Liver cirrhosis was observed in 251 (68.8%) subjects, while 47 (12.9%) and 67 (18.3%) patients showed severe (Metavir F3) and mild/moderate (F0-F2) fibrosis, respectively. The most represented genotype was 1b (n=168, 46%), followed by 1a (n=54, 14.8%), 3 (n=59, 16.2%), 2 (n=43, 11.8%) and 4 (n=36, 9.9%). Median HCV-RNA before DAA initiation was 5.91 log U/mL. One hundred ninety-four (53.2%) patients were treated with DAA regimens recommended in the 2018 EASL guidelines: sofosbuvir/velpatasvir (n=51, 26.3%), ombitasvir/paritaprevir/ritonavir + dasabuvir (n=45, 23.2%), glecaprevir/pibrentasvir (n=37, 19.1%), grazoprevir/elbasvir (n=33, 17%), sofosbuvir/ledipasvir (n=28, 14.4%). DAA were discontinued a median of 1 (IQR 1-4) weeks before the pre-defined EOT, with 164 (44.9%) patients stopping DAA at least two weeks before the planned schedule. Treatment duration was <8 weeks in 30.7% of F0-F3 and <12 weeks in 64.5% of F4. Overall, SVR12 was observed in 345 (94.5%) patients. SVR12 was similar across all HCV genotypes and was not significantly different in: cirrhosis vs F0-F3 fibrosis (93.2% vs 97.4%, p=0.138), regimens recommended by current guidelines vs past regimens (95.4% vs 93.6%, p=0.602), ribavirin vs no ribavirin use (93.7% vs 95%, p=0.754), HIV+ vs HIV- (92.5% vs 95%, p=0.611). A trend toward higher rates of SVR12 in naïve patients was observed (97% vs 91.3% in experienced, p=0.067). An association between length of DAA treatment and SVR12 was observed: lower rates of SVR12 were observed in patients treated for <4 weeks (50% vs 99.1% for >=4 weeks, p=0.003) if F0-F3 and <8 weeks (83.3% vs 94.6% for >=8 weeks, p=0.038) if F4.

Conclusions: Despite premature discontinuation of DAA, high SVR12 rates were observed in a real-life setting for treatment lasting at least 4 weeks if F0-3 and 8 weeks if F4. On this basis, feasibility of reducing DAA treatment duration should be explored in randomized clinical trials.

Management and treatment of viral hepatitis

P 108 ANALYSIS OF URINARY METABOTYPES BY NUCLEAR MAGNETIC RESONANCE BASED-METABOLOMICS IN HCV PATIENTS WITH SEVERE LIVER FIBROSIS RECEIVING DIRECT-ACTING ANTIVIRAL AGENTS

E. Biliotti[1], O. Giampaoli[2,3], L. Volpicelli[1], G. Capuani[2], A. Tomassini[2,3], D. Palazzo[1], R. Esvan[1], M. Spaziante[1], E. Gaudio[5], A. Miccheli[3,4], G. Taliani[1]

[1]Department of Translational and Precision Medicine, Sapienza University of Rome, Italy, [2]Department of Chemistry, Sapienza University of Rome, Italy, [3]NMR based Metabolomics Laboratory, Sapienza University of Rome, Italy, [4]Department of Environmental Biology, Sapienza University of Rome, Italy, [5]Department of Anatomical, Histological, Forensic Medicine and Orthopedics Sciences, Sapienza University of Rome, Italy

Background: Hepatitis C virus (HCV) infection triggers liver inflammation, induces a long-term inflammatory response and causes oxidative stress, leading to important modifications of the liver microenvironment characterized by hepatic fibrosis and metabolic alterations. Direct-acting antiviral agents (DAAs) induce HCV-clearance, but does not completely restore liver dyshomeostasis. Understanding the impact of viral eradication on the liver metabolic activities could allow the optimization of patient's metabolic care during and after HCV cure. The aim of the present prospective longitudinal study was to characterize the urinary metabolic profile of HCV-induced severe liver fibrosis and the metabolic changes induced by DAAs and HCV clearance by Nuclear Magnetic Resonance (NMR)-based metabolomics.

Material and methods: The urinary metabolic profile of 23 HCV males with severe liver fibrosis and 20 age-matched healthy-controls was analyzed by NMR-based metabolomics before starting DAAs, at the end-of-therapy, after one and three months of follow-up. 1H-NMR spectra were acquired at 298 K using a Bruker AVANCE 400 spectrometer (Bruker BioSpin GmbH, Karlsruhe, Germany) equipped with a magnet operating at 9.4 Tesla and at 400.13 MHz for 1H frequency. Principal components analysis (PCA) was used as a preliminary analysis to explore inherent clustering and to identify outliers. Partial least squares-discriminant analysis (PLS-DA) was applied to maximize the differences between groups and identify the discriminating variables.

Results: The urinary metabolic profile of patients with severe liver fibrosis was characterized by higher levels of four metabolites related to oxidative stress (pseudouridine, hypoxanthine, methyl-guanidine, dimethylamine) and two amino-acids (glutamine, tyrosine) compared to healthy-controls. N-methyl-nicotinamide, a catabolic intermediate of nicotinamide-adenine-dinucleotide, and 3-hydroxy-3-methylbutyric-acid, an intermediate of leucine catabolism, returned to control levels with viral eradication. Finally, 3-hydroxyisobutyrate and 2,3-dihydroxy-2-methyl-butyrate, intermediates of valine catabolism, increased temporarily during therapy, resulting as potential urinary biomarkers of the systemic effects of DAA treatment.

Conclusions: The identified metabolic profiles suggest that oxidative stress persists despite HCV eradication in the context of severe liver fibrosis, suggesting a potential benefit of an antioxidant treatment concurrently with or after DAA therapy. HCV clearance permanently modifies leucine metabolism, while DAA administration temporarily influences valine metabolism, therefore in case of amino-acid supplementation such modifications should be taken into account.

Management and treatment of viral hepatitis

P 109 AN UNDEFINED CASE OF VIROLOGICAL FAILURE IN AN HIV-POSITIVE PATIENT TREATED WITH DAAS FOR HCV RECURRENCE AFTER LIVER TRANSPLANT

D. Testi[1], L. Vizioli[2], L. Badia[1], V. Guardigni[1], G. Ferraro[1], V. Vero[2], M. Ravaioli[3], G. Verucchi[1], P. Viale[1], M. Cescon[3], M.C. Morelli[2]

[1]Dipartimento di Malattie Infettive, S.Orsola-Malpighi, Bologna, [2]Medicina interna trattamento gravi insuf. d'organo-Morelli, S.Orsola-Malpighi, Bologna, [3]Chirurgia Generale e trapianti, S.Orsola-Malpighi, Bologna

Background: Primary non-response to 12-weeks of SOF + NS5A in HCV recurrence after liver transplantation (LT) is rare (less than 1%). We describe the case of an HCV/HIV patient who underwent LT and experienced an apparently unexplained virological treatment failure.

Material and methods: We reviewed all patient's medical records and compared our case to other published cases of virological treatment failure to DAAs after liver transplant.

Results: The patient is a 55-year-old Caucasian male with HCV/HIV co-infection (both diagnosed in 1981) and no other comorbidities. He started ART in 2011 with TDF+3TC+NVP and switched to 3TC+DTG in 2015 with viral suppression. HCV infection (genotype 3a, Metavir F4) was previously treated with IFN+RBV with no response. In 2015 he received 2-lines of DAAs (first SOF+RBV and then SOF+DCV+RBV) with relapse in both cases. After the second DAAs treatment, a genotypic resistance test showed no resistance associated substitutions (RAS). Then, his cirrhosis status got worse (MELD 21, CHILD-PUGH C10) with several episodes that required hospital admissions. For this reason, in 2017 he was put on waiting list for LT. During the waiting time he was also diagnosed with an HCC nodule in IIs. On May 15th 2018 the patient underwent LT successfully. On May 22nd, according to the medical team decision, he started SOF/VEL treatment. HCV-RNA at the baseline was 3.050 IU/mL. After 3-weeks viral load was 1.719.729 IU/mL. Despite the complete adherence to the therapy of the patient, therapeutic drug monitoring of SOF showed very low concentrations (peak to trough between <10 ng/mL and 33 ng/mL, GS331007 between 20 ng/mL and 179 ng/mL). In addition, no drugs-drugs interactions and no NS5A RAS associated were found. Four days later HCV-RNA was even higher (2.793.225 Ui/mL). As the patient showed severe cholestasis with acholic stools, Kehr's T-tube was clumped; 2 days later the viral load decreased to 147.938 IUi/mL.

DAAs regimen was switched to GLE/PIB, keeping Kehr's T-tube clumped only half-day. After 16-weeks of this treatment, the patient achieved SVR24.

Conclusions: Liver recipients with HCV recurrence have always been considered as a difficult-to manage population, especially if HIV co-infected and/or with HCV-genotype 3 and with decompensated cirrhosis. We didn't find any satisfactory explication for the virological treatment failure. We can speculate that all the patient's bile was released by Kehr's T-tube and this had an effect on SOF pharmacokinetic. In addition, we find interesting that the patient had always failed SOF-based regimens. In conclusion, it appears that in this kind of patients therapeutic monitoring drug can have an important role, together with case-to-case medical team evaluation.

Management and treatment of viral hepatitis

P 110 EVALUATION OF A PAN-GENOTYPING FULL POPULATION-BASED SEQUENCING METHOD FOR HEPATITIS C NS3, NS5A AND NS5B DRUG RESISTANCE IDENTIFICATION

T. Allice[1], M.G. Milia[1], E. Burdino[1], G. Gregori[1], L. Boglione[2], A. Bottoni[1], M. Cazzadore[1], P. Tremante[1], E. Scuccimarra[1], S. Bonora[2], V. Ghisetti[1]

[1]Laboratory of Microbiology and Virology, ASL Città di Torino, Torino, [2]Department of Infectious Disease, University of Torino, Torino

Introduction: In spite of the high sustained virological response with Direct Antiviral Agents (DAAs) against hepatitis C virus (HCV) in chronically infected patients, about 5–10% of them do not respond to first-line DAA regimens and drug resistance is the leading cause of virological failure. Patient retreatment is hampered by the presence of resistance antiviral variants (RAVs) in the majority of patients. Due to HCV high genetic variability, the development of a standardized genotype resistance testing (GRT) is complicated by the need for HCV genotype-subtype-specific protocols. Objective of this study was to evaluate the performance of a pan-genotypic full-population-based sequencing method for HCV-NS3, NS5A e NS5B drug resistance mutations (DeepCheck HCV Drug Resistance assays, DeC-HCV-DR assay, ABL Luxembourg distributed in Italy by Technogenetics, Milan). DeC-HCV-DR covers genomic regions within known DAA drug-resistant variants for NS3, NS5A and NS5B inhibitors (NS3: 1-206 aa; NS5A: 1-222 aa and NS5B: 1-579 aa).

Materials and Methods: Plasma (1 ml) from 11 patients (pts) with chronic HCV hepatitis, infected by HCV genotype 1a (n=2 pts), 1b (n=3 pts), 3 (n=2 pts), 4 (n=2 pts), 2 (n=1 pt) and 1+4d (n=1 pt), mean viral load 5.1 x 106 UI/ml (range 6.526-12.419.541 UI/ml) was tested with DeC-HCV-DR assay. Results were compared with an in-house NS3, NS5A and NS5B GRT consisting of 10 HCV genotype-subtype-specific protocols for HCV genotypes 1, 3 and 4 (Standard of Care-GRT: SoC-GTR, validated against QCMD proficiency HCV panels). Both DeC-HCV-DR and the in-house GTR assays were performed on the Sanger Sequencing 3130xl Genetic Analyzer (Applied Biosystems). RAVs were analyzed with the Viroscore Software provided by ABL and Geno2pheno (hhttps://hcv.geno2pheno.org).

Results: While the SoC-GTR allowed successful sequences in 70% of samples (25/33), the DeC-HCV-DR was successful in all samples (100%) and for all HCV genomic regions. DeC-HCV-DR was able to successfully amplify and sequence NS3, NS5A and NS5B genes from patients with HCV genotype 2 infection (N=1), HCV genotype 1 and 4 coinfection (N=1). NS5B regions were successfully amplified in other 2 patients with HCV genotype 3 in whom the SoC-GRT was negative.

Conclusions: DeC-HCV-DR is a pan-genotypic GRT using three highly efficient protocols for NS3, NS5A and NS5B amplification across HCV genotype 1-4 allowing the easily and fast achievement of HCV RAV analysis. DeC-HCV-DR is easy to perform, with a high successful rate and can be customized allowing HCV RAV study with different algorithms. In the laboratory work-flow DeC-HCV-DR may be a good option against complex, intensive SoC-GRT, improving successful sample processing rates.

In conclusion, in the view of re-treating patients failing first-line DAA regimens, DeC-HCV-DR seems to be an interesting novel all-in-one GTR method for HCV RAV detection to optimize second-line treatment options.

Management of HIV infection

P 111 THE CLINICAL HETEROGENEITY OF PLWH SWITCHING TO DUAL THERAPY IS LEVELLED IN 2 YEAR FOLLOW UP IN A REAL-LIFE COHORT

G. Guaraldi, I. Franconi, A. Malagoli, J. Milic, A. Santoro, M. Menozzi, A Mariani, F. Carli, S. Zona, C. Mussini

Modena HIV Metabolic Clinic, Infectious Diseases Unit, University of Modena and Reggio Emilia, Italy

Objective: Patients living with HIV (PLWH) treated with "two drug regimens" (2DR) antiretrovirals (ARV) are frequently described as a homogeneous minority of HIV cohorts. The objective of this study was to compare PLWH switching from a three-drug regimen (3DR) to a 2DR or a new 3DR.

Methods: Patients were selected from the Modena HIV Metabolic Clinic (MHMC) from Jan 2006 to Dec 2017 who had a multidisciplinary assessment (baseline) before switching from a 3DR to current 3DR or 2DR with no further ARV change. Data were censored at last observation for follow up. 2DR regimens were sub-grouped according to anchor drug: protease inhibitor (2DR-PI), integrase inhibitor (2DR-INSTI) or protease inhibitor with integrase inhibitor (2DR-PI/INSTI). Multi-morbidity (MM) was defined as the simultaneous presence of >2 co-morbidities, polypharmacy (PP) as the use of >5 drugs other than ARV. Quality of life (QoL) was assessed with EQ-5D-5L questionnaire.

Results: Our study included 807 patients: 548 switched to a new 3DR, 103 switched to 2DR-INSTI (RAL in 44 and DTG in 59 pts); 83 to 2DR-PI and 73 to 2DR-PI/INSTI (RAL in 59 pts and DTG in14 pts). At baseline, we observed heterogeneity in PLWH switching to 2DR when compared to those switching to a new 3DR. Differences included both viro-immunological and clinical variables (CKD-epi, MM, PP), being more severe in 2DR-PI/INSTI switch.

After median period of 2.07 (1.2-3.75) years of follow up, the inter-group diversity observed at baseline were levelled to a none significant difference. However, all patient groups demonstrated a non-significant intra and inter group increase in BMI and waist circumference. PP, MM and QoL did not change significantly.

Conclusion: Switch from 3DR to 2DR are not uncommon. Clinical heterogeneity of PLWH justify different 2DR. Older age seems to level the homogeneous increase of age related variables including BMI, waist circumference, co-morbidities and polypharmacy.

Management of HIV infection

P 112 LACK OF HIV SEROLOGICAL DIAGNOSIS WITH NEW GENERATION TESTS IN AN AIDS PATIENT : WHICH CONSEQUENCES ON HIV EPIDEMIOLOGY?

I. Uccella[1], R. Pulselli[1], I. Abbate[2], C. Gori[2], K. Casinelli[1], P. Fabrizi[1], C. Falco[1], G. Farinelli[1], M. Limodio[1], L. Sarracino[1], M. Sebastiani[1], E. Anzalone[1]

[1]Ospedale Fabrizio Spaziani, Frosinone, [2]INMI Lazzaro Spallanzani, Roma

Background: The reaching of undiagnosed HIV patients and the expanded HIV screening are the priorities to obtain the WHO targets 90'-90'-90'. The new generation EIA tests, milestones of "test and treat "strategy because their high sensibility and specificity, are useful to detection of acute infection, self-testing expansion and partner notification.

Material and Methods: We describe a case of a 48-year-old Italian woman HIV late presenter with 4th and 5th HIVAb/Ag EIA generation tests negative. On April 18, 2018 she attended in Frosinone Hospital for dyspnoea and recovered on Infection Disease Department. Her husband died with AIDS diagnosis in another closer hospital few months before. The Chest X-ray documented bilateral diffuse ground-glass opacities. Empiric treatment with intravenous daily dose of TMP 15–20 mg/kg plus SMX 75–100 mg/kg and steroidal anti-inflammatory drugs for the treatment of PCP was started and clinical response was observed. The fundus oculi documented bilateral exudative lesions. The CMV-PCR on blood plus the CMV antigen resulted positives and ganciclovir at the dose of 5 mg/kg iv was administered: at the end of the treatment ocular lesions disappears. Lymphocyte analysis documented CD4-T cell count 46 cells/ul (23%) with CD4/CD8 ratio 0.6. At the entry, the 4th generation Architect HIV Ag/Ab Combo (Abbott) with sensitivity 100% (95% CI: 99,63-100%) and specificity 99,77% (95%CI :99,62-99,88%), and p24 sensitivity of 1.032 IU/mL, (considering WHO Standard NIBSC 90/636), resulted negative. Laboratory diagnosis was possible only by HIV-1 RNA quantification in plasma (1.850.000 copies/ml). At the Spallanzani Hospital of Rome the 5th Generation BioPlex 2200 HIVAg-Ab EIA (Bio-Rad) with sensitivity 100% (95%CI: 99,50-100%) and specificity 99,96% (95%CI :99,90-100%), resulted negative for HIV-1/2 and p24 (sensitivity 0.637 IU/mL- WHO Standard NIBSC 90/636). HIV-1 infection was confirmed by RNA quantification after 3 and 6 months with 235.000 and 130.000 copies/ml, respectively, and at 6 months by PBMC-DNA quantification (2178 copies/million cells). The genotype indicated wild type subtype B. Antibodies for Measles, Toxoplasma gondii, Rubeo, CMV, and HSV1/2 were positives. The HLA-B 57 resulted negative. On the basis of viremia positivity, antiviral therapy (ARV) was started. The 4th and 5th generation immunoassay were repeated one and three months after, but they resulted ever negatives, too. (Table1)

Results: The patients actually is clinically healed, but after six month viroimmunological failure was documented, done to her low adherence. A new ARV based on second genotype is in progress.

Conclusion: We described the first case of HIV patient- CDC stage C3, with lack of antibodies and p24 in the era of new generation tests. Memory antibodies for other viruses were not lost. This case open a new scenario on HIV knowledge and epidemiology and for the approach on testing.

Management of HIV infection

P 113 HIV-1 DNA TEST: A RELIABLE METHOD FOR THE MANAGEMENT OF HIV INFECTION

E. Carloni[1], E. Omiccioli[1], C. Orlandi[2], L. Pucci[1], V. Ceppetelli[1,2], I. Bon[3], A. Bertoldi[3], B. Canovari[4], Z. Pasquini[4,5], F. Barchiesi[4,5], M. Menotta[2], A. Casabianca[2], M. Magnani[2]

[1]Diatheva srl, Cartoceto, Fano (PU), [2]Dipartimento di Scienze Biomolecolari, Università di Urbino "Carlo Bo", Urbino (PU), [3]Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale, Università di Bologna, Bologna (BO), [4]Malattie Infettive, Azienda Ospedaliera Ospedali Riuniti Marche Nord, Pesaro (PU), [5]Dipartimento di Scienze Biomediche e Sanità Pubblica, Università Politecnica delle Marche, Clinica Malattie Infettive Ospedali Riuniti di Ancona, Ancona (AN)

Background: The most widely used marker of HIV persistence in infected cells is total HIV-DNA. HIV-1 DNA levels may vary among patients, according to the stages of HIV disease and the effectiveness of anti-HIV therapy.
The "HIV-1 DNA Test" (Diatheva srl) is a real-time PCR (qPCR), based on dual-labelled probes, that includes a Standard Curve based on a linearized recombinant plasmid containing the HIV-1 LTR target region. The kit allows the measurement of HIV DNA in whole blood and PBMC samples from HIV+ patients.
The aims of this work are: a) comparison between Standard Curve of the kit and pNL4-3 plasmid (N.:114; NIH AIDS Reagent Program); b) HIV quantification using different quantities of DNA in comparison with 1 µg of DNA (recommended quantity); c) application of the kit to quantify HIV-DNA in HIV+ patient blood; d) comparison with digital-PCR (dPCR).
Material and methods: Standard curves starting from circular and linearized pNL4-3 plasmids, were compared to Standard Curve provided in the kit and four HIV+ DNA samples were analysed. Three, 5, 10 and 20 µl of 5 HIV-1 positive DNA samples were amplified in comparison with 1 µg of DNA. DNA from 50 blood samples collected from HIV+ patients followed up within a program for surveillance and treatment of HIV infection and 50 blood samples from healthy donors were analysed.
Moreover, the plasmid copies number of the Standard Curve was verified by QS 3D Digital PCR System (Applied Biosystem). Eight DNA samples were analysed also by dPCR and correlation of the two systems was calculated.
Results: Standard curve prepared using circular pNL4-3 plasmid showed increased Ct values compared to the standard curve of the kit at any concentration applied (5 to 50,000 HIV cps/reaction). However, using linearized pNL4-3 plasmid, a perfect overlap of the two standard curves was observed and similar quantification of HIV DNA copies in HIV+ samples was obtained. Quantification results obtained using different DNA quantities, ranging from 0.27 to 2.8 µg DNA/reaction, were similar to results obtained amplifying 1 µg DNA/reaction. No amplification signals were obtained testing HIV- samples while 100% of HIV+ samples were quantified. Positive samples ranged from 2.5 to 487.5 HIV cps/µg DNA and the median [IQR] value was 34.75 [20.20-68.03] cps/µg. Digital PCR quantifications of the recombinant plasmid in the first two points of the qPCR curve (2,500 and 250 cps/µl) were 1,996.1 and 211.4 HIV cps/µl, respectively. Moreover, dPCR showed false positive signals when testing HIV- samples. However, the Pearson Coefficient value was 0.929 (P=0.0072) showing a positive significant correlation between the two assays.
Conclusions: The "HIV-1 DNA Test" showed good amplification performances ensuring reliable quantification results, trueness and precision of the assay were confirmed by the comparation with pNL4-3 plasmid and by the comparative study carried out using dPCR assay.

