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ABSTRACT BOOK

Promosso da
SIMIT Società Italiana di Malattie Infettive e Tropicali

e da
INMI, Istituto Nazionale per le Malattie Infettive
ISS, Istituto Superiore di Sanità
AMCLI, Associazione Microbiologi Clinici Italiani
SIICA, Società Italiana di Immunologia, Immunologia Clinica e Allergologia
SIMaST, Società Interdisciplinare per lo Studio delle Malattie Sessualmente Trasmissibili
SITA, Società italiana per la Terapia Antinfettiva
SIV-ISV, Società Italiana di Virologia - Italian Society for Virology
ANLAIDS, Associazione Nazionale per la lotta all'AIDS
ARCIGAY, Associazione LGBT Italiana
ASA Onlus, Associazione Solidarietà AIDS Onlus
EpaC Onlus, Associazione EpaC Onlus
LILA, Lega Italiana per la Lotta contro l'AIDS
MARIO MIELI, Circolo di Cultura Omosessuale
NADIR, Associazione Nadir Onlus
NPS Italia Onlus, Network Persone Sieropositive
PLUS, Rete persone LGBT+ sieropositive Aps

Social Science

OC 1 AWARENESS AND PERCEPTION OF ACCURACY OF THE U = U MESSAGE IN PEOPLE LIVING WITH HIV (PLWHIV), IN ITALY AND CORRELATION WITH THE LEVEL OF CONFIDENCE IN REFERENCE PHYSICIANS

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Background: Recent studies have definitively confirmed the absence of risk of sexual transmission of HIV by the HIV+ partner with undetectable plasma HIV-RNA (HIV-RNA <200 c/ml), leading to worldwide campaign "U=U" (undetectable = untransmittable). Purpose of this study was to evaluate the perceived accuracy of the message among PLWHIV, HIV-neg people with sexual risky behaviors (PWSRB) and HIV physicians, in order to inform subsequent efforts and implementation of HIV prevention strategies.

Methods: A nationwide survey among ICONA centers, Community based voluntary test&counselling (CBVTC) centers and fast-rack cities websites has been conducted (January 30th, 2020-ongoing), using an online web-application for conducting surveys (Limesurvey). The answers have been collected through a mysql database on the Icona Foundation server. Three different anonymus questionnaires containing several identical questions (for physicians, for PLWHIV and for PWSRB) were set up.

Results: At interim analysis after the first 20 days, 930 participant filled the questionnaires: 266 PLWHA [82% male, 93% Italian, median age 47y (IQR 36-54), 42.5% >University degree, 69% MSM, 49% more than 10 y from HIV diagnosis, 41% on cART for >10 y, 50% without a stable partner, median number of partners in the last year 2 (1-10)]; 85 physicians -[41% male, 73% <50 y, 47% individually following <100 PLWHIV]; 579 PWSRB [69% male, median age 32 (IQR 26 -40), 96% italian, 59% MSM, 52% without a stable sexual partner, 38% tested for HIV <6 months, median number of partners in the last year 2 (1-10)]. Awareness of U=U ("Do you know the message U=U?") has been reported in 73%, 46% and 93% of PLWHIV, PWSRB and physicians, respectively. The accuracy ("How accurate do you consider U=U") has been rated as high in 80%in PLWHIV vs 66% in PWSRB and 79% in physicians. Physicians perceived that 11% of PLWHA have a high rate of perception of U=U, whereas among PLWHIV, only 34% reported definitive positive messages from physicians. Among PLWHIV, factors associated to the awareness of U=U were level of education (University vs lower AOR 2.20, 95%CI 1.11-4.37, p0.024), being MSM/bisexual (vs heterosexual AOR 4.32, 95%CI 1.68-11.1, p 0.002) and being on cART for 5-10 ys (vs <5 ys OR 2.63, 95%CI 1.05-6.57, p 0.038). Factors associated with a perception of high accuracy of message in the three groups are reported in table 1.

Conclusions: Although preliminary, these findigs clearly indicate that a difference exists between awareness and perception of accuracy about the U=U message both among PLWHIV and physicians. This insufficient certainty might undermine the strength of the U=U message that should be spread particularly among selected subgroups who might benefit from targeted educational campaigns.

Dissemination of the message among people with sexual risky behaviors is far from being efficaciously implemented and should represent a priority for increasing HIV knowledge and decreasing HIV stigma.

Social Science

OC 2 HEPATITIS C, HIV AND TUBERCOLOSIS AMONG VULNERABLE POPULATIONS IN AN OUT-OF-HOSPITAL SETTING: A SEROPREVALENCE ANALYSIS FROM "THE WEEK OF THE POOR" EXPERIENCE

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Background: Vulnerable populations (poor, homeless, unemployed, foreigners and people who use drugs) represent a challenging cohort of patients as they often don't access to hospital for screening and treatment because of economic and social barriers. However, they often have several risk factors for infectious diseases such as poor hygienic conditions, malnutrition, immunodeficiency and drug use. The implementation of programs aimed at screening and linking to care these marginalised populations is crucial to assess the real burden of contagious infectious diseases and finally to achieve their eradication.

Methods: Vulnerable populations were screened for HCV, HIV and tuberculosis (TB) during the 2nd and 3th edition of "The Week of the Poor" organized by the Vatican in November 2018 and 2019 in a temporary street field clinic. The medical staff interviewed patients and collected demographic data and information about their risk behaviours for infectious diseases. HCV Ab and HIV Ag/Ab rapid tests were used as first step evaluation to assess serostatus, while the Xpert HCV and HIV Viral Load Finger-Stick to confirm the diagnosis in 60 minutes. Tuberculin skin test (TST) was used for the screening of TB. People with positive results have been taken in charge by the Infectious Diseases Clinic of Tor Vergata Hospital in Rome.

Results: 345 people were recruited by the staff (77.9% male, median age 42 y): 84.6% foreigners (27% from Asia, 26.4% from Africa, 20.3% from Eastern Europe, 9.8% from South America), 66.6% unemployed, 11.3% drug users, 6.4% received no school education. Most of the tested subjects reported no prior screening for HCV (65.1%) or HIV (55.5%). HCV seroprevalence was 4.6% (16/345): 12/16 (75%) male, median age 46 y, 8/16 (50%) were drug users, 8/16 (50%) were Italian, 10/16 (62.5%) were unemployed and 6/16 (37.5%) reported no previous test or a negative test showing that they were unaware of their serostatus. 9/16 received an HCV-RNA positive confirmation. Factors associated with HCV Ab positivity included having already run a test in the past, having a tattoo/body piercing, drug use disorder (heroin and cocaine consumption both injecting or inhaling), bisexual/with PWID sexual intercourses (p

Conclusion: The implementation of HCV/HIV screening campaigns among vulnerable populations with quick tests and then Xpert Viral load may provide a useful tool to find undiagnosed infected people in out-of-hospital setting. Also the TB screening is important from a public health perspective as it improves the health of the patient but it also prevents the potential spread

Social Science

OC 3 ENGAGEMENT OF YOUNGER GENERATIONS IN THE FIGHT AGAINST HIV/AIDS

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Background: #cHIVuoleconoscere is a project to promote sensitization, information and formation about HIV/AIDS in high schools aiming to improve the knowledge about the prevention, increment the acceptability of screening tests and fight the stigma.
The initiative is connected to the Bergamo Fast-Track City network that involves the Municipality, the Representative Council of Mayors, the Territorial School Office, ASST Papa Giovanni XXIII, the Bergamo ATS, Arcigay Bergamo-Cives, The Italian red cross Bergamo Committee, the Caritas Diocesana Bergamasca and the associations La Melarancia, ALT, Coop. di Bessimo, Coop. Il Pugno Aperto, Coop. L'Impronta.
Methods: The project, started in Oct. 2019, involves 18 High Schools and about 2000 students through interactive programs. The courses (3 meetings of 2 hours each) for single classes are evaluated by means of a pre- and post-intervention questionnaire, borrowed from those of the AIDS project of Caritas Italiana. The questionnaire includes 9 questions on scientific aspects of HIV infection, 7 about the perception of infective risk and stigma and a final part with socio-demographic variables.
Besides, we offer students to participate in an art contest submitting works aiming at the prevention of infection, the promotion of testing and the fight of stigma. The prized art-works will be used to run a sensitization campaign both for their peers and for the general population.
Results: The preliminary analysis based on about 1000 pre- and post-intervention questionnaires allows an interesting evaluation of efficacy.
Particularly significant is, as an example, the concept U=U: if before the formation process only 40% of the students thinks that the statement "A person with HIV that is successfully treated does not transmit the infection through unprotected sex" is true after the intervention the same proportion raises to 84%. Similarly, if before 36% of the teenagers thinks that HIV can be transmitted through saliva, the proportion drops to 3% after the intervention (all differences $P < 0.001$).
More difficult is to cope with stigma. Nevertheless, it is significant that a question like "Do you think that it is appropriate for a person living with HIV to work with children?" being the possible choices in the range from 0 (not at all) to 10 (yes, absolutely) the proportion of negative responses is 71% before the intervention, while drops to 32% after it. Again, at the question "would you feel uneasy staying close to a person with HIV?" 58% of the participants declared that they do not feel uneasy before the training intervention and becomes 80% after the intervention (all differences $P < 0.001$).
Conclusion: Data of all questionnaires, the outcomes of the art contest and of the final sensitization campaign will give the comprehensive picture. In the meantime, we believe that bet on younger generations is a winning strategy to obtain 2030 WHO endpoints to end the HIV epidemics and defeat stigma.

Social Science

OC 4 POST-MIGRATION HIV INFECTION IN THE FOREIGN-BORN POPULATION ENROLLED IN THE ICONA COHORT

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Background: Migrants account for 40% of all new HIV diagnoses in Europe and 30% in Italy in last years. According to recent studies, a high rate (nearly 60%) of these infections are acquired after migrating to Europe, attesting a gap in prevention strategies targeted to this special population. Only limited data are available on the extent of post-migration HIV infection in Italy. Herein, we aimed to assess the proportion of post-migration HIV acquisition in migrants enrolled in the ICONA cohort.

Methods: All foreigners (birth country other than Italy; hereafter "migrants"), for whom information regarding date of arrival to Italy was available in ICONA database, were included. Timing of HIV infection was estimated based on: i) date of seroconversion (when available), or calculated as midpoint between dates of last negative and first HIV positive test with a maximum of 2 years (yrs) between test dates; ii) CD4 depletion model parameters [Lodi et al, CID 2011]; iii) rate of ambiguous nucleotides (NT) (R/Y/K/M/S/W/B/D/H/V/N) in pre-ART pol sequences (when available) using BioEdit. A sequence ambiguity threshold of 0.5% was used to discriminate recent (<1yr) from non-recent (>1yr) infections [Kouyos et al, CID 2011]. Logistic regression was used to investigate factors associated with probability of HIV infection after arrival.

Results: A total of 1,002 migrants [58% males, median [IQR] age 33 (27-39) yrs, 44% from Africa], whose information regarding date of arrival to Italy was available, were included in the analysis (Figure 1). For 117 subjects, either the date of seroconversion (34 patients) or of a negative test in the 2 yrs before HIV diagnosis (83 patients) was known, while in the remaining 885 subjects timing of infection was estimated according to the CD4 depletion model. For a total of 519/1,002 subjects (51.8%), the duration of infection was estimated shorter than the period of stay in Italy. By multivariate analysis, older age (p<0.001), stable employment (p=0.015) and better immunological condition (p<0.001) at enrolment were significantly associated with HIV acquisition in Italy. In addition, in a subgroup of 147/885 subjects without documented date of seroconversion (16.6%), the ambiguous NT% was evaluable: 41(27.9%), who resided in Italy for >2 yrs, had an ambiguity rate <0.5%, indicating a post migration infection, while for 29 (19.7%) individuals, in Italy for <1yr, the ambiguity rate was >0.5%, therefore HIV was certainly acquired abroad. In 52.4% of cases timing of infection remained undetermined.

Conclusions: Based on a statistical approach combining information on arrival date, last testing and CD4 count, >50% of HIV infections was estimated to be acquired post-migration, similarly to other European studies. Based on sequence data, we also were able to confirm that in >25% of cases HIV transmission occurred in Italy. This calls for urgent actions in order to prevent exposure to HIV in migrants.

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Social Science

OC 5 BLQ CHECKPOINT: CHARACTERISTICS OF USERS AND SERVICES OFFERED. A 5 YEARS REVIEW

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Plus, rete persone LGBT+ sieropositive

Background and Methods: BLQ Checkpoint is the first community-based centre offering sexual health services using a peer-to-peer approach outside of the hospital in Italy; it was opened by Plus in September 2015, thanks to a collaboration with the municipality of Bologna and the local health authorities. It is open on Tuesdays and Thursdays, from 6 PM to 9 PM, for HIV, HCV, syphilis testing upon reservation; on Mondays and Wednesdays for a molecular testing offered periodically to individuals with high-risk behaviour in a cohort study (Sex Check). Data on users are collected using a web-based platform.

Results: We present data from its first 5 years (15 September 2015 – 31 December 2019) of testing activity (Tuesdays and Wednesdays, plus special activities, such as the European HIV and hepatitis Testing Week, the San Valentino Testing Day, the AIDS Day on 1st December). During the reporting period, the BLQ Checkpoint was open for 564 days, with a steady increase of opening days across years (Fig. 1). Overall, 4,428 HIV tests, 2,338 HCV tests and 1,324 Syphilis tests were performed (Table 1).

In the reporting period, 4,410 single users accessed the Checkpoint and a total number of 8,112 accesses were registered (median 15,6 accesses per day) (Table 2.).

Of the 4,410 users, 77.0% were male (range 74.6-82.5), 22.7% female (range 17.0-25.0), 0.2% transgender (Fig. 2). The most represented age group was 26-35 (38.4%), followed by 18-25 (32.2%), and 36-45 (17.2%); 12.1% of the users were older than 46 with 9 users older than 66 (Fig. 3). Among male users, 67.2% had sex with men only, 6.8% with men and women, 1.0% with men, women and transgender persons (total men who have sex with men (MSM) 75.2% of male users, 59.5% of all users) (Fig. 4).

Among those with available data, average number of sexual partners in the past 3 months was 8.1, while 10% of users with available data reported ≥12 partners in the past 3 months. Among all user, 18.9% said they used a condom during their last anal intercourse. A subgroup of users engaged in group sex (7.2%) or fisting (2.6%) in the previous 3 months. The most common chemsex dru used by those with available data was cocaine (60.4%), followed by MDMA (29.2%), mephedrone (24.5%), GHB/GBL (19.8%) and ketamine (16.7%).

Out of the 4,428 HIV tests performed, 29 gave a reactive result. All users with reactive results were MSM. All were confirmed by test ELISA at the hospital and were linked to care. Six users were diagnosed with HCV infection and 16 with syphilis.

Conclusions: The BLQ Checkpoint has become an important tool for providing sexual health services in Bologna, especially to MSM. A subgroup of users access the testing services regularly, thus supporting an attitude towards frequent testing and counselling within the community. Next steps include reaching out to a larger group of people at higher risk for HIV and STIs infections and fund raise for offering more services to the gay community.

Social Science

OC 6 SEXUAL BEHAVIOUR AND ASSOCIATED RISK FOR SEXUAL HEALTH AMONG MEN WHO HAVE SEX WITH MEN (MSM) IN ITALY: DATA FROM THE EMIS 2017 SURVEY

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Background: Differences in health and behaviour among MSM have been observed regarding STIs prevention strategies (e.g., condom use, PEP, PrEP, TasP) and risky behaviours such as casual sex and chemsex. A better understanding of sexual behaviour amongst MSM can be useful to strategically focus both prevention programmes and sexual health services.

Methods: Data from 11,025 Italian participants of EMIS 2017 were analysed considering sexual behaviour and associated risk factors. EMIS 2017, part of the European ESTICOM project funded by the EU Health Programme 2014 -2020, was an internet based, self-completion survey conducted in 33 languages and included 127,000 MSM from 47 countries in Europe and Central Asia between October 2017 and January 2018.

Results: 74.15% of respondents (CI: 73.32-74.95) identified themselves as gay or homosexual, while 17.60% (CI: 16.90 -18.32) identified as bisexual. Mean age was 38.78 (St Dev: 12.36), with a minimum of 14 and a maximum of 84 years of age. Considering the number of non-steady male partners (NSP) in the last year, 23.57% (IC: 22.77-24.38) of the respondents reported more than 10 NSP. When exploring the frequency of condom use during sexual intercourse with a NSP in the last 12 months, 46.31% (IC: 45.21-47.41) MSM declared they used condoms in all sexual encounters, 30.30% (IC: 29.29-31.32) in the majority of them and 23.39% (IC: 22.46-24.33) in few/none of their sexual encounters. Condomless anal intercourse (CAI) with NSP with unknown HIV serostatus was reported by 59.55% (IC: 58.05-61.02) of respondents, whereas 12.87% (IC: 11.88-13.91) declared CAI with one or more HIV positive NSP. Amongst those who reported CAI with unknown HIV status NSP in the last 12 months, 19.72% (IC: 18.2-21.32) were HIV+. More than 99% of the HIV+ respondents reported to be on antiretroviral treatment (ART).

Conclusions: The Italian EMIS 2017 data show that one in four MSM had a high number of NSP. CAI was frequent even when NSP HIV serostatus was unknown. Whilst the U=U acronym is well established/embedded in HIV positive MSM's vernacular, one fifth engaged in CAI with NSP with an unknown HIV status. Beyond the high efficacy of ART as prevention, there remains a need to strengthen HIV/STI prevention programmes that focus on the risk-reduction strategies available to MSM (including PrEP and condoms) as well as highlight the need for regular STI testing and treatment

Antiretroviral Therapy

OC 7 DURABILITY OF DOLUTEGRAVIR-BASED REGIMENS AFTER THE FIRST YEAR OF THERAPY

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Background: Dolutegravir (DTG)-based regimens demonstrated good tolerability and durability in the first year. We have less information on the frequency and causes of drug discontinuation after 48 weeks and late onset adverse events.
Methods: Multicentre prospective cohort study performed in the context of SCOLTA (Surveillance Cohort Long-Term Toxicity Antiretrovirals). Patients were included if they were on DTG since at least one year of observation. Two definitions of durability were used. DTG-durability: time to DTG discontinuation; regimen-durability: time to regimen (DTG or backbone) discontinuation. Hazard ratio for discontinuations were calculated from fitting a Cox regression model and durability was represented throughout Kaplan-Meyer plot.
Results: Among 988 taking DTG in SCOLTA, 629 met inclusion criteria (136 ART-naıve, 493 experienced). 24.5% were women, mean age was 47.7 ±11.1 years and mean CD4+T cells were 379 ±244 in naïve and 608 ±362 in experienced patients. The estimated proportion of patients discontinuing DTG at year 2, 3 and 4 were 8.3%, 7.4% and 9.0%, while those who discontinued the regimen were 23.9%, 21.3% and 18.4%. At Kaplan-Meier analysis, DTG-durability was similar across regimens and treatment experience, whereas regimen-durability was higher in ART-experienced than naïve patients ($p<0.0001$) and in dual than in triple therapy ($p=0.003$), Figure. In the multivariable Cox regression model including sex, age, CDC stage, dual/triple therapy, and naïve/experienced status, none of these factors resulted predictive of DTG-durability. When analyzing regimen-durability, naïve patients were more likely to discontinue the regimen with HR= 2.32 (95% CI 1.73-3.12), whereas those on dual therapy were less likely (HR=0.64, 95% CI 0.44-0.93). The more frequent regimen changes were switches from TDF/FTC to ABC/3TC (N=44) and from TDF/FTC to TAF/FTC (N=39).
When considering only DTG discontinuations due to adverse events, naïve status and older age resulted predictive of discontinuation (HR=2.33, 95%CI 1.10-4.91 and HR 1.03 for 1year increase, 95%CI 1.003-1.066).
The causes of discontinuations changed from year 2 to 5, with toxicities leading to the majority of DTG interruptions in the first period of observation (from 56% at year 2 to 7% at year 4, $p<.0001$) and simplifications being more frequent in late discontinuations (from 4% at year 2 to 28% at year 4). Late adverse events, although rare, were present in our cohort and were mainly central nervous system (N=14, 8 in experienced and 6 in naïve) and gastrointestinal events (N=8, 7 in experienced and 1 in naïve).
Conclusions: Regimen-durability was higher in experienced than naïve patients and in dual compared to triple therapy. However, discontinuations of the regimen were mainly driven by changes in the ART strategy, rather than to DTG interruptions. Naïve patients were those more likely to experience adverse events owing to DTG discontinuation, also after the first year of therapy.

Antiretroviral Therapy

OC 8 SWITCH TO RPV+DRV/COBI: 48WEEK RESULTS OF THE PROBE 2 STUDY

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Objective: To evaluate Rilpivirine plus cobi-boosted darunavir (RPV+DRV/cobi) as simplication 2DR in virologically suppressed patients.

Methods: Randomized, non-inferiority trial in chronically HIV-1 infected patients >18 years-old on a stable, effective (>6 months) three-drug cART (CAR). The primary endpoint was non-inferiority of the virological response at 6 months between treatment groups, according to FDA snapshot. After 6 months patients in the CAR group were switched to RPV+DRV/cobi (CARswitch group), too. Their results were used to confirm findings of the controlled phase, while early shifted subjects completed the 48 weeks follow-up.

Results: 160 patients received RPV+DRV/cobi or continued CAR. Patients were 73% males with a median age of 50 years and more than 10 years of cART history.

Baseline median CD4 were 761 cells/mcL and median time below detection was 7.4 years.

RPV+DRV/cobi was non-inferior. At 24 weeks, 0% of patients with RPV+DRV/cobi presented a HIV-RNA level >50 copies/ml compared to 3.7% of controls (difference 3.75%, 95%CI -0.4+7.9). A HIV-RNA level <50 copies/ml was detected in 90.0% of patients on 2DR and in 93.8% of controls (difference -3.75%, 95%CI -11.6+5.6)(figure). At 48 weeks, 87.5% of patients in the RPV+DRV/cobi group still presented a HIV-RNA level <50 copies/ml and 0% failed virologically. Patients of the CARswitch group were still with a HIV-RNA level <50 copies/ml in 94.8% of cases, while 2 patients failed virologically with a viremia < 200 copies/ml not allowing for virological sequencing. No significant changes of immunological status, creatinine levels and body weight were observed in any group of patients switched to RPV +DRV/cobi. After the switch to RPV+DRV/cobi there was a tendency to the increment of total cholesterol, LDL-cholesterol and triglycerids, but not of HDL cholesterol. The increment was statistically significant only for patients that, before switch, were taking a 3DR including TDF (figure). Bone mineral density (ultrasound bone stiffness) median increment was 1.0 g/cm2 at 24 weeks and 2.15 g/ cm2 at 48 weeks in the RPV+DRV/cobi group, while bone stiffness decreased by 0.7 g/ cm2 in patients on CAR (first 24 months) and then increased by 1.7 g/ cm2 when they were switched to RPV+DRV/cobi, too.

Conclusion: RPV+DRV/cobi 2DR was non-inferior over 6 months to an ongoing triple cART according and within the limits of the standard FDA snapshot approach. The high virologic efficacy of the combination was confirmed over the 48 week extended follow-up and further supported by the 94.8% response rate at 24 weeks of the CARswitch group. The dual therapy may be considered lipid friendly as all significant variation depended more from the withdrawal of TDF than from the new ARV regimen. It resulted friendly on bone metabolism, too.

Antiretroviral Therapy

OC 9 PREDICTORS OF VIROLOGICAL FAILURE AMONG HIV-1 INFECTED PATIENTS SWITCHING FROM AN EFFECTIVE FIRST LINE ANTIRETROVIRAL REGIMEN. A PRELIMINARY ANALYSIS

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Background: Optimization strategies have been widely used in everyday HIV clinical practice to minimize long-term side effects or adherence issues deriving from life-long antiretroviral therapy (ART) exposure.
Material and methods: Multicentre, retrospective study conducted in the ARCA cohort. Inclusion criteria were: ART started after 2010, available baseline genotypic resistance test (GRT), stable virological suppression (HIV RNA <50 copies/ml for ≥ 6 months from reach of virological suppression) and at least 42 months of follow-up following either ART initiation (for patients maintaining their first line regimen) or following ART switch, where applicable. Virological failure (VF) was defined as two consecutive HIV RNA ≥50 copies/ml or a single determination ≥1,000 copies/ml. ART switch was defined as a change in backbone or in the anchor drug or reduction in the number of drugs. Statistical analysis was conducted with univariable logistic regression and with Cox's multivariable regression.
Results: A total of 1,022 patients were included; characteristics of the study population are outlined in Table 1. Predictors of VF were higher HIV RNA load at baseline (aHR 1.61, 95%CI 1.19-2.18) and a first line protease inhibitor (PI)-containing ART (aHR 3.32, 95%CI 1.85-5.94), while protective factors were homosexuality as risk factor for HIV acquisition compared to heterosexual behaviour (aHR 0.36, 95%CI 0.18-0.70) and undergoing ART switch (aHR 0.17, 95%CI 0.10-0.27, in particular when switching from a PI-containing ART to any other regimen (aHR 0.30, 95%CI 0.16 -0.54). At baseline GRT, 14.7% of patients presented resistance-associated mutation (RAM) to at least one antiretroviral class; GRT at VF was available for 47 (43.5% out of 108) and new RAMs were observed in 24 (51.1% out of 47) of these patients (p=0.75).
Conclusions: For evaluable patients, the rate of emerging resistance was not negligible in our cohort. We observed about a 5-fold higher incidence of VF among the patients maintaining their first-line regimen (18% vs 5%). Predictors of VF were higher baseline HIV-RNA load and first line PI-containing regimens, variables usually associated with more difficult-to-treat patients.

Antiretroviral Therapy

OC 10 LONG TERM EFFICACY OF DOLUTEGRAVIR + LAMIVUDINE AS SIMPLIFICATION CART IN PATIENTS WITH SUPPRESSED HIV-RNA

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Objectives: Availability of new potent drugs allows to explore the feasibility of less-drug regimens but their durability, especially on the long run is unknown.
Methods: Prospective, multi-center, cohort study in patients on stable cART , with a confirmed (>6 months) viremia <50 copies/ml, absence of M184V mutation or HBsAg. Patients were switched to a dual DTG+3TC regimen and prospectively monitored. Survival analysis (Kaplan-Meier curves), Cox-regression analysis and general linear model for repeated measures were used in the analysis.
Results: 218 patients, 75.2% males, median age 52 years (IQR 12) were enrolled. At switch patients were on ARV drugs for a median of 10.2 years (IQR 13) and virologically suppressed for a median of 75 (IQR 217) months. Most patients presented with a non-infectious chronic co-morbidity (median 2; IQR 1) because of which, beside ARV drugs they were taking a median of 2 other drugs (IQR 11). Over 788.7 patient/years of follow-up (median follow-up 4 years) treatment was discontinued in 42 (19.3%) subjects (figure). Eleven subjects stopped therapy because of death (occurring at a median age of 61 years), further 1 subjects because of intolerance (figure); 16 because of other causes mostly related to losses at follow-up (8), transfer to other Center (3), while 4 patients were re-shifted to a 3 drugs regimen. Mean KM estimate of treatment duration was 4.57 years and older age (P = 0.025), female sex (P = 0.016) and risk factor for HIV (P = 0.018) were significantly associated to treatment durability in the Cox-regression model. On the other hand, time on cART before switch, time with HIV-RNA below detection limit and the number of previous ART lines were not linked to treatment durability. For the whole follow-up no virological failure was documented and only sporadic virological blips recorded (figure). Over time CD4 median increment was of 40 cells/mcL (P = NS), while CD8 cells decreased of a median of 122 cells/mcL (P = 0.012) without any significant change in CD4/CD8 ratio. Tolerability was high and median blood creatinine increment was negligible 0.04 mg/dl. Median total cholesterol levels lowered by 38 mg/dl (P = 0.042) and LDL cholesterol by 32 mg/dl (P = 0.028), without significant variations of both HDL cholesterol and triglycerids.
Conclusion: DTG-3TC dual ART is a durable, effective and well tolerated alternative to standard three drug regimens in virologically controlled patients.

Antiretroviral Therapy

OC 11 LAMIVUDINE+DOLUTEGRAVIR (3TC+DTG) SWITCH STRATEGY COMPARED WITH THE SINGLE-TABLET REGIMEN OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) IN VIROLOGICALLY SUPPRESSED HIV PATIENTS: PRELIMINARY RESULTS FROM AN ITALIAN CENTER

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Background: We tried to investigate and compare the safety of a dual therapy (DT) with DTG+3TC versus a single tablet regimen with BIC/FTC/TAF (BIC).
Methods: We performed a retrospective analysis in a cohort of virologically suppressed HIV+ pts switching to DT or BIC in our center. Primary endpoint was to evaluate time to treatment discontinuation (TD) for any cause. Survival analysis was employed to determine time to TD and its predictors were analyzed by Cox regression. Moreover, we collected viro-immunological parameters as well as markers of renal function and lipid profile at baseline and after 24 weeks and assessed changes via non-parametric tests. Predictors of changes were analyzed by linear regression.
Results: We analyzed 476 patients: 350 starting a DT and 126 starting BIC. Patients in the BIC group were more frequently coinfected with HCV and had a a shorter median time of virological suppression compared with those in DT. Moreover, patients in the BIC group switched mainly for treatment simplification and more frequently from a 3-drug regimen with a backbone of 2 NRTIs and an INI. Full baseline characteristics and differences between groups are summarized in Table 1. Overall, we registered 21 TD: 15 in the DT group during 170 PYFU (a rate of 8.8 per 100 PYFU) and 6 in the BIC one during 48 PYFU (12.5 per 100 PYFU). Reasons for TD in the DT group were GI toxicity in 5 cases (1.4% of the group), CNS toxicity in 3 (0.8%), other toxicity in 4 cases (1.1%) and other/unknown reasons in 3 cases (0.9%); in the BIC group reasons for TD were GI toxicity in 2 cases (1.6%), CNS toxicity in 2 cases and other/unknown reasons in other 2 cases. Estimated probability of maintaining study regimen after 24 weeks were 95.5% (SD±1.1) in the DT group and 94.9% (SD±2.0) in the BIC group, with no significant differences between them (log-rank p=0.639). In a dedicated sub-analysis, we found no differences in the estimated probability of discontinuing study regimen for CNS toxicity at 24 weeks between the DT and BIC groups (98.3% vs 94.5%, respectively, p=0.742). Concerning metabolic profile, in the DT group, after 24 weeks, triglycerides decreased significantly (median change -14 mg/dL, p<0.001) while HDL cholesterol increased (+3 mg/dL, p=0.031). In the BIC group, meanwhile, we observed a significant decrease in LDL cholesterol after 24 weeks (-13 mg/dL, p=0.026). As to renal function, pts in the DT group saw their estimated glomerular filtration rate (eGFR) decrease (-8.36 ml/min, p<0.001). The decrease of eGFR was worse in pts with a higher baseline eGFR (per 10 ml/min more, -8.6, 95%CI -10.1 to -7.1, p<0.001). No significant variations were observed in the BIC group. However, eGFR changes between groups were not significant.
Conclusions: Both optimization strategies showed high tolerability in the short term in experienced pts, we few differences between them. Further studies are needed to properly assess the matter.

Antiretroviral Therapy

OC 12 DURABILITY OF F/TAF REGIMENS IN THE ERA OF INTEGRASE INHIBITORS IN A LARGE COHORT OF PLWH SEEN FOR CARE IN ITALY

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Background: F/TAF showed a comparable efficacy to F/TDF with a better safety profile, nevertheless long-term virological and treatment response data from the real-life setting are sparse.

Material and methods: ART-naïve and virologically suppressed (HIV RNA ≤50copies/mL) patients enrolled in the Icona cohort who started TAF-based triple regimens, from 2015 to 2019 were included. Cumulative probability of TAF discontinuation for any cause, for toxicity and time to treatment failure (TF, confirmed HIV RNA >50 copies/mL -after six months for ART naïve- or discontinuation for any cause) were estimated by Kaplan-Meier curves. Factors associated with the risk of the same outcomes were identified by multivariable Cox proportional hazard model, separately in the two groups.

Results: 4,110 patients included:965 ART-naïve and 3,145 ART-experienced (ART-exp). General characteristics of the enrolled population are described in Table 1. Main TAF-based combination regimens were: E/C/F/TAF (27% naïve;32% ART-exp), DTG+F/TAF (35%;6.4%), R/F/TAF (12%;38%), D/C/F/TAF (18%;9%). The main reason for discontinuation was simplification (57% ART-naïve,52% ART-exp). In the ART-naïve group, the 2-year risk of discontinuing F/TAF was 19.4% (95% CI 15.5, 23.4) for any causes and 2.7% (1.1, 4.4) for toxicity, while for TF was 21.6% (16.9, 26.3) (Figure 1, upper panel). In the ART-exp group, the 2-year risk was estimated at 5.2% (95% CI 4.3, 6.1), 1.1% (0.6, 1.6) and 6.5% (5.3, 7.6) for discontinuation for any cause, for toxicity and TF, respectively (Figure 1, lower panel). In the subset of people using F/TAF as single tablet regimen (STR) the rate of TF by 2 years was even lower: 13.4% (6.6;20.3) in the ART-naïve and 5.4% (4,1,6.7) in the ART-exp group. The most frequently regimens chosen after F/TAF discontinuation were ABC/3TC/DTG (59.4% naive;26% exp) and DTG-based 2DR (26%;45%). In a multivariable regression model with time-fixed covariates at baseline, in the ART-naïve group, using F/TAF as multiple tablet regimen (MTR) was associated with an increased risk of TF [2.59 (1.45, 4.61);p=0.001]. In the ART-exp group, the risk of discontinuation was higher per more recent time of baseline [1.47 per 6 months (1.03, 2.10)p=0.034], while using F/TAF as MTR was associated with higher risk of both discontinuing TAF and of TF [1.67(1.19, 2.35);p=0.003 and 1.67 (1.18, 2.36);p=0.004, respectively]. In contrast, a longer duration of virological suppression before baseline was associated with a reduced risk of TF [0.95 (0.91, 0.98);p=0.002].

Conclusions: Approximately 1 in 5 PLWH starting TAF-based regimens from ART-naïve in the real-life setting discontinue this drug by 2 years but only 3% for toxicity and around 2% because of failure. As expected, rates of failure and discontinuation were even less frequent in the ART-experienced group. Our analysis suggests that a low pill burden is a key factor for longer durability of modern TAF-based cART regardless of previous drug history

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HIV Prevention

OC 13 ENGAGEMENT, ADHERENCE AND RATE OF DISCONTINUATION IN AN ITALIAN ACCESS PROGRAM OF HIV PRE-EXPOSURE PROPHYLAXIS (ITAPREP)

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Background: Pre-exposure prophylaxis (PrEP) currently represents one of the main HIV prevention strategies. Despite consistent evidence of efficacy in clinical trials as well as observational studies, there is a limited knowledge about PrEP persistence in real life. Aim of this study is to evaluate PrEP persistence and adherence and factors associated in a multicentric access program in Italy.

Methods: Observational study on people taking PrEP in 11 Italian centers. PrEP discontinuation was defined as PrEP definitive stop or lost to follow-up (at least two consecutive missed visits). Non-adherence was defined as wrong reported schedule of assumption, temporary interruption or at least one reported sexual intercourse off of PrEP. Kaplan-Meier was used to estimate outcome probability. Poisson regression was used to investigate factor associated with non-adherence and discontinuation.

Results: 456 persons enrolled. Median follow-up 5.5. months (IQR 2.8-10.9). 98% men, 1% TGW, 1% women; 98% MSM, 2% heterosexual. Median age 39 (IQR 32-48) years, 12% non-Italian origin, 46% university degree, 65% employed. Criteria for starting PrEP were condomless sexual intercourses in 78%, previous STI in 28%, previous PEP in 14%, chemsex use in 36%. 262 persons were observed at baseline and at a subsequent follow-up visit and evaluable for this analysis, 27% used on-demand schedule, 33% daily schedule and 26% changed schedule during observation (21% from daily to on-demand, 5% viceversa). 15 (3,2%) persons presented at least one non-communicable comorbidity. No HIV seroconversion was observed during 194 person-years of follow up. The 1-year probability of discontinuation was estimated as 20.9% (95%CI 14.9%-28.7%) (Fig. 1A) and no significant associated factors were identified. The 1-year probability of non-adherence was 34.1% (95%CI 26.2%-43.7%) (Fig. 1B). Non-adherent participants were more frequently chemsex users (IRR 2.88 95%CI 1,77-4,69), older (IRR 1,26 per 10 yrs older 95%CI 1,06-1,51 p=0,009) and with at least one comorbidity (IRR 3,78 95%CI 1,19-12.03). On-demand schedule (IRR 0.41 95%CI 0.23-0.73) was associated with lower risk of incorrect assumption respect to daily schedule. Non-Italian nationality (IRR 0,30 95%CI 0,12 -0,75) and having a stable partner (IRR 0,48 95%CI 0,25-0,91) were associated with a lower risk of poor adherence. Only 58 persons (22%) reported side effects and only 2 (<1%) stopped PrEP for adverse events. During observation, overall IR of STIs were 10.3 (95%CI 6.6-16.1) per 100 PYFU, with 10.3 for syphilis, 19.9 for gonorrhea, and 15,3 for Chlamydia.

Conclusions: Adherence to PrEP remains critical as well as discontinuation rate, consistently with real-life data observed in other countries. Predictors of poorer adherence was older age, chemsex, comorbidities and daily schedule compared to on-demand. These informations may be crucial to define intervention strategies to improve PrEP access and persistence

HIV Prevention

OC 14 PRE-EXPOSURE PROPHYLAXIS (PREP) USE AT FIVE INFECTIOUS DISEASES UNITS IN NORTHERN ITALY (PREP-ITALY STUDY)

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Background: Pre-Exposure Prophylaxis (PrEP) has been proved to be effective as HIV prevention strategy. Both EACS and SIMIT guidelines provide recommendations on PrEP use. According to the Italian National Health System, FTC/TDF is prescribed by the Infectious Disease (ID) specialist, but is paid by consumers (the cost of generic drug is approximately 60 euros/30 pills) while the cost of follow-up testing/visit is provided on a free basis. So far, few ID Units in Italy have been offering PrEP services and limited data are available on PrEP users.

Methods: A retrospective study was performed, including all the patients who were initiated on PrEP at 5 Infectious Diseases Units, from February 2018 to February 2020, in northern Italy. We collected demographic data and reviewed history of previous Sexually Transmitted Infections (STIs), Post Exposure Prophylaxis (PEP) use, PrEP regimen, time of starting PrEP since first visit, PrEP side effects, incident STIs, duration of PrEP and the reasons for discontinuation.

Results: A total of 178 individuals were enrolled, 94% were male (92% MSM) and median age was 36 years (19-64). Out of 117 patients with available information, 64% possessed a degree. A total of 28% of patients were not living in the same area where the PrEP service was provided. Previous PEP use was reported by 25% of patients. 111 patients (62%) reported past STI (mostly syphilis and urethral gonorrhea). On-demand PrEP was prescribed to 73% of patients. PrEP was started in 47% of patients on the same day of first visit, in 12% within 7 days, in 28% within 30 days and in 6% within 3 months. As transferring from other hospital, 7% of patients were already on PrEP at first visit. The standard follow-up visits were planned every three months in all the centers. A total of 66%, 10% and 1% of patients have reached the 4-month, 12-month and 18-month follow-up visit, respectively. Overall, 40 adverse events (the most common was diarrhoea) were reported in 33 patients. A total of 86 incident STIs were documented in 58 (33%) patients (mostly rectal chlamydia). PrEP was discontinued in 37 (21%) patients. Median time to discontinuation was 71 days (range 0-328) and the main reasons were: patient's choice (13), patients lost at follow-up (10) and moving to another Centre (8). Only two patients discontinued PrEP due to adverse events (renal impairment and erectile dysfunction). Two patients who discontinued PrEP have restarted it after 4 and 14 months, respectively, and they were counted as new users at re-presentation. Two patients started PrEP despite virological suppressed HIV-infected partners due to psychological reasons. No incident HIV infection was diagnosed.

Conclusions: Most patients were prescribed on-demand PrEP (73%) and showed a high rate of retention with rectal chlamydia being the most common incident STI. PrEP services, as well as the continuous collection of data on PrEP users, should be more extensively implemented in Italy

HIV Prevention

OC 15 UPTAKE AND EFFECTS ON SEXUAL BEHAVIOUR IN A COHORT OF PREP USERS

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Background: ASA Onlus started a free PrEP programme in Sept 2017 to follow up those taking PrEP outside a clinical setting. The programme was moved to the community-based Milano Checkpoint after its establishment in Feb 2019.
Material and methods: All participants in the PrEP programme are included in a longitudinal open cohort. Participants enter in the programme at an evaluation appt. (T-1), then PrEP is generally started after a 1-month non-exposure period (T0) and regular follow-up appts. are scheduled after PrEP start. At each appt. participants: see an infectious diseases doctor and a psychologist or counsellor; complete a questionnaire investigating sexual behaviour and PrEP uptake; are screened for HIV, syphilis, HCV and additionally for C. trachomatis (CT) and N. gonorrhoeae (NG) since Feb. 2019. Changes over time were assessed using paired t-test and McNemar test; standard survival analysis was used to asses incidence of first CT and NG event from PrEP start and Cox regression model to identify predictive factors of CT/NG acquisition.
Results: Participants were 206 (Table 1). At T-1 70% were single, 8% sex workers, 29% had ≥1 STI in the last 12 months, 17% practiced chemsex in the last 30 days, 20% took PEP ≥1 time and 12% have been on PrEP previously. 91% were MSM. Out of 206, 7(3%) were on PrEP at T-1, 19 (9%) started PrEP same-day at T-1 (due to a high and not abatable risk for HIV) and 109 (53%) started at T0; of the remaining 71, 52(69%) dropped out (attended no appts. in ≥6 months after the previous one) before PrEP start, while 19(31%) were not at T0 yet. 17/135(13%) participants who have been on PrEP dropped out, only 1 due to side effects. The mean no. of condomless anal/vaginal sexual intercourses (CSIs) occurring in the previous month declined from T-1 to T0 (T-1/T0:-1.6;p=0.001), then increased at the first appt. after PrEP start (T1) (T -1/T1:+1.6;p=0.008), while no significant change was seen at latest appt. after T1 (T2) (T-1/T2:+0.5;p=0.439) (Fig. 1). At the same time the mean no. of occasional partners in the last 30 days didn't change at T0 (T-1/T0: +0.67;p=0.349), then increased at T1 (T-1/T1: +3.4;p<.001), and went back to T-1 levels at T2 (T-1/T2: +0.6;p=0.231). With 6 events for CT and 7 for NG after T0, incidence rates were 22.8 and 25.3 per 100 PYFU, respectively, with a cumulative CT/NG incidence rate of 47.8 per 100 PYFU (Fig. 2). Having >5 CSIs in the previous month brought a threefold non-significant increase in risk for CT/NG acquisition (HR 2.91; 95%CI 0.91-9.29; p=0.071) (Table 2). There were no changes in chemsex use.
Conclusions: Risky sexual behaviours increased only at T1, but after T1 PrEP had no significant effect on sexual behaviours. The PrEP programme has been effective in retaining PrEP users in care. Retention in care is essential to regularly assess PrEP uptake, and also to diagnose and treat STIs acquired during PrEP, as risk exposure remains considerable over time.
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HIV Prevention

OC 16 PREVENTIVE MEASURES AGAINST HIV AND SEXUALLY TRANSMITTED INFECTIONS AMONG KEY POPULATIONS REFERRING TO A COUNSELING AND TESTING CENTER IN THE METROPOLITAN AREA OF ROME

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Background: Persons at high risk of contracting HIV and sexually transmitted infections (STI) should have access to preventive measures, including pre-exposure prophylaxis (PrEP). In Rome, men who have sex with men (MSM) and transgender women (TGW) are key populations for interventions.
Materials and Methods: Among those referring to the Counseling and Testing Centre (CTC) at the National Institute for Infectious Diseases L. Spallanzani (INMI), high-risk persons are identified using a baseline questionnaire as those who reported at least one of the following risk factors in the previous 3 months: unprotected anal intercourse (UAI), STI, chemsex. We analyzed demographics, behavioral, laboratory and clinical data, and preventive measures prescribed to, MSM and TGW who attended our CTC since we started PrEP stewardship in 2018.
Results: Of 4257 persons referring to our CTC in 2018-19, 3340 were males at birth, 1444 of whom MSM or TGW. Their median age was 33 yrs (IQR 27-42); 19% were non-Italians; 11% were first-testers. All were offered risk reduction counselling for STI prevention, information on post-exposure prophylaxis (PEP) and PrEP, STI testing and vaccinations. Vaccination was prescribed to 35% who were susceptible for hepatitis B and 53% susceptible for hepatitis A; 2 persons unaware of hepatitis C infection were treated with Directly Acting Antivirals; 7.9% who had active syphilis, 4.5% and 1.5% with rectal and urinary chlamydia, respectively, and 3.7% with rectal gonorrhea, received antibiotic treatment. Ten percent were already vaccinated against Human Papilloma Virus; those who were not, were referred to territorial services, and anti-meningococcal vaccination was also suggested.
Of 1444, 395 had at least one risk factor, and 70 had more than one. HIV-1 infection was diagnosed in 54 of these (11.6%) at baseline, 4 (0.97%) seroconverted in the period of observation. Of the 411 uninfected at baseline, 266 asked for PrEP; 20% had performed at least 1 PEP treatment in the past, and 11.2% over the last 24 weeks. Of 266, 27 had no indications (single partner, either uninfected or undetectable; consistent condom use), 3 refused after discussing PrEP in detail, 1 seroconverting was immediately started on ARV. Therefore, 235 were referred to the INMI PrEP clinic; 200 started PrEP, while 35 missed the visit and were lost to follow-up.
Conclusions: Access for HIV testing represents an important chance to enroll high-risk persons in continuum of prevention programs, to decrease the likelihood of acquiring and spreading not only HIV but also STI, including viral hepatitis. However, costs and organization of services may hinder a more widespread access of high-risk persons to preventive interventions. Free access to PrEP and viral hepatitis/STI screening and vaccinations was progressively available at our center over the study period. Follow-up studies are needed to assess whether this will enhance participation and impact on local epidemics

HIV Prevention

OC 17 INCIDENCE OF STIS AND HIV IN A COHORT OF MSM AND MTF WITH HIGH PREVALENCE OF RISK FACTORS FOR HIV ACQUISITION EVALUATED IN A PREP COMMUNITY-BASED SERVICE IN ITALY: ONE-YEAR FOLLOW-UP DATA FROM SEX-CHECK STUDY

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Background: Men who have sex with men (MSM) and transgender women (MtF) are at higher risk of HIV and other sexually transmitted infections (STIs). Pre-exposure prophylaxis (PrEP) is effective in preventing HIV but does not protect from STIs; indeed, concerns remain that PrEP use may lead to increased STIs acquisition. Thus, frequent screening, early detection and timely treatment remain a key prevention tool, and extra-hospital setting could represent, in this scenario, a valuable help.

Materials and methods: At BLQ Checkpoint, a community-based service peer oriented in Bologna (Italy) run by Plus, we conducted a retrospective/prospective study in a cohort of HIV negative MSM and MtF with high prevalence of risk factors for HIV acquisition. Participants were enrolled between March 2018 and January 2019 and each has been followed for 1 year. Every three months were performed: a counseling session, administration of anonymous questionnaire about sexual habits, risk self-perception and rapid diagnostic tests for HIV, HCV, syphilis, Chlamydia trachomatis and Neisseria gonorrhoeae (CT/NG) on urine sample, rectum and pharyngeal swab. Participants were free to choose to start and stop PrEP at any time during the study, in accordance with good clinical practice and national guidelines. Primary aim was to evaluate the incidence of STIs and HIV infection.

Results: Overall, 71 MSM and 2 transgender women (T=73) were enrolled; 53 participants took PrEP at some time during the study whereas 20 never took it. The average age was 41 years (IQR 19-58).

4 participants underwent just a single evaluation; 6 participants were lost at follow-up. Altogether, we identified 45 person-years of follow-up in PrEP group and 22 in non-PrEP group.

During the study period, we diagnosed 26 infections caused by CT and/or NG (21 in PrEP group and 5 in non-PrEP group) and 8 syphilis (all in PrEP group). Total STIs incidence was 51,5/100 p-yrs/follow-up (64.4/100 p-yrs/follow-up and 22.7/100 p-yrs/follow-up in PrEP group and non-PrEP group respectively). Moreover, we found a single case of previously undiagnosed HCV infection (PrEP group) and 2 new HIV infections (both in MSM who were not taking PrEP) with an incidence of 9,1/100 p-yrs/follow-up.

Conclusions: We found a high global incidence of STIs according to international literature, especially in PrEP group. Our results support the importance of a quarterly STIs screening and peer counseling.

We also found a high incidence of HIV in non-PrEP population; of note, both new HIV infections were diagnosed in participants who recently voluntarily interrupted PrEP because of a reduction in self-estimated risk of HIV acquisition.

In conclusion, our community-based service has proven to guarantee an adequate follow-up for PrEP users and early diagnosis and treatment of both HIV and STIs in people at high risk who voluntarily do not assume PrEP.

HIV Prevention

OC 18 HIV AND MOTHERHOOD – A SURVEY ON WOMEN'S EXPERIENCES IN THE U=U ERA

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Background: In Italy, thanks to ART, women with HIV can now experience motherhood in safe conditions and more naturally if compared to the past. However, while in last years a lot of knowledge has been gained on clinical aspects, little is known about the emotional issues and well-being of women with HIV who choose to be mothers. The aim of this study was to investigate their experiences before conception, during pregnancy, childbirth and breastfeeding, to gain insight on eventual shortcomings preventing achievement of their psycho-physical well-being.

Material and methods: The study targeted women with HIV who gave birth in Italy from 2016 onwards and was conducted through a survey available both online as well as in hard copy in some infectious disease depts and in accredited SIGO centers. It consisted of 32 questions; hard copies were available in Italian, English, French, Arabic.

Results: Sixty-one women took part to the survey (36 Italian; 25 foreigners). Only 32 (52,5%) declared to have been undetectable at conception; 4 of them had resorted to self-insemination. 4 women did not know their HIV status before pregnancy; other 12 had not yet started ART. 46 respondents referred to have been undetectable at the time of childbirth; among them, only 22 (47,8%) could undertake vaginal delivery. 3 women breastfed their newborns and only 37 of 58 (63,8%) received free milk formula; 14 did not know they could have it free of charge and 3 did not want to ask their family doctors for privacy issues.

Concerning their emotional experience, most women described it as serene but added to have been concerned about the risk of passing HIV to their child. Information received on HIV and motherhood were mainly evaluated as satisfactory, except for the topic of breastfeeding. Giving-up breastfeeding represented a painful decision and generated the concern that relatives and acquaintances could relate such choice to the HIV condition. 18 women (29,5%) felt discriminated against, mostly by hospital nurses.

Conclusions: Although the survey involved only a small sample, it succeeded in capturing some critical issues. Let aside the well known problems (delays in HIV diagnoses and in access to ARV), the experiences of HIV undetectable women in the U=U era highlighted paradoxes, such as the choice of self-insemination and of caesarean section: proportion of caesarean sections in our sample (52,2%) was much higher than national average (24%; OASI report 2018). Breastfeeding represented a delicate matter, highlighting peremptory indications by doctors for avoiding it which translated into painful choices. Many women did not know they were entitled to free milk formula or they gave up such opportunity not to disclose HIV status to GPs.

It is important to strengthen women's awareness of U=U, to deepen clinical research on risks associated with breastfeeding and to inform women they can have milk formula for free, simplifying procedures for obtaining it.

Virology

OC 19 DEFINING STABLE REFERENCE GENES TO ANALYZE CELL ASSOCIATED HIV RNA INDUCED BY LATENCY REVERSING AGENTS

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Background: Latency-reversing agents (LRAs) are ubiquitous in the "shock-and-kill" HIV Cure strategy. Ex-vivo quantification of cell associated HIV RNA (CA-RNA) is one of the most important assays used to evaluate the performance of LRAs. HIV RNA copies, measured by qPCR, is often normalized to the input extracted RNA amount (ng) or cell number. However, these could be affected by biological variability and/or technical errors, which can be avoided by using an internal reference gene. To obtain reliable data, it is essential to select stable reference genes (RGs) for which the expression is not influenced by biological variability, the type of cells, or the LRAs used. However, to date, no studies have carefully evaluated reference gene stability following LRA exposure.

Material and methods: We analyzed the stability of six widely used RGs (GAPDH, TBP, YWHAZ, UBE2D2, HPRT1 and RPL27A) in human PBMC (n=4) and CD4+ (n=4) cells cultured for 6 and 24 hours with DMSO (control), PHA, PMA +Ionomycin (PMA+ION), Vorinostat (VOR), Romidepsin (ROM), PEP005, AZD-5582, IBET-151, or STING agonist (STINGa). We evaluated the fold change expression of each RG in the LRA versus the DMSO conditions. A value of 0.5 to 2.0 fold is considered stable in previous publications. We identified the best RGs using RefFinder, an online program that incorporates the four most common tools (GeNorm, NormFinder, BestKeeper and the comparative ΔCt method) to rank reference genes. Finally, using resting CD4+ T cells from an ART suppressed donor, we evaluated the impact of applying different normalizers to the HIV RNA copies comparing DMSO, PHA, and VOR conditions.

Results: We observed a significant downregulation of UBE2D2 in STINGa ($p=0.0413$), YWHAZ in both PMA+ION ($p=0.0021$) and in STINGa ($p=0.0306$) after 6 hours and downregulation of YWHAZ in ROM ($p=0.0262$) after 24 hours. PMA+ION significantly upregulated the expression of UBE2D2 after 24 hours ($p=0.0164$) and HPRT1 after 6 and 24 hours ($p=0.0225$, $p=0.0262$). GAPDH gene was highly upregulated after 24 hours in PHA, PMA+ION and PEP005 conditions ($p<0.0001$, $p<0.0001$, $p=0.0101$) (Fig. A). Overall, TBP, UBE2D2, or RPL27A were the most stable RGs in all conditions tested. TBP was generally the most stable RG in the analysis, whereas GAPDH varied the most (Fig. B). Altered results were observed in HIV CA-RNA when normalized to TBP versus GAPDH. Using GAPDH as a reference, a statistically significant decrease of HIV CA-RNA was found in PHA in comparison with DMSO ($p=0.0258$). This difference was absent when TBP was used ($p=0.2768$) (Fig. C).

Conclusions: We identified TBP as the most stable RG in experiments using LRAs. Our data underline the importance of testing the stability of RG for HIV CA-RNA evaluations for rigor. To our knowledge, this is the first careful evaluation of the stability of RGs after LRA exposure, and will significantly contribute to the quality of data analysis in regards to gene expression.

Virology

OC 20 PREVALENCE OF DRUG RESISTANCE MUTATIONS TO RILPIVIRINE AND DORAVIRINE AMONG NNRTI - EXPERIENCED PATIENTS IN ITALY: A CROSS-SECTIONAL STUDY

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Background: NNRTI class still represents a cornerstone of combination HAART, mainly thanks to new generation drugs with lower drug-drug interaction and side effects and higher genetic barrier, but drug resistance mutations (DRM) surveillance is warmly recommended by WHO.

Materials and Methods: This was a cross-sectional analysis from the Antiviral Response Cohort Analysis (ARCA) database. To assess pre-treatment DRM prevalence to rilpivirine (RPV), we included only genotypic resistance tests (GRT) from NNRTIs-experienced patients (pts) who were naïve to RPV (RPV group); to assess pretreatment DRM prevalence to doravirine (DOR), GRT from all NNRTIs-experienced pts (DOR group) were included in our analysis. All GRT performed at least three months after NNRTI containing regimen start since 1998 onwards were collected. Resistance interpretation was made according to the Stanford algorithm [Potential Low-level (PL), Low-level (L), Intermediate (I) and High-level(H)].

Results: Overall, 3214 GRTs were included from 1773 pts of RPV group, and 3530 from 1911 pts of DOR group: mostly men (69.1%), Caucasian (75%) and B subtype (around 12-13%) in both groups.

Prevalence of susceptible strands were 71.5% in RPV group and 73.5%in DOR group; GRT labelled as PL, L, I and H resistant were observed much less frequently, with a prevalence of 2.7%, 8.6%, 4.7%, 10.2% and 3.5%, 7.8%, 7.3%, 7.5%, respectively.

Similar overall prevalence of DRMs was observed for the RPV (16.9%) and the DOR (16.5%) groups. L resistance was mainly attributable to E138A (3.4%) in RPV group, while DOR group it was principally due to V108I (3.1%) and K101E (2.3%); the latter showed the same percentage in RPV group, where in confers I resistance, such as L100I around 2.2%. L100I in combination with K103N confers I resistance to DOR and H resistance to RPV (1.7% vs 1.5%), being this pattern second only to Y188L among all H DRM considered in our analyses (1.8% vs 1.9%) (Tables 1A&1B).

Regarding the single DRM V106A, this was significantly more frequent among Caucasian race (1.8% vs 0%, P=.002) and B subtype (27,4% vs 20.6%, P=.001).

In both RPV and DOR groups, statistically significant association has been found between B subtype and the presence of at least one DRM (P=.003 and .001, respectively), and between male sex and the presence of at least one I/H DRM (P=.005 and <.001, respectively), later confirmed in multivariable logistic regression: male sex and number of previous cART regimens were associated with detection of DRM, while a CD4+ count <50/ L associated with a lower risk of DRM, in both groups. By contrast, calendar year of GRT and controlled viremia were inversely associated with DRM in the RPV group only, and subtype B decreases DRM odds in DOR group only (Table 2).

Conclusion: High level DRM to both RPV and DOR are uncommon in our samples. Relative higher prevalence of Y188L and K103N+L100I arises concern about use of both drugs among efavirenz and nevirapine experienced pts.

Virology

OC 21 HIV-DNA FROM RECTAL GALT IS A VALID MARKER TO CHARACTERIZE THE VIRAL RESERVOIR

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Background: The extension of HIV reservoir in the gut associated lymphoid tissue (GALT) and the ART influence on this compartment are still poorly studied. Aim of our study is to evaluate the extent of HIV-DNA in undetectable pts' rectal GALT.

Methods: 26 HIV1+ pts on ART were included in this ongoing study. Among these, 25 were undetectable (HIV-RNA <50 cp/ml), 1 had 54 cp/ml. Blood and GALT HIV-DNA levels and residual viremia were quantified by using digital droplet-PCR (detection limit: 32cp/106CD4+ for HIV-DNA and 2 cp/ml for residual RNA). Rectal biopsies were collected during High Resolution Anoscopy, subjected to collagenase digestion, mechanical disruption and filtering through cell strainer. Washed cells were analysed to characterize the lymphocyte subsets and activation markers by flow cytometry.

Results: Pts median age (IQR) was 37 (32-47), 24 were males, 1 female, 1 MtoF transexual. 61.6% had B subtype. Median (IQR) CD4 count and viremia at diagnosis were 463 (310-625) cells/μL and 124527 (28606-522298) cp/ml, respectively. Instead, at the enrolment, median (IQR) CD4 count was 679 (552-1070) cells/μL. All pts were under NRTI-based regimen (3rd drug: 14 INSTI, 8 NNRTI, 4 PI). Median (IQR) time of undetectability was 36 (30-57) months.

Median (IQR) residual viremia was 5 (2-11) cp/ml. Although without statistical significance, HIV-DNA levels in GALT were higher than peripheral ones (median [IQR]: 736 [237-1620] vs 539 [137-927] cp/106CD4. p=0.527) (table 1). Moreover, lower median (IQR) levels of HIV-DNA were observed in GALT among those on INSTI-based regimen when compared with non-INSTI (522 [0-1590] vs 930[468-1538] cp/106CD4. p=0.462) as well as in peripheral compartment (163[29-2409] vs 688[444-840] cp/106CD4. p=0.297).

Focusing on GALT HIV-DNA, a positive correlation emerged with peripheral HIV-DNA (Rho= 0.685; p <0.001), residual viremia (Rho=0.425; p=0.030), pre-ART viremia (Rho=0.563; p=0.023), pre-ART peripheral HIV-DNA (9 samples available; Rho=0.783; p=0.013), time (weeks) necessary to achieve the undetectability (Rho 0.439; p=0.068). Moreover, the immunophenotype analysis showed that the percentage of CD19+CD38+ subpopulation from GALT negatively correlated with both GALT HIV-DNA (although not significantly, Rho= -0.448; p =0.108) and peripheral HIV-DNA (Rho= -0.587; p <0.027). 2 pts had undetectable HIV-DNA levels in both blood and GALT compartments. These were on INSTI-based treatment and interestingly, the HIV-DNA in their seminal fluid was undetectable too. The former had started ART during acute infection and his residual viremia was 5cp/ml. The latter had undergone allogeneic bone marrow transplant and his residual viremia was completely undetectable.

Conclusions: These preliminary results show that HIV-DNA from rectal GALT is a valid marker to characterize the viral reservoir. Further details on a larger cohort are needed to assess possible correlations with drugs regimens, viral latency and mucosal immunoactivation status

Virology

OC 22 EVALUATION OF HIV-1 TROPISM IN MULTIDRUG-RESISTANT CART FAILING PATIENTS

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Background: Heavily treatment-experienced (HTE) patients (pts) still represent a fragile population for whom few therapeutic options might be available. According to this consideration, aim of this study was to evaluate HIV-1 tropism in cART-experienced failing pts to characterize those with exhausted treatment options.

Material and methods: HIV-1 infected pts failing cART with at least one available plasma genotypic resistance test (GRT) for PR/RT and gp120-V3 performed for clinical purposes were analysed. HIV-1 tropism was inferred through Geno2Pheno algorithm (G2P). In particular, G2P was set at FPR of 10%, thus pts with false positive rate [FPR] ≤10% were considered infected with X4-dual-mixed tropic viruses. In X4/dual-mixed tropic specimens, FPR was further stratified into 2 levels: ≤5% and 5-10%. For each patient, plasma cumulative resistance at the last V3 genotyping available was evaluated by cumulating major resistance mutations (MRM) to PI, NRTI, NNRTI and INI detected in all GRTs available. Multi-drug resistant (MDR) pts were defined as those who accumulated resistance to at least 3 drug classes among NRTI, NNRTI, PI or INI. Associations between FPR levels and demographic, viro-immunological and resistance parameters were investigated.

Results: Overall, 1262 cART failing pts were analysed. Most of them were males (68.1%) and infected with HIV-1 B-subtype (78.5%) (Table). Median (IQR) nadir and contextual CD4 cell count (cells/mm3) were 98 (34-211) and 307 (157 -509), respectively.

Three-hundred and thirty-two (26.3%) pts were infected with X4/dual-mixed strains (FPR≤5%, n= 240; FPR:5-10%, n=92) and 725 (57.5%) accumulated at least 1 class resistance. In particular, 22.2%, 21.5%, 12.4% and 1.4% pts harboured a resistant virus to 1, 2, 3 and 4 drug classes, respectively. Resistance to PI, NRTI, NNRTI and INI was 21.1%, 43.7%, 39.7% and 11.1%, respectively. Sixty-six (5.2%) MDR pts harboured X4/dual-mixed strains. Of them, 54 (81.8%) showed an FPR ≤5%.

By stratifying according to FPR levels, compared to pts with FPR 5-10% and FPR >10%, those with FPR≤5% showed the highest prevalence of resistance to 3 classes (18.8% vs. 12% vs. 10.8%), 4 classes (3.8% vs. 1.1% vs. 0.9%), PI (29.6% vs. 18.5% vs. 19.1%) and NRTI (50.4% vs. 47.8% vs. 41.6%) (Table, p<0.05). Moreover, by decreasing FPR, a decrease of nadir (median [IQR] cells/mm3: from 110 [44-220] to 47 [8-131], p<0.001) and contextual (median [IQR] cells/mm3: from 324 [178-524] to 243 [87-433], p=0.002) CD4 cell count was found, while the proportion of HTE-pts, who were perinatally infected, who experienced >10 previous regimens or were exposed to maraviroc/enfuvirtide increased (p<0.05, Table).

Conclusions: Among pts failing cART tested also for HIV-1 tropism, about 5% of pts harboured MDR and X4/dual-mixed tropic strains, and for this reason with a very limited treatment options. Low FPR values (≤5%) were associated with a long history of HIV-1 infection and high level of resistance.

Virology

OC 23 DOES DUAL THERAPY HAVE AN IMPACT ON HIV-DNA DECAY IN VIROLOGICALLY-SUPPRESSED PATIENTS COMPARED TO TRIPLE THERAPY? RESULTS FROM A MULTICENTRIC STUDY

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Background: Virological efficacy of certain dual therapies (DT) as maintenance strategy in virologically-suppressed patients (pts) has been well established, but little is known about their impact on HIV reservoir compared to triple therapies (TT). Our aim was to evaluate the changes in HIV-DNA levels in blood of virologically-suppressed pts maintaining a TT versus pts switching to a DT with 3TC+DTG or 3TC+ATV/b.

Material and methods: We retrospectively analyzed pooled data from virologically-suppressed HIV+ pts that, in the setting of different prospective studies, switched to a DT with 3TC+DTG or 3TC+ATV/boosted or maintained a TT. Total blood-associated HIV 1-DNA levels were assessed by droplet digital PCR at baseline (BL) and after 48 weeks (T48) and results were expressed as log10HIV-DNA copies/106 leucocytes. The Student's T test was used to compare the characteristics of pts at BL and the HIV-DNA levels among the groups. The Student's t test for paired samples was used to compare the change in HIV-DNA levels intra each group at BL and T48. Univariable and multivariable linear regressions were used to study predictors of changes in HIV-DNA.

Results: We enrolled 308 pts, 131 on TT and 177 switching to a DT 3TC-based (135 with ATV/b and 42 with DTG). Overall, 241 pts (78.2%) were males, with a median age of 45 yrs (IQR 38-53), a median time of HIV infection of 6.7 yrs (IQR 3.8-13.5) and a median time of virological suppression of 3.5 yrs (IQR 1.5-8.3). At BL, median CD4 cells count was 634 cell/mm3, without differences among the groups (p 0.105). Differences among the 3 groups are shown in table 1. Median changes in log10HIV-DNA from BL to T48 were -0.063 for TT, -0.058 for DT, -0.058 for ATV/b and -0.077 for DTG group (fig. 1). A significantly higher decrease in log10HIV-DNA from BL to T48 was observed in DTG group when compared to TT (p=0.038) and ATV group (p=0.016).

Exploring predictors of change in HIV-DNA levels between BL and week 48, DTG+3TC did not confirm an association with higher decay at multivariable analysis. Overall, we only found a weak association between zenith viral load and delta log10HIV-DNA (per 100,000 copies more -0.005, CI 95% -0.010 to 0.000, p 0.062). Among pts on DT, nadir CD4 <200 cells/mmc and a zenith viral load >500,000 copies/ml were weakly associated with the decline of logHIV-DNA (respectively, +0.107, CI 95% -0.013-0.227, p 0.081 and -0.200, CI 95% -0.415-0.016, p 0.069). A lower Log10 HIV-DNA at BL was predicted by CD4 cells count at nadir (per 10 cells more, -0.007, CI 95% -0.011 to -0.003, p 0.01).

Conclusions: In our population, we observed a higher decrease in HIV-DNA levels at 48 weeks after simplification to DTG+3TC when compared to ATV/rit+3TC or TT. However, such findings were not confirmed after adjusting for potential confounders. These results seem to confirm the safety of DT on HIV reservoir when compared to TT and seem not to show a significant advantage of one DT strategy over the other.

Virology

OC 24 PREVALENCE OF HIGH-RISK HPV GENOTYPES AND HPV GENOTYPES TARGETED BY THE NINE-VALENT VACCINE GARDASIL-9 AND THE ASSOCIATED RISK FACTORS

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Background: Human papillomavirus (HPV) immunization is currently recommended for young men who have sex with men (MSM) with <45 years of age.
The aim of the study is to assess the prevalence of anal HPV serotypes in MSM living with HIV over the past 5 years and to determine factors associated with the risk of anal infection: i) by high-risk (HR)-HPV genotypes or ii) by genotypes targeted in the nine-valent Gardasil-9 vaccine.
Methods: Time-trend study on adult people living with HIV (PLWH), who self-identify as MSM, followed at the San Raffaele Hospital, with ≥1 HPV test on anal swabs collected from 2014-2019. In case of multiple tests, the earliest was considered and the first HPV test was always performed before HPV vaccination, if occurred. The detection of 28 HPV genotypes was performed on anal samples by multiplex real-time PCR (CFX96™, Seegene).
All the considered characteristics were determined at or within 180 days before the date of HPV testing.
Cochran-Armitage test was used to assess for linear trend in HPV prevalence over time. Logistic regression models were applied to estimate risk factors for having ≥1 HPV-high risk genotype or ≥1 genotype targeted by the 9-valent vaccine.
Results: Overall, 1352 PLWH were included in the analyses: 147 (11%), 553 (41%) and 652 (48%) were ≤30, >30-45 and >45 years old, respectively; median (IQR) CD4 nadir was 333 (227-483) cell/uL, CD4+ 742 (565-945) cells/uL, CD4/CD8 ratio 0.8 (0.56-1.09), on ART since 6.5 (2.1-14.0) years, 61% with ≥1 previous STI including HCV, HBV, gonorrhea, ureaplasma, chlamydia and syphilis.
168 (12%) PLWH had no evidence of HPV infection.
Overall, 1184 (88%) had ≥1 genotype of any type; prevalence ranged from 86% to 90% with no difference over time (p =0.634). At least one HR-HPV genotype was found in 1072 (79%) PLWH: prevalence ranged from 77% to 84% with no trend difference over the last 5 years (p=0.859); the most prevalent was HPV-53 (27%). HPV-16 and 6 were prevalent in the MSM population (23% and 22%, respectively), while HPV-18 and 11 were less frequent (11% and 13%, respectively). Interestingly, 956 (71%) PLWH resulted to carry ≥1 serotype covered by the 9-valent vaccine, 547/956 (57%) carried ≥2 genotypes and only 6 (0.6%) ≥6, with no change in prevalence of HPV serotypes included in Gradasil-9 (p=0.197) from 2014 to 2019.
At multivariate regression, we found that the risk of ≥1 HPV-high risk genotype and ≥1 genotype included in Gardasil-9 vaccine were associated with age at different gradient and a history of gonorrhea (Table 1).
Conclusion: The findings of this study reinforce the recommendation of proposing Gardasil-9 vaccine in MSM living with HIV. Those younger than 30 years and with a prior gonococcal infection have a higher risk of infection with HR-HPV serotypes, probably reflecting number of sexual partners. We can hypothesize that the interaction of gonorrhea and HIV could create an inflammatory milieu in which HPV infection and oncogenesis are favored.

Comorbidities

OC 25 FAT DISTRIBUTION AND DENSITY IN PLWH WITH >=5% WEIGHT GAIN

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Background: Weight gain (WG) with INSTI-based ART has been reported, but it is unclear whether INSTIs are also associated with fat deposition in ectopic sites. We assessed ectopic fat quantity and density in virally suppressed ART-experienced people with HIV (PLWH) who had WG after switching to INSTI-based ART (INSTI-s) vs remaining INSTI-naive (INSTI-n) on stable ART.

Methods: In an observational cohort study from 2007 to 2019 at Modena HIV Metabolic Clinic, PLWH were grouped as INSTI-s vs INSTI-n and matched for sex, age, 1st visit BMI and follow-up duration. Significant WG was defined as an increase of ≥5% from 1st visit weight over follow-up. Body composition was assessed at 1st visit and at last evaluation. In the INSTI-s group, the 1st visit was prior to switch. DXA assessed weight and total lean and fat mass. Computed tomography assessed visceral (VAT), subcutaneous (SAT) and epicardial (EAT) adipose tissue area and density (VAT-d, SAT-d, and EAT-d), liver-to-spleen density ratio (L/S), and psoas muscle density (P-d).

Results: A total of 418 PLWH (71% males), mean age 50 (±8) years with median HIV duration of 17.4 years (IQR 12.3 -22.6) were analyzed at 1st visit and after 4 years (±2.2). INSTI-s switched to DTG in 68 (32%), RAL in 131 (62%) and ELV/c in 11 (6%) cases. INSTI-n were on stable PI in 96 (46%) and on NNRTI in 105 (51%) cases. Two-drug regimens in INSTI-s and INSTI-n were 37% and 6%. At the 1st visit, all body composition measurements were not different in INSTI-s and INSTI-n groups (all p>0.05). At follow-up, the mean change in body weight (1.6kg vs 2.4kg, p=0.3) and the prevalence of WG (24.6% vs 27%, p=0.66) were similar for INSTI-n vs INSTI-s. However, among weight gainers only, the change in BMI and absolute weight was greater in the INSTI-s vs INSTI-n group (11.8kg vs 9.4kg, p=0.02). While the VAT increase over the interval was similar in both groups, the VAT-d decreased in the INSTI-s group, suggests a change in fat quality. Other changes in body composition were not observed (Table).

Conclusions: Over a four-year interval, virologically controlled PLWH with ≥5% WG INSTI-s had a greater gain in BMI compared to those who remained INSTI-naïve, but there were no differences in the changes in ectopic fat depots. Further work is needed to understand whether the differences in VAT density associated with INSTI impact adipose function

Comorbidities

OC 26 STATIN ELIGIBILITY IN PEOPLE LIVING WITH HIV: ARE WE USING THE RIGHT TOOLS TO IDENTIFY PATIENTS AT RISK OF DEVELOPING MAJOR CARDIOVASCULAR DISEASE?

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Background: Cardiovascular disease (CVD) risk assessment remains a critical step in defining primary prevention strategies in people living with HIV (PLWH). The aim of this study was to evaluate whether coronary artery calcium (CAC) scoring (known to have a very high negative predictive value for CVD events when reported as zero) allowed a more accurate selection of patients that may benefit from statin therapy, compared to Framingham Risk Score (FRS) and D:A:D.
Methods: We performed a cross-sectional study in a cohort of PLWH over the age of 50 years without known CVD that underwent CT scans to measure CAC scores between 2009-2019 at Chelsea and Westminster Hospital NHS Foundation Trust in London, UK. FRS and full D:A:D scores were calculated for each patient at the time of CAC scoring. We estimated the proportion of patients eligible for statin therapy based on current European risk-assessment guidelines (10-year risk ≥ 10% using FRS or full D:A:D score) and evaluated modifications to statin eligibility after measuring CAC scores.
Results: A total of 739 patients were included in the study (mean age 56±5 years, 92.9% male, 84% White). CAC scores of individuals categorized as being at low (<10%), intermediate (10–20%) or high (>20%) risk using FRS and DAD scores are shown in Table 1. According to current guidelines, 477 (56.4%) of patients were eligible for moderate-intensity statin based on a 10-year FRS≥10%. A CAC score of zero was found in 174 (41.7%) of these patients. Conversely, 93 (12.6%) of patients with a CAC score>50th centile) were identified as low-risk (FRS<10%). Overall, when compared to FRS, CAC scoring allowed a reclassification of CVD risk in 36.1% of patients, prevented the unnecessary use of statins in 23.5% and indicated the use in 12.6% of patients that would not have been treated. Similarly, D:A:D score underestimated the presence of significant coronary calcification in 16.1% vs 12.6% and overestimated CVD risk in 18.8% vs 23.5% patients with CAC score of zero.
Conclusion: This is the first study showing that the inclusion of CAC scores in CVD risk assessment of PLWH over 50 may prevent the unnecessary use of statins, reducing costs and potential toxicity of these drugs, and allow a more accurate selection of patients that benefit from pharmacological CVD risk primary prevention.

Comorbidities

OC 27 PREVALENCE, PREDICTORS AND EVOLUTION OF LEAN NON-ALCOHOLIC FATTY LIVER DISEASE IN HIV MONO-INFECTED PATIENTS

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Objective: The burden of NAFLD is growing in people living with HIV. NAFLD is usually associated with obesity, however it can occur in normoweight (lean) patients. We aimed to investigate: (i) prevalence and predictors of lean NAFLD in HIV-infected patients; (ii) prevalence of significant liver fibrosis by BMI category and rates of liver fibrosis progression in patients with lean NAFLD.

Methods: We included HIV mono-infected patients from three prospective cohorts (LIVEHIV in Montreal, MHMC in Modena and LHIVPA in Palermo). NAFLD was diagnosed by transient elastography (TE) and defined as controlled attenuation parameter ≥248 dB/m, in absence of alcohol abuse and HBV/HCV co-infection. Lean NAFLD was defined when BMI <25 kg/m2. Fibrosis progression was defined as development of significant liver fibrosis (TE ≥7.1 kPa), or transition to cirrhosis (TE ≥13 kPa) for those with significant liver fibrosis at baseline. A patient was defined as metabolically abnormal in presence of diabetes, hypertension or hyperlipidemia. Predictors of lean NAFLD were investigated in multivariable analysis, using logistic regression. Kaplan-Meier plot and log-rank tests were performed to study liver fibrosis progression in lean NAFLD patients compared to and overweight/obese NAFLD patients.

Results: 1511 HIV mono-infected patients were included, of whom 45% were lean. Prevalence of NAFLD and liver fibrosis in lean patients were 13.9% and 5.5%, respectively. NAFLD affected 24% lean vs. 59% overweight patients (p<0.001). Interestingly, lean NAFLD patients were similarly metabolically abnormal as overweight ones (75% vs. 77.2%). Lean NAFLD patients had similar prevalence of elevated alanine aminotransferase (ALT) as overweight patients (36.7% vs. 31.6%), as well as similar prevalence of significant liver fibrosis (14.3% vs. 19.1%) (see Figure 1). After adjusting for sex, ethnicity, hypertension, low HDL cholesterol, CD4 cell count, and time since HIV infection diagnosis, independent predictors of NAFLD in lean patients were older age (aOR 1.34, 95% CI 1.08-1.64, p=0.007), higher triglycerides (aOR 1.37, 95% CI 1.13-1.65, p=0.001) and higher ALT (aOR 1.14, 95% CI 1.04-1.24, p=0.003), while higher HDL was protective (aOR 0.44, 95% CI 0.25-0.75, p=0.003) (see Table). 142 patients with NAFLD were followed for a median of 26 months (interquartile range 6-54). Incidence rate of fibrosis progression was 24.5 per 100 persons-year (PY) (95% CI 11.0-54.5) vs. 17.6 per 100 PY (95% CI 12.5-24.9) in lean vs. overweight/obese patients (p=0.438).

Conclusion: NAFLD affects one in four lean HIV mono-infected patients. Although lean NAFLD has been previously considered benign, these patients have similar degree of liver fibrosis and similar rates of liver fibrosis progression as overweight/obese NAFLD patients. Investigations for NAFLD should be proposed in older patients with dyslipidemia and elevated ALT even if normoweight.

Comorbidities

OC 28 NAFLD WITH SIGNIFICANT FIBROSIS IN PLWH INFORMS THE NATURAL HISTORY OF CARDIOVASCULAR DISEASE

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Background: Non-alcoholic fatty liver disease (NAFLD) is associated with intrahepatic and extrahepatic manifestations such as fatal and non-fatal cardiovascular diseases (CVD). We hypothesized that the natural history of CVD and NAFLD are parallel. We postulated that NAFLD with/without significant fibrosis were independently associated with various stages of CVD in people living with HIV (PLWH).
The aim of the study was to compare the performance of NAFLD and significant fibrosis in comparison to ASCVD algorithm in the prediction of high CV risk, subclinical CVD and major CVD event (MACE) in PLWH.
Methods: This was a cross-sectional study that included consecutive PLWH attending Modena HIV Metabolic Clinic (MHMC) from June 2018 to October 2019. We included ART-experienced PLWH who were evaluated for NAFLD and clinical and subclinical cardiovascular disease. Liver steatosis and fibrosis was assessed by transient elastography (TE). Patients with hepatitis B, hepatitis C co-infection and hazardous alcohol intake were excluded from the study. Cardiovascular disease was assessed through MACE history, CVR algorithm estimator and assessment tools for subclinical cardiovascular disease. The primary study outcomes were: 1) CVR algorithm estimator using the ASCVD risk score; a 10-year risk for CVD was categorised as low (<7.5%) and high (≥7.5%); 2) subclinical CVD was assessed with one of the following tools: ultrasound carotid intima-media thickness (cIMT), carotid-femoral pulse wave velocity, coronary calcium score by computed tomography; 3) MACE including myocardial infarction, coronary artery disease, peripheral vascular disease, stroke, and angina pectoris, as well as coronary artery bypass grafting and angioplasty. Nonparametric receiver operating characteristic curve (ROC) analysis was conducted to assess the performance of NAFLD and NAFLD with significant fibrosis in the prediction of CVD stages compared to ASCVD algorithm.
Results: We analysed 616 PLWH. Mean age was 56 (±7.8) years, 79.2% were males, mean BMI was 24.6 (±3.8), median CD4 was 707 µL (IQR=540.3-907.8), HIV RNA viral load was undetectable in 98.9% of cases. Low ASCVD, high ASCVD, subclinical CVD and MACE were present in 209 (33.9%), 123 (20%), 216 (35.1%), 68 (11%) respectively. NAFLD and NAFLD with significant fibrosis was present in 443 (39.7%) and 92 (8.2%), respectively. Subclinical CVD was well predicted by NAFLD and NAFLD with fibrosis (ROC=0.738 and ROC=0.727 respectively) and it was not inferior to ASCVD risk score (ROC=0.738), p>0.05. MACE is also well predicted NAFLD and NAFLD with fibrosis (ROC=0.71 and ROC=0.714 respectively) and it was not inferior to ASCVD risk score (ROC=0.710), p>0.05.
Conclusions: NAFLD and NAFLD with fibrosis have the same performance in prediction of CVD as traditionally used ASCVD risk algorithm. NAFLD and NAFLD with fibrosis can be used as a biomarker of metabolic age in the prediction of CVD events.

Comorbidities

OC 29 DECLINE OF METABOLIC SYNDROME AND INCREASE IN OVERWEIGHT IN HIV INFECTED PATIENTS FROM 2005-2015

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Background: Metabolic alterations obtained high level of attention in HIV investigations, and recently available antiretroviral (ARV) drugs have improved efficacy and safety profile, compared with older ones. The aim of the study was to assess, in the clinical setting the proportion of overweight and the prevalence of metabolic syndrome (MS) among patients with HIV infection in three different cross-sectional investigations from CISAI group.
Design: Multicenter, nationwide study assessing overweight and MS prevalence in three cross-sectional study periods: 2005, 2011 and 2015.
Methods: Date were collected in three previous studies from CISAI group: SIMone, HIVHy, STOPSHIV including overall 3512 subjects. We analyzed anthropometric and laboratory characteristics in 3014 Caucasian HIV infected patients, with evaluable MS, enrolled in these studies performed in 2005, 2011 and 2015 with similar investigation procedures. The MS was diagnosed according to the National Cholesterol Education Program (ATP III) definition. Variables were described as frequency (%), mean (standard deviation) or median (interquartile range). Logistic regression (odds ratio, 95% confidence interval) was used to account for age and gender difference among three groups when comparing MS prevalence and overweight.
Results: Overall mean age was 46.9 ± 10.2 years, and men were 73.3%. Comparing respectively 2005, 2011 and 2015, MS was present in 34.5% vs 33.0% vs 29.3% (ATP III). Adjusting for age, OR for MS was 0.64 (95% CI 0.52 -0.78) in 2011 and 0.56 (95% CI 0.46-0.69) in 2015. Mean blood glucose (95 ± 27 vs 93 ± 21 vs 93 ± 21 mg/dL) and median triglycerides (151, 98-126, vs 132, 94-197, vs 119, 84-178, mg/dL) were significantly higher in 2005 compared with 2011 and 2015. The atherogenic index of plasma (AIP), that is the logarithmically transformed ratio of molar concentrations of triglyceride and high-density lipoprotein cholesterol was respectively 0.16, -0.1-042, vs 0.12, -010-035, vs 0.06 -0.15-0.30, significantly improved over time. Total cholesterol was higher in 2011 but significantly lower in 2015 than in 2005, HDL cholesterol and systolic blood pressure were similar, whereas diastolic blood pressure declined over time, with increasing use of antihypertensive drugs. CD4 cells counts was significantly lower in 2005 compared with 2011 and with 2015 (median 440 vs 638 vs 640 cells/mm3, p<0.0001).
BMI increased from 23.6 to 24.5 and 24.5, with a concurrent increase of overweight from 29.4% to 39.5% to 39.6% (p<0.0001).
Conclusions: In the last years, the relevant effort in educational intervention and therapeutic options in HIV infected people had significantly improved metabolic profile in new ARV therapy era. In contrast an increase of weight and BMI could be considered attributable to several factors, including the "return to health" weight gain with reversal of the catabolic effects of HIV-infection.

Comorbidities

OC 30 PROGRESSION OF ANAL/CERVICAL DYSPLASIA IS ASSOCIATED WITH HUMAN PAPILLOMAVIRUS (HPV) AND SYPHILIS COINFECTION IN HIV-INFECTED PATIENTS

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Background: HPV-related dysplasia is a precursor of anal/cervical cancer. HIV-infected subjects are at risk of HPV-related disease progression. The reasons for this are multifactorial: increased exposure of HPV and other sexually-transmitted diseases (STDs), the state of immune-depression and the impairment of HPV-specific immunity. Understanding which factors are associated with the progression of anal/cervical squamous intraepithelial lesions (SIL) is of importance for prevention strategies.

Materials and methods: Longitudinal study enrolling male/female HIV-positive patients who underwent anal/cervical PAP smears and HPV genotyping in the period 01/2006-11/2019. Patients repeated PAP smears every 8-12 months depending on the clinical indication. Follow-up accrued from the enrollment in the cohort (i.e. the first surgical/gynecological examination with PAP smears) to the last available examination. SIL progression was defined as development of a higher grade of HPV-related dysplasia.

Demographic (including HCV, HBV and syphilis coinfection) and viro-immunological parameters (CD4+ and CD8+ T-cell count, CD4/CD8 T-cell ratio; CD8+CD38+; CD8+CD38R0+; CD4+ and CD8+ CD127-expressing cells) were collected at the time of the cytological evaluation.

Chi-squared/Mann-Whitney test, Kaplan Meier survival analysis with log-rank test and Cox proportional hazards regression analysis were used for statistics.

Results: 398 patients were enrolled. The median age, time since HIV diagnosis and time since cART initiation were 41 years (IQR 34-46), 46 months (IQR 9-136) and 39 months (IQR 9-99), respectively. 96 (24%) patients displayed progression from no SIL to any grade of SIL or from Low (L) SIL to High (H) SIL. SIL progressors were more commonly males, co-infected with HPV, HCV and syphilis, compared to subjects presenting with a stable/regression of SIL (Table 1). No differences were observed in viro-immunological characteristics between the two groups (Table 1).

In a mean time of 97 months (IC95% 92,7-102,2), the 24- and the 48-month probability of SIL progression was 5% (IC95% 3-7%) and 14% (IC95% 10-18%), respectively. The 48-month probability of SIL progression was 9,8% (95%CI 4 -15%) in syphilis-positive patients and 3,9% (95%CI 1-6,7%) in syphilis-negative subjects (log-rank p=0,006) (Figure 1). In the adjusted Cox regression model, syphilis was confirmed associated with a trend toward a higher probability of SIL progression (AHR 1,57, 95%CI 0,999-2,48; p=0,05, adjusting for HPV infection and gender (Table 2).

Conclusion: In the context of HIV-HPV coinfection, syphilis was associated with SIL progression, while immunological parameters were not. These findings suggest that exposure to HPV and other STDs are drivers of SIL pathogenesis in HIV-infected subjects rather than peripheral immune impairment. HPV vaccination and prevention of syphilis infection should be therefore considered in the management of HPV dysplasia in HIV disease

Clinical Hepatitis and coinfections

OC 31 THE CONTRIBUTION OF LATE PRESENTATION AND LATE ART INITIATION TO TB-HIV OCCURRENCE ACROSS FOUR COUNTRIES

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Background: Tuberculosis (TB) remains the leading cause of mortality worldwide in people living with HIV (PLWH). Late presentation to care (LP) and late ART initiation (LI) appear to be associated with the TB risk but supporting data are scarce. We aimed at analyzing the causal link between LP and LI and the risk of TB and at quantifying the contribution of LP and LI to TB-HIV incidence by using the attributable risk(AR) and population attributable fraction(PAF), in four countries with different TB-HIV burden.

Methods: Patients enrolled from 2007-2 016 with recent HIV diagnosis (< 3mo), were included. LP was defined as accessing care with CD4≤350cells/mm3; and LI as starting ART with CD4≤350cells/mm3 among non-LP. The risk of TB was compared in LP vs. non-LP using survival curves and a weighted Cox regression model with inverse probability weights (IPW). A marginal structural model (MSM) which mimicked a 2 arm-randomized trial: 1) Initiating ART with CD4>350(non-LI) vs. 2) initiating ART with CD4≤350(LI) was used to evaluate the impact of LI on risk of TB. Weighted hazard ratios (wHR) for TB in LI vs. non-LI were estimated by pooled logistic regression with interaction between time and strategy of ART initiation. Results were used to estimate AR and PAF.

Results: 20,112 patients included: 54% from Uganda, 29% from Italy, 14% from Peru and 3% from Mexico; 59% were LP. 420 TB cases were diagnosed prior to ART initiation, 68% in LP. wHR for TB among LP vs. non-LP was 4.94 (95% CI: 4.27-5.71). Among LP, AR was 81% at 1-year and 66% at 5 year while PAF was 72% and 58%, respectively. 422 TB cases were observed after ART initiation, 86% in LP; wHR for LP vs. non-LP was 3.16 (95% CI: 2.36 - 4.24). AR were 68% and 67% and PAF were 57% and 56% by 1 and 5 years respectively. Among 7,899 non-LP wHR for LI compared to non-LI was 0.54 (95% CI: 0.23 - 1.26). Among LI, AR was -3% and 31 % and PAF was 2% and 26% by 1 and 5 years, respectively, risk of TB attributable to late initiation by 1, 3 and 5 years were -3% , 21% and 31 % respectively.

Conclusions: In this 4-country cohort of PLWH with different TB burden, a high proportion of incident TB occurring both before and after ART initiation could be attributed to late diagnosis of HIV. Delaying ART initiation among non-LP also increased incidence TB, with variation among countries. Our findings suggest that efforts to expand HIV testing and immediate ART initiation may have a major impact on TB-HIV incidence.

Clinical Hepatitis and coinfections

OC 32 HPV 16 AND 18 INFECTIONS CONTRIBUTE TO DEVELOPMENT OF ANAL CYTOLOGICAL ABNORMALITIES IN A COHORT OF PLWH

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Background: Our aim was to investigate prevalence and incidence of HPV infection and cytological abnomalities in anal swabs of People Living With HIV (PLWH) according to gender and sexual orientation: Men who have sex with Men (MSM), Men who have sex with Women (MSW) and women (W).
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. Persistance and acquisition of HR HPV were described among patients who repeated anal swab tests during the course of follow-up.
Results: 354 PLWH (people living with HIV) were screened both for cytological examination and HPV genotyping MSM were 174, MSW 90 and W 61. Patients' characteristics and HPV prevalence were shown in table 1 and 2 respectively. Median number of HPV were found higher in MSM vs MSW and W (4 [3-6 IQR] vs 2[1-4] and 3 [1-4] respectively, p<0.001) as well as median number of HR-HPV (3 [2-4] vs 1 [1-3] and 2 [1-3] respectively, p<0.001). Prevalence of at least one HR-HPV was higher in MSM (91%) and W (85%) vs MSW (77%) (p<0.05). Cytological abnormalities were found in 21.1% of entire population with no significant differences among the groups (MSM 22.4%, MSW 20%, W 13.1%) . At multivariable regression analysis (adjusted for age, nadir Cd4, last Cd4 cell count and HIV-RNA) for HPV infection a lower risk was found for W vs MSM [OR 0.24 (95% CI 0.115; 0.513)] and for MSW group vs MSM [0.37 (0.180; 0.773]. At multivariate regression for HR-HPV was found a significant lower risk for MSW vs MSM [0.261 (0.121;0.564)]. Multivariate analysis for cytological abnormalities showed a significant higher risk in PLWH with HPV 16 and 18 [3.3 (1.04; 10.49)]. 175 PLWH had at least 1 follow-up visit (T1) median follow up time between T0 and T1 was 3.6 years [IQR:2.1-5.7]. In this subgroup 103 were MSM, 33 MSW and 26 W. The acquisition of new HR-HPV infection was high with 66.7% (16 of 24) of PLWH negative for HR-HPV at T0 that became positive at T1 (p<0.001) and 40% (14 of 40) of PLWH negative for preventable HPV by vaccine acquired a preventable genotype (p<0.001). Prevalence of cytological abnormalities was stable at T1 (20.6%). Progression and clearance of cytological abnormalities was highly variable with 17.2% of new cytological abnormalities and a 70.2% of clearance (p<0.001). Evaluating persistence of HPV 16 and/or 18 according to cytological results a significant association between development of positive cytology at T1 and persistence of HPV-16 and or 18 was found (p<0.05).
Conclusions: Prevalence of cytological abnormalities in our sample is low despite the high prevalence of HPV infection and HR-HPV. HPV 16 and 18 infections and persistence are associated with development of cytological abnormalities.

Clinical Hepatitis and coinfections

OC 33 IMPACT OF SYPHILIS ON THE RISK OF HIV VIRAL REBOUND IN HIV POSITIVE PATIENTS UNDER EFFECTIVE ANTIRETROVIRAL TREATMENT: DATA FROM THE ICONA COHORT

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Background: A transient HIV load rebound in people living with HIV (PLWH) under effective antiretroviral treatment (ART) has potential implications for the risk of transmission. The aim of the study is to assess the impact of syphilis infection on the risk of transient HIV-RNA elevation in PLWH with current HIV-RNA ≤50 cp/mL.

Material and methods: All PLWH in the ICONA cohort (2009-2019) under ART with at least 2 consecutive HIV-RNA values ≤50 cp/mL before the date of syphilis diagnosis and at least one HIV-RNA determination after the syphilis event were enrolled. A control group of PLWH without syphilis who after the same amount of time from enrolment of the syphilis case (index date) were free from syphilis was matched for age, mode of HIV transmission and CD4 cell count at the enrolment in the ICONA cohort. Outcomes were defined using the first HIV-RNA measure in the time window ranging between -2 and +6 months of the index date. The primary outcome used the cut-off of >200 cp/mL to define failure and the secondary outcome >50 cp/mL. The association between syphilis infection and the protocol defined outcomes was evaluated using logistic regression analysis. The multivariable logistic analysis was adjusted for potential confounders: previous AIDS, CD4 cell count, previous virological failure and time of virological suppression before the index date. Age, mode of transmission and CD4 cell count at ICONA enrolment were controlled by matching. An interrupted time series analysis (ITS) was used to assess the trend of HIV-RNA in PLWH with syphilis.

Results: Six hundred and ninety-two PLWH with syphilis were enrolled and matched with 993 PLWH without syphilis. The first HIV-RNA in the time window was >200 copies/mL in 12/692 (1.7%) syphilis exposed and 17/933 (1.8%) non-exposed whereas an HIV-RNA >50 cp/mL occurred in 28/692 (4.0%) exposed and 31/933 (3.3%) non-exposed. In the multivariable analysis syphilis infection was not associated with the risk of HIV-RNA >200 cp/mL [adjusted Odds Ratio (AOR) 1.37 (CI95% 0.59-3.17)]. Previous virological failure [0 vs 1-3, AOR 12.05 (CI95% 3.22-45.10); 0 vs >3, AOR 39.37 (CI95% 10.94-141.7)] and the time of virological suppression (per 6 months longer duration) before the index event [AOR 0.79 (CI95% 0.68-0.91)] were associated with the risk of HIV-RNA >200 cp/mL. Patients with syphilis had an increased risk of HIV-RNA >50 cp/mL in the multivariate analysis [AOR 1.64 (CI95% 0.92-2.90)] compared to controls. ITS analysis for PLWH with syphilis showed some evidence of an increase in average HIV-RNA corresponding to the date of syphilis.

Conclusions: Although people with syphilis showed some evidence for an increased risk of viral blips (single value >50 cp/mL) less convincing evidence was found for the association between syphilis infection and transient viral elevation with the potential of HIV transmission (single value >200 cp/mL), suggesting that the role of syphilis in HIV rebound is still to be determined.

Clinical Hepatitis and coinfections

OC 34 DECREASE OF PREVALENCE OF SUBJECTS HARBORING REPLICATING HCV AMONG PLWHIV IN ITALY: RESULTS FROM THE NOCO STUDY

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Background: The aims of these analyses from the NoCo study are to estimate the prevalence of active HCV infection in HIV+ individuals in care in 2017-2019, to estimate the DAA-uptake and the incidence of new HCV infections and re-infections.

Methods: Cross-sectional and longitudinal analyses within the NoCo (=No Coinfections) study. Subjects included are those screened for HCV from September 2017 to January 2020, independent of their HCV status, belonging to centres of the Icona network. Prevalence of HCV infection (HCVAb+) and active HCV infection (HCV-RNA+) was evaluated at baseline. Proportion of active HCV infection has been also evaluated according to calendar year of screening (2017 -2019) using a chi-square for trend. Independent predictors of being HCVAb+ were identified by logistic regression (cross sectional analysis). Subjects retested for HCV at 1 year follow up participate to the longitudinal analysis. Incidence of HCV seroconversions, in those negative for HCVAb at NoCo screening, and of HCV re-infections (in those HCVAb+/HCV-RNA- who turned to HCV-RNA+) were evaluated and predictors identified by Poisson regression. Standard survival methods used to estimate the probability of DAA-start from first NoCo screening, for those screened HCV-RNA + at first screening.

Results: 12,443 patients included. At the first NoCo screening 3,744 (30.1%) were HCV-Ab+, 1,483 HCVAb+ subjects (39.6%) were HCV viremic, 2,151 (57.4%) were HCV-RNA negative and 110 (3.0%) were not tested. All the independent predictors of HCV positivity are shown in Table1.

A total of 1,954 HCVAb- were retested after 1 year: 15 seroconverted to HCVAb+. Incidence rate was 0.8/100 PYFU (95%CI: 0.3-1.8); 1.0/100 PYFU (0.5-1.8) in MSM. MSM showed an unadjusted non significant 1.41-fold (0.4-4.5) higher risk of HCV seroconversion as compared to heterosexuals.

A total of 767 HCV-RNA- individuals were retested and 19 resulted to be HCV-RNA+: 7 were relapses, 12 were reinfections, giving an incidence rate of reinfections of 2.2/100 PYFU (1.1-3.5) 4.8/100 PYFU in MSM. MSM had an unadjusted non significant 1.8 fold (0.3-9.8) higher risk of HCV reinfection as compared to heterosexuals.

1,152/1,483 (77.7%) HCV viremic subjects at baseline had a follow-up thereafter, 1,013/1,152 (87.9%) started a DAA with a 1-yr cumulative probability of DAA-start of 87.7% (95%CI: 85.5-89.7). 611 had HCV-RNA data >=12weeks after end of treatment with a SVR12 reached for 595 (97.4%).

Taking into account both screening and 1-year follow up tests, the prevalence of individuals harbouring replicating HCV decreased from 42% in 2017, to 24% in 2018 and 17% in 2019 ($p<0.001$, Figure1).

Conclusions: IDUs are the group at highest risk of being HCV co-infected in Italy. Circulation of HCV among MSM appears low. Most (83%) of the HCVAb + individuals tested in 2019 have achieved viral eradication, suggesting that the target of HCV coinfection elimination in PLWHIV could be achievable. This study is supported by a grant from Gilead International

Clinical Hepatitis and coinfections

OC 35 INNOVATIVE PROCEDURES FOR MICRO-ELIMINATION OF HCV INFECTION IN A HIGH-RISK POPULATION OF UNDOCUMENTED MIGRANTS AND LOW-INCOME REFUGEES

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Background: Because of the intermediate HCV endemicity in immigrant populations and the high efficacy of DAA therapy, programs should be undertaken to eradicate the infection in this difficult-to-manage setting. The aim of this study was to evaluate an innovative model to eliminate HCV infection in this population

Materials/methods: A prospective, multicenter, collaborative study, based on the long-term cooperation between five first-level clinical points and two corresponding third-level units of Infectious Diseases (ID) was performed in Campania, Southern Italy.

A screening to identify the subjects with HCV infection, free of charge and without bureaucratic procedures, was proposed to all undocumented migrants and low-income refugees prospectively observed by a physician and a cultural mediator at one of the first-level clinical centers from June 2018 to March 2019. All migrants received correct information and illustrated brochures on transmission and prevention of HCV infection, related diseases and available treatments. All anti-HCV positive subjects were addressed at one of the two ID units for further clinical investigation including HCV-RNA determination and, if positive, HCV-genotyping (GT). HCV-RNA positive patients were treated with sofosbuvir plus velpatasvir+ribavirin for 12 weeks and followed up for 12 weeks after treatment withdrawal.

Results: Of the 3,401 migrants observed, 3,286 (96.6%) accepted to be screened. They were young (median age 27 years), predominantly male (83.3%) and came mainly from Northern Africa (4%), Sub-Saharan Africa (67.1%), Eastern Europe (9.3%), and Indo-Pakistan region (16.4%). Of the 3,286 enrolled subjects, 180 (5.4%) resulted anti-HCV positive. The Figure shows the HCV-cure cascade. All the 180 anti-HCV-positive subjects were linked to care at 3rd level center and tested for HCV-RNA, and 48 (26.6%) resulted HCV-RNA positive. Of these, 40 (83.3%) started DAA regimen (14 with GT 1b, 21 with 1a, 18 with 3, 4 with 4 and 2 with 2): 38 completed the follow-up with a SVR rate of 100% and 2 are still pending. No subject had adverse neither was drop-out.

Conclusions: This innovative procedures for micro-elimination of HCV infection seems to be effective in undocumented migrants and low-income refugees with rates of diagnosis, linkage to care and cure in line with the WHO goals.

Clinical Hepatitis and coinfections

OC 36 HCV TREATMENT AND REINFECTION RISK IN INJECTING DRUG USERS IN RESIDENTIAL TREATMENT SETTING FOR DRUG ADDICTION. SAN PATRIGNANO HCV-FREE

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Background: HCV eradication in injecting drug users (PWID) can be reached with direct acting antivirals (DAA). The main obstacles to this goal are insufficient screening and linkage to care, and the HCV-reinfection risk. We investigated the feasibility of HCV eradication in the context of a drug free Therapeutic Community (TC) and analysed the pros and cons of the model.

Methods: We collected data on HCV test performed in all subjects present in the San Patrignano TC during the DAA-era (2015-2019). Data on HCV Antibody (Ab) and ribonucleic acid (RNA) testing, care and treatment were used to populate the HCV cascade among San Patrignano TC. DAA treatment were prescribed according to AIFA criteria and following the Regional (Emilia Romagna) guidelines.

Results: The study group was constituted by 648 PWID (75.3% males), with a median age at TC-entry of 29 years (Interquartile Range: 24-35), mostly Italians (604, 93.2%). Among them 643/648 (99.2%) were screened for HCV infection at entry. HCV antibodies were detected in 418 subjects (65% overall). In 263 individuals HCVAb positive serology was a confirmation of previous test performed pre-TC entry, while 155 individuals (37.1%) were newly diagnosed (see Fig.1); in 40 subjects acute HCV infection was diagnosed after admission. Among 418 HCVAb-pos individuals, 406 (97.1%) were screened for HCV-RNA. Detectable RNA was found in 291 (71.7%) individuals; among the remaining 115 RNA-negative individuals, 74 had spontaneous clearance (18.2%) and 41 (10.1%) were considered cured due to HCV treatment before TC-entry. Among the 291 viraemic subjects, 17 (5.8%) were not considered suitable for treatment (10 foreigners, 1 jailed, 2 refuses, 4 with comorbidities). Further 37 subjects enlisted were not treated (11 drop-out and 26 discharged from TC before HCV treatment) and 27 are still in the waiting list for treatment. Finally, DAA treatment was prescribed in 210 (72.2%) and SVR obtained in 207 (98.6%), while 3 individuals were not cured (2 suspension due to complicancies and 1 not-respondent). No cases of HCV reinfection were observed. Overall cascade of care is synthesized in Fig.2.

Conclusions: HCV screening in PWID is still insufficient: over a third of them is unaware of being HCVAb-pos at TC-entry. However, once identified through screening HCVAb-pos individuals are almost universally linked to care and the quota of those who initiated treatment was above 70%, and success of cure virtually complete. The major drawback of this strategy is the drop out of patients, but recent modification of AIFA criteria will probably lead to a progressive improvement of the quota of not treated. Environments like TC, Rehab centres and jail, can be considered optimal points of care for HCV eradication. Treating both addiction and HCV infection reduces the risk of HCV among PWID toward zero. Supported by: Grant Gilead IN-IT-987-5396, part of the LEGA-C™ program "Local Elimination Programs leading to Global Action in HCV"

Basic science and immunology

OC 37 REDUCED PROBABILITY OF ACHIEVING OPTIMAL VIRO-IMMUNOLOGICAL CONDITION IN SUBJECTS WITH VERTICAL TRANSMISSION OF HIV REACHING ADULT AGE WITH UNSUPPRESSED HIV RNA OR INCOMPLETE IMMUNOLOGICAL RECOVERY

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Background: This study explored viro-immunological status (through the evaluation of HIV-RNA, CD4 and CD4/CD8 ratio) and factors associated with viro-immunological outcome in young adults with vertical transmission (VT) of HIV.
Methods: Multicenter study including VT HIV-1 infected subjects ≥18 years old and already transited to the adult care, from six large Italian clinics. Subjects were observed from birth to death, lost to follow up or last visit until June 2019. Demographical, clinical, viro-immunological and antiretrovirals data were collected. We defined optimal viro-immunological condition (OC) as the simultaneous presence of HIV RNA <50 cp/ml & CD4 >500/mm3 & CD4/CD8 ≥1, while any other combination as not-optimal viro-immunological condition (nOC). We analyzed categorical and continuous variables; a Markovian multi-state model was used to assess the viro-immunological condition and the transition from OC to nOC.
Results: 126 subjects were enrolled, 70 females and 56 males, with a median age of 27.8±4.4 years. Most of subjects (84.1%) were born before the introduction of cART in 1996. After the transition to the adult care, 15.1% of subjects was lost to follow up, while 2.4% died. Median follow-up period (since patients were followed in the adult care) was 12.7 ±10.1 years. At 18 years of age, 52/126 (44.4%) subjects had HIV-RNA >50 cp/ml, 47/126 (38.2%) had a CD4 <500/mm3 and 78/126 (67.2%) a CD4/CD8 ratio <1, thus a great part of subjects (90/126; 76.3%) reached adult age with nOC.
For subjects reaching adult age in nOC, overall probability of staying in that condition during follow-up was 89% (85.8 -91%), while probability of migration from nOC to OC was 11% (8.8-14%).
Subjects presenting OC at 18 years had a probability of preserving that state of 70% (62.6-77%) and a probability of migration to nOC of 30% (23.3-37%).
Probability of a status change from nOC to OC was improved in patients with a CD4/CD8 ratio ≥1 at 18 years of age [Hazard Ratio, HR, 7.70 (95% CI 4.23-14.04)]. On the contrary the presence of at least one AIDS event strongly reduced this probability [HR 0.09 (0.03-0.30)]. Moreover, the probability of a status change overtime from OC to nOC was increased in those with a HIV RNA ≥50 cp/ml at 18 years of age [HR 6.13 (3.04-12.36)] and reduced in those with CD4/CD8 ratio ≥1 at 18 years of age [HR 0.49 (0.26-0.92)].
Other variables analyzed as gender, presence of resistance associated mutations (RAMs), hepatitis and syphilis coinfections and non-AIDS comorbidities did not predict any migration from a state to the other one.
Conclusions: Our study shows that only a small proportion of subjects with HIV VT reached the adult age with OC, and that transition to the adult care with a compromised viro-immunological state represents a severe negative driver for future improvement of viro-immunological condition. CD4/CD8 ratio remain a strong predictor of viro-immunolgical condition and its modifications during follow-up.

Basic science and immunology

OC 38 IMMUNOLOGICAL RECOVERY IN T-CELL ACTIVATION AFTER DAA TREATMENT AND SVR IN HIV POSITIVE SUBJECTS WITH CHRONIC HEPATITIS C

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Introduction: HIV/HCV-co-infected patients have higher levels of activated CD4+ and CD8+ T-cells (HLA-DR+ and CD38 + co-expression) as compared to patients HCV-mono-infected, HIV-mono-infected and healthy controls. Little is known about the effect of HCV clearance in HIV/HCV-co-infected subjects on CD4+ and CD8+ T-cell activation.
Methods: We investigated the changes in immune parameters of T-lymphocytes from pre-DAA therapy to post-SVR among HIV+ patients with chronic hepatitis C. Repeated measurements of activated CD4+ and CD8+ T cells were analyzed by flow cytometry from 16 months before DAA therapy to up to 16 months after. All patients with at least one measure before and after DAA therapy were included. A general linear model for repeated measurements was used to estimate the mean outcome at each time-point and changes between time-points.
Results: We analyzed 270 PLWHIV successfully treated with DAAs. They were mostly males (81.5%), of Italian origin (98.5%) and having intravenous drug use as main risk factor (79.6%). Their median age at HIV diagnosis was 27 years (IQR 23-35), while the median age at DAA treatment was 52 years (IQR 49-55).
Before DAA treatment the CD4+; CD8+; CD4+CD38+HLA-DR+ and CD8+CD38+HLA-DR+ median counts were: 648 cells/mcL (IQR 431-856); 839 cells/mcL (IQR 577-1148); 1.2% (IQR 0.8-1.9) and 4.35% (IQR 2.6-8.1). After DAA treatment CD4+ raised to a median of 679 cells/mcL (IQR 477-932; P = 0.003); CD8+ raised to 908 cells/mcL (IQR 581 -1274; P = 0.004) and CD4+CD38+HLA-DR+ and CD8+CD38+HLA-DR+ median values dramatically lowered to 0.8% (IQR 0.6-1.2; P < 0.0001) and 2.8% (IQR 1.6-4.9; P < 0.0001), respectively (see figure).
The relevant factor is that the reduction of T-cell activation was evident soon after DAA treatment at SVR, but persisted over time (figure). As an example,CD8+CD38+HLA-DR+ median counts were 3.8% (IQR 2.5-6) soon after SVR and 3.5% (IQR 2.1-9.8, P = 0.77) 16 months after SVR (figure).
Conclusion: This longitudinal study shows that HIV/HCV co-infected patients treated with DAAs and obtaining SVR have continued improvements in immunological recovery in T-cell activation, highlighting a novel long-term clinical benefit of HCV clearance on morbidity.

Basic science and immunology

OC 39 HIGHER FREQUENCY OF CD4+PD1+ T CELLS AND INTERFERON-STIMULATE GENES ARE ASSOCIATED TO A DECREASE IN CD4+ TREG LEVELS IN HIV-1 INFECTED PATIENTS

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Background: The relationship between CD4+ T cell exhaustion, regulatory T cells (Tregs) and type I interferon (IFN-I) response is not well characterized during HIV-1 infection. Our aim was to evaluate whether expression of PD-1 on CD4+ T cells was associated with an alteration of the distributional profiles of CD4+CD25+FOXP3+ (CD4+ Tregs) and interferon (IFN) gene response in long term antiretroviral therapy-experienced HIV-1 male positive patients.

Material and Methods: Peripheral blood mononuclear cells of HIV-1 male positive patients (n=30) and age and gender matched healthy subjects (n=20) were examined. In order to perform immunophenotype analysis, PD-1+ expression within the total gate of CD4+ T cells and CD4+ Treg expressing CD25+ FOXP3+ frequencies were evaluated by multiparametric flow cytometry. The RNA copy numbers of FOXP3 and IFN stimulated genes (ISG56 and GBP1) were measured by quantitative RT/TaqMan assays.

Results: CD4+ T-cell counts of HIV-1 positive patients at enrolment ranged from 270 to 1300 cells/mm3 blood and plasma viral load was <37 HIV-1 RNA copies/ml. Levels of CD4+ T cells expressing PD-1+ in HIV-1 infected patients were higher compared to that of healthy donors ($p<0.005$). Moreover, the frequency of CD4+PD-1+ T cells in HIV-1 infected patients correlated with the duration of antiretroviral treatment ($p<0.05$, $r=0.47$). By contrast, CD4+ Treg percentage was reduced in HIV-1 positive patients as compared to healthy controls ($p<0.005$). A negative correlation was recorded between the frequency of CD4+ Treg and mRNA levels of FOXP3 ($p<0.05$, $r=-0.601$) in HIV-1 positive patients. Of note, CD4+ Treg levels correlated negatively with the age in elderly patients ($p<0.005$, $r=-0.7906$). Median values analysis of IFN-stimulated genes indicated that HIV-1 infected patients exhibited an increased gene expression of ISG56 and GBP1 compared to healthy subjects ($p<0.005$).

Conclusions: Overall this study indicated that increased blood levels of CD4+ PD-1+ T cells are associated with a reduction of CD4+ Tregs frequencies expressing FOXP3 and an higher gene expression of IFN stimulated genes in treated HIV-1 male positive patients. This data suggest that immune T exhaustion, paucity of CD4+ Tregs and a dysreguation of antiviral immunity could be involved in the immunopathogenesis of HIV-1 infection.