Management of HIV infection

P 114 ORGANIZATIONAL AND ECONOMIC IMPACT OF A REGIONAL CLINICAL PATHWAY ON HIV PRESCRIPTION PATTERNS: 3 YEAR-ANALYSIS IN 4 CENTRES IN LAZIO REGION

R. Di Bidino[1], A. Cicchetti[2], R. Cauda[1], M. Andreoni[3], A. Antinori[4], C. Mastroianni[5], V. Vullo[5], C. Mastroianni[5], G. D'Ettorre[5], A. Borghetti[1], S. Lamonica[1], C. Cerva[3], V. Malagnino[3], A. Giannetti[4]

[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, [2]Alta Scuola di Economia e Management dei Sistemi Sanitari (ALTEMS), Rome
[3]Fondazione Policlinico Tor Vergata, Rome, [4]Istituto Nazionale per le Malattie Infettive "Lazzaro Spallanzani" IRCCS, Rome, [5]Azienda Policlinico Umberto I, Sapienza Università di Roma, Rome

Background: In 2017 Lazio Region (Italy) published a new care and therapeutic pathway (PDTA) to guide the choice of treatments for HIV naive and experienced patients. Recommended treatments were identified on the base of both clinical and economical criteria to guarantee the most appropriate care and substainability of regional NHS.
Lazio Region has planned a full HTA assessment to evalute how the new PDTA impact on clinical practice. Meanwhile, an pilot assessement is under way for economical and organizational domains.
The assessement is focused on the four main HIV treatment centers at regional level. Each center provides data on the frequency of prescriptions of each available treatment option for HIV in the period January-June 2017 -2018-2019. The goal is to compare and analyze prescribing behaviours pre and post the introduction of the new PDTA.
Results: Data (January-June 2017-2018, 100% coverage) show that the number of experienced patients increases (+10.1%. n= 7249 in 2018), while that of naive patients slighlty decreases (-3%, n=220 in 2018). Trends are common among HIV centres. In terms of prescribed treatments, adoption of PDTA-recommended regimes is more common for naive (prescribed to > 80% of HIV patients) while improved from 2017 to 2018 for experienced patients (from 36% to 62%) (Figure 1). First 10 most prescribed treatments cover > 88% of naive and > 65% of experienced patients in both semesters. Prescribing variability emerged among HIV centres, more for for experienced patients.
Mean expenditure in recommended treatments was stable for naive patients (€775-765/month, - 1.40%) was slightly incresead for experienced ones (€605-652/month, + 7.9%). Indeed, not only more patients were treated with recommended regimes but the increased involved regimes with a cost per month > € 700 as showed in Table 1. A decline in expenditure is expected in 2018 due to new generic treatments available at regional level, which will allow to improve the adherence to PDTA. Data will be collected for the period January-June 2018.
Conclusions: The implementation of a regional therapeutic pathway on HIV should be assessed to guide health policies and improve communication among decision makers and clinicians, who are responsible to prescribe appropriate treatments.
Our analysis is based on administrative databases and that represents its major limitation. Therefore, a semi-structured survey is under way to collect both quantitative and qualitative evidence both on case-mix of patients under treatment, the organizational structure of each HIV center and on factors able to influence clinician decisions, including market evolution. It will support a SWOT analysis on the role played by the regional therapeutic pathway. Furthermore, survey will help to interpreted prescribing variability among HIV centres.
Our pilot analysis aims to support regional policies identifing critical aspects able to influence the implementation of PDTA.

Management of HIV infection

P 115 HIV RAPID TEST IN COMMUNITY SETTING: DATA FROM AN EXPERIENCE IN 6 ITALIAN CITIES (OPEN-TEST PROJECT)

C. Falanga[1], S. Negri[1], F. Di Gennaro[2], M.C. Poliseno[2], D.F. Bavaro[2], A. Saracino[2], S. Lo Caputo[2], G. Angarano[2]

[1]ANLAIDS Sezione Lombarda, Milan, Italy, [2]Clinic of Infectious Diseases University of Bari, Italy

Introduction: Despite the undeniable successes achieved against HIV infection in the last 30 years, about 4,000 new HIV diagnoses and approximately 800 AIDS cases are still reported yearly in Italy, with a steady trend observed in the last decade. Improving the awareness of general population and bringing out the HIV undiagnosed individuals are the keystones to progress towards the control of the HIV epidemic. To this purpose, the "OPEN-TEST" was organized and delivered by the Anlaids Lombardia, together with local infectious diseases specialists, in order to provide free access HIV testing outside the healthcare settings in different Italian cities.
Methods: Between October 2017 and February 2019, 6 "OPEN-TEST" initiatives have been delivered in 6 Italian cities (3 North, 1 Central and 2 South). Eligible criteria for HIV testing were: 18+ years and the ability to provide informed consent. Each subject underwent to a HIV rapid test performed on oral fluid and while waiting for the results, socio-demographic information and attitudes towards the initiatives were collected. Descriptive and comparative analyses by geographic macroarea were performed using STATA 13.0. All categorical variables were reported as absolute and relative frequencies; Chi-square test (with the Fisher's correction when appropriate) was performed to compare them.
Results: 581 people were tested; they were mainly male (57%) and Italian (96%), without differences among geographic areas. The age group 18-25 was the most represented in the northern (69%) and southern (51%) areas, while in the centre the majority were in the 26-30 (40%) and 31-40 (17%) age group ($p<0.001$). Moreover, in northern and southern cities the greater part of participants was students, respectively the 43% and 47%, compared with the 26% in central Italy ($p<0.001$). The overall prevalence of HIV tests' reactivity was of 0.7%.
The majority of subjects from all the cities denied a previous HIV test (73%). Among those who referred previous testing, 59% did not report the reason for testing, while, when referred, the principal reason was unprotected sexual intercourse. Notably, a HIV screening due to pregnancy or surgical procedures was reported mainly by participants in northern centers ($p<0.001$). Lastly, the initiative was considered useful and remarkable from 99% of people participating.
Conclusion: Prevalence of HIV tests' reactivity in our experience was in line with national data. Moreover, our experience confirmed that the HIV rapid testing in community setting is an efficacy strategy to reach the young population, difficult to test in healthcare setting. The initiative was also a good occasion to spread awareness among the community, gaining a good success from the general population. In conclusion, our experience suggested that such testing and counselling strategies in community setting should be institutionalized from local health authorities also in Italy, in line with the 90-90-90 global strategy.

Management of HIV infection

P 116 MILTEFOSINE TREATMENT OF AMFOTERICIN-B RESISTANT LEISHMANIASIS IN HIV

F. Bulla, P. Scerbo, A. Priamo, L. Cosco

U.O.C. Malattie Infettive A.O. "Pugliese-Ciaccio" Catanzaro

Background: When visceral leishmaniasis (VL) occurs in HIV patients, it presents several challenges. These include changes in clinical manifestations that may result in delayed diagnosis; changes in immunological response to the infection that affect the performance of diagnostic tools; and poor treatment response, in terms of low initial cure, relapse and mortality, due mainly to the combined effects of both infections increase immunosuppression.

The anti-leishmanial medicines available cannot completely eradicate the Leishmania parasites from the body.

In HIV patients, who are declared parasitologically cured at the end of treatment are, in reality, left with some parasites in the tissues that are not undetectable by microscopy, this small number of remaining parasites continues to replicate resulting in relapse of disease, which then becomes more difficult to cure. These patients tend to have a persistent infection with flare-ups of clinical disease, described as active chronic disease.

Despite repeated treatment courses, such patients remain poorly responsive to treatment and deteriorate in their long term outcomes of VL in HIV infected patients.

Materials and methods: We report a clinical case of an italian HIV late-presenter with lower CD4+ lymphocyte count (<50cell/µl).

The diagnosis was difficult because of the poor immunologic response that made vain serologic assays. Leishmanial DNA (L. infantum) was detected by real-time PCR in the bone marrow aspirates.

The patient started an HAART INI-based but was recalcitrant to therapy with liposomal Amphotericin-B (40 mg/kg) followed by secondary prophylaxis (3 mg/kg every 4 weeks).

He was successfully treated with Miltefosine (100 mg/day for 28 days).

Results: The salvage therapy in HIV-infected patient suffering with visceral leishmaniasis, recalcitrant to liposomal Amphotericin B, is today an increasing topic. After the employment of combination anti-leishmanial treatment (first liposomal Amphotericin B then Miltefosine), parasite genomes were not detectable up to the last follow up visit, 57 and 78 weeks after treatment onset, respectively.

CD4+ lymphocyte counts fluctuated over time, but were generally higher than counts detected at treatment onset, which likely contributed to protection against VL relapse.

Conclusions: Results achieved with the anti-leishmanial combination treatment (liposomal Amphotericin-B followed by Miltefosine) were promising. Miltefosine was efficacious, safe and well tolerated, suggesting that it can play an important role in the treatment of severe VL.

Further investigations are necessary to confirm the efficacy of this salvage therapy in sustaining the immunological response and control of VL in Italians and foreign people.

Management of HIV infection

P 117 THE EFFICACY AND SAFETY OF DUAL THERAPY REGIMENS IN AN HIV-INFECTED COHORT

G. Piazza[1], A. Rutter[1], S. Vitale[1], L. Appolloni[1], G. Pensalfine[1], C. Bitello[1], M. Morotti[1], L. Calza[2], C. Puggioli[1]

[1]Clinical Pharmacy, S. Orsola-Malpighi Polyclinic, Bologna, [2]Infectious Disease S. Orsola-Malpighi Polyclinic, Bologna

Background: The use of three drugs in combination antiretroviral therapy (cART) has been the cornerstone of first-line HIV treatments since 25 years. In virologically suppressed patients, dual therapies based on a boosted protease inhibitor (PI) or an integrase inhibitor (INI) and a single nucleoside analogue have recently emerged as safe, cost-saving and equally effective approach to maintain virological suppression while optimizing cART regimens.

Materials and methods: A retrospective study was performed to investigate the maintenance of virological suppression with a dual therapy and the eventual need to switch to triple cART regimens in our HIV infected outpatients between January and December 2018. Virological data and cART regimes were collected from our medical records and tracked in an Excel database.

Results: The study involved 230 patients (76 female and 154 male) with a mean age of 51 years (range 16-81). N=92 of these received DRV/c+3TC, N=5 DRV/r+3TC, N=37 ATV/c+3TC, N=22 ATV/r+3TC, N=52 DTG+3TC, N=22 DTG+RPV. Plasma HIV RNA remained < 50 copies/mL in 224 patients (97.4%); the other 6 patients were in virological failure (N=4 had viral load between 40 and 1000 copies/mL and N=2 above 10000 copies/mL). The high viral load in these 2 patients was related to lack of adherence and did not lead to a cART regimen modification.

N=15 patients required a switch of therapy of which N=13 towards a triple cART regimen and N=2 towards another dual therapy regimen. Only 10 patients (4.3%) were affected by side effects related to the dual therapy (N=6 hyperbilirubinemia caused by ATV, N=2 metabolic disorders by DRV, N=1 diarrhoea by 3TC and N=1 insomnia by DTG). Other reasons for therapy switch were N=1 pregnancy, N=1 simplification to a single tablet regimen (STR), N=1 concomitant treatment with direct acting antiviral therapy (DAA), N=1 low increase of viral load (28 copies/mL) and N=1 unknown cause.

Conclusions: In the patient cohort considered, the use of dual therapy was safe, well-tolerated and effective in the maintenance of virological suppression.

None of our patients needed a change of cART regimen related to a lack of efficacy of dual therapy. In fact, HIV RNA viral load remained undetectable while a dual drug regimen was prescribed.

The main limiting factor of dual therapies is that they actually require a multiple tablet regimen (MTR) instead of a STR which would contribute to a further simplification of the therapy and an improvement of adherence. Therefore, it would also be desirable that new dual therapy regimens become available in a STR form as it happened with triple cART.

Management of HIV infection

P 118 KNOWLEDGE AND BEHAVIOURS OF ITALIAN HIV CLINICIANS TOWARD VACCINATIONS RECOMMENDED FOR PEOPLE LIVING WITH HIV: RESULTS OF A QUESTIONNAIRE-BASED INVESTIGATION

A.L. Ridolfo[1], S. Nozza[2], L. Oreni[1], G. Mazzola[3], G.P. Carosi[4], S. Lo Caputo[5], A. Di Biagio[6], A. Muscatello[7], A. Cascio[8], A. Ranzani[1], M. Galli[1], for the Gruppo di Studio HIV/Vaccinazioni, Società Italiana di Malattie Infettive e Tropicali (SIMIT)

[1]Infectious Diseases Unit, DIBIC Luigi Sacco, University of Milan,Italy, [2]Department of Infectious Diseases, IRCCS San Raffaele Scientific Institute, University Vita-Salute San Raffaele, Milan, Italy, [3]Infectious Diseases Unit, Paolo Giaccone/Azienda Ospedaliera Universitaria Policlinico, Palermo, Italy, [4]Member of the Società Italiana di Malattie Infettive e Tropicali, [5]Clinic of Infectious Diseases, Policlinico, University of Bari, Italy, [6]Infectious Diseases Unit, Hospital Policlinico San Martino, University of Genoa, Italy, [7]Infectious Diseases Unit, IRCCS Ca' Granda Ospedale Maggiore Policlinico Foundation, University of Milan, Milan, Italy, [8]Department of Sciences for Health Promotion and Mother-Child Care, University of Palermo, Italy

Background: Despite vaccinations represent an important part of healthcare of people living with HIV (PLWH), studies indicate that vaccination coverage remains sub-optimal in this population. To understand potential physician-related barriers we investigated the attitudes of Italian HIV specialists regarding vaccinations recommended for PLWH.

Material and methods: A cross-sectional survey based on a self-administered questionnaire was conducted among HIV clinicians attending the 10th ICAR Conference that took place in Rome on May 2018.

Data were analysed and results presented as numbers and percentages.

Results: A total of 322 (55.1%) out of 602 HIV physicians completed the questionnaire. They were 176 females and 156 males working in northern (40.1%), central (30.7%) and southern (29.2%) regions; the 44% were working in general hospitals and the 56% in academic hospitals, with 46% having a working experience >15 years and 31% <5 years. The 73.3% of respondents stated to have good/optimal knowledge about vaccinations and almost all (99.3%) considered vaccinations important/quite important for PLWH; specifically, >80% considered important to vaccinate PLWH against influenza, pneumococcus, meningococcus, HBV, HAV, HPV, whereas only the 60.8% considered important the chickenpox (shingles) vaccination; very few respondents stated to be concerned about potential harm of vaccines for PLWH regardless of ongoing treatment and vaccine type, while the majority (76.3%) acknowledged that vaccines efficacy may be reduced in immune compromised patients; almost all respondents (90.5%) indicated HIV physicians as the key figure in the offer of vaccinations to PLWH (Table 1).

The majority of respondents agreed with guidelines on extending to all PLWH the vaccination against influenza (82.4%), pneumoccocus (74.1%) and meningococcus (60.7%); however, only the 47.4% agreed on recommending HAV vaccination for only males who have sex with males (MSM) and patients with additional risk factors, while the 45.5% would have extended it to all PLWH; furthermore, only 12% of them agreed on recommending HPV vaccination for women <45 years and males <26 years old, while the majority would have extended it to all MSM and people with multiple partners up to the age of 45, or even to all PLWH (Figure 1).

Most of respondents declared to always/often collect information on patients' immunization status and to always advise them about required vaccinations (89.7% and 79.4%, respectively), but only the 58.5% and the 49% of them stated to assess the patients' vaccination response and to recommend revaccination for non–responders, respectively (Table 2).

Conclusions: Italian HIV clinicians are aware of the importance of vaccinating PLWH and of their own key role in promoting vaccinations in their practice. Still, a not negligible number of physicians do not fully agree with current guidelines and do not pay due attention to the patients' vaccination history.

Management of HIV infection

P 119 MEAN PLATELET VOLUME CORRELATES WITH CD4+ IMMUNE ACTIVATION IN HIV+ OLDER PATIENTS: RESULTS FROM THE 36 MONTHS FOLLOW-UP OF THE RAL-AGE COHORT

L. Celani[1], C. Borrazzo[1], P. Pavone[1], L. Santinelli[1], P. Vassalini[1], G.P. Innocenti[1], C. Fimiani[2], C. Mastroianni[3], F. Di Sora [4], I. Mezzaroma[1], V. Vullo[1], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases - "Sapienza" University of Rome, [2]Azienda Ospedaliero-Universitaria Policlinico Umberto I, Rome, [3]Department of Sense Organs University Sapienza Rome Azienda Ospedaliera, [4]S. Giovanni Department of Sense Organs University Sapienza Rome Addolorata, Rome

Background: Raltegravir (RAL) is considered one of the better-tolerated antiretroviral medications. Long-term treatment with raltegravir (RAL)-containing regimens seems to be safe and effective in the older population. In a previous study by our group, RAL-containing regimens were associated with reduction in triglycerides and platelets count in aged patients. Despite many studies, the role of the platelets in the HIV infection and in cardiovascular risk remains debated. Larger platelets seem to be more active metabolically with an increased prothrombotic activity. Aim of the study was to confirm previous result and investigate relationship between mean platelet volume (MPV) and CD4+ cells immune activation.

Material and Methods: This real-life cohort describe RAL-regimens data in 96 aged HIV patients compared with a control group of 50 HIV+ patients under 60 years old. The time of observation was at least 36 months. To confirm preliminary findings modification observed in the RAL-AGE study we decide to compare lipid profile data, platelets count and mean platelet volume (MPV) and in a sub-set of patients, we measured the levels of immune activation by CD38 and HLA-DR.

Results: The median age of the 96 HIV+ aged patients was 69 (IQR: 65-74.8) years with undetectable HIV-RNA at the baseline in most of the patients, median CD4+ count was 453 (IQR: 339-712) cell/mmc. The control group was composed by 50 HIV+ patients and the median age was 54 (IQR: 51-57) years. The median of CD4+ cells was 554 (IQR: 444-765) cell/mmc.

Only in the aged group we observed triglycerides significant reduction compared to the baseline (from 188 ±73.3 mg/dl to 148.5±66.4 mg/dl, p=0.002). We also observed LDL cholesterol decrease (from 113.1±31.1 mg/dl to 110.5±31.2 mg/dl), increase in HDL values (from 42.0±15.1 mg/dl vs 47.5 ±14.3 mg/dl) and Framingham Score reduction after 36 months (from 16.4±7.5% to 12.5±7.6%), but not significant for Student's t-test (p>0.05). Platelet count values showed a reduction while maintaining normal values (226770±45735/mmc to 208454±49182/mmc) as previously observed. MPV values appeared to be reduced after 36 months of RAL treatment only in patients over 60 years-old (p=0.015). In addition, we evaluate in 41 patients from the older group and 28 patients from the control group, CD4+ immune activation. At time of follow-up CD4+ immune activation was reduced in older and younger patients as expressed by reduction of all the tested CD4+ subsets, but MPV had moderate correlation with immune activation only in the older cohort as expressed by CD4+CD38+ % (r = 0.5, p= 0.025) and CD4+CD38+HLA-DR+% (r=0.4, p= 0.035) Fig1 A-B.

Conclusions: At 36 months, patients over 60 years old seem to benefit more than younger population from RAL treatment in terms of hypertriglyceridemia and immune activation. Lower MPV values showed in the aged group, should be interpreted as beneficial, considering the association with lower levels of CD4+ immune activation.

Management of HIV infection

P 120 PREVALENCE AND PERSISTENCE OF HPV IN ANAL SWABS OF A COHORT OF PEOPLE LIVING WITH HIV

N. Squillace[1], G. Lapadula[1], A. Soria[1], L. Rocca[1], F. Sabbatini[1], E. Colella[1], P. Vitiello[1], M. Rossi[1], S. Malandrin[2], A. Cavallero[2], A. Di Lucia[3], M. Braga[3], G.M. Migliorino[1]

[1]Azienda Socio Sanitaria Territoriale Monza, Ospedale San Gerardo, Unità Operativa di Malattie infettive, Monza, [2]Azienda Socio Sanitaria Territoriale Monza, Ospedale San Gerardo, Laboratorio di Microbiologia e Virologia, Monza, [3]Azienda Socio Sanitaria Territoriale Monza, Ospedale San Gerardo, Chirurgia generale e d'urgenza I, Monza

Background: Anal HPV infection is frequently observed in people living with HIV (PLWH) and widely studied among men who have sex with men (MSM). The aim of our study was to compare prevalence, persistence and genotype distribution of HPV of HIV-positive MSM with those of women (W) and of men who have sex with women (MSW).

Materials and Methods: Between March 2010 and January 2019, anal swab for cytological smear and HPV-DNA test was offered to all PLWH attending our clinic, regardless of gender and sexual orientation. Logistic regression analysis was conducted to identify predictors of infection by high risk (HR) HPV infection, as defined by the International Agency for Research on Cancer (2011). Persistance and acquisition of HR HPV were described among patients who repeated anal swab tests during the course of follow-up.

Results: A total of 325 PLWH (171MSM, 91MSW, 61 W) were included (Table 1). Prevalence of HPV infection was: 90.1% among MSM, 75.8% among MSW and 68.9% among women. One or more HR HPV genotype was detected in 82.0% of MSM, 52.2% of MSW and 58.6 of W.