Basic science and immunology

OC 40 MACROPHAGE TRANSCRIPTOME PROFILING UPON CCL2 NEUTRALIZATION IDENTIFIES AN ASSOCIATION BETWEEN ACTIVATION OF ANTIVIRAL RESPONSES AND HIV-1 RESTRICTION

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Background: Whilst CD4+ T cells are the main target of HIV-1, macrophages are also infected in vivo and contribute to viral persistence in patients undergoing combined antiretroviral therapy. These cells produce high levels of the pro-inflammatory chemokine CCL2, either constitutively or following HIV-1 infection. We previously found that exposure of monocyte derived-macrophages (MDMs) to CCL2 neutralizing antibody (Ab) causes a strong inhibition of HIV-1 replication affecting post-entry steps of the viral life cycle. This study aimed at a deep characterization of the cellular factors and pathways modulated by CCL2 blocking in MDMs and potentially involved in the restriction of HIV-1 replication.
Material and methods: Three RNA-seq datasets were generated from total RNA samples extracted from MDMs treated or not with anti-CCL2 or control Ab for 4 or 20 h (dataset 1), 4 h (dataset 2), and 4 h before HIV-1 infection for 1 or 4 days (dataset 3). Reads were aligned to hg19 and the differentially expressed genes were identified using DESeq2. DAVID and TRRUST were used for functional analysis. Reads not mapped to hg19 were aligned to the HIV-1 genome to quantitate viral transcripts. Microarray miRNA profiling was performed on MDMs from 3 additional donors, treated or not with anti-CCL2 or control Ab for 4 h. Potential regulatory networks among genes and miRNAs were identified by bioinformatics/literature search. The expression profile of some miRNAs/transcripts was confirmed by quantitative RT-PCR on samples used in RNA-seq/microarray or obtained from other donors.
Results: Early exposure to CCL2 neutralizing Ab profoundly affected the MDM transcriptome. Functional annotation clustering of the upregulated genes identified 2 clusters enriched for molecular pathways related to antiviral defense and immune response, comprising several IFN-stimulated genes and restriction factor coding genes. Transcripts in the clusters were enriched for RELA and NFKB1 targets, suggesting the activation of the canonical NF-kB pathway as part of a regulatory network involving miR-155 up-regulation observed following CCL2 neutralization. Moreover, while HIV-1 infection caused small changes to the MDM transcriptome and did not induce a type I IFN signature, CCL2 blocking restored the activation of the host innate response in infected cells and potently inhibited viral gene expression. Notably, an inverse correlation was observed between expression levels of the restriction factors APOBEC3A, OAS3 and EIF2AK2 and of viral transcripts.
Conclusion: Collectively, these findings highlight an association between activation of innate immune pathways and inhibition of HIV-1 gene expression upon CCL2 blocking in MDMs and identify this chemokine as an endogenous factor contributing to the deficient macrophage response to HIV-1. Therapeutic targeting of CCL2 may thus strengthen host innate immunity and restrict HIV-1 replication.
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Basic science and immunology

OC 41 HIGH FREQUENCY OF MYELOID DERIVED SUPPRESSOR CELLS IN IMMUNOLOGICAL NON RESPONDERS: POSSIBLE INVOLVEMENT IN CD4 T CELL RECOVERY

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Background: Myeloid Derived Suppressor Cells (MDSC) are expanded during HIV-1 infection and correlated with disease progression. In primary HIV infections, we previously demonstrated that successful ART failed to decrease MDSC frequency after 48 weeks, their frequency inversely correlated with CD4 T cell number, and these cells were able to affect the expansion of early progenitors from hematopoietic stem cells. Aim of the present work was to evaluate whether ART treatment duration and response are associated with MDSC modulation.
Methods: Fifty-eight patients with chronic HIV infection under ART from one to more than ten years were enrolled. Five individuals were virological non responders (VNR, HIV RNA>50 copies/ml), and eleven were immunological non responders (INR, CD4 T cell count<350/µl). Healthy donors (HD) were enrolled as control. Circulating MDSC frequency, T cell differentiation and activation profile were evaluated by flow cytometry.
Results: As previously observed, despite ART initiation, polymorphonuclear MDSC frequency was higher in HIV patients compared to HD (median=4.5 IQR= 3.3-9.59 vs. median=0.9, IQR=0.5-1.3 respectively, p<0.0001). Moreover, when grouped based on ART duration (1-2, >2-5, >5-10, >10 years) no differences were found in PMN-MDSC percentage, suggesting that long lasting effective ART failed to reduce circulating MDSCs. Grouping HIV+ patients in Responder (R), VNR, and INR, we observed that in all HIV+ groups MDSC frequency was higher than in HD. Interestingly, we observed that the INR had the highest MDSC frequency: in particular, a significant difference was found between R and INR (median=3.74 IQR=3.1-9.6 vs. median=15.99 IQR=4.8-23.8 respectively, p=0.004). Of note, MDSC from VNR were comparable to R (median=3.74 IQR=3.1-9.6 vs. median=5.6 IQR=4.4-8.3 respectively), indicating that virological failure is not the driver of MDSC maintenance. As expected, an inverse correlation was found between MDSC and CD4 T cell number (r=-0.42, p=0.001), while a positive one was observed with CD4 T cells expressing HLA-DR (r=0.43, p=0.001). Moreover, a weak but significant inverse correlation was observed between the frequency of MDSC and naïve CD4 T cells (r=-0.29, p=0.031), that was stronger when only INR were analyzed (r=-0.62, p=0.047).
Conclusion: MDSC persist higher in HIV+ treated patients than HD also after long lasting effective ART, and is associated to a worst CD4 T cell recovery, indicating a new player in the regulation of CD4 T cell replenishment after ART-induced HIV clearance

Basic science and immunology

OC 42 HIV-BINDING SPECIFICITY AND -NEUTRALIZING POTENCY AFTER ART INTERRUPTION IN CHRONICALLY HIV-1 INFECTED SUBJECTS WITH LONG-LASTING VIROLOGICAL SUPPRESSION (APACHE STUDY).

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Background: Control of HIV-1 would require the elicitation of broadly neutralizing antibodies (bNAbs), which are directed to conserved epitopes on the HIV envelope spike and therefore neutralize the majority of HIV isolates. Few studies have investigated chronically infected individuals after ART interruption (AI) and in particular little is known on the role of HIV specific antibodies involved in the viral control after AI. The aim of this study was to investigate the modulation of HIV specific antibodies such as binding (Babs) and neutralizing antibodies (Nabs) in 9 patients who underwent AI.
Methods: Prospective, open-label, single arm, non-randomized, proof-of-concept study (NCT03198325) on HIV-1 chronically infected subjects, followed at San Raffaele Hospital, with HIV-RNA <50 cps/mL for ≥10 years, CD4+ cell count >500 cells/µL and HIV-DNA <100 copies/106PBMC (real-time PCR, ABI Prism 7900). Enrolled patients were intensively followed-up with weekly viral load monitoring. The ART regimen in use at the time of AI was resumed when viral rebound was confirmed (CVR, 2 consecutive HIV-RNA >50 cps/mL). We evaluated the levels of both Babs and Nabs at 3 different time points: time of AI, time of CVR and time of viral re-suppression after ART resumption. To define bAbs specificity, ELISA with solid phase of recombinant gp160, gp120 and gp41 was used. To evaluate neutralization potency by sera, 5 different viruses were used: two Tier 1A (SF162-R5 tropic and MN-X4 tropic), one Tier 2 Clade B (QH0692.42) and two Tier2 clade C (Du172.17 and Zm214M.PL15). To establish whether the neutralizaton was due to HIV specific antibodies, purified IgG fractions with their subclasses (IgG1, IgG2, IgG3 and IgG4) from the 4 patients with highest levels of neutralization were used to block SF162 infection.
Results: All subjects had CVR after AI at a median time of 21 days (14-56) and restarted ART. HIV-RNA at viral rebound was 3.38 (2.23-6.16) log10copies/ml and 4.84 (3.47-6.47) log10copies/ml at CVR. After ART resumption, all the enrolled subjects achieved HIV-RNA<50 copies/ml in 42 days (21-98). We observed a strong increase of either Babs (both IgG and IgA to all env proteins tested) or Nabs titers from AI to viral re-suppression in one patient, who was the only one to have CVR at 56 days after AI. Very interesting is that, in this patient, Babs and Nabs was specifically due to both IgG1 and IgG4 subclasses directed to gp120 antigen only.
Conclusion: Modulation of both Babs and Nabs titers was shown in our patients following ART interruption and subsequent resumption. Of interest is that the highest Babs and Nabs titers were associated with a longer time to virological rebound after ART interruption in one patient. In addition, the presence of systemic antigen specific IgG1 and IgG4 suggests that antibody profile can provide insight into whether the antibody response is coordinated in response to pathogen.

Clinical HIV

OC 43 MACHINE LEARNING STATISTICAL APPROACH TO IDENTIFY HIV CO-INFECTED PATIENTS WITH ASYMPTOMATIC NEUROSYPHILIS

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Background: People living with HIV (PLWH) are at increased risk of asymptomatic neurosyphilis (ANS). The guidelines suggest performing lumbar puncture (LP) in asymptomatic PLWH in cases of: late syphilis (acquired > 1 year previously) and CD4+ cells ≤ 350/mm3 and/or a serum Venereal Disease Research Laboratory/Rapid Plasma Reagin (VDRL/RPR) title ≥ 1:32, "serological failure" after syphilis therapy, and the use of alternative treatment for syphilis. However, this practice varies widely among clinicians. The aim of this study was to provide a novel machine learning statistical approach to verify the accuracy of the guideline's criteria for the indication of LP in the suspicion of ANS, in a cohort of PLWH.
Method: We retrospectively analyzed 455 HIV-infected patients with diagnosis of late syphilis stage from 2014 to 2019. LP to determine RPR and Treponema Pallidum Hemagglutination Assay (TPHA) in cerebrospinal fluid was offered to all participants with at least one of the following conditions: CD4+ ≤350 cell/µL and/or serum RPR ≥1:32, refusal to start antiretroviral therapy or lack of serological response after syphilis treatment. We first evaluate the number of LPs required to diagnose a single case of ANS and then a machine learning approach with a cohort decision tree using a time-homogeneous Markov model (entropy) to predict asymptomatic neurosyphilis cases. Decision tree was used to explore diagnostic indicators, and ROC analysis was performed to assess diagnostic accuracy.
Results: Among 93 episodes in which LP was performed, neurosyphilis was diagnosed in 15% of cases (n=14). Out of 93 patients, 88 (94.6%) were male, 84 (90%) were virologically suppressed with VL <50 cp/ml and 78 (83.9%) had CD4+ ≥350 cell/mm3. The number of LP necessary to identify a case of ANS in our cohort was approximately 7. ROC analysis was performed to identify the predictors of accuracy in the diagnosis of ANS (Fig. 1A). For threshold combining CD4 +≤350 cells/mm3 and/or RPR ≥1:32, sensitivity was 63% and specificity 83%, with a diagnostic accuracy of 83%; if we used threshold combining CD4+≤350 cells/mm3 and/or RPR ≥1:32 or TPHA ≥ 1:1280 the sensitivity was 64% and specificity was 86%, with a diagnostic accuracy of 85%. Using machine learning approach with decisional tree in our cohort, we found that adding serum TPHA ≥ 1:1280 to CD4+ count ≤350 cell/µL and serum RPR ≥1:32 could reduce the LP necessary to identify a case of ANS to approximately 3, decreasing the LPs performed from 93 to 35 with an increase of the percentage of patients with diagnosis of ANS up to 37% (Fig. 1B).
Conclusion: Machine learning statistical approach could help the clinicians to improve the selection of asymptomatic patients to whom to propose lumbar puncture with a consequent reduction of the number of LPs necessary to identify a case of ANS. Further investigations and larger databases for statistical model training are needed to verify the advantages of this approach

Clinical HIV

OC 44 BODY COMPOSITION CHANGES IN HIV: DO INSTI MATTER?

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Objectives: The aim was to assess weight gain (WG) and body composition changes in people living with HIV (PLWH) switching to INSTI-based regimens in comparison to INSTI-naïve patients. We assessed WG impact on incidence of co-morbidities.

Methods: In a prospective observational study, we included ART-experienced INSTI-naïve PLWH from 2007 to 2019. Patients were divided in two groups: patients who remained INSTI naïve and patients who switched to an INSTI regimen either in 3-drugs regimens (3DR) or in 2-drug regimens (2DR). The groups were matched for sex, age, baseline BMI and switch duration. WG was defined as an annualized increase of 7% in BMI. Predictors of WG were analyzed in a multivariable regression model comparing INSTI naïve 3DR to INSTI naïve 2DR, and patients who switched to INSTI either in 3DR or 2DR.

Results: A total of 1158 PLWH (68.7% males) were analyzed at baseline and at 4 years (2.23) follow-up. Patients who switched to INSTI showed significant changes in age, BMI, waist circumference (WC), fat-free mass index (FFMI), appendicular skeletal muscle index (ASMI) and leg fat % ($p<0.001$). Mixed lipodystrophy, visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) did not change over time. INSTI naïve showed significant changes in age, BMI, WC, FFMI, ASMI, leg fat %, sarcopenia, VAT and SAT. Higher prevalence of WG was observed in patients who switched to INSTI (68.9% vs. 31.2%, $p<0.001$). Figure describes independent predictors of WG. PLWH who experienced WG had higher incidence of T2DM (1.97 vs 1.22), CVD (1.67 vs 0.53), HTN (13.2 vs 7.07), CKD (6.82 vs 3.49), COPD (3.4 vs 1.06) cases per 100 patient-year, with the latter being the only statically significant.

Conclusions: A significant BMI increase was observed two times more frequently in patients who switch to INSTI, regardless of 3DR or 2DR regimens. TAF/TDF contributed to WG in PLWH switching to a 3DR INSTI regimen but not never INSTI. Clinical relevance of this phenomenon needs to be explored in larger cohorts. Weight gain should be part of counselling with PLWH switching to INSTI.

Clinical HIV

OC 45 RISK OF WEIGHT GAIN (WG) ACCORDING TO TYPE OF SWITCHING STRATEGY IN A LARGE COHORT OF HIV-INFECTED INDIVIDUALS WITH STABLE SUPPRESSED HIV-RNA

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Background: There is rising evidence that INSTIs may be associated with WG in ART-naïve patients. Data on WG in virologically suppressed patients switching to INSTIs are still limited.
Methods: ART-treated patients in the Icona Foundation Cohort with stable viral suppression (<200 copies/mL), no history of virological failure who switched for the first time over 2009-2019 to cART regimen with anchor drug belonging to a drug class (INSTI or PI/b or NNRTI) to which they were currently naïve (baseline), were included. Primary endpoint was to evaluate WG defined as an increase of ≥3 kg or ≥5 % or BMI over 2 units from baseline (Outcome 1). A more stringent WG definition (≥10% weight increase or BMI ≥30 from baseline), identifying "greater gainers" and treatment-emergent obesity, was also used (Outcome 2). Sensitivity analysis, excluding patients with BMI≥30 or ≤18.5 at baseline or receiving TAF, was performed. Follow-up accrued until to change/stop of drug class or last observation. Inverse Probability Weighted Cox regression was used to estimate causal HR of WG, adjusting for the main confounders (see Table).
Results: 720 patients (male 79%; Caucasian 94.5%) included, 348 (48%) switching to INSTI, 138 (19%) to PI/b and 234 (33%) to NNRTI. WG occurred in 320/720 patients by Outcome 1 and in 109/660 by Outcome 2, with IR of 24.4 [95%CI 21.9-27.2] and 7.3 [6.0-8.8] per 100 PYFU, respectively. Causal HR of WG for INSTIs versus other drug-classes did not show any significant difference (Table). In the sensitivity analysis, only using Outcome 2, an increased risk of WG for INSTI compared to NNRTI was observed (Table).
Conclusions: No clear evidence of WG after switching to INSTIs was observed in overall population. However, an increased risk of greater WG (>10%) or obesity was found in those switching to INSTIs compared to NNRTI when considering normal/overweight patients not receiving TAF.

Clinical HIV

OC 46 IMPACT OF ANTIRETROVIRAL THERAPY ON GUT CD4 T CELLS ACTIVATION: DIFFERENCES BETWEEN NAÏVE AND LONG-TERM TREATED HIV-1 INFECTED PATIENTS

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Background: A rapid and substantial damage of the gastrointestinal tract occurs during Human Immunodeficiency Virus -1 (HIV-1) infection, with a massive depletion of T helper type 17 (Th17), a CD4+ T cell subset involved in normal mucosal defense and epithelial barrier maintenance. This loss is linked to chronic levels of immune activation, that persist despite antiretroviral therapy (cART).
Material and Methods: Twentytwo male HIV-1-infected individuals, eleven undergoing long-term fully suppressive cART (>5 years)(group A) and eleven HIV-1 cART naïve patients (group B) were enrolled in this study. Lamina Propria Lymphocytes (LPL) were freshly isolated from gut biopsies collected by pancolonoscopy. The expression of immuno-activation markers CD38 and HLADR and IFN-gamma or IL-17A in CD4+ T-Cell, Th1 and Th17 respectively, was evaluated by multiparametric flow cytometry analysis and expressed by median frequencies. Comparisons among patient groups were performed using the Mann–Whitney test. The level of significance was set at 0.05.
Results: The cART-naïve HIV+ patients (median age: 46; IQR 39-49) had a detectable plasma viral load >50 copies/ml, with a CD4+ T cell count ranged from 277 to 621 cells/mm3, while ART-treated HIV+ individuals (median age: 48; IQR 32 -56) were virologically suppressed and showed a peripheral blood CD4+ T cell count ranged from 708 to 1350 cells/mm3. A statistically significant reconstitution of intestinal CD4+ T cells percentage was observed in Group A (median 11%; IQR 7.5–16.1) as compared to Group B (median 46.12%; IQR 42.4–51.2) (p <0.0001). Regarding the effects of antiretroviral treatment on immune activation levels, our findings indicated that the frequencies of CD4+ T cells expressing CD38+ and/or HLA-DR+ decreased in Group A compared to Group B [CD4+ CD38+: 6.5% versus 40% (p =0.005); CD4+ HLA-DR+: 5.8% versus 17.8% (p = 0.001); CD4+ CD38+ DR+: 9.2% versus 1.3% (p=0.004)](Fig.1). Interestingly, data, obtained from a comparison of Th1 and Th17 T cells frequencies between cART-treated and naïve patients, highlighted no significant differences between the two groups.
Conclusions: Although long-term antiretroviral therapy resulted in a significant increase in the levels of total CD4+ T-cells in gut mucosa and in decline of T-cell activation, it fails to restore the frequencies of Th1 and Th17. To this extent, cART may not be effective on the complete recovery of the gastrointestinal damage during HIV-1 infection

Clinical HIV

OC 47 RESIDUAL INFLAMMATION AND CD4/CD8 RECOVERY AFTER SWITCHING TO DUAL THERAPY

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Background: Dual cART has set up a new paradigm in HIV treatment and is now appointed by guidelines. However, a concern endures on its ability to control residual inflammation, in turn affecting immune recovery. We investigated whether the level of plasma pro-inflammatory markers, measured early after switch, might result in differences in CD4/CD8 changes 12 months later, in patients switching to dual (DT) as compared to triple (TT) therapy.

Methods: Inclusion criteria: patients (pts) from Icona, 3-drugs cART regimen from ART-naïve, switching to DT or different TT after HIV-RNA suppression, maintenance of switch regimen for at least 12 months (T12), 1 stored plasma sample between 2-6 months from switch. Lab analyses: sCD14, CRP, IL6 (Luminex). Statistical analyses: multivariable linear regression: association between T12 change in CD4/CD8 and inflammatory markers at 2-6 months from switch; Poisson regression: association between biomarkers and the confirmed reduction of ratio<0.45, in pts with ratio>0.45 at switch.

Results: We included 407 pts; median (IQR) CD4 592cell/mmc (410-797), duration of HIV-RNA suppression 24 moths (11-41). 376 (92%) pts switched to a different triple regimen, 31 (8%) to a dual therapy. Baseline epidemiological, clinical and HIV-related characteristics were comparable between the two groups. Inflammatory markers were measured at a median (IQR) of 3.6 months (2-5) after switch. Patients switching to dual therapy featured higher plasma IL-6 (2vs1.6pg/ml, p=.039) and CRP (3.5vs1.4 g/ml; p=.061) early after switch, and lower CD4/CD8 rise at T12 (0.04vs0.09; p=.031) versus pts switching to triple therapy.

The multivariable linear regression showed no association between inflammatory markers early after switch and T12 CD4/CD8 ratio, when patients are pulled together (Fig1a) and when patients are separated according to switch regimens (Fig1b-c), with the exception of a modest association with high CRP in dual therapy group (Fig1c). We next explored whether inflammatory markers might predict the CD4/CD8 descent to <0.45, finding a modest association with high level of IL-6 (>1.7pg/ml, p=.052), albeit not reaching statistical significance in the multivariate model (p=.082; Fig1d).

Conclusions: In our cohort of cART-treated HIV+ patienst, switching to dual therapy seemed to disturb 12-month CD4/CD8 stability, seemingly associated with higher CRP. Interestingly, high circulating IL-6 early after switch seemed to exert a modest independent effect on the reduction of 12-month CD4/CD8 to below 0.45, supporting the need to better elucidate the potential role of residual inflammation early upon cART switch as possible predictor of subsequent immune failure, mainly in the setting of dual therapy.

Clinical HIV

OC 48 EVALUATION OF THE IMPACT OF RESISTANCE ON VIROLOGICAL EFFICACY OF STR REGIMENS AND EMERGENCE OF RESISTANCE AT VIROLOGICAL FAILURE

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Background: Despite the increasing use of single tablet regimens (STRs), few data from real life are available regarding potential impact of pre-existent drug resistance to each single drug. The study aimed to evaluate the impact of resistance in patients (pts) who start STR and the emergence of resistance at virological failure (VF).
Methods: We selected from the ARCA database treatment-naïve (G1), treatment-experienced aviremic (G2) and viremic (G3) HIV-1 infected pts genotyped from 2008 to 2019 for protease/reverse transcriptase and integrase (when available). Cumulative resistance associated mutations (RAMs) before STR start and cumulative STR genotypic susceptibility score (cGSS=3: full susceptibility; <3: reduced susceptibility to at last 1 drug) were evaluated according to the Stanford algorithm (HIVdb version 8.9-1). The impact on VF of pre-treatment resistance to at least 1 component included in the following STRs was evaluated: EFV/FTC/TDF, FTC/RPV/TDF, FTC/RPV/TAF, EVG/COBI/FTC/TDF, EVG/COBI/FTC/TAF, ABC/DTG/3TC. Survival analysis (Kaplan-Meier curves and Cox regression) was used to assess the probability and predictors of VF. In pts who failed STR and for whom a genotypic resistance test at VF was available, the emergence of RAMs was also evaluated.
Results: Overall, 3918 pts (73.1% males, median [IQR] age 44 [36-52] years) were included, of whom 678 (17.3%) in G1, 2309 (58.9%) in G2, and 931 (23.8%) in G3 (Table). Viral subtype was reported B in 2928 (74.7%) pts. Zenith viral load (VL) was 5 (4.3-5.5) cps/mL. Before STR start, RAMs were present in 82 (12.1%) pts in G1, 580 (25.1%) pts in G2 and 279 (30.0%) in G3. Median cGSS was 3 (IQR 3-3) in G1, 3 (IQR 2.5-3) in G2, 3 (IQR 2.5-3) in G3. By one year of STR treatment, VF probability was higher in pts with cGSS <3 than in those with cGSS =3 both in G2 (respectively 6.9% and 4.5%, p=0.003) and in G3 (respectively 22.5% and 10.5%, p<0.001), without significant difference in G1. Adjusting for confounder factors, at multivariable analyses, the risk of VF was predicted by zenith VL (per 1 log increase; aHR [95% CI] 1.47 [1.01-2.15], p= 0.047) in G1, by female gender (vs. male; 1.94 [1.01-3.72], p=0.046) in G2 and by CD4 cells count nadir (per 100 cells increase; 0.83 [0.74-0.94], p=0.003) and previous use of PI (per 1 drug increase; 1.74 [1.07 -2.81], p=0.024) in G3. Among pts who failed STR, only in those in G3 exposed to EFV/FTC/TDF we observed a significant selection of RAMs: K103N (pre-STR= 15.7%, post-STR =56.9%, p<0.001) and M184V (pre-STR =19.6%, post-STR =47.1%, p<0.001).
Conclusions: Despite high virological efficacy of STR regimens, higher VL and the reduced predicted susceptibility score to at least 1 drug seems influence virological efficacy of STR. In treatment-experienced viraemic pts who started EFV/FTC/TDF, an increment of K103N and M184V mutations was observed. Conversely, no significant increment of mutations was observed in naïve and treatment experienced aviraemic pts.

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OC 49 SARS-COV-2 INFECTION IN PLWHIV: A LARGE SINGLE CENTER COHORT

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Background: Information about SARS-CoV-2 infection in PLWHIV is limited to a few case-series and even less, quite small cohorts exclusively dealing with COVID-19 affected patients.
Methods: In this observational prospective study, we included PLWHIV (aged ≥18 years) with confirmed SARS-CoV-2 infection independently by the presence of COVID-19 disease and compared them with PLWHIV negative for SARS-CoV-2. Confirmed COVID-19 was defined by positive RT-PCR or a positive serological test. Suspected cases were individuals with clinical and radiological findings compatible with COVID-19, but whose RT-PCR results were inconclusive and without any other proven cause.
Results: We identified 70 cases of SARS-CoV-2 infection either by RT-PCR test (16 cases, 23%), serology (48, 69%) or clinical grounds (6, 8%). We compared these cases with 104 mostly asymptomatic PLWHIV who tested negative for SARS-CoV-2 RT-PCR and/or serology. No significant difference was observed between SARS-CoV-2 positive and negative patients for age distribution, gender, risk factor for HIV infection, time with HIV infection, nadir CD4 cell counts, type and number of co-morbidities, current CD4 and CD8 counts and type of anti-HIV therapy (see table). Positive patients presented with a median of 3 symptoms (IQR 1-3). The most common symptoms were fever (78.6%), dyspnoea (32.9%), anosmia and ageusia (30%) non-productive cough (224.3%) and fatigue (21.4%). Ten patients (14.3%) were, however, completely asymptomatic. The severity of COVID-19 was graded according to the worse type of respiratory support needed. Fifty-4 subjects (77%) did not receive oxygen support, in 5 (7%) it was limited to an oxygen mask and 11 (16%) were put on C-PAP or intubated. If no baseline characteristic was linked to the risk of infection, age increased with the increasing severity of COVID-19. Mean age was 52.6 years (95%CI 50-55) for patients not receiving oxygen, 52.9 years (95%CI 46-58) for those with oxygen mask and 61.3 years (95%CI 56-67) for the worst cases (P =0.006). COVID-19 had a fatal outcome in 4 (6%) subjects. Factors significantly associated with death included age, number of co-morbidities, and a lower current CD4 count (see table). According to a binary logistic model however, only the first two variable retained statistical significance. The odds ratio for age (1 year increment) was 1.237 (95%CI 1.027-1.489; P = 0.012) and for the number of co-morbidities was 2.659 (95%CI 1.105-6.396; P = 0.029).
Conclusions: Although no HIV-related characteristic is linked to the risk of acquiring SARS-CoV-2 infection, PLWHIV should not be considered protected from SARS-CoV-2 infection or as having lower risk of severe disease. Indeed, those with low CD4 cell counts might have worse outcomes than individuals with restored immunity. Infection may be asymptomatic in a large proportion of subjects and this variable must be counted when epidemiological studies are implemented in PLWHIV

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OC 50 NEWLY DIAGNOSED HIV INFECTIONS AT A COUNSELING AND TESTING SERVICE DURING COVID-19 PANDEMIC

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Introduction: in response to COVID-19 pandemic, lockdown measures, including the deferral of non urgent outpatient care visits, have been implemented in most Countries, including Italy. These measures could have had a significant impact on HIV at-risk population in terms of behaviors as well as access to early diagnosis and antiretroviral therapy.
Aim of the report is to describe new HIV diagnoses linked to care during the lockdown period at the HIV Counseling, Testing and Referral Centre (CTC) of the National Institute for Infectious Diseases (INMI) "L. Spallanzani" in Rome, Italy, with a comparison to the same period of the previous year.
Methods: the INMI "L. Spallanzani" in Rome, Latium, has been the first Italian hospital to admit and manage patients affected by COVID-19 on January 29, 2020 peaking more than two hundred in-patient daily presences during all March 2020. The HIV CTC of the Institute represents the AIDS Reference Centre in Latium region.
During the COVID-19 lockdown the CTC continued to offer free direct-access, although limiting some face-to-face services, while ensuring the application of evidence-based measures to reduce possible SARS-CoV-2 transmission (patients' triage, physical distancing, universal masking, hand hygiene, personal protective equipment for staff).
We did a casenote review of all individuals newly diagnosed with HIV at our CTC from March 10 to May 18 2020 and from March 10 to May 18 2019. Primary HIV infection(PHI) was classified according to Fiebig criteria, from stage I to stage V
Results: Of 383 persons referring to our CTC during the 2020 study period, 15 (3.9%) were newly diagnosed with HIV infection. In the same period of the previous year, of 1033 persons referring to our CTC, 32 were new HIV diagnoses (3.1%)(p=0.44).
Comparison between the main epidemiological, clinical, virological and immunological characteristics of patients newly diagnosed with HIV in 2019 and in 2020 is shown in Table 1.
5 patients were diagnosed with primary HIV infection (PHI) in 2019 (15.6%) and 4 in 2020 (26.7%) (p=0.43). The patients with PHI observed in 2020 were all Italian males, reporting sex with men (MSM)(Table 2).All patients reported clinical symptoms, and fever was the most common one.
Conclusions: Although the proportion of new HIV diagnosis and of PHI in 2020 were not statistically different from the previous year, it was noteworthy that they were diagnosed in the midst of the lockdown and therefore of the social distancing measures and stay-at-home recommendations. These findings may also suggest a low risk perception not only for acquiring HIV but even for SARS-CoV-2 infection, in vulnerable persons including members of HIV key populations like MSM, which may be at increased risk of both infections.
Increased efforts are imperative to assure direct-access to essential HIV prevention, counseling, testing and treatment services also where confinement measures are implemented in response to the COVID-19 pandemic

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OC 51 HIV AND SARS-COV-2 CO-INFECTION: EPIDEMIOLOGICAL, CLINICAL AND IMMUNOLOGICAL ASPECTS AMONG HIV-POSITIVE YOUNG INDIVIDUALS

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Introduction: To date, few data have been published on the spreading of SARS-CoV-2 among HIV-positive children and adolescent individuals. In this study, we report the epidemiologic, clinical and immunological profiles in a cohort of HIV-infected young patients, treated with antiretroviral therapy, followed at the Unit of Paediatric Infectious Disease at Sacco Hospital, Milan.

Methods: 86 HIV-infected young patients (36 M/50 F) were enrolled in the study. Real–time PCR was performed to detect SARS-CoV-2 on sputum and plasma samples were tested for anti-SARS-CoV-2-specific antibodies IgG (Euroimmun). RNA expression and quantification of genes involved in the anti-viral immune response was performed on PBMCs upon stimulation with SARS-CoV-2 antigens as well as with Aldrithiol-2-inactivated HIV (Quantigene Plex Gene expression assay). Secreted cytokines/chemokines were quantified on plasma and cell culture supernatants (Multiplex Cytokine Array).

Results: HIV-infection was vertically transmitted in all but 5 of the patients enrolled in the study. Mean age was 21.7 years (range 1-37 years); HIV-RNA < 20 cp/ml in 67 on 86 patients; the mean of CD4 T cells was 741 mm3 (range 187 -2554 mm3). All the HIV-infected patients were undergoing antiretroviral treatments with INI (41), PI (32), NRTI (1) or NNRTI (12). SARV-CoV-2 co-infection was documented only in 4 patients, 3 of whom were IgG seropositive and one resulted positive in sputum sample.

In the course of the lockdown, 14 patients declared not having stayed at home, principally for working reasons. Among them, only 2 resulted positive for SARS-CoV-2-specific IgG. None of them was hospitalized for coronavirus-related symptoms. HIV-infected SARS-CoV-2-positive subjects displayed an increase in MCP-1, IL-6, and IL-10 in comparison to SARS-CoV-2-negative patients both at RNA and protein level, ($p < 0.05$). Notably, the concentration of the same factors was upregulated following both SARS-CoV-2 and HIV-specific stimulation.

Conclusions: The low rate of SARS-CoV-2 infection (2 of 86 patients enrolled) could suggest a protective role of the antiretroviral therapy among HIV-positive young individuals. The immune activation profile of SARS-CoV-2 HIV-co-infected patients resembles the picture described in other SARS-CoV-2 HIV-negative subjects. Conversely, despite the presence of an immunocompromised background, the absence of severe clinical manifestations in SARS-CoV-2 HIV-co-infected subjects could be justify by the hyper production of IL-10 , which could play a role in the protection from detrimental immune activation

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OC 52 CLINICAL FEATURES AND OUTCOMES OF HIV PATIENTS WITH CORONAVIRUS DISEASE 2019

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Background: Little is known about the clinical outcomes of HIV patients infected with SARS-CoV-2. The aim of this retrospective study was to describe the clinical characteristics and outcomes of HIV-infected patients with a probable/proven diagnosis of SARS-CoV-2 infection who have been regularly followed up by our hospital.
Methods: We searched our database for HIV patients diagnosed as having probable or proven SARS-CoV-2 infection between 21 February and 20 April 2020. A diagnosis of probable SARS-CoV-2 infection was based on the presence of fever and respiratory symptoms, epidemiological risk factors (relatives or close colleagues with a proven diagnosis of COVID-19), and/or a chest X-ray or CT diagnosis of interstitial pneumonia; proven SARS-CoV-2 infection required a throat swab positive for viral nucleic acid.
Results: During the observation period, 47 HIV patients with proven or probable SARS-CoV-2 infection were identified. They were mainly males (76%) and had a mean age of 51±11 years. At least 80% receiving integrase inhibitor-based antiretroviral treatment and 11% a protease inhibitor-based regimen (11%); 42% were receiving a tenofovir-based regimen. Characteristics and symptoms are shown in Table 1. Twenty-eight patients (>50%) tested positive for SARS-CoV-2; the remainder were not tested mainly because they lived in the high-risk provinces of Bergamo and Brescia (Lombardy) but were isolated at home and cared for by their general practitioners. The COVID-19 diagnosis of the untested patients was based on their clinical symptoms and the presence of risk factors (13% were healthcare providers; 9% had been in close contact with SARS-CoV-2 positive working colleagues and 23% with SARS-CoV-2 positive relatives). Interstitial pneumonia was diagnosed by means of an X-ray in three cases, and ground-glass opacity was identified by means of CT in one. Thirteen of the 28 SARS-CoV-2 positive patients were hospitalised. Six had severe lung disease, two of whom required mechanical ventilation: one recovered and was discharged and the other (a 47-year-old overweight man without other co-morbidities) died. Another patient with CVD and a recent diagnosis of lung cancer died during hospitalisation. For comparative purposes, the crude mortality rate of the HIV-negative COVID-19 patients in our hospital (n=502, 67% males, mean age 61±16 years) is currently about 17%. Fewer than 50% of the patients were given potential anti-SARS-CoV-2 treatments, specifically hydroxychloroquine (17%), azithromycin (15%), lopinavir/ritonavir (11%); one was treated with tocilizumab and remdesivir, and one with toxicizumab alone.
Conclusions: As in the general population, the large majority of our patients were males, but their mean age was nearly 10 years lower than that observed in HIV-negative COVID-19 patients. Our findings suggest that HIV-positive patients with SARS-CoV-2 infection are not at greater risk of severe disease or death than HIV-negative patients.

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OC 53 ANTIBODY RESPONSES TO SARS -COV-2 IN PEOPLE LIVING WITH HIV (PLWH) IN UMBRIA

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Introduction: In Umbria, where over 880000 residents are living, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic has affected 1412 subjects (11-5-2020), causing 71 deaths. Currently there are 142 positive cases. People living with HIV (PLWH) can be considered a category at high risk of serious disease due to SARS-CoV-2 for the potential interactions between COVID-19, HIV, and other risk factors for COVID-19 complications such as diabetes and hypertension that are common in PLWH. The Day Hospital of Infectious Diseases Clinic of Perugia cares for about 800 PLWH, none of whom, until now, has been hospitalized for SARS-CoV-2 infection. Here we describe the prevalence of SARS-CoV-2 positive antibodies in PLWH attending our center.
Method: Since the beginning of "Phase 2", all PLWH who consecutively referred to our Day Hospital, have been offered a rapid test for qualitative detection of IgG and IgM antibodies to 2019-nCov (Rapid Test Cassette, Sensitivity and Specificity of 100% and 98% respectively). All patients signed the informed consent.
Results: One hundred fifty-seven out of 161 PLWH underwent rapid test for antibody to SARS-CoV-2, 4 subjects refused. Male gender (79.6%) and Caucasian ethnicity (85%) were mainly represented, median age was 53(24-84). Current smoking rate was 35%. The demographic and immuno-virologic characteristics of patients are shown in table 1. Four out of 157 (2.5%) PLWH tested positive for IgG antibodies to 2019-nCov, but negative to RT-PCR on naso-pharyngeal swab obtained the same day.
Conclusions: In this PLWH case series the prevalence of SARS-CoV-2 antibodies is quite low (2.5%).

Immunopathogenesis

OC 54 PSYCOSEXUAL HEALTH AND SYSTEMIC, MUCOSAL IMMUNE ACTIVATION AND IN HIV-INFECTED ART SUPPRESSED AND UNINFECTED WOMEN: EVALUATION OF BIOMARKERS AND ENVIRONMENTAL STIMULI

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Background: Despite successful ART, HIV infection in women remains a grave concern over the years in disproportionate ratios as compared to men . It is directly proportional to various reproductive and hormonal differences making women in general more vulnerable. It elicits an Immune response which can be monitored by analysing various factors such as biomarkers in the plasma, serum and vaginal lavage, mucosal immunity, sexual behaviour and other vaginal infections.
Aim: To evaluate the systemic and mucosal immuno-inflammatory status, the female sexual function (FSF) and generalized anxiety in a group of HIV positive women receiving successful HAART(CD4>200 mm^3 and VL<20) and comparing them to healthy women (HW). Methodology: We enrolled 53 subjects, 23 HIV Positive women on successful HAART and 30 Healthy women (HW) with no statistical differences in the age. Figure 1 shows inclusion criteria and the methods applied. Cytometry and Kit ELISA (R&D) were used for estimation of lymphocytes and all cytokines. The women were also tested for co-morbidities such as diabetes, blood pressure, HCV, cervical cancer etc. Statistical analysis was performed using PRISM 8.0.
Results: No differences in terms of CD4 in the 2 groups were observed. A higher CD4/CD8 ratio and CD8 cell count was observed in HW as compared to HIV + women
(respectively p=0.004, p=0.007). Plasma levels of the sCD163, CXCL-10, IL-1 , IL-6 and IL-8 were significantly higher in HIV women as compared to HW(p<0.001), while IL-6 and IL8 were lower in the VL of HIV women. Regarding PAP test, only an ASCUS in HD was found. Moreover, estradiol levels correlated to plasmatic CXCL-10 (r=-0.7, p=0.005) and vaginal CXCL-10 (p=0.02, r=-0.57). 50% of HIV women reported a FSFI compare to 26% of HW. We found an association with HIV positivity and sexual dysfunction (p=0.03). A significant difference between the two groups in the FSFI score (p=0.02) was found, particularly in sexual desire and lubrification. A positive correlation between level of testosterone and FSFI score only in HIV women was found (p=0.005; r= 0.56) where a a correlation between testosterone and age was also found (p=0.008, r=-0.52). Moreover, only in HIV group a correlation between testosterone and plasmatic sCD14 (p=0.03, r=0.53), CXCL-10 (p=0.04, r=-0.52), IL-6 (p=0.01; r=-0.51). The anxiety disorders was similar into the 2 groups: 27% in HIV positive and 25% in HW. Z-index was associated with orgasm domains (p=0.01; r=-0.4) and CD4+ T cells (p=0.02; r=-0.45).
Conclusion: In HIV positive women under a succesfull HAART a dissociation between plasma and mucosa's immune activation is observed with high plasma levels in plasma and decreased levels in mucosa enviroment. Femal sexual dysfunction seems to be associated to HIV positivity and 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

Immunopathogenesis

OC 55 INFLAMMATORY BURDEN IN PEOPLE LIVING WITH FOUR-CLASS DRUG RESISTANT HIV: DATA FROM THE PRESTIGIO REGISTRY

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Background: Four-class drug resistant (4DCR) people living with HIV (PLWH) are a fragile population with a 22% probability of AIDS- or non-AIDS-events or death for any cause over 48 months. No data on biomarkers of inflammation, immune activation, microbial translocation and T-cell exhaustion are available for this population.
Methods: Cross-sectional study on PLWH, on antiretroviral therapy (ART), classified into three groups:
- 4DCR (defined as at least intermediate resistance to NRTI, NNRTI, PI, INSTI) with HIV-1 RNA ≥50 copies/mL (group 1; n=30);
- 4DCR with HIV-1 RNA <50 copies/mL (group 2; n=30);
- non-4DCR with HIV-1 RNA <50 copies/mL (group 3; n=20).
Groups were matched by age (±5 years),sex, smoking habit.
Markers of inflammation (hs-CRP, IL-6, TNF-α, D-dimer), immune activation (sCD163 and CXCL13) and microbial translocation (sCD14, endotoxin core IgG (EndoCAb) and 1-3-β-D-glucan (BDG)) were measured using specific ELISA kits.
An inflammation burden score (IBS) was defined as the number of biomarkers with an abnormal level, including all the aforementioned markers. An abnormal biomarker level was defined as a value at or above the 75th percentile (elevated); for EndoCAb, abnormal level was defined as a value at or below the 25th percentile (reduced).
In 4DCR-PLWH, markers of T-cell activation (HLA-DR/CD38 coexpression) and exhaustion (PD-1, CTLA-4 and TIM-3) on CD4+ and CD8+ T-cells were assessed by multiparameter flow-cytometry.
Linear regression was fitted to estimate factors associated with IBS.
Results: Overall, 80 subjects were evaluated: median age was 51.7 (IQR=45.9-55.2) years, 86% male, 60% smokers, 12.5% with a previous cancer diagnosis, on ART since 17.8 (IQR=8.0-23.7) years, with 472 (IQR=237-766) CD4+ cells/mm3, 817 (IQR=509-1064) CD8+ cells/mm3, CD4+ nadir of 156 (IQR=47-260) cells/mm3. IBS was higher in 4DCR-PLWH, even when virologically suppressed, compared to non-4DCR-PLWH (Table1). Among 4DCR-PLWH, the highest T-cell activation and exhaustion marker levels were observed in people with HIV-1 RNA ≥50 copies/mL (Table1).
After adjusting for age, CD4+ T-cell count, CD4+ nadir, HCV serostatus, use of statin and previous major adverse cardiovascular events, higher values of IBS were significantly associated with 4DCR condition (slope=+1.74, 95%CI=0.26 -3.23, p=0.022), increasing values of viral load (slope=+0.50, 95%CI=0.16-0.84, p=0.005) and the presence of a previous cancer diagnosis (slope=+2.03, 95%CI=0.69-3.36, p=0.004).
Conclusions: People living with 4DCR HIV showed higher values of inflammatory markers, in presence of either detectable or undetectable viral load, as compared to non-4DCR people. Moreover, HIV-1 RNA levels and a previous cancer diagnosis were associated with an increased inflammatory burden.
Finally, in 4DCR-PLWH, detectable viremia was also related with a higher degree of T-cell exhaustion. Therapeutic approaches aimed to reduce inflammation and T-cell exhaustion in 4DCR-PLWH need to be investigated.

Immunopathogenesis

OC 56 GUT MICROBIAL DYSBIOSIS IS LINKED TO IMMUNE-RECONSTITUTION AND CD4+ T-CELL SKEWING IN MSM WITH HIGH FRAMINGHAM RISK SCORE

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Background: HIV-related gut dysbiosis may fuel the pro-inflammatory and activated immune milieu which is linked to a higher risk of cardiovascular disease (CVD) in this population. Our preliminary findings showed different microbial composition according to sexual behavior and that cardiovascular risk may be modulated by the combined effect of microbes and antiretroviral drug exposure (IAS 2019). Open questions still remain, however, as to whether specific shifts of the intestinal microbiota may be linked to T-cell phenotype skewing in HIV-infected individuals at risk for CVD.
Methods: 44 male, HIV-infected subjects on virologically suppressed cART, comparable for demographics, HIV-related parameters and food consumption, were stratified according to Framingham Score (FS) using a cutoff of 10 (<10: Low FS; ≥10 Intermediate/High FS) and sexual behavior (Men having Sex with Men: MSM; Men having Sex with Women, MSW). Faecal microbiota composition (α and β-diversity; MiSeq Illumina® technology) was correlated to measures of T-cell recovery (CD4+ T-cell counts; CD4/CD8 T-cell ratio) and homeostasis (naïve: CD45RA+; central memory: CD127+; activated CD8+CD38+; memory/activated CD8+CD38+R0+).
Results: In MSM, α-diversity indexes which describe microbial richness and evenness, were consistently associated with CD8+ T-cell activation and memory phenotypes, regardless the FS. Indeed, CD8+CD38R0+ cells correlated with Observed (r=0.60, p=0.02) and Faith indexes (r=0.53, p=0.04) (Fig 1A) in MSM with a L_FS and CD8+CD38+ cells with Evenness index (r=0.66, p=0.04; Fig 1A, B) in MSM with an I/H_FS. Similarly, CD8+CD38+ levels positively correlated with Observed and Faith indexes in MSW with a L_FS (r=0.84, p=0.01; Fig 1A), Of note, the CD4/CD8+ T-cell ratio, marker of immune-reconstitution and independent predictor of clinical events, was inversely correlated with α-diversity solely in MSM, in both L (Shannon, r=-0.53, p=0.04; Fig 1A) and I/H_FS groups (Evenness, r=-0.66, p=0.04) (Fig 1A,C). Further, in the latter, also the CD4+ T-cell count and CD4+CD127+ subpopulations were inversely correlated with α-diversity (Evenness, respectively: r=-0.68, p=0.04, Fig 1A,D; and r=-0.71, p=0.03; Fig 1A,E). When analyzing the possible correlation between Principal Components-1, which measure the microbial cores extrapolated by each β diversity index, and peripheral T-cell homeostasis, scant and inconsistent data were found (Fig 1A). However, in MSW with I/H_FS, Weighted-Unifrac-PC1 index inversely correlated with the CD4/CD8 T-cell ratio (r=-0.64, p=0.04; Fig 1A).
Conclusions: In this pilot study, HIV-related dysbiosis may be linked to skewing of the T-cell compartment thus favoring CVD. Our findings of α-diversity linked to elevated T-cell activation and reduced measures of CD4+ T-cell reconstitution in MSM with high CVD risk, suggest that the microbiome may be a driver of sex-related, inflammatory diseases in the setting of cART-treated HIV infection.

Hepatitis and clinical virology

OC 57 UNEXPECTED RISING IN THE CIRCULATION OF COMPLEX HBV VARIANTS ENRICHED OF HBSAG VACCINE-ESCAPE MUTATIONS IN HBV GENOTYPE-D: POTENTIAL IMPACT ON HBSAG DETECTION/QUANTIFICATION AND VACCINATION STRATEGIES

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Introduction: HBsAg vaccine-escape mutations can alter HBsAg recognition by antibodies thus challenging vaccine efficacy, promoting immunosuppression-driven HBV-reactivation, and impairing HBsAg detection by immunoassays. In HBV genotype-D infection, limited information is available on the circulation of vaccine-escape HBsAg mutations overtime.
Here, we investigate the circulation of vaccine-escape mutations, the burden of complex mutational profiles and their impact on serological parameters in a large cohort of patients (pts) infected with HBV genotype-D.
Methods: This study includes HBsAg sequences from 947 viremic pts infected with HBV genotype-D, collected for routine clinical practice from 2005 to 2019. 21 vaccine-escape mutations(T116N, P120E/S, T126A/I/N/S, Q129H/R, T131I/N, M133I/L, C139S, K141E, P142S, D144A/E, G145A/R, A159G by Lazarevic, 2014) are analyzed.
Results: Median (IQR) HBV-DNA and ALT are 3.5(2.6-5.0)logIU/mL and 39(26-73)U/L, respectively. 4.2% is HBsAg-negative despite HBV-DNA positivity. Overall, 17.7% (168/947) of pts harbor >1 vaccine escape mutation with the highest prevalence in subgenotype-D3 (23% for D3 vs 13.6% for other subgenotypes, P<0.001). Among them, 17.3% (29/168) show complex profiles of vaccine-escape mutations characterized by the co-presence of 2 or more vaccine-escape mutations.
Notably, the proportion of pts with complex profiles of vaccine escape mutations increased over time: from 0.4% (1/237) in 2005-2009 to 3.0% (12/396) in 2010-2014 and to 5.1% (16/314) in 2015-2019, P= 0.007, suggesting an increased circulation of viral strains endowed with enhanced capability to evade humoral responses.
Moreover, the presence of complex profiles of vaccine-escape mutations correlates with lower HBsAg levels: median (IQR) 40(0-2905)IU/mL for pts with complex mutational profile vs 1688(348-6090) without them (p=0.0007), suggesting their role in altering HBsAg quantification.
Focusing on HBsAg-negativity, the presence of complex profiles of vaccine-escape mutations also correlates with an HBsAg-negative result despite HBV-DNA positivity (34.8% of pts with >2 vaccine-escape mutations vs 6.7% and 2.3% of those with a single or no vaccine-escape mutations are HBsAg-negative, p=0.007 and <0.0001). Interestingly, HBsAg-negativity is strongly associated with the presence of T126I/A in combination with >1 additional vaccine-escape mutation (50% of pts with T126I/A-containing profiles vs 3.3% without them were HBsAg-negative, p<0.0001). In HBsAg-negative pts, T126I/A frequently co-occurs with P120S and Q129H.
Conclusions: Complex profiles of vaccine-escape mutations are detected in a not negligible fraction of HBV genotype-D infected pts, and correlate with lower HBsAg quantification and HBsAg-negativity despite ongoing viral replication. These mutations should be considered for a proper clinical interpretation of HBsAg results and their circulation should be taken into account for the development of novel vaccine formulation

Hepatitis and clinical virology

OC 58 HCV GENETIC VARIABILITY IN PATIENTS WITH RELATED HEPATOCELLULAR CARCINOMA

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Background: Recently some reports showed that amino acid substitution (aas) 70 and/or 91 in the CORE region of HCV are predictor of hepatocarcinogenesis. Aims: evaluate genetic variability of HCV in patients with hepatocellular carcinoma (HCC) analyzing aas in NS3, NS5A and CORE regions.
Methods: 30 patients with chronic HCV (CCH), 25 genotype 1b, 3 genotype 2c and 2 genotype 2a, were enrolled. 17 patients had HCC (Cases) and 13 showed CCH without HCC (Controls). All were naïve to DAAs. For the Cases, a sample of neoplastic liver tissue, non-neoplastic liver tissue and a serum sample were collected. For the Controls, a sample of liver tissue was collected. Sanger sequencing of three regions was performed by homemade protocols. The phylogenetic trees were created with the Mega 10 program. Mutations and quasi-species were identified by the seqescape program software (Applied Biosystems) with a tolerance> 20% for improper sequences.
Results: Table 1 shows patients characteristics. 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 25% of the Cases and in 9,1% of the Controls, p=0.2957. Analyzing the NS3 region, aas in position 103 and 122 have been found in 50% of the Cases and 9,1% of Controls, p=0.0267. 2 aas conferring resistance to anti-NS3 inhibitors were identified, 4 Cases and 1 Control presented S122G and 1 Case showed D168E. Analyzing the NS5A region, aas at position 37 (90%) and 54 (80%) are more present in the Cases compared to the Controls without statistical significance. Aas that confer resistance to DAAs have been identified, Y93H in two Cases and in 1 Control, L31M in 1 Control.
Conclusions: In the literature there are few studies analyzing the genetic variability of HCV in cancer and in non-cancer tissue moreover without univocal results. In our opinion with the increase of the Cases we can better study this phenomenon and identify other aas associated to HCC.

Hepatitis and clinical virology

OC 59 PREVALENCE AND RESISTANCE ANALYSIS OF "UNUSUAL" HEPATITIS C VIRUS (HCV) SUBTYPES WITHIN THE ITALIAN RESISTANCE NETWORK VIRONET-C

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Background: Recent data has shown that specific "unusual" hepatitis C virus (HCV) subtypes had a lower response rate to direct-acting antivirals (DAAs) compared to the other most prevalent subtypes. Our aim was to investigate the prevalence and resistance profile of "unusual" HCV subtypes in Italy.

Methods: Clinical and virological data of "unusual" HCV genotype(GT)/subtypes, defined as GT1 non1a/b, GT2 non2a/b, GT3 non3a, GT4 non4a/d, and GT5, collected within the Italian Resistance VIRONET-C database, were retrospectively analyzed. Subtype assignment was confirmed by phylogenetic analyses on NS3±NS5A±NS5B sequences. Prevalence of resistance-associated substitutions (RASs) was evaluated at key positions (Sorbo et al 2018).

Results: A total of 311/3358 (9.3%) individuals with an available NS3±NS5A±NS5B sequence were found to be infected with "unusual" subtypes (GT1c/g/i/l=1/5/1/2; GT2c/i/j=267/1/2; GT3b/g/h/k=2/1/9/1; GT4c/i/l/m/n/o/r/v=1/1/1/1/3/5/5/1; GT5a=1). 245 patients (78.8%) were DAA-naïve, while 66 were DAA-failures (21.2%; Table 1). A different geographic distribution of these "unusual" subtypes was observed considering the patient's ethnicity: in particular, GT2c and GT3h were mainly found in Italians (91% and 100%, respectively), the other "unusual" GT3 subtypes were found mainly in patients from Asia (75%), while "unusual" GT1 and GT4 in patients from Africa (77.8% and 77.8%, respectively). Patients failed several DAA regimens such as glecaprevir(G)/pibrentasvir(P) (n=22), sofosbuvir(SOF)/velapatasvir(VEL)+/-ribavirin(RBV) (n=13), grazoprevir(GZR)/elbasvir(EBR) (n=2), or SOF/daclatasvir (DCV) (n=14), SOF/ledipasvir(LDV)+/-RBV (n=2), 3D/2D (paritaprevir/ombitasvir+dasabuvir)+RBV (n=6/2) or other DAAs (n=5). Analyzing the 60 NS5A-failures, all patients (100%) with the "unusual" subtypes GT1l, GT3b/g/h/k and GT4n/o/r/v had combinations of multiple NS5A RASs (from 3 to 6; Table 2). A similar pattern was also confirmed in DAA-naïve patients. Differently, in GT2c, only 53.5% of failures harbored >2 NS5A RASs, and this prevalence was decreased in DAA-naive patients (40.1%; p= 0.12). Substitutions at position 93 (H/F/S) were detected only at failure in GT3h/k and GT4o/v. Considering NS3-RASs, few patients showed resistance and only at failure (12.5%: 1 GT3h:80R; 3 GT2c:56H ±168V/A), while NS3 polymorphisms were observed in some "unusual" subtypes, from both naïve and failures (GT1g/GT2c/GT3h/GT4n/r). The NS5B 316H+321I pattern occurred in 66.7% of GT4r failures (2/3). No other SOF RASs were found at failure, with the exception of 282G in one GT2c patient.