HPV 16 and HPV 31 were the two most frequently detected HPV genotypes in all groups. HPV 58 was present in 23% of MSM but less frequently detected in other groups, whilst HPV 53 was more frequently detected among W than among male patients. Table 2 shows prevalence of all HR-HPV genotypes by gender and sexual orientation. Using logistic regression, MSW (OR 0.24; 95%CI 0.14-0.42) and W (OR 0.31; 95%CI 0.16-0.59) had a significantly lower risk of HR-HPV infection than MSM. No statistically significant difference was detected comparing W with MSW. In addition, older age (per year increase, OR 0.97; 95%CI 0.94-0.99) and CD4+ Nadir (per 100 cells/mm3 increase, OR 1.13; 95% CI 1.02-1.24) were both significantly associated with risk of HR-HPVdetection. No statistically significant association was found between HR-HPV infection and other patient characteristics, including current CD4+ count, HIV-RNA and antiretroviral treatment history. Follow-up swabs were available for 159 patients. Among them, 47.8% (76 patients, of whom 12 were previously completely negative for HR HPV) acquired at least 1 new HR genotype and 35.2% (56 patients) acquired >1 HPV genotype which could have been prevented by vaccination. Conversely, among those already positive for HR-HPV at the first test, 14/120 (11.7%) reverted HPV-HR positivity at the latest test. While MSW had a significantly lower risk than MSM of acquiring new HPV-HR genotypes during the follow-up (OR 0.21; 95%CI 0.08-0.53), this was not the case for W (OR 0.79; 95%CI 0.32-1.92).

Conclusions: Despite a lower prevalence than MSM, HIV-positive MSW and W too have high risk of being infected by HR-HPV in the anal canal. High rates of new acquisitions of HR HPV (many of whom preventable by vaccination) and low rates of spontaneous HR HPV clearance were observed in all groups, with MSM running the highest risk of new acquisitions and MSW the lowest.

Management of HIV infection

P 121 RISK OF FAILURE IN DUAL THERAPY VERSUS TRIPLE THERAPY IN NAÏVE HIV-PATIENTS: A META-ANALYSIS

A. Russo[1], M. Pisaturo[1], L. Onorato[1], S. Martini[1], P. Maggi[1], N. Coppola[1,2]

[1]Department of Mental Health and Public Medicine – Infectious Diseases Unit. University of Campania Luigi Vanvitelli, [2]Infectious Disease Unit. AORN Caserta

Background: in recent years, given the documented efficacy of the different therapeutic schemes of anti-HIV drugs, the scientific community has focused its attention on optimizing antiretroviral therapy. Thus, many studies have tried to reduce the pharmacological load and therefore the side effects, searching for schemes that include only two equally effective drugs. The objective of this meta-analysis is to evaluate the relative risk of failure of two-drug therapies compared to three-drug therapies in HIV-naïve patients.

Methods: A systematic review and meta- analysis conducted using MEDLINE Google Scholar and the Cochrane Library. All studies included had to fulfill the following inclusion criteria: : (a) present original data from randomized or non-randomized trials; (b) investigate in antiviral therapy-naïve HIV subjects the efficacy of a conventional triple ARV (control group), based on three antiretroviral drugs, versus a dual ARV (experimental group), based on two antiretroviral drugs; (c) report the primary outcomes clearly defined as virological failure, i.e. HIV RNA more than 50 copies/ml at week 24, at week 48 and at week 96; (d) report data allowing the odds ratio estimates of relative risk (RR) to be calculated for the different outcomes of therapy with triple versus dual therapy; (e) be written in English; (f) be published as a full paper from January 2007 up to January, 2019.

Results: Fourteen studies, from a total of 4,743, meet the inclusion criteria allowing a meta-analysis of 5,931 patients. For the primary outcome, fourteen studies providing data for 3,079 in dual-therapy group and 2,852 in control group (table 1). Overall, the Relative Risk (RR) of failure with dual therapy compared with control group was 1.10 (95% CI 0.91–1.34; I2 39.1%) (fig.1). Excluding the papers including the maraviroc, as drug included in experimental group, the RR was 1.04 (95% CI 0.90-1.20; I2 0%) (fig.2). In maraviroc-sparing studies, no difference were observed in the different dual therapy-regimen used: precisely, in the 7 studies including INI the RR was 1.16 (95% CI 0.94-1,43; I2 0%) (table 2) ; in the 7 studies including PI the RR was 1.02 (95% CI 0.86 -1.21; I2 0%) (table 2); in the 3 studies including NNRTI the RR was 0.90 (95% CI 0.7-1.15; I2 0%) (table 2); in the 3 studies including NRTI the RR was 1.04 (95% CI 0.82-1.31; I2 28.5%) (table 2).

Findings: dual therapy, excluding those based on maraviroc, are as effective as those with three drugs, showing no difference according different dual therapy. Further sub-analyzes are necessary to establish safety, selection of resistances and if there are groups of patients at greater risk of failure.

Management of HIV infection

P 122 HIV DNA FORM QUANTIFICATION IN BLOOD, TISSUES, CD4+ T LYMPHOCYTES AND MACROPHAGES

C. Orlandi[1], B. Canovari[2], M. Surdo[3], S. Cannizzo[4], F. Bozzano[5], E. Merlini[4], M.F. Cortese[3], C. Tincati[4], F. Marras[6], C. Luigiano[4], Z. Pasquini[2,7], S. Aquaro[8], G. Marchetti[4], F. Ceccherini-Silberstein[3], F. Barchiesi[2,7], A. De Maria[6], C.F. Perno[9], M. Magnani[1], A. Casabianca[1]

[1]Department of Biomolecular Sciences, University of Urbino "Carlo Bo", [2]Malattie Infettive, Azienda Ospedaliera Ospedali Riuniti Marche Nord, Pesaro, [3]Department of Experimental Medicine and Surgery, University of Rome Tor Vergata, [4]Clinic of Infectious Diseases ASST Santi Paolo e Carlo, Department of Health Sciences-University of Milan, [5]Bambino Gesù Hospital, Rome, [6]Center for Excellence in Biomedical Research, University of Genova, [7]Dipartimento di Scienze Biomediche e Sanità Pubblica, Università Politecnica delle Marche, Clinica Malattie Infettive Ospedali Riuniti di Ancona, [8]Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, Arcavacata di Rende (CS), [9]Department of Oncology and Hemato-Oncology, University of Milan

Background: Among all reservoir markers, HIV DNA can reliably characterize the global size of HIV reservoirs allowing an overall quantification of all viral forms of HIV DNA (both integrated and unintegrated, representing the stable and the dynamic form of reservoir, respectively) in infected cells, each playing a different role in HIV replication and pathophysiology. Level of HIV DNA in peripheral blood is representative of the total reservoir but the dissemination and retention of infected cells in a wide variety of tissues, often with distinct viral and cellular characteristics, underscores the importance of studying tissue reservoirs in the development and assessment of cure strategies. We analyzed the range of HIV DNA levels and assayed the feasibility and of the simultaneous measurements of all viral DNA forms in blood, tissues (colon biopsy) and different type of cells from in vitro studies by TotUFsys qPCR platform.

Material/Methods: Cellular DNA was isolated from the different samples with home-made protocol and spin column method tailored to specific blood/tissue/sorted cell samples. Some optimizations were performed to provide pure, concentrated and amplifiable DNA. Quality control measures to ensure the validity of the quantification of total/unintegrated/integrated/2-LTR forms were tested. HIV DNAs were quantified by TotUFsys qPCR platform (LOD 1 copy/1,5x10^5 cells; Casabianca et al., PlosOne 2014, Surdo et al., Antiviral Res 2018).

Results: Sample purification is the crucial first step for the vast majority of molecular biology techniques. The parameters of quality control showed high purity, quality and concentration, absence of degradation and of inhibitors in the isolated DNAs. Preliminary data on the application of HIV DNA forms measurement in more than 1300 samples from different DNA sources (625 from WBC, PBMC, sorted CD4+ T lymphocytes and colon biopsies of HIV subjects, 732 from sorted blood cells for in vitro experiments) and clinical conditions (383 ART-naïve/untreated and 974 ART-treated) were reported in Tables.

Conclusion: The reservoirs are disseminated throughout the body and HIV DNA measurement applied to many kinds of samples permits to estimate the total number of all infected cells, resting or activated, present in blood and tissues. In this study, we demonstrated the feasibility of TotUFsys qPCR platform, after specific DNAs isolation procedure, in measuring a broad range of HIV reservoir size in different biological samples. Our method has proven to be a specific and sensitive system for the analysis of HIV DNA levels in blood, colon biopsies, CD4+ T lymphocytes and in-vitro experiments.

Management of HIV infection

P 123 SOLID ORGAN TRANSPLANT IN HIV POSITIVE PATIENTS WITH 10 OR MORE YEARS FOLLOW-UP: A SUSTAINED GERO-PROTECTIVE OUTCOME

G. Dolci[1], E. Franceschini[1], J. Milic[1], G. Ciusa[1], I. Franconi[1], V. Serra[2], G. Alfano[3], P. Magistri[2], F. Di Benedetto[2], C. Mussini[1], G. Guaraldi[1]

[1]Unità di Malattie Infettive, Policlinico di Modena, Università di Modena e Reggio Emilia, Modena, [2]Chirurgia Oncologica Epato-Bilio-Pancreatica e dei Trapianti di Fegato, Policlinico di Modena, Università di Modena e Reggio Emilia, Modena, [3]Struttura Complessa di Nefrologia e Dialisi , Policlinico di Modena, Università di Modena e Reggio Emilia, Modena

Background: While health generally worsens with age, the relationship between aging and health is dynamic and gero-inducer or gero-protective interventions can be identified. We previously validated frailty index (FI) as a valuable health measure in HIV transplant patients.
We found a relevant correlation between FI strata at baseline and first year mortality as well as a significant correlation between, ΔFI and survival. In this study we sought to describe FI change in HIV patients who underwent OLT before 2009 to address the impact of this health intervention on sustained biological age transition.
Results: From 2003 to March 2009 at total of 22 HIV-positive patients underwent solid organ transplantation at the Policlinico di Modena Hospital, Italy. Nine individuals (40%) are still alive after more than 10 years of post-transplant follow-up. The last death in this cohort occurred in 2012.
Table 1 shows the main demographic and HIV-related characteristics of these patients. Biological age was assessed with a previously validated 30-items FI
At baseline mean FI value was 0.4 (range 0.24-0.48), at follow up mean FI value was 0.3 (range 0.17-0.36).
Seven out of nine survivors have improved their frailty index, one has maintained it stable, while one patient only had a the last one has faced an minor increment. All the patients have sustained undetectability of HIV and HBV (in the 2 co-infected) and SVR to DAA (in the 3 co-infected). Four patients are on a Ciclosporine-based immunosuppressive regimen, while other four are on Sirolimus, only one on Tacrolimus therapy. The two patients that did not improve FI were on Ciclosporine-based immunosuppression.
Discussion: We describe a unique population of long term HIV-positive survivors after SOT.
All the patients underwent a CD4-cells increase and sustained suppression of virus replication.
An extraordinary improvement in health index witness the excellent health profile of these patients and suggest SOT as a powerful gero-protective health intervention. In this particular setting the impact of different immune-suppressive agents can be speculated.

Management of HIV infection

P 124 DR APOLLO CHATBOT: A DIGITAL CONTRIBUTION TO THE ACHIEVEMENT OF THE "FOURTH 90" FOR PEOPLE LIVING WITH HIV

S. Vita[1], R. Marocco[1], G. Morlino[3], V. Palmacci[2], A. Carraro[2], I. Pozzetto[2], M. Renzelli[1], C. Del Borgo[1], V.S. Mercurio[1], C.M. Mastroianni[2], M. Lichtner[1,2]

[1]Infectious Disease Unit, SM Goretti Hospital Latina, [2]Department of Public health and Infectious disease, Sapienza, University of Rome, [3]Snapback, Rome

Background: Integration of mobile phone technology into HIV care has been proposed not only to increase ART adherence bur also to facilitate the long term follow-up of people living with HIV. Aim of the project is to design, develop and evaluate a digital health personnel-patient interface to strengthen their therapeutic alliance a fundamental for the improvement of the disease prognosis.

Materials and Methods: The project phases (analysis of needs and expectations, development, enrollments of study population and evaluation) have been conducted with a user centered approach. Interview were made with HIV positive pts, nurses, HIV specialists. The bot was building with the Microsoft Bot Framework and Cognitive Services and the LUI Service.

Inclusion criteria were: own a smartphone, age >18 yo, to be under effective ART, to have an HIV diagnosis for > 1 year. A semi-structured questionnaire before and after (B/A) Dr Apollo use to evaluate the current interaction modalities with the clinical center and the degree of satisfaction was administered. Non-parametric tests were used for statistical analysis.

Results: The identified needs of HIV pts were: a diversified level of required privacy, the possibility to receive the results of blood test in real time, have a contact with the center also during closing times and a leaner appointment management. The need of HIV doctor specialist were: avoid to lose the pts at the follow up (FU), to communicate a personalized FU program for each pts; while for the nurses: optimize work and avoid to lose time to contact pts. Telegram was the instant messaging platform chosen for Dr Apollo. Figure 1a shows a bot scheme usage and its functions. 31 pts have been enrolled into the study. Table 1 lists the characteristics of the population. In the 9 month period 4720 messages between pts and Dr Apollo were exchanged, many of those outside working hours. The most used function was "Book appointment" (23%), "Results" (22%) (Fig. 1b). Analyzing the results of the questionnaire B/A a decreasing in missed appointments was observed (respectively 31% vs 16%, $p<0.001$).

Conclusions: The design of a digital tool to promote the interaction between health professionals and pts with HIV infection has posed an interesting challenge on the topic of privacy, which, being perceived in a variety of ways, requires flexible approaches and tools, adaptable to individual needs. Conversational interfaces based on instant messaging platforms such as Telegram have proved to be a suitable tool to tackle this problem. The need to be in continuous contact with the clinical center was a major issue for enrolled pts as to know their exam results. In fact, since the first enrollment, the system has shown a high level of acceptability both by the operators, thanks to the reduction of the workload of health care, and by the pts, for the reduction of the impact of the management of HIV infection in everyday life.

Management of HIV infection

P 125 FOOD INTAKE AND HIV INFECTION: A PILOT STUDY OF NUTRITION EDUCATION IN A GROUP OF PATIENTS

P. Vitiello, G. Lapadula, F. Sabbatini, G.M. Migliorino, A. Soria, E. Colella, M. Rossi, N. Squillace

U.O Malattie Infettive, Ospedale S. Gerardo, ASST Monza

Introduction: a balanced nutrional intake in people living with HIV (PLWH) is demonstrated to be effective both for the immunity system integrity and for the control of the metabolic comorbidities. There are few data about the food habits of PLWH; This project aims to evaluate the nutritional assessment and the efficacy of a nutrition education intervention in a group of patients (pts).

Materials and Methods: we enrolled PLWH of age> 18 years-old, on stable antiretroviral treatment for at least 6 months, followed up at the Infectious Diseases Outpatient Clinic of Ospedale San Gerardo, Monza. From October to December 2018 we performed 3 educational meetings (2 hours long, each) every three weeks time. Nutritional records were taken by a multiple choice homemade questionnaire at the beginning of the first (T0), at the end of the third meeting (T1) and three months after (T2). Considering the poor numerosity of the study population, we only report a descriptive analysis of our results.

Results: 14 patients (10 female, 4 male) partecipated to the project. Mean age was 56, mean BMI (Body Mass Index) for women was 22,1 (range:16-31,6), for men was 30,6 (range:26,2-32,8).

At T0 80% of pts had at least 3 meals per day, (20% did not have breakfast), this percentage increased to 90% at T1. At T0 The food style of 77% of pts was characterised by poorly nutritional balanced meals that were a unique first course with a prevalent carbohydrates composition or a unique second course with prevalent proteins. According to suggestions of the Italian guidelines for a healthy diet(last edition,2003), at T0 72% of pts had a low intake of legumes (less than 3-4 portions/week), 100% low intake of fish (less than 3 portions/week), 64% and 71% took less than 2 portions respectively of vegetables and fruits per day. Only 22% of pts took an adequate daily intake of calcium (at least 1 portion of dairy products per day).

The habit of taking high proportion of carbohydrates at lunch and of proteins at dinner did not change at the different time points (respectively T0:63% vs T1:63% vs T2: 63% and T0: 55% vs T1:90% vs T2: 90%)

The frequency of intake of different food classes are reported in the table 1. At T1 we observed an increased intake of cereals (56% took 1 portion/day at T1 and 78% at T2), fruits and vegetables (at least 2 portions of fruits and vegetables in 67% and 50%) and water (67% drank more than 1 liter/day). No remarkable differences were reported from T1 to T2, except for the progressive increase of cereals intake.

Physical exercise was practised by 50% of pts at T0,T1 and 67% at T2.

Conclusions: Although the group education intervention did not substantially modified the patients' eating habits, we observed a positive trend in increase of cereals, fruits-vegetables and water intake. Individual meetings and personalised diet advices could be more effective; they will be our next project to sensitize PLWH to lead a healthy life style.

Non infectious comorbidities in HIV

P 126 ANEMIA IS ONE OF THE GREATEST COMPLICATIONS IN HIV. USE OF ERYTHROPOIETINS IN ASL ROMA 5: BIOSIMILAR AND ORIGINATOR COMPARED

F. Ferrara[1], *M. Mensurati*[1], *M. Latini*[1], *M. Rizzica*[2]

[1]ASL Roma 5, Tivoli (RM), [2]INMI "L. Spallanzani", Roma

Biosimilar medicines, available on average at a price about 30% lower than the reference medicine, represent a great opportunity for the economic sustainability of the NHS. However, clinicians appear reluctant to consider biosimilars as a therapeutic option for their patients. Therefore it is increasingly important the role of Pharmacy UOCs to extend the knowledge on the biosimilars of erythropoietins and to provide the information needed to comprehensively clarify the aspects related to the safety and efficacy of these medicines. The purpose of this work is to raise awareness and encourage clinicians to practice swich in a more vigorous manner.
After analyzing all the therapeutic indications of ESA drugs, regional data, epidemiological data and available evidence on ESA comparative efficacy and safety, two documents shared with clinicians on the preferential use of biosimilar in dialysis and an experimental phase of gradual shift to evaluate therapeutic safety through a company series. In the first half of 2018, as already highlighted in December 2017, a comparison analysis was undertaken between the first half of 2017 and the first half of 2018 on the use of ESAs in dialysis across the Rome 5 ASL.
In the first half of 2018 compared to the same period of 2017, in the 9 Dialysis present at the ASL Roma 5 company and in the Tivoli Nephrology we find conflicting data regarding the use of the biosimilar drug with respect to the originator. Only the agreed dialysis (except CFTGM) and the dialysis of Palestrina and Subiaco reduced the use of darbepoetin, while in the remaining dialysis its consumption increased (+ 3.3% Tivoli, + 10.3% CFTGM, +0, 4% Colleferro) highlighting a surge in prescriptions from the Nephrology department alone (+ 57.2%). The other originator drugs (epoietin alfa and epoietin beta) used in 2017 by almost all dialysis, in 2018 the only departments that continued to prescribe it were the dialysis of Colleferro (+ 2.2% and -11%), Palestrina (-11.4% and -0.4%), Dialysis Villa Luana (-4.7% and -2.3%). Biosimilar consumption increases in all Dialysis except for Nephrology and Tivoli CFTGM (-43.4% and -15.2%).
In literature there is no supporting evidence on the use of an ESA compared to another in terms of safety and effectiveness. Furthermore, the advantage of darbepoetin mono-administration is completely irrelevant in the dialysis field due to the numerous accesses that do not change the patient's compliance. In 2018, in the light of the absence of ADR or less efficacy, a greater prescriptive push of biosimilar drugs was expected. After analyzing the consumption of epoetins in the first half of 2018, it is necessary not only to reaffirm the company appropriateness lines for the prescription of factors stimulating erythropoiesis but also to further strengthen them in favor of biosimilarity

Non infectious comorbidities in HIV

P 127 EMERGENCY CARDIAC TRANSPLANTATION IN NEWLY DIAGNOSED HIV INFECTION: A CASE REPORT

M.C. Moioli[1], D. Motta[1], G. Travi[1], R. Rossotti[1], M. Merli[1], S. Chiappetta[1], C. Orcese[1], C. Santolamazza[2], A. Garascia[2], G. Foti[2], M. Cottini[3], G. Tata[3], A. Costetti[3], M. Mininni[4], G. Pedrazzini[4], A. Nava[5], D. Fanti[5], C.F. Perno[5], M. Puoti[1]

[1]Infectious diseases Unit, ASST Grande Ospedale Metropolitano Niguarda ,Milan Italy, [2]Cardiology Unit Transplant Center, ASST Grande Ospedale Metroplitano Niguarda , Milan, Italy, [3]Cardiac Surgery Unit , Cardio Thoraco-Vascular Department , ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [4]Cardiothoracic Anesthesiology Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [5]Chemical-clinic and Microbiological Analysis, ASST Grande Ospedale Metropolitano Niguarda, Milan italy

A 49-year-old male patient was admitted to a peripheral hospital on November 17th, 2017 for a late presenting myocardial infarction, complicated by severe left ventricular dysfunction and endoventricular thrombotic appositions. Initially a PTCA was performed, but the procedure was unsuccessful. A subsequent cardiac MRI showed a left ventricular pseudoaneurysm, therefore the patient was referred to our Hospital. Upon arrival in intensive care, the patient was in inotropic support with adrenaline and dopamine: a cardiac US confirmed dilated left ventricle, akinesia of the distal middle segments of all walls with rupture of the apex supplying pseudoaneurysm. The only possible treatment in this complicated scenario was cardiac transplantation, and instability due to rapid clinical evolution justified the need to request the inclusion of the patient in a national emergency regime list.

Serological screening tests for heart transplantation showed HIVAb positivity, previously unknown to the patient

The patient had no history of diabetes mellitus, peripheral vascular disease, or hepatitis A, B, or C, and he was not a smoker.

A rapid NAT test confirmed the infection and, as soon as possible, viro-immunological profile was performed, showing HIV RNA 7951 copies/ml and CD4+ T-cell count 730/mmc (26%).

We started antiretroviral therapy with Raltegravir, Darunavir, Emtricitabine and TAF.

After obtaining consensus and exception to the National protocol after a collegial discussion, favourable NIT opinion and favourable second opinion, we decided to register the patient in the national emergency transplantation list.

On December 9th, 2017 the patient underwent orthotic cardiac transplantation, complicated by cardioembolic stenosis of the right renal artery resulting in renal failure.

He was treated with standard immunosuppressive therapy according to protocol with Thymoglobulin-Cyclosporine and Mycophenolate, and the antiretroviral therapy was subsequently modified to Dolutegravir, Emtricitabine, Maraviroc and TAF. We introduced prophylaxis with sulfamethoxazole for pneumocystosis and toxoplasmosis, and with ganciclovir since the recipient serology was not known at the time of transplantation and the donor was CMV IgG-positive. Drugs dosing was adjusted to GFR and TDM when possible.

Conclusion: Sixteen months after the transplantation the patient is in good condition, presented an episode of mild rejection treated with steroids 2 months after transplantation, he continued therapy antiretroviral maintaining undetectable HIVRNA and stationary values of CD4+ T-cell. He did not present opportunistic pathologies except for CMV reactivation in the first year.

Cardiac transplantation remains an option for patients with HIV infection and terminal heart disease.

Non infectious comorbidities in HIV

P 128 STEVENS-JOHNSON SYNDROME/TOXIC EPIDERMAL NECROLYSIS (TEN) AND NON-HODGKIN LYMPHOMA HIV-RELATED: FORTUITOUS ASSOCIATION OR PARANEOPLASTIC SYNDROME?

V. Barocci, S. Mazzanti, M. Di Pietrantonio, A. Polenta, P. Mantini, V. Iencinella, L. Brescini, A. Giacometti

Clinica malattie infettive Ancona, Università Politecnica delle marche

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are serious hypersensitivity reactions characterized by muco-cutaneous and systemic involvement with possible lethal outcome. The prognosis of these diseases is severe, with mortality of 5% in the SJS and 40% in the TEN.
Our case is about a trans-sexual sex worker, HIV positive, in cART with moderate viroimmunological control. History of previous pleuro-pulmonary and lymphoglandular TB and HBV-related hepatitis. A chest abdominal CT scan, performed for low back pain, highlighted multiple lymphoglandular swelling along the main abdominal-pelvic vessels, in particular in the left inguinal area, the largest of which of 27 x 44 mm. The patient was submitted to lymph node biopsy that confirm the diagnosis of Hodgkin's lymphoma nodular sclerosis IV stage/B. During the hospitalization for the first cycle of ABVD scheme, appeared erythematous lesions spread to the face, involving also the oral mucosa, the trunk and the root of the limbs. The drugs in place at the time of the onset of lesions were not newly introduced: the patient took Cotrimoxazole (one of the main suspects in the genesis of SJS/TEN) for many years as a prophylaxis for PCP.
Therefore, in the suspicion of a SJS/TEN, it was decided to assume a wait-and-see attitude. The patient was therefore treated with Betamethasone 5.5 g iv with slow, but gradual resolution of the lesions, not requiring the use of immunoglobulins or any other diagnostic and therapeutic measures. Approximately 7 days after the resolution of the lesions, the patient underwent the ABVD scheme as scheduled, without re-presenting the SJS/TEN post-chemotherapy.
In this case, the absence of a certain pharmacological or infectious cause, argues in favor of a non-random association between LH and SJS. The linkage between the two diseases could be the state of immunodepression induced by LH (and in this case exacerbated by the state of HIV positivity) that would favor an infection triggering the SJS, or the secretion by tumor cells of mediators (such as Granulisin) responsible for apoptosis of keratinocytes.
SJS therapy is based on the discontinuation of potentially involved drugs and on the support of the patient's vital functions. In the case described, the patient was treated with steroid therapy with associated antibiotic therapy in light of the patient's significant infectious risk (LH and HIV).
It was a rare and interesting case of SJS/TEN, fortunately, with the regression of the picture and the complete resolution of the lesions, causing only a slight delay in the administration of chemotherapy.
In our opinion two hypothesis are possible to explain the pathogenesis: the first hypothesis is the multifactorial state of immunosuppression of the patient (HIV infection, cachexia and paraneoplastic state), while the second one is that tumor cells could be responsible for the secretions of factors that determine apoptosis of keratinocytes.

Non infectious comorbidities in HIV

P 129 T-CELL MEDIATED POLYMYOSITIS AS AN UNUSUAL PRESENTATION OF PRIMARY HUMAN IMMUNODEFICIENCY VIRUS INFECTION

M. Di Pietrantonio, V. Barocci, A. Polenta, S. Mazzanti, P. Mantini, V. Iencinella, L. Brescini, A. Giacometti

Clinica Malattie Infettive Ancona, Università Politecnica delle Marche

Myalgias and weakness are common in human immunodeficiency virus (HIV)–infected patients. These symptoms are caused by a heterogeneous group of disorders. Whereas uncomplicated myalgias associated with viremia (HIV or hepatitis C) and fibromyalgia typically require only symptomatic treatment, myopathies associated with HIV or its treatment deserve special consideration because these disorders are potentially disabling and life threatening. Patients with HIV infection may develop various forms of myositis (HIV-myositis), including polymyositis, dermatomyositis, or inclusion body myositis. The occurrence of polymyositis (PM) in HIV-infected individuals (HIV-PM) has been more commonly reported. These cases appear to be clinically and pathologically similar to sporadic PM (sPM), although it was noted that a higher proportion of cases in the HIV-PM cohort showed normal or near-normal creatine kinase (CK) levels. There was no difference in the age of diagnosis between HIV-PM and sPM cases. Recent reports demonstrate that CD4-positive regulatory T cells, known to be dysregulated in HIV, play a critical role in suppressing muscle inflammation and injury and facilitating muscle repair.

Our case is about a 47 years old black woman with new diagnosis of HIV infection. History of HBV infection, hypertension, IGT, MGUS. She presented to the ED with over a year history of lower and upper limbs weakness, generalized myalgias, mild dysphagia and polyuria.

Initial laboratory investigations showed: increased creatine kinase (CK) levels: 28.000 U/L, positive HIV test, anemia, hypereosinophilia, slightly increased cholesterol and triglycerides levels, positive ANA, monoclonal IgG K gammopathy of the undetermined significance, HIV-RNA: 19918 copies/ml with no significant mutations, CD4 + 371 cells/mmc, HIV-RNA: 613 copies/ml in the CSF. Myoglobin and CK-MB levels had increased since the onset of symptoms.

A chest-abdominal CT, performed for staging HIV infection, highlighted small nodular lesions interesting both lungs, ground glass opacities on the lower lobes and consolidation on the right middle lobe. Diffuse lymphadenopathy in mediastinum, abdomen. Splenomegaly.

Electromyography- electroneurography (EMG-ENG) showed findings consistent with myositis and signs of muscle inflammation/necrosis.

Left quadriceps muscle biopsy revealed T-cell CD8+ mediated severe primary inflammation consistent with HIV-polymyositis.

Therapy was initiated with antiretroviral drugs: darunavir/cobicistat/tenofovir/emtricitabine, 1 tablet/day and, after a week, with prednisone 50 mg/day. After two weeks was administrated intravenous immunoglobulin (0.4 g/kg/day for 5 days), which resulted in progressive improvement of weakness and myalgia.

Laboratory tests show decreasing myoglobin, CK-MB, CPK levels.

After 6 weeks patient was discharged with antiretroviral and FANS therapy.

Non infectious comorbidities in HIV

P 130 RAPIDLY PROGRESSIVE AUTOIMMUNE HEPATITIS IN AN HIV-POSITIVE PATIENT: A CASE REPORT

A. Borioni, L. Badia, V. Guardigni, P. Viale, G. Verucchi, G. Piazza

Osp. S.Orsola Bologna; Alma Mater Studiorum, Università di Bologna

Background: Autoimmune hepatitis (AIH) is a progressive, chronic hepatitis that has rarely been reported in HIV-infected individuals. We describe the case of a patient with HIV infection and an extremely fast worsening of liver function due to a likely undiagnosed AIH.

Material and methods: We retrospectively reviewed the charts of the patient and compared our case with other previous published cases about HIV-infected and concomitant AIH.

Results: The patient is a 57-year-old Caucasian male diagnosed with HIV in 2003, with a CD4 cell count of 609/mmc and HIV load of 22000 copies/ml. ART with 3TC/AZT and EFV was initiated on January 2004, and switched to 3TC/ABC and EFV on April 2012. One year after introduction of the new ART regimen, a moderate elevation in serum aminotransferase values was found, with ALT 384 U/l and AST 287 U/l, so that ART was discontinued (because considered a possible cause of liver injury) and an extended diagnostic workup was undertaken. All tests for infectious and autoimmune diseases were negative. Aminotransferase levels continued to increase despite therapy discontinuation (ALT 930 U/l and AST 528 U/l) so a liver biopsy was performed which showed hepatocyte cells with confluent and spotty periportal necrosis with plasma cells in the portal and perisinusoidal space. This histology was suggestive for an exacerbated chronic hepatitis, but alone did not allow the pathologist to reach the diagnosis of AIH. HIV viral load remained spontaneously undetectable until June 2017, when an HIV RNA of 2116 cp/ml with CD4+ 808/mmc was found and cART with 3TC/ABC/DTG was resumed. Ten months later a further worsening of liver function occurred: a progressive deterioration of liver markers (bilirubin up to 10.65 mg/dl, AST 792 U/l and ALT 337 U/l) and pleural and ascitic effusion led to a second liver biopsy that showed severe liver cirrhosis (Ishak 6, Metavir 4). ART was reintroduced (with TAF/FTC + RAL) and after a month, immunomodulatory therapy (with azathioprine and steroid) was started with subsequent improvement of liver function.

Conclusions: Despite the favourable CD4 count, all laboratory markers of AIH have always been negatives, in contrast to other 13 HIV-infected AIH cases described in literature, none of whom had completely negative markers. Our case suggests that AIH in HIV patient could be an underestimated diagnosis due to ART acting as a confounding factor, and it is important to consider that the absence of detectable circulating autoantibodies does not preclude a diagnosis of AIH. Our patient changed ART an year prior to presentation (from 3TC/AZT+EFV to 3TC/ABC+EFV), so we can assume that ART could be one possible trigger of immune response directed against liver antigens. Meanwhile the virus itself may somehow be causative agent in certain instances, so low level viremia could have played a role in determining such a rapid cirrhosis progression in our patient.

Non infectious comorbidities in HIV

P 131 DOLUTEGRAVIR DOES NOT INDUCE BONE MINERAL DENSITY DECREASE IN A REAL LIFE SETTING

P. Bonfanti[1], E. Ricci[2], B. Menzaghi[3], G. Orofino[4], N. Squillace[5], G.V. De Socio[6], F. Vichi[7], M. Celesia[8], C. Dentone[9], S. Rusconi[10], S. Mameli[11], C. Molteni[1], M Guastavigna[4], M. Nofri[6], E. Salomoni[7], V. Colombo[10], G. Madeddu[11] on Behalf of CISAI study group

[1]Unit of Infectious Diseases, A. Manzoni Hospital, ASST di Lecco, Lecco, [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, [3]Unit of Infectious Diseases, ASST della Valle Olona – Busto Arsizio (VA), [4]Division I of infectious and Tropical Diseases, ASL Città di Torino, Torino, [5]Infectious Diseases Unit, ASST-MONZA, San Gerardo Hospital-University of Milano-Bicocca, Monza, [6]Department of Internal Medicine 2, Infectious Diseases Unit, "Santa Maria della Misericordia" General Hospital, Perugia, [7]Infectious Diseases Unit, Santa Maria Annunziata Hospital, Uslcentro, Florence, [8]Infectious Diseases University of Catania ARNAS Garibaldi, Catania, [9]Unit of Infectious Diseases, Department of Graduated Medical Care, Sanremo Hospital, Sanremo, [10]Infectious Diseases Unit, DIBIC "Luigi Sacco", University of Milan, Milan, [11]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari

Background. The integrase inhibitor Dolutegravir (DTG) is one of the most widely used drugs for the treatment of patients with HIV infection. Few data exist about the effect of DTG on Bone Mineral Density (BMD) in real life. Aim of this study is to determine rates of change in BMD over time in patients treated with DTG.

Methods: The SCOLTA project is a multicentre observational study enrolling HIV-infected people who start newly commercialized drugs prospectively, both ART naïve and experienced patients, with the aim of identifying toxicities and adverse events (AE) in real life setting. Dual-energy X-ray absorptiometry at femoral neck (FN) and lumbar spine (LS) were performed at study entry (baseline, BL) and after 96 weeks (follow-up, FU). Percentage BMD change from BL was evaluated using a general linear model, including factors potentially associated with bone loss: age, sex, BMI, HCV, past intravenous drug use (IVDU), naïve status, CD4 at BL < 350 cells/mm3, week at last observation.

Results: 160 patients were enrolled (26.2% F, median age 50 yrs, IQR 42-56) from April 2015 to April 2017. Both baseline and follow-up BMD measures were present in 130 pts at LS and 120 at FN (Table). Most subjects (69%) were on lamivudine/abacavir/DTG; 21% pts started DTG-containing regimen as first treatment and 11% were currently on Tenofovir (TDF)-containing regimen. At univariate analysis, change from BL was 9 (95% confidence interval, CI, -5, 23) mg/cm2 for FN (p=0.22 for H0=0) and 12 (95% CI 1, 24) mg/cm2 for LS (p=0.03). Percentage variations were 1.5 (95% CI -0.5, 1.4, p=0.13) and 1.5 (95% CI 0.2, 2.8, p=0.02) respectively. These results were confirmed using the T- and Z-score variation from baseline.

Accounting for potential confounders, comparisons between groups were not significant, with the exception of BMI class: overweight patients showed a significant LS percentage increase as compared with normal weight ones (p=0.002).

Conclusions: DTG-containing regimens do not seem to induce bone loss in a cohort of HIV-patients, predominantly treatment-experienced, in a real life setting. Further research is required to determine the robustness of these results, in particular for naïve patients.

Non infectious comorbidities in HIV

P 132 HYPERTENSION AND HIV-RELATED RISK FACTORS IN YOUNG SUBJECTS ON ANTI-RETROVIRAL THERAPY IN TANZANIA

S. Trifirò[1], F. Cavallin[2], S. Mangi[3], L. Mhaluka[3], S. Maffoni[4], S. Taddei[5], G. Putoto[6], G.F. Torelli[3,7]

[1]Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy, [2]Independent statistician, Solagna, Italy, [3]Tosamaganga Council Designated Hospital, Iringa, Tanzania, [4]University of Pavia, Italy, [5]University of Pisa, Italy, [6]CUAMM Doctors with Africa, Padua, Italy, [7]CUAMM Doctors with Africa, Iringa, Tanzania

Background: HIV infection is a global public health concern especially in SSA where the majority of PLHIV reside. The use of ART has shifted the course of HIV infection to a chronic condition, increasing the survival of PLHIV and posing the new challenge of non-AIDS-related chronic diseases, such as cardiovascular diseases, adding an extra burden for health care services especially in low-resource settings.
Hypertension is the most important cardiovascular risk factor and the first cause of death worldwide. PLHIV have been found to be at an increased cardiovascular risk, possibly since HIV infection accelerates inflammatory processes known to promote atherosclerosis and hypertension, and patients on ART have a metabolic profile at increased risk of hypertension as well. In addition, traditional cardiovascular risk factors such as smoking and physical inactivity are frequently reported in PLHIV.
However, the links between NCDs and HIV infection/therapy and the relative role of viral infection, ART and traditional cardiovascular risk factors remain controversial.
Material and Methods: PLHIV regularly attending the HIV clinic of Tosamaganga Hospital were retrospectively evaluated. Tosamaganga is a district hospital supported by Doctors with Africa CUAMM and located in Iringa Region, Tanzania.
Inclusion criteria were age between 26 and 80 years and regular ART. Exclusion criteria were acute febrile illnesses, pregnancy/lactation. Demographic data, social and past medical history were retrieved from hospital records. Data regarding CD4 count, ART history, biometry, blood pressure, glucose levels were also collected.
Results: 242 patients (median age 43 years, 98 males and 146 females) were included in the analysis. Median HIV infection was 6 years, median ART duration was 5 years. 79% of subjects were on first line ART and the most used combination was tenofovir, efavirenz and lamivudine. The preferred second line ART was tenofovir, emtricitabine and lopinavir/ritonavir. ART improved CD4 count from 213 cells/µl (at diagnosis) to 518 cells/µl (last visit).
62 subjects were found hypertensive (26%), 19 subjects with central obesity (8%), 10 with diabetes (4%) and 8 with cardiac diseases (3%).
Hypertension was associated with age, family history for hypertension, obesity, cardiac diseases and diabetes. Hypertension was also found to be associated with more advanced WHO clinical stage and more depressed CD4 counts at HIV diagnosis, longer HIV infection and longer exposure to ART.
Conclusions: Hypertension was the most prevalent NCDs in a cohort of young HIV positive subjects on regular ART. Hypertension was found to be associated with both traditional cardiovascular risk factors and HIV related features, such as more severe immunosuppression at HIV diagnosis, longer HIV infection duration and longer use of ART. Further studies to confirm this association and surveys with active screening for NCDs in PLHIV are warranted.

Non infectious comorbidities in HIV

P 133 ALEXITHYMIA IS LINKED TO NEUROCOGNITIVE FUNCTION INDEPENDENTLY OF SOCIODEMOGRAPHIC AND CLINICAL PREDICTORS. A MULTICENTRIC HIV COHORT STUDY

F. Vadini[1], G. Madeddu[2], P. Di Stefano[1], B. Zizi[2], P. Maggi[3], E. Tracanna[1], F. Sozio[1], F. Trave[1], D. Cibelli[1], V. Lai[2], F. Vichi[4], G. De Socio[5], C. Bartolozzi[4], A. Sciacca[1], A. Agostinone[1], P. Bonfanti[6], G. Parruti[1], and CISAI Study Group

[1]Infectious Disease Unit, Pescara General Hospital, Pescara, Italy, [2]Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Sassari, Sassari, Italy, [3]Infectious diseases Clinic, Policlinico Hospital, Bari, Italy, [4]Infectious Diseases Unit, Santa Maria Annunziata Hospital, Bagno a Ripoli, Florence, Italy, [5]Infectious Diseases Unit, Santa Maria Hospital, Perugia, Italy, [6]Infectious Diseases Unit, A. Manzoni Hospital, Lecco, Italy

Background: Alexithymia is construed as a stable personality trait characterized especially by an impairment of affective and cognitive emotional processing. Several brain areas and their associated networks have been implicated in alexithymic behavior, suggesting a neurobiological underpinning for the trait. We hypothesized that there might be a correlation between extent of alexithymia and cognitive performance associated with these brain areas.

Material and methods: A cross-sectional analysis to evaluate the predictors of neurocognitive performance. HIV-positive patients followed at the Infectious Disease Units of four Italian regions (Pescara, Sassari, Bari, Firenze), were consecutively enrolled. Patients were characterized for sociodemographic, clinical and viro-immunological parameters. The 20-item Toronto Alexithymia Scale (TAS-20) was administered to evaluate alexithymia. Neuropsychological tests evaluated visual attention (Trail making A), executive function (Trail making B), short-term memory (Digit span), and processing speed (Digit symbol). A composite neuropsychological summary Z-score (NPZ-4) was calculated by averaging z-scores from each test.

Results: A cohort of 404 subjects (72.7% male, age 46±9.7 yr), was recruited. Of them, 96.4% had been on HAART for 118.6±92.9 months. Mean CD4 T-cell counts at enrollment were 717.4±396.5/mmc. Three hundred sixty-two patients (90%) completed both the neurocognitive tests and the TAS-20. As expected, at univariate analysis lower neurocognitive performance was associated with increasing age (p>0.001), low education (p=0.0003), time living with HIV (p=0.038), unemployment status (p=0.007), higher systolic blood pressure (p=0.009), lower CD4 T-cell counts (p=0.05), and higher alexithymic scores (p=0.0009). The diagnosis of AIDS, CD4 nadir, HCV co-infection, cigarette smoking, poor physical activity and depression were not associated with cognitive performance. At multiple linear regression analysis alexithymia was inversely associated with the NPZ-4 (β= -.006, p=0.040), regardless of age (β= -.012, p=0.008), unemployment status (β= .150, p=0.047), and systolic blood pressure (β= -.004, p=0.046). NPZ-4 progressively decreased across increasing TAS-20 tertiles (Kruskal-Wallis test: chi-squared =14.4, p= 0.0007; fig.1).

Conclusion: With the limits of a cross-sectional design, this multicentric study confirms the role of alexithymia in HIV-associated comorbidities, as already reported for cardiovascular disease. These data add an additional line of evidence on the importance of assessing and treating alexithymia to prevent adverse health outcomes associated with HIV.

Non infectious comorbidities in HIV

P 134 EVALUATION OF LIPID PROFILE IN HIV NAIVE PATIENTS, TREATED BY TAF-BASED REGIMENS

S. Martini[1], P. Maggi[1], L. Onorato[1], S. Ferrara[2], L. Alessio[3], C. Bellacosa[4], V. Esposito[5], G. Di Filippo[6], A. Masiello[7], A. Maddaloni[8], R. Santoro[9], G. D'Alessio[10], S.R. Bruno[2], V. Rizzo[5], S. Parente[6], A. Iodice[3], N. Coppola[1,3]

[1]Infectious Disease, University of Campania, Luigi Vanvitelli, [2]University of studies of Foggia, [3]AORN Sant'Anna e San Sebastiano of Caserta, [4]University of studies of Bari, [5]IV Division AORN dei Colli, [6]University Federico II of Naples, [7]AO San Giuseppe Moscati of Avellino, [8]VII Divisione AORN dei Colli, [9]AOU San Giovanni di Dio e Ruggi d'Aragona of Salerno, [10]AORN San Pio of Benevento

Background: Tenofovir alafenamide(TAF) has deeply changed the choice of backbone in antiretroviral regimens, since maintaining virological efficacy of tenofovir disoproxil fumarato (TDF), it has strongly improved long term bone and renal tolerability. However there are many data in literature that show an amount of lipid levels after switch from TDF to TAF. Few data are available in naïve patients.
Aim: Our aim is to analyze if TAF is associated to higher lipid levels than regimen with abacavir/lamivudine as backbone in treatment of HIV naïve patients.
Material and method: We have enrolled, in an observational, retrospective, longitudinal, multicentric study,175 patients with HIV infection at the time of the start of ART and with a follow-up of at least 24 weeks after starting therapy. Exclusion criteria was the use of TDF or boosted protease inhibitor. Patients have been divided in relationship to the type of adopted regimen: TAF/FTC/RIL (Case group A), TAF/FTC/EVT/Cobi (Case group B), TAF/FTC/INI (Case group C) and a control group without TAF and Cobicistat [ABC/3TC/DTV (Control group)]. We have evaluated Tryglicerides, Cholesterol, HDL and LDL levels. Case groups has been compared to control one analyzing data at baseline (T0), at 24 weeks (T1) and 48 weeks (T2) of follow-up, although data at T2 were incomplete. The endpoint was evidence along follow-up of lipid abnormalities (serum values upper normal values) and/or introduction of statin treatment.
Results: There were no differences between Case and Control groups at baseline (tab.1). At T1 and T2, we observed an increase of incidence of hypercholesterolemia in TAF groups, not associated to alteration of LDL and HDL values (Fig.A/tab.2). Table 3 shows the results of a multivariate analysis to analyze the factors associated to hypercholesterolemia at T1 and T2 (tab.3): at T1 only age was related to hypercholesterolemia, while at T2 also TAF/FTC/EVT/Cobi and TAF/FTC/INI seem to be associated to hypercholesterolemia, with TAF/FTC/RIL that appears protective in this setting.
Conclusions: Our preliminary data from a real-life multicentric study show that,in HIV naïve patients, TAF, if associated to INI with or without cobicistat, may be involved in onset of hypercholesterolemia after 48 weeks of follow-up compared to control group and anyway the age of patients plays a major role.This effect must be in every case confirmed in successive analysis and is so far clinically unclear, but it may be an important focus for the management of patients showing aging, comorbidities and possible cardiovascular risk.