Conclusions: Overall, our study provided a characterization of "unusual" subtype circulating in Italy. The majority of DAA-failures carried complex NS5A RAS patterns, some conferring high level of resistance. Further studies are needed to better characterize the impact on DAA efficacy of these "unusual" HCV subtypes, particularly for those with natural complex RASs at baseline

Social Science and epidemiology

OC 60 A LESS RECENT DIAGNOSIS IS ASSOCIATED WITH LOCAL TRANSMISSION CLUSTERS AMONG HIV-1 PRIMARY INFECTIONS IN ROME

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Background: Phylogeny represents one of the most important tools to better describe and monitor local HIV epidemics. Identifying recent spread of HIV can help prioritize prevention and early treatment for those at highest risk of transmission.
Objective: We evaluated characteristics and transmission dynamics of a cohort of individuals with primary HIV-1 infection (PHI) presenting and linked to care at the HIV regional reference center in Rome, Italy, from 2013 to 2020.
Materials and Methods: At diagnosis, we collected epidemiological, clinical and viro-immunological data of all individuals with PHI, promptly managed and treated at the INMI L.Spallanzani of Rome (SIREA cohort). We performed a phylogenetic analysis to identify transmission clusters (TCs) through HIV pol sequences, using Maximum-Likelihood (genetic distance ≤0.015) and Bayesian methods. Factors evaluated at univariate analysis for possible association with TCs inclusion were gender, age, nationality, transmission risk, year of diagnosis, Fiebig stage, CD4 count and viral load at diagnosis, HIV subtype, transmitted drug resistance, and time to virological suppression.
Results: Of 238 PHI diagnosed, 229 were linked to care, with a median follow-up of 168 weeks (IQR 96-232). Median (IQR) age was 39 (32-48) years; 94.8% were males, 86.5% Italians; 83.4% were men who have sex with men (MSM). HIV-1 B subtype was predominant (56.8%). Acute infections (Fiebig II to IV: 51.1%) had a higher viral load than recent infections (Fiebig V-VI) [log10 copies/mL, median (IQR), 6.2 (5.4-7.0) vs 5.0 (4.3-5.5), p< 0.001)]. Of 229 individuals, 92.6% started treatment within a median of 4 days [IQR 2-7] from diagnosis, with 2NRTI+DRV/b+RAL, or (from May 2015) 2NRTI+DTG. Most of those for whom treatment was delayed (15/17) were diagnosed in 2013-2014. Overall, 95 (46.6%) and 109 (53.4%) individuals reached undetectable viral loads >24 and ≤ 24 weeks follow-up, respectively.
From the 229 sequences analysed, we identified 68 persons (29.7%) involved into 20 TCs (median size 3, range 2-9). Among epidemiological, clinical and virological factors (Table 1), only a less recent year of diagnosis was found to be significantly associated with TCs inclusion, with a higher probability to be included in a TCs in the past with respect to present days. Of those individuals in the small group with delayed treatment, 3 (17.6%) were included in TCs.
Conclusions: Studies on TCs during PHI give the opportunity to take a more realistic snapshot on how the epidemic is developing in a specific geographical area. In our cohort, PHI involved predominantly Italian males and MSM, suggesting local TCs among this population. Since the only factor significantly involved in TCs inclusion was a less recent year of diagnosis, we suppose that the implementation of the test and treat approach in the overall HIV population during the course of the study may have probably played a role in restricting the size of TCs over time

Social Science and epidemiology

OC 61 HIGH HIV PREVALENCE FOLLOWING SCREENING OF SUBJECTS WITH HIV INDICATOR CONDITIONS IN A HOSPITAL SETTING

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Background: In Europe, approximately half of new HIV diagnoses are identified with CD4+ T-cell counts <350/uL. European recommendations suggest that subjects presenting with medical conditions associated with HIV prevalence >0.1% (HIV Indicator Conditions, HIV-ICs) should be tested for HIV. Aim of the present study is to verify the feasibility of offering HIV testing to individuals suffering from one or more HIV-ICs during hospital admittance.

Material and Methods: We organized a screening campaign (HIV sCreening tEsts BEyond the taRGet, "Iceberg" project) to detect undiagnosed HIV infections in subjects presenting HIV-ICs admitted in hospital wards, from January 2019 to December 2019. All patients provided informed consent for the collection of demographic and clinical data.

Results: 768 subjects suffering from a total of 846 HIV-ICs were tested (Table 1). The most frequently screened HIV-IC was pregnancy (n=385; 45.5% of total ICs screened; 50% of total subjects screened). 698/768 (90.9%) presented with 1 HIV-IC, 62/768 (8%) with 2, and 8/768 (1.1%) with 3. 282 subjects (36.7%) were males, with median age of 34 (28-44) years. The majority (520, 67.7%) were Caucasian, with 462 (60.2%) Italians.

13 patients were diagnosed with HIV (Table 2). Overall HIV prevalence in our hospital setting was 1.7%; excluding pregnancies, HIV prevalence was 3.1 %. Among the 13 HIV+ patients, 9 were Italian, 3 African and one was Latin American. Median age was 40 (33–46) years. Median CD4 T-cell absolute count and percentage were 83(22-212)/uL, and 8% (5-19) respectively. One patient (#3) died during hospital stay because of severe clinical complications despite minimal immunological impairment.

Conclusions: Prevalence of HIV infection in a hospital setting was relatively high, supporting the implementation of HIV-ICs screening. Most subjects presented with low CD4+ T-cell counts and 25% with AIDS-defining events, 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 HIV diagnosis.

Social Science and epidemiology

OC 62 THE CASCADE OF CARE AS TOOL TO PROMOTE A MORE EFFECTIVE CITY-WIDE PROGRAM AGAINST HIV/AIDS

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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 modeling 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 2019. 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 January 2020 patients actively followed at our Center were 2766. According to our calculation the total estimated number of PLWHIV was 3314 of whom 207 (6.5%) unaware of their infection. Over the considered 36 years of epidemics, 341 subjects (10.2%) resulted either transferred to other centers or lost to follow-up. Therefore patients aware of their HIV status and actively followed were 83.5% of all infected subjects. The number of diagnosed and alive subjects actively taking cART was 2755 (99.6%) of those in follow-up and 83.1% if compared to all PLWHIV. Finally, 95.0% of patients taking cART had their last viral load < 50 copies/ml and 97.7% below the 200 copies cut-off to define non-infectivity. That brought to a final proportion of people living with HIV and virally suppressed of 79.0% or 81.2% according to the cut-off[figure] above the 90-90-90 goal.

In our area, over time, the proportion of undiagnosed subjects dropped drastically from 28% in 2000 to 6.5% at the beginning of 2020 (figure), but the time between infection and diagnosis remains quite stable (mean 3.4 years)in the last years.

Conclusions: The Achille's heel of our cascade of care is 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. To achieve the 95-95-95 target we have to reduce it by at least three fourths. A city-wide program named "friendly test" is in place to address this problem and try to reach the general population and the most fragile groups of subjects at risk. The project is based on an independent check-point that is a place to perform tests but also a place for listening and counseling for PLWHIV and their relatives. Furthermore multiple spot-events (for tests) are planned during the year along with educational and promotional activities within the fast track city project concentrated in improving the rate of diagnosed PLWHIV and to shorten the time between infection and diagnosis.

Social Science and epidemiology

OC 63 CAUSES AND INCIDENCE OF HOSPITALIZATION IN PATIENTS ENROLLED IN THE ICONA COHORT

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Background: Data on the rates of hospitalizations in the more recent HAART era are useful for both healthcare planning and the development of strategies to improve health status of persons living with HIV (PLWHIV). We aimed to describe the change in the incidence of hospitalization between 2008 and 2018, and the reasons for hospitalization among patients who started antiretroviral therapy (cART) from 2008 onwards.

Methods: We included participants in the ICONA cohort who started cART from 2008. All the hospitalizations occurred during the first 30 days from the start of cART were excluded. The study differentiated hospitalizations in: AIDS defining conditions (ADC), infections non-ADC and non-infections/non-ADC (i.e. cardiovascular, pulmonary, renal-genitourinary, cancers, gastrointestinal-liver, psychiatric and other diseases). Hospitalization rates were reported per 100 person-years (PY). An individual patient could contribute multiple hospitalizations during the study period. Comparisons of rates across time were assessed using Poisson regression. Poisson multivariable model evaluated risk factors for hospitalizations, including both demographic and clinical characteristics.

Results: 9705 PLWHIV were included. During 36167 PY there were 1058 hospitalizations in 748 (7.7%) subjects (2.9/100 PY): 12.4% IDU, 36.5% MSM, 43.6% heterosexuals, 74.6% males, 42.3% smokers, 16.6% coinfected with HCV and 6.8% with HBV. At hospitalization 34.9% had HIVRNA>50 copies mL, 25.8% CD4<200/mmc. Causes of hospitalization were: 23.3% ADC, 22.7% infections non-ADC, 54.1% non-infections/non-ADC (11.1% cancers; 8.8% gastrointestinal-liver; 6.2% cardiovascular; 4.6% renal-genitourinary; 4.5% psychiatric; 3.9% pulmonary; 14.9% other). Over the study period, IR decreased significantly (from 5.8, in 2008-2011 to 2.2 in 2016-2018); this decrease was confirmed after adjusting for all the characteristics. Whereas hospitalization rates for ADC and for non-infections/non-ADC also showed a decreasing trend, the infections non-ADC remained stable throughout the period (Table 1a). Female, age>50 years, IDU, familiarity for cardiovascular disease, HIV-RNA>50, CD4 <200, longer time from HIV diagnosis to first cART were independently associated with a higher hospitalization risk; age, nationality, HCV coinfection were not. Results of multivariate analysis in Table 1b.

Conclusions: Chronic degenerative diseases, and not infectious diseases, are the main cause of morbidity leading to hospitalization, in PLWHIV after cART start in recent calendar years.

Social Science and epidemiology

OC 64 THE 4TH NINETY IN THE 4TH DECADE

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Background: With the use of ARV the life expectancy of PLWH is almost equivalent to that of the general population but, is it comparable in terms of quality? Beyond the concept of 90 90 90, we have questioned how PLWH day by day are to face the unexpected extension. Nadir elaborated a first survey in November 2017 to investigate the self-perception of the health related QoL. We presented the results at ICAR 2018.
In December 2019 we elaborated a second survey to investigate other aspects of the QoL perception among PLWH.
Material and Methods: We launched the questionnaire at the Nadir Seminar last October to 25 Organizations who attended and we also put it on our website www.nadironlus.org for 2 months. Only people using ARV were invited to give answers. We received 330 questionnaires filled from 35 cities in Italy, spread along the country. People were diagnosed between 1985 and 2019 and had started treatment from 1988 until 2019. The diversification of ages, genders, regions, periods of starting treatment, the duration of the HIV virus in their bodies gave us a wide vision of the participants perception, unbiased by external influences. We did not verify if their caregivers provided a range of clinical services that may include counseling or home assistance. We have considered two main variables: age and years from diagnosis and compared them to understand if and how the perception of QoL is affected.
Results: A high percentage of people who declare they live a good QoL is experimenting psychological distress particularly with reference to the aging that imposes several medications due to co-pathologies or frailty. We found the 33% of participants cannot interpret the difference between aging/frailty and HIV related or non-related symptoms. They pinpointed the social attitude and discrimination as a major obstacle to enjoy a stable QoL (52%) and evidenced their emotional and professional lives have been influenced by the fear of discriminating attitudes as well as the capacity of building long term plans (70%). These answers were based on personal experiences with family and friends (76%) and they witnessed the outing of their serostatus is an obstacle that still cannot be bypassed. Though the unexpected success of the new generation ARV decreases the life threatening challenge, the fear to face sexual disfunction remains one of the most difficult problems to cope with (42%).
Conclusions: Two diverse aspects emerge from the survey: 1) satisfaction towards the treatment efficacy even in the presence of co-pathologies and polypharmacy. 2) the QoL is strongly influenced by the social attitude in the judgemental and marginalizing milieu of small or midsize cities where the participants live. The sample shows the undetectability has improved QoL for the 76%, but 34% of this sample declares to have an insufficient sexual QoL and the 11% defines his/her sexual QoL as very bad because of sexual disfunctioning.

Social Science and epidemiology

OC 65 GENERAL PRACTITIONERS AND PLWH: WHAT DO PATIENTS THINK?

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Background: HIV infection today is a chronic condition, in which age-related co morbidities and poly-pharmacy are issues that must be taken into account. In this setting, General Practitioners (GPs) could play a key-role.
Our study was aimed to assess, among a multicentre cohort of People Living With HIV (PLWH), the relationship withthe GPs, the level of subjective illness awareness and the perception of stigma, using patient reported experience measures (PREMS).
Methods: From 1st December 2019 to 14th February 2020 an anonymous survey was administered to patients attending the outpatient service for PLWH of four Italian Infectious Diseases Centers: Foggia, Bari, Genoa, Florence.
The survey questions covered four main topics: communication of HIV positivity to GPs, subjective perception of the disease, presence of co-medications and management of Drug-Drug Interactions (DDIs). Socio-demographic data were collected. Proportions were compared using χ2statistics. Analysis was performed using R v.3.60. A $p<0.05$ was considered statistically significant.
Results: During the observation period a total of 672 patients participated in the survey. The majority were male (462, 69%), Italian (605, 90%) and older than 30years (632, 94%). Most subjects had high education level (387,58%) and were unmarried (431, 64%).
508 pts (76%) had informed the GP about HIV-positivity. Factors related with a better communication with GPs were: lower level of education ($p<0.001$), longer history of disease ($p=0.001$), being unmarried ($p= 0.003$) (Table 1). 164 patients (24%) said they had not informed their GP about HIV, mainly due to fear of indiscretion (39%) and fear of stigma (36%).
The concept of "Undetectable=Untrasmittable" (U=U) was investigated and taken as an indirect measure of perceived stigma. Almost a half of the subjects (334, 50%) referred that being undetectable did not help them in communicating their status to GPs. The perceived stigma was higher in married patients ($p= 0.003$) and in patients with higher education level ($p= 0.007$) (Table 2).
Patients from Northern Italy had better communication levels with GPs and less perceived stigma, when compared to patients from the South ($p<0.001$). No significant difference was found for age or sex.
Overall, 264 pts (39%) took other medications; 510 pts (76%) referred to the Infectious Diseases Specialist for the evaluation of DDIs.
476 pts (74%) advised the need of a better communication between the GP and the Infectious Diseases Specialist.
Conclusions: Even in presence of a general acceptable level of communication between PLWH and GPs, remarkable disparities exists over the country and, especially in South Italy, patients still feels stigmatized. According to our results, improving the co-operation between GPs and Infectious Diseases Specialists appears mandatory, as these figures are currently entirely taking on the responsibility of the management of co morbidities and DDIs related to this chronic infection

Pharmacology

OC 66 USE OF DIRECT ORAL ANTICOAGULANTS IN PEOPLE LIVING WITH HIV: A SINGLE-CENTER EXPERIENCE

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Background: Direct oral anticoagulants (DOACs), specifically developed to overcome the challenges posed by vitamin K inhibitors, have changed the outlook towards stroke and thromboembolic events prevention with anticoagulation. Indeed, more than 70% of HIV-negative patients requiring anticoagulant therapy are actually treated with these drugs. Here, we sought to assess the use of DOACs in HIV-infected patients from our Clinics.
Materials and Methods: The database of our Infective Diseases Clinics (with nearly 2300 HIV-infected patients on active follow-up) was investigated in search for patients starting antithrombotic therapy after January 2012 or starting therapy on any date but suspending it after 2012 (year of the marketing of the first DOAC). The risk of drug-drug interactions (DDIs) between antiretroviral and antithrombotic therapies was scored using the University of Liverpool HIV Drug Interactions checker (https://www.hiv-druginteractions.org/checker).
Results: Fifty out of the 76 HIV-infected patients on antithrombotic therapy from our database fulfilling the inclusion criteria were considered (clinical characteristics are given in Table 1). All patients except one have started anticoagulant therapy after being diagnosed with HIV. The anticoagulant therapy resulted in a significant increase in the haemoglobin concentrations (from 13.7±2.4 to 14.3±2.2 mg/dL, p=0.036) with no effects on serum creatinine (from 1.0±0.4 to 1.1 ±0.4 mg/dL, p=0.409) or on alanine aminotransferase (from 35±31 to 30±39 mg/dL, p=0.513). Only 14% of the patients were given DOACs, with the large majority being still treated with a vitamin K inhibitor (66% with warfarin and 16% with acenocoumarol), despite the fact that these regimens resulted in 58% of cases at risk of potential DDI (orange flag). We subsequently proposed a hypothetical scenario in which all patients were ideally shifted to DOACs by checking their DDIs with the actual antiretroviral regimens. We found that all patients could have been theoretically shifted to the novel anticoagulant therapy. Remarkably, this shift, if applied, would have been resulted in a further reduction in the orange flag DDIs (from 58% to 42%, Table 1)
Conclusions: In the HIV-infected patients there is still an underuse of DOACs probably linked to an unjustified fear for DDIs. A rationale selection of the best antithrombotic agent for each antiretroviral therapy would improve the quality of life of people living with HIV.

Pharmacology

OC 67 PHARMACOKINETICS OF ONCE-DAILY DORAVIRINE OVER 72 HOURS FOLLOWING DRUG CESSATION

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Background: HIV drug treatment relies on adherence to combination antiretroviral therapy (cART) every day, ideally at the same time. However, cART is for life and doses can be forgotten or delayed. Therefore, antiretrovirals with long half-lives (t1/2) are desirable. We investigated the pharmacokinetic (PK) 'forgiveness' of the new non nucleoside reverse transcriptase inhibitor doravirine (DOR) to advise clinicians and patients on delayed or missed doses.

Methods: Healthy volunteers received DOR 100mg once daily for 7 days. Full PK profiles were assessed for 72 hours (h) following day 7. DOR plasma concentrations were measured predose and 2, 4, 8, 12, 24, 30, 36, 48, 54, 60 and 72h postdose using a validated liquid chromatography-mass spectrometry method. The lower limit of quantification for DOR was 2.5ng/mL over a calibration range of 2.5–1000ng/mL (r=0.9997). The PK parameters were calculated using noncompartmental modelling techniques, which were trough concentration (Ctrough), maximum concentration (Cmax), elimination t1/2 to last measurable time-point, and total drug exposure, expressed as the area under the plasma concentration-time curve from 0-24h after dosing (AUC0-24h) and 0-72h (AUC0-72h).

Results: Fourteen subjects completed the study. Geometric mean (GM) values and 95% confidence intervals for the steady-state PK parameters measured over 24h and 72h are summarised in the table. The GM t1/2 to 24h of DOR (14.56h) was similar to that to 72h (13.97h). At 48h and even 72h postdose, all subjects had DOR concentrations higher than the 50% inhibitory concentration [IC50] for wild-type virus (5.4ng/mL).

Conclusions: Our data contribute to the understanding of DOR behavior following treatment interruption and provide reassurance to clincians and patients about the PK forgiveness of DOR, which maintains above IC50 at 72h following a missed dose. Furthermore, when DOR is combined with TDF and 3TC, it provides a balanced cART in terms of PK forgiveness, as all 3 drugs are characterised by prolonged t1/2.

Pharmacology

OC 68 INFLAMMATION AFFECTS ANTIRETROVIRALS PLASMA AND INTRACELLULAR EXPOSURE

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Background: Antiretroviral therapy (ARV) reduces systemic inflammation and immune activation, but not to levels like HIV negative . Limited drug penetration within tissues and presence of immune sanctuaries has been argued as potential mechanisms of persistent inflammation. Limited data are available on the role of inflammation on plasma/intracellular (IC) pharmacokinetics (PK) of ARV drugs through to downregulation of cytochrome P450 3A (Cyp 3A4), protein expression1 and suppression of expression of P-glycoprotein (P-gp)2 in several tissues. Understanding the effect of inflammation on IC of modern ARV drugs may be relevant for designing appropriate interventions in the setting of the functional cure of HIV. Thus, aim of this study was to investigate the correlation between inflammation markers (IM) (CRP, IL-6), microbial translocation (sCD14, LPS) and plasma/IC PK of different ARVs regimen in stable HIV-positive patients (pts).
Methods: We included in the study ART-treated HIV+ pts switching to 3 different ARV regimens: i)Dolutegravir based dual therapy (DTG-DT) plus boosted Protease Inhibitors [PI, atazanavir (ATV) or darunavir (DRV)], ii) DTG based triple therapy (DTG-TT; without PI), and iii) DRV/c based triple therapy (DRV/c-TT). Lab analyses: (a) plasma and IC ARV drugs concentration means of UHPLC-MSMS validated method at the end of dosing interval (T0) b) IM on samples concomitantly with ARV PK determination: soluble CD14 (sCD14), C-reactive protein (CRP) (Luminex), Inteleukin-6 (IL-6) (ELISA) and Lipopolysaccharide (LPS). Non-compartmental PK parameters were calculated and reported as ng/ml and expressed as geometric mean (CI95%). We analysed the correlation between IM and ARVs PK with non-parametric tests.
Results: 60 samples from pts included in the switching study, were used for measuring plasma and intra-PBMC concentrations of HIV drugs: 9 on DTG-DT, 25 on DTG-TT and 26 on DRV/c-TT. They were mostly male (80%), with median age and BMI of 53 years (48-59) and 23 Kg/m2 (20-24). No significative differences between CRP, sCD14, IL-6 and LPS values in 3 arms of therapy were observed (Table 1).
Interestingly, a significant correlation was observed between tenofovir plasma concentrations and sCD14 (rho=-0.79, p<0.001), between DRV plasma concentration and sCD14 (rho=0,31, p=0,07) and between DRV IC/plasma ratio and Log10 transformed IL-6 concentrations (rho= -0.36, p=0.04). In all 34 pts on DTG, DTG IC concentrations were associated with age (rho=0.4, p=0.01). Furthermore, in 24 pts on DTG-TT, we observed a negative trend between IC DTG concentrations and sCD14 levels (rho=-0.34, p=0.09).
Conclusions: In our study we evaluated IC ARVs PK in 60 pts, according to markers of inflammation. Our preliminary data support the hypothesis of lower IC concentrations of DRV and DTG in pts with higher plasma IM, suggesting an interplay between HIV drug penetration and persistent inflammation in cART- treated HIV positive pts.

Pharmacology

OC 69 BICTEGRAVIR PLASMA AND INTRACELLULAR PHARMACOKINETICS IN IN THE CLINICAL SETTING

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Background: Bictegravir (BIC) co-formulated with Emtricitabine/Tenofovir alafenamide (BIC/F/TAF) is the newest three-drug regimen (3DR) fixed dose combination available in clinical practice. Since few data on BIC plasma1,2 and no data on intracellular (IC) pharmacokinetics (PK) are available, aim of this study was to measure BIC plasma exposure and accumulation within peripheral blood mononuclear cells (PBMCs) in our experienced patients (pts) in the clinical setting.
Methods: We included patients who switched to BIC/F/TAF, according to clinicians' judgement. BIC plasma and IC Ctrough samples were collected from 46 experienced patients switching from different antiretroviral (ARV) regimens, mostly integrase inhibitor (INI)-based, after one month of BIC exposure. BIC plasma and IC concentration were measured by means of UHPLC-MSMS validated method. Non-compartmental PK parameters were calculated and expressed as geometric mean (CI95%). Concentrations were expressed as ng/ml. Descriptive analysis were expressed as geometric mean; variables were tested using non-parametric tests (Mann-Whitney and Spearman's rank test).
Results: We enrolled 46 patients : 80% were male of median age and BMI of 50 years (IQR 44-58) and 23,7 Kg/m2 (IQR 22,2-29,5). All pts switched for optimization: 36% from F/TAF/Elvitegravir/Cobicistat, 16% F/TAF and Dolutegravir (DTG), 11% F/TAF/Rilpivirine, 9% Abacavir/Lamivudine/DTG, and 27% from Protease Inhibitors (PIs) and Raltegravir based regimen. BIC plasma, IC Ctrough and IC/plasma ratio were 2828 ng/mL (2206-3450), 610 ng/mL (392-828) and 0,222 (0,173-0,271). Significant linear correlations between BIC plasma and age (rho=0,305, p=0,036) and IC Ctrough (rho=0,660, p<0,001) were observed. No correlation between BIC PK and BMI or gender was found.
Conclusions: This is the first evaluation of BIC plasma and IC concentration in the setting of experienced pts switching from different regimens. PK analysis showed a correlation between plasma exposure and IC accumulation. BIC plasma concentration resulted to be comparable with those reported in literature.

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Pharmacology

OC 70 GENERIC PRE-EXPOSURE PROPHYLAXIS FORMULATIONS: A COMPARISON OF TENOFOVIR TROUGH CONCENTRATIONS

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Background: Extensive evidence is available showing that Pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate (TDF)-based formulations dramatically reduces the risk of HIV acquisition among HIV-negative individuals. Here, we aimed to compare tenofovir plasma trough concentrations in subjects taking PrEP daily versus on demand and using different TDF-based formulations.

Material and Methods: Consecutive subjects who provided a signed informed consent form for the measurement of tenofovir plasma levels were considered. The measurement was carried out after ≥3 consecutive days of PrEP intake. Drug trough concentrations were stratified according to PrEP schedule (daily or on demand), TDF-based formulation and drug source. HIV-positive patients with renal function matching that of subjects on PrEP and taking branded TDF/FTC not combined with boosted-antiretroviral drugs were considered as control group.

Results: 140 subjects were included in the present study. They had a mean age 39±10 years, a body weight 76±11 kg, and had normal kidney (serum creatinine 0.9±0.1 mg/dL) and liver function (serum AST 29±18 IU/L). 21% took PrEP on demand and 79% daily at the time of measurement, respectively. Those taking the drug daily started PrEP 200±191 days before the assessment of tenofovir concentrations. PrEP was mainly purchased online from secure suppliers (42%) or in a pharmacy (39%); the remaining received PrEP directly at the Milano Checkpoint, generic TDF/FTC donated by Mylan (11%) and branded TDF/FTC supplied by Gilead within the ItaPrEP observational study (8%). 8 different generic PrEP formulations were recorded (Table 1).

No significant differences were found in tenofovir trough concentrations when comparing subjects taking PrEP on demand versus daily (115±80 vs. 110±73 ng/mL; p=0.573). Similarly, no significant differences were found when comparing trough tenofovir concentrations between the 8 generic PrEP formulations or when comparing generic PrEP formulations, considered singularly or collectively, with values measured in the control group of HIV-positive patients on Truvada®. When drug sources were considered, no statistically significant differences were found in tenofovir trough concentrations when comparing the secure online suppliers to Milano Checkpoint and to pharmacies (112±85 vs. 130±75 vs. 112±65 ng/mL; p=0.463); a trend for lower drug concentrations was observed in the 12 subjects taking Truvada® within the ItaPrep study (65±70 ng/mL).

Conclusions: Generic formulations of TDF/FTC sourced through secure suppliers delivered tenofovir plasma trough concentrations comparable to each other and with values measured in HIV-positive patients taking Truvada®. This is a reassuring message for subjects at high risk for HIV transmission and caregivers on the high quality of generic PrEP formulations available on the market. More data is needed to reach the same level of significance for all the formulations considered.

Antiretroviral Therapy

OP 1 EVALUATION OF TOTAL HIV-DNA AND RESIDUAL VIREMIA IN HIV-1 INFECTED PATIENTS WHO CONTINUE A TWO-DRUG REGIMEN WITH DOLUTEGRAVIR PLUS ONE REVERSE TRANSCRIPTASE INHIBITOR OR SWITCH TO ELVITEGRAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR ALAFENAMIDE ENROLLED IN THE BE-ONE STUDY

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Background: To investigate HIV-DNA and residual viremia levels through 48 weeks (W48) in virologically suppressed HIV-1 infected patients randomized to continue a two-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).

Material and Methods: This is a randomized, single-center, open-label, 96-week superiority study (NCT03493568; Be-OnE Study). Total HIV-DNA (normalized for copies/106 CD4+ T-cells) and residual viremia were measured with standardized in-house digital droplet PCR assays. Spearman correlation coefficients (rs) were calculated to assess linear relationship between HIV-DNA, viremia levels and several immunological parameters (including D-Dimer, C-reactive protein [CRP], %CD8+CD38+HLA-DR+, %CD4+CD38+HLA-DR+, CD4+ T-cells, CD8+ T-cells, CD4/CD8) both at baseline (BL) and at W48. Differences in HIV-DNA and residual viremia levels were evaluated by using Wilcoxon signed-rank test among patients within the same arm or the Mann-Whitney test between the 2 arms.

Results: HIV-DNA and residual viremia measurements at BL and at W48 were available for 40/50 patients (Figure). Overall, median (IQR) HIV-DNA levels were 2247 (767;4268) and 1587 (556;3543) copies/106 CD4+ T-cells at BL and at W48, respectively, while median (IQR) residual viremia levels were 2.9 (1.1;5.3) and 1.2 (0.0;5.5) copies/mL, without significant differences between arms (Table). No significant correlations were found between HIV-DNA and viremia levels or immunological parameters at either BL or W48, with the exception of HIV-DNA levels and CD8+ T-cells at W48 (rs=0.411, p=0.008). No significant changes in HIV-DNA and viremia levels were found from BL to W48 (Table). However, the proportion of patients with target not detected plasma HIV-RNA (TND=0 copies/mL) increased from BL to W48, overall (10% vs. 40%, p= 0.004) and in both arms (E/C/F/TAF: from 4.8% to 38.1%, p=0.008; DTG+1RTI: from 15.8% to 42.1%, p=0.074). Moreover, at W48, a modest decrease in HIV-DNA from BL was found: -226 (-1189; 890) copies/106 CD4+T-cells (p=0.465) in the DTG+1RTI-arm and -137 (-983; 133) copies/106 CD4+T-cells (p=0.334) in the E/C/F/TAF-arm, without significant differences between the two arms (p=0.968). In a few participants, HIV-DNA slightly increased from BL to W48 (DTG+1RTI: 7/19; E/C/F/TAF: 5/21, p=0.495), despite a residual viremia decrease. In a single participant on the DTG+1RTI arm, an increase of both HIV-DNA (from 320 to 1210 copies/106 CD4+ T-cells) and residual viremia (from 1.1 to 9.6 copies/mL) was observed.

Conclusions: Changes in HIV-DNA and residual viremia from BL to W48 in virologically suppressed individuals who switched from a 2DR with DTG+1RTI to E/C/F/TAF were negligible and did not significantly differ from changes in those who continued the 2DR.

Antiretroviral Therapy

OP 2 DURABILITY AND LIVER SAFETY OF INSTI-BASED REGIMENS IN HIV-INFECTED PATIENTS WITH ADVANCED LIVER FIBROSIS OR CIRRHOSIS: DATA FROM THE ODOACRE COHORT

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Background: Integrase strand transfer inhibitors (InSTI) have become the reference drug class for the treatment of HIV infection for their efficacy and tolerability. Safety is a critical factor in antiretroviral drugs choice in patients with advanced chronic liver disease (aCLD)/cirrhosis but few data are available for newer InSTI in this setting. Our study aimed to explore durability of different InSTI-based regimens in subjects with aCLD/cirrhosis.
Methods: Retrospective multicenter (3 clinical centers in Italy) observational study including HIV-1 infected, treatment-experienced patients with HIV-RNA (VL)<50 cp/mL and aCLD/cirrhosis (defined as Fib-4 score>3.25, stiffness>9 kPa or by clinical criteria) switching to InSTI-based regimens. Patients were followed from the time of InSTI initiation to the time of InSTI discontinuation, to the last available visit or to a maximum of 36 months of follow-up. Kaplan-Meier curves and Cox regression analysis were used to explore incidence and predictors of InSTI discontinuation (TD), virological failure (VF, defined as one VL>1,000 cp/mL, or two consecutive VL>50 cp/mL or one VL>50 cp/mL followed by therapeutic switch), treatment failure (TF, the first of VF or TD), liver enzyme elevation (LEE, defined as aminotransferases ≥2.5 times the upper limit of normal) and occurrence of hepatic events (HE).
Results: Overall, 124 patients (72% males, 85% with HBV or HCV coinfection, median age 52 years, median time of HIV 23 years, median baseline CD4 593 cells/mmc) were included, of which 67 (54%) treated with raltegravir (RAL) [n=16 (24%) in 2-drug regimen (2DR)] and 57 (46%) with dolutegravir (DTG) [n=27 (47%) in 2DR].
Overall, the incidence of TD, VF, TF, LEE and HE were 19.8, 3.9, 22.2, 6.4, 5.2 per 100 PYFU, respectively.
The estimated probability of TD for any reason (52.1% vs 30%; p=0.019), TD for simplification (22.8% vs 2%, p=0.005), TF (53.3% vs 36.1%; p=0.051) and LEE (30.1% vs 2.6%, p=0.001) at 36 months were higher in RAL when compared to DTG group (Figures). No significant differences in the incidence of VF and HE were observed between DTG and RAL.
Exploring predictors of TD, DTG use (aHR 0.5; p=0.03) and longer time of ART exposure (aHR 0.9; p=0.05) confirmed an association with a lower risk at multivariate analysis. DTG use (aHR 0.5; p=0.03) and higher zenith VL (aHR 1,15; p=0.02) were also associated with a lower risk of TF after adjusting for potential confounders. Finally, DTG use (aHR 0.08; p=0.02) was an independent negative predictor of LEE, a while a higher Fib-4 score (aHR 1.7, p=0.003) conferred an increased risk. Higher Fib-4 score (aHR 1.8; p<0.001) was also independently associated with a higher risk of HE.
Conclusions: In HIV-infected patients with aCLD/cirrhosis, InSTI-based regimens showed high efficacy. Regimens including DTG were associated with a lower risk of discontinuation and seemed to have a lower impact on liver function.

Antiretroviral Therapy

OP 3 PREVALENCE OF TRANSMITTED RESISTANCE MUTATIONS TO RILPIVIRINE AND DORAVIRINE IN TREATMENT-NAIVE PATIENTS IN A LARGE CLINICAL AND RESISTANCE DATABASE

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Background: Non-nucleoside reverse transcriptase inhibitors (NNRTIs), first approved in 1996, have historically been a cornerstone of antiretroviral therapy. However, their low genetic barrier to resistance may affect the HIV transmitted drug resistance (TDR). TDR, therefore, can lead to virological failure as a consequence of pre-existing resistance to one or more drugs in the first-line antiretroviral regimen. The aim of this study was to investigate the prevalence of TDR to both rilpivirine (RPV) and doravirine (DOR) among naive patients from a large Italian cohort, in the 1996-2019 period.

Materials and methods: In this retrospective study, we selected all ART-naïve HIV-1 infected patients with at least one plasma RT/PR genotypic resistance test (GRT) available, performed from 1996 to 2019 from the ARCA database. We considered major resistance mutations paneled by the Stanford HIV Drug-Resistance Database 2019. We evaluated the overall and 5-year prevalence of TDR to RPV and DOR in all isolates.

Results: We retrieved 2,441 isolates from 1,667 ART-naive patients: mostly males(69%), Caucasian (82%) with subtype B (71%) and with a median age of 51 (IQR 42-58) years. The overall prevalence of DOR and RPV resistance-associated mutations were 3.6% and 10.6% respectively, while 3.6% was the prevalence of TDR affecting both DOR and RPV (Fig1). The DOR-TDR frequency decreased from 9% in 1996-2000 to 2% in 2006-2010 (0.001), remaining stable until 2016 -2019 (0.500) (Fig1). On the contrary, the frequency of RPV-TDR increased from 3% in 1996-2000 to 15% in 2001-2005 (<0.001) and thereafter decreased, but not significantly, to 12% in 2006-2010 (0.257), staying stable until 2016-2019 (0.158) (Fig1). Resistance to both DOR and RPV was comparable to RPV-TDR trend. The percentage of GRTs suscebtible to both DOR and RPV remained stable around 85% during the study period except for a minimum percentage (70%) reached in 2001-2005. The most frequent DOR mutation was V106I (68 GRTs), followed by Y188L (26 GRTs); the most frequent RPV substitutions were E138A and Y181C (96 and 71 GRTs, respectively). Similar TDR frequency and prevalence were observed when classifying the isolates according to B and non-B subtype over time.

Based on Stanford algorithm, the prevalence of GRTs considered with Potential Low-level, Low-level, Intermediate and High-level resistance to DOR and RPV were 3, 6, 5 and 4% and 3, 8, 3 and 7%, respectively.

After stratifying by viral load and CD4 done at GRT, DOR and RPV-TDRs were more frequent in patients with HIV-RNA ranging between 100 and 25,000 copies/mL (p=0.138 and <0.001, respectively) and CD4 cells <350/µL (p<0.001 and 0.274, respectively).

Conclusion: Overall DOR and RPV-TDRs showed a decrease from 2001 to date. However, in the last decade their frequency seems stable, thus to be monitored. Genotype test in newly HIV-diagnosed patients remains crucial to drive the clinicians in building the optimal first-line antiretroviral regimen.

Antiretroviral Therapy

OP 4 EFFICACY AND TOLERABILITY OF BICTEGRAVIR/ TENOFOVIR ALAFENAMIDE/ EMTRICITABINE AS A SWITCH STRATEGY IN A COHORT OF ANTIRETROVIRAL THERAPY TREATMENT-EXPERIENCED HIV-1-INFECTED PATIENTS

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Background: The bictegravir/emtricitabine/tenofovir alafenamide single tablet regimen (BIC-STR) has recently been approved for use in antiretroviral therapy (ART) treatment-naive and ART-experienced subjects.
Objectives: The primary endpoint was BIC-STR discontinuation for any reason.
Methods: All ART-experienced patients starting BIC-STR, from July 2019 to January 2020 were retrospectively selected at our center. Demographic, clinical and laboratory data along were analyzed. Categorical variables were analyzed with X2/Fisher's exact test and continuous variables with Wilcoxon signed-rank test for paired data.
Results: Overall, 90 patients were included [median age 53 years (IQR 40- 57)], including 16 females (17.8%) and 2 transgenders (2.2%), who reported mostly [70 (77.8%)] a sexual risk of acquiring HIV infection. Median follow-up was 3 months [IQR 2.5-4.8]. Most subjects 72 (80%) had HIV-RNA <50 copies/mL at baseline and come from a 3-Drug INSTI-based regimen 72 (80%); 5 (5.6%) come from a 3-Drug PI-based regimen, 3 (3.3%) from a 3-Drug NNRTI-based, 3 (3.3%) from dual-therapy, 7 (7.8%) from other regimens. Baseline data are shown in Tab 1. Of the 69 patients with a genotype available at baseline 29 (32.2%) had at least 1 major mutation: 10 had reduced sensitivity to TDF, 8 had 184V mutation; 19 had mutations for NNRTI (27.5%), 6 for PI (8.7%). Overall 50 patients (55.6%) had comorbidities at baseline: dyslipidaemia 23 (25.5), hypertension 12 (13.3%), osteopenia/osteoporosis 11 (12.2%), diabetes 4 (4.4%). Fourteen patients used statins at baseline. Reasons to switch were simplification 83 (92.2%), virologic failure 6 (6.7%), drug interaction 1 (1.1%). Overall, 4 subjects stopped BIC-STR: 1 for arthralgia, 1 for repeated blips <50 copies/mL, 1 for virologic failure, 1 for edema in the lower limbs. The discontinuation rate for all causes was 0.43 x 1000 person-year (95% CI 0.16-1.17).
The patient who experienced virologic failure had a virus harboring transmitted resistance mutations 67N 69N 181C 219Q 221Y and 13V 20R 36I 60E 63P 84V conferring drug resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PI), respectively, and no integrase-strand-transfer-inhibitor mutations. No significant change in the CD4 count from baseline was observed. Conversely, at 12 weeks a statistically significant mean reduction of 20.4 mg/dL in total triglycerides (on a sample of 22 patients) was observed ($p = 0.0271$). The difference was evident only in the subgroup of patients who came from a previous boosted regimen (EVG/b or PI /b).
Conclusions: Switching to BIC-STR was well tolerated and effective also in those with a not completely effective backbone. A significant reduction in triglycerides in patients who came from a booster regimen was observed. This result is particularly significant because a large part of the population that switches to BIC-STR in our sample is over fifty and has numerous comorbidities.

Antiretroviral Therapy

OP 5 VIRAL REBOUND IN PTS WITH SUPPRESSED HIV-RNA ON A 2 OR 3-DRUG REGIMEN: A COMPARISON

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Background: 3TC-based maintenance dual therapies (DT) have demonstrated non-inferiority as compared with triple therapies (TT) in randomized trials. We compared the efficacy of DT and TT in clinical practice.

Methods: In a retrospective (2011-2019) study involving 6 third-level Italian hospitals, we analysed the time to viral rebound (VR, defined as an increase from undetectable plasma HIV-RNA to any value above 0 cps/mL) in patients (pts) with negative HBsAg-serostatus, either on a DT with 3TC plus either a boosted protease inhibitor (bPI; atazanavir or darunavir) or dolutegravir, or a on a standard TT (2NRTIs plus bPI or dolutegravir), followed-up from the third consecutive undetectable HIV-RNA determination (i.e. HIV-RNA=0 copies/mL) in one year-period. To estimate the effect of DT (versus TT) on the time to VR, both in the overall population and separately for pts on bPIs and INIs, a Cox model was adjusted for potential confounders; another one was adjusted for the propensity-score (PS) of receiving a DT; the last one after calculating the inverse probability of treatment weights (IPTW).

Results: Eight hundred sixty pts were eligible for the analysis: 344 (40.0%) were on a DT (21.7% with bPI, 18.3% with DTG), 516 (60.0%) on a TT (31.2% with bPI, 28.8% with DTG). The population was mainly composed of men (69.7%), with 51 years of median age. Characteristics of study groups are summarized in table 1.

Overall, there were 164 and 267 VR over 382 and 491 persons-years of follow-up with DT and TT, respectively, with a statistically significant difference in favour of the DT (log-rank p=0.020). After adjusting for ethnicity, age, number of HIV determinations in the previous year, time of ARV exposure and HIV duration, baseline CD4 count, previous therapy and reason for switch to the current one, previous virological failure and genotypic susceptibility score of current regimen, DT showed no association with VR (aHR 0.84, 95% CI 0.67-1.06; p=0.142). A zenith HIV-RNA>100k cps/mL (versus <100k cps/mL, aHR 1.45; p<0.001) and male gender (vs female, aHR 1.33, p=0.015) predicted VR, whereas a longer time of viral suppression (per 1 year more, aHR 0.96; p=0.005) was protective. Cox models with PS and IPTW confirmed the lack of association between DT and VR (OR: 0.87, 95% CI 0.70-1.09; p=0.236 and 0.92, 95% CI 0.73-1.16; p=0.487, respectively).

In the subgroup of pts on PI, DT was not predictive of VR at multivariable Cox regression (aHR 0.76, 95% CI 0.56-1.02; p=0.069), nor after adjusting for PS (aHR 0.83, 95% CI 0.62-1.12; p=0.224) nor after calculating IPTW (aHR 0.88, 95% CI 0.62-1.23; p=0.447). Similarly, DT with dolutegravir did not show any association with the outcome at Cox regression (aHR 0.98, 95% CI 0.68-1.41; p=0.931), PS-adjusted Cox model (aHR 0.97, 95% CI 0.68-1.39; p=0.860) nor with IPTW (aHR 0.94, 95% CI 0.66-1.34; p=0.747).

Conclusions: 3TC-based DT did not increase the risk of VR as compared to TT even in the setting of clinical practice.

Antiretroviral Therapy

OP 6 OPTICALLY TRACEABLE PLGA NANOPARTICLES IMPROVE THE ABILITY OF DARUNAVIR TO CROSS THE BLOOD BRAIN BARRIER AND INHIBIT MMP-9. IMPLICATIONS FOR THE TREATMENT OF HIV-ASSOCIATED NEUROLOGICAL DISORDERS

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Background and aim: The central nervous system (CNS) is a sanctuary in which HIV can independently replicate causing neurocognitive impairment even in patients with suppressed plasma viral load.
Darunavir (DRV), an antiretroviral drug belonging to the class of HIV protease inhibitors, has been approved for treatment of HIV-infected patients in combination with other antiretroviral drugs. However, the efficacy of DRV in the treatment of HIV-associated neurological disorders (HAND) is limited due to the low penetration through the blood brain barrier (BBB).
Therefore, innovations in DRV formulations, based on its encapsulation in optically traceable nanoparticles (NPs) may improve its transport through the BBB providing optical monitoring of drug delivery within the CNS.
Aim of this study was to synthetize biodegradable polymeric NPs loaded with DRV and investigate on their ability to cross an artificial BBB and inhibit in vitro gelatinase B (MMP–9), which represents a factor responsible for the development of HIV-related neurological disorders [1].
Material and Methods: Luminescent carbon dots (C-Dots) were synthesized by exploiting a one-step procedure [2] and co-encapsulated in poly lactic-co-glycolic acid (PLGA) based NPs with DRV (PLGA-NPs). For this purpose, oil in water emulsification–solvent evaporation method was used [3]. PLGA-NPs were fully characterized in terms of size, colloidal stability, morphology, optical properties, drug loading and drug release by means of complementary techniques. Astrocytes and brain immortalized endothelial cells (bEnd-3) were treated with different amounts of PLGA-NPs and their biocompatibility was evaluated by the MTT assay. Colture supernatants from astrocytes treated with both free DRV and PLGA-NPs were subjected to zymography to assess MMP-9 levels. The ability of PLGA-NPs to cross the BBB was evaluated on an artificial model of BBB obtained by a co-colture of primary astrocytes and bEnd-3.
Results: Biodegradable PLGA-NPs resulted characterized by average hydrodynamic diameter of about 130 nm, high colloidal stability in aqueous medium, good drug encapsulation efficiency, and relevant emitting optical properties in the visible region of spectrum.
The treatment of primary cultures of astrocytes with PLGA-NPs indicated the high degree of biocompatibility and their ability to inhibit the MMP-9 expression levels.
Interestingly, the assay on the BBB artificial model showed that a larger amount of DRV was able to cross BBB when incorporated in the NP-PLGA system rather than as free DRV.
Conclusions: The overall results highlight the great promise hold by these luminescent nanoformulations as optically traceable delivery nanovectors of DRV for the treatment of HAND.
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Antiretroviral Therapy

OP 7 EFFECTIVENESS AND LONG-TERM DURABILITY OF RILPIVIRINE-BASED SINGLE TABLET REGIMENS IN A LARGE COHORT OF HIV-INFECTED PATIENTS. A PRELIMINARY ANALYSIS

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Background: Single tablet regimens (STR) promote adherence among patients needing life-long antiretroviral therapy (ART). Among antiretrovirals, rilpivirine (RPV) shows a favorable profile with regards to long-term side effects. Aim of our study was to assess durability of RPV-containing STRs (RPV-STR) and to identify predictors of RPV discontinuation.

Materials and methods: Multicentre, retrospective study including all patients treated with a RPV-STR in the period 2013-2019 in a large cohort of patients in Italy. Virological failure (VF) was defined as two consecutive determination of detectable (≥50 copies/ml) HIV-RNA, or a single determination of HIV-RNA ≥200 copies/ml. ART simplification was defined as a reduction in pill burden or in the number of drugs composing the regimen; ART optimization as a switch to prevent long-term side effects. Univariable Cox's regression was performed to asses statistical association among variables with RPV-STR discontinuation.

Results: Five-hundred and eighty-nine HIV-1 infected patients were enrolled. Characteristics of the study population are outlined in Table 1, as well as statistical associations of each variable with RPV discontinuation. Median duration of RPV-STR treatment was 238 weeks (IQR 134-279 weeks). Reason for switch to RPV-STR in our cohort were optimization (n=266, 45.2%), simplification (n= 146, 24.8%), side effects (n=66, 11.2%), drug-drug interactions (n= 9,1.5%), VF or intensification (n=10, 1.7%) and unknown (n=7, 1.2%). Overall, 107 patients (18.2%) discontinued their RPV-STR during the study period. The reasons for discontinuation were loss to follow-up (n=30, 28.0%), drug intolerance or side effects (n=21, 19.6%), VF (n=19, 17.8%), patients' preference (n=11, 10.3%), drug-drug interactions (n=9, 8.4%), simplification (n=9, 8.4%) and other/unknown cases (n=8, 7.5%). Predictors of RPV-STR discontinuation at univariable analysis were found to be previous virological failures (HR 1.64 [95%CI 1.12-2.41], p=0.012).

Conclusions: In our multicenter cohort the rate of discontinuation of RPV-STR was lower than 20%. Such a low rate of VF might be explained by the easy administration and the few side effects of RPV-STR. However, it is important to correctly select patients especially in case of previous virological failures. Considering the need to life-long ART, such a durable drug might pose great advantage.

Antiretroviral Therapy

OP 8 Increase In body weight after a year of INI-exposure in a multicenter italian cohort

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Background: The use of Integrase Inhibitors (INI) has been related to weight gain. The aim of our study is to evaluate body weight changes in our cohort and assess differences between dolutegravir (DTG), raltegravir (RAL) and elvitegravir (EVG).

Methods: We retrospectively analyzed all patients (pts) starting a INI-based regimen in our multicenter cohort with an available weight measure 1 year before, at baseline and after 1 year. To assess changes, we used parametric and non-parametric tests, as appropriate. Logistic regression analysis was performed to evaluate predictors of weight gain.

Results: We enrolled 1899 pts: 1356 (71.4%) were males, 357 (18.8%) were naive and 555 (29.7%) were AIDS-presenters. Median age was 48 years (IQR 40-55), median time from HIV diagnosis for experienced pts was 15 years (IQR 9-22) and median time of ARV exposure was 12 years (IQR 6-18). As to INI regimens: 1010 (53.2%) were on a DTG-based regimen, 657 (34.6%) on a RAL-based one and 232 (12.2%) on a EVG-based one. Median body weight at baseline was 74Kg (IQR 63-85). After a year of follow-up, overall we observed a significant median increase in body weight +0.7Kg (+0.95%, IQR -1.1;+3.1, p<0.001). In our cohort, 102 pts (5.4%) had a body weight increase >5% in a year and 69 (3.6%) >7%. Treatment-naïve pts had a more pronounced increase in body weight compared to experienced pts (+3.0% vs +1.2%, p=0.034). When considering the 3 INIs separately, body weight increase was significant in all 3 groups: +0.94Kg (+1.4%, p<0.001) for DTG, +0.97Kg (+1.5%, p<0.001) for RAL and +1.3Kg (+1.9%, p<0.001) for EVG. No significant difference was observed between groups (p=0.717). In a multivariate analysis, being younger than 50 years (p=0.003), a peak HIV-RNA >500.000 copies/mL (p=0.045) and a previous increase in body weight over 5% in the year before the switch (p<0.001), resulted predictors of an increase in body weight >5%. Furthermore, a peak HIV-RNA >500.000 copies/mL (p=0.006) and a previous increase in body weight >7% in the year before the switch (p<0.001), resulted predictors of an increase in body weight >7%. In both analyses, no specific INI was predictor of weight gain compared to the others.

Conclusions: In our cohort INI exposure was related to an increase in body weight that was more pronounced in naive pts. No difference emerged between the 3 analyzed INIs. However, a high peak HIV-RNA and a previous increase in body weight before INI start were predictors of significant weight gain.

Antiretroviral Therapy

OP 9 TREATMENT OUTCOME AMONG HIV-1 INFECTED PATIENTS WHO STARTED FIRST-LINE ART PENDING GRT RESULTS FROM 2015 TO 2018

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Introduction: In daily clinical practice, it is sometimes mandatory to begin a rapid antiretroviral therapy (ART), before the Genotypic Resistance Test (GRT) result has been obtained.
However, a possible increased risk of virologic failure of a rapid ART, especially if compared with a GRT-based ART prescription, is still debated.
Herein, we aimed to investigate the incidence of virologic suppression (VS) in a cohort of HIV-1 infected patients who started first-line ART pending GRT versus a cohort of patients whose ART prescription was GRT-based.
Patients and methods: HIV-1 sequences from 521 subjects who started first-line ART between 2015 and 2018, with at least 1 year of follow up available, were retrieved from ARCA database. Mann-Whitney, Pearson $\chi 2$ or Fisher's exact tests were used to compare features of patients who started a rapid ART (defined as ART started pending GRT) versus those who started after GRT. Survival analysis (Kaplan-Meier curves with Log rank test and Cox Regression Model) was used to evaluate the probability and predictors of VS stratifying for the two groups.
Results: Overall, 398 (76%) of patients were males; median (IQR) age 40 (31–49) years, 30 (6%) diagnosed with AIDS, without significant difference in post-GRT vs pre-GRT group. Conversely, median (IQR) BL CD4 cells count [383 (253 -564) in post-GRT vs 257 (93-448) cells/μL in pre-GRT, p<0.001] and median (IQR) BL viral load (BLVL) [4.61 (4.01–5.08) in post-GRT vs 4.98 (4.40 – 5.57)log10 cp/mL in pre-GRT, p<0.001] were dissimilar between groups.
VS was observed in 120 (96.8%) vs 386 (97.2%) of subjects starting ART post-GRT vs pre-GRT, respectively (p=0.765).
By analyzing baseline GRTs, at least one resistance associated mutation (RAM) was observed in 15% vs 18% of patients (post-GRT vs pre-GRT respectively, p=0.563), without significant difference in terms of per-class drug RAM between the two groups. Overall, 138A/G/K was the most frequently observed (7%), followed by 106I (3.2%) and 33F (2.8%).
Overall, an INSTI-based regimen was prescribed in 59.7% and 59.4% (post-GRT vs pre-GRT, respectively); differently, a NNRTI-based regimen was more frequently prescribed in post-GRT group (27% vs 14%, p<0.001), while a PI-based regimen was preferred in pre-GRT group (24% vs 12%, p=0.004).
Kaplan Meier curves did not show a significant difference in terms of VS probability between the two groups. Conversely, it was influenced in both groups by calendar year of starting ART and different third drug class (logrank p<0.001 in both cases).
By performing a semi-parametric Cox-regression, a more recent calendar year of starting ART was associated with increased probability of VS, while a NNRTI-based regimen was associated with increased risk of viral failure (TABLE 1).
Conclusions: In this cohort, a rapid ART strategy did not influence the achievement of a high rate of VS. Indeed, main predictors of VS were calendar year of starting ART and first line regimen prescribed.

Antiretroviral Therapy

OP 10 RETROSPECTIVE ANALYSIS OF REASONS AND CHARACTERISTICS OF SWITCHES IN A COHORT OF WOMEN AFFECTED BY HIV INFECTION REFERRING TO "D. COTUGNO" HOSPITAL, NAPLES, PERIOD 2017 -2019

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Background: Persons living with HIV should remain on antiretroviral therapy (ART) indefinitely; however a switch in the drug regimen is often necessary. Recently, switching ART has become a strategy in clinical practice in order to reduce drug-to-drug interactions (DDI), prevent long-term toxicity, simplify the therapy and improve the adherence.
Women living with HIV (WLWH) are more likely to discontinue therapy than men (1). Despite they represent about 50% of worldwide population affected by HIV, nowadays data about ART switches among WLWH are lacking (2). Aim of this study was to evaluate the main reasons of ART switches, and characteristics of switches in a cohort of WLWH, experienced to ART.
Methods: We retrospectively analyzed the main reasons for switching ART and characteristics of switches among a cohort of experienced WLWH referring to the UOC "Immunodeficienze e Malattie Infettive di Genere", Cotugno Hospital in Naples, in the period 2017-2019. We classified the causes of switches in: optimization/simplification/proactive switch, virological failure, adverse events/toxicity and comorbidities causing DDI or other conditions requiring ART modifications, such as pregnancy. Moreover, we analyzed the causes of ART switches related to the characteristics of new ART regimens.
Results: In the study period we enrolled 247 WLWH (median age 45 years, 49% not Italian), who made at least one switch in the ART, with a total number of 346 switches: 163 patients underwent only one ART switch, 69 patients 2 switches and 15 patients 3 switches.
Table 1 shows the main reasons of switch: in 83% of cases, switch was secondary to optimization/simplification. Moreover, 30.3% of women changed ART in favour of STR regimens.
Table 2 shows the correlation between main ART switches and new therapy regimens. ART switches to TAF-based regimen or within the same drug class were more frequently secondary to optimization/simplification ($p<0.001$). Appearance of adverse events/toxicity and DDI/comorbidities mainly led to change ART in favour of INI-based regimens ($p<0.001$). In this group, 4 women changed ART because of pregnancy, starting RAL-based regimen. Switch to PI-regimens was mostly due to virological failure ($p=0.04$). Moreover, switches to 2-drug regimen were reported in 4% of WLWH and mainly contained INI + PI.
Discussion: According to current literature data, in our cohort of WLWH the main reason for switching was optimization/simplification, reflecting the recent changes in recommendations aimed to improve adherence and minimize drug toxicity and side effects. Similarly, INI-based regimens are preferred among switches for other reasons.
Real-life data shows that women experience more adverse events, comorbidities, polypharmacy and may face a pregnancy (3): therefore, when planning a ART regimen among WLWH, clinicians should be mindful of the peculiar characteristic of this population.

Antiretroviral Therapy

OP 11 ASSESSING THE FEASIBILITY OF 2-DRUG REGIMENS AS SWITCH STRATEGIES IN A MULTICENTER COHORT

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Background: 3TC-based 2-drug regimens (2DR) have become clinicians' preferred switch strategies in treatment-experienced patients (pts) with a better tolerability and lower costs compared with 3-drug regimens; however the risk of virological failure (VF) in pts on a 2DR requires attention in selecting patients more suitable for these strategies. We aimed to assess how many pts in our multicenter cohort could safely benefit from a 2DR.

Methods: We analyzed a cohort of virologically suppressed (i.e. HIV-RNA below each center's lowest limit of detection for at least one year), HIV-positive pts on a standard 3-drug regimen from 5 clinical centers from the Lazio region. We collected patients' clinical history and viro-immunological parameters and used a recently published predictive score to assess pts' risk of VF with a 2DR.

Results: We collected data on 1813 pts. Among them, 77 were HBsAg-positive while 88 had no available data on HBV-coinfection; moreover, 527 had no available genotypic resistance test and for 10 pts other data needed to calculate the score were missing. These pts were therefore excluded from the analysis. Overall, 1118 pts were left for analysis: 845 (81.2%) were males, with a median age was 48 years (IQR 40-56), a median time from HIV diagnosis of 9.6 years (IQR 4.7-15.6). Two-hundred and sixteen pts (11.9%) had a previous AIDS event while 125 (6.9%) were HCV-coinfected. Most common viral subtype was B (853 pts, 47.0%). Median time of virological suppression was 69.5 months (IQR 36.0-82.8). Full pts characteristics are shown in Table 1.

Considering all parameters, overall median score was 2 (IQR 0-4). To put this in perspective, 507 pts (45.3%) had a predictive score lower than 2 (negative predictive value for VF of 95%) and could therefore switch relatively safely to a 2DR. Moreover, raising the threshold to a score of 4 (negative predictive value for VF of almost 92%), the number of pts suitable for a 2DR increases to 869 (77.7%). Few of these pts (6 when considering a score ≤2 or 9 considering ≤4) have the V32I resistance mutation in last available genotypic test: this mutation is associated with reduced efficacy of darunavir. Moreover, 1 of the analyzed pts has the R263K mutation, which is associated with resistance to dolutegravir.

Conclusions: In the 5 analyzed clinical centers we found that more than 500 pts, today on a 3-drug regimen, could be safely switched to a 3TC-based 2DR possibly resulting in lower toxicity for pts and better use of financial resources for the healthcare system. The use of a decision algorithm appears a useful tool for Clinicians struggling with various simplification strategies.

Antiretroviral Therapy

OP 12 RISK OF FAILURE IN DUAL VS TRIPLE THERAPY IN NAÏVE HIV-PATIENTS: A META-ANALYSIS

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Background: 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: present original data from randomized or non-randomized trials; investigate in antiviral therapy-naïve HIV subjects the efficacy of a conventional triple ARV (control group), versus a dual ARV (experimental group); report the primary outcomes clearly defined as regimen failure; 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; be published from January 2007 up to January, 2019.
Results: Fourteen studies, from a total of 5,278, meet the inclusion criteria allowing a meta-analysis of 5,205 patients. The meta-analysis performed on study presenting data at 48 weeks, 10 studies, 3495 patients, reveals: the RR of treatment failure at 48 weeks was 1.20 (95%CI: 0.91-1.59), the analysis by subgroup didn't reveal statistical difference between subgroups: the RR of virological failure in 8 studies on 3184 patients was 1.54 (95%CI: 0.84-2.84). The RR of adverse drug reaction leading to discontinuation of regimen at 48 weeks in 8 study, on a total of 3204 patients, was 0.76 (95%CI: 0.43-1.33). In patients with less of 200 CD4+, the RR of treatment failure, in 2 studies without MRV on 172 patients, was 2.09 (95%CI: 1.05-4.17); in patients with equal to or greater than 200 CD4+, the RR of treatment failure, in 2 studies without MRV on 1467 patients, was 1.06 (95%CI: 0.74-1.52). Regarding the studies at 96 weeks, the RR of treatment failure, in 3 studies on 2,991 patients, was 1.15 (95%CI: 0.93-1.44); the virological failure, in 3 papers on 2,991 patients, was 1.10 (95%CI: 0.84-1.44).
Conclusion: Dual therapy, excluding those based on maraviroc, are as effective as those with three drugs, showing no difference according different dual therapy, except in patients with less than 200 CD4 considering data at 48 and 96 weeks.

Basic science and immunology

OP 13 DAA TREATMENT FAILS TO RESTORE THE INFLAMMATORY PROFILE BOTH IN HCV/HIV AND IN HCV INFECTED PATIENTS

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Background: Hepatitis C virus (HCV) co-infection represents a worsening condition in HIV-infected patients. The Direct Antiviral Agents (DAA) are highly effective in eradicating HCV also in HCV/HIV co-infected patients but the evaluation of their impact on inflammation and fibrosis is not still well defined. Aim of our study was to analyze the impact of DAA therapy on pro-fibrotic/inflammatory profile in HIV/HCV co-infected patients.

Methods: HIV/HCV co-infected patients (n=34) were enrolled on the basis of Fibrosis index (F3-F4) and sampled before DAA (T0) and after 12 (SVR12) and 24 (SVR24) weeks from the end of treatment. A matched groups of HCV mono-infected patients (n=20) were also enrolled at T0 and at SVR12. Healthy donor (HD, n=10) were also recruited as controls. Plasma samples were analyzed to define the soluble profile using ELLA platform (IL-6, sCD14, IL-17A, TGF-β, VEGF, TNF-α, free light chains (K and L). Principal Component Analysis (PCA) was performed to investigate the variance in the soluble mediators levels in enrolled patients before and after DAA.

Results: DAA treatment improved liver function (AST, ALT) both in HCV and in HIV/HCV infected patients (T0 vs SVR12 $p<0.0001$). Before treatment, in HIV/HCV patients, K+L, IL-6, TNF-α and sCD14 were significantly higher than HD ($p<0.001$). Although K+L decreased at SVR12 ($p<0.001$), TNFα decreased at SVR24 ($p<0.001$), they persisted higher than HD ($p<0.001$). No effects of DAA on sCD14 and IL-6 were observed. A comparable unbalanced profile involving K +L, IL-6, TNF-α was observed also in HCV patients before and after treatment. Differently, TGFβ levels in both groups were comparable to HD and slightly influenced by treatment.

PCA analysis allowed defining the contribution of each mediator within the profile. Using this approach, we confirmed that the pro-fibrotic/inflammatory profile in HIV/HCV co-infected and HCV mono-infected patients was different respect to HD and persisted altered after effective DAA treatment (Figure 1). The following cytokines were identified by PCA as responsible for the bulk of the variations in mediators levels at T0 and SVR12 and SVR24: in HIV/HCV patients K+L and TNF-α contributed to define PC1 (42% and 23 % respectively); IL-6, VEGF and TNF-α contributed to define PC2 (31%, 29% and 18% respectively). In HCV patients, IL-6 and K+L contributed to define PC1 (27% and 25% respectively) and K/L ratio, IL-17 and sCD14 contributed to define PC2 (32%, 25% and 21% respectively). Finally, a positive correlation between K+L and IL-6 was observed both in HCV and in HIV/HCV co-infected patients.

Conclusions: In conclusion, our study showed that DAA treatment reduces some pro-fibrotic/inflammatory mediators but the overall profile was not restored both in HIV/HCV co-infected than in HCV-mono-infected patients. We identified K+L, IL -6 and TNF-α as the main players in defining the altered inflammatory profile both in HIV/HCV and HCV infected patients

Basic science and immunology

OP 14 STEROL METABOLISM MODULATES SUSCEPTIBILITY TO HIV-1 INFECTION

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Background: 25-hydroxylase (CH25H) is an Interferon stimulated gene (ISG), which catalyzes the synthesis of 25-Hydroxycholesterol (25-HC). 25-HC plays a pivotal role in metabolic and infectious processes as this compound controls cholesterol homeostasis and sterol biosynthesis and influences the entry of several viruses, including HIV, into host cells.
We verified whether natural resistance to HIV-1 infection in HIV-1-exposed seronegative (HESN) individuals is at least partially mediated by particularities in sterol biosynthesis.
Methods: Peripheral blood mononuclear cells (PBMCs) and monocyte-derived macrophages (MDMs) isolated from 15 sexually-exposed HESN and 15 healthy controls (HC) were in vitro HIV-infected and analyzed for: 1) percentage of IFNa-producing plasmacytoid Dendritic Cells (pDCs); 2) lipoprotein Signaling and Cholesterol Metabolism RNA expression; 3) resistance to HIV-1 infection by p24 viral antigen quantification. Moreover, MDMs from 5 HC were in vitro HIV-infected in the absence/presence of exogenously added 25-HC to verify its effect on susceptibility to HIV-infection.
Results: IFNa-producing pDCs were significantly augmented in HESN compared to HCs both in unstimulated and in in vitro HIV-infected PBMCs ($p<0.001$ in both cases). This resulted in an increased expression of CH25H and of a number of genes involved in cholesterol metabolism (LXR, ABCA1, SCARB, HMGCS1, PPARg) and was associated with a significantly reduced susceptibility to in vitro HIV-1-infection in PBMCs and MDMs ($p<0.01$). Notably, addition of 25-HC to MDM of HC resulted in increased cholesterol efflux and augmented resistance to in vitro HIV infection.
Conclusions: Results herein show that in HESN sterol metabolism might be particularly efficient. This could be related to the activation of the IFNa pathway and results in a reduced susceptibility to in vitro HIV-1 infection. Further analyses are needed to examine the cholesterol pathway involvement in natural resistance to HIV-1 infection. These results, nevertheless, suggest a possible basis for therapeutic interventions to control of HIV-1 infection.

Basic science and immunology

OP 15 DIFFERENT AMOUNTS OF ACTIVATED OR EXHAUSTED EFFECTOR MEMORY T CELLS AMONG DIFFERENTIATED CD4+ OR CD8+ T LYMPHOCYTES DURING PRIMARY, ACUTE HIV INFECTION

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Background and Aim: Studies on primary, acute HIV infection (AHI) are crucial to understand the first interactions between the virus and the immune system. By using the most sophisticated technologies and the novel analytical tools required to investigate high-dimensional data in an unsupervised manner, we analysed peripheral blood mononuclear cell (PBMC) from patients experiencing AHI. Aim of the study was to identify subtle differences in exhaustion or cell senescence between CD4+ and CD8+ T lymphocytes.

Material and methods: We analysed PBMC from 14 HIV patients collected during AHI before HAART using a novel 18 parameter, 16 colour flow cytometry panel. Cells were thawed, washed and stained with PromoFluor-840 for cell viability (Promokine) and with the 10-colour IM T Duraclone panel (Beckman Coulter, BC), then added with other 5 mAbs recognizing CD25, CD127, CD38, CD95 and HLA-DR. A minimum of 0.5 million cells per sample were acquired using a 6 laser CytoflexLX (BC). Then, ".fcs" files were exported and pre-analysed using Flowjo, and CD3+,CD4+ or CD3+,CD8+ T cells were electronically gated and exported to CATALYST package under R-studio environment to perform high-dimensional data analysis (as depicted in the Figure, related to CD4+ T cells). As shown in the figure, the dimensional reduction was performed using Uniform Manifold Approximation and Projection (UMAP), while clustering was performed using FlowSOM algorithm based on artificial neural network.

Results: Concerning CD4+ T cells, 50.1% were naïve and 14.21% expressed the T-cell activation marker CD38, while 18.39% CD8+ T lymphocytes were naïve and 2.66% expressed CD38 protein. Central memory T cells (TCM) expressed detectable levels of CD38 too: 5.92% and 1.08% of total CD4 or CD8 T cells respectively. Both CD4+ and CD8+ effector memory T cells (TEM) showed high level of heterogeneity. More than 40% of CD8+ T cells were TEM, 31.75% of which expressed PD-1low, T cell activation markers like CD38 and HLA-DR but not CD57, that indicates cell senescence. About 5% of CD4+ T cells were TEM. Concerning CD8+ T cells, 20% were effector memory CD45RA+ (TEMRA) and 17.77% showed senescent characteristic since they were expressing CD57 but not PD-1. Of total CD4 T cells, only 1.26% were TEMRA and all of them expressed high level of CD57 but not PD-1. Finally, we could find the recently described population of T stem cell memory (Tscm), that were 0.28% and 0.5% of CD4+ and CD8+ T lymphocytes, respectively.

Conclusions: By using a novel bioinformatic approach, we could unravel, at least in part, the complexity of the T lymphocyte compartment in the early phases of the response to HIV. Indeed, we could observe that markers of exhaustion, activation and cell senescence are differently distributed among CD4+ or CD8+ T cells that were in the same differentiation status. Moreover, we could describe for the first time the presence of detectable amounts of circulating Tscm in patients experiencing AHI.

Basic science and immunology

OP 16 HIV+ PATIENTS: MODULATING EFFECTS OF ANTIRETROVIRAL THERAPY ON CYTOKINES' PROFILE AND MICROBIOTA COMPOSITION

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Background:
HIV infection remains a major public health problem globally, and systemic inflammation is one of the primary contributors to morbidity and mortality in HIV+ patients despite antiretroviral therapy (ART). An altered interplay between gut mucosa and microbiota during HIV infection may contribute to increased bacterial translocation and chronic immune activation.
For this reasons the aims of our study were:
- to define the gut microbiota composition in HIV+ patients before and after ART
- to characterize the systemic cytokines' profile of HIV+ patients before and after ART
- to evaluate the ART effects on gut microbiota and clarify the reciprocal influence between HIV infection, gut microbiome functions and correlated immune response

Material and methods: 22 HIV-infected patients were enrolled in the study. In ten patients, we characterized the fecal microbiota before (t0), and at 4(t4), 24(t24) and 48(t48) weeks after starting ART, through the "Next Generation Sequencing". We also evaluated in the same timing points the cytokines' profile in serum samples through Luminex MagPix analysis. In detail, we have assessed the level of 22 cytokines (MIP-1α, IL-7, IL-1ß, IL-4, IP-10, IL-6, IL-8, IL-10, IL-17A, IFN-ɣ, GM-CSF, TNF-α, IFN-α, MCP1, IL-9, P-selectin, IL-1α, IL-18, IL-21, sICAM1, IL-22, E-selectin).

Results: About the cytokines' modulation, after 48 weeks of treatment, we have obtained significant results only for some cytokines. In detail, MIP-1α (P. value 0,0234), IL-7 (P. value 0,022), IL-1ß (P. value 0,0223), IL-4 (P. value 0,0156), IL-8 (P. value 0,0391), IL-17A (P. value 0,0223), IFN-ɣ (P. value 0,0156), TNF-α (P. value 0,0078), IFN-α (P. value 0,0313), MCP1 (P. value 0,0234), IL-18 (P. value 0,0156) and E-selectin
(0,0391). While at t=24, only the IP-10 (P. value 0,0244) decreased as well as the IL-22 (P. value 0,0371) after 4 week of the ART treatment.
The microbiota analyses revealed that no differences in alpha-diversity (Shannon index) were detected according to the therapy regimen at different sampling time (t0, t4, t24, t48). Instead, analysis of beta-diversity (Bray-Curtis) suggested the presence of two clusters (PERMANOVA P=0.001) which mainly differed in the relative abundance of Enterobacteriaceae, Prevotellaceae and Bacteroidaceae, regardless of the therapy regimen and sampling point.
Finally, correlation analyses showed that Prevotellaceae were negatively correlated with P-selectin (Spearman P<0.0001; r: -0.57) and Enterobacteriaceae with IL-22 (Spearman P=0.0004; r: -0.51), whereas Bacteroidaceae were positively correlated with MIP-1α (Spearman P=0.0004; r: 0.53).

Conclusion: Our preliminary data showed that the ART treatment is able to modulate the serum profile of some cytokines and the composition of intestinal microbiota. In addition, because increasing data suggest a close relationship between gut microbiota and immunity, we have notably documented that the relative abundance changing of Prevotellaceae, Enterobacteriaceae, and Bacteroidaceae are correlated with P-selectin, IL-22 and MIP-1α.

Basic science and immunology

OP 17 ASSOCIATION BETWEEN SUBCLINICAL ATHEROSCLEROSIS AND IFN-I RESPONSE IN HIV-1 INFECTED PATIENTS

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Background: After the introduction of antiretroviral therapy (ART), people living with HIV-1 exhibit a longer life expectancy, but also increased inflammation and cardiovascular disease (CVD) compared to healthy individuals. The pathogenesis behind CVD involves traditional risk factors, metabolic disorders related to ART, chronic inflammation and immune activation associated with the virus itself. Of note, innate immune responses have a major role in the initiation of atherosclerosis. In this context, we aimed to study whether increased production of IFN-I and/or IFN related pathways might be involved in the development and progression of atherosclerosis during HIV-1 infection.
Materials and methods: A total of 34 HIV-1+ patients under ART and 21 healthy subjects asymptomatic for CVD were enrolled. Quantitative real-time PCR was carried out to analyze the mRNA expression of IFN-α, IFN-β and IFN-stimulated-gene (ISG) 56 in all subjects. Coronary CT scan was conducted in all HIV-1+ patients to evaluate stenosis degree (> or < 50%), calcium volume score, calcium Agatston score and myocardial extracellular volume (ECV). Carotid intima-media thickness (cIMT) was also measured in all HIV+ patients, and considered a sign of subclinical atherosclerosis if ≥ 0.9 mm. Clinical scores as Framingham, ASCVD and D:A:D were calculated in order to evaluate the clinical risk of CVD.
Results: An average 80-fold increase in IFN-α/β and ISG56 production was observed in HIV-1+ patients compared to healthy subjects. Among HIV-1+ patients, those with a coronary luminal stenosis >50% reported higher levels of ISG56 ($p=0.017$) and an increasing trend of IFN-α ($p=0.100$) expression compared to patients with stenosis <50%. No differences were recorded between these two groups regarding IFN-β expression. Patients with coronary stenosis degree >50% also showed higher Framingham ($p=0.019$), ASCVD ($p=0.011$) and D:A:D (0.004) score risk. The stenosis degree resulted to be related to a higher cIMT ($p<0.001$), which was directly associated to CVD development. In fact, higher calcium volume score ($p<0.001$), calcium Agatston score ($p<0.001$) and ECV fraction ($p=0.008$) were recorded in patients with cIMT >0.9 mm. However, no relationship was recorded between higher IFN-I expression and cIMT.
Conclusions: The expression of IFN-I can play a double role in HIV-1+ patients, as it is a major weapon to control cellular viral replication but it can also lead to chronic inflammation and enhanced risk of CVD. The overproduction of IFN-I may represent an interesting topic for further studies and a useful tool in the management of CVD in HIV-1+ patients in clinical practice.

Basic science and immunology

OP 18 P53/MIR34A/SIRT1 LOOP AND IMMUNE RECONSTITUTION RELATIONSHIP DURING CHRONIC HIV INFECTION

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Background: microRNA (mirRNA) are small non coding RNAs that endogenously regulate the gene expression at the post transcriptional level and can be modulated by HIV infection. miR-34a, belonging to a miRNA family able to regulate cell cycle progression, cellular senescence and apoptosis, has been up-regulated in T cells by HIV infection. miR-34 targets sirtuin 1 (SIRT1), a gene that regulates cellular senescence and limits longevity, that in turn, modulates p53 dependent apoptosis. In a previous study we showed that SIRT1 expression is lower on circulating hematopoietic progenitor cells in HIV infected patients under successful ART, highlighting that SIRT1 may play an important role in the regulation of correct replenishment of lymphocyte pool. The aim of this study was to analyse the loop p53/mir34/SIRT1 during chronic HIV infection and its relationship with lymphocyte activation/differentiation pathways.
Methods: Gene expression analysis was performed in PBMC by real time PCR in 26 HIV infected patients under successful ART and 16 healthy donors (HD). HIV patients were grouped on basis of CD4 T cell count (CD4>500/mmc, n=14 and HIV CD4<500/mmc, n=12).
Results: Our results showed that SIRT1 expression in PBMC decreased in HIV+ patients with CD4 T cell count <500 respect to HD ($p<0.01$). Accordingly, p53 and mir34 are significantly overexpressed in HIV+ patients respect to HD ($p=0.05$ and $p=0.0082$ respectively). To evaluate the effect of the upregulation of mir34 and p53 on lymphocytes homeostasis, we analysed their correlation with the expression of key regulators of lymphopoiesis such as BLNK, FOXP3, IL7, IL7R and IL6. We found that in HIV infected patients only BLNK, that regulates B cells development and activation, is negatively correlated with mir34 ($r=-0.5$, $p=0.04$) and positively with CD4 count ($r=0.5$, $p=0.04$). Noteworthy, a lower BLNK expression was found in HIV+ patients with low CD4 count ($p=0.015$, HIV CD4<500 vs HD and $p=0.008$, HIV CD4<500 vs HIV CD4>500), suggesting a possible impact on T cell homeostasis. These results therefore highlight as the regulating factor BLNK may play an important role in the loop p53/mir34/SIRT1 and in immune reconstitution impairment.
Conclusion: These data suggest that during chronic HIV infection the overexpression of p53/mir34 axis may downregulate SIRT1 that in turn affect the correct lympocytes pool replenishment involving key regulating factors such as BLNK.

Basic science and immunology

OP 19 LOWER IMMUNE ACTIVATION IN PERINATALLY THAN IN HORIZONTALLY HIV-INFECTED ADULTS

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Background: The aim of this study was to compare the level of activation, exhaustion and ageing of immune system in perinatally HIV-infected young adults (PHIV) and patients with similar age, but infected in adulthood (AHIV).

Methods: This was a cross-sectional study including young HIV-infected patients aged >18 and <40 years and on ART since at least 12 months. Patients with HIV-RNA>50 copies/mL or active AIDS-defining diseases were excluded. We comparatively measured by flow cytometry the expression of: A) immune exhaustion and activation markers on CD4+ and CD8+ T cells; B) soluble markers of inflammation (VCAM1, sCD163, IL-6, adiponectin); C) telomere length in PHIV and AHIV patients. Values were expressed as medians (interquartile range) and analysed by Mann Whitney U test.

Results: We enrolled 26 PHIV and 18 AHIV with median age of 26 (8.0) and 18 (6.8) years (p 0.080). While percentages of total CD4+ and CD8+ T lymphocytes were comparable in PHIV and AHIV (Table), PHIV showed significantly higher percentages of naïve CD4+ and CD8+ T cells (p 0.003 and p <0.001) and lower percentages of Terminal Effector Memory CD4+ and CD8+ T cells (p <0.001 and p <0.001). On both CD4+ and CD8+ T lymphocytes AHIV exhibited significantly higher expression of exhaustion markers, namely PD-1, TIM-3, Lag-3 (p<0.001 for all) and EOMES (p 0.021), than PHIV (Table). In line with these results, also the percentage of activated CD8+CD38+HLA-DR+ T cells resulted higher in AHIV than in PHIV (p 0.007). Concerning the T regulatory arm, the percentages of CD4+CD25 +FOXP3+ and CD8+CD28-CD127-CD39+ T regulatory cells (Treg) were similar in the two groups: however, a higher percentage of activated CD4+ Treg (CD45RA-FOXP3high) showing increased expression of PD-1, TIM-3, Lag-3 and EOMES was present in AHIV than in PHIV (p 0.005) (Table). Among soluble markers of inflammation, only adiponectin showed different (reduced) concentrations in PHIV than in AHIV (p 0.008, Table). Telomere length, a biomarker of ageing, was comparable in the two groups.

Conclusions: These data exclude alterations of lymphopoiesis in PHIV, suggesting a normal development of the immune system in children perinatally infected by HIV.

Signs of immune-exhaustion/activation prevailed in AHIV than in PHIV, suggesting a different dynamic of interaction between HIV and the immune system in the two groups. It will be of interest to monitor PHIV to verify whether their lower level of immune activation will have a clinical impact on the frequency of HIV-associated comorbidities.

Basic science and immunology

OP 20 MICROBIOTA COMPOSITION IN HIV-POSITIVE AND HIV-EXPOSED UNINFECTED PEDIATRIC SUBJECTS

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Background: A profound gut dysbiosis has been described in HIV+ adults, destabilizing the intestinal barrier and promoting disease progression. While in infants in utero HIV exposure and maternal microbiota seem to be the major players in shaping the microbiota composition and immune system, little is known on what happens in older pediatric subjects. We investigated fecal microbiota composition, intestinal barrier integrity and monocyte activation in HIV+ vs HIV-exposed uninfected (HEU) pediatric subjects.

Methods: We enrolled 80 pediatric subjects (<18 yrs), born from HIV+ mothers. Exclusion criteria: age <1year, hepatitis co-infection, prebiotic supplementation, antibiotic use in the past 2 weeks. Specimen: plasma, stool. Lab analyses: gut damage (I-FABP, E-Cadherin) and monocyte activation (sCD14) markers by ELISA; microbiota composition (alpha, beta diversity, relative abundance) by MiSeq Illumina tech. Statistical analyses as appropriate.

Results: 47 (59%) were HIV+ on cART, 33 (41%) HEU, with median age of 14 and 12 yrs respectively. As shown in Fig1a, the 2 groups significantly differ for feeding practice (p<.0001), delivery mode (p=.0005) and maternal cART during pregnancy (p<.0001). Interestingly, while I-FABP and E-Cadherin levels were similar (p=.960, p=.931, Fig1a), HIV+ showed higher sCD14 vs HEU (p<.0001; Fig1a). The gut microbiota analyses revealed a similar bacterial composition in terms of alpha diversity (Fig1b), beta diversity (Fig1c) and relative abundance (Fig1d). Few differences were observed following the LEfSe analyses, with HIV+ showing bacteria belonging to the class of Clostridia alone, while HEU bacteria belonging to the class Clostridia, Bacteroidetes, Alphaproteobacteria (Fig1e). We restricted the analyses to individuals >5yrs (n=64), confirming no differences in microbiota composition. The LEfSe analyses highlighted higher prevalence of Clostridia in HIV+, Bacteroidetes and Actinobacteria in HEU (Fig1f).

Conclusions: In our cohort of HIV+ and HEU pediatric subjects, we describe similar gut microbiota and intestinal barrier integrity, yet higher sCD14 in HIV+. While the observation of comparable intestinal barrier integrity might support the positive role of cART in preserving gut integrity in pediatric subjects, the finding of higher monocyte activation seems to imply that residual inflammation, known driver of disease progression in the course of cART, lays its foundation already in the pediatric age.

Basic science and immunology

OP 21 SWITCHING TO INTEGRASE INHIBITORS IS NOT LINKED TO WEIGHT INCREASE IN YOUNG ADULTS AND ADOLESCENTS PERINATALLY INFECTED WITH HIV, RESULTS FROM A 10-YEARS OBSERVATIONAL STUDY

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Background: An unexpected excess in weight gain has recently been reported in course of integrase strand transfer inhibitors (INSTI) treatment, but little data is available on this effect in the long-term exposure to treatment. Moreover, the possibility of weight gain in people who are perinatally infected with HIV (PHIV), and thus exposed to lifelong therapy, still needs to be explored. Aim of this study is to investigate whether weight gain differs among adult PHIV treated with INSTI compared to other regimens, over 10 years of follow up.

Methods: Retrospective multicenter case-control study. Adult PHIV followed between 2010 and 2019 in two outpatient services in Northern Italy were included if they had at least two weight measures available in two successive years of observation. Patients were considered as cases if they were switched to an INSTI containing regimen at any time of the study (INSTI group) or controls if they were never exposed to INSTI (non-INSTI group). Baseline (T0) was considered the date of the switch for the INSTI group, while T0 was randomly assigned for non-INSTI group. Mixed effects models were used to compare the post-T0 change weight between INSTI and non-INSTI groups and to assess the change weight per year pre- and post- T0.

Results: A total of 66 participants, 50.0% women, 92.4% Caucasian were included. They had a median follow-up of 9 years (range 2-10); 4 years (range 1-8) before-T0 and 3 years (range 1-9) after-T0. Mean age at last study visit was 27.3 (SD± 4.8) years and the mean CD4+ T-cell count was 820.8 (SD± 323.6) cells/mm3. None of the study participants was in treatment with an INSTI-regimen at the first observation. Among them, 45 were subsequently switched to INSTI, while 21 remined in the non-INSTI group. The INSTI group experienced a mean increase (pre-post T0) in body weight of 0.66 Kg/year (95%CI 0.38;0.95, p<.0001), while in non-INSTI group the mean increase was 0.53 Kg/year (95%CI 0.11;0.95, p=0.013), without a significant difference between groups (p for interaction between time and treatment regimen=0.867, Figure).

Analyzing the change in weight by gender, we noticed that male patients seemed to gain slightly less weight after switching to an INSTI regimen (-0.08 kg/year, 95%CI: -0.79;0.62) compared to female (+0.16 kg/year, 95%CI: -0.60 -0.92). However, both differences were not significant (p for interaction between time and treatment regimen=0.884 and 0.732, respectively).

Among patients on INSTI, the weight gain after T0 was higher than pre-T0, of +0.28 kg/year (95%CI -0.30;0.85), although this difference did not reach significance (p=0.340). Also, weight change was similar in patients who started an INSTI-regimen either with detectable HIV RNA (>50 copies/mL) or not (-0.66 kg/year, [95% CI -1.83;0.50], p=0.256).

Conclusions: PHIV switched to an INSTI-based regimen did not experienced an excessive weight gain compared to those who were treated with a non-INSTI based regimen in our cohort.

Basic science and immunology

OP 22 AN ATYPICAL CASE OF HIV-1 ELITE CONTROLLER: 15 YEARS OF FOLLOW UP

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Background: Up to now, little is known about the mechanism by which some patients spontaneously control HIV viral load below the limit of detection, a group known as "elite controllers". We identified an unusual elite controller who resulted both HIV-RNA and HIV-DNA undetectable for more than 15 years follow-up. At the same time, even with CD4 +Tcells always below 100 cells/mm3, the patient never presented any opportunistic infection.

Material and methods: A 34-year-old white female was diagnosed with HIV infection in 2004 by ELISA assay. Her Western Blot (WB) met all the reactivity criteria. She denied any symptoms, but she had HIV risk factors. Despite seropositivity, HIV-RNA was undetectable. In order to identify factors underlying this virological control, we performed several laboratory tests. HLA class I and class II antigens were identified by using serological and genomic typing. HIV-DNA was measured in bone marrow and ileum biopsies (RT-PCR). Lymphocyte subpopulations, CCR5 and CXCR4 coreceptor expression were evaluated by flow cytometry. mRNAs expression of innate immunity was measured by RT-PCR. HIV-RNA (Versant KPCR Siemens Healthcare) and HIV-DNA were measured over years.

Results: Since her HIV diagnosis, patient remained clinically well in the following 15 years, even if her CD4+Tcells counts never exceeded 100 cells/mm3. Patient resulted positive for A32/33, B39/6 and DRB1 1/13 HLA alleles. Bone marrow analysis showed a poor white blood cell cellularity, a normal red blood lineage and 68 copies/106 cells of HIV-DNA were found. An inflammatory infiltrate of lymphocytes, mainly CD8+ suppressor phenotype, was found in ileum biopsy as well as 23 copies/106 cells HIV-DNA. Patient showed a permanent leucopenia, reduced lymphocyte percentage and increased values of monocytes. Lymphocyte subpopulations showed NK cell value higher than normal. CXCR4 and CCR5 coreceptor expression was evaluated at baseline and after PHA stimulation resulting higher than normal intracellularly but much lower than healthy donors (HD) at surface level. HIV-RNA and HIV-DNA quantifications resulted always undetectable even if a persistent positive WB assay was detected also 15 years later. The levels of mRNAs coding for factors involved in viral control (IL32A, P56, MXA, SAMHD1) were the same as those found in HD but lower than ART naïve HIV+ patients. Levels of APOBEC 3G and APOBEC 3F mRNAs were also investigated and resulted inferior compared to HD and HIV+ controls. In contrast, in our patient levels of ISG15 mRNA were higher than HD.

Conclusions: Given her characteristics, our patient does not fulfil any of the current classifications of spontaneous control. The WB positivity with undetectable HIV-RNA and HIV-DNA may suggest some virus presence in tissue reservoir. Further, due to her deep immunodepression, it might be assumed that the patient developed unique defence mechanisms which contribute to avoid both HIV replication and opportunistic infections.

Clinical HIV

OP 23 NEWLY DIAGNOSED HIV INFECTED PATIENTS IN BRESCIA, NORTHERN ITALY: EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS AND POSSIBLE TARGETS OF PREVENTION AND EARLY DIAGNOSIS CAMPAIGN

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Background: An active surveillance of socio-demographic, behavioural and clinical characteristics of patients with new HIV diagnosis in a high HIV prevalence Province (Brescia, Northern Italy) was conducted since 2010. Here we report the findings for the period 2010-2018.

Matherial and Methods: A retrospective, single-center study was conducted on newly HIV-infected patients evaluated in Outpatient HIV Clinic in Brescia, Northern Italy, from January, 1st, 2010 to December, 31st, 2018, using a database generated with clinical and biochemical data of patients. A descriptive analysis of patients characteristics was performed.

Results: 968 patients were diagnosed with HIV infection in the study period. Mean age was 40 years (SD 11), 73.9% were male and 67.7% were Italian. Among females, only 37.5% were Italian ($p<0.001$ vs males). Foreign patients were from 30 different countries, mostly from Africa (17%) and Eastern Europe (7.6%). 58.4% of patients declared heterosexual intercourses as risk factor for HIV acquisition, while 33.7% classified themselves as MSM (men who have sex with men) or bisexuals; only 5% were IVDU (intravenous drug users). HBV and HCV co-infection were detected in 4.4% and 8.6% (detectable HCV RNA in 55/84) of patients, respectively. Mean CD4+ T-cell count at the time of diagnosis was 354 cells/microL (SD 282 cells/microL). The proportion of late presenters (CD4+ T-cells <200 cells/microL at diagnosis) was 35%. Patients characteristics according to calendar year of HIV diagnosis are shown in Figure 1, 2 and 3. AIDS-defining events were detected in 19.5% patients at HIV diagnosis. The most frequent opportunistic infection was pneumocystis jirovecii pneumonia (53/189), associated in 43.4% of cases with a further AIDS-defining event, mostly disseminated CMV (cytomegalovirus) infection. HIV diagnosis was made during pregnancy in 17.4% of women, significantly more frequently in foreigners than in Italians ($p<0.001$). 116 (12%) study patients were lost to follow up at the end of the study, while 40 (4.1%) were deceased

Conclusions: A mean of 107 new HIV cases entered every year our Outpatient HIV Clinic. In line with national data, most newly infected patients are male, Italian and heterosexuals. Female patients are mostly non-Italian also in our Cohort and frequently diagnosed during pregnancy. A significant proportion of patients are late or AIDS-presenters. The surveillance of recent HIV infection in our geographical region is a useful tool to identify sub-population at risk (e.g. foreign women), which can be addressed in prevention and early diagnosis programs.

Clinical HIV

OP 24 ROSUVASTATIN DECREASES SERUM INFLAMMATORY MARKERS AND SLOWS ATHEROSCLEROSIS PROGRESSION RATE IN HIV-INFECTED PATIENTS WITH METABOLIC SYNDROME

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Objectives: Metabolic syndrome is usually associated in general population with systemic inflammation and higher cardiovascular risk, and statins have shown beneficial effects on reducing serum inflammatory markers in these subjects. However, data about the effect of statins in patients with HIV infection and metabolic syndrome are lacking to date.

Methods: Prospective cohort study of HIV-infected patients aged from 40 to 60 years, on combination antiretroviral therapy (cART), with or without metabolic syndrome (MetS), who started a lipid-lowering therapy with rosuvastatin (10 mg daily), and were followed-up for 12 months. The primary endpoint was change in serum levels of inflammation markers: high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α). The secondary endpoint was change in the intima-media thickness (IMT) assessed by a carotid ultrasonography performed at baseline and after 12 months.

Results: On the whole, 98 patients were enrolled in the study: 51 with MetS (MetS group) and 47 without MetS (control group). Overall 86% were men, 94% Caucasian, and the mean age was 48.7 years. The mean CD4 T lymphocyte count was 564 cells/mm3, 91 (93%) had plasma HIV RNA <20 copies/mL, 58% were smoker, 16% had hypertension, 61% triglycerides >150 mg/dL, 65% HDL cholesterol <50 mg/dL, 24% BMI >25 Kg/m2, and the mean 10-year cardiovascular disease risk (by the 2013 ACC/AHA equation) was 8.2%. After 12 months, rosuvastatin produced a significant decrease in median serum levels of hsCRP (-0.31 mg/dL; 95% CI -0.55, -0.09; p=0.025), IL-6 (-2.3 pg/mL; 95% CI, -3.5, -1.1; p=0.007), and TNF-α (-6.5 pg/mL; 95% CI, -9.9, -3.3; p=0.011) in patients with MetS. On the contrary, in controls rosuvastatin did not lead to a significant change in median levels of hsCRP (-0.06 mg/dL; 95% CI -0.33, +0.27; p=0.388), IL-6 (-0.8 pg/mL; 95% CI, -1.9, +1.4; p=0.311), and TNF-α (-1 pg/mL; 95% CI, -1.9, +0.9 p=0.447). After 12 months, the mean IMT increase at the carotid bifurcation was significantly lower in the MetS group than in the control group (0.019 vs 0.033 mm; p=0.031), and mean IMT increases were significantly lower in the MetS group than in the control group in all the evaluated anatomical sites.

Conclusion: Our findings suggest that rosuvastatin is effective in reducing serum inflammation markers and slowing atherosclerosis progression rate in HIV-infected patients on cART and with MetS, while its effect on serum biomarkers and IMT increase seems to be not significant in those without MetS. These preliminary data stress the potential role of rosuvastatin in the management of cardiovascular disease risk in HIV-positive subjects with MetS.

Clinical HIV

OP 25 DURABILITY OF INSTI-BASED REGIMEN IN GERIATRIC PEOPLE LIVING WITH HIV. DATA FROM THE ITALIAN MULTICENTER GEPPO COHORT

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Background: No randomised clinical trials studied cART effectiveness in geriatric HIV patients. In particular, durability of InSTI-based in people living with HIV aged >65 years is still unknown. The aim of the study is to describe the durability of first InSTI regimen in a geriatric HIV population.

Methods: People were prospectively recruited in the period 2017-2019 from the Geriatric Patients Living with HIV/AIDS (GEPPO) cohort, an Italian prospective observational multicentre study characterising multimorbidity and geriatric syndromes in people living with HIV >= 65 years with a special focus on antiretroviral (ART) prescription. Inclusion criteria was the initiation of InSTI based regimen after 2017. InSTI included were dolutegravir (DTG), elvitegravir/cobicistat (ELV) and raltegravir (RAL). Study end point was time to discontinuation of first InSTI regimen. We modelled descriptive and survival analysis as well as a Cox regression analysis to assess predictors of InSTI discontinuation.

Results: Among a total of 1531 patients aged >= 65 years enrolled between 2017 and 2019 in the GEPPO cohort, we included a total of 823 patients in this analysis. At baseline, median age was 69.7 (IQR 7.28), 667 (81%) were males, median CD4+ t-cell count at baseline was 618 (IQR 390); 94.9% had HIV RNA <50 copies. Multimorbidity was present in 348 (42.3%) subjects, while 221 (26.9%) were in polypharmacy (more than 5 drugs excluding cART).

Overall, 485, 96 and 242 patients received (as first InSTI) DTG, ELV and RAL respectively, in particular 168 (20.4 %) received 2DR DTG-based, among whose 75 (44.6%) with 3TC, 43 (25.6%) with RPV and 50 (29.7%) with other molecules; 477 (57.9%) received a standard triple therapy. Patients included were in ART for (median and IQR) 16.1 (9.87), 12.8 (11.1) and 18.3 (9.98) years respectively, with significant differences among the three InSTIs (Kruskal-Wallis test, $p < 0.001$). The median follow-up time was 16.20 months (using KM estimator).

At the end of follow up 31, 22 and 51 patients discontinued DTG, ELV and RAL respectively with a proportion of discontinuation estimated in 6.4%, 22.9%, 21.1% respectively for DTG, ELV and RAL estimated (KM) median discontinuation time for ELV was 29 months and 36 months for RAL while DTG didn't reach 50% discontinuation.

The curve of InSTI regimen discontinuation is showed in figure 1, the log rank test among the three InSTIs was significant ($p<0.001$). Among patients who discontinued their regimen (104) we found 0 (0%) virological failure, 30 (28.8%) simplification/deprescription, 11 (25.9%) other reasons, including toxicity.

Conclusions: This longitudinal study in elderly people demonstrated that DTG-based regimens (regardless of accompanying drugs) were highly durable. While several reasons account for drug discontinuation in this group of fragile patients virological failure was not observed.

Clinical HIV

OP 26 WEIGHT GAIN AND BODY COMPOSITION CHANGES IN PEOPLE LIVING WITH HIV TREATED WITH INTEGRASE STRAND TRANSFER INHIBITORS: A LONGITUDINAL ASSESSMENT WITH BIOIMPEDANCE VECTORIAL ANALYSIS

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Introduction: Weight gain and body composition changes are common in people living with HIV (PLWH) on Antiretroviral Therapies (ART). Growing focus has been recently paid to the possible implication in this process of Integrase Strand Transfer Inhibitors (INSTI), although discordant evidence come from recent works. Aim of our study was to prospectively evaluate, using Bioimpedance Vectorial Analysis (BIVA), to which extent body composition changes occur in a cohort of PLWH initiating a INSTI-based regimen both as a first- or a second-line ART.

Methods: From January 2018,after informed consent, a nutritional counseling and a BIVA test were offered at baseline and at month 3, 6 and 12 to all newly-diagnosed patients starting any ART regimen (group A) and to PLWH switching their first line ART in favor of an INSTI-based regimen (group B). Weight, BMI,Free Fat Mass (FFM) and Fat Mass (FM) were obtained. PREDIMED questionnaire on adherence to Mediterranean diet was proposed and physical activity level was assessed. For each group, univariate and multivariate analyses were performed to determine clinical, immune-virological and therapeutic features associated with changes in nutritional status and body composition. A p value <0.05 was considered statistically significant.

Results: At time of writing, a total of 49 pts, 77% males, mean (SD) age 44.4 (±12.8),with at least 3 months of follow-up (FU) have been enrolled, 34 of whom naïve to ART and 15 switching to an INSTI-based second line therapy. In group A, at baseline mean(±SD) weight was 68.7(±4.4) kg and BMI was 23.6 (±4.6). An INSTI regimen was started in 15 (44%) PLWH, a PI-based in 16 (47%), and a NNRTI-based in the remaining 9%. Overall, over a FU time of 8.3 (±3.8) months, a mean (SD) of 4.5(±7.9) kg of weight was gained (both in FM and FFM). In Table 1a, mean increment of weight, FM and FFM according to different clinical and virologic features are reported. At multivariate analysis, also taking into account adherence to Mediterranean diet and physical activity level, no relation was found between weight, FM and FFM gain and a specific ART regimen. Factors related with FM gain were instead female sex and AIDS stage at diagnosis (r2=-9.25, p=0.004 and r2=7.00, p=0.001, respectively). Conversely, detectable viremia at the end of FU and lower baseline CD4 count were respectively related to an increase (r2=2.41, p= 0.017) and a decrease(r2=-0.007, p<0.001) in FFM. In group B (Table 1b), over a mean (SD) of 8.2 (±3.2) months of FU after switch to INSTI, only a slight, not statistically significant, weight gain [mean (±SD) of 0.5±1.7 Kg] was observed, mainly in FFM [mean (±SD) of 0.9±1.8 Kg/m].

Conclusions: Several factors could affect weight gain and body composition in PLWH; according to our interim analysis, however, the type of ART seems not to play a major role. BIVA could represent a useful tool to deeply understand this process, once extended to a larger population.

Clinical HIV

OP 27 TRANSMITTED DRUG RESISTANCE IN NEWLY DIAGNOSED HIV-1-INFECTED PATIENTS IN A LARGE TEACHING HOSPITAL OF THE NORTHERN ITALY

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Background: Resistance to antiretroviral drugs can complicate the management of HIV-1 infection and impair control of its spread. The aim of the current study was to investigate the prevalence of transmitted drug resistance (TDR) among antiretroviral therapy (ART)-naïve patients with new diagnosis of HIV-1 infection made in the S.Orsola Teaching Hospital (Bologna) between 2017 and 2020.

Material and Methods: The protease/reverse transcriptase sequences and the integrase sequences (nucleotide positions 2268-3287 and 3776-4639 of HXB2, respectively) were analyzed using the calibrated population resistance (CPR) tool in the Stanford University HIV drug resistance database (http://cpr.stanford.edu/cpr.cgi).

The 2009 Stanford Surveillance Drug Resistance Mutation (SDRMs) list include the following codon sites in the protease region (PR): 23, 24, 30, 32, 46, 47, 48, 50, 53, 54, 73, 76, 82, 83, 84, 85, 88, 90; the following codon sites in the reverse transcriptase region (RT): 41, 65, 67, 69, 70, 74, 75, 77, 100, 101, 103, 106, 115, 116, 151, 179, 181, 184, 188, 190, 210, 215, 219, 225, 230 and the following codon site in the integrase region (IN): 66A, 92, 118, 121, 138, 140, 143, 147, 148, 155, 230, 263.

Results: Among 178 HIV-1-infected, ART-naïve patients, 162/178 (91%) were men and 101/178 (57%) harbored a B subtype. In detail, 178 PR/RT and 117 IN sequences were analyzed. A TDR to any class of antiretroviral agents was detected in 14 out of 178 sequences (7.9%). The prevalence of TDR to each class of drugs was 3.9% for nucleoside reverse transcriptase inhibitors (NRTIs), 3.4% for non-nucleoside reverse transcriptase inhibitors (NNRTIs), 2.8% for protease inhibitors (PIs), and 0.9% for integrase strand transfer inhibitors (INSTIs). The most frequent NRTI mutations were T215S/I/D (n=6), M41L (n=3), D67N/G (n=3), L210W (n=3) and K219Q (n=3). K103N (n=3) was the most prevalent mutation in the NNRTIs class, following by G190A (n=1) and Y188L (n=1). In PR, the mutations M46I/L (n=2) and F53Y (n=3) were detected. The only drug resistance mutation identified in the integrase was E138K, observed in one patient diagnosed in January 2020 and infected with a CRF01_AE subtype. TDR was also more prevalent among patients infected with B subtype compared to all non-B subtypes (9.9% vs 5.2%) and was higher among non-Italian patients (8 cases). The trend analysis showed a decrease in the prevalence of TDR in PR and RT sequences in comparison with previous years, but a sentinel mutation in the integrase region was detected for the first time during the observation period.

Conclusions: Overall, the phenomenon of TDR in newly diagnosed HIV-1-infected patients in our hospital was limited and comparable or lower than the prevalence observed in other European countries. However, a continuous virological surveillance is necessary, particularly with the increasing clinical use of INSTIs, in order to border its local spread and to optimize the ART management.

Clinical HIV

OP 28 SAME DAY TREATMENT AND RAPID ANTIRETROVIRAL THERAPY INTRODUCTION IN A COHORT OF UNSELECTED NEWLY-DIAGNOSED HIV-POSITIVE INDIVIDUALS

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Introduction: Rapid antiretroviral (ARV) treatment initiation has been demonstrated to be feasible and associated with good clinical outcomes in various settings, from rural Africa to large US cities. Scaling up this approach can contribute to improve treatment access and take universal HIV treatment to population scale. Its feasibility, acceptability and effectiveness in unselected Italian populations has not been explored yet.

Methods: In 2017, a recommendation in our clinic was issued to conflate as much as possible the time between HIV diagnosis and ARV initiation in the outpatient setting, ideally initiating ARV during the first visit (same day treatment [SDT]) or within 48-72h. Herein, we describe how this recommendation affected the time to treatment initiation, HIV-RNA suppression and retention in care of newly diagnosed patients.

Results: Between Jan 1st 2018 and Jan 31st 2020, 75 HIV-positive patients accessed for the first time to our outpatient clinic while naïve to ARV and with no history of recent hospitalization or diagnosis of AIDS-defining conditions contraindicating rapid ARV introduction. Their characteristics are depicted in Table 1. ARV was initiated in 74/75 patients, after a median (IQR) of 7 (1-14) days, significantly more quickly than in 2017 (14 [8.75-27.25] days, P<0.001); in 2018 -2020, 23%, 32% and 55% of the patients initiated ARV during the first visit, within 3 days and within 1 week versus 8%, 10% and 21% in 2017, respectively. As shown in Table 2, time to ARV introduction progressively reduced across time.

No association was found between SDT or "within 3 days" treatment and gender at birth, sexual orientation or baseline CD4 T-cell count. Conversely, SDT was significantly less likely among older people (per year increase, OR 0.94; 95%CI 0.89-0.99; P=0.02) and more frequent among transgender female sex workers (OR 6; 95%CI 0.91-39.4; P=0.06).

Regarding treatment efficacy, the proportion of patients with HIV-RNA <200 at month 1, 3 and 6 were 54% vs. 61%, 81% vs. 80% and 85% vs. 91% among those treated within ≤3 or >3 days, respectively (all P >0.05). Also, median time to first HIV-RNA <50 was comparable in the two groups (47 [32-96] vs. 47 [30-103] days; P=0.97). Six patients interrupted the follow-up: 3 (12.5%) among those who initiated treatment within 3 days (2 lost when HIVRNA was <200 cp/ml, 1 never showed up after the first visit) and 3 (5.9%) among those in whom treatment was deferred (1 lost before treatment initiation, 1 moved abroad, 1 died). [P=0.32] No treatment was changed because of transmitted drug resistance or due to the results of other baseline exams, when they became available.

Discussion: Rapid ARV treatment initiation among HIV-positive patients presenting for the first time was feasible and associated with high rates of virological suppression and retention in care. Efforts to promote SDT led to an overall significant reduction of time to ARV introduction, even when SDT was not feasible.

Clinical HIV

OP 29 CHANGES IN HOMEOSTATIC MODEL ASSESSMENT FOR INSULIN RESISTANCE (HOMA-IR) INDEX IN TREATED HIV-1 INFECTED PEOPLE ON VIROLOGICAL SUPPRESSION

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Background: Antiretroviral therapy (ART) may play a role in increasing insulin resistance (IR) among HIV−1 infected people; recently, attention was focused on metabolic impact of newer drug regimens.
Aim of this study was to assess change in homeostatic model assessment for insulin resistance (HOMA-IR) index in HIV-1-treated people, virologically suppressed, who switched to a different ART regimen.
Methods: Cohort study on adult HIV-1 infected people receiving ART, with HIV-1 RNA <50 copies/mL, who switched the anchor drug (the last available switch was considered), with a HOMA-IR determination at or within 90 days the date of switch (baseline, BL) and ≥1 determination after 6 months of follow up from BL; follow up was censored at discontinuation of at least one drug of the considered regimen or at last available visit. Patients with a diagnosis of diabetes mellitus were excluded. HOMA-IR was considered normal if ≤2.5, according to the literature data.
To avoid effects of extreme values on estimates of HOMA-IR, values were winsorized at the 1st and 99th percentile. Mixed linear models were used to estimate mean changes in HOMA-IR over time.
Results: We evaluated 526 individuals followed for a median of 2.5 years (IQR=1.7-3.8). At BL, median age was 50 (IQR=43-55) and males were 79.3%. BL HOMA-IR ≤2.5 was observed in 335 (63.7%) subjects. Other characteristics are shown in Table.
At BL, IR positively correlated with BMI (r=0.305, p<0.001): body mass index (BMI) ≤25 Kg/m2, >25-≤30 Kg/m2 and >30 Kg/m2 was found in 68%, 28% and 4% of people with HOMA-IR ≤2.5 compared to 49%, 35% and 16%, among individuals with HOMA-IR >2.5 (chi-square test: p<0.001); similarly, changes in HOMA-IR were associated with changes in BMI (r=0.135, p<0.0001).
Overall, mean (95% confidence interval, CI) values of HOMA-IR at BL, 6, 12, 24 and 36 months, were 2.6 (2.42-2.77), 2.85 (2.58-3.12), 2.74 (2.47-3.02), 2.79 (2.53-3.05), 3.08 (2.59-3.56) respectively, for an overall unadjusted mean change of +0.12 (95%CI=0.02-0.22, p=0.017).
At multivariable analysis, the adjusted mean change in HOMA-IR was +0.15 units/year (95%CI=0.02-0.28, p=0.03); use of an integrase strand inhibitor (InSTI) regimen at switch was associated with an increase in HOMA-IR [adjusted mean change +1.04 units/year (95%CI=0.03/2.05), p=0.004], while the use of tenofovir alafenamide (TAF) was associated with a reduction in HOMA-IR [adjusted mean changes -1.24 units/year (95%CI=-1.89/-0.60), p=<0.001], after adjusting for age, gender, HIV risk factor, BL BMI, duration of viral suppression, BL CD4, BL triglycerides and total cholesterol, and use of a protease inhibitor or non-nucleoside reverse transcriptase inhibitor at switch.
Conclusions: In people with HIV-1 infection, increases in HOMA-IR index were associated with switching to InSTI−based regimens whereas the use of TAF was significantly associated with reduction in HOMA-IR values. An accurate evaluation of ART should be considered in individuals with IR.

Clinical HIV

OP 30 A DESCRIPTIVE ANALYSIS ON DUAL REGIMENS' DISCONTINUATIONS IN A MULTICENTRE ITALIAN COHORT

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Background: Dual therapies (DT) represent an effective switch strategy for virologically suppressed people living with HIV (PLWHIV) and recent studies show acceptable efficacy of selected DT also in treatment naïve PLWHIV. In this study we aim to analyse the main reasons for DT discontinuation in our cohort.

Methods: We performed an observational, retrospective analysis on a multicentre cohort of PLWHIV on a DT strategy that discontinued such regimen. We collected population characteristics, clinical history and reasons for treatment discontinuation (TD). Parametric and non-parametric tests were used to compare variables, as appropriate. Kaplan-Meier survival analysis was performed to assess probability of discontinuing DT for various reasons.

Results: We analysed 312 patients: 63% of them were males, with a median age of 50 years (IQR 44-55) and a median time from HIV diagnosis of 15 years (IQR 7-23). Median follow-up time was 15 months (IQR 7-31).

Two hundred patients (64%) were treated with a protease inhibitor (PI)-based regimen, while the other 36% was treated with an integrase inhibitor (INI)-based regimen. Full patients' characteristics are displayed in Table 1.

Causes of TD were different between PI-based and INI-based strategies (p=0.003): main reasons for TD of a PI-based DT were simplification (i.e. pill reduction, 32.0%), viro-immunologic failure (VF, 15.0%), drug interactions (DDI, 8.5%) and gastrointestinal toxicity (6.0%) while with INI-based DT main reasons were VF (15.2%), simplification (15.2%), patients' request (12.5%) and CNS toxicity (8.0%).

After interrupting a DT most patients (131, 42%) started a new regimen with a "backbone" of 2 nucleoside reverse transcriptase inhibitors (NRTI) plus an INI, 72 (23.1%) switched to 2NRTI plus a NNRTI, 57 (18.3%) started a therapy with 2NRTI plus a PI.

We found no significant differences in probability of discontinuing study regimen for viro-immunological failure between PI-based DT and INI-based ones (after 3 years 22% vs 30%, respectively, log-rank p=0=232); similarly the 3-year cumulative probability of interruption because of treatment simplification in PI-treated patients was 37% and in INI-treated patients was 30% (log rank p=0.483). We observed a significant difference regarding overall toxicity: the 3-year probability of TD due to drug toxicity was 29% for patients in a PI-regimen and 36% for those in an INI-regimen (log rank p=0.013).

Comparing the companion "nuke" agent, we found no differences between NNRTI-containing regimens and 3TC-containing regimens in probability of discontinuation due to virological failure (log-rank p=0.126), treatment simplification (p=0.646) and overall toxicity (p=0.132).

Conclusions: In our cohort no differences regarding discontinuations of DT strategies due to VF were observed. PI-based strategies showed a higher rate of TD due to simplification and DDI whereas INI-based regimens were characterized by a higher rate of TD due to CNS toxicity.

Clinical HIV

OP 31 VIROLOGICAL RESPONSE AND RESISTANCE PROFILE IN HIGHLY TREATMENT-EXPERIENCED HIV-1 INFECTED PATIENTS SWITCHING TO DOLUTEGRAVIR PLUS BOOSTED-DARUNAVIR IN CLINICAL PRACTICE

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Background: We evaluated virological response and resistance profile in cART-experienced HIV-1 infected patients (pts) starting for the first time a dual therapy with dolutegravir (DTG) and ritonavir/cobicistat boosted-darunavir (DRV).
Materials and Methods: Pts included in the study were either viremic or virologically suppressed. Survival analysis was used to assess probability of virological success (VS) in viremic pts and of virological rebound (VR) in virologically suppresses pts. Major resistance mutations (MRM) and genotypic susceptibility score (GSS) were evaluated at baseline (BL, as cumulative plasma resistance) and after switch.
Results: Overall, 130 pts were analyzed (62 [47.7%] viremic; 68 [52.3%] virologically suppressed). Pts had a long treatment history with a median IQR of 9 (4-12) previous regimens; most of them had previously received DRV (75.4%) and INI (60%; DTG: 9.2%, Table 1). Even though at BL 81.5% of pts had accumulated ≥1 MRM (PI: 35.7%, NRTI: 77.5%; NNRTI: 69.0%; INI:10.1%), 77.7% of pts harbored strains fully susceptible to DTG+DRV (DTG: 93.8%; DRV: 82.3%). Compared to viremic pts, virologically suppressed pts showed a higher level of BL DRV-resistance (≥3 DRV MRMs: 13.2% vs. 0%, P<0.001; fully susceptible DRV-GSS: 44.9% vs. 95.2%, P<0.001), while DTG susceptibility was high in both groups (INI resistance: 6.7% vs. 12%; fully susceptible DTG-GSS: 92.6% vs. 95.2%, P=0.720).
By 12 months after treatment start, the overall probability of VS in viremic pts was 91.2%; the median time (95% C.I.) of VS was 2 (1-3) months. The few pts receiving a non-fully active regimen had a lower probability of VS (80.0%) compared to those who received a fully active treatment (92.8%), even though statistical significance was not reached (P=0.658), probably due to the low sample size.
Concerning response in virologically suppressed pts, by 24 months after therapy switch, the probability of VR was 10.5% with only 6 VR events recorded at a median viremia of 266 (104-142,761) cps/mL. Pts with a previous time under virological suppression ≤6 months showed a higher VR probability compared to others (37.5% vs. 6.7%, P<0.001). No significant association with resistance was found due to the low number of events.
Among 24 pts who did not respond (5 who never achieved VS; 12 who experienced VR), 12 (50%) were tested for resistance in a median (IQR) time of 12.4 (9.3-27.4) months after switch. 8 (66.7%) of them were previously exposed to raltegravir or DTG. Two pts (16.7%), both with non-fully susceptible BL-GSS, accumulated further resistance in integrase and protease (ID 357: Y143C/H/R; ID 392: S147G, N155H and V32I, L33F, I54L) (Table 2).
Conclusions: Dual therapy with DTG+DRV in highly treatment experienced pts ensures a high rate of virological control. In the few failures recorded, the majority of previous resistance mutations are no longer present in plasma genotypic resistance test; selection of new resistance is a rare event

Clinical HIV

OP 32 DOES RAPID INITIATION OF ART AT HIV DIAGNOSIS IMPACT ON VIROLOGICAL RESPONSE AND RETENTION IN CARE? A SINGLE CENTER EXPERIENCE (BRESCIA, NORTHERN ITALY)

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Background: In 2017 WHO introduced rapid (≤7 days from diagnosis) or immediate ART initiation, in order to reduce HIV transmission and loss of care after diagnosis. In 2018, a systematic review showed improved viral suppression and retention in care at 12 months with ART rapid start (<14 days from diagnosis), particularly in low-income settings. Recently, Italian researchers from ICONA Foundation Study Cohort did not observe differences in virological response and retention in care according to timing of ART initiation.