Non infectious comorbidities in HIV

P 135 ARCHI-PREVALEAT PROJECT. A NATIONAL REGISTER OF COLOR-DOPPLER ULTRASONOGRAPHY OF THE EPI-AORTIC VESSELS IN PATIENTS LIVING WITH HIV

S. Martini[1], S. Ferrara[2], C. Bellacosa[3], B.M. Celesia[4], A. Tartaglia[2], P. Maggi[1]

[1]Università degli studi della Campania, Luigi Vanvitelli, [2]Università degli studi di Foggia, [3]Università degli Studi di Bari, [4]Università di Catania ARNAS Garibaldi

Background: The introduction of effective antiretroviral (ARV) regimens has produced a deep impact on the natural history of HIV infection, leading to a dramatic decrease in its mortality improving life expectancy of Persons Living with HIV (PLWH), nevertheless, in these patients cardiovascular disease (CVD) is more frequently than the general population. Measurement of carotid Intima Media Thickness (IMT) with color-Doppler ultrasonography is a non-invasive, sensitive and highly reproducible technique for identifying and quantifying atherosclerotic lesions, even at a very premature stage. It is a well-validated research tool and is widely used in clinical practice. In preventive medicine, IMT measurement is especially important for subjects with an intermediate CV risk, being consistently related to future CV events. Aim: PREVALEAT (PREmature VAscular LEsions and Antiretroviral Therapy) is a multicenter, longitudinal cohort study involving several Italian centers, aimed to the evaluation of CV risk in HIV-infected patients since 1998.The cohort produced, during years, several studies in this field. Our aim is to generate a National Register of color-Doppler ultrasonography (Archi-Prevaleat) to evaluate the characteristics of vascular lesions in PLWH on a large number of data.

Material and Mehods: The project involves, at present,9 Italian centers in which the ultrasonographic examination is performed by specifically trained physicians during a Continuing Medical Education stage. The Register is based on a on-line platform (www.archiprevaleat.com) aimed at collecting data regarding patients routinely submitted to the examination for the first time and at all the subsequent follow-up examinations. We have enrolled until now 116 patients who performed color-Doppler ultrasonography whose data are summarized in Table 1.IMT of common and internal carotid for both left and right sides is registered. A minimum of three measurements are requested: on the common carotid artery:1 cm before the carotid bifurcation and at carotid bifurcation; on the internal carotid:1 cm after the carotid bifurcation and 2 cm after the carotid bifurcation. An IMT of >1 mm is considered pathological. Atherosclerotic plaques, if present, are described.

Results: The tendency is to perform the investigation in older patients, in males and subjects with an history of AIDS. The prevalence of IMT has been 26,4% at left carotid bulb,18,8% at right carotid bulb, 21.1 % at left common carotid and 22.5% at right common carotid (Fig.A).

Conclusions: The preliminary data of our Register show an unexpectedly high prevalence of pathological IMT even if the investigation is performed in patients at higher risk. This will prompt extend the investigation to all patients and will help to proactively prevent CVD, that, in association to aging, inflammation and dyslipidemia, will have a negative impact on good prognosis conquered by advent of safer antiretroviral drugs.

Non infectious comorbidities in HIV

P 136 ABACAVIR HIPERSENSIVITY REACTION (HSR), ASSOCIATED TO BASELINE FALSE NEGATIVE HLAB5701 SCREENING, IN ANTIRETROVIRAL TREATMENT NAIVE HIV-1 PATIENT

S. Martini, P. Maggi, A. Russo, A. Cascone, N. Coppola

University of studies of Campania, Luigi Vanvitelli

Background: Patients with HIV infection,generally,perform at enrollment a pharmacogenetic test for detection of HLAB5701 allele,that is related to abacavir(ABC)hipersensivity reaction(HSR).Aim:Describing a rare case of HSR to ABC in antiretroviral treatment naive HIV-1 patient with baseline false negative HLAB5701 test.

Material and Methods: This case report is about a Ukrainian woman,40 years old,with HIV infection.She arrived at our Unit since November 2017 and first baseline exams showed CD4+ 460 cell/µL,HIV-RNA 1030 copies/ml, no viral resistances,no B and C viral hepatitis,negative Mantoux test,no alcohol intake,no other drugs or addiction,normal liver enzymes,classified as CDC A1.Baseline HLAB5701 screening,performed by cytofluorimetric assay,resulted negative.

Results: At the end of November,patient started antiretroviral treatment(ART)by a co-formulated regimen based on ABC+3TC+Dolutegravir,but after only 2 weeks,began to show fever,articular pain,nausea,stomach cramps. ART was early stopped and exams were performed showing elevate liver enzymes(ALT 503 U/L;AST 218 U/L). Other causes of hepatitis were analyzed,but all resulted negative(Table 1).After 1 month from stopping ART, patient showed CD4+ 394 cell/µL,HIV-RNA 713 copies/ml,no viral resistances and normalization of liver enzymes(ALT 18 U/L;AST 9 U/L).In January 2018,she began a new co-formulated regimen with Elvitegravir +Cobicistat+Emtricitabina+Tenofovir Alafenamide.showing,after 1 month,good tolerability,with persistent normal liver enzymes,not detectable HIV-RNA and increased CD4 count(Fig. A/B).In September 2018,in the suspect of baseline false negative HLAB5701 test,screening was repeated,but this time using a PCR assay,that resulted positive.This test has clarified that patient had developed an HSR to ABC,after drug administration due to a baseline false negative HLAB5701 test.This screening,performed by 2 different assays,had given discordant results,therefore it was repeated for the third time,using again a cytofluorimetric assay with result defined as doubt.

Conclusions: HSR to ABC is a rare and dangerous condition and so the screening is important to avoid drug intolerance and false negative tests. Data of literature show that cytofluorimetric or PCR assay have the same high sensitivity to detect HLAB5701 allele,avoiding false negative tests.Cytofluorimetric is generally preferred for baseline screening,being less expensive.In contrast with these data,our case report shows a discrepancy between 2 assays,underlying that in rare cases,it is possible to obtain a false negative test,performing cytofluorimetric test. It is important therefore to pay attention to liver function and general tolerability when ABC is administered,also in case of baseline negative HLAB5701 screening.

Non infectious comorbidities in HIV

P 137 CARDIOVASCULAR RISK SCORE AND INFLAMMATORY MARKERS IN HIV POPULATION

A. Auricchio[1], C. Ucciferri[1,2], F. Vignale[1], J. Vecchiet[1], K. Falasca[1]

[1]Clinic of Infectious Diseases Department of Medicine and Science of Aging, University "G. d'Annunzio" Chieti-Pescara, Chieti, [2]University of Molise Department of Medicine and Health Sciences Campobasso Italy

Background: The life expectancy of HIV-infected patients in high income countries is approaching that of the general population. Along with improved survival, the practice and complexity of HIV management have changed. Because the HIV infected are living longer, diseases such as cardiovascular disease (CVD), now emerge as prominent causes of death in this population. This phenomenon can be explained by the presence of an HIV-related chronic inflammatory state. A lot of algorithms have been used to predict cardiovascular risk (CVR): FraminghamRiskScore (FRS), Atherosclerotic CardiovascularDisease (ASCVD), the Prospective Cardiovascular Münster study score (PROCAM) and the DAD-5 Years Estimated Risk but none of these considers the inflammatory state in the assessment. The aim of the study is to show the relationship between CVR scores and plasma inflammatory markers.

Material and Methods: A total of 90 virologically suppressed HIV-positive outpatients attending at the Infectious Diseases Clinics of Chieti were enrolled. Demographic and anamnestic data were collected, blood and immunological parameters were measured in addition to the Cystatin C, PCR, microalbuminuria, IL-18, IL-2, IL4, IL-6, IL-10, TNF-α and IFN- γ and CVR scores.

Results: We enrolled 70 males (78%) and 20 females (22%) with a mean age of 48,86±10,01years and a mean BMI of 25,97±3,94 Kg/m2. Biochemical parameters showed a mean of CD4+lymphocytes of 686.09 ±311.51 cells/ml, CD4/CD8 ratio of 0.81±0.12, PCR of 0.41±0.23 mg/dl, eGFR of 88.22±22.02 ml/min/1.73m2, total cholesterol of 184.14 ±34.58 mg/dl while Cystatin C was 1.02±0.25 mg/dl. Interleukin levels showed the following mean values: IL-18 of 270.10±7.44 pg/mL, IL-2 of 1.69 ±1.33 pg/mL, IL-4 of 1.92 ±3.02 pg/mL, IL-6 of 3.87±2.58 pg/mL, IL-10 of 1.17±1.75 pg/mL whereas TNF-α was 1.31±0.8 pg/mL and IFN- γ equal to 32.65±17.1 IU/mL. The study of cardiovascular risk scores showed a mean of FRS of 6.98 ± 6.11%, ASCVD of 7.18 ± 6.25%, PROCAM of 6.7 ± 7.4% and DAD- 5 Years Estimated Risk of 3.10 ± 3.41%. There was a correlation between all the scores for CVR prediction and the years of HIV diagnosis ($p < 0.001$); a correlation between all the CVR scores and IL-18 ($p < 0.001$); a correlation between circulating IL-2 with both the FRS and the DAD-5 Years Estimated Risk; a correlation between these scores and levels of Cystatin C ($p < 0.001$), PCR ($p < 0.01$) and microalbuminuria($p < 0.01$).

Conclusions: We found a correlation between the inflammatory markers and the results from the CVR scores, highlighting how the inflammatory process participates in the pathogenesis of cardiovascular damage in the HIV-positive population. Use of biological markers could be a valid tool to be used in association with the calculators to improve the sensibility and specificity of CVR calculators.

Pediatric, adolescent, maternal, fetal aspects

P 138 Noninvasive liver assessment in a population of vertically HIV-infected children adolescents and young adults

E. Longoni[1], F.W. Basile[1], F. Forlanini[1], P. Nannini[1], GV. Zuccotti[2], V. Giacomet[1]

[1]Unit of Paediatric Infectious Diseases, ASST FBF Sacco, University of Milan, Milan, [2]Department of Paediatrics, V. Buzzi Hospital, ASST FBF Sacco, University of Milan, Milan

Background and Objective: The advances in antiretroviral therapy in the Human Immunodeficiency Virus (HIV) infection have led to increased longevity but also to long term complications, mostly represented by drug-induced liver injury, viral hepatitis and both alcohol and non-alcohol-related steatohepatitis. Vertically HIV-infected patients are more likely susceptible to liver injury, because of the duration of the disease, the longer exposition to drug toxicity, and the higher possibility of co-infections. To date, there are few studies with a complete assessment of liver function combining both noninvasive clinical tests and instrumental imaging in vertically-HIV-infected patients.

Methods: A cross-sectional study performed at Luigi Sacco Hospital of Milan. We enrolled 41 vertically-HIV-infected patients aged 8 to 30 years old, HBV and HCV negative, and compared them with 16 healthy controls matched for age and sex. All patients underwent anthropometric evaluation, complete liver biochemical profile (AST, ALT, γGT, total bilirubin, total and fractioned cholesterol, apolipoprotein A1, alpha 2macroglobulin), abdominal ultrasound (US) and transient elastography (FibroScan) during their follow-up at the Pediatric Infectious Diseases Unit. Fatty Liver Index (FLI), AST to Platelet Ratio Index (APRI) and FIB-4 score were calculated with the obtained results. Statistical analysis was performed using STATA 14 software.

Results: Mean age was 18.7 years old (8-27), 95% of patients were on antiretroviral therapy (HAART), of whom 44% were on protease inhibitors (PI) regimens. Viral load was under 37 copies/mL in 90% of patients. BMI did not differ significantly between the two groups (21.3 kg/m2 vs 20 kg/m2; p=0.11). Mean values of liver transaminases, γGT and LDL cholesterol were higher in the HIV cohort (Tab. 1, p<0.01). A significant difference of mean values of FLI and APRI between the two groups was found (15.3 vs 8.6 and 0.32 vs 0.16 respectively; p<0.01), whereas no significant differences between the FIB-4 mean values were observed. Mild liver steatosis was appreciated in 15% of the HIV-infected patients. None of the individuals of both groups had liver fibrosis, however mean TE stiffness at FibroScan varied significantly between HIV-patients and controls (5.59 vs 5, p<0.01).

Conclusions: Vertically HIV-infected patients on HAART do not exhibit relevant biochemical and structural liver abnormalities. Although both within a normal range, the statistically significant difference between the two groups in mean liver biomarkers, liver steatosis and stiffness, suggests that a complete liver function evaluation should be routinely performed during the long-term follow up of vertically HIV-infected patients to detect the insurgence of liver damage as early as possible.

Pediatric, adolescent, maternal, fetal aspects

P 139 AN INTEGRATED MODEL OF PREVENTIVE MANAGEMENT OF HIV-POSITIVE WOMEN DURING PREGNANCY AND FOLLOW-UP OF THE FIRST YEAR CHILD'S LIFE

V. Boscolo[1], G. Marini[2], S. Cavinato[2], S. Oletto[1], O. Rampon[1], S. Marinello[2], A. Zambon[3], M. Granci[3], C. Giaquinto[1], A. Cattelan[2]

[1]Women's and Children's Health Department, University of Padua, [2]Infectious Diseases Unit, University of Padua, [3]Obstetrics and Ginecology Clinic, University of Padua

Background: HIV counseling, antiretroviral therapy, adherence and retention in care during pregnancy are topics mostly dealt by literature of developing countries. The migratory flows put the need also for European countries. As advised within the guidelines (Simit, 2017), we present a retrospective study on HIV-infected pregnant women cared through a multidisciplinary protocol.

Material and Methods: The project provides professional collaboration by Infectious Diseases/Gynecology and Obstetric/Paediatric Infectious Diseases Departments of our University Hospital. The protocol schedules monthly blood tests, a gynecology and obstetric consultation and an infectious diseases consultation. Together with medical controls, it is proposed a psychosocial assessment and counseling to the pregnant women. One month before the delivery it is held an interview to the parents with the pediatrician. The project also foreseen a monthly meeting by all involved professionals to share clinical and psychosocial information. The team settles personalized interventions for maternal antiretroviral treatment, diagnosis disclosure and testing for HIV of the partner, counseling about delivery and feeding, administration of therapy to the newborn. To the foreign women it is also offered a space to explore thoughts and cultural beliefs about infection, pregnancy and childbirth. The main objective is to highlight any critical issue/risk factors on pshysical and psychosocial mother and newborn well-being in order to prevent MTCT.

Results: From January 2014 to December 2018, we involved 57 pregnant women: 38 (66.7%) are African, 12 (21.05%) from Eastern Europe, 6 (10,5%) Italian, 1 (1,75%) from Brazil. HIV infection was diagnosed in 43 women (74,4%) before pregnancy, in 13 (22,8%) during pregnancy and in 1(2,8%) at delivery.To date, 48 women have given birth. 64 children were born, 54 (84,3%) by a caesarian section,10 (15,7%) by a vaginal delivery. HIV-RNA < 40 copies/ml was reported in 72% and 86% of cases during the 3rd trimester and at delivery, respectively. In women with detectable HIV viremia at delivery median viral load was 6310 cp/ml. 95% of the women maintained viral suppression sixth months after delivery. The median CD4+ cells count increased from 470 cells/µl (28%) at third month of pregnancy to 527 cells/µl (32%) at delivery. All women had IgG anti-CMV before pregnancy; 2 women had reactivation of CMV during pregnancy. No cases of HIV transmission to the baby were reported. The majority of women received social/psychological supports showing a positive correlation with virological outcome.

Conclusion:The antiretroviral treatment allowed pregnant women to maintain suppressed HIV viral load at delivery and to design a protective maternity respect to the risk of MTCT. Psychosocial and environmental factors play a crucial role and an integrated work model of maternal and childcare services with high specialization in HIV infection could ensure successful outcomes.

Pediatric, adolescent, maternal, fetal aspects

P 140 A PICTURE OF CLINICAL, IMMUNOLOGICAL, AND SOCIAL SITUATION IN A POPULATION OF HIV-INFECTED YOUTH FOLLOWED AT A REFERENCE PAEDIATRIC CENTER

V. Giacomet[1], P. Erba[2], F.W. Basile[2], L. Folgori[2], A.R. Benincaso[2], G.V. Zuccotti[3]

[1]Unit of Paediatric Infectious Disease- ASST FBF SACCO- Department of Biomedical and Clinical Sciences, University of Milan,[2]Unit of Paediatric Infectious Disease- ASST FBF SACCO, University of Milan, [3]Clinic of Paediatrics, V Buzzi Hospital, ASST-FBF-SACCO, University of Milan

Background and Objective: Nowadays, due to the efficacy of antiretroviral therapy, most HIV-infected children and adolescents survive into adulthood, and the acute infection has become a chronical infection. Nevertheless, HIV infection is unique among chronic diseases because it implies stigma, often poverty, and the fact that some members of the same family may be living with or died because of AIDS. The aim of this study was to analyze clinical and immunological data together withsocial behavior of a cohort of HIV patients followed from the childhood to the adult age.

Methods: A cross sectional analysis was performed in the Paediatric Infectious Disease Unit at Sacco Hospital in Milan. One hundred and sixtyfive HIV-infected children were followed since 1990.

Results: We are currently following 104 HIV-infected children, adolescents and youth patients (age range 3-33 years, median 16.9 years). Fourteen children died before 2005 (pre-HHART era) whereas 35 patients were transferred to the Adult Clinic. Of 104 patients, 52 are now older than 18 years. Clinically, 14 patients reached the AIDS stage during their childhood but are currently fine. However, two of them are on transplant list (renal and liver transplantation). The first one has a chronic renal failure due to adverse events of antiretroviral drugs with the HIV-infection not well controlled. The second patients is a HCV-coinfected child with a history of non-Hodgking lymphoma at 6 years of age with residual thrombocytopenia; he was treated for HCV infection only when Direct Active Antivirals (DAA) drugs arrived.

Virologically, 50 out of 52 patients show a HIV RNA < 37 cp/ml. Of these 52, 24 patients are currently treated with a INI-based regime, 18 with a PI-based regimen, 3 with a NNRTI- based regimen, and 7 with a combined therapy including PI and INI because of resistant testing. From the social point of view, 34 out of 52 have a job whereas 8 patients are currently unemployed. Ten frequented middle and high school and one graduated; 32 of these 52 patients lost one or both parents during the childhood and 10 were adopted. Nine patients (7 female and 2 male) had a child.

Of the 35 patients transferred to Adult Clinic of Infectious Diseases, 15 are in care with a good compliance. Data on the remaining 20 patients were not available.

Conclusion: This analysis describes the situation of a cohort of patients followed since birth at a Paediatric Center. We now must optimize the transition to the adult clinic while maintaining the retention in care and adherence to therapy.

Pharmacology, pharmacogenomics and drug interactions

P 141 COBICISTAT (COBI)-BOOSTED PROTEASE INHIBITORS (PIS) PLASMA AND INTRACELLULAR (IC) PHARMACOKINETICS (PK) IN NICOTINE USERS

M. Ferrara, A. Trentalange, C. Alcantarini, L. Marinaro, V. Pirriatore, A. Ianniello, A. De Nicolò, A. D'Avolio, A. Calcagno, G. Di Perri, S. Bonora

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

Background: Substance Users among HIV positive patients (pts) are numerous and in the real life setting Nicotine Users (NU) are the most frequent. The impact of nicotine and its metabolites on antiretroviral (ARV) therapy has been scarsely described in vitro and in vivo, underlying a role of nicotine as inductor of membrane transporters (Pgp and BRCP) and cytochromes (Cyp1A1, Cyp1B1, UGT etc) involved in ARV metabolism.
Aim of our study was to evaluate the role of nicotine on the COBI-boosted PIs PK both at plasma and intracellular level comparing Smoking (S) and Non-smoking (NS) pts.
Material and Methods: Sixty-eight patients (pts) admistered with COBI-boosted PIs, 32 S and 36 NS were enrolled in our study. Plasma and IC samples were collected at midpoint (12 hours) or at the end (24 hours) of dosing interval. COBI, ATV, DRV plasma and IC concentration were measured by means of UHPLC-MSMS validated method, respectively and results compared between S and NS. Non-compartmental pharmacokinetic parameters were calculated and expressed as geometric mean (CI95%). Concentrations were expressed as ng/ml. Descriptive analysis were expressed as median (IQR) and geometric mean (CI95%) and patients characteristics were compared by Mann Whitney and Correlation analyzed with Spearman test.
Results: 68 pts were 72% male, median age 51 (IQR 48; 56), BMI 25,4 (IQR 23; 27,5).
COBI plasma, IC concentration and ratio IC/plasma in S and NS pts were respectively 26,9 (-70,2; 124,1) and 65,2 (-21,2; 151,6) ng/mL; 85,7 (-7,0; 178,4) ng/mL and 156,2 (-25,9; 338,5) ng/mL; 3,177 (0,268; 6,087) and 2,396 (1,383; 3,409). ATV plasma, IC concentration and ratio IC/plasma in S and NS pts were respectively 519,6 (215,6; 823,6) and 920,6 (281,8; 1559,3) ng/mL; 798,8 (488,4; 1109,2) and 1229,1 (582,9; 1875,4) ng/mL; 1,537 (0,985; 2,089) and 0,866 (0,476; 1,255).
We found a significative reduction of plasma and IC concentration of COBI ($p= 0,021$ and $p=0,059$) and ATV plasma concentration ($p=0,037$) in S pts. All plasma and IC COBI, ATV and DRV concentrations showed to be significantly correlated ($p<0,001$) both in S and NS pts.
Discussion and Conclusion: The impact of Nicotine on ARV PK in HIV positive population is scarsely described. In our study a significative decrease of ATV plasma concentration was confirmed, as previously described, and, for the first time, a significative reduction of COBI plasma exposure and a trend toward significance for IC Cobi penetration in S population were showed. The role of nicotine in induction of efflux pump, as P-gp or BCRP, and the impact on cytochrome metabolism has to be taken into account in smoking population and further analysis should investigate the potential drug-drug interactions with ARV PK.