Methods: A retrospective, single-center study was conducted on newly HIV-infected patients in a large Outpatient HIV Clinic, from September, 1st, 2015 to July, 31st, 2019. Patients were grouped according to the time between the first HIV care access and ART initiation: Group 1 ≤ 7 days, Group 2 7-30 days and Group 3 >30 days. Multivariable logistic regression models were used to investigate factors associated with virological response (HIV RNA< 50 cp/mL) and retention in care at month 6 and 12.

Results: 320 patients were included; however, we focused the analysis on outpatients excluding 114 patients (35,6%) hospitalized at diagnosis.

Among 206 patients included, median age was 39.3 years (IQR 30.4-50.6), 72.3% were male and 66.5% were Italian. Patients characteristics summarized in Table 1.

The median interval between the first HIV positive test and the first access to our HIV Outpatient clinic was 19 days (IQR 12-32). Patients were grouped as follows: 46 (23.4%) in Group 1, 40 (20.3%) in Group 2 and 111 (56.3%) in Group 3. The median interval between the first access and the ART prescription was 34 days (IQR 9-44). 9 patients never started ART. 195 patients received 2 NRTI plus a 3rd agent: integrase inhibitor in 145 cases (73.6%, with dolutegravir-DTG as preferred choice in 119 patients [82%]), PIs (mostly darunavir) in 15.7% and NNRTI (only rilpivirine) in 12.2% of cases. Dual therapy with DTG+lamivudine was prescribed in only 2 cases.

At 6 months 85.6% achieved viral suppression, 5,3% were LTFU and 3 patients were transferred to another Clinic. At 12 months 94.9% achieved viral suppression, 11,2% were LTFU, 1 patient deceased and 4 more patients were transferred. According to regression analysis, there was no significant association between timing of ART initiation and probability of HIV RNA suppression or retention in care at 6 and 12 months. We found a lower probability of being virosuppressed at 6 months among those subjects in group 2 or 3 but not statistically significant (OR 0.36,95CI 0.1-1.6, OR 0.4, 95CI 0.1-1.5, respectively). As expected, the only predictor of viral suppression at 6 months after ART initiation is a baseline HIV RNA <100.000 cp/mL.

Conclusions: in our cohort the 3rd 90% (viral suppression) of the UNAIDS 90-90-90 goals is achieved 12 months after ART initiation but, in our study, we did not observe any differences in virological response and retention in care according to timing of ART initiation

Clinical HIV

OP 33 EFFICACY AND DURABILITY OF DOLUTEGRAVIR- OR DARUNAVIR-BASED REGIMENS IN ART-NAÏVE AIDS- OR LATE-PRESENTER PATIENTS

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Background: Dolutegravir (DTG) and Darunavir (DRV) are both recommended in first-line regimens; however, limited data are available in advanced naïve HIV+ patients. We aimed to describe and compare efficacy and durability of DTG- and DRV-based regimens in ART-naïve AIDS- or late-presenter patients in clinical practice.

Methods: Retrospective multicenter study (6 centers in Italy) including ART-naïve AIDS- or late-presenter (def. CD4≤200/μL) HIV-infected patients starting treatment with DTG 50mg or ritonavir/cobicistat-boosted DRV 800mg once daily + 2NRTIs from January 2009. Exclusion criteria were acute HIV infection, lack of clinical or laboratory follow-up. Patients were followed from the date of first-line ART initiation (baseline, BL) to the discontinuation of DRV or DTG, last visit, death, loss to follow-up or a maximum of 36 months of follow-up, whichever occurred first. Kaplan-Meier curves and Cox regression analysis were used to estimate incidence and predictors of time to treatment discontinuation of DTG or DRV (TD), virological failure (VF, defined as a single HIV-RNA>1000cp/mL or two consecutive HIV-RNA>50cp/mL after 6 months of therapy or after virological suppression had been achieved), treatment failure (TF, the first of TD or VF), optimal immunological recovery (OIR, defined as CD4≥500/μL+CD4≥30%+CD4/CD8≥1).

Results: Overall, 308 patients (79.2% males, median age 43 years, 45.5% heterosexual, 36.7% homosexual, 40.3% AIDS-presenter, median CD4 66 cells/μL, median CD4/CD8 0.10, median HIV-RNA 5.29 log10cp/mL at BL) were enrolled, of which 181 (58.8%) and 127 (41.2%) in the DTG and DRV arm, respectively. NRTIs backbone were represented by TDF-TAF/FTC and ABC/3TC in 240 (77.9%) and 66 (21.4%) patients, respectively. The median time from HIV diagnosis to ART initiation was 0.43 months. The two arms did not significantly differ for baseline characteristics. Incidence of TD, VF, TF and OIR were 21.9, 5.2, 25.6 and 1.4 per 100 person-year of follow-up, respectively, without significant differences between DTG and DRV groups (log rank p>0.05 for all outcomes). However, a higher estimated probability of TD for central nervous system (CNS) toxicity (at 36 months: 11.7% vs 0%, p=0.002) was observed for patients treated with DTG while those treated with DRV showed a higher probability of TD for simplification (at 36 months: 21.3% vs 5.7%, p=0.046)(see figures). At multivariable analyses, when adjusting for potential confounders, use of DTG vs DRV was not a significant predictor of the different outcomes. Independent predictors of TD for toxicity were older age (aHR 1.40 per 10 years increase, p=0.019) and baseline AIDS events (aHR 2.13, p=0.018).

Conclusions: DTG and DRV showed similar efficacy and durability as anchor drugs for first-line therapy in AIDS- or late-presenter naïve patients. Survival analyses showed a higher risk of TD for CNS toxicity with DTG, while patients treated with DRV had higher probabilities of treatment simplification.

Clinical HIV

OP 34 EFFICACY SAFETY AND TOLERABILITY OF THE SWITCH FROM EFAVIRENZ/EMTRICITABINE/TENOFOVIR DISOPROXIL ON ALTERNATE DAYS OR CONTINUOUS TREATMENT TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE IN VIROLOGICALLY SUPPRESSED HIV+ (EBONY STUDY)

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Background: The aim of this study was to evaluate efficacy, safety and patient reported outcomes (PROs) of treatment switch from efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) given quod die (qd) or on alternate days (ATAD) to bictegravir/emtricitabine/tenofovir alafenamide (BIC/F/TAF) in virologically suppressed HIV+ patients (pts).
Material and methods: EBONY is a pilot 48-week (w), single-arm, monocentric, open-label, phase IV trial. Virologically-suppressed pts on EFV/TDF/FTC qd or ATAD, without resistant mutation on genotype resistance test or previous virological failure (VF) were eligible. Enrolment of 240 pts was planned: at baseline (BL) pts were switched to BIC/F/TAF. HIV-RNA and HIV-DNA levels, immunological parameters, renal function, metabolic profile and neurocognitive performance were monitored in total population. Bictegravir plasma level, PROs and evolution of bone composition were evaluated in the three different subgroups of 80 pts each. VF was defined as two consecutive HIV-1 RNA tests ≥ 50 copies/ml. We report an interim analysis including pts who completed 24w, considering viroimmunological, metabolic and adherence/quality of life (QoL) outcomes.
Results: Overall 195 pts were enrolled of whom 90 completed 24 w. BL characteristics were: 87.8% male, 56.7% MSM, median age 52 yrs, median 13 yrs from HIV diagnosis, CD4 count 645 cells/mm3, median CD4/CD8 ratio 1.01, median HIV-DNA 3.5 log10 copies/106 PBMC. 72.2% pts switched from EFV/FTC/TDF qd, 27.8% from EFV/TDF/FTC ATAD. At 24w CD4 count improved from 645 to 752 cells/mm3 ($p<0.001$) and CD8 count from 647 to 769 cells/mm3 ($p<0.001$). The CD4/CD8 ratio changed from 1.01 to 0.98 ($p=0.04$). Median HIV DNA was unchanged at w24 (Table1). 2/90 (2.2%) pts experienced VF, neither of whom developed drug resistance mutations and both achieved resuppression without antiretroviral therapy (ART) changes. 8/90 (8.8%) pts experienced adverse events (AE), 1 was severe (SAE): ictus cerebri. 4/8 AEs were considered related to BIC/F/TAF and study ART was not interrupted in any case. Adherence and QoL parameters showed a stable trend over time (Table2-Table3). Fasting glucose slightly decreased from 89 mg/dL to 82 mg/dL ($p<0.001$). Total cholesterol showed an improving trend from 191 mg/dL to 184 mg/dL ($p=0.176$) and triglycerides increased from 103 mg/dL to 112 mg/dL ($p= 0.949$) (Table 4). Regarding renal function, a slight increase in creatinine levels was observed ($p<0.001$) while the proportion of pts with proteinuria decreased from 31% to 15.5% ($p=0.048$) (Table 4).
Conclusions: Our preliminary data showed that BIC/F/TAF demonstrated virologic and immunologic efficacy and safety comparable to that of EFV/FTC/TDF both administered qd and ATAD. Metabolic parameters slightly improved, whereas blood creatinine showed a mild increase probably due to the inhibition of hOCT2 mediated by BIC. The small sample size and short follow-up limit generalizability of the results.

Clinical HIV II

OP 35 ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN HIV-POSITIVE RECIPIENTS: A CASE SERIES

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Background: although attractive for the impact on HIV-reservoir to achieve eradication, allogeneic hematopoietic cell transplant (allo-HCT) is challenging because of concerns on infectious complications and interactions between antiretroviral therapy (ART) and immunosuppressive agents. Data on allo-HCT in HIV patients are scanty; only one prospective trial is available on HCT from HLA-matched donor. Here, we describe the infectious complications, T-cell immune-reconstitution, ART management and overall survival in a series of HIV people who received HCT.

Material and methods: case series analysis of HIV-positive adults who received allo-HCT at San Raffaele Hospital from Jan-2014 to Dec-2019 for hematological malignancy.

Results: Five people with a median age of 48 years received HCT: 2 from haploidentical donor [1 for acute leukemia (AL), 1 for Hodgkin-lymphoma], 1 from matched-unrelated donor (MUD) for Burkitt-lymphoma and 1 from matched-related donor (MRD) for AL. The last patient received cord-blood transplant (CBT) for AL. At HCT, all patients had HIVRNA <50 copies/mL and median CD4+ count was 523 cells/μL. At HCT, 1 switched from triple therapy NNRTI-based to a triple therapy INSTI-based, 2 were maintained on a triple therapy INSTI-based and 1 and 1 simplified, respectively, from a triple therapy NNRTI-based and INSTI-based to a dual-therapy (3TC+DTG).

No HCT recipients developed pre-engraftment blood-stream infection.

The individual who received MRD HCT experienced HHV6-reactivation at day +25, the one who received MUD HCT developed adenovirus reactivation with possible esophagitis at day +12; both didn't developed graft-versus host disease (GVHD). After HCT, they were maintained on the same ART.

Two patients who received haplo-HCT experienced HHV6-reactivation: one at day +25 associated with cutaneous rash, the other-one at day +120 associated with pancytopenia. Both developed acute and chronic GVHD. After HCT, one patient was maintained on the same ART and the other was simplified from TAF/FTC+DTG to BIC/TAF/FTC.

The patient who underwent CBT developed concomitant acute GVHD and proven CMV-colitis at day +20; she experienced also proven HHV6-encephalitis at day +25 and adenovirus reactivation associated with duodenal perforation at day +60. After HCT, ART was changed from TAF/FTC+DTG to DRV/COBI/TAF/FTC to minimize neurotoxicity in a patient with HHV6 encephalitis sequelae.

After HCT, median CD4+ count at day +60 and +120 was 382 and 540 cells/μL, respectively (Figure 1), and HIVRNA remained undetectable.

The patient who received CBT died of transplant-related mortality (GVHD, sepsis) 7-months after HCT; the other 4 patients are alive in complete remission at a median follow-up of 38-months after HCT.

Conclusions: allo-HCT is feasible in HIV people. Despite fast CD4+ T-cell immune-reconstitution, viral infections are the main concern: it is conceivable that mismatched donor and virus-specific T-cell immune-response affect their occurrence.

Clinical HIV II

OP 36 ITALIAN SURVEY ON CLINICIANS' APPROACH TO LATENT TUBERCULAR INFECTION IN PEOPLE LIVING WITH HIV

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Background: Tuberculosis is the leading preventable cause of death among people living with HIV worldwide.(1). The WHO TB Global report 2017 pointed out that people living with HIV (PLWH) have a 23-fold probability to develop an active tuberculosis than non-HIV. 2

The WHO and SIMIT-Italian guidelines recommend to screen and treat all PLWH and LTBI, but their implementation is lacking and two European studies identified the opinions and clinical practice approach of HIV clinicians as the main barrier to guideline implementation. (3-4)

Material and methods: Aim of the study was to evaluate the opinions and clinical approach of Italian HIV physicians. From the 1st of december 2019, an online multiple-choice questionnaire was sent to all members of SIMIT Società Italiana di Malattie Infettive)

Results: Eighty physicians completed the questionnaire: 43.75% from the north of Italy, 26.25% from the centre and 28.75% from the south. The mean age of experience in HIV was 15.54 years +/- 10.87.

Almost everybody resulted familiar with the guideline recommendations (98.75%) and the 67.5% of the sample consider the above-mentioned guidelines to be evidence-based. Moreover a vast majority (82.5%) believe that the recommendations are relevant for the daily practice in their HIV setting. Nevertheless only 52.5% of the HIV centre in our sample adopt them and 16:25% partially; in the 28.75% of the cases the clinicians decide individually how to manage the LTBI. (Fig.1)

In only 58.75% of cases PLWH are screened for LTBI at HIV diagnosis, and few clinicians screen the patients according to anamnestic risk factors (13.75%).(Fig.2)

Surprisingly the 30% of our sample do not prescribe LTBI preventive therapy despite a positive test; in some cases (18.75%) LTBI screening is never repeated in the patient's lifetime.

Quantiferon test alone is the preferred strategy (66.25%). The exclusion of active TB is done through clinical plus microbiological plus radiological criteria (61.25%) or through a radiological plus clinical strategy (33.75%).

Finally, despite most clinicians believe that PLWH are not enough informed about TB risk (77.5%) almost no one provides informative material (96.25%) even if they largely believe it would be useful (75%).

Conclusion: This questionnaire-based survey on LTBI screening in PLWH reveals a significant heterogeneity in the strategies applied by Italian HIV clinicians and a partial implementation of guidelines.

Evidence based updated guidelines and shared diagnostic/therapeutic protocols may improve the management of LTBI in PLWH.

1- WHO TB report 2015.

2- WHO TB report 2017

3- Implementation of latent tuberculosis screening in HIV care centres: evaluation in a low tuberculosis incidence setting. C Wyndham-Thomas

4- Intention of physicians to implement guidelines for screening and treatment of latent tuberculosis infection in HIV-infected patients in The Nethederlands: a mixed method design. K Evenblij.

Clinical HIV II

OP 37 A POOR IMMUNOLOGICAL RECOVERY IS ASSOCIATED WITH NON-AIDS-DEFINING CANCERS IN THE ERA OF HAART: A CASE-CONTROL STUDY

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Background: In the era of HAART, incidence of non-AIDS-defining diseases is increasing among HIV+ patients (pts). Particularly, non-AIDS-defining cancers (NADC) are a major cause of morbidity and mortality. Our aim was to evaluate the changes of incidence of NADC trough years and the association with viro-immunological factors.

Materials and methods: We selected all patients with a diagnosis of NADCs made in our Clinic of Infectious Diseases after January 2006 (data shown in figure 1), excluding cancers diagnosed within the first year from HIV diagnosis. We compared these cases with a control population of HIV+ pts without history of cancer, matched (1:2) for age, time of HIV infection and CDC stage. Differences between groups were analyzed with Chi-square test and Mann-Whitney test. Predictors of cancer risk were studied with conditional logistic regression.

Results: We analyzed 561 pts, 187 cases and 374 controls. Most of them were males (68.5%), with a median age of 51.7 years (IQR 46.4-57.9), a median time of HAART of 10.9 years (IQR 5.6-16.9) and a median CD4 cells count of 533 cells/mm3(IQR 343-735). At the time of diagnosis of cancer, the case group was different from control group for median time of HAART (9.9 yrs vs 11.4 yrs, p 0.011), time of virological suppression (8.8 yrs vs 10.4 yrs, p 0.039), CD4 cells count (445 vs 562cells/mm3, p 0.001) e CD4/CD8 ratio (0.59 vs 0.70, p 0.010), as shown in table 1. At univariate analysis, receiving an HIV diagnosis after 1996 (for the period 2006-2019 vs period before 1996 OR 0.14, CI95% 0.07 -0.30, p 0.001), years of virological suppression (OR 0.92, CI95% 0.88-0.96, p 0.001) and years of HAART (OR 0.93, CI95% 0.90-0.97, p 0.001) were protective against risk of cancer. Cigarette smoke (OR 2.05, CI95% 1.19-3.53, p 0.009) and HCV-coinfection (OR 1.83, CI95% 1.16-2.87, p 0.008) were associated with higher risk of cancer. At multivariable analysis, only yrs of virological suppression and cumulative exposure to integrase strand inhibitors resulted protective against cancers (respectively, aOR 0.815, CI9%% 0.69-0.95, p 0.01 and aOR 0.98, CI95% 0.95-0.99, p 0.25). Among immunological factors, a CD4 percentage>15% and a CD4/CD8 ratio>0.4 were protective against cancer risk (respectively, compared to CD4%<15% aOR 0.12, CI95% 0.02-0.60, p 0.010 and compared to CD4/CD8<0.4 aOR 0.36, CI95% 0.14-0.93, p 0.036). Having a CD4 cells count >500 cells/mm3 compared to CD4 <200 cells/mm3 predicted a lower risk of cancers (OR 0.12, CI95% 0.15-1.02, p 0.053).

Conclusions: In our cohort, yrs of virological suppression resulted the most important protective factor against risk of cancer, confirming the importance of an early start of antiretroviral therapy to prevent AIDS and NAD illnesses. In this context, the result of a protective role of a higher CD4/CD8 ratio and of CD4 percentage can help the physician to identify patients at higher risk of cancer that may need more prevention and screening measures.

Clinical HIV II

OP 38 HPV INFECTION IN HIV+, MSM PATIENTS FOLLOWED AT A LARGE HIV CLINIC IN NORTHERN ITALY

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Background: HPV infection has been linked to the development of cervical, anal and head-and-neck cancer. In HIV + population, MSMs have been consistently demonstrated as the most vulnerable risk group for acquiring HPV and developing anorectal cancer. While the link between HPV carriage and histological changes (cervical) has been extensively studies in seronegative women, we still lack a comparable degree of knowledge in HIV+ MSMs. HPV serotype (ST) distribution and rates of progression to high-degree lesions may indeed be different in this population. This study aimed to describe the epidemiology of anal HPV infection in a cohort of HIV+ MSMs followed at a teaching hospital in Northern Italy.
Material and methods: We retrospectively examined data from HIV+ MSMs who had an anal swab performed from February 2018 to January 2020. Data were extrapolated from the clinical records and included epidemiological and virological data, HPV history, proctological consultation results (when available).
Results: An anal swab was done in 65 MSM patients (aged 47.4±11,6) years, with a mean nadir CD4 count of 294 ±214 cell/ul. At the time of sampling the most recent CD4 count was 647±295 cell/ul and all but 2 patients had plasma HIV-RNA undetectable (1 naive, 1 non-adherent).
In 10 patients a previous history of HPV infection was elicited. A positive anal swab was obtained in 49 patients (75.8%). ST distribution was as follows: 16 cases (32.7%) w/ ST of unknown risk, 14 (28.6%) w/ low risk ST, 7 (14.3%) w/ probable high risk ST and 12 (24.5%) w/ high risk ST (5 of them infected by ST 16). In 6 patients (12.2%) a mixed ST infection was shown. Proctological evaluation was performed in 26 cases (53.1%): 2 AIN1 lesion, 2 unspecified lesion, 4 had non-HPV related diagnosis (abscess, haemorrhoids). In summary, our screening identified 4 (6.1%) patients with HPV-related anal changes and 19 cases (29.2%) infected w/ high risk or probable high risk ST infection.
Conclusions: We identified a HPV anal infection in more than 3/4 of patients, and nearly 30% of these had high risk or probable high risk ST infection, with around 6% w/ an anal pathology (related or unrelated to HPV). Most cases had no previous HPV infection demonstrated. Contrary to other studies on HPV epidemiology in HIV+ MSMs, we found a significantly lower prevalence of HPV ST 16 (2% vs. 38% (Patel 2017) and 22% (Va Aar, 2012).

Clinical HIV II

OP 39 RISK OF MULTIPLE PRIMARY NEOPLASMS AND IMPACT ON SURVIVAL OF PERSON LIVING WITH HIV (PLWH)

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Background: PLWH are diagnosed with cancer, both AIDS-defining (ADC) and Non-AIDS-defining (NADC), at an increased rate over the general population. Expanding ART use and standardized cancer treatment protocols dramatically increased life expectancy, increasing the number of cancer survivors, who are at high risk of other primary neoplasms. Proportion of multiple primary cancer in PLWH has been recently reported about 14-18%, close to that observed in the general population. Aims of this study were to investigate possible risk factors for multiple primary cancers in PLWH and to examine survival probability according to the number of cancer diagnoses (1, >=2).

Methods: Patients (pts) in ICONA Foundation cohort enrolled between 1997 and 2019 were analyzed for relative frequencies of first or subsequent primary cancer diagnosed till 5 years before first HIV test. Poisson regression was used to investigate factors recorded at first cancer associated with the onset of a second diagnosis. Weighted Cox regression was used to estimate causal HR of death for patients with a second diagnosis of cancers (time-varying exposure), adjusting for the main confounders (age, gender, HCV/HBV/CMV coinfection at baseline and time-varying CD4, CD4/CD8 ratio, HIVRNA and virus-related first cancer). Baseline of this analysis was the date of first cancer.

Results: 1177 pts with cancer were observed, 1116 (94,8%) with single and 61 (5,2%) with a second cancers; only one of 61 had a third primary cancer. Incidence of multiple cancer was 1.1 per 100 PYFU (95%CI 0.8-1.4) (1988-1999 IR 1,1, 2000-2009 IR 1, 2010-2019 IR 1,2). Kaposi sarcoma, Non-Hodgkin Lymphoma and Hodgkin Lymphoma were the 3 more common first neoplasm in the two groups (55.2%, 32% and 14.7% in single and 47.2%, 36.1% and 20% in multiple, respectively). Comparing pts with single cancer vs those with multiple diagnoses (Table 1) HCV coinfection (20% vs 26%) and HIV RNA>200 cp/mL (45% vs 49%) were more frequent in multiple cancers group. At multivariable Poisson regression, HCV coinfection, older age and CD4<200 mmc were associated with higher probability of a subsequent diagnosis of cancer. The 5-years survival probability was 72.6% (95% CI 69.6%-75.4%) and 65.5% (95%CI 51.7% -76.2%) in single and multiple, respectively. The causal HR of death for pts with a second cancers was 4-fold higher than those who had single cancer (HR 4.09 [95%CI 2.06 -8.13]) after adjusting for main confounders.

Conclusions: Multiple primary cancers occurred in our cohort at a relatively low frequency than previously reported and stable over time. Immunological impairment, older age and HCV coinfection seem to increase risk of subsequent neoplasms. Role of oncogenic viruses as persistent predisposing factor could be responsible for the relative frequencies of multiple cancers. The finding of worse survival in pts with multiple neoplasms, suggests the importance of early identification of risk group and of better prevention strategies

Clinical HIV II

OP 40 DEVELOPMENT AND STANDARDIZATION OF A REAL TIME PCR FOR THE QUANTIFICATION OF HTLV-1 PROVIRAL LOAD

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Background: The human retrovirus HTLV-1 is the etiologic agent of adult T cell leukemia (ATL) and HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). The main target of the virus is represented by peripheral blood mononuclear cells (PBMCs), in particular CD4+ T lymphocyte but also CD8+ T cells, macrophages and dendritic cells. HTLV-1 replication cycle occurs preferentially through cell-to-cell transmission or "clonal expansion" of infected cells rather than the release of new virions. PCR-based molecular assays represent the most appropriate methods for proviral detection and confirmation of HTLV-1 infection; furthermore, quantitative, real-time PCR is required for quantification of the proviral load (PVL) in positive samples since the burden of PVL seems to be an important factor in the development and progression of HTLV-1 associated diseases.
Currently there are no commercially available real time PCR kit or international standards for quantification of HTLV-1 DNA. Our aim was the development and validation of an in house real time PCR assay for HTLV-1 PVL quantification in PBMCs.
Materials And Methods: We cloned a 910 bp length fragment containing part of the pol region of HTLV-1 DNA from a HTLV-1 infected cell line, MT-2, into a pUC18 vector, obtaining the "pUC18-XH" plasmid. The latter was used to generate a standard curve, first in H2O in order to test the detection limit and subsequently in an uninfected cell line (Jurkat) cellular matrix in order to reproduce the ex vivo condition of biological samples. Standard curves were analysed in real time PCR using SYBR Green chemistry and the previously published SK111-SK112 primers, opportunely modified. Routine samples from HTLV-1 infected patients referring to Sant'Orsola Hospital in Bologna were collected and analysed for quantification of PVL. PVL was normalized to the amount of cellular DNA by quantification of the albumin gene.
Results: We tested a dynamic range of target from 105 to 101 copies of pUC18-XH/reaction. Each run was performed in triplicate. Overall, our assay showed high sensitivity and a good intra- and inter-assay reproducibility (CV inter-run from 2,35% to 5,73%; CV intra-run from 1,80% to 5,88%). The PCR efficiency, slope and correlation coefficients ranged from 95% to 103%, from -3,41 to -3,25 and from 0,95 to 0,99, respectively. Based on the validated assay, we were able to quantify PVL in 9 samples from HTLV-1 infected patients: values ranged from 104 to 105 copies/106 PBMCs.
Conclusions: Our data highlight the robustness and the specificity of this in house assay as an essential tool for diagnosis and management of HTLV-1 infected patients, allowing the quantitation of PVL. Moreover, it is a low cost and simple set-up method. Importantly, its application will facilitate the follow up of patients under therapeutic regimens and the correlation between PVL and pathogenesis.

Clinical HIV II

OP 41 IS PRETREATMENT HIV-1 INTEGRASE RESISTANCE INCREASING? A LARGE ITALIAN CENTRE EXPERIENCE

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Background: Testing ART-naïve people living with HIV (PLWH) for HIV drug resistance is important to define the risk of virological failure and to attempt to prevent it. The aim of this study was to evaluate the prevalence of integrase strand inhibitor regimen (InSTI) pretreatment HIV-1 drug resistance in a large cohort of naïve PLWH over the past decade.
Material and methods: Time-trend study on adult naïve PLWH followed at San Raffaele Hospital, with paired NRTI/NNRTI/PI/InSTI Genotypic Resistance Tests (GRT) determined on RNA before ART start, in the period 2009-2019. GRT was determined by Sanger sequencing using ABI PRISM 3130xl Genetic Analyzer (Applied Biosystems, Foster City, CA, USA). We retrospectively calculated the degree of resistance to each InSTI drug using the Genotypic Resistance Interpretation Algorithm of the Stanford HIV Drug Resistance database Program (version 9.1.1). The obtained scores were used to classify the presence of potential low-level, low-level, intermediate or high-level resistance to each InSTI drug and to the InSTI drug class. Drug resistance (DR) within the InSTI class was defined by the presence of at least low-level resistance to ≥1 drug of the InSTI class. All the considered characteristics were measured at or within 180 days before the GRT date. Cochran-Armitage test was used to assess the linear trend in pretreatment HIV-1 InSTI-DR prevalence over time.
Results: We analyzed 1223 ART-naïve PLWH: 91% were males, with a median age of 37 years (IQR=30-45); other characteristics are described in Table 1. Overall, 18 (1.5%) people had at least low-level InSTI DR and 5 (0.4%) had at least intermediate InSTI DR. Major InSTI-resistance mutations were very uncommon: both E138K and R263K were found in 2 (0.2%) people while each of G118R, G140S, Y143C, Y143R, S147G, and Q148H were inferred in 1 individual. The most frequent accessory InSTI-resistance mutations were: 19 (1.6%) people with T97A, 12 (1%) with L74I, 11 (0.9%) with E157Q, 10 (0.8%) with G163R.
Over the decade 2009-2019, prevalence of at least low-level InSTI DR was almost null between 2009-2013 and then gradually raised from 1.3% in 2014 to 3.9% in 2019 (p-for-trend=0.0003, Figure 1); prevalence of at least intermediate InSTI DR increased from 0% in 2009 to 2% in 2019 (p-for-trend=0.188, Figure 1).
We also evaluated trend over time of DR prevalence (and at least intermediate) of first-generation InSTIs (raltegravir, elvitegravir) and second-generation InSTIs (dolutegravir, bictegravir): a significant increase over time in at least low-level DR prevalence was found only in relation to first-generation InSTIs (p-for-trend=0.0003, Figure 1).
Conclusions: Our findings confirm that in naïve PLWH the prevalence of pretreatment HIV-1 integrase resistance is still rare but significantly increased over the past decade, mainly due to first-generation InSTI. Increase in low-level pretreatment resistance in InSTI may deserve to be monitored.

Clinical HIV II

OP 42 ASSOCIATION BETWEEN LOW LEVELS OF HIV-1 DNA AND HLA CLASS I MOLECULES IN CHRONIC HIV-1 INFECTION

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Background: Up to now, no data are available on the association between human leukocyte antigen (HLA) profile and low levels of HIV-1 DNA in chronic HIV-1 infection.
The aim of the study was to evaluate if there were HLA class I molecules associated with low HIV-1 DNA in adults with chronic HIV-1 infection, prolonged suppressive antiretroviral therapy (ART) and good immunological asset.
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, HLA-A, -B and -C were tested on genomic DNA with polymerase chain reaction (PCR) sequence-specific oligonucleotides and sequence-specific primers; 16 HLA-A, 24 HLA-B and 12 HLA-C were tested.
Patients' characteristics were reported as median (quartile 1- quartile 3) or frequency (%).
Multivariate logistic regression was used to determine factors associated with low levels of 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, HIV-1 RNA <50 copies/mL for 11.7 (10.6-14.0) years and absence of plasma residual viremia for 6.9 (6.2-7.2) years. Nadir CD4 was 253 (167-339) cells/μL among patients with HIV-1 DNA ≥100 copies/106PBMCs and 353 (212-434) cells/μL among those with HIV-1 DNA <100 copies/106PBMCs (p=0.055). Other patients' characteristics are reported in Table.
Overall, only 3 HLA class I molecules showed at least a marginal association with HIV-1 DNA: HLA A-24 was present in 21 (29.6%) among subjects with HIV-1 DNA ≥100 copies/106PBMCs and 1 (5.9%) among those with HIV-1 DNA <100 copies/106PBMCs (p=0.060); HLA B-39 in 1 (1.4%) with HIV-1 DNA ≥100 copies/106PBMCs and in 3 (17.6%) with HIV -1 DNA <100 copies/106PBMCs (p=0.021) and HLA B-55 in 3 (4.2%) and 3 (17.6%), respectively (p=0.081).
All the three patients with HLA B-39 and HIV-1 DNA <100 copies/106PBMCs did not have HLA A-24.
At multivariate analysis, the presence of HLA B-39 [adjusted odds ratio (AOR) 204.82 (95%CI=5.14->999), p=0.046] and B-55 [AOR 18.09 (95%CI=1.45-225.52), p=0.025] were associated with low HIV-1 DNA, after adjusting for age, gender, years of HIV-1 RNA <50 copies/ml, zenith HIV-1 RNA, hepatitis C coinfection, HLA A-24, nadir and current CD4.
Conclusions: In patients with chronic HIV-1 infection, prolonged suppressive ART, absence of plasma residual viremia for ≥5 years and good immunological profile, HLA B-39 and B-55 were associated with a lower viral reservoir, suggesting that HLA class I may have a role in establishing the size of reservoir.

Clinical HIV II

OP 43 EVOLVING EPIDEMIOLOGY OF HIV/AIDS IN CAMPANIA REGION, 2008-19: IS HIV/AIDS POPULATION IN CAMPANIA DIFFERENT?

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Background: Epidemiology of HIV/AIDS in Italy is continuously evolving. The Italian National HIV Surveillance, instituted in 2008, is based on 21 regional surveillance systems and adopts an essential Data Collection Form with a definite data flow. Regional epidemiology may be very different, because of different social determinants. We briefly describe the epidemiological characteristics of newly diagnosed cases of HIV/AIDS at "D.Cotugno" hospital, Naples, in 2008-2019, as a representative sample of incident cases in Campania Region.
Methods: Data about newly diagnosed HIV/AIDS cases in 2008-19, derived from Forms sent yearly to Italian National HIV Surveillance system, were extracted and analysed. "D.Cotugno" hospital is a Infectious Diseases specialistic hospital, accounting for the most part of all HIV/AIDS new diagnoses in Campania Region. A substantial part of these new diagnosis were performed at the "Gruppo C" service, an HIV Counselling and Testing site based at "D.Cotugno".
Results: In the study period, a total of 1676 HIV/AIDS cases were diagnosed at "D.Cotugno" hospital, being about 70% of total cases in the Campania Region. Males represented 73,5%, with Male-to-Female ratio increasing in the recent years (Figure 1). Median age was 38,3, stable across years (Figure 1). Foreign patients, 68% coming from Africa, represented 33%, with proportion not significantly changing over years (Figure 2). Figure 3 summarized the evolving rates of risk factors in the study population: as occurred at National level, Men who have Sex with Men (MSM) is increasing over years, while Injection Drug Users (IDU) decreased. Main reasons for performing the HIV test was at risk behaviours in 45,6%, and symptoms suggestive for HIV in 33,2%.
Overall, mean of first CD4 was 311, with patients with CD4 <350 being the most part in the whole study period (Figure 4). The proportion of patients with fist HIV-RNA > 100.000 copies is 55%: this proportion significantly increase over years, from 42% in 2008 to 70% in 2019 (p for correlation <0,002). In the study period, patients with AIDS at diagnosis was 22,7% with proportion stable across years
Discussion: Evolving epidemiology of HIV/AIDS in Campania region mostly reflects the National data. Distribution and evolution over years for gender, age and origin are similar of that reported at National Level. Despite that, some remarkable differences emerge. The distribution of Risk Factor reflects the national trend, but the population of IDU, even if decreasing starting from 2010, is more represented in Campania: in 2018, more than 10% of incident cases were IDU, still, and this proportion never was lower than 6%, vs about 3% reported in Italy. Moreover, the clinical picture among Campania patients is more severe: patients with initial CD4 <350 were 60%, and about 1 out of 4 is an advanced-naïve AIDS presenter. Regional prevention and management strategies should consider these peculiarities of HIV/AIDS population in Campania.

Clinical HIV II

OP 44 IMPACT OF BOOSTED VS UNBOOSTED ANTIRETROVIRAL REGIMEN ON DOLUTEGRAVIR PLASMA AND INTRACELLULAR PHARMACOKINETICS

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Background: Dolutegravir (DTG) 50 mg qd plus boosted Protease Inhibitors (bPIs) has been described as a possible high-genetic barrier to resistance nucleoside (NUC)-sparing dual regimen. On the other hand, DTG has been used often with other PI-free regimens in the clinical practice, including two or three-drug regimen (2DR or 3DR). Since comparison of DTG plasma and intracellular (IC) pharmacokinetics (PK) between boosted and PI-free therapy have not been reported in literature, aim of our study was to evaluate the role of boosters on plasma and IC DTG exposure in the clinical setting.

Methods: Patients (pts) administered with DTG plus Ritonavir (RTV) or Cobicistat (COBI)-boosted Atazanavir (ATV) and Darunavir (DRV) and DTG plus a PI-free regimen were included. PI-free regimen included 2DR or 3DR as DTG and Lamivudine (3TC), DTG and Rilpivirine (RPV), DTG and Emtricitabine/Tenofovir alafenamide (F/TAF) or co-formulated with Abacavir/3TC (ABC/3TC). Plasma and IC DTG Ctrough samples were collected and results compared between bPIs and PI-free regimens. Plasma and IC DTG Ctrough were measured by means of UHPLC-MSMS validated method. Non-compartmental PK parameters were calculated and reported as ng/ml and expressed as geometric mean (CI95%). Concentrations were expressed as ng/ml. Pts characteristics were compared by Mann-Whitney and Kruskal-Wallis test and correlations by Spearman's rank test.

Results: 74 pts were included in our study, 34 on DTG PI-free regimen (17 DTG+F/TAF, 11 ABC/3TC, 5 DTG+3TC, 1 DTG+RPV) and 40 on DTG plus bPIs (17 COBI, 23 RTV). 73% of pts were male, age and BMI were 52 years (44-59) and 23,4 Kg/m2 (22,0-25,6). DTG plasma concentrations with COBI, RTV and in those not receiving boosters were 1611,5 ng/mL (-0,5-3223,6), 1226,0 ng/mL (568,1-1883,8) and 1012,6 ng/mL (740,4-1284,8). DTG IC concentrations were 232,0 ng/mL (103,2-360,7), 240,5 ng/mL (130,1-350,9) and 211,7 ng/mL (104,3-319,0). DTG IC/plasma ratio were 0,149 (0,055-0,243), 0,210 (0,118-0,302) and 0,199 (0,169-0,230). Correlation between DTG plasma and IC was linear and significative ($p<0,001$) in all different groups. No significative difference in DTG PK parameters among three groups was found. Moreover no difference by gender and no correlation with age and BMI was observed.

Conclusions: This is the first evaluation of DTG plasma and IC concentration dosed with bPIs vs PI-free regimens. In this study we found no difference in DTG PK with or without boosters: this is in contrast with previous finding reporting higher DTG plasma exposure dosed with COBI than dosed with unboosted ATV. More data are needed to evaluate DTG PK especially in contest of new 2DR strategy based on DTG and 3TC or RPV

Comorbidities

OP 45 INFLAMMATORY AND NEUROMETABOLITE CHANGES AMONG PATIENTS SWITCHING AWAY FROM EFAVIRENZ AND THEIR CORRELATION WITH NEUROTOXICITY: RESULTS FROM THE SUB-STUDY OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: The potential of efavirenz (EFV) for neurotoxicity is well-established. However, whether and the mechanisms by which it could cause neurocognitive (NC) side-effects is less known. We aimed at correlating neurometabolites and immunologic markers with NC performances and central nervous system (CNS) side-effects in patients chronically treated with EFV, before and after switching to rilpvirine (RPV).

Methods: We conducted a substudy of a randomized controlled trial in which patients who had mild neurocognitive alteration and/or sleep or mood disturbances during treatment with TDF/FTC/EFV were randomized 1:1 to continue the same treatment or switch to TDF/FTC/RPV. Complete NC and symptom assessments were performed at screening and after 24 weeks. Plasma levels of immune-inflammatory markers (neopterin, MCP-1 and sCD163), tryptophan metabolites (kynurenic and quinolinic acid) and glial activation markers (GFAP and S100b) were measured using ELISA at screening and at week 24. Kruskal Wallis test was used to analyze group differences and Spearman's test to explore correlations.

Results: At screening, inflammatory markers and neurometabolites did not significantly correlate with presence of NC impairment (ie, z-scores below -1 in ≥2 domains) nor with domain z-scores. Levels of kynurenic acid were higher among patients with depression (Beck Depressory Inventory ≥90th vs. <90 percentile, 709 vs. 491, P=0.048) and among those who reported more intense CNS symptoms (symptom score ≥6 vs <6; 858 vs. 632, P=0.033).

At week 24, comparing 37 patients switching to RPV with 36 maintaining EFV, a significant improvement in CNS symptoms but no differences in NC function were found. Nonetheless, compared with patients remaining on EFV, those who had switched to RPV had a significant reduction of GFAP (median change since baseline, -1.23 vs. +0.28 ng/ml, P=0.003) and S100B (-342 vs. -5 pg/ml, P=0.01) levels. A significant association between such changes and NC performances was present. As a matter of fact, among those switching to RPV, but not among those continuing EFV, global z-score change at week 24 was inversely correlated with changes in GFAP (R=-0.38, P=0.028) and S100B (R=-0.45, P<0.001). No association was found between the extent of CNS symptom improvement and changes in the levels of S100B, GFAP or of the other explored markers.

Discussion: A decrease in glial activation markers was observed after EFV discontinuation and it correlated with improvement in NC performances. These findings suggest that astrocytes and glial cells could play a significant role in the pathogenesis of EFV-associated neuropsychological side-effect.

Comorbidities

OP 46 CONTRIBUTION OF INSTI, BMI, PHYSICAL ACTIVITY OR CALORIC INTAKE TO WEIGHT GAIN IN PLWH

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Background: Weight gain in people living with HIV (PLWH) is a multifactorial phenomenon in which the relative contribution of traditional and HIV specific modifiable risk factors is not known. The aim was to assess the population attributable fractions (PAFs) of lifestyles and INSTI regimens in PWH who experienced a 5% weight gain over 4 years.
Methods: In an observational cohort study from 2007 to 2019 at Modena HIV Metabolic Clinic, virally suppressed ART-experienced but INSTI-naive PWH were grouped in INSTI-switchers vs non-INSTI on stable ART. Groups were matched for sex, age, 1st visit BMI and follow-up duration. Significant weight gain was defined as an increase
of ≥5% from 1st visit weight over follow-up. Physical activity was assessed with International Physical Activity Questionnaire (IPAQ) as metabolic equivalent of task (MET). Daily caloric intake (DCI) was evaluated with a 3 day food diary. PAFs and 95% CIs were estimated to quantify the proportion of outcomes that could be avoided if the risk factor was prevented, using the following dichotomic variables: BMI >25 kg/m2 vs <25 kg/m2, DCI >2500 kcal vs <2500 kcal, IPAQ MET <600 vs MET>600, quitting vs continuing smoking, INSTI vs no-INSTI regimens, and CD4/CD8 ratio <1 vs >1.
Results: Of 304 PWH (74% males), mean follow-up was 4.2 years (±1.8 SD), age 54.3 (±7.8 SD) years, median duration since HIV diagnosis 22.3 years (IQR 15.5-27.5), CD4 cell count 716 cells/μL (IQR 564-893);98.7% had undetectable HIV-1 RNA (Table).
PAF for weight gain was the greatest for BMI (41%, 24-56, p<0.001), followed by CD4/CD8 ratio (38%, 19-55, p<0.001) and physical activity (33%, 95% CI 8-53, p<0.02). PAF was not significant for DCI (-1%, 9-13, p=0.99), smoking cessation (5%, 0-13, p=0.1) and INSTI switch (9%, -20-33; p<0.51).
Conclusions: Our findings suggest that weight gain is mostly influenced by pre-existing weight and low physical activity. High CD4/CD8 ratio suggest additional immunologic mechanisms linked to weight gain.

Comorbidities

OP 47 CEREBROSPINAL FLUID CXCL13 AS A MARKER OF INTRATHECAL IMMUNOGLOBULIN SYNTHESIS AND IMMUNE-ACTIVATION IN TREATMENT-NAÏVE PEOPLE LIVING WITH HIV

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Background: CXCL13 is a chemokine secreted by follicular T-helpers to attract B cells to germinal centres. In people living with HIV (PLWH) plasma CXCL13 seems to predict the neutralization breadth of humoral responses to vaccines. Data on cerebrospinal fluid (CSF) CXCL13 are missing, but central nervous system (CNS) represents one of the reservoirs threatening eradication strategies. Therefore, we evaluated whether CXCL13 can be detected in CSF and associate with CNS environment among treatment-naïve PLWH.

Material and methods: Retrospective cross-sectional study. Inclusion criteria: treatment-naïve adult PLWH undergoing lumbar puncture for clinical/research reasons. Exclusion criteria: spirochetal infections, lymphoproliferative disorders, infective or inflammatory CNS disorders unrelated to HIV. Eight CSF biomarkers were measured by ELISA (including CXCL13, limit of quantification 7 pg/mL) or immunoturbidimetry. Data were analysed through non-parametric tests.

Results: Sixty-six patients were included; 50 were Caucasian males (75.8%). Median age, current CD4 count, plasma and CSF HIV-RNA were 44 years (38-50), 57 cells/mmc (23-126), 5.42 (4.93-6.01) and 3.90 Log10 cp/mL (2.98-4.77), respectively. 25 had advanced diagnosis without CNS complications (37.9%), 14 HIV-associated neurocognitive disorders (21.2%), 15 isolated brain MRI abnormalities (22.7%), 4 HIV encephalitis (6.1%) and 8 neurological complaints of unknown origin (12.1%). CSF CXCL13 was detectable in 20 patients (30.3%; 30 pg/mL [9.5-91.5]). Patients with detectable CSF CXCL13 differed for higher prevalence of low-level detectable CSF EBV and CMV (33.3% vs 7.9%, p.02 and 17.6% vs 2.5%, p.04) and higher CSF neopterin (7.3 [2.9-15.5] vs 1.4 [1.1-2.7], p<.01), Tourtelotte and IgG indices (24.0 [6.47-47.8] vs 2.35 [0-11.5] and 0.68 [0.42-1.1] vs 0.36 [0.24-0.65], p.02 both) and CSF HIV-RNA (4.6 [4.2-5.3] vs 3.5 Log10 cp/mL [2.4-4.2], p<.01). Significant correlations are shown in the figure. For every unit more in log10 CSF HIV-RNA and EBV-DNA a log10 increase of 0.26 (p.04) and 0.56 (p<.01) was observed in CSF CXCL13, respectively. At multivariable analysis, CSF HIV-RNA was the only predictor of detectable CSF CXCL13 (aOR 2.2 [1.2-4.6], p.02), independently of CSF EBV and CMV-DNA.

Conclusion: About one third of treatment-naïve PLWH showed detectable CSF CXCL13. This CSF chemokine correlated with the magnitude of intrathecal immunoglobulin synthesis and compartmentalized immune-activation. CSF HIV seems to be the main driver to its production, but herpesviridae contribution deserves further evaluation as well as the role of CSF CXCL13 in CNS viral control.

Comorbidities

OP 48 EVALUATION OF THE ASSOCIATION BETWEEN COGNITIVE PERFORMANCE AND HAND DIAGNOSIS WITH THE COGNITIVE RESERVE IN NAÏVE HIV-INFECTED PATIENTS

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Background: Cognitive Reserve (CR) is usually used to assess the brain resilience in relation to brain damage and it is not a fixed entity but can change across the lifespan depending on exposures to work, education and behaviors .The relationship between cognitive reserve and cognition suggests that people living with HIV with low CR might be more prone to show neurocognitive deficits. Aims of this study were to investigate the association between cognitive abilities and CR in a group of naïve HIV-infected individuals and to evaluate the potential association between CR and the anxiety/depression symptoms.

Material and methods: We included HIV positive naïve persons with more than 18yrs attending an Italian HIV/AIDS clinical center. Participants (pts) underwent: neuropsychological assessment (NPA) through a standardized battery of 12 tests on 5 different domains, a questionnaire for cognitive reserve (CRI-q) that provides four index [CRI-total(CRI-T), CRI-education (CRI-E), CRI-working(CRI-W), and CRI-leisure time (CRI-LT)] and two questionnaires for the symptoms of anxiety (BAI) and depression (BDI-II). Pts were classified as having HIV associated neurocognitive disorders (HAND) according to Frascati's criteria. Pts with confounding factors (opportunistic infections/neoplasia involving the CNS, major depression, not Italian speaking, physical disabilities) were excluded. Logistic and linear regression were used to investigate the association of HAND and NPZ12 with CR, respectively.

Results: 107 pts were included: 23 (21.5%) were impaired (19 ANI, 4 MND). Main characteristics: male 93.5%, median age 40yrs (IQR 30-51), MSM 62.2%, median yrs of education 13 (IQR 12-16). Median CD4+ count at NPA was 339 cells/mm3 (IQR 104 - 556). The median CRI-Tscore was 98 (IQR 92-110), while the median scores on CRI-E, CRI-W and CRI-LT 98 (90-110), 97 (89-109) ,99 (91-110), respectively.

By adjusted multivariable logistic regression for CD4 count at NPA and Age, HAND diagnosis was found to be associated with lower CRI scores (total, education, working and leisure time) (Table 1, Figure1). Similarly, an adjusted multivariable linear regression model (for the same variables) showed a correlation among all CRI index and NPZ12 [CRI-T : B 0.025,95%CI 0.017-0.033,p<0.001; (Figure 2); CRI-E: B 0.020, 95%CI 0.011-0.028, p<0.001; CRI-W: B 0.023, 95%CI 0.012-0.034, p<0.001; CRI-LT: B 0.0177, 95%CI 0.009-0.025, p<0.001]. No association of the BAI/BDI-II questionnaires with cognitive status and with CR was found.

Conclusions: Our findings suggest that all four CR index (total, education, working and leisure time) might have an impact on cognition. Moreover, CR could represent a protective factor for HAND in a group of HIV naïve PLWH. Further data are needed to confirm these preliminary findings and to assess if CR could be introduced in neuropsychological evaluation in order to monitor the evolution of the cognitive ability

Comorbidities

OP 49 ARE LOW VITAMIN D PLASMA LEVELS ASSOCIATED WITH INTRATHECAL IMMUNEACTIVATION IN PLWH?

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Background: Low levels of vitamin D (25OHD) have been linked to some neurodegenerative diseases and worse cognitive performance. Few data are available on 25OHD in CNS. HIV plays a role in the genesis of neurodegenerative phenomenon due to immune activation and inflammation. Aim of our study was to assess the CSF 25OHD levels and to determine correlations of plasma 25OHD levels and CSF immune-activation in person living with HIV (PLWH).
Methods: Single-center retrospective study on CSF/plasma paired samples from HIV positive patients undergoing lumbar puncture (LP) because CNS staging of lymphoma or neurological signs/symptoms. Concentrations of IL-17A, IL-6, TNFa, VEGF-A, TGFb and CD14s were quantified using ELLA system (ProteinSimple). Total plasma and CSF 25OHD was quantified using a chemiluminescence immunoassay (CLIA; DiaSorin LIAISON 25 OH Vitamin D TOTAL Assay). Plasma/liquor ratio 25OHD was calculated. Pearson correlation coefficient and linear regression were used to investigate the association between 25OHD and biomarkers.
Results: 33 CSF/plasma pairs from 26 HIV+ patients were included: 94% male, median age 55y, heterosexual 45%, MSM 27.3%, median CD4 129 (IQR 60-278) cells/mm3, 80% CDC stage C. At LP, 76% of patients were receiving cART. Median HIV-RNA was 1.64 (IQR 0-2.93) log copies/mL in plasma, 1.59 (0-2.72) in CSF. Median value of plasma 25OHD was 23.3 (9.9-33.7) ng/ml and in 21 (63.6%) patients 25OHD was under threshold in CSF, with median ratio of 5.0 (2.4 -7.7).
Higher levels of 25OHD in plasma and 25OHD ratio were associated with lower levels of CSF sCD14 (r=-2.8, p=0.009; r= -2.5, p=0.020) (Figure 1). No correlation between levels of 25OHD (plasma, CSF and ratio) and remaining biomarkers was found. At univariable analysis, AIDS vs non-AIDS conditions was significantly associated with higher levels of CSF sCD14 (Beta 327.0 (95%CI -8.51; 662.6), p=0.06). Low level of 25OHD plasma remained still associated with higher level sCD14, after adjusting for AIDS condition (Beta -10.2 per 1 ng/mL (95%CI -19.3.3; -1.16), p=0.03).
Conclusions: Low serum level of vitamin D, but not CSF levels seems to play a role in CSF immune activation in PLWH. Nevertheless, more study are needed to better define the exact pathogenetic mechanism and if a supplementation of vitamin D could reduce central immune activation and potential neurodamage.

Comorbidities

OP 50 GENDER DIFFERENCES IN NEUROCOGNITIVE FUNCTIONS IN PLWK

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Background: Recently, gender differences in brain function and disorders were well documented although yet very few studies deepened possible gender differences in neurocognitive complications of HIV. In fact women may be more vulnerable than men to HIV related cognitive dysfunction due to sociodemographic, lifestyle, mental health and biological factors.Our aim was to compare global cognitive performance (GCP) in a HIV positive population among men and women.

Method: We performed a retrospective, cross-sectional analysis of a monocenter dataset including 351 subjects on cART who underwent a comprehensive neuropsychological assessment (NPA) during routine clinical care between November 2008 and March 2019.Global performance (GCP) was measured by transforming raw scores at each task into standardized Z-scores and averaging to calculate a composite total score.Zung Depression Scale was also administered. We compared GCP and Zung pathological scores (ZPS) among groups based on gender: women and man living with HIV (1=WLWH;2=MLWH).Factors associated to GPC and ZPS were explored in the overall population.

Results: The sample included 228 MLWH e 123 WLWH.Subjects belonging 2 groups significantly differed in mean age (p=0.019) and education (p=0.003) [supplementary clinic and demographic charateristics in table1].GCP was significantly higher in group 2 when compared to group 1 [mean 0.01 (SD 0.89) vs -0.02 (SD 0.86); p 0.009]. Considering each cognitive domain separately, group 2 showed a better performance than group 1 regarding memory [mean -0.45 (SD 1.14) vs -0.71 (SD 1.2); p 0.046], attention [mean -0.01 (SD 0.71) vs -0.42 (SD 0.69); p <0.000] and executive functions [mean 0.24 (SD 0.75) vs 0.13 (SD 0.73); p 0.007].Higher GCP was associated to male gender (β 0.165; 95% CI 0.009/0.322; p 0.039), higher age (β 0.010; 95% CI 0.003/0.018; p 0.007) and higher education (β 0.068; 95% CI 0.049/0.088; p<0.001), after adjusting for time from HIV diagnosis, CDC stage C and CD4 cell count.In the same regression model, male gender was associated significantly to better attention abilities (β 0.323; 95% CI 0.171/0.474; p <0.000) and with a trend toward significance to higher executive skills (β 0.153; 95% CI -0.014/0.320; p 0.073). Furthermore group 1 showed significantly higher percentage of subjects with ZPS [15,4% n=19 vs 7,9% n=18 (p. 0.029)]. Group 1 had 2.46 times the odds of showing clinical depressive symptoms (OR 2.46; 95% CI 1.19/5.05; p 0.014), after adjusting for past injecting drug use CDC stage C and cholesterol level.

Conclusions: In our population, GCP was significantly higher in MLWH independently by age and education. Furthermore MLWH seemed to better perform in attention and executive skills domains, and WLWH seemed to have higher odds of showing clinical depressive symptoms.WLWH seemed to show cognitive disadvantages and elucidating the mechanisms underlining these differences is critical for tailoring cognitive interventions.

Comorbidities

OP 51 MENOPAUSE IN AGING WOMEN LIVING WITH HIV: CHANGES IN BONE MINERAL DENSITY AND TRABECULAR BONE SCORE

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Objective: HIV infection and tenofovir disoproxil fumarate (TDF)-containing antiretroviral regimens alone or in association with boosted protease inhibitors are associated with impaired bone quality and quantity and high fracture risk. Bone loss has never been studied across the menopausal transition in women living with HIV (WLWH). The aim of the study was to describe pattern of bone quantity (lumbar bone mineral density (BMD)) and bone quality (trabecular bone score (TBS)) changes across menopause in WLWH undergoing ART with or without TDF.

Methods: We conducted a longitudinal retrospective study including WLWH attending Modena HIV Metabolic Clinic from 2012 to 2019. The observation period was divided into reproductive, transitional, early and late menopause according to STRAW criteria. Lumbar BMD and TBS derived from DEXA evaluation. GEE models were built to predict changes in BMD and TBS across menopause and TDF or TDF+PI/r/c containing ART regimens.