Pharmacology, pharmacogenomics and drug interactions

P 142 TDF TUBULOPATHY IN A SWITCHBACK PATIENT. A CASE REPORT

N. Forni, C. Alcantarini, A. Lazzaro, V. Pirriatore, R. Angilletta, M. Ferrara, M. Tettoni, A. Ianniello, A. De Nicolò, A. D'Avolio, A. Calcagno, G. Di Perri, S. Bonora

Clinica Malattie Infettive, Ospedale Amedeo di Savoia, Università di Torino

Woman, 52 years old, PWID, HIV-HCV coinfection known from 2009. At the time of diagnosis PJP and CMV systemic infection, CDC C3. HIV genotype B, wild type , HLA-B5701 positive. The patient started ART in 2009 with TDF/FTC+ LPV/r , followed by TDF/FTC/EFV. In 2014 switch to TDF/FTC/RPV. In 2018 switch to TAF/FTC/RPV. The patient was treated with PegIFn and ribavirine for HCV infection with SVR.
The patient had some comorbities: STEMI in 2014 treated with PTCA plus DES (drug eluting stent)in therapy with bisoprolol and c-asa, depressive disorder for which she was taking sertraline.
the patient did not tolerate the new TAF regimen. The patient referred depression, loss of appetite, weight loss, so a decision was taken to go back to the previous treatment with TDF. The symptoms gradually disappeared with the new old regimen and a standard regular follow up was started.
After a 6 months period at regular blood test follow up a marked increase in serum creatinine, 2,7 mg/dl, was observed, associated with glucose and protein loss at urine analysis. In order to understand the cause of the creatinine elevation a 24 hour urine collection analysis was made. The test showed a severe tubular damage: serum creatinine 2,7 mg/dl, creatinine clearance 14 cc/min, urinary phosphorus 283 mg/24h, , urinary calcium 1 mmol/24h, urinary albumin 161 mg/24h, urinary proteins 763 mg/24h. The main culprit was identified in TDF that was subsequentially interrupted and a new combo was started with DTG+RPV.
In order to understand the role of TDF in the tubular damage a TDM (therapeutic drug monitoring) was performed after the withdrawal of TDF. After 7 days, 168 hours, the plasmatic concentration of TFV was 88 ng/m (FTC 210 ng/ml)l, the TFV urinary concentration 7023 ng/ml with an Urinary-plasma ratio of 79.
TDM was sequentially repeated after 2 weeks from TDF discontinuation. Plasmatic TFV 18 ng/ml (FTC 26 ng/ml), urinary TFV 2924 ng/ml , U/P ratio 162.
The 24 hours urinary collection was repeated after 4 weeks from TDF discontinuation. The analysis showed an improvement in all tubular parameters. Serum creatinine 2,2 mg/dl, creatinine clearance 21 cc/min, urinary phosphorus 221 mg/24h, urinary calcium 1,6 mmol/24h, urinary albumin 46 mg/24h, urinary proteins 285 mg/24h. Plasmatic TFV 6 ng/ml (FTC undetectable), urinary TFV 426 ng/ml , U/P ratio 71.
The case show how an obliged choice to go back to TDF led to a severe tubular damage. It is important to underline that the patient tolerated TDF in the past. TFV plasma halflife is 12-18 h, the elimination is mainly renal. It is not clear what is the role of bisoprolol in the development of tubular necrosis, in fact it is partly eliminates unchanged in the urine, but there is no evidence that bisoprolol and TFV are eliminated by the same transporters. Finally is not known the weight of rilpivirine on the intracellular TFV entrapment into the proximal tubular cells in this case.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 143 HEALTH CONSTRUCTION IN MSM PEOPLE WHO ARE LIVING WITH HIV IN VENETO

M. Costacurta
Università degli Studi di Padova, Padova

Background: In 2017 men who have sex with men living with HIV (MSMLWH) are estimated as the 57% of the new infections in Western Europe and North America (UNAIDS, 2018). We also know certainly that people undetectable since more than six month are also unable to transmit the virus to other partners. Furthermore, it has to be taken into consideration that the quality of life of people treated by ART is very similar to the one of people who are living without the virus. The aim of our study is to understand how MSMLWH face stigmatisation by adapting their habits (social relations and sexual practices) and representation of health to the consciousness of their own serum conversion.
Material and methods: This ongoing qualitative study has been developed through in-depth dialogic interviews lasted 2 hours with 15 MSMLWH participants followed by a doctor in Veneto. Then the records were transcribed and analyzed by themes. The inclusion criteria of the sample considered the concept of saturation: we recruited participants through dating apps, the network of the association Arcigay and the help of some infectivologists in Veneto, selecting the most important cases of study. In particular some variables were taken into consideration for the analysis, such as age, coming out, year of the diagnosis, way of transmission, race, level of study, activism, provenance and sexual orientation. The position and the standpoint of the researcher was very important to appear at first without prejudice on the HIV-positivity and to reduce the distance with the participants during the interviews.
Results: All participants consider the diagnosis as one of the most important events of their whole life. It changed a lot the perception of their own body and the other not only considering the personal social representation of the disease, but also the complete sexual sphere, approaching it to the feelings of shame and guilty. It seems that some people got worried and less disposed to have sexual meetings, while people with less stigmatization became more open to new intimate experiences especially with other MSMLWH. Linked to the serum conversion some people are currently being
followed by a psychotherapist, whereas others found support from the group of peers. The latter case shows that the serum conversion is perceived not only as a medical problem, but also as a social-political problem.
Conclusions: Considering the narrations on the worries and the desires of the participants, it seems that the problem of the stigmatization is not related only to the HIV, but to the social representation of sex and the concept of promiscuity. The lack of a national law aimed at providing young students with an inclusive and positive sexual education is not a problem only for the high number of diagnosis, but in particular for the psychological well-being of new cases of infection and the people around them.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 144 PREVENTION DURING THE APPS ERA. ANLAIDS IS ONLINE ON GRINDR

S. Negri[1], A. Chinelli[3], R. Galipò[4], M. Longhi[5], J.D. Pamphilj[4], M. Ramadori[6], B. Marchini[2]

[1]Anlaids Lombardia,[2]Anlaids Onlus, [3]Anlaids Liguria, [4]Anlaids Lazio, [5]Anlaids Mantova, [6]Anlaids Umbria

Background: The Italian newspaper Il Sole24Ore on February 2016 stated that there are 91 millions internet users chatting and the numbers were increasing in 2018. People between 25 and 34 years old are those who look for online dating. In Europe there are 33 million people browsing online dating websites and apps, and in Italy they are 9 millions. Focus magazine, within an article back on October 2017, stated that online dating could support integration (a study carried on by a Cornell University team).
One of the best Apps that "supports" online dating system is, without any doubt, Grindr. Born in 2009, Grindr is a geo-localization based social network dedicated to men who have sex with men which aim is to put in connection users in the same area. The number of users touched 2 millions after 2 years: today, they are 4 millions.
Anlaids Lazio had already experienced spreading prevention via apps: back in 2016 it launched an ad hoc counselling service through app, then National headquarters of Anlaids extended the service into other cities through their own sections in the country. Chatting on GRINDR, users can ask questions about HIV/AIDS/STIs to the expert via Joe Condom's profile.
Material and Methods: In the picture of the Profile there is a toned guy (JOE CONDOM) with the Logo of Anlaids (and the
section) on the shirt. In it, the type of service is clearly displayed as well as from whom it is supplied. The operators are appropriately trained psychologists or counsellors, who connect at different times of the day, guaranteeing at least 2 hours a day coverage.
Results: Anlaids Lazio (from June 2016 to August 2018), has collected almost 2000 contacts and about 4000 questions addressed to JOE Condom.
From September 2018, JOE Condom is active in five cities, mainly in Rome, Milan, Mantua,
Genoa and Perugia; in February 2019, Anlaids Lombardia had 125 contacts; Anlaids Lazio 137;
Anlaids Liguria 72; Anlaids Mantova 25; Anlaids Umbria 28. The data of these 2 last sections are
relating to less than 3 months of activity.
A significant percentage of users (over 50%) try to hook the operator for meetings even after asking questions or becoming aware of the type of service. The service is widely accepted also because of its immediacy and the questions are mainly about:

- HIV risk after oral intercourse (80%)
- Info about the test (60%)
- Where, when and info requests on quick tests
- HIV risk with practices such as pissing and rimming (25%)
- Symptoms of the infection (30%)
- PreP (40%) and Tasp (about 20%)
- Other STIs (18%)
- Other (15%)

Conclusions: The results suggest that it is possible to use mobile technologies and the popularity of GPS-based social media networks as complementary tools for education and information on sexual health with a successful outcome in the terms of number of contacts.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 145 ANLAIDS ONLINE FORUM IS AN EFFECTIVE TOOL TO MONITOR THE PERCEPTION OF HIV TRANSMISSION RISK AND THE HIV-RELATED SOCIAL STIGMA IN GENERAL POPULATION

G.V. Calvino[1], A. Venturelli[1], M.Galli[2], C. Balotta[2], B. Marchini[1]

[1]Anlaids – Associazione Nazionale per la lotta contro l'Aids Onlus, [2]Infectious Diseases Unit, Department of Biomedical and Clinical Sciences, University of Milan, Italy

Background: Since 2007, ANLAIDS Onlus offers an online forum where questions about HIV prevention, transmission and diagnosis are answered by a doctor. On average, 4.1 messages are posted every day on the online forum.
Our aim is to analyze systematically the nature of users requests to monitor the levels of awareness of HIV transmission, potential risk of infection and perception of social consequences of disease.
Methods: Our study was conducted considering the 1° semester of 2018 for a total of 730 posted messages. Due to privacy issues, it was not possible to identify the age and geographical origin of the users which were classified, only by gender. The sex of the users was deduced, when possible, by the contents of their questions.
The risk of transmission has been classified as "real transmission risk" (RTR) and "no risk"(NR). The criteria used to classify the message were: 1) lack of information, when the post clearly indicated the absence of knowledge of true transmission modalities; 2) phobia, when the content of the post clearly showed phobic elements, in the latter case further considered factors were detailed description of supposed symptoms and reiterations of questions by the same user.
The alleged mode of HIV transmission in sexual intercourses and social life was then considered.
Results: We examined 730 posts. Of these, 586 (80%) were from men. 28% of the posts were containing questions about RTR; in half of them it was described a low transmission risk (active oral sex, unclear exchange of secretions). 475 posts (65%) were questions classified as NR; of these 58% were related to not-at-risk-sexual intercourses and 42% to aspects of social life.
The posts that showed an evident lack of information were 42%; they were not related to sex, such as frequenting public places, toilets or handshakes. With regard to sex, the large majority of questions were related to masturbation in the presence of abrasions of the finger skin or related to doubts about the efficacy of the condoms in preventing HIV transmission.
Almost half of posts that openly manifested phobias, both for the used tones and the number of reiterations; 9% of users have posted over 15 messages asking the same question in different style. Furthermore, 15% of users lamented HIV acute infection related symptoms. 63 of these persons were not exposed HIV.
Conclusions: A relevant number of recent posts show that there is still a great lack of information regarding the modalities of HIV transmission. The perception of HIV infection, transmission and therapy of many users is obsolete. For many users HIV is linked to transgressive sexual behaviors and fear the stigma related to HIV infection.
Health care providers, together with non-profit association and patient communities need to work together to transfer up-to-date information to the public to increase awareness about HIV infection and to eradicate the social stigma associated with HIV infection.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 146 PROMOTING MIGRANT ACCESS TO SEXUAL AND REPRODUCTIVE HEALTH SERVICES FOR SEXUAL GENDER BASED VIOLENCE (SGBV) PREVENTION AND RESPONSE (PRO-ACCESS). PRELIMINARY DATA ON HIV AND HCV PREVALENCE

*K. Ceesay, D. Di Dio, S.B. Dhiab, G. Floridia, M.C. Longo, M. Manuli, D. Matheson, G. Petrelli, S. Reale, S. Scalzo, A.A. Sleemankhel, M. G. Di Benedetto, F. Bellissimo and L. Nigro for the ProAccess/LILA Volunteer Group**

Lega Italiana per la Lotta contro l'AIDS - Catania

Background: In Italy, although the number of new diagnoses of HIV infection among migrants has remained relatively stable, the percentage has increased from 28.6% in 2010 to 34.4% in 2017.
Living in a high prevalence country does not necessarily increase the individual risk for acquiring HIV, however, studies has shown that migrants, in their country of origin, have an increased vulnerability for HIV infection, because access to HIV prevention, testing and counselling is often limited due to legal, cultural, socio-economic issues. Also, the migration process itself can impact HIV risk and access to care, because migrants might experience (sexual) trauma, discrimination and marginalization as well as problems with legal status.
A question frequently asked in the case of migrants is: migrants arrive in our country already suffering from the infections or acquire the infections in our country.
Promoting migrant access to sexual and reproductive health services for sexual gender based violence (SGBV) prevention and response (Pro-access) is a program that aims to offer, among others services, HIV and HCV testing. The program is addressed to economic refugees and asylum seekers (People of Concern, PoCs).
Objective: The aim of this study is to establish the prevalence of HIV and HCV infection in PoCs who live in: 1) houses / flats, "Protection system for asylum seekers and refugees" (SPRAR); 2) reception centers for asylum seekers (CARA); 3) other reception centers (centers for minors); 4) urban areas (refugees).
Materials and methods: The preliminary data of the study refer to the period from January to December 2018. The study began in August 2017 and is still ongoing.
All the PoCs encountered were offered HIV and HCV testing; those who accepted were given pre and post test counselled.
Counseling and testing, at receptions centers and drop-in were performed by a psychologist and a doctor.
Tests used OraQuick® Rapid Antibody HIV and HCV by Meridian.
Results: The PoCs enrolled arrived in Italy during the last three years and were from Nigeria, The Gambia, Senegal, Bangladesh, Guinea, Ghana, Cameroon, Ivory Coast, Sudan, Morocco, Mali, Eritrea, Libya, Tunisia, Pakistan, Afghanistan.
A total of 2185 PoCs were informed on STI prevention. Of these, 585 accepted to be counseled and tested. All tested negative for HIV and 4 tested positive for HCV.
Conclusion: Our findings suggest that PoCs are healthy when leave the country of origin and become infected in the countries of arrival. These is due to the fact that PoCs women/girls and men/boys continue to be victims of trafficking and sexual exploitation even after reaching Europe. There is a need to identify: gaps regarding STI prevention programs, services access, sexual risk behaviors and gender differences.
*ProAccess/LILA Volunteer Group: J. Alieu, S. Bruno, G. Cacciatore, A. De Cristofaro, A. Leo, S. Maccarrone, M. Maresca, S. Timpanaro.
The program, started in 2017 and still ongoing, is fund by UNHCR.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 147 HEPATITIS A AWARENESS AMONG HOMOSEXUALS AND THE GENERAL POPULATION: RESULTS OF A SURVEY

M. Properzi, B. Boldrini, A. Chiesa, D. Coletto, N. Gregori, F. Castelli, E. Quiros-Roldan

Departement of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy

Aims: To assess the awareness of Hepatitis A disease, prevention and transmission among a local community of homosexuals and the general population and to compare the populations examined.

Methods: We performed a cross-sectional study from 14th March to 30th August 2018 in Brescia province. An anonymous Web questionnaire evaluating the awareness of HAV infection was administered through social networks (Facebook) to 3 different groups:

A) Homosexual persons aged >18 years old enrolled in a territorial gay community (Orlando - Comitato Territorale Arcigay di Brescia)

B) Heterosexual general population aged between 18 and 35 years old

C) Heterosexual general population >50 years old

The questionnaire was composed of different questions regarding sexual behavior, HAV epidemiology, disease and prevention plus a narrative comment section.

Fisher's exact test was performed; a p value <0.05 was considered statistically significant.

Results: A total of 222 questionnaires was collected (87: Group A, 111: Group B, 24: Group C). In Group A the majority were men (n=70, 80%) with a median age of 28.9 years (range:18-55); in Group B 43% (n=42) were females (median age 24.5 years, range 18-35), while in Group C 54% (n=13) were males (median age 62.3 years, range:53-71). Condoms were more likely to be used by Group A (40%) compared to Group B and C (35% and 17% respectively, p=0.226); having 5-15 and > 15 sexual partners in the last year was significantly associated with Group A (p<0.05). The majority of Group A performed at least one HIV test in his life (60.9% vs Group B: 19.8% and Group C: 20.8%, p <0.05). Over 99% of interviewed in Group A knew HAV (vs Group B: 94%, Group C: 71%); group B identified less well Hepatitis A symptoms (83.8% vs 90.8% for Group A and 91.7% for Group C, p=0.300). Only few people knew the possibility of spread through contaminated food or water (Group A: 6%, Group B: 10%, Group C: 13%) while over 76% for Group A and 74% for Group B was aware of HAV sexual route of transmission (Group C: 38%). Group A and B were more informed about HAV vaccine compared to Group C (p<0.05), but only few got vaccinated (Group A: 48%, Group B: 29%). Regarding Group A, 51.7% knew that HAV vaccine is free; however, 35.7% did not get vaccinated because ignored whom to consult. In the comments, homosexuals told that the biggest obstacle to free vaccination was to declare to be gay.

Conclusions: Although a sensitized MSM community, HAV infection is still unacknowledged. Much should be done to implement knowledge, prevention and vaccination strategies not only in typically at-risk groups but also in general population.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 148 HIV-RELATED STIGMA AS A MULTI-LAYERED CATEGORY: AN ANTHROPOLOGICAL INQUIRY

A. Gattari

Università Alma Mater Studiorum, Bologna

This work is the result of a MA Thesis research in Cultural Anthropology. The ethnographic inquiry investigated the experiences and troubles of HIV patients in their daily lives. Illness, disease and stigma peculiarities, when it comes to seropositivity, are deeply bond with politics, economics and sociocultural dynamics which are tremendously decisive: in fact, they continuously trace the invisible boundaries that define concepts such as health, disease, normality and a-normality. The focus of the research was the close examination of these topics, using the qualitative approach that characterizes anthropology as a social science.

The fieldwork started in June 2017 with the collection of ethnographic data; the resulting monograph was finalized in March 2018. 11 qualitative interviews were collected during the inquiry: all of them were entirely recorded and transcribed. The informants were all located in Emilia-Romagna: they took part in the research thanks to the collaboration of three non-profit associations. The semi-structured format of the interviews allowed the researcher the exploration of a wide range of themes, spanning from the relation with drugs and biomedical institutions, to the organization of support groups. Stigma and prejudice emerged as dominant topics of each person's story: they were closely investigated through the analysis of practices, discourses and representations connected to these concepts.

The results of the research cleared three important aspects: first of all, stigmatizing episodes have a strong influence on the strategies and behaviors of people with HIV. Prejudice takes action in many manners but, paradoxically, it is reinforced and made invisibile by the dynamics of biomedical and political institutions. Secondly, stigma is a powerful narrative which has been historically and socially developed; some of the informants never experienced negative episodes, yet they embraced the cause of those who feel oppressed and rejected. This is what we may call the embodiment of perceived stigma. Lastly, stigma as a category evolved into a discursive tool, actively used by people with HIV to reclaim their neglected identity through the constitution of support groups. These organizations often keep their doors closed to strangers – i.e. seronegative people; they act as isolated entities that in the end, contrary to their purpose, remark the distinction between normality and a-normality.

In conclusion, the experience of HIV in everyday life is linked to the theme of prejudice, in certain cases passively suffered, in others actively exploited. Stigma is a category made of several layers: social phenomena are mixed with biological data and experienced as history unfolds. Support groups, then, are based on a form of bio-sociality, the dynamics of which result in a zero-sum game: as they fight the discriminations, they reinforce the same distinctions that the lack of understanding of biomedical and political institutions created.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 149 "MASSIMA SICUREZZA": INTERVENTIONS FOR THE PREVENTION OF HIV, HEPATITIS AND OTHER INFECTIONS IN THE MILAN PRISONS OF SAN VITTORE AND BOLLATE

S. Penon, L. Cosmaro, S. Curridori, D. Savarino, M. Oldrini

Fondazione LILA Milano ONLUS, Milano

Background: The Italian National AIDS Plan (PNAIDS) aims to target prisoners with prevention interventions. At the moment the Plan was issued, Italian prisons hosted 103.840 inmates with estimated 5.000 PLHIV. Estimates on HCV prevalence suggest that up to 1/3 prisoners might be HCV positive, often unaware of HCV status. Prisoners engage in risky behaviors (unprotected sex, use of non-sterile needles); no data available on HIV and HCV incidence within prisons. In 2016, approximately 1/4 of inmates were considered drug dependent, a proportion that remained stable over the years (EMCDDA, Italy Country Drug Report 2018). PNAIDS suggests specific training programs for prison police, healthcare staff and detainees and provision of informative materials.

LILA Milano has been addressing HIV prevention in Milan prisons for over 25 yrs and from Oct 2017 to Sep 2018 carried out an intervention in two prisons: San Vittore and Bollate.

Material and methods:

Structure of the intervention:

-meetings with prison mgmt and healthcare staff prior and after the trainings, to agree on contents/methods and share outcomes

-2 separate training modules targeting prisoners and prison police staff conducted by an infectious disease specialist and 2 educators

-provision of kits containing hygiene and personal care items -together with multilingual brochures on HIV/HCV prevention and treatment- to prisoners

-completion of pre/post-training questionnaires to measure improvement of competences in detainees and prison police staff

-completion of questionnaires on quality, usefulness and effectiveness of interventions

Topics addressed:

-health and wellbeing in prison settings

-prevention and care of infectious diseases (viruses, bacteria, fungi, parasites); focus on doctor/patient interactions

-HAV, HBV, HCV, HIV: prevention, diagnosis and treatment; PPE and TasP for HIV

-other infections in prison settings: scabies, tuberculosis, legionellosis

Results:

The following activities were carried out:

-3 meetings with both management and healthcare staff in 2 prisons

-26 training modules (2 sessions each) to a total of 370 prisoners

-4 training modules (2 sessions each) to a total of 66 prison police staff

Comparison between pre/post training questionnaires indicated overall improvement of competences and decrease in stigma towards PLHIV. Training sessions contributed to clarify doubts and diminish fears related to potential transmission of HIV/HCV, thus improving relationships among inmates who share overcrowded cells. Also police staff reported a reduction in concerns connected to daily contacts with prisoners.

Conclusions: All actors involved evaluated the intervention as concrete and useful, as they could benefit from information directly connected to their daily prison routine/professional tasks. Prison management requested continuation of activities. Interventions might be replicated with even improved effectiveness, thanks to the experience gained during 1st year of activities.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 150 POSITIVE PROJECTIONS: THE THEMATIC APPERCEPTION TEST (TAT) AND THE IMMUNOLOGICAL RESPONSE IN HIV+ PATIENTS

C. De Guglielmo, A. Masiello, S. Giglio, M. Talamo, S. Leone

A.O.R.N "S.Giuseppe Moscati" Malattie Infettive, Avellino

Background: The Thematic Apperception Test (TAT) is a projective personality test that evaluates the content of the thoughts expressed and the fantasies of the subject, allowing the clinician to know the subject's emotions, attitudes and cognitive processes. Our goal was to analyze projective capacity and emotional expression through TAT test in HIV + patients related to immunological attitude and gender emotional differences. Our goal was also to evaluate the possible differences between the various emotional themes expressed.

Material and methods: We enrolled consecutively 20 Hiv+ patients pair-matched for age and level of schooling. Projective and expressive capacity was evaluated using the TAT test and the Bellak method which consists of the administration of 10 standard tables. The tables present various life situations. The ambiguity and poor structuring of the stimulus are the fundamental characteristics of the techniques based on projection. For each patient were evaluated Nadir CD4+ and the immunological attitude at the time of test somministration. All patients present HIV-RNA not detectable for at least 2 years. The patients were divided into two groups based on a formal analysis (length and processing of stories) and evaluation of the content (scores 1-5 based on the quality of the emotional content).GroupA, 13 patients with medium-high projective and expressive capacity(> 600 words;scores >3 quality of contents) and group B, 7 patients with Medium-Low projective and expressive capacity (<600 words; scores<3 quality of contents). Subsequently, they were subdivided into three groups for gender and sexual orientation. MSM(n.7), heterosexual women (n.6), heterosexual men (n.7). They were compared with the control group of 20 healthy subjects matched by age, sex and sexual orientation. The characteristics of the patients are shown in Table1. For statistical analysis, we used the Student t test and the X2 test.

Results: GroupA shows higher values of CD4 than GroupB. (p = 0.01) (Chart1). Hiv+ women (p = 0.04) and Hiv+ MSM (p = 0.03) show greater projective and expressive capacity
than Hiv+ men (chart3). Hiv+ women and women Hiv- showed a statistically significant difference in the expression of sexuality (p = 0.04). HIV + women more express the desire for protection and aggressiveness. HIV + men don't expess the desire for success and sexuality (Chart 3-4).

Conclusion: the quantitatively and qualitatively poor stories in TAT, corresponding to greater emotional resistance, are associated with a low immunological response. This data confirms the psychoimmunological analysis of the relationship between expression of emotions and the immune system.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 151 TREATMENT OF HCV IN THE AGE OF NEW DIRECT-ACTING ANTIVIRAL DRUGS (DAAS): INNOVATIVE ASPECTS, MANAGEMENT IMPACTS AND BIOETHICAL IMPLICATIONS

D. Piccioni[1], S. Bertini[1], A. Ferrero[1], C.B. Traversi[1] , C. Carcieri[1], G. Cinnirella[1], A. Consoli[2]

[1]Amedeo di Savoia Hospital Pharmacy, ASL City of Turin, [2]Department of Addictions, ASL TO 5

The new DAA drugs changed the prognosis of chronic hepatitis C with the possibility of HCV eradication in 96 -68% of cases;however the high cost was the main obstacle to their use.This issue provided numerous general and subjective reflections in the bioethical field.

Several questions,tab.1,were evaluated in order to respond with particular attention to the ethical point of view.

1.Since the end of 2014, the Italian Medicines Agency (AIFA), authorized progressively all the drugs available in Europe, modulating, however, the access to therapy for economic reasons.The exclusion from the eligibility criteria of some patients generated the serious ethical problem to initially deny them the treatment,contradictory to the universal ethical principles of medicine.
2.The ethical principle of equitable access to care must be defended and protected by the excessive profit attempts of Pharmaceutical Companies, which, in this perspective,would gain the added value of "social good" producers.
3.The cost of these drugs varies in the countries according to the system of price graduation, proportionally to the national income;this situation resulted in a migration toward middle-low income countries of patients not eligible for treatment according to the AIFA criteria.The phenomenon of migration accentuates the problem that access to care depends on the economic conditions of patients or to National Healthcare budget: this fact is contrary to the principles of fairness and universalism that characterize our National Healthcare System.
4.Despite the decisions of AIFA,some Regions have proposed to treat all patients,creating an important diversity in the way they access to care.
5.With a view to safeguarding public health,it would be better to treat this type of patient as a priority,thus reducing the risk of infection and therefore a final economic saving for the NHS.
6.The patient's lifestyle (active alcoholics,drug addicts,sex workers)could affect the outcome of the therapy or nullify the benefit in the event of re-infection. Faced with the cost borne by the community, there is therefore a moral responsibility of the patient who is called to assess his own risk behavior.Fragile patients with limited cognitive abilities, low degree of motivation or with psychiatric problems may not correctly and consistently take a therapy for which it is known that adherence to the recruitment schedule represents a guarantee of therapeutic success over time.

The decision makers did not work on the goal of maximizing care,but tried to perfect the prescriptive environment, effectively reducing the supply of therapy.The reflection on this case can be an indicator of how much bioethical education is necessary in general terms and with reference to the concrete exercise of clinical and health planning tasks.The hope is to use complex and critical events,like this one,to avoid the repetition of poorly adequate behaviors in situations of great impact on public health.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 152 YOUNG PEOPLE AND HIV: KNOWLEDGE AND ATTITUDES ABOUT CONDOM OF HIGH SCHOOL STUDENTS IN THE LAST FIVE YEARS IN ITALY

M. Galli[1,2,5], L. Oreni[1], M. Pedretti[2], E. Zambon[2], T. Ferrario[2], R. Galipò[3], M. Longhi[4], G. Del Bene[2,5], B. Marchini[5]

[1]UOC clinicizzata di Malattie Infettive, DIBIC L. Sacco – UNIMI, [2]ANLAIDS Sezione Lombarda, [3]ANLAIDS Lazio, [4]ANLAIDS Mantova, [5]ANLAIDS Onlus - Progetto Scuola

Background: High school is a strategic site to perform prevention programs and for the monitoring of knowledge on HIV/STI issues. Since 1993 ANLAIDS has promoted information and prevention on HIV and STI in schools with specific initiatives aimed at students. Here we present the results of a five-year survey of the orientations and knowledge of a large sample of high school students.

Material and methods: A pre-intervention anonymous questionnaire was administered to students in large majority attending the third year of Second Degree Secondary Schools of different educational orientation (lyceum, technical institutes and professional institutes). The students were mostly not yet involved in specific initiatives addressed to HIV prevention. Questionnaires were structured with multiple choice questions. Statistical analysis was performed by logistic regression.

Results: In five consecutive school years (September 2013 - June 2018) 13,905 students from the provinces of Milan, Monza/Brianza, Mantua, Rome and Latina completed their questionnaires. Of them, 6876 (49,45%) were female. The median age was 17 years (interquartile range 15-18). The 53% was attending a technical institute. Rome and Milano contributed for 30,51% and 47,36% of participants, respectively. The 45,22% of females and the 47,33% of males reported having had complete sexual intercourses. Of them, 81% reported they have used condoms, but only 58% of them declared that they do not associate any problems with their use. Among the problems related to the use of condoms, 2% of students report that their partner does not want to use it (1,32% of males), 3% don't think it's safe, 1% don't know how it works, 4% prefer other methods of protection, 1% say that it is against religion (2% of males), 10% think that it disturbs the atmosphere of the relationship (12,26% of males), 16% report other reasons or provide no further explanation. Factors independently associated with perceiving problems with the use of condoms were reported in the Figure 1.

Conclusions: A relevant percentage of students reported problems with condom use, which increased with age. The problems were related to individual information (possible confusion between condom as a contraceptive and as a protection against HIV, and erroneous extension to other contraceptives, such as the contraceptive pill, of a protective role against HIV), family education (children of foreign parents had significantly more problems than other), personal behaviour (association with smoking and alcohol consumption, which suggests a greater aptitude for risky behaviour, capable of negatively influencing condom use). The high number, especially of males, which states that the condom 'disturbs the atmosphere' might be a signal of insecurity on the ability to maintain an penis erection during the entire sexual intercourse.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 153 KNOWLEDGE AND SOURCES OF INFORMATION ON HIV FROM A LARGE SAMPLE OF ITALIAN STUDENTS IN THE FIVE-YEAR PERIOD 2013-2018

M. Galli[1,2,5], L. Oreni[1], M. Pedretti[2], E. Zambon[2], T. Ferrario[2], R. Galipò[3], M. Longhi[4], G. Del Bene[2,5], B. Marchini[5]

[1]UOC clinicizzata di Malattie Infettive, DIBIC L. Sacco – UNIMI, [2]ANLAIDS Sezione Lombarda, [3]ANLAIDS Lazio, [4]ANLAIDS Mantova, [5]ANLAIDS Onlus - Progetto Scuola

Background: Information on HIV plays a fundamental role in guiding individual behaviour and implementing prevention attitude among young people. Over time, the degree of information has undergone significant variations, due to several factors, including the attention dedicated by the media and the quantity and quality of prevention programs. Here we present the results of a five-year survey of the knowledge of a large sample of high school students on HIV.

Material and methods: An anonymous questionnaire was administered to students in large majority attending the third year of Second Degree Secondary Schools of different educational orientation (lyceum, technical institutes and professional institutes). Statistical analysis was performed by logistic regression.

Results: From September 2013 to June 2018 a total of 13,905 students from the provinces of Milan, Monza/Brianza, Mantua, Rome and Latina responded to the questionnaire. Of them, 6876 (49,45%) were female. The median age was 17 years (interquartile range 15-18). The factors independently associated to correct answering to all HIV questions are reported in the Figure 1. Students with both non-Italian parents were at greater risk of not answering the proposed questions correctly. The knowledge was more scarce in males, in the students of technical institutes than in those of Lyceum, and in those practicing a religion compared to those who claimed not to practice any religion. The level of knowledge was increasing with age and better in smokers and alcohol consumers, in those who had already had a complete sexual relationship, in those who had had information in the family, at school, on television or from the internet. There was a trend towards increasing knowledge over the years. The sources of information from which the students claim to have had or to expect information on HIV or STIs are the school (67%) or television (63%). The family (37%) and the web (35%) are in third and fourth place only. Latest newspapers (22%) and friends (15%). Males, in particular, seem to talk less about it in the family, but to turn to more web and friends.

Conclusions: Insufficient, sometimes even totally lacking, information remain particularly in the children of non-Italian parents and among technical school students. The fact that school and television are indicated, more than the family and much more than friends or the web as main sources of information suggests that the HIV topic is experienced as limitedly involving the direct interests of students. In any case, it seems to remain difficult to be faced in the family context.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 154 ANLAIDS PROGRAMME ON HIV/AIDS/STI PREVENTION AMONG HIGH SCHOOL STUDENTS IN MILAN METROPOLITAN AREA, IN COLLABORATION WITH DEPARTMENT OF BIOMEDICAL AND CLINICAL SCIENCES 'L.SACCO' (DIBIC) – UNIMI AND SISM OF MILAN

M. Pedretti[1], *E. Bonomessi*[1], *G. Del Bene*[1], *M. Massa*[1], *E. Zambon*[1], *E. Torazzi*[3], *M. Galli*[1,2]

[1]Anlaids Sezione Lombarda, [2]Department of Biomedical and Clinical Sciences 'L.Sacco' (DIBIC)-UNIMI, [3]SISM Milano Hunimed

Background: The data of the Italian AIDS operation centre (COA) referring to 2017 report the highest incidence of new diagnosis of HIV infection among the 25-29 age group (15.4 new cases per 100,000 residents). The Italian National Plan on HIV e AIDS (PNAIDS) 2017-2019 has focused attention on youth, favouring educational meetings at school. The School Project (Progetto Scuola) of Anlaids Lombardia dates since 1993 and has enabled us to reach over the years thousands of students with prevention initiatives. A collaboration with Segretariato Italiano Studenti in Medicina – SISM (Italian Segretariat of Medical Students) of Milan has been active since 2014.

Material and methods: Progetto Scuola aims to raise the awareness among Middle and High School students (age group 13-19) through informative and experience-based trainings addressed to HIV and STD prevention. Project is carried out by a multidisciplinary team with expertise on scientific topics and communication methods. Furthermore, teachers of the schools involved received recurring training.

Together with the interventions carried out on the class group, students are involved in Peer Education courses, laboratory activities and/or event organization, whenever possible. Finally, alternanza scuola/lavoro activities have been activated to favour youth involvement in educational projects of non-profit organizations.

Each activity includes a survey before and after the trainings based on structured questionnaires.

Results: From 1993 to 2018 Progetto Scuola has involved each year 20 to 45 schools in Milan metropolitan area (including Monza and surroundings since 2002). Every year from 150 to 250 awareness-raising interventions are carried out, involving an average of 4.500 students.

In support of this programme, 23 courses for teachers, 19 courses of communication methods for doctors , 8 courses for parents, 22 Peer Education trainings, 12 Alternanza Scuola/Lavoro trainings and 8 affectivity trainings had carried out. Students created many products (graphics, videos, expressions...) shown at school or in specific initiatives (including ICAR).

Moreover, thanks to the numerous tests administered over the years, a large amount of data useful for planning further interventions has been collected.

Conclusions: Due to its characteristics, the Project can be proposed as a possible model to extend information and prevention against HIV and STI among adolescents. It could be facilitated and implemented through its integration into an overall health education project promoted by the Ministry of Education.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 155 "EXTERNA" PROJECT DEVELOPMENT: FROM LINKAGE TO CARE TO QUALITY OF LIFE FOR PEOPLE LIVING WITH HIV

A. Antonino[1], G. Fracca[2], A. Bianchi[3], F. Rossi[4], N. Gianotti[5], A. Castagna[6], M. Cernuschi[7]

Associazione Solidarietà AIDS, Centro S. Luigi HSR

Background: "EXTERNA" is a free-of-charge service offered since November 2010 by Associazione Solidarietà AIDS Milan to Hiv+ people followed up by the Infectious Diseases Center "San Luigi" (HSR). The service offers counseling: after first doctor's visit; on appointment in the afternoons under patient's request or doctor's suggestion. Recently, and as a pilot program, a psychologist attends to patients.

Methods: Qualitative meta-analysis on experience collected over the past years.

Aim: To define an evolution line of the upcoming and ongoing projects. EXTERNA has been conceived in two steps: 1) counseling to facilitate a link between hospitals and territory; 2) to fight isolation and stigma against HIV+ patients. EXTERNA's first target concerns understanding of issues connected with the first medical visit. Aimed by linkage to care, during the first visit, after HIV+ diagnosis the doctor collects anamnesis focusing on the condition of the infection, based on laboratory analysis, while the certified counselor allots appropriate time to listen to patient's questions, answering them on HIV related key aspects (transmission, therapy, sexual activity, life style), with the additional benefit of touching up on emotional impact of the diagnosis and encouraging self-empowerment.

Results: The analysis identifies key categories – standard and measurable in frequency. In step 2, HIV+ patients refer difficulties not strictly correlated to engagement in care but to subjective and personal experiences connected to diagnosis' interiorization and acceptance. No significant difference was found between patients on or off therapy. Patients carry with them their personal needs, their subjective experience of HIV+ diagnosis, and their own functioning system. The subjectivity of the individual arises rather that their sickness. Retention in care focuses not only on adherence to treatment plan and empowerment but on the possibility of becoming protagonist of their own healing process.

Conclusions: To get a better quality of life, different working hypothesizes arose from the care taker staff, since 2018, introducing ASA psychologists into the outpatient services program with two aims: retention of patients with risk of treatment failure (10%), low adherence and multi-factorial vulnerability; and support of proper doctor-patient communication, more oriented towards the patient as a whole instead of symptoms. The doctor is increasingly becoming the subject of seropositive person's care taking regime, and he is exposed to long lasting doctor-patient relationship.

ASA was supported by ViiV Healthcare.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 156 CHEMSEX BEHAVIOURS IN HIV RISK POPULATIONS IN PADOVA: A CASE-CONTROL ANALYSIS

V. Vazzoler[1], L. Sasset[2], L. Fabbris[1], A.M. Cattelan[2]

[1]Dipartimento di Scienze Statistiche, Università di Padova, Padova, [2]UOC Malattie infettive e Tropicali - Azienda Ospedaliera e Università di Padova, Padova

Background: Chemsex refers to combining sex and illicit drugs to intensify and extend sexual sessions. Chemsex has been associated with a number of HIV risk factors such as multiple sexual partners, group sex and condomless sex in men who have sex with other men (MSM). An association between chemsex and sexually transmitted infections (STIs) in HIV-infected individuals was founded. However, there is a paucity of studies in Italian cohorts on chemsex among MSM, heterosexual population and HIV infected people. The aims of this study were to measure the prevalence of recreational drug use among different HIV risk populations and the relations between chemsex and other STIs.

Material and methods: We conducted a case-control study analyzing routinely collected data from people attending to the Infectious Diseases Department of Padua between September 2017 to September 2018. The cases were HIV positive patients in care at the Department, while the controls were HIV negative individuals who came to our centre to perform an HIV test. Everyone filled out a questionnaire about recreational drug use prior to being evaluated clinically and tested.

A multivariate logistic regression was used to analyse the data.

Results: 554 persons were investigated. 376 (67.9%) HIV pos, 178 (32.1%) HIV neg. 326 (58.8%) MSM, 228 (41.2%) heterosexuals. MSM HIV+ 232 (41.9%), MSM HIV- 94 (17%), heterosexuals HIV+ 144 (26%), heterosexuals HIV- 84 (15,1%). 25,7% of heterosexual HIV + persons self-reported chemsex use at least once in their life vs 16.7% of heterosexual controls, HIV-. A prevalence of 33.2% of chemsex was found in MSM HIV+ vs 17% in MSM HIV-. In the MSM population, chemsex was strongly associated with the presence of the HIV with an excess adjusted odds ratio (aOR) of 3.819 (95% CI: 2.178-6.811) and with excess prevalence of another STIs infection in the last year of aOR 2.292(95% CI: 1.481-3.582). In the heterosexual population chemsex was not associated with the HIV occurrence with aOR of (1.217, 95% CI: 0.628-2.357) but it was strongly associated with the occurrence of another STIs in the last year with aOR of 5.297(95%CI: 2.951 -9.955).

Conclusion: In our population chemsex was a widespread practice and was strongly associated with a STI in both heterosexual and MSM persons. In addition, in MSM, chemsex was significantly associated with the HIV infection. The analysis also showed the presence of a large group of individuals, mostly in the MSM group, who began practicing chemsex only after an HIV diagnosis. Our findings provide further evidence of the importance of asking MSM HIV infected patients about the use of psychoactive substances during consultations. This report also highlights the need for more frequent STI screening in risk populations.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 157 MA.S.D.HIV PROJECT: SURVEY ON SEXUALLY TRANSMITTED DISEASES, SEXUAL BEHAVIORS AND DRUG ABUSE IN HIV-POSITIVE YOUNG PATIENTS

V. Rizzo[1], M.A. Carleo[1], V. Penta[2], V. Iodice[2], P. Rosario[1], M. D'Abbraccio[1], A. Busto[1], R. Viglietti[2], V. Sangiovanni[2], V. Esposito[1]

[1]UOC Immunodeficienze e Malattie Infettive di genere, Ospedale Cotugno, Napoli, [2]UOC Infezioni Sistemiche e dell'immunodepresso, Ospedale Cotugno, Napoli

Background: More than 1 million of sexually transmitted infections (STIs) are worldwide acquired every day, mostly in the population aged 15-25years. These numbers are mainly related to misinformation and to the poor awareness of the infectious risk due to unsafe sexual behavior, abuse of psychotropic substances and infrequent use of condom, even among individuals with known HIV infection.
The project Ma.SDHIV (sexually transmitted diseases, sexual behaviors and drug abuse in HIV-positive young patients) aimed to analyze sexual behaviors and toxic/alcoholic substance consumption in this particular subset of patients, in order to optimize the doctor-patient approach through targeted multidisciplinary care pathways.
Materials and methods: From November 2017 to February 2019 we performed a 3-phases study at Cotugno Hospital in Naples. First, we offered to naïve and experienced HIV-positive patients ≤35 years of age anonymous questionnaires including the 5-item of the World Health Organization Well-Being Index (WHO-5), aimed to collect socio-demographic data and information about sexual habits and substances abuse. Secondly, evaluating the frequency of HIV-STIs tests, use of condoms, use of psychotropic substances and WHO score, we identified 3 levels (LOW-MEDIUM-HIGH) of risky sexual behavior. Lastly, we administered to the same population enrolled non-anonymous questionnaires in order to identify the risk level of each patient and to establish multidisciplinary targeted interventions.
Results: We enrolled 50 HIV+ patients (main characteristics are reported in Tab.1). A total of 46% reported to be aware of the main STIs, mainly through web sites. Only 2% had never undergone HIV test before the diagnosis of HIV infection, 14% of subjects never screened for STIs and 22% declared an occasional use of condom. A part of subjects (66%) reported the use of alcohol or cannabis during the last 12 months, while no one declared the abuse of different drugs. Forty-two non-anonymous questionnaires were then performed: 18 identified LOW risk patients, 20 MEDIUM risk patients and 4 HIGH risk patients. For subjects at MEDIUM risk level, an individual venerological counseling and psychological co-counseling sessions were proposed. Moreover, ad hoc prevention activities, group sessions for targeted health education and frontal seminars were organized. Regarding subjects at HIGH risk level, we offered 2 venerological visits for diagnostic assessment and then 2 cycles of 4 sessions of individual psychological counseling.
Conclusions: Counseling and behavioral interventions offer primary prevention and may reduce the risk of STIs. In our population we reformulated counseling strategies in order to encourage patients to avoid risky sexual behaviours, through an individual or groups psychological support. Moreover, since the abuse of substances is often omitted by patient, we suggest to carefully investigate about these practices to avoid underestimation of the phenomenon.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 158 CHEMSEX AND RELATED ADDITIONAL RISK FACTORS FOR HIV POSITIVE MSM: PRELIMINARY RESULTS FROM THE SCREENING CHEMSEX STUDY

P. Vinti[1], M. Cernuschi[1,2], A. Castagna[2], S. Bossolasco[2], S. Nozza[2], C. Raddato[2], A. Bianchi[1], M. Lanza[1], E. Messina[2], V. Spagnuolo[2], M. Maillard[2]

[1]ASA onlus, Milano, [2]IRCCS Ospedale San Raffaele, Milano

Background: Chemsex consists in using sexually enhancing drugs (SEDs) to increase pleasure, arousal and endurance and is practiced mainly by men who have sex with men (MSM). Data on its prevalence in Italy stems from anecdotal evidence or online surveys. Chemsex is a public health concern: it plays a part in HIV and STIs transmission dynamics and can also entail serious consequences both for physical and mental health. Solid and reliable data is needed in order to design and implement effective prevention and harm reduction policies and interventions.