Results: We included 185 (mean age=49.3 years) ART-experienced WLWH observed for a median of 6.1 years. At baseline, median duration of HIV infection was 244 months, median CD4 cell count was 635 cells/uL. 134 observations were assessed in the "Reproductive Period", 180 in the "Menopause Transition Period", 185 in the "Early Menopause Period" and 20 in the "Late Menopause Period", for a total of 519 DEXA observations. Across menopause, LDL, HDL, CRP, vitamin D and PTH significantly increased, while ASMI, FFMI, lumbar BMD, TBS score and FRAX® score worsened ($p<0.001$). Loess curves of TBS and BMD trend across menopause did not reach statistical difference between the two, both TBS and BMD show decrement over time windows. Both TBS and BMD rapidly reduced in the first year of menopause, then improved in the second year post menopause, and stabilized after third year post menopause. Independent predictors of BMD and TBS changes are explored in GEE multivariate linear regression models and are shown in Table 1.

Conclusions: Bone decrement with both BMD and TBS was the greatest during early menopause period. Current TDF exposure was independently associated with BMD, but not TBS lowering in menopause, suggesting that TDF use should be avoided in WLWH entering the menopause. The similar was not observed for PI. The exact role and potential benefit of TAF over TDF in the menopause transition should be studied.

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OP 52 NAFLD PHENOTYPE AND PREVALENCE ACROSS THE MENOPAUSE SPECTRUM IN WOMEN WITH HIV

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Background and Aims: Both menopause and non-alcoholic fatty liver disease (NAFLD) are major metabolic events with potential systemic effects. The objective of the study was to describe natural history of NAFLD during menopause transition and the interplay between these two conditions in women living with HIV (WLWH).
Method: This was a cross-sectional study of consecutive WLWH attending Modena HIV Metabolic Clinic in 2018-2019. Women with hazardous alcohol intake and hepatitis B or hepatitis C virus co-infection were excluded. NAFLD and significant liver fibrosis were assessed with transient elastography and defined as controlled attenuation parameter (CAP) >248 dB/m and as liver stiffness measurement >= 7.1 kPa respectively. Menopause was determined according to STRAW criteria including 4 periods: reproductive, transitional, early and late menopause. Due to low absolute number of NAFLD cases, these criteria were further simplified dividing WLWH as "pre-menopause" if being in the first two periods and "post-menopause" if being in the last two periods. Two logistic regression models were built to explore predictors associated with NAFLD in pre-menopause and post-menopause periods, using as covariates metabolic and anthropometric variables.
Results: We analyzed 296 WLWH with mean age=54.3 (+-7.9) years, current median CD4=710 µL (IQR=543-896) and HIV RNA undetectability in 98.3% of cases. Overall, NAFLD and significant fibrosis prevalence in WLWH were 33.8% and 11.8% respectively. NAFLD and significant fibrosis were observed in 33.3% and 7.4% in reproductive, 29.4% and 11.8% in menopause transition, 32.6% and 12.9% in early menopause and 56.3% and 12.5% in late menopause respectively (p=0.07 and p=0.66). Table shows characteristics between WLWH with NAFLD in reproductive and menopause period. In two multivariate logistic models, HIV duration, lipoatrophy, CD4/CD8 ratio and obesity were not associated with an increased risk of NAFLD in pre-menopause and post-menopause, while the HOMA was the only co-variate to predict NAFLD in post-menopausal WLWH (OR=0.38, 0.15-0.8; p=0.03).
Conclusion: Prevalence and phenotype of NAFLD and liver fibrosis did not differ across the menopause in WLWH, suggesting that more complex immune-metabolic pathways, not captured by STRAW criteria, are involved in NAFLD natural history in aging WLWH.

Comorbidities

OP 53 INCIDENCE OF DIABETES IN A COHORT OF PLWH PEOPLE LIVING WITH HIV IN PERUGIA

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Introduction: Diabetes mellitus (DM) is a common condition with significant associated morbidity and mortality. In PLWH (people living with HIV) a DM prevalence up to 14 % (4 times more than HIV negative subjects) is reported. In PLWH, in addition to increasing age, obesity and genetic factors, risk factors for DM are: HIV infection itself, ART, HCV-coinfection, medications (antipsychotics, corticosteroids), visceral fat and HIV-related inflammation. Therefore, the early detection of dysglicaemic conditions and atherosclerotic progression, especially in patients with DM , are important clinical aspects to prevent the onset of DM and to follow up the cardiovascular risk in those already diabetic. We investigated the incidence of impaired fasting glucose (IFG) and DM in ART treated PLWH without previous diagnosis, comparing their glycol-metabolic profile and analysing the presence of carotid plaques before starting antidiabetic drugs.

Methods: In order to identify individuals with IFG (at least 2 fasting glucose >100 mg/dl) or new DM (2 fast blood sugar ≥126 mg/dl or HbA1c ≥ 6.5% or blood sugar> 200 mg/dl 2 hours after OGTT), an observational study on all patients attending the DH of Infectious Diseases Clinic of Perugia from October 2018 to March 2019 was performed.

In diabetic PLWH, anthropometric measurements, immune-virologic and metabolic parameters, carotid intima-media thickness (cIMT), presence of carotid bifurcation plaques were evaluated. An endocrinological visit was performed before starting metformin 500 mg/die.

Results: Five hundred PLWH were evaluated. Out of them 73 (14.6%) showed an IFG and 21 of these (4.2%) satisfied a new diagnosis of DM. Both in diabetics and in IFG patients, the male gender (66.6%vs84.6%) and the Caucasian ethnicity (81% vs 84.6%) were mainly represented.The demographic, immuno-virologic and metabolic characteristics of patients with DM and IFG are shown in the table 1. All PLWH were on stable ART and under virological suppression. We did not observe any significant difference in immune-virological parameters and in total cholesterol, HDL-c and LDL-c plasma levels between the two groups.

Higher triglyceride plasma levels (p0.04) and larger waist circumference (p0.01) were seen in DM than in IFG. The 14.2% of patients with DM had carotid plaques > 20%. Metformin 500 mg daily was started in 18/21 patients: 2 required insulin treatment and 1 refused any treatment.

Conclusions: In our experience 28.7% of patients with IFG were diabetic. Therefore, improved screening of dysglycemic conditions could ameliorate the early diagnosis of DM and prevention and management of cardiovascular complication in PLWH.

Comorbidities

OP 54 STANDARD VS HIGHER DOSE OF RIFAMPICIN IN PATIENTS WITH TUBERCULOSIS: A META-ANALYSIS

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Background: evidence suggests that Rifampicin doses could be increased to achieve more effective tuberculosis treatment. We compared clinical and microbiological outcomes of patients with pulmonary tuberculosis treated with either standard dose (10mg/kg) or higher dose (>10/kg) of Rifampicin.

Materials/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) reported clinical (treatment failure and/or mortality and/or ADR) and/or microbiological outcomes (culture conversion at 8 weeks) comparing standard dose and higher dose of Rifampicin;(b) were available as a full text manuscript;(c) written in English;(d) included pulmonary tuberculosis;(e) enrolled either children or adult HIV-positive or HIV-negative patients. The exclusion criteria were:(a) letters, case reports, meeting abstracts, or editorial comments;(b) enrolled patients with Rifampin resistant or MDR infection;(c) studies enrolling less than 5 subjects.

Results: From a total of 11,686, 6 studies met the inclusion criteria, allowing a meta-analysis on 1,110 patients. Two studies examined treatment failure showing no significant difference in the two observed groups (RR 0.64, 95%CI 0.24 -1.68). In terms of mortality in pulmonary TB there was no significant difference between the intensified treated patients and the control groups (RR 1.48,CI 0.29-7.63). Five studies investigated ADR grade 3 and 4, showing no statistical difference in terms of events between the intensive treated group and the control group (RR 1.35, CI 0.86-2.10, p 0.192). Similarly, investigating into ADR leading to discontinuation of therapy there was no statistical difference among the intensive therapy group compared to the control group (RR 2.24, CI 0.53-9.56; p 0.275). Moreover, four studies analyzed ADR grade 3 or 4 related to hepatic events, showing no significant difference in the two groups (RR 1.29, CI 0.48-3.49, p 0.620). Treatment with higher doses of Rifampin was more efficacious compared to the treatment with a standard dose in negativization of culture at eight weeks (RR 1.06, CI 1.00-1.13, p 0.037).

Conclusions: the meta-analysis showed higher rate in negativization of culture at eight weeks when treating patients affected by pulmonary TB with higher doses of Rifampicin. There was no difference in terms of ADR grade 3 or 4, ADR grade 3 or 4 hepatic related, ADR leading to discontinuation, mortality and rate of treatment failure. Further studies are needed to clarify the role of higher dose of rifampicin in patients with pulmonary tuberculosis.

Hepatitis and coinfections

OP 55 RAPID DETECTION OF MYCOBACTERIUM TUBERCULOSIS DNA IN PULMONARY AND EXTRAPULMONARY PARAFFINIZED SAMPLES BY DDPCR

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Background: Rapid, reliable diagnosis of tuberculosis (TB) is essential to initiate correct treatment, avoid complications, and prevent transmission. Mycobacterial culture, the gold standard for TB diagnosis, may not be an option if samples are formalin-fixed and paraffin-embedded (FFPE) for histopathological examination. Even though nucleic acid amplification tests by real-time (rtPCR) are improving, their accuracy remains uncertain. Here, we attempted a novel molecular approach based on droplet digital PCR (ddPCR, Biorad) to rapid detect Mycobacterium tuberculosis (MTB) DNA in clinical FFPE samples.

Methods: MTB detection was performed by ddPCR in 36 mycobacterial culture positive and 10 mycobacterial culture negative samples from different anatomical sites from patients with clinical suspect for TB, retrospectively collected at Niguarda Hosp (Milan, Italy) between 2013 and 2019. The reactions were carried out using primers and probes targeting the multicopy gene IS6110. At least 2 positive droplets were considered for a positive test result. Analytical sensitivity of ddPCR assay was evaluated using serial diluition of H37rv strain. Limit of detection (LOD) was calculated by probit analysis for a 95% positive result.

Results: Of the 46 subjects, 22 (46.8%) were males, with a median age of 35 (IQR:26-42) years, and 3 (6.5%) were HIV-1 coinfected. Pulmonary and extrapulmonary samples were 8 (17.4%) and 38 (82.6%), respectively.

Looking at ddPCR performance assays, IS6110 assay showed a good linear correlation between expected and observed values (R2=0.99). Probit analyses predicted a LOD of 23 (95%CI: 14-127) ISS6110 copy number.

Considering mycobacterial culture as a reference method, ddPCR yielded 34/36 (94.4%) positive results, with a median of 378 (99-1,358) IS6110 copies number. Interestingly, among these positive results, 4 were PCR negative (11.7%), and only 16 (47.0%) had a positive AFB smear result. Of the 12 ddPCR negative results, 2 (16.7%) were culture positive (after 10 and 12 days of culture). The sensitivity and specificity of ddPCR assay were 94.4% (95%CI: 81.3-99.3) and 100% (95%CI: 69.1-100) respectively, with a test accuracy of 95.6. Similar performances were observed in pulmonary and extrapulmonary samples. ROC curve analysis showed that the area under the curve was 0.96 (95%CI 0.91-1.00), confirming the high accuracy of the method in predicting MTB culture positivity. Notably, these data confirmed the superiority of ddPCR assay in detecting MTB in FFPE over rtPCR, characterized by an accuracy of 89.1 and a sensitivity of 86.1% (95%CI: 70.5-95.3).

Conclusions: This preliminary study suggests that ddPCR has the potential to provide a highly sensitive, accurate and rapid method for diagnosis of pulmonary and extrapulmonary MTB infection in FFPE samples. This approach could be helpful when culture is not performed or where TB differential diagnosis is needed, like in the setting of HIV-1 coinfected and immunocompromised patients.

Hepatitis and coinfections

OP 56 PHARYNGEAL CONTAMINATION IS A MAJOR DRIVER FOR SEXUALLY TRANSMITTED INFECTIONS EPIDEMIC IN MEN WHO HAVE SEX WITH MEN

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Background: Sexually transmitted infections (STIs) – especially C. trachomatis (Ct), N. gonorrhoeae (Ng), M. genitalium (Mg) and syphilis – are increasing among men who have sex with men (MSM). Since condom is reported to be used in less than 10% of oral sexual acts, condomless oral sex was suggested to have a pivotal role in the current STI epidemics. Aim of present study is to describe pharyngeal STIs epidemiology and clinical features in a cohort of MSM.

Methods: This monocentric, retrospective analysis included all MSM who attended our STI Clinic for routine periodical screening between 2017 and 2019 and who collected pharyngeal swabs for standard culture and multiplex nucleic acid testing (mNAT). This mNAT essay tested simultaneously for Ct, Ng, Mg and for microorganisms generally not clinically relevant for MSM (M. hominis, Ureaplasmas and T. vaginalis). Data from clinical evaluation for HSV and HPV, serology for syphilis and viral hepatitis and mNAT from urine and anus were collected. Subjects were stratified into symptomatic and asymptomatic. Demographic, behavioral and clinical features were collected. Descriptive statistics and non-parametric Chi-square test were used.

Results: 383 subjects were included in the analysis: they were mainly Italians (81.2%) and with a median age of 36 (IQR 30-45) years. HIV+ subjects were 49.6%, pre-exposure prophylaxis users were 20.9%. A large majority (63.2%) had at least one previous STI, 36.2% reported recreational drugs use during sex.

862 pharyngeal swabs were collected (256 for mNAT) and were paired to 862 serologic tests; 819 urine samples and 240 anal swabs were also available. None complained of pharyngeal symptoms; 815 urine and 226 anal swabs were collected from asymptomatic subjects.

Syphilis was the most common STI found in the study period (5.2%, p<0.001). Standard culture from pharyngeal swabs resulted positive for Ng in 2 cases (0.2%), while 66 (7.7%) showed a meningococcal contamination. Cumulatively, mNAT from pharyngeal swabs was positive in 5.0% of samples (4.6% including only clinically relevant pathogens): pharynx was significantly more commonly contaminated than the other anatomical sites (p<0.001). Figure 1 shows mNAT isolates: Ng was the most common microorganism in the pharynx. Ng and T. vaginalis were more frequently isolated from the pharynx than from other sites (p<0.001 both), while Ct and Mg were more common in anal swabs (p<0.001 and 0.026, respectively). No difference in terms of pharyngeal infections was observed for each pathogen among HIV+ and HIV- individuals.

Conclusions: Pharynx is the most contaminated anatomical site for STI. Pharyngeal infection is mainly due to Ng: this diagnosis relies essentially on mNAT and not on standard culture. Given the absence of symptoms and the reported low condom use during oral sex, our data support the observation that this sexual practice is a major driver for STI spread.

Hepatitis and coinfections

OP 57 HCV INFECTION IN PWUD: A MICROELIMINATION INTERVENTION IN ROME

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Background: People who use drugs (PWUD) are considered an important reservoir of HCV infection. Data on the number of infected PWUD in Italy are patchy. Moreover, PWUD move continuously between services for addiction (SerD), therapeutic communities and prisons.
We analyzed the effectiveness of an intervention aimed to improve the diagnosis and treatment access for HCV through a facilitation model in a PWUD population who is in charge to a center for addiction in Rome (SerD ASL Rome 3).
Material and methods: We conducted a prospective cohort study in a PWUD population in Rome.
Medical harts were reviewed to identify the clinical features of PWUD in charge to center.
HCV rapid test was offered on site to PWUD who had not HCV infection data, or had a previous negative test and a recent exposure.
Individuals testing positive and those with already diagnosed HCV infection were referred to the clinical center to perform in the same week HCVRNA test.
Viremic individuals were offered to perform in the same day the blood tests, fibroscan and clinical evaluation. During the visit, antiviral treatment and follow-up were scheduled.
Reasons for declining screening, HCVRNA test and treatment were recorded.
Results: 721 clinical files had been consulted. The most important routes of drug's administrations were intravenous (58.7%) and inhaling (20.3%).
Overall, 454 PWUD in charge to the center were enrolled in the study from March 2018 to January 2020.
47.4% (n=215/454) of individuals resulted positive for HCV Ab, 162 performed HCVRNA blood test and 106 (49.3%) resulted viremic. About one third of pts never did the HCVRNA test (24.7 % n=53/215).
267 PWUD refused the screening. Reported reasons were: a HCVAb negativity during the last year in 17.2% (n=46/267) of cases, a recent HCV treatment in 28.5% (n=76/267), a spontaneous HCV clearance in the 12.0% (n=32/267). 29 (10.9%) PWUD had a known HCVAb positivity, but declined the screening, of whom 14 were HCVRNA positive. 48 (18.0%) PWUD were unreachable, of whom 14 had a documented HCVAb positivity.
Almost all viremic pts (97.0%; n=100/106) performed blood test, fibroscan and clinical assessment; 97 started antiviral therapy with DAA while 3 never attended the therapy because of oncological diagnosis. Six pts dropped out the clinical assessment.
35.1% had advanced fibrosis (F3-F4) (n=34/97). One pt presented HCC and underwent to hepatic resection, another pt presented multifocal HCC.
Pts who executed follow up blood examination achieved SVR12.
Conclusions: Our data confirm an important reservoir of HCV infection in PWUD population.
This study demonstrated feasibility and effectiveness of a program based on site offer of HCV test and immediate referral for treatment. Nevertheless important gaps remain in the cascade of care, that call for further efforts in order to improve the health perception, diagnosis, treatment adherence in these pts.

Hepatitis and coinfections

OP 58 DIRECT-ACTING ANTIVIRAL BASED TREATMENT FOR HCV-INFECTED PERSONS WHO INJECT DRUGS: A MULTI-CENTRE REAL-LIFE STUDY

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Background: People who inject drugs (PWID) have always been regarded as a key population to treat in order to achieve a global elimination of HCV infection. During the last years, the advent of oral direct acting antiviral (DAA) regimens has offered a highly effective and well tolerated therapy, leading to a substantial increase in treatment uptake in difficult-to-treat populations. In the present study we aimed to evaluate the factors associated with virological response in a cohort of HCV infected PWID treated with DAAs.

Materials and methods: We conducted a multicentre retrospective cohort study enrolling all HCV infected subjects treated with DAAs, who reported a former or recent injection of illicit drugs, for which HCV-RNA loads at 12 weeks after end of treatment were available. The primary outcome evaluated was the SVR12 rate; the epidemiological, clinical and virological characteristics associated with the viral response were analyzed. A logistic regression analysis was applied to identify independent predictors of virological failure.

Results: During the study period, 520 HCV-infected injection drug users treated with all oral DAA-based regimens were enrolled; Most of patients (456, 87.5%) were male; the mean age was 47.7+9.3 years.; 168 (32.3%) patients presented a genotype 1a, 109 (21.0%) a genotype 1b, and 174 (33.5%) a genotype 3; 152 out of 520 subjects (29.2%) were cirrhotic; 118 (22.7%) and 373 (71.7%) were treated with a DAA regimen of second and third generation, respectively; 169 (33.6%) patients were receiving an opioid agonist at the start of antiviral therapy. Only 11 subjects (2.1%) showed a positive HCV-RNA at 12 weeks after EOT, 3 of which had dropped out before the scheduled duration of therapy. No epidemiological or biochemical characteristic was associated with treatment failure. A significant correlation was found between treatment with opioid substitution therapy (OST) and viral failure ($p<0.001$) Similarly, HIV coinfection was more frequent between patients who failed to achieve the SVR ($p=0.002$). Finally, subjects treated with first or second generation regimens showed an higher rate of virologic failure than those treated with third generation DAAs (5.5% vs 0.8% respectively, $p=0.006$). At the multivariate analysis, the treatment with a first or second generation DAA resulted the only factor independently associated with failure (OR 10.4, 95% CI: 1.43 to 76.1, $p=0.02$).

Conclusions: The treatment with DAAs led to a high SVR12 rate (97.9%) among a large cohort of HCV-infected PWID. The only predictor of viral failure found in our analysis was the treatment received. Systematic screening and treatment with highly effective third generation regimens will make the elimination of HCV in this setting a feasible goal.

Hepatitis and coinfections

OP 59 ARE NON-INJECTING DRUG USERS AT RISK OF HCV-INFECTION? DATA FROM THE SAN PATRIGNANO COHORT

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Background: Non-injecting drug users (NIDU) are considered at risk of HCV infection, but few and inconsistent epidemiological data are available, with HCV antibodies prevalence estimates ranging between 2% to 35%, depending on study methodology, type of drug used, way of use, and cultural context. We investigated the epidemiology and risk factors of HCV infection in a cohort of NIDU admitted to a residential treatment setting for drug addiction.
Methods: We collected data of NIDU admitted to the San Patrignano Therapeutic Community (SPTC) during the DAA-era (2015-2019). At entry all clients undergo a medical examination, including a detailed toxicological anamnesis, and blood chemistry, including HCV screening. The Study was approved by local Ethical Committee.
Results: Among 892 NIDU (17% F, median age at entry 28 years, Interquartile Range: 22-34), mostly Italians (94.9%). Cocaine/crack use was reported by 93.7%, while heroin addiction by 264 subjects (29.6%). Before entry in SPTC 236 (26.5%) were already followed by Public Health Services for drug addiction (SerD), 202 (22.6%) attended other TC, while 100 (11.2%) experienced carceration. Seven subjects (0.9%) were HIV infected. Before SPTC admission 135 (15.1%) had been previously screened for HCV, of which 3 positive (2.2%). At SPTC admission, 848 (95.1%) were screened for HCV, 5 resulting HCVAb positive (0.6%), including the 3 cases found positive before entry and 2 newly diagnosed (none HIV-pos). A deeper interview on these cases indicated a possible way of HCV infection in 4 out of 5 cases: connatal infection (1 patient), unsterile tattoo in jail (1), accidental sting (1) with a just used syringe, and voluntary intranasal spray of dissolved drug from a just used syringe (1). The remaining subject had no explanation other than snorting or smoking drugs and/or heterosexual exposure. Two subjects resulted HCV RNA negative, one because of spontaneous clearance, the other cured with DAA before SPTC admission; among the 3 patients eligible for treatment, 2 were successfully treated with DAA, while the last patient ended his period in the TC before HCV treatment.
Discussion: In Italy, NIDU population consist mainly by cocaine/stimulant users, who don't attend Drug Treatment Services. Moreover, in comparison with injecting drug users, they have less experiences of jail and other TC. For these reason, HCV screening is very unlikely performed in NIDU. HCV prevalence in NIDU is much lower than that observed in injecting drug users, and in most of the cases the mode of exposure may be not directly related to drug using behaviors. Nonetheless, screening of this population would be still cost-effective at the prevalence level recorded in our study population. Supported by: Grant Gilead IN-IT- 987-5396, part of the LEGA-C™ program "Local Elimination Programs leading to Global Action in HCV"

Hepatitis and coinfections

OP 60 REAL LIFE DAAS IN A LARGE COHORT OF PEOPLE WHO USE DRUGS WITH HEPATITIS C VIRUS INFECTION IN TOR VERGATA HOSPITAL IN ROME: ADHERENCE, EFFICACY AND REINFECTIONS OF A KEY POPULATION

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Background: People who use drugs (PWUD) are a great concern among patients with HCV infection. Treatment in this key population could be difficult because of poor adherence, psychiatric comorbidities and high rate of reinfections. The aim of our study was to describe PWUD demographic features, adherence rates to therapy and follow up and efficacy of treatment with direct-acting antivirals (DAAs) at the Infectious Diseases Clinic of Tor Vergata Hospital.

Methods: A retrospective study was conducted among PWUD with chronic hepatitis C treated at the Infectious Disease Clinic of Policlinico Tor Vergata in Rome, from april 2015 to december 2019. Among the total amount of patients treated for HCV infection in our Clinic, 69% had an anamnestic data positive for drug use disorder in the past years or still continue during the treatment.

Results: Patients' cohort (n=265, male 81%, median age 42 y) was so represented: current PWUD (n=40, 15%), opioid substitution therapy (OST) PWUD (n=46, 17.7%), chaotic PWUD (n=142, 5.9%) who declared both current drug-use and opioid substitution therapy (OST), rehab PWUD (n=37, 13.9%). OST more used was methadone, less frequently buprenorphine (87% vs 9%). 135/265 (81.9%) of patients had advanced liver fibrosis (F3-F4); 24/265 (9%) of patients was HIV-coinfected; almost half of the population showed a concomitant occult HBV infection (129/265, 48.1%); 34.3% had psychiatric comorbidities.

The majority of patients (n=244/265, 92%) completed treatment, but 21/265 (8%) discontinued DAAs and 67/265 (25%) didn't comply with the medical appointments. Among PWUD that completed treatment, 157/244 (64.3%) comply with medical visits until follow-up at 12 weeks after the end of treatment (FU12, even if 36,9% out of appointment during treatment and 36.9% during follow-up); 97/265 patients (39.7%) drop out at FU12, 4 of them died for other comorbidities before FU12. 18/97 (18.5%) were recalled or come spontaneously at Follow Up 24 (FU24). Sustained virologic response (SVR12) rate in patients who completed treatment at the time of the analysis was 96.8% (152/157). Data of 3 patients were not available at FU12 but at FU4 they presented HCVRNA undetectable. At FU24 we observed that 10 patients were viremic (6 cases were reinfections and 4 relapses that were lost at FU12). Features of reinfections and relapses are reported in table 1.

Conclusions: PWUD are a difficult to treat population. Even if the majority of patients completed treatment, retention in follow up is a challenge. People lost to follow up represent a problem because not having data about SVR12 they can constitute carrier of HCV infection, so it becomes very important to focus on PWUD population in order to achieve the HCV eradication target.

Hepatitis and coinfections

OP 61 EFFECTS OF HCV ERADICATION ON LIVER FUNCTION IN HAEMOPHILIC HIV/HCV CO-INFECTED PATIENTS

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Background: Challenge to eradicate HCV in haemophilic patients started in 1987, firstly with interferon, then with first generation Direct Acting Antivirals (DAAs) and from 2015 with interferon-free DAAs. According to AIFA criteria, from March 2017 patients with coagulopathy, a condition documented in accelerating the course of HCV-related liver dysfunction, are eligible to DAA treatment independently from their stage of liver fibrosis.
The efficacy in eradicating HCV of interferon-free regimens in haemophilia is already documented in literature, but only few studies have investigated whether liver function and metabolic profile improve after HCV eradication, especially in presence of human Immunodeficiency Virus (HIV) co-infection, a condition known to accelerate the course of HCV hepatopathy. Aim of our study is to investigate whether in co-infected HIV-HCV haemophilic patients the eradication of HCV leads to an improvement in liver function, metabolic profile, renal function and immunological recovery.
Methods: We retrospectively analyzed the clinical and biochemical data of patients affected by coagulopathies with HIV/HCV co-infection before and after eradicating HCV both with interferon and interferon-free therapeutic regimes. The trend of biochemical data and FIB4 and APRI scores across the study period was evaluated using a generalised linear model for repeated measures and a pair comparison performed with the Bonferroni adjustment.
Results: A total of 70 patients with HIV/HCV co-infection were enrolled. This population was made up of 69 men and 1 woman. 59 patients had haemophilia A, 10 patients had haemophilia B, and one female patient was affected from Von Willebrand disease.
Nine patients were lost during follow-up and 4 patients died, 57 patients were included in our analysis.
Between 1998 and 2019, 55 patients aged 28-70 (median 44) years successfully eradicated HCV. Two patients are currently on ongoing HCV treatment. Four patients had spontaneous clearance of HCV, 48 were treated with IFN-based therapies and 33 with DAA.
After HCV eradication both FIB-4 (p=0.001) and APRI score (p=0.001) reduced significantly, accordingly with transaminases decrease (p=0.001), as shown in Table. A trend towards an amelioration of albumin and alpha-fetoprotein levels was also seen, although the post-hoc analysis did not find a significant changing in the timeframe following HCV treatment. On the contrary, creatinine levels tended to increase during the follow up, without a significant difference in the trend before and after treatment (Table). Blood cholesterol and triglyceride levels remained stable after HCV eradication, as well as CD4+ T cell count.
Conclusion: Eradication of HCV leads to an improvement in liver function documented as a reduction of FIB-4 and APRI scores one year after the beginning of anti-HCV therapy in coagulopathic patients with HIV infection

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OP 62 VIROLOGICAL PATTERNS OF HCV-PATIENTS WITH FAILURE TO SECOND GENERATION DIRECT-ACTING ANTIVIRALS

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Background: Despite the excellent efficacy, direct-acting antivirals (DAA)-regimens are associated with failure in 5% of cases.

Aims: To characterize the virological patterns and the resistant-associated substitutions (RASs) in the patients with failure to second-line DAA-regimen.

Methods: All the consecutive 79 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 April 2019 were enrolled. All the pts had been treated with second DAA-regimens(Sofosbuvir+Velpatasvir, Glecaprevir+Pibrentasvir, Grazoprevir/Elbasvir) according 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 characteristics of patients enrolled and type of treatment. According to therapeutic outcome, 90 % relapse, 6 % breakthrough and 4 % non-response. Among the 79 patients failed at three therapeutic regimens, 24 (30.3%) were been treated with Sofosbuvir+Velpatasvir, 16 (20.2%) with Glecaprevir/Pibrentasvir and 39 (49.3%) with Elbasvir/Grazoprevir. The duration of DAA in months, median (range) 12 (8-24), the timing of resistence test in months at the end of treatment, median (range) 5 (1-19). The NS5A-RASs were more frequent in Sofosbuvir+Velpatasvir (21/24, 87.5%) and in Grazoprevir/Elbasvir (38/39, 97.4%) failed patients than in Glecaprevir/Pibrentasvir (4/16, 25%) failed patients (p=0,002 and 0,000 respectively). According to Sofosbuvir/Velpatasvir regimen 34.1% pts showed at least 2 RASs in at least two HCV region including NS5A and 70.3% pts showed at least 2 RASs only in NS5A region. Considering Grazoprevir/Elbasvir regimen 25.6% pts showed at least 2 RASs in at least two HCV region including NS5A and 89% pts showed at least 2 RASs only in NS5A region.(p=0.00).

All 23 re-treated patients with Sofosbuvir/Velpatasvir /Voxilaprevir, obtained with SVR. The re-treatment was guided by genotyping test.

Conclusions: At failure Patients showed mutations in the NS5A region, more frequently in patients experienced Sofosbuvir/Velpatasvir and in Grazoprevir/Elbasvir regimen than in patients experienced Glecaprevir/Pibrentasvir failure probably due to short lasting of the last cited therapy.

Hepatitis and coinfections

OP 63 ADVANCED LIVER DISEASE OUTCOMES AFTER HEPATITIS C VIRAL ERADICATION ACCORDING TO HUMAN IMMUNODEFICIENCY VIRUS COINFECTION IN PITER COHORT

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Background: Liver disease progression after Hepatitis C Virus (HCV) eradication following direct-acting antiviral (DAA) treatment in the real-life setting according to Human Immunodeficiency Virus (HIV) coinfection was evaluated.
Methods: Patients consecutively enrolled in PITER between April 2014 and May 2018, were included. Factors associated with liver disease outcomes following viral eradication were evaluated in DAA treated patients with pre-treatment diagnosis of liver cirrhosis who achieved SVR12 by propensity score analysis and Cox regression analysis.
Results: 108 HCV/HIV coinfected and 1242 HCV monoinfected patients were evaluated during a median follow-up of 27.1 (range 6-44.6) and 24.7 (range 6.8-47.5) months, respectively. No difference in the cumulative HCC incidence, liver transplantation, hepatic decompensation and Child-Pugh (C-P) class changes was observed between coinfected and monoinfected patients. Age (Hazard Ratio [HR]=1.08; 95%:CI:1.04-1.12), alcohol use (HR=2.20 95% CI=1.11-4.39), lower albumin levels (HR=3.93 95% CI=1.86-8.30), genotype 3 (HR=2.99; 95% CI=1.07-8.37) and serum anti-HBc positivity (HR=1.89, 95% CI=1.00-3.58) were independently associated with HCC incidence. Factors independently associated with C-P class increase were: male sex (HR=2.01; 95% CI=1.19-3.40), platelet count <100,000/µl (HR=1.88; 95% CI 1.17-3.03) and higher INR value (HR=2.34; 95% CI 1.47-3.71). Platelet count <100,000/µl (HR=2.05; 95% CI 1.29-3.25), lower albumin levels (HR=1.99; 95% CI 1.25-3.17), HCC (HR=2.02; 95% CI 1.04-3.92) and liver decompensation prior to treatment (HR=7.47; 95% CI 4.69-11.89) were independently associated with a new decompensating event after viral eradication.
Conclusion: HIV coinfection was not associated with a higher probability of liver complications in patients with cirrhosis, after viral eradication.

Hepatitis and coinfections

OP 64 THE COMBINATION OF ACCURATE SEROLOGICAL AND VIROLOGICAL HBV MARKERS CAN HELP TO PREDICT THE OCCURRENCE OF HBV REACTIVATION AND TO OPTIMIZE PROPHYLAXIS DURATION IN HBSAG-NEGATIVE/ANTI-HBC-POSITIVE PATIENTS WITH ONCOHEMATOLOGICAL DISEASES

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Background: Prevention of HBV-reactivation (HBV-R) in patients undergoing immunosuppressive therapy is still challenging. This study is aimed at investigating the role of HBV markers in predicting HBV-R in HBsAg-negative/anti-HBc-positive patients with oncohematological diseases.

Methods: HBV-R rate is estimated in 107 HBsAg-negative/anti-HBc-positive patients (42 receiving rituximab [RTX], 40 hematopoietic stem cell transplantation [HSCT], 25 other chemotherapies). All patients received lamivudine-prophylaxis for >18 months after stopping immunosuppression (EASL guidelines) and were prospectively monitored every 3 months. 58/107 patients have completed lamivudine-prophylaxis and were monitored for a median time of 25.4 (9-32) months after prophylaxis completion. The role of HBV markers in predicting HBV-R is evaluated by testing 831 serum samples for highly-sensitive HBsAg (Fujirebio, HS-HBs; lower limit of quantification [LLOQ]: 5 vs 50 mIU/ml of routinely-used assays), HBV-DNA (Roche, LLOQ:20IU/ml), quantitative anti-HBs and anti-HBc (Fujirebio, LLOQ:1.0COI). HBV-R is defined as serum HBV-DNA >20IU/ml (Seto, 2016).

Results: At baseline-screening, all patients have undetectable HBV-DNA and 67.3% is anti-HBs positive (median [IQR]:152[47-976] mIU/ml]. HBV-R occurs in 14/107 patients with the highest 5-year cumulative reactivation rate in HSCT (63.4% vs 15.8% for RTX and 9.6% for other chemotherapies, P=0.026).

At HBV-R, median (IQR) HBV-DNA is 42(23-682) IU/ml and ALT>ULN for 46% (median [IQR]: 88[60-763] U/L). Among HBV-R cases, 6 develops HBV-R during and 8 after completing prophylaxis (median [min-max] months after prophylaxis completion: 3[1-27]).

The analysis of serological markers during the entire monitoring reveals that the combination of anti-HBc>3COI and anti-HBs persistently or declining to <50mIU/ml correlates with a higher risk to develop HBV-R (53.8% of patients with anti-HBc>3COI+anti-HBs<50mIU/ml vs 14% without this combination experiences HBV-R, P=0.004, OR [95%CI]: 7.1[1.9 -26.1]). Results confirmed in the subset of 58 patients completing lamivudine-prophylaxis (63% of patients with anti-HBc>3COI+anti-HBs<50mIU/ml vs 26% without this combination experiences HBV-R, P=0.038, OR [95%CI]: 4.7[1-22.7]).

Furthermore, by monitoring virological markers, the positivity, confirmed in at least 2 time-points, to HS-HBs (detection failed by routinely used HBsAg-assays) and/or to HBV-DNA (detected below LLOQ) is another factor predicting HBV-R (44.4% of patients positive to HS-HBs and/or HBV-DNA vs 7.4% never positive to these markers experiences HBV-R, P=0.007, OR [95%CI]: 10.1[2.2-46.1]).

Conclusions: In the setting of oncohematological diseases, HBV-R frequently occurs in anti-HBc-positive/HBsAg-negative patients, particularly after completing antiviral prophylaxis. The combined usage of accurate HBV-markers can guide to identify patients at higher HBV-R risk who need an extended prophylaxis

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OP 65 HBV AND HDV INFECTION IN IMMIGRANTS LIVING IN SOUTH ITALY: EPIDEMIOLOGICAL AND VIROLOGICAL CHARACTERISTICS

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Background: in several European countries, there has been an increase in migration from countries with a high prevalence of HBV. In Italy epidemiological data relating to HBV and HDV infection in the migrant population are scanty. Aim of our study was to investigate the demographic and virological characteristics of HBV and HDV infection in a cohort of migrants living in Southern Italy.
Methods: Between January 2012 and december 2018 all the migrants attending to one of the 5 first-level centers, 2 in Naples, 2 in Caserta and 1 in Foggia were tested for HBV. Data for demographic characteristics and risk factors for HBV infection were collected. All HBsAg positive subjects were tested for HDV. HBV genotype was evaluated in viremic subjects. For all HDV positive subjects was performed HDVRNA.
Results: 3184 subjects were tested; the 243 (7.6%) HBsAg positive subjects had median age of 26 (range 15-55) years and 277 (94%) were males; 214 (88%) came from Sub-Sahariana Africa, 3 (1.2%) from North Africa, 17 (7%) from Eastern Europe, 8 (3.2%) from IndoPakistan area, one from South America; 8 of 243 subjects (3.2%) were HDVAb positive. Table 2 shows the characteristics of the 243 HBsAg positive patients enrolled and stratified according HDV serostatus.
We found that HDVAb negative subjects lived in Italy for a longer period (p = 0.001) compared to HDVAb positive patients. No variables independently associated with HDVAb positivity were identified at multivariate analysis. HBV-DNA levels were similar in the two groups. The HBV genotype was available for 90 samples in the group of HDVAb negative patients; genotype A was present in 17%, C in 3%, D in 12% and E in 69%. HDV-RNA was performed for all HDV Ab positive patients but only one patients (12.5%) was found HDV-RNA positive genotype 1. None of the patients 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 migrants 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 and coinfections

OP 66 HEV INFECTION AS AN EMERGENT PUBLIC HEALTH ISSUE: IS IT A CONCERN FOR ITALIAN BLOOD DONORS?

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Background: In high-income countries, HEV infection is usually associated with an asymptomatic, self-limiting, acute or mild hepatitis. However, the risk of HEV transmission through blood or blood products raises concerns, especially in the setting of immunosuppressed patients. The aim of the present study was to determine the presence of HEV infection in blood donors at ASST GOM Niguarda Hospital using a combined approach (HEV-RNA/seroprevalence).

Material And Methods: From January to July 2019, 9,081 sera and plasma samples from blood donors were retrospectively analysed. Pools of 6 plasma donations were assessed to detect HEV-RNA using the commercial Cobas® HEV Test (Roche Molecular Diagnostics, LLOD 18,6 IU/mL). Among them, 7,771 serum samples were tested for anti-HEV total IgM/IgG with ELISA test (DIA.PRO).

Results: Overall, the blood donors were predominantly men (73.6%; 5,720/7,771) with a median age of 42 (IQR: 31 -50). HEV-IgM/IgG positivity was found in 4.3% (334/7,771) of blood donations, however none of them carried detectable HEV-RNA.

The rate of HEV-infection in this healthy population was compared with that of symptomatic patients (with altered transaminases). HEV-IgM/IgG positivity was found in 4.3%(14/324) and 10.6%(50/472) of patients, respectively. Among them, 1.6% (3/184) of patients had detectable HEV-RNA: two of them were mother and son from Egypt with acute HEV-infection and the third was an italian man with chronic HEV-infection.

Conclusions: The circulation of HEV-RNA in blood donations at Niguarda Hospital results to be absent, with an HEV-IgM/IgG prevalence of 4.3%, one of the lowest reported among blood donors in Italy (8.7%, Spada et al., Blood Transfusion 2018). At the same time, HEV active infection has been detected in few patients whose HEV-RNA was assessed for hepatic symptoms (elevated ALT). From these data, the screening for HEV-RNA appears not to be crucial in our population of blood donors, while further studies are warranted to define its relevance in case of liver pathologies.

Social Science and prevention

OP 67 HIV SELFTESTING: A SURVEY OF SELF-TESTS AVAILABILITY IN ITALIAN PHARMACIES

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Background: HIV Self-Tests (HIVST) became available for private purchase in Italian pharmacies on 1st December 2016. Despite National AIDS plan including several actions to assess its impact and spread, there is a lack of data about its role in the national HIV testing strategy. A survey was carried out in order to collect information about the availability and experience of trying to buy an HIVST.

Materials and methods: ARCIGAY and LILA volunteers visited 167 pharmacies in 18 cities across Italy from Jun to Aug 2019 (List of cities and no. of pharmacies shown in Figure 1). Quantitative and qualitative data were collected through an online form after the attempt to buy an HIVST. The survey was carried out in collaboration with Public Health England as a part of European project INTEGRATE.

Results: HIVST were immediately available in 95/167 (57%) pharmacies; when including those with a short time to order to store (one day), it increased to 136/167 (80%). HIVST were out on the shelf in 41 pharmacies and in storage in 79 [Figure 2]. Prices ranged from €18 to €32, with most common price of €20 [Figure 3]. In pharmacies were HIVST was unavailable (n=31), according to pharmacists this was due to:

- Lack of demand (n=8)
- Never heard about it (n=5)
- It is possible to order but it takes more than one day to receive it (n=17)

As for information provided, only 91 (67%) of pharmacists gave information about the HIVST, either unprompted or after request. Some gave incorrect information (n=20, 22%), especially about the window period. Additionally, 109 comments were collected about the experience overall:

- 62 were positive, often focusing on non-judgmental environment and kindness of the pharmacist, regardless of information quality
- 15 were neutral
- 32 were negative, mainly focused on lack of privacy

Conclusions: Overall, most pharmacies have HIVST available. This is encouraging and in line with previous surveys[1] . Cost differed by pharmacy, possibly according to the brand of HIVST available. This was not investigated by the survey, although in one pharmacy two different brands of HIVST were available. Concerns about privacy issues and stigma reported by volunteers were uncommon, but lack of/incorrect information about how to use the HIVST was often reported.
It is important to involve the associations of pharmacists in the national HIV testing strategy, in order to complement it with higher access to HIVST. Points for discussion should include improving the availability of HIVST by allowing clients to order them when unavailable, placing them out on the shelves or even in automatic machines to improve visibility and allow for a high level of privacy and 24h/7 availability). Training of pharmacists on HIVST should be ensured, to provide users with adequate/correct information.

[1]HIV Auto-test and PrEP in Milan's pharmacies: a survey Calzavara et al. ICAR2019

Social Science and prevention

OP 68 TESTING MSM IN CRUISING VENUES

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Background: A.S.A. and CIG-Arcigay Milano have administered HIV rapid finger-prick tests, anonymously and free of charge,from March 2019 to february 2020, in MSM cruising venues. Inside the venues is one welcome area and one testing area were set up. The test is carried out by a doctor who also gives the results in a space designed to protect privacy. In case of reactive result, the doctor plans an appointment in a hospital in Milan for the confirmation HIV blood test.

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 STATA software.

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 during sex, sexual behaviours related to HIV status of the sexual partner, U=U concept, and follow up.

Results: 749 test were administered:92,70% Male users,of these 69,27% omo,55,66% Age 31-50,86,81% Already tested,of these 36,96% within 6 months and 36,38% whitin 1 year,48,27% last test took in unconventional context, Out of 8 GHB users, 5 declare having sex under alcohol.72,29% Knowledge of PrEP,13,35% avoided sex with PLWHIV 1 at least,8,44% had penetration intercourse with PLWHIV in the last year, of these 32,18% no condom with undetectable.36,15% Ejaculation In Mouth 1 at least.70 clients use to take Chems/Drugs during sex (13,45%), of these 61,42% popper, 33,71% cocaine,18,57% MDMA, 17,14% GHB, 17,14% Mephedrone,11.42% Meth.41 clients declare not using condom during penetration intercourse. Out of 8 GHB users, 5 declare having sex under alcohol.8 persons turned out to be reactive (table 1).

Conclusions: In general,the variables on sexual behavior in the last 12 months are in line with previous same studies. Out of 794 tests repeated in the last year,330 took it in unconventional context.These datas show that the service, during the evening hours and the week ends,is essential for reaching UNAIDS 90-90-90 targets in the Fast Track City of Milan. In comparison with the previous study,less people avoided having sex with PLWHIV(4%) and more people accept having sex with PLWHIV on treatment without condom. Supposedly due to the effect of U=U or for using PREP. Moreover,the trend of not knowing the HIV status of the partner persists.A 3% increase of those who have never tested before,a 4% increase of last test within 6 months and a 4% increase of knowledge of PrEP was observed.A 2% decrease of individuals(287) who had ejaculation in mouth at least once was observed, of these 64 of them never tested before. Out of 8 reactive tests, linkage to HIV units and related support was ensured to 5 clients. ASA has been supported by VIIV Healthcare and ARCO ong.

Social Science and prevention

OP 69 BEHAVIORAL ASPECTS OF MSM TESTED IN COMMUNITY-BASED SETTINGS IN 5 CITIES

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Background: HIV prevalence among men having sex with men (MSM) in Italy remains high. Community-based testing has proved to be an effective way to increase awareness of HIV and of HIV status among this key population. Arcigay offers free community-based HIV testing in non-conventional settings relevant for the community since 2016: LGBTI associations, saunas and clubs, public events, cruising areas. Some of these settings, such as associations, public events and cruising areas, are attended also by non-MSM and testing is delivered to everybody who requires it.

Methods: Behavioral data are collected through common anonymous self-administered risk-assessment questionnaires in Verona, Milano, Padova, Modena, Roma and Napoli before testing. 3979 HIV tests and questionnaires have been delivered in these cities from July 2016 to December 2019. Questionnaires include topics about testing settings preference, chemsex and attitudes towards HIV+ partners. Peer-operators are available in case clients need information related to the questionnaires or to the topics.

Results: 3458 (86.9%) respondents were male, 505 (12.7%) were women and 16 (0.4%) transgender. 3130 men (78.6%) self identified as gay, bisexual or queer or had sex with men in the last 12 months, and were defined as MSM. 15.6% of MSM never tested before, compared to 62.6% of women. 33.1% of MSM tested more than 1 year ago. 97.2% of respondents in saunas and clubs and 86.1% of respondents in Arcigay associations were MSM, whilst this figure is lower among those tested in bars (72.9%), special events (62.4%) and cruising areas 57.2%).

Considering all the sample, 54% of those who never tested before reported that they prefer community-based settings, while this figure decrease among those who tested more than 1 year ago (44.3%) or less than 1 year ago (39.6%). 45 on 3979 HIV tests were reactive and never tested positive before (1.13%), 6 tested reactive but were already aware of their positive result. Amongst those newly diagnosed, 43 were MSM, 2 were heterosexual or non self-identified men.

Only 7.3% of MSM reported they had sex with HIV+ men in the last 12 months, whilst 49.6% reported that they excluded they had sex with HIV+ men and 41.3% that they couldn't know if they did it. Among those who reported sex with HIV+ men, 58.2% did it with condom, 31.7% with TasP and only 3.9% said they didn't know anything about the viral load of the partner. 12.45% reported that they refused having sex with an HIV+ man because of his HIV status, 19% said they never refused and 65.4% said that they never met self declared HIV+ men or men whose they knew the HIV+ status.

Conclusions: The setting were MSM can be more easily reached are saunas and clubs. Most of those tested reactive were MSM. A large percentage of MSM have sex assuming that their partners are HIV negative although they know nothing about the HIV status of the partner.

Social Science and prevention

OP 70 PRE-EXPOSURE PROPHYLAXIS IN MODENA: A WIDE SPREAD OF SEXUALLY TRANSMITTED INFECTIONS AMONG USERS ATTENDING THE DEDICATED OUTPATIENT CLINIC

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Background: Pre-exposure prophylaxis (PrEP) with the association of tenofovir disoproxil (TDF)/emtricitabine (FTC) is effective in the prevention of HIV transmission when taken daily or according to an event-driven dosing schedule. This study aims to investigate the epidemiological characteristics of users, the effectiveness and security of PrEP, the incidence of sexually transmitted infections (STIs), and the adequacy of PrEP prescriptions.
Materials/methods: A prospective observational study was conducted enrolling all the users attending our PrEP outpatient Clinic from July 2018 until February 2020. We collected epidemiological and clinical data at baseline and during follow-up visits at one month, and then every three months. We performed serological test for HIV, HBV, HCV, HAV, Syphilis and research by PCR for Chlamydia and Gonorrhea on urine, rectal and pharyngeal swabs; in addition, renal function and phosphatemia were monitored.
Results: 39 people underwent the basal check-up and obtained PrEP, with a follow-up of at least one month; 6 suspended PrEP: 1 had acute renal failure (2.6%), 4 considered PrEP no longer needed, 1 moved to another city.
38 (97.4%) of the users were MSM and one was transgender woman; 33 (84.6%) were Italian, median age was 46 years. Regarding indications, 15 people (38.5%) reported an inconstant condom use, 15 (38.5%) a previous STI (14 treated syphilis, 2 previous HAV infections, 1 treated HCV infection, 1 treated gonorrhea infection), 2 (5%) practiced chemsex, 3 (1.7%) received post-exposure prophylaxis, 4 (10.2%) people did not report risky behavior. 29 (74.3%) of them chose event-driven regimen and 7 (18%) the daily scheme. At baseline, 10 people (25.6%) were diagnosed with at least one STI. During the follow-up period, 12 people (30.8%) contracted at least one STI, with a total of 24 new infections diagnosed (6 users were repeatedly diagnosed with STIs, one of these had three STIs). Table 1 shows the proportion of diagnosed STIs. No new HIV infection was observed. Condom use in PrEP-users was mostly discontinuous. 9 users (23.1%) reported side effects, mostly minor gastrointestinal except for 1 acute renal failure which required PrEP suspension.
Conclusions: In our experience, PrEp is effective in preventing new HIV infections in people with other STIs, and therefore with increased risk of transmission. More than 30% of the users at the baseline already had a STI, and more than 30% of the users contracted a STI during the prophylaxis, with a large number of people diagnosed with multiple STIs at the same time, repeatedly, particularly with asymptomatic infections such as rectal and pharyngeal gonorrhea and chlamydia. For this reason, we believe that prescription and delivery of PrEP should be done under medical supervision in order to closely monitor and promptly treat this high-risk population. Since the assumption of PrEP also correlates with serious side effects, close medical monitoring is mandatory.

Social Science and prevention

OP 71 PREVALENCE AND RISK FACTORS FOR HPV ANAL INFECTION IN PREP USERS: IMPLICATIONS FOR VACCINATION POLICY

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Background: Anal HPV infection is common in men who have sex with men (MSM), especially in HIV infection. Several studies have demonstrated a prevalence around 85% in HIV+ and 50-60% in HIV-. High risk HPV genotypes (hrHPV) have been found in 65% in HIV+ and in 45% in HIV-. Few data are available in pre-exposure prophylaxis (PrEP) users, who share similar high-risk sexual behaviors. Aim of present study is to describe epidemiology and clinical features of HPV anal infection in PrEP users.

Methods: This monocentric, retrospective analysis included all subjects who started PrEP between January 2018 and January 2020, underwent digital ano-rectal examination (DARE) and HPV testing. Demographic, behavioral and clinical features were collected. Descriptive statistics and non-parametric (Chi-square and Mann-Whitney U, as appropriate) tests were used. Odd Ratios (ORs) were calculated to describe potential risk factors for HPV infection.

Results: 76 subjects were included in the analysis: they were mainly MSM (96.1%), Italian (84.2%), and with a median age of 35 (IQR 30-42) years. A large majority (69.7%) had at least one previous STI; 21.1% had HPV-related disease. Two subjects completed the tetravalent vaccination course, two started the nonavalent and received the first two doses before sample collection.

HPV was found in 85.5% subjects (68.4% of them had hrHPV). Figure 1 shows genotype distribution: genotype 16 was the most common (23.7%). Nonavalent vaccine would be protective in 47.0% of cases. PrEP users showed to be infected by more than one genotype: the median number of viral strains for each individual was 2 (IQR 1-4). Vaccinated subjects tested positive for genotypes 6 and 16 (and other six strains not covered by immunization).

No difference in terms of clinical or demographic features was observed among HPV+ and HPV- individuals; subjects older than 45 years had the same prevalence of younger individuals (80.0% versus 86.4%, p=0.594). Engaging only in insertive anal sex had a protective role against the infection (OR 0.25, 95% CI 0.07-0.94, p=0.031), while a previous STI showed a tendency to be a risk factor (OR 3.39, 95% CI 0.91-12.55, p=0.058). After PrEP start, HPV+ had more condomless anal sex than HPV- subjects (48.5% versus 7.2%, p<0.001).

Fourteen subjects (18.4%) showed an abnormal finding on DARE, but only two (2.6%) underwent surgical excision. Pathologic findings were consistent with dysplastic lesions and no anal intra-epithelial neoplasia was observed.

Conclusions: The rate of anal HPV infection was high and similar to what reported in HIV+ population. Nonavalent vaccine could be protective in half of this population, while the previous immunizations courses would be less suitable. Although this administration is currently off label, nonavalent vaccine use would be justified also in MSM older than 45 years given the high rate of hrHPV infection in this population.

Social Science and prevention

OP 72 NEETAGERS FOR THE PREVENTION OF HIV AND AIDS

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Background: In Italy, 2 million young people between the age of 15 and 29 do not study nor work and can be defined as "Neet" (Not in Education, Employment or Training). Since 2017, Italy has confirmed the highest Neet rate in Europe with 19.9% against a European average of 11.5%. In Umbria, the Neet rate was 21% in 2017.
The Neet phenomenon represents the "condition of overt youth unease". The greatest risk is that these young people start on a path to social exclusion and impairment of social well-being. They are a difficult target to reach, existing outside the contexts of prevention of risky behavior, thus showing gaps transversal to the rest of society on the progress of treatment, fight and prevention of HIV and AIDS.
Material and methods: NEETagers is an experimental project implemented in the Umbrian territory, with the aim of reaching the Neet population and beyond.
It proposed prevention and awareness actions through the distribution of (ad hoc) material and condoms, information through counselling interviews with trained personnel, and prevention actions through the offer of fast-response fourth generation combo tests (HIV, HCV). In the event of a positive test, it guaranteed rapid and facilitated access to the confirmation test, and possibly, access to care at a public facility in the area.
Further objectives were:
Promotion of the culture of prevention, and dissemination of information by raising the awareness of peers;
Emergence of the Identikit of Neet Umbro;
Street education / intervention;
Activation of a telephone service aimed at offering the possibility of staying in touch, access to testing, and of being able to express one's cognitive needs.
The promotion of the project took place through two distinct plans: institutional channels (logo, project blog and online newspapers, social networks) and unconventional channels (short and original video spots that will be circulated in social networks, captivating brochures directed to the target).
Results: The questionnaires submitted to users who carried out the Hiv and Hcv TEST between the provinces of Perugia and Terni were 142. The three questions to measure the level of information on Hiv / ist had the following answers:
Question 1 about masturbation:
Right answers 89
Wrong answers 53
Question 2 about mosquito bite:
Right answers 93
Wrong answers 49
Question 3 about U = U and HIV transmission in undetectable situations:
Right answers 54
Wrong answers 86
He doesn't know 2
Conclusions: The NEETagers project found a low level of knowledge regarding the prevention of sexually transmitted diseases. The data resulting from question number 3 is very significant: it is necessary to continue working with the U = U campaign. Most people believe that the risk of transmission with a person living with HIV is possible even if with an undetectable viral load.

Social Science and prevention

OP 73 CLINICAL RESEARCH INTEGRATED WITH NARRATIVE MEDICINE TO UNDERSTAND LIVING AND COPING WITH HIV: TMC114FD1HTX4011 - DIAMANTE STUDY

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Background: Notwithstanding HAART's crucial impact on HIV morbidity and mortality decreasing, psychological burden and social stigma still characterize the living with this condition; therefore, coping with this disease remains challenging. The interdisciplinary methodology of narrative-based research allows gaining insight into illness and coping experience - defined as the set of conscious strategies used by the patients in order to accept the living with this condition - through collecting and analyzing patients' written narratives.

Methods: The non-interventional DIAMANTE study aimed to collect data on HIV-1 positive patients treated with D/C/F/TAF, to evaluate therapy effectiveness and Patient-Reported Outcomes (PROs). The study started in June 2018 and involved 18 centers across Italy; 246 HIV-1+ patients, 125 experienced and 121 naïve, were enrolled, and followed up for 48 weeks. PROs were registered by the administration of HIV-Treatment Satisfaction Questionnaires together with the narratives collected at enrollment and at last study visit. Narratives were analyzed independently by 2 epidemiologists through NVivo10 software on the basis of content analysis.

Results: 246 HIV-1+ patients were enrolled in the study; 137 already completed their narratives at enrollment (Visit 1). Written narratives showed that HIV infection impacted patients' daily activities in 10% of cases; nevertheless, 51% coped with the disease. Coping was not influenced by gender, age, degree, sexual orientation, nor disease history (Fig.1).