Methods: The Screening chemsex study is being conducted in the infectious diseases clinics of the main hospitals in Milano (Italy) to gather chemsex epidemiological data among outpatients. The study is a no-profit, national, multicenter, cross-sectional observational study, sponsored by ASA onlus. Enrolment is proposed to outpatients satisfying enrolment criteria: >18 years, literacy, adequate understanding of Italian, sexual activity in the last year. The data is collected through an anonymous self-administered questionnaire investigating sexual use of recreational drugs in the last year, alcohol drinking habits, use of erectile disfunction drugs (EDDs), sexual habits, STI diagnoses and HAV, HBV and HCV serostatus. For HIV+ subjects treatment regimen and viral load are investigated. All subjects are profiled for age, sex, sexual orientation, place of birth, education, relationship and occupational status. Coding: sexual use of crystal meth, GHB/GBL or mephedrone="chemsex"; sexual use of cocaine, ketamine, MDMA, or MDPV="use of other SEDs"; sexual use of any of the aforementioned drugs= "use of any SED".

Results: The study is still ongoing, up to 1000 subjects are expected to be enrolled. Data analysis has been carried out on the first 310 completed subjects enrolled at San Raffaele Hospital. This sample is made up of 276 HIV+ and 16 HIV- men, 12 HIV+ and 1 HIV- women and 5 HIV+ trans women. MSM represent the 86,7% (n=269) of this sample, while HIV+ MSM the 81,6% (n=253). 49 participants (15,8%) reported chemsex; 59 (19,0%) reported use of other SEDs; 72 (23,2%) reported use of any SED. 25,3% (n=64) of HIV+ MSM reported use of any SED. Among them: the 29,7% take COBI or RTV as part of their treatment regimen, 60,9% take either DTG, EVG or RAL; 37,5% has mixed SEDs with alcoholic drinks, 31,3% with popper and 6,3% with both alcohol and popper; 67,2% used EDDs at least occasionally; 65,5% used SEDs during group sex events; 25 out of 40 who last had sex with an occasional partner didn't use a condom.

Conclusions: There is a significant prevalence of sexualised use of drugs among HIV+ MSM attending infectious diseases clinics Milano. Moreover, recreational drugs are often mixed with other substances that can bring additional health risks. Yet the main risk of serious health consequences may come from HIV treatment. Final results will shed more light on these issues.

ASA has been supported by ViiV Healthcare

Social and behavioural science, marginalized groups, community aspects and community surveys

P 159 THERAPY ADHERENCE, EMOTIONAL AWARENESS AND CARDIOVASCULAR RISK IN PERSONS WITH HIV

S.A. Sofia[1], C. Iacobello[1], G. Pantò[1], B. Cacopardo[2], B.M. Celesia[2]

[1]Unit of Infectious Diseases, Cannizzaro Hospital, Catania, [2]Unit of Infectious Diseases, University of Catania, ARNAS Garibaldi, Catania

Background: Psychological factors, as capacity to recognize emotions in self and others and to regulate own emotions, have been associated to negative outcomes in persons with HIV. In fact, exploring this issue, we have recently showed that alexithymia and impairment of the ability to recognize other's emotions contribute to antiretroviral therapies (ART) non-adherence, as assessed with both self-report and viral load testing.
Aim of this study was to detect if the same psychological factors driving to ART non-adherence, could predict heightened cardiovascular risk in a group of subjects HIV+ on treatment.
Materials and Methods: We assessed 124 HIV+ patients, 81% males, media age 45.24±9.27 years. Demographic and biological parameters and cardiovascular predictors were considered. Intima-Media Thickness (cIMT continuous measure) was examined by B-mode ultrasonography, while depressive symptoms were studied by the Beck Depression Inventory (BDI-II), emotional inhibition by the Emotional Inhibition Scale (EIS), alexithymia by the Toronto Alexithymia Scale (TAS-20) and emotional disregulation by the Difficulties in Emotional Regulation Scale (DERS).
Analyses were conducted in three phases. First, we used T-Tests and Pearson correlations to explore whether IMT was related to demographic and medical related data. Second, we correlated the IMT scores with the psychological assessments including the TAS, DERS, EIS and BDI. Finally in case of multiple variables related to IMT, we planned a stepwise regression in which any general demographic variable linked with IMT was allowed to enter to predict IMT scores in the first step, medical and behavioral variables specifically linked with HIV in the second step and then any psychological variables correlated with the IMT score in the third step.
Results: Subjects with hypertension had significant greater IMT scores (1.01±0.41 vs 0.81±0.33; $p < 0.05$). Patients with detectable viral loads had significant greater IMT scores (1.02±0.33 vs 0.75±0.33 $p < .0001$). Participants who reported adherence had significantly lower IMT scores (0.77±0.31 vs 1.05 ± 0.37; $p < .0001$). IMT was significantly correlated with age ($r=0.44$; $p<.0001$), total cholesterol ($r=0.23$ $P<.05$), years since infection ($r=0.42$; $P<.0001$), and C reactive protein ($r=0.34$; $p<.0001$). IMT was not significant related to BMI. Only TAS and DERS total score were significant linked with the IMT total.
Conclusions: Alexithymia and emotion dysregulation were significantly linked with the IMT total. The BDI and EIS total were not significantly correlated with the IMT scores. Alexithymia resulted as an independent predictor or cardiovascular risk, independently from other psychological and biological parameters, including viral load. Pychological treatments for persons with HIV are increasingly needed. Clinicians able to address them might gain benefits in terms of higher therapeutic adherence.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 160 HIV RELATED STIGMA IN A COHORT OF PATIENTS CHRONICALLY TREATED IN EASTERN SICILY

L.Vinci, B. Cacopardo, B.M. Celesia

Unit of Infectious Diseses. University of Catania. ARNAS Garibaldi Catania

Background: Stigma is a condition that appears when an attribute becomes deeply discrediting within certain relations and context. HIV related stigma is a well known condition, has been described since the beginning of HIV infection, has negatively influenced the attitude of patient to the disclosure and represented a barrier to diagnosis, linkage to care, treatment and prevention. Aim of this cross sectional study was to measure the level of stigma in a cohort of HIV+ patient followed in a outpatient unit and detect any association with socio-demographics data and self-reported level of depression.

Materials and methods: A battery of self-administered psychometric test were proposed to more than 140 patients in our outpatient unit. This analysis was a part of a project aimed to exploring social and psychological aspects of patients with chronic HIV infection that was specifically supported by Gilead fellowship 2017. A 12-items short version of HIV Stigma Scale by Berger was used to measure the stigma perceived by people with HIV infection. 4 different areas were explored (3 questions/area) and specifically: personalized stigma, disclosures concerns, concern about public attitudes and negative self image. For every question, 4 different answers were permitted (always, often, sometime, never). The short form 13-item of Beck Depression Inventory (BDI-SF) was used to screen symptoms related to depression. Socio-demographics data were also collected.

Results: Data extrapolated from 68 out of 82 returned questionnaires were analysed. 59 (86.7%) were males, median age 48 (IQR 37-57) years, 42 (61.7%) were MSM, 18 (26.5%) heterosexuals, 8 (11.7%) IVDU. 28 (41.2%) live in provincial county town. 45 (66.2%) has an high educational level (secondary school or degree). 14 (20.6%) were unemployed, 10 (14.7%) retired. 46 (67.6%) perceived any type of personal stigma, only 8 (11.7%) referred no problem to disclose while 19 (27.9%) referred always. 51 (75%) felt any negative concern about PLWHA. Finally 36 (52.2%) perceived a negative self image due to HIV infection. 50 (75.7%) refer no depressive associated symptoms, 11 (16.6%) soft depression, 5 (7.6%) moderate depression. We didn't show any difference associated to age, sex, risk, residence, educational level while soft or moderate depression was associated with perceived stigma ($p=0.011$) and negative self image ($p<0.001$).

Discussion: although the battle against HIV infection began more than 30 years ago, also now HIV related stigma is not won and it represents a problem for a high percentage of patients. Some depressive symptoms could be related to this issue with potential consequences on adherence, residual HIV viremia and increased risk of transmission.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 161 SURVEY ON HUMAN PAPILLOMAVIRUS (HPV) KNOWLEDGE AND PERCEPTION IN A SAMPLE OF MSM POPULATION

A. Marcandalli

C.I.G. - Arcigay Milano, Milano

Background: The 2017-2019 National Programme for Immunization (PNPV) recommends the anti-HPV (Human Papillomavirus) vaccine for MSM (men having sex with men), considered as subjects at higher risk. In the administrative region of Lombardy, the Regional Programme for Immunization provides a free anti-HPV vaccine for MSM up to the age of 30. Yet, to this day, the vaccination uptake for these at risk groups is very low, probably because of a lack of knowledge on the HPV infection and consequently on the possible available prevention options. The aim of this study is to research the knowledge of HPV infection and the HPV vaccine in a MSM ≥ 18-year-old population sample.

Material and Methods: For this specific purpose a questionnaire has been produced and submitted to a sample of MSM, reached thanks to the collaboration of the Centre for Gay's initiatives – Milan Arcigay between 28th and 30th June 2018, during the Milano Pride. Overall have been gathered 271 questionnaires filled by as much as MSM (average age: 28-year-old, range 18-60-year-old), with a medium-high level of education (64% graduates, 30% high school graduates).

Results: Even though 94% of the survey respondents declared to have heard about HPV (mainly through TV, internet and social media), approximately 40% believes that the infection cannot affect them, even when most of the respondents have several different risk factors for the HPV infection, as early sexual intercourse (65%), numerousness of sexual partners (63%), previous transmitted sexual infections (42%). 85% of the respondents knows that HPV infection can be caught by men, while knowledge of the HPV-related diseases is more limited. 30% of the respondents never heard about HPV vaccination, of them approximately half has less than 26 years old. More of 90% would accept the inoculation of the HPV vaccine if it was proposed to them.

Conclusions: The analysis of the results highlighted that in MSM the level of knowledge about HPV infection is lacking and it is even worse for the HPV vaccine. Therefore, the initial hypothesis has been confirmed, that the low adhesion to the HPV vaccine in homosexual male population is associated to the lack of knowledge regarding the HPV infection and the possible preventive options.

On the base of the observed inadequacies of knowledge an informative action dedicated to MSM has been developed: the realization of flyers providing information about HPV infection, related diseases and above all about the HPV vaccine and the immunization offer, giving also practical information, with a view to distributing the flyers at lesbian associations, gay, bisexuals and transgender in the city of Milan.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 162 HIV AUTO-TEST AND PREP IN MILAN'S PHARMACIES: A SURVEY

D. Calzavara, D. Deserti, S. Betti, M. Corbetta, D. Papagna, M. Pilloni

CIG - Arcigay Milano

Since many years, no decrease has been registered in new HIV diagnosis, especially in MSM communities. Milan and Lombardy have most new diagnosis, despite the whole range of possible testing and prevention activities offered on the territory. In recent years pharmacies became agents of an important role in the fight against HIV. Since 1st of December 2016 it is possible to buy a rapid HIV self-testing, without need of health professionals. Moreover since 2018 it's possible to buy at pharmacies the Emtricitabine/tenofovir, a medication used for pre-exposure prophylaxis (PrEP). We wanted to verify how much these tools affected the Milan population, inquiring the sales volume and the knowledge level of local pharmacies.

After alerting the Pharmacists Association's President, we realized an anonymous and concise test, examining the availability and cost of self-testing and the medication used for PrEP, the knowledge of the PrEP and of the medication itself, together with a letter presenting the project. During February 2019, through a net of volunteers we went personally to local pharmacies distributing the test. We reached 137 pharmacies from the overall 440, selected randomly in the area of Milan.

We took notice that it is possible to purchase the HIV test in 131 pharmacies (96%). The most common is the Autotest VIH with a cost between €20 and €25. The test is always available in the 82% of the pharmacies, with no need to order it in advance. Only six pharmacies declare that they sold more than 10 tests in January 2019. During 2018, 84 pharmacies sold less than 10 tests, and only 3 sold more than 70. As for the PrEP, only 42% of the pharmacists is aware of the drug tenofovir/emtricitabina and only 44% knows what profilaxis pre exposition is. It can be purchased in less than half of the pharmacies and it is always available only in 8(6%). The most common is the generic of DOC, with a cost between €58 and €66. Regarding sales, only 5 pharmacies sold the treatment in January 2019, while in 2018, 83 out of 100 didn't sell any treatment and only one was able to sell over 50 doses.

About two years after the placing onto the market of the HIV self-testing, data demonstrate an inadequate awareness on the local population, inadequate as the engagement of the pharmacies which might depend on the people unfamiliarity in getting regularly the test, on high costs and lack of privacy while requesting it in the pharmacy. Probably a less expensive self-testing and the possibility to buy it at vending machines would increase the use. We express judgment reserve on inadequate support and information, particularly on reactive result. In this scenario the service offered by associations at the forefront on the fight against HIV is still essential. As for PrEP, despite the recent appearance on Italian markets, we stressed the inadequate knowledge of the tool and of the medication. Therefor it is necessary a specific training for pharmacists both on the test and the PrEP.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 163 RISK OF DEVELOPING BODY DYSMORPHIC DISORDERS IN HIV-INFECTED INDIVIDUALS ASSESSED BY SELF-REPORTED QUESTIONNAIRES. THE VIGOR STUDY

F. De Zottis[1], G. Passavanti[1], M.M. Plazzi[1], A. Giannetti[1], R. Bellagamba[1], S. Cicalini[1], G.M. Corbelli[2], A. Antinori[1], A. Ammassari[1]

[1]Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani IRCCS, Roma, [2]PLUS Onlus, Bologna

Background: Muscle dysmorphia (MD) is a body dysmorphic disorders (BDD) characterized by body image disturbance that leads to a pathological research for muscularity and excessive exercising. It implies considerable functional impairment on a psychological and behavioral dimension. MD affects mainly young adults and can be as prevalent as 10% among who train in fitness centers. Due to forced training, dieting behaviors and consumption of anabolic steroids MD can lead to organic dysfunction such as dysmetabolic and musculoskeletal disorders and increased cardiovascular risk. MD was investigated mainly for its psychological aspects, but little is known about proper diagnostic criteria and clinical implications. To our knowledge, this topic was not previously explored in HIV infection. Aim of study was evaluate risk factors for MD in a population of men living with HIV.

Methods: We enrolled HIV+ men from Jan to Apr '18, in a single center, cross-sectional study to evaluate socio-demographic, behavioral and clinical factors associated with MD. Patients who by the judgment of attending physician could have a BDD were enrolled. They underwent anthropometric, biochemistry, viro-immunological, and metabolic assessment. Questionnaires included: Muscle Appearance Satisfaction Score and ADONIS Complex to asses degree of DM, quality of life, HAART adherence, depressive and auto-reporting symptoms. Multiple Correspondence and Cluster Analysis were performed to stratify patients into different phycological risk profile groups for MD, based on questionnaire answers. While logistic regression was applied to evaluate clinical risk factors for MD.

Results: 51 male patients were enrolled. Demographics and anamnestic data are summarized in Table 1. One was diagnosed with MD. Base on questionnaires answers, cluster analysis divided patients into "low risk" and "medium-high risk" for developing MD, respectively 78,4% and 21,6%. the latter group comprehend those more concerned about physical appearance in a way that affects social life, moreover, they show healthier lifestyle and, as expected, spend more time training. At multivariate analysis no clinical or laboratory data showed statistical significance of increased risk for MD, in both groups.

Conclusion: In our sample population only one patient had MD. However, 21% resulted having a medium-high risk of developing a BDD, based on questionnaires results. This preliminary data suggests that awareness for this condition is needed among clinicians who manage HIV patients and that, in case of suspicion, referral to psychological and nutritional evaluations is needed. In the beginning of HIV/AIDS era, physical appearance was a concern for patients because of wasting syndrome and drugs side effect, such as lipodystrophy. Today, improved clinical management of HIV requires clinicians to be highly aware of different kind of patient's body perception, which could otherwise go unnoticed with routine controls.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 164 WHAT DO ITALIAN PEOPLE THINK ABOUT PREP FOR HIV PREVENTION IN 2018/2019? A NETWORK ANALYSIS APPROACH TO SOCIAL REPRESENTATION: A NEW SURVEY

A. Toscano[1], A. Bignardi[2], L. Gozzi[2]

[1]Polo Universitario di Milano - Università degli Studi eCampus, [1]Centro Studi Airone, Taranto, [2]Arcigay "Matthew Shepard", Modena

Background: In 2016, when we conducted our former study, PrEP was an emerging community issue in Italy and its Social Representation was still in course of definition. Nowadays, we can consider it as a defined object of social knowledge and therefore deepen how people represent it in terms of concepts and associations between concepts.
Network Analysis (NA) is a good way to identify content and affective polarization of social knowledge since it allows to build graphs based on the identification of nodes and links.
Methods: We sent an online questionnaire to the National LGBT association Arcigay mailing list, and got back 43 responses [age=33.9, SD=8.48]. We asked people to write the first 15 words coming into mind about PrEP, and to evaluate each one on a polarity scale (positive, neuter, negative). We also asked how they evaluate their own knowledge about PrEP on a 1-4 scale.
After receiving compiled questionnaires, we transformed each word into its lexical entry and we indicated lexical root for those words reported as nouns or verbs, in order to minimise grammatical variability. Each entry and root has been treated as a node in a chain, and the very preceding and following words as coming-to and coming-from links. Then, we counted each entry's occurrence and calculated Polarity and Neutrality Indexes.
Results: We were able to identify that prevention (28 occurrences), safety (21), HIV (21), cure (20) and sex (20) were the most occurrent entries. Prevention was associated to moral issues, community and medicality; safety with morality, utility and medicality; HIV with medicality, prevention and community. People's self-evaluated knowledge on a 1-4 scale was placed toward the middle [2.79, SD=0.99]
Polarity scale index results were .07 (positivity index, neither positive, nor negative) and .62 (neutrality index, strongly polarized into negative and positive).
We also found a significative correlation (r = -.62) between neutrality and knowledge, meaning that the more people know about PrEP, the less they're neutral about it.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 165 PEER EDUCATION -SISM

E. Clemente, D. Rosini

SISM - Segretariato Italiano Studenti in Medicina, Anlaids

SISM Peer Education: a national project realized by Italian Medical students that involves 151 classes of 55 Italian Middle and High Schools. SISM also collaborates with Intercultura doing Peer Education activities for Italian and foreign students in 25 different Italian cities.

Background: SISM is a no-profit Association of the International Federation of Medical Students' Associations, recognized as a Non-Governmental Organization within the UN and the WHO. Since 1970 SISM, thanks to peer-to-peer activities, is involved in the social promotion of: Sexual and Reproductive Health Education, Intercultural Learning; Conflict of Interest; Stigma Prevenction; Gender Based Violence; Gender Identity and LGBTQI+ Community; Global Health and Human Rights. UNESCO defines Peer Education as "the use of subjects belonging to a specific group in order to facilitate change at other members of the same group ". This strategy shifts the centrality of the pedagogical role from the traditional adult expert to the young and qualified one.

Material, Methods: SISM's Peer Education allows Middle and High School students (13-18 years old) to inform themselves about their health and rights in an interactive and free from prejudice way. Trainings are managed by students who are not more than ten years older than school children, who feel free to express their doubts and curiosities. Activities are managed through explanations, games, exchange of understandable information; always in a very precise way, following a nationally established agenda. Every session is preceded and followed by the administration to children of a national Impact Assessment module, useful for evaluating the actual impact of the activities carried out and for collecting reusable data throughout Italy, now in the collection phase.

Results: SISM's Peer Education in 2018 has involved 151 classes of 55 Italian Middle and High Schools. SISM also collaborates with Intercultura doing Peer Education for Italian and foreign students in 25 different Italian cities. Every year it involves about 4600 Students. Activities are appreciated both by children and Peer Educators and SISM constantly works to improve them. SISM is collecting the latest updated data on the Peer Education Impact Assessment. Peer Educators are Medical students, trained by experts during a specific Non-Formal Education Training.

Conclusions: This project is a great opportunity for the growth and education of the youngest, who are increasingly at risk of coming into contact with incorrect information and illnesses, especially STIs and HIV. One of the most effective ways to avoid this is Education, especially if carried out by young and qualified people with whom students can build a trusting relationship. In this way Italian medical students hope to contribute in building a world in which every citizen is informed about their own risks, possibilities, rights and duties.

Presenting Authors Index