On the other hand, previous knowledge of HIV (68%) and regular examination for STDs (65%) facilitated coping. Forty-one percent of patients shared their experience about HIV-positivity diagnosis; patients recalling a complicated past, coped in 69% of cases. Furthermore, the emotions felt at diagnosis and after the first visit influenced good acceptance of HIV-seropositivity: 81% of patients feeling regretful or peaceful at diagnosis showed a higher coping, compared with a lower coping reported by patients feeling anguish (51%) or pain (24%). 68% felt relieved after the first visit with the clinicians. The main difficulties arise from the stigma associated with HIV, depicted in 67% of experiences. Stigma influenced particularly relationship with friends (76%) and colleagues (83%).

Metaphors chosen by participants to describe HIV mirrored their coping status: acceptance of HIV was reported by 81% of patients describing battle or new journey, by 58% of those reporting malignant nature or constant presence and by 34% of patients recalling a monster.

Conclusions: Use of narratives in an observational setting in HIV-1 positive patients highlights how coping with HIV diagnosis is still a challenge and how the relationship with the treating physicians could play a positive role in this process.

Social Science and prevention

OP 74 WOMEN AND HIV IN PRISON SETTING: A DATA UP DATE FROM THE ITALIAN ROSE NETWORK

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Background: HIV infection in the female prison population shows a higher prevalence both to the general population and to the same male prison population. An in-depth knowledge of this minority reality is needed to share effective actions both during and after detention. The aim of the project is to build and implement a national network to study the characteristics and health needs of the population of women detained with HIV infection.

Material and methods: a specific network was set up in 2017 involving 17 infectious specialists who follow the women detained in the following Italian prisons and during these 3 years it was implemented involving 21 italian prisons: Chieti, Reggio Calabria, Pesaro, Paliano, Latina, Civitavecchia, Rome, Genoa, Milan Bollate, Milan San Vittore, Lecce, Foggia, Trani, Catania, Turin, Sassari, Palermo, Perugia, Avellino, Pozzuoli, Salerno. A one year observational study was performed, collecting the demographic, clinical and virological data of the sample of women detained during the period in the various institutions in a database.

Results: preliminary data of 853 women were enrolled (32% of the female prison population in Italy as of 31 Genuary 2020). The timely prevalence of HIV-Ab in this cohort was 5.0%, with 40 women being positive, of whom 23 were Italian and 17 were foreign. The average age is 44 years. Antiretroviral therapy was not taken by 3 patients for refusal (8%); 10 women on treatment had CD4 + <350 / mmc (28% of the observed population). Of the 37 in antiretroviral treatment 6 were viremic with HIV-RNA> 50 cp / ml (16%): 3 of them because of poor compliance, 2 of them because they have started therapy recently, 1 of them because of a viral blip. Therapeutic regimens were observed: 44% in treatment with INI, 39% in treatment with PI, 17% in treatment with NNRTI. The mode of transmission of HIV is predominantly parenteral in italian women while the sexual one is predominantly in foreign women. Co-infection with HCV virus was present in 9 patients (23%): genotype 3a in 2 women, genotype 1a in 7 women. One patient is with positive HBSAg, and HBV-DNA was negative.

Conclusions: HIV infection in our cohort is confirmed higher than that seen in detained men. The prevalence of co-infection with HCV appears high but decreased with the DAA era. Refusal of therapy and poor compliance are the main causes of non-control of the HIV infection. The implementation of the network and planning an out of prisons network for the therapeutic continuity togheter with actions to enhance adherence will allow to control the HIV infection in this population.

This project has been unconditionally supported by Viiv Healthcare

Social Science and prevention

OP 75 FIRST-YEAR EXPERIENCE OF AN HIV CLINIC-BASED STOP-SMOKING SERVICE

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Background: Lung cancer (LC) and major cardiovascular events (MACE) are two leading causes of death in people living with HIV (PLWH). Smoking habit is a clear risk factor both for LC and MACE and is more frequent in PLWH than it is among the general population. Previous studies have shown that stop-smoking services (SSS) are effective in supporting patients to quit smoking. Therefore, simplified access for PLWH to SSS is highly desirable.
We report herein the experience of the first Italian HIV clinic-based SSS.
Methods: An SSS based in the San Raffaele "Centro San Luigi" HIV clinic commenced activity on March 1, 2019. Access to SSS was restricted to PLWH until June 2019; from July 1, 2019, access was extended to HIV-seronegative persons.
The SSS intervention scheme, detailed in Figure 1, included visits for both medical and psychological assessment and phone counselling. During the first visit, tobacco dependence and smoking cessation motivation were assessed using the Fagerström and Mondor questionnaires, respectively, and patients' basal expired carbon monoxide (CO) levels were measured using Smokerlyzer (Bedfont®). Oral pharmacotherapy (PCT) for smoking cessation (varenicline or cytisine) was also proposed according to SITAB guidelines and the patient's preference.
During the intervention period, a patient was defined as abstinent based on the combination of self-reported continuous abstinence and an expired CO level < 5 ppm.
Results are reported as median (interquartile range) or frequencies (%). Continuous and categorical characteristics were compared using the Mann-Whitney test and Chi-square or Fisher's exact test, respectively.
Results: On January 30, 2020 (freezing date), 44 persons accessed the SSS. The patients' median age was 53.3 (44.1 -59.0) years; 72% were male, 86% were Italian, and 2 (5%) and 3 (7%) had previous diagnoses of cancer and MACE, respectively. Twenty-eight were (64%) PLWH.
A PCT was initiated in 30 (68%) patients (varenicline 43%; cytisine 57%). Although not all patients completed the six-month intervention period, 18 (41%) subjects were abstinent at the freezing date.
Patients' characteristics, PCTs and proportion of abstinence, according to HIV serostatus, are reported in Table 1. Use of PCT was associated with higher smoking cessation rates (53% in PCT users vs 7% in non-users; p=0.021). No differences were observed with respect to cytisine or varenicline use among those who ceased smoking (p=0.484). Proportion of smoking cessation did not differ between PLWH and HIV-seronegative persons (43% vs 38%, respectively; p= 0.761).
Conclusions: Based on our experience, the creation of an HIV clinic-based SSS appears feasible. We believe that this strategy should be implemented, in view of the overall good smoking cessation rates observed. Considering the high rate of active smoking among PLWH, smoking cessation interventions must be considered as a priority among this population.

Social Science and prevention

OP 76 PSYCHIATRIC DISTURBANCES ARE COMMON IN PREP USERS: AN ANALYSIS OF COMORBIDITIES AND COMEDICATIONS IN REAL LIFE

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Background: Pre-exposure prophylaxis (PrEP) demonstrated to be highly effective in reducing the risk of acquiring HIV infection. Few real-life data are available about comorbidities and comedications in PrEP users. Although pharmacokinetics interactions with tenofovir disoproxil fumarate are uncommon, several drugs could hamper its safety profile given a concurrent toxicity. Aim of present study is to describe the clinical features of the reported comorbidities and comedications in PrEP users.
Methods: This monocentric, retrospective analysis included all subjects who started PrEP between January 2018 and January 2020. Demographic, behavioral and clinical features were collected. Descriptive statistics and non-parametric (Chi-square and Mann-Whitney U, as appropriate) tests were used.
Results: 80 subjects were included in the analysis: they were mainly MSM (95%), Italians (85%), with a median age of 35 (IQR 30-42) years and with a high level of education (61.3% took a University degree). Alcohol use was stated by 51.3% while recreational drugs and Chems practice were reported by 40.0% and 13.8%, respectively.
The majority (62.5%) showed no comorbidity. A psychiatric disease (mainly belonging to the anxiety-depressive spectrum) was the most common disorder (18.8%). Other reported clinical conditions included cardiovascular (13.8%), gastrointestinal (11.3%), and autoimmune (8.8%) diseases. Figure 1 shows the comedications: protein supplements for anabolic gym activity and finasteride were frequently used (15.0% and 6.3%, respectively). Individuals taking protein supplements and other nephrotoxic drugs such as cyclosporine showed a lower median baseline eGFR (92 versus 101 mL/min, p=0.018), but they did not worsen later on (data not shown).
Besides the over-the-counter drugs, psycho-active substances were the most common (10.0%); they were not limited to benzodiazepines and selective serotonin re-uptake inhibitors (SSRI) and included also some second-line drugs like anti-epileptics and butyrophenones. Subjects with a psychiatric comorbidity showed a tendency to have a less risky behavior (lower numbers of recreational drugs, Chemsex, post-exposure prophylaxis and previous sexually transmitted infection), but the only statistically significant difference was a lesser alcohol use (26.9% versus 56.9%, p=0.035).
Conclusions: Drugs intended to have an aesthetic purpose are frequently used. Even if subjects taking protein supplements had a worse baseline renal function, they did not show a further worsening after PrEP start, suggesting that tenofovir had no additive effect. Despite the young median age, around 40% of PrEP users showed at least one comorbidity: psychiatric disorders resulted the most common. Psycho-active drugs were also the most used comedications besides over-the-counter products. Our data suggest that PrEP users with psychiatric disturbances might have a less risky behavior.

Virology and pharmacology

OP 77 THE HIV-1 PROVIRUS EXCISED BY CRISPR/CAS9 MAY BE INTEGRATED BACK INTO THE CELL GENOME IN PRESENCE OF THE VIRAL INTEGRASE

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Background: Large part of the reverse transcribed HIV RNA genome (cDNA) produced during viral replication does not integrate. These unintegrated viral molecules may either be destroyed, aid productive infection through expression of several genes or have a second chance of integrating through complementation or rearrangement events. Emerging evidences propose CRISPR gene-editing strategies to eradicate the HIV infection. This study explores the fate of the provirus once excised from the host cell genome. We used a single CRISPR/Cas9 RNA guide targeting both LTRs. This treatment leads to excision of full-length provirus indistinguishable from the unintegrated genome molecules generated during HIV replication.

Materials and Methods: We used the droplet digital PCR to evaluate the presence of NEF-LTR junctions. HIV-1 re-integration was examined in 293T cells and J-Lat cells by using the Alu-PCR.

ddPCR and Alu-PCR results were analyzed using one-way ANOVA, $^{**}p < 0.01$, n.s. not significant.

Results: ddPCR revealed that the basal numbers of LTR circle molecules in J-Lat prior or after the transcriptional induction using the TNF- addition, were 15 and 30 every 1000 cells, respectively. Similar counts were found after treatment with CRISPR/Cas9 NR gRNA and TNF- . Treatment with the LTR targeting gRNA1 and gRNA2 dramatically increased the number of LTR circle molecules that raised to 140 (about 1 out of 8 cells) and 320 (1 out of 3 cells) every 1000 cells, respectively. Furthermore, excision with both gRNA1 and gRNA2 led to lower production of LTR circle molecules compared to single gRNA. Interestingly, formation of LTR circle molecules upon CRISPR/Cas9 treatment did not occur in the absence of TNF- We hypothesize that IN played a role in circularization of the excised provirus. To probe this idea, we repeated the experiments described above in the presence of HIV-1 IN inhibitor Raltegravir (RAL) added 24 hours prior to CRISPR/Cas9 transfection. LTR circle molecules were counted by ddPCR. RAL abolished LTR circle formation strengthening the idea that IN is required for circularization of the excised provirus. Alu-PCR did not reach detection threshold (100 copies/100,000 cells) with J-Lat untreated or treated with NR gRNA. Conversely, treatment with g1, g2 and, to a much lower extent, g1+g2 scored positive indicating de novo integration of the provirus in Alu sites. The numbers found were proportional to the number of circular forms generated following CRISPR/Cas9 treatment. Most notably the addition of RAL blocked the re-integration of excised provirus.

Conclusions: We show that if the HIV-1 genome is excised, it may persist and reorganize in a way that gives the virus a second chance to rebuild an infectious form. This work aims to implement the efficacy of delivery systems and CRISPR/Cas9 strategies in vivo to achieve cleavage of HIV genome in more sites and in all cells, and evidences the crucial role of IN during the re-integration event.

Virology and pharmacology

OP 78 ANALYSIS OF HIV LATENCY ESTABLISHMENT AND MAINTENANCE IN CD4 T CELLS STIMULATED WITH IL -15

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Background: HIV integrates into the host genome creating a viral reservoir, which persists despite effective antiretroviral treatment. Indeed, considerable work has been done on finding drugs, which can reactivate latent HIV. However, all the Latency Reversing Agents (LRAs) that have been tested so far failed in inducing a significant reactivation of latent HIV and reduction of the reservoir when tested in HIV infected patients.
It has been recently reported that the IL-15 superagonist N-803, in combination with CD8 depletion, induced a robust reactivation of latent SIV in ART-treated macaques (McBrien et al., Nature 2020).
Aim of this study was investigating what CD4 T cell subsets support latency even under IL-15 stimulation, and dissecting the molecular mechanism governing this effect.
Methods: To directly study latency establishment, we took advantage of a dual reporter HIV construct, which allows discrimination between LTR-silent ("latent") and LTR-active ("productive") infection at a single cell level. To investigate expression of proteins important for HIV transcription in the different CD4 T cell subsets, we isolated Central Memory [TCM], Effector Memory [TEM], Transitional Memory [TTM], naïve and stem memory T cells [TSCM] through FACSAria™ III sorter by expression of CD45RA, D45RO, CCR7, CD27 and CD95 markers. Expression of pTEFb complex was determined by Western Blot analyses.
Results: We observed that primary human CD4 T memory cells, cultured in IL-15, support both latent and productive HIV infection with the more differentiated memory T subsets (e.g., TCM, TEM, TTM) being the most susceptible to infection. Interestingly, naïve and TSCM were more likely to harbor latent infections compared to the other subsets. Thus, the more undifferentiated CD4 T cells likely play a pivotal role in maintaining the HIV latent reservoir.
In order to investigate the molecular bases of differential HIV transcription in the diverse CD4 T cell subsets we sorted Naïve, TSCM, TEM, TCM and TTM from healthy donors and determined the levels of expression of the pTEFb complex, a key component of HIV transcription, in the presence or in the absence of IL-15. We observed that at steady state all subsets expressed similar levels of the two proteins that constitute the pTEFb complex (CDK9 and Cyclin T1). On the other hand, upon IL-15 stimulation, TEM, TCM and TTM expressed higher levels of CDK9 and Cyclin T1 compared to Naïve and TSCM.
Conclusion: Taken together, our data suggest that IL-15 may have different effects on HIV transcription in the diverse CD4 T cells subsets. This difference may be due to IL-15 ability to increase pTEFb specifically in the more differentiated CD4 T memory cells.

Virology and pharmacology

OP 79 PHYLOGENETIC ANALYSES APPLIED TO THE STUDY OF TRANSMISSION VARIANTS AND THEIR EVOLUTION IN A HIV-1 POSITIVE COUPLE

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Background: During infection, HIV-1 typically accumulates a high level of genetic diversity. Such high mutation rate plays a pivotal role in conveniently escaping the immune system as well as pharmacological approaches, while adapting to the host. Indeed, the generation of such genetic diversity is a strong advantage for HIV-1 to infect new hosts.
It is now well established that in the vast majority of the infections it is just one out of potentially thousands of HIV-1 variants to colonize the new host, named transmitted/founder (T/F) variant. T/F variants are modeled by both stochastic and selective pressures, and the bottleneck of the mucosa plays a major role.
Based on such premises, the present study aims to characterize T/F variants tracing the HIV-1 infection in a young couple who become infected through sexual activity. This is the first time that a phylogenetic analysis is performed on both components before therapy, very likely within few weeks from infection, and verifying the effect of antiretroviral therapy on viral evolution.
Methods: Blood was collected from a fourteen-year-old couple upon HIV-1 diagnosis and after six months of anti-retroviral treatment. NGS (next generation sequencing) technique was employed for sequencing. As the phylogenetic analyses actually represent the gold standard in the study of HIV evolution and transmission, we adopted the Bayesian inference methods to study the variants transmitted between the two individuals.
Results: Both partners were infected with an HIV-1 B subtype and genetic distance increased over time. By sequencing different HIV-1 regions (protease, RT, V1V2 and gp41), one HIV-1 single variant resulted dominant, although some minor variants could be observed in all the analyzed viral regions. The same tree structure was observed both at baseline and after 6 months of therapy. Data herein indicate that primary HIV-1 infection was supported by two viral variants that can be considered the early T/F variants.
Conclusions: This unfortunate event offered us the unprecedented opportunity to study the T/F variants in the naïve couple and upon administration of the antiretroviral therapy. Indeed, we observed two T/F variants transmitted from the boy (G) to the girl (M), confirming for the first time in an untreated human couple what previously observed. Understanding which HIV-1 variants are most likely to be transmitted would allow a better understanding of viral evolution, playing a relevant role in vaccine design and prevention strategies.

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OP 80 CREATION OF AN ITALIAN HIV DNA NETWORK FOR THE VALIDATION AND CLINICAL USE OF HIV-1 DNA QUANTIFICATION ASSAYS

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Background: Although total cell-associated HIV-1 DNA (CAD) has gained attention as a rough estimate of the HIV-1 reservoir, certified systems for CAD quantification are not available and many different quantitative PCR-based methods are being used to determine CAD levels in blood of HIV-1 infected patients. Assays include commercial kits not yet marked for in vitro diagnostic use and homebrew quantitative PCR protocols based on digital (ddPCR) or real time (rtPCR) formats. The "Italian HIV DNA network" was launched to create a collaborative network to test and validate CAD quantification methods in use at University and Hospital laboratories.

Material and methods: In the stage 1 of Network, detailed information was collected from all participating centers concerning sensitivity, specificity, accuracy, linear range and precision of the individual methods, generated by self-assessment. Each parameter was assigned a score based on the type and number of standards used and on results obtained. A minimum threshold score of 39/65 points had to be reached to access the stage 2 of the Network, consisting in analyzing blindly a panel of reference material and reconstructed samples as an extensive quality control and assay validation. We report data of stage 1 with mean±SD or median (IQR) values.

Results: Of the 12 selected centers, 9 perform rtPCR, 2 ddPCR and 1 both methodologies. Quantification standards used included certified international standards (n=5), home-made (n=3) or commercial (n=1) plasmids, DNA from cell lines harboring known numbers of HIV-1 proviruses, quantified either by user (n=2) or by provider (n=1). The lower limit of detection (CAD copies/reaction) was calculated through single-reaction limiting dilution by 1 center (6.0), replicate limiting dilution by 4 centers (8.5 [6.0-10.0]) or complete Probit analysis by 7 centers (8.7 [3.0-13.0], 95% Hit rate). To assess precision, the centers used 3-5 different standard input copies and a median of 5 (3-5) replicates and obtained a coefficient of variation (CV) value 10.3±7.7%. On a median of 8 (4-20) blood/PBMCs clinical samples, precision testing yielded 14.0±9.1% CV values. For linear range assessment, the centers tested 4 (3.8-4.0) standard input copies and CAD quantification was linear over the tested range. To assess accuracy, 5, 4 and 3 centers tested 4, 3 and 5 standard input copies, respectively. The accuracy (log [expected–measured] values) was 0.1±0.2. Only 6 centers verified the alignment of their probe/primers on publicly available HIV-1 sequences, however 8 declared to be able to quantify CAD across different subtypes. All centers reached a passing score to proceed to stage 2.

Conclusions: The centers had broadly but variably investigated the performance of their own assay and data based on self-assessment were reassuring. However, a blind and comprehensive analysis planned in stage 2 is required for external validation of the systems.

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OP 81 INITIAL CHARACTERIZATION OF ELEMENTS DETECTED AND QUANTIFIED EXCLUSIVELY ON THE BASIS OF LTR REGION BY APTIMA HIV-1 QUANT DX DUAL-TARGET ASSAY IN PLASMA OF HIV-POSITIVE PATIENTS

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Background: Aptima HIV-1 Quant Dx (Aptima) is a dual-target (pol and LTR) diagnostic assay for the detection and quantification of HIV-1 RNA in plasma of HIV-infected patients. Recently, we reported that Aptima measures HIV-1 RNA levels mainly with pol target, in 94% of plasma samples; in the remaining specimens, HIV-1 RNA is recognized only with LTR target (being pol signal absent) spanning in the range of <30–12,000 cp/mL. To characterize virological properties (such as infectivity and structure) of these elements detected only with LTR region, we tried to isolate viral particles from PBMC of HIV-infected patients. The presence of LTR elements in exosomes obtained from their plasma was also investigated.
Material and methods: Co-cultures of PBMC from 5 HIV-positive patients with LTR-detected viral load (VL) and from HIV-negative donors were set up. PBMC were previously deprived of CD8 lymphocytes and stimulated with PHA for 3-5 days. Supernatants (SN) collected every 3-4 days were analyzed with Aptima for LTR-detected HIV-1 RNA (LTR-HIV) and with ELISA test to measure p24 levels. LTR-detected particles contained in the SN of co-colture were then analyzed for their ability to infect HIV-negative PBMC. SN containing 600,000cp of LTR-HIV was ultra-centrifuged at 20,000g for 180min at 4°C and virus-containing pellet was re-suspended in complete medium and incubated with 1,2x106 PBMC from HIV-sero-negative blood donor for 90min. Cells were re-suspended at 2x106/mL in complete medium with IL-2 at 50,000 IU/mL and maintained in culture for up to 6 weeks, stimulated with fresh PBMC at 7-10 day intervals. Every 3-4 days, SN was tested to monitor LTR-HIV. Virus-containing pellet and exosomes obtained both from plasma and co-colture SN were also analyzed with Aptima.
Results: Viral isolation was observed only in co-cultures of PBMC from patients showing pol-detected HIV-1 RNA: in fact, significant increase of both p24 viral antigen and pol-detected HIV-RNA levels were measured over time, together with typical cytopathic effects (syncitya and/or apoptosis). On the contrary, with PBMC from LTR-HIV patients, after an initial detection of a fair amount of LTR-positive viral elements, a progressive decline was observed until complete disappearance around the fifth week of co-culture. LTR elements obtained from these co-coltures were utilized to infect fresh HIV-negative PBMC, but no evidence of productive infection was highlighted. Interestingly, after ultra-centrifugation of both plasma samples and co-colture SNs, LTR elements can be detected almost exclusively in the sediment. Consequently, exosomes were analyzed for a possible presence of LTR-HIV, but no LTR signal emerged.
Conclusions: These findings suggests that viral elements detected in HIV+ patients with LTR target by Aptima are not able to trigger efficient productive infection, although they seem show corpuscular shape. Sequence analyzes of LTR-HIV elements are ongoing to complete their characterization.

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OP 82 STABLE TOTAL HIV-DNA AFTER 1 YEAR ON SWITCH TO TAF-BASED REGIMENS IN REAL WORLD DATA

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Background: TAF more efficiently delivers TFV to HIV-1 target cells resulting in lower plasma and kidney exposures. However, the impact of TDF-TAF switch on peripheral reservoir is poorly investigated. Here, we study the change of peripheral HIV-DNA over 1 year of therapy with TAF after a switch from either RPV/FTC/TDF or EVG/FTC/TDF in virologically suppressed patients.

Methods: This is a prospective study of 79 patients with HIV-RNA <50 copies/ml) switching from TDF to TAF from either RPV/FTC/TDF (n=49) or EVG/FTC/TDF (n=30) who remained with suppressed viral load for 12 months. Total HIV-DNA (LTR-5' ddPCR assay, normalized by copies/10^6 CD4), CD4 (cell/mm^3), CD4/CD8, IL-6 (pg/ml) and c-reactive protein (CRP, Luminex, µg/ml), CD38+HLA-DR+CD8+ (Flow Cytometry, %) were retrospectively tested on stored samples at baseline of switch (T0) and 12 months after (T12). Pearson correlation and multiple linear regression analyses were used to estimate biomarkers changes from T0 to T12 and the association with specific anchor drugs used. Results are described as mean [±SD] and 95% CI.

Results: Patients had a median age of 47 [40-55] years and were HIV-1 infected by 5.6 [3.8-12.0] years. Exposure to TDF was 3 [2-6] years. At T0, HIV-DNA, CD4, CD4/CD8 were 554 [±711] copies/10^6 CD4, 723 [±297] cell/mm^3 and 0.90 [±0.40], while IL6, CRP and CD38+HLA-DR+CD8+ were 2.7 [±2.1] pg/ml, 2.8 [±3.4] µg/ml, and 10.2% [±11.2%], respectively. Patients receiving EFV or RPV were balanced for demographics and laboratory markers at T0 (not shown). Overall, HIV-DNA remained stable (mean difference [±SD]: -20.1 [±619] copies/10^6 CD4, P=0.77), and similarly, no changes in CD4 and CD4/CD8 were found from over T0-T12 (+4.8 [±197] cell/mm^3 and 0.0 [±0.21], P=0.83 and 0.76). A significant reduction in IL6 and CD38+HLA-DR+CD8+ at T12 as compared to T0 was found in the overall population in unadjusted analysis and after controlling for HIV-DNA change over T0-T12 (-0.56 pg/ml and -2.22 µg/ml, p<0.005, respectively). No evidence for an association between change of HIV-DNA, CD4, CD4/CD8, inflammatory markers and use of RPV- or EVG-FTC/TAF groups was found (Table).

Conclusions: Twelve months of TAF-containing regimens resulted in containment of HIV-DNA levels, despite a reduction in inflammatory markers. While suggesting that maintenance of peripheral reservoir appears to be independent of the containment of residual inflammation, these data also indicate a possible role of TAF in the containment of other sources of residual inflammation upon suppressive cART. Results were similar regardless of the third drug used.

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OP 83 HIV-1 RNA AND DNA MUTATIONAL LOAD IN HTE PATIENTS WITH MDR VIRUS: A TOOL FOR DECIDING OBR?

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Background: Heavily treatment-experienced (HTE) people living with HIV-1 with multi drug-resistance (MDR) need careful assessment to plan an effective therapy. Mutational load (ML) in isolates from plasma and PBMC could impact virological outcome.

Material and Methods: We analysed 20 HTE persons with resistance to NRTI/NNRTI/PI/INSTI, failing ART, enrolled in the PRESTIGIO registry. Resistant and APOBEC-related variants (Stanford HIVdb version 9.1.1) in HIV RNA and DNA were evaluated through next generation sequencing (NGS, Illumina MiSeq) and compared to those present in the historical Sanger genotypic resistance test (GRT). Gp120-V3 NGS was performed to infer tropism through geno2pheno algorithm. ML was calculated based on mutant frequency and HIV DNA (through ddPCR) and RNA levels (Fig).

Results: Main characteristics [median (IQR)] at sample collection were: age 47 (37-53) years; time from diagnosis 23 (19 -26) years; time on ART 19 (17-22) years; number of previously failed regimens 11 (6-32); plasma HIV-RNA 4.5 (4.1-5.0) log10 cps/ml; proviral DNA 4.5 (4.0-5.2) log10 cps/10^6 CD4+; CD4 count 204 (97-329) cells/mm3. By NGS, 4-class resistance was detected in 26% and 68% of patients in plasma and PBMC, respectively. Among 255 resistant variants detected in either compartment, 182 (71.4%; 148 in plasma and PBMC; 33 only in PBMC; 1 only in plasma) were already present in historical GRT. NGS detected 73 additional variants (28.6%).

Complex resistance patterns were detected in all individuals (Fig); 12 (60%) persons harboured an X4-tropic virus in at least one compartment. Median (IQR) DNA ML was 3.9 (3.1-4.6) log10 cps/10^6 CD4+, while median (IQR) RNA ML was 4.5 (4.0-4.9) log10 cps/ml. APOBEC-related proviral resistance mutations (PI: M46I, D30N; NRTI: D67N, M184I; NNRTI: E138K, G190E) were found in 9 patients (45%, median [IQR] ML: 2.7 [2.2-2.9] log10 cps/10^6 CD4+), while substitutions at enzymatic catalytic sites (PR: G27E; RT: M184I, D186N; INT: E152K) were present in 8 patients (40%, ML [IQR]: 2.8 [2.3-3.1] log10 cps/10^6 CD4+). 14 people (70%) showed variants with stop codons in proviral DNA with intra-patients' frequency <17% (median [IQR] frequency: 2.4% [1.4%-3.4%]; median ML [IQR]: 2.9 [2.4-3.2] log10 cps/10^6 CD4+).

Fourteen individuals modified ART after sample collection: 5/14 (35.7%) experienced virological failure and, compared to responders, had higher resistant ML in both proviral DNA (4.1 [3.0-5.4] vs. 3.5 [3.0-4.1], log10 cps/10^6 CD4+, p<0.001) and in plasma (4.7 [4.0-4.9] vs. 4.1 [3.9-4.5], log10 cps/ml, p<0.001). Moreover, a higher proportion of failing people presented all resistant variants with a ML >3 log in both compartments (60% vs. 11%, p=0.095).

Conclusions: APOBEC activity can be detected in HIV-1 DNA in most HTE people with 4-drug class resistance, with a low viral burden. HIV-1 RNA/DNA ML might help to identify individuals more prone to experience VF and guide salvage therapy optimization.

Virology and pharmacology

OP 84 VIRAL TROPISM DOES NOT HAVE ANY IMPACT ON CD4 RECOVERY IN ACUTE HIV INFECTION OR AIDS

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Background: The impact of viral tropism on immunological recovery during different stages of HIV infection is still a matter of debate. The aim of our study was to assess the impact of viral tropism determined by population sequence analysis and next-generation sequencing (NGS) on the immunological recovery of HIV positive patients with acute/recent HIV-1 infection or AIDS presentation.
Methods: We conducted a prospective observational study on a cohort of HIV-1 infected patients. Study participants were enrolled at the III Division of Infectious Diseases of the Luigi Sacco Hospital, Milan between 2012 and 2015. We included antiretroviral treatment (ART)-naive AIDS presenters or acutely/recently infected patients who started ART within 4 weeks from the HIV diagnosis. The follow-up time was 36 months for each patient. We collected data regarding viral load and CD4 count from baseline every 6 months and CD4/CD8 ratio every 12 months. Viral tropism at baseline was measured using population-sequencing in all recruited patients and NGS in a subset of patients. CD4 and CD4/CD8 ratio were studied by uni- and multivariate analysis using a SAS proc mixed model for repeated measures. Concordance in determining tropism between population-sequencing and NGS was measured using Cohen's kappa coefficient (κ). A value of $p < 0.05$ was considered statistically significant.
Results: Forty-six patients were enrolled. Baseline characteristics are reported in Table 1.
Tropism at baseline was tested in each patient using population-sequencing. X4-tropic virus had a prevalence of 33% in the whole cohort. Nine patients were re-tested at 12 months using population-sequencing and none of them had had a tropism switch. The prevalence of X4-tropic virus at 12 months with population sequencing was 22%. Patients in the acute/recent phase of the infection had a better CD4 recovery when compared to AIDS presenters [β 259.59 standard error (SE) 110.64; p=0.0241]. Moreover, baseline CD4 cell count correlated with CD4 recovery [β -0.47 (SE) 0.18; p=0.0124]. No correlation between tropism at baseline, determined by population sequence analysis and NGS, and the number of drugs in the ART regimen (3 vs ≥ 4 drugs), CD4 count and CD4/CD8 ratio recovery was observed in either groups.
Population sequence analysis and NGS showed a moderate level of concordance in determining HIV-1 tropism [κ = 0.534]. Nine patients had an available tropism performed by population-sequencing at 12 months and none had a tropism switch from baseline. Thirty patients had a baseline tropism performed by NGS; we observed one switch from X4- to R5-tropic virus among the 9 patients who were re-tested at 12 months.
Conclusions: Our study confirms that the timing of ART start is the most important factor for CD4 recovery. Whereas, neither viral tropism nor number of drugs composing the regimen showed an impact on immunological recovery in our study.

Virology and pharmacology

OP 85 ANTIVIRAL EFFECT OF HIV1 TAT/REV SIRNA CARRIED BY NANOPARTICLES IN HUMAN CD4+ T CELL LINE

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Background: RNA interference pathways to target HIV-1 replication offers a novel treatment strategy for HIV infection. The successful therapeutic application of siRNAs requires their efficient delivery to specific cells. Polymers such as chitosan, have been shown great potential for gene delivery in various cell types. Chitosan bind to cell surface glycoproteins and enter the cells through endocytosis. In addition, the encapsulation of siRNA into liposomes was described. Liposome fuse with the cell membrane, releasing the nucleic acid into the cytoplasm. The aim of the study was to evaluate the antiviral effect of HIV1 tat/rev siRNA carried by chitosan and liposomes (ESCORT) and directed against HIV-1 tat/rev transcripts, in C8166 cell line infected with HIV-P1.

Methods: To determine the efficacy of uptake in C8166 cells, nanoparticles (np) was labelled with FITC and fluorescence was measured with cytofluorimetric assay. MTT-assay was used to determine dose-related toxicity. To achieve experiments, chitosan and liposomes carrying siRNA were prepared. Also, np carrying synthetic DNA with the same molecular size of siRNA were prepared as control. C8166 were subjected to pre and post treatment. Specifically, cells were pre-treated with np for 4 hours (h), washed, infected with HIV-1 P1 at high multiplicity of infection (MOI=1) and incubated at 37°C. In post-treatment, C8166 were infected with HIV-1 P1 (MOI=1), washed, treated for 4h with np and incubated. After 24h of incubation supernatants were collected and HIV RNA was measured to determine percentage of HIV replication reduction.

Results: No toxicity was observed when cells were treated with 100, 20 or 10 ug/ml of chitosan np. The efficiency of 20 ug/ml np uptake was lower in infected than in control cells (infected: pre-treatment 46%, post-treatment 63%; not infected 80%) suggesting that the presence of virus may interfere with np. In agreement with internalization studies, chitosan carrying siRNA reduce of 40% and 70% viral replication in pre and post treatment, respectively.

No inhibition of viral replication was observed for chitosan carrying DNA in pre-treatment; instead, in post treatment 50% of viral replication reduction was observed. Also, post-treatment with chitosan not complexed with siRNA or DNA reduced viral replication of 60%.

About ESCORT with siRNA, HIV replication inhibition was 35% in pre-treatment experiment and 61% in post treatment. Again, a 45% of reduction was observed in post-treatment with ESCORT carrying DNA.

Conclusions: These data demonstrated the efficacy internalization of chitosan in C8166 cells line suggesting their use as potential carrier of siRNA to reduce HIV replication. However, the reduction of HIV replication observed in cells treated with np without siRNA, after HIV infection, suggest that np may interfere with early step of HIV life cycle and that can have a synergic effect with siRNA to reduce antiviral replication

Virology and pharmacology

OP 86 A REAL-LIFE EXPERIENCE OF VACCINATION STRATEGIES FOR HBV PREVENTION IN HIV PATIENTS

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Background: HBV Hepatitis is a preventable disease among HIV patients undergoing an appropriate vaccination schedule. At present, two preparations are available: Engerix-B Hepatitis B (rDNA) vaccine (adsorbed) and Fendrix Hepatitis B (rDNA) vaccine (adjuvanted, adsorbed).
Materials and methods: Upon accessing our in-hospital vaccination program, all HIV patients underwent HBV susceptibility screening and evaluation of viro-immunological parameters. Previous HBV vaccination was assessed through anamnestic interview. According to Italian guidelines, HBV susceptible patients (HBsAg, HBsAb and HBcAb negative) with no history of previous vaccination were proposed HBV vaccination. We initially administered Engerix-B (3-doses vaccination schedule) and later switched to Fendrix (4-doses vaccination schedule) as the preparation became available. Patients with a previous history of HBV vaccination and HBsAb titer <100UI/mL were offered a single-dose booster with Fendrix. All patients with a complete vaccination schedule and a following assessment of HBsAb titer were included in this study. Factors associated with no-response (HBsAb titer <10UI/mL) were investigated using univariate logistic regression analysis.
Results: From December 2017 to January 2020, 118 patients were included in our study: 52 HBcAb-negative patients with HBsAb<10UI/mL and no history of previous HBV vaccination completed the HBV vaccination schedule (38 with Engerix, 7 with Fendrix); 66 patients had a previous history of HBV vaccination with Engerix. Clinical characteristics of the study population were: median age of 43years (IQR 36-50), 84.3% male, median CD4+ cell count 703/uL (IQR 522 -896); HIV-RNA <50cp/mL 96%.
Overall, 71/118 patients (60%) responded to HBV vaccination (HBsAb>10UI/mL). We observed a higher response to 4-doses Fendrix schedule comparing to 3-doses Engerix scheme: 8/8 patients (100%) vs 63/110 patients (57%) (p=0.02). When investigated using univariate logistic regression, response was not affected by sex, age category (>40 y.o. vs <=40 y.o.), CD4+ cell count (>500cell/uL vs <=500cell/uL), and time between end of vaccination and titer control. [Figure 1A]
Forty-nine patients with a HBsAb titer control <100UI/mL after a complete Engerix vaccination, received a single-dose booster with Fendrix. Only 28 patients assessed HBsAb titer after booster administration: among these, 27 (96.4%) responded to the vaccine, showing an increased HBsAb titer >100UI/mL; only one patient maintained HBsAb <10UI/mL. [Figure 1B]
Conclusions: Response to HBV vaccination regimen with 4-doses Fendrix was superior compared to 3-doses Engerix in our real-life experience of HIV patients. In patients not responding to previous Engerix vaccination, a single-dose booster with Fendrix has proven effective in generating protective immunological response. Further studies are needed to compare other vaccination strategies

Virology and pharmacology

OP 87 A SUCCESSFUL EXPERIENCE OF AN IMMUNIZATION PROGRAM IN HIV-POSITIVE ADULTS

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Background: Compared to HIV-negative individuals, HIV-positive adults often have an increased risk of infection or experience more severe morbidity following exposure to vaccine-preventable diseases. Objectives were to evaluate the safety and efficacy of vaccinations in HIV-positive adults and to propose an immunization schedule specific to HIV-positive subjects.
Materials/methods: This retrospective cohort-study was conducted at the Infectious Diseases Department of Busto Arsizio Hospital in Italy, between 1st February 2018 and 31th January 2020. HIV-positive adults who received a recommended immunization schedule were included. Virological suppression was defined as HIV-RNA <50 copies/mL for at least 6 months. Live-attenuated vaccines were not administered if CD4 count was <200 cells/µL.
Results: 300 subjects were enrolled, all on antiretroviral therapy: 204 (68%) were males, mean age was 49.9 years. The rate of virological suppression was 96%. Median CD4 count was 730 cell/µL (CD4%=34%). 90 subjects (30%) were IVDU, 80 (27%) MSM. HCV or HBV coinfection occurred in 94 (31%) patients, cardiovascular diseases in 80 (12%), tumours in 24 (8%), diabetes in 21 (7%). Five patients (3%) were candidates for organ transplantation, 3 (1%) to chemo or radiotherapy, 13 (4%) were on immunosuppressant drugs or biological agents. Immunization schedule included the following vaccines: 13-valent (PCV-13) and 23-valent (PPV-23) pneumococcal, seasonal influenza, 2-dose meningococcal ACWY (Men-ACWY) and B (Men-B), diphtheria-tetanus-acellular pertussis (dTPa), 9-valent HPV (males and females aged <45 years), HBV and HAV in seronegative individuals, measles/mumps/rubella/varicella (MMRV) for subjects not immunized against one or more of those diseases, live-attenuated herpes zoster (HZ) in subjects aged > 50 years with COPD, diabetes, heart diseases, previous shingles episodes or starting immunosuppressive therapies, Haemophilus influenzae type B (Hib) in severely immunocompromised patients. Adherence to total immunization program was 89% (267/300 patients). PCV-13 and PPV-23 were administered to 97% (n=291) and 73% (n=220) of patients, respectively. Men-ACWY and Men-B were performed in 89% (n=266) and 78% (n=235) of cases, dTPa in 63% (n=189), inactivated influenza vaccine in 50% (n=151), HAV in 32% (n=97), HBV in 31% (n=92), HPV in 20% (n=60), Hib in 12% (n=36), HZ in 8% (n=24), MRPV in 3% (n=10). Rare adverse reactions included local swelling/redness in 27 (9%) cases, fever >37.5°C in 8 (3%), gastrointestinal disorders in 4 (2%). Among patients immunized for HBV, 18 (36%) resulted as non-responders to a 4-dose schedule.
Conclusions: Immunization program for HIV-positive adults was safe and well tolerated with satisfactory coverage rates for most vaccine-preventable diseases, considering a suboptimal adherence.

Virology and pharmacology

OP 88 PLASMA EXCHANGE AND DOLUTEGRAVIR EXPOSURE. A CASE REPORT

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Total Plasma Exchange (TPE) is nonselective a procedure where a volume of plasma is removed together with pathological substances and replaced with other fluids. Also drugs can be removed.
The extent of drug removal is affected by several factors; a low volume of distribution (<0.2 L/kg) and a high protein binding (>80%) are associated with a higher likelihood of drug removal during the procedure.
Dolutegravir (DTG) has a high volume of distribution (17.4 L), high Protein binding (>99%) and a half-life of 13 to 14 hours. Less than 1% of DTG is excreted unchanged in the urine, no dose reduction is required in severe kidney injury.
To the best of our Knowledge no data on DTG PK in TPE are available.
We report the case of an HIV patient receiving DTG, requiring plasma exchange (TPE) for a thrombotic thrombocytopenic purpura. Written consent for publication was obtained from the patient.
A 34 years old man was diagnosed with an HIV infection at the admission. Baseline parameters were HIV-RNA>300000 copies/ml; CD4: 75 cell/uL; glomerular filtration rate: 43 ml/min/1.73m2 (by Cockroft and Gault Formula, creatinine 1.89 mg/dl). HAART was started during hospitalization (day 2) with Tenofovir alafenamide fumarate/emtricitabine and dolutegravir (200/25 mg + 50 mg/OD).
TPE for thrombotic thrombocytopenic purpura was empirically started on day 6 and continued through day 11, restarted on day 17, at that time the patient was suffering of a nephrotic syndrome, with a proteinuria of 10 g/day.
DTG was administered on day 17 after TPE and on day 18 we analyzed DTG plasma concentrations immediately before and after TPE. Further plasma samples were collected at 1, 2, 4 and 6 hours after DTG oral administration (post-TPE). On day 19 an extra dose was administered 4 hours before apheresis and the usual dose after TPE and we analyzed DTG plasma concentrations immediately before and after TPE to calculate the elimination rate of DTG.
DTG concentrations were determined by a specific and validated HPLC-UV method.
On day 18, DTG trough concentration was 1.7 mcg/mL pre-TPE and 1.0 mcg/mL post-TPE (48% extraction). On day 19 (4 hours after the extra 50 mg dose) the corresponding values were 2.7 mcg/mL and 1.3 mcg/mL (50% extraction). Both pre and post-TPE concentrations remained within the suggested therapeutic range (0.7 – 2.35 mcg/mL). AUC 0-24h value, calculated on day 18, was 45.8 mcg.h/mL, with a t1/2 of 9.7 h, and fell within the pre-defined target pharmacokinetic exposure range (37.0-67.0 mcg.h/mL).
Unfortunately, we did not determine the amount of DTG removed in the plasmapheresate to estimate the extent of drug extraction with TPE.
TPE is a relatively uncommon practice and PK data are generally scanty. This report seems to show that DTG concentrations are not deeply affected by TPE. Even though the PK data in our data are incomplete, to the best of our knowledge this is the first case report describing DTG plasma biodisposition in this setting.

Bacterial and fungal infections in immunocompromised host

P 1 A DESCRIPTIVE ANALYSIS OF BLOODSTREAM INFECTIONS IN PATIENTS LIVING WITH HIV IN A LARGE ITALIAN CENTER

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Background: Even after the introduction of HAART and the onsuing decline in AIDS-related deaths, HIV-positive patients (pts) remain a "fragile" population, and various works depict them as more susceptible to bloodstream infection (BSI) compared to HIV-negative individuals. In this work we aim to describe the etiology, clinical characteristics and outcome of bloodstream infections (BSI) in HIV-positive pts in our center.

Methods: We retrospectively analyzed all cases of BSI in HIV-positive pts in our center between January 2013 and July 2019. For each case we collected informations about the isolated pathogen, viro-immunological parameters at BSI diagnosis, patient's clinical history and evalueted the outcome (i.e. all-cause mortality in the first 90 days following BSI diagnosis). We did not include cases of probable contamination of blood cultures (i.e. single blood culture positive for CoNS, no improvement after targeted antibiotic therapy, spontaneous symptoms resolution without therapy). Predictors were assessed via regression analyses.

Results: Throughout the study period, a total of 69 pts had at least 1 BSI, for a total of 77 episodes and 101 isolated pathogens. Pts with BSI were prevalently males (56.4%), with a median age of 55 years old (InterQuartile Range [IQR] 47-64), a median time from HIV diagnosis of 16 years (IQR 3-22) and a median time on HAART of 11.1 years (IQR 0.8 -16.5). Among them, 36.6% were CDC stage C, 18.8% were HCV-coinfected and 27.7% had a previous virological failure. General characteristics of the study population are available in Table 1.

Most frequently isolated germs were: Enterobacteriacae (33, 32.7%), Staphylococcus aureus (14, 13.9%), Coagulase-negative staphylococci (13, 12.9%) and Enterococci (11, 10.9%). Four cases (4%) of candidemia were observed. Among isolated germs, 35 (34.7%) presented multi-drug resistance profiles; in particular, among the 14 isolated Staph. aureus, 6 (43%) were meticillin-resistant (MRSA) while among the 33 isolated enterobacteriacae, 12 (36%) presented an ESBL-positive phenotype. In our cohort, pts with MRSA-related BSI had a significant lower CD4+ cell count (p=0.020) and an older age (p=0.030) compared with the others.

Twenty-one pts (20.8%) died within 90-days from the BSI diagnosis. At a multivariate analysis, death was predicted by an older age (aHR 1.10, 95%CI 1.01-1.18, p=0.030), concomitant haematologic malignancy (aHR 18.80, 95%CI 2.29 -147.74) and polimicrobic BSI (aHR 12.32, 95%CI 2.06-73.83, p=0.006), after adjusting for sex and previous virological failure.

Conclusions: BSI in HIV-infected pts have a wide spectrum of possible etiologies and are still marked by high mortality, correlated not only to an advanced HIV stage but also to other major comorbidities.

Bacterial and fungal infections in immunocompromised host

P 2 AMEBIC ABSCESS OF THE SPLEEN WITH SEVERE SEPSIS AND BRONCHIAL FISTULISATION IN HIV +PATIENT: CASE REPORT

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Background: Amebiasis is an infection caused by the intestinal parasite, Entamoeba histolytica. It is transmitted through fecal-oral route. The most frequent extraintestinal location of Entamoeba histolyca is in the abdominal area, where it gives rise to hardly manageable pseudo-abscessual lesions mainly located in the liver. In this case report we described the diagnostic difficulties for an uncommon case of amebic abscess of the spleen in an immunodeficiency patient.
Material and methods: patient A.P. (male 34 yo, black, HIV+ since 2018, CD4 312, HIV-RNA undetectable, in ART regimen on FTC/TAF/RPV) was admitted twice in our hospital between May and September 2019, for a total of one hundred days for "septic fever and abdominal colic in HIV+ patient". During his second stay, we noticed a voluminous round shape in the spleen, which was absent before and seemed to have the characteristics of an echinococcal cyst. The anty-hydatid antibody did not confirm this theory. In fact, they turned out to be positive for Entamoeba histolyca. In the following days, the patient had three episodes of severe abdominal sepsis, probably correlated with the bacterial contamination from the amebic abscess. In addition to the abdominal pain on the left side, he presented fever, neutrophilic leukocytosis, hyperprocalcitoninemy, thrombocytosis, anemy (the patient was transfused several times) and a serious renal impairment (which gave rise to the need for haemodyalitic assistance in the first hospitalization only). Furthermore, the case became more complicated during the patient's second hospital admission due to a multiple vein thrombosis (inferior vena cava, common iliac vein LH, external iliac LH, internal iliax RH). Case was solved thanks to a medical approach (therapy under metronidazole iv + ceftazidime/avibactamiv iv + paromomycin per os + sodium enoxaparin subcutaneous); therapy went on discontinuously (except for enoxaparin and metronidazole) along with repeated abdominal sepses treated with different drugs and posologies, while keeping renal functionality under control. A pulmonary vomit episode twenty days after the patient's dismissal positively influenced the improvement of his general medical condition. In fact, it created a volumetric reduction of the mass, despite having caused a fistulisation of the right bronchial tree (as proven by the abdominal TC performed on 22.08.2019 see Fig.1). The patient, after six months of oral therapy under paromomycin and metronidazole, is in optimal condition. The latest TC (February 2020) shows a complete resolution of the abscess both in the liver and in the spleen.
Conclusions: the case proposed here sounds quite unfamiliar for the infrequent location of the amebic abscess (in the spleen, not in the liver). Particularly striking is the recurrence of severe abdominal sepsis and of thrombosis, probably correlated with the overlapping bacterial colonization.

Bacterial and fungal infections in immunocompromised host

P 3 PNEUMOCYSTIS JIROVECII PNEUMONIA IN HIV-NEGATIVE PATIENTS, A FREQUENTLY OVERLOOKED PROBLEM: CASE SERIES FROM A LARGE ITALIAN CENTER

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A classic AIDS-defining condition, Pneumocystis jirovecii pneumonia (PJP) still has substantial morbidity and mortality among immunocompromised individuals. For patients with haematologic malignancies and stem-cell transplant recipients course of infection is severe, and management guidelines relatively recent.
We collected all PJP cases diagnosed in adult inpatients in 2019 at our Center (900 total beds), encompassing Hematology, Bone marrow and Solid organ transplant wards. Aim was assessing the characteristics of HIV-negative patients with PJP in a large general hospital and raise awareness on risk factors and management.
Throughout 2019, 11 patients were diagnosed with PJP, on the basis of clinical symptoms + compatible radiologic exams + microbiologic evidence: positive RT-PCR for P. jirovecii DNA on BAL (sputum in 1 case); for 7/11 immunofluorescence was also positive. Of them, 8/11 were HIV-negative and 3/11 AIDS presenters. For HIV-negative pts, female gender was 75% and median age 66.5 y.
Of the 8 HIV-negative patients, 2 had undergone allogeneic hematopoietic stem cell transplantation (HSCT) in 2017 and 2018 for acute myeloid leukemia (AML) and Sezary syndrome, respectively; 1 had AML; 2 Diffuse Large B-cell Lymphoma (DLBCL) undergoing chemotherapy, 1 follicular lymphoma in complete remission (CR); 1 primary biliary cholangitis (PBC); 1 dermatomyositis (DM).
At time of PJP diagnosis all patients were not on prophylaxis for PJP.
Based on ECIL guidelines and the Sanford guide, 2/8 patients had indication for PJP prophylaxis: 1 had allo-HSCT with ongoing immunosuppression (GVHD on sirolimus and 5 mg prednisone) and had recently discontinued TMP/SMX after clinical risk assessment, 1 was on chronic prednisone >20 mg/day for PBC and had never been on prophylaxis.
Of the others, 1 had history of allo-HSCT and was recently briefly (<4 wks) treated with high-dose prednisone; 2 had undergone rituximab-based therapies (R-CHOP, R-CVP) for DLBCL <6 months before; 1 (AML) was on chronic prednisone 10 mg/day, on azacitidine and was lymphopaenic (CD4 count not performed); 1 (follicular lymphoma, CR) had a recent short course of high dose steroids for hip inflammation; 1 (DM) did not have any known risk factor. CD4 count was available for 4/8 patients, and was >200/mcL for all. 5/8 patients had pO2 <70 mmHg.
All patients were treated in accordance to guidelines (21 days, 7/8 TMP/SMX, 1/8 IV pentamidine due to past hepatitis during TMP/SMX prophylaxis). 2/8 died (day 12 and 21). 1/6 started with oral TMP/SMX, 4/6 switched to oral during treatment, 6/6 progressed to secondary prophylaxis. Our case series confirms that, despite appropriate treatment, PJP is still associated to high mortality (25%) among patients with hematologic or autoimmune conditions. Strict adherence to prophylaxis guidelines, awareness of grey areas (minor risk factors not among prophylaxis indications) and prompt diagnosis can help managing this frequently overlooked infection.

Bacterial and fungal infections in immunocompromised host

P 4 INFECTION BY MYCOBACTERIUM CHIMAERA IN TWO SUBJECTED UNDERGOING CARDIAC SURGERY

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Background: Mycobacterium chimaera is a slow-growing non-tuberculous mycobacterium grouped with Mycobacterium intracellulare and Mycobacterium avium to make up the Mycobacterium avium complex (gram-positive, non-motile, and acid-fast).
Evidence suggests that it is responsible for symptoms similar to those found in disseminated mycobacterial diseases, prosthetic valve endocarditis, ocular emboli, vertebral osteomyelitis, hepatitis, and renal dysfunction, along with other life-threatening conditions.
Additionally, it can cause pneumonia in patients with underlying respiratory complaints, such as cystic fibrosis and other immunodeficiencies.
Mycobacterium chimaera did not come to the forefront until 2015, when this infectious agent was identified as a culprit responsible for two prolonged outbreaks involving prosthetic valves and associated systemic infection in the United States and Europe.
Material and methods: Two patients were accepted in our yard after a period of two weeks or more with aspecific syntoms: unexplained fevers, night sweats, joint or muscular pain, increasing shortness of breath and unexplained weight loss.
We conducted ematologic and radiologic screening that shows us a systemic failure (pancytopenia, lung, liver, kidney and heart faliure) without a clear evidence of an eziological identification.
Moreover they didn't had improvement on health after antibiotic therapy.
They both referred cardiac surgery history more than five years before.
Results: In one case we reach during the recovery bloodcolture for intracellular Mycobacteria then was subject to immunochromatographic assay, so we treated him with specific treatment.
The other case regarded a subject that was recovered in 2013 - 2014 and dead in 2015.
We analyzed blood samples collected in our laboratory.
Both samples showed presence of intracellular Mycobacteria after identified as Mycobacterium chimaera.
Conclusions: The importance of heating-cooling units lies in their ability to regulate the body temperature of the patients during cardiac surgery; evidence suggests that the airborne transmission of aerosolized bacteria from the water tanks was responsible for this infection.
The infection remains clinically dormant for years, making a diagnosis of Mycobacterium chimaera in a timely manner challenging.
Only specific research of the pathogen can identify the cause and allow the specific treatment that frequently comes too late.

Bacterial and fungal infections in immunocompromised host

P 5 A CASE OF PERSISTENT RELAPSING ABDOMINAL MYCOBACTERIAL INFECTION REQUIRING PROLONGED INTRAVENOUS MULTI-DRUG TREATMENT

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Mycobacterium genavense (Mg) is a rare pathogen that can cause severe infection in HIV. Difficult culturing and the absence of specific symptoms make the diagnosis challenging. Type and duration of treatment are unclear.
A middle-age man with advanced HIV diagnosis (CD4 4/ l) was admitted in March 2017 for fever, pancytopenia and weight loss. Computed tomography (CT) revealed enlarged intrabdominal lymph nodes, hepatosplenomegaly and left pleural effusion. Acid-fast bacilli (AFB) were seen in microscopic stool and bronchoalveolar lavage examination, BKDNA was negative. Antimycobacterial treatment for atypical Mycobacteria was started, (rifabutin, clarithromycin, ethambutol), followed in 2 weeks by antiretroviral therapy (tenofovir/emtricitabine+dolutegravir); 2 weeks later, stool cultures grew Mg. No antibiogram was available (fastidious organism). As fever persisted, thrice weekly amikacin was added to antimycobacterial treatment for 3 months. In September 2017 HIVRNA was <200 copies/mL and CD4 were 104/ l. However, despite >3 months of treatment, monthly stool examination remained positive for AFB up to October 2017. Further attempts to isolate the organism were unsuccessful. Amikacin was then replaced by a fluoroquinolone (FQ) (moxifloxacin, then levofloxacin) obtaining 3 negative consecutive stool samples for AFB. Unfortunately, FQ was withdrawn for QT prolongation in August 2018, when he was again hospitalized for clinical deterioration. He presented with pancytopenia, low albuminemia (1.8 g/dl), no proteinuria, bilateral leg edema, bilateral pleural effusion and ascites. Abdominal CT showed enlargement of intrabdominal lymph nodes with duodenal compression, and severe hepatosplenomegaly. Deep intrabdominal lymph node and bone marrow biopsies revealed granulomas, although cultures were negative. Antimycobacterial therapy was implemented adding linezolid, discontinued after 2 weeks for nausea and vomiting, which resolved rapidly after linezolid stop. Therapeutic drug monitoring for rifabutin and ethambutol was below normal range, while for dolutegravir was normal. Then, azithromycin, ethambutol, rifampicin, tedizolid (thrice weekly) intravenous, oral clofazimine and albumin supplementation were administered. After 7 months of intravenous therapy, lower limbs edema, ascites and abdominal lymph nodes improved, thus anti-mycobacterial therapy was shifted orally (azithromycin, rifampicin, ethambutol and clofazimine). Rapid clinical deterioration was observed, with onset of abdominal pain and development of chylous ascites: microscopic stool examination revealed AFB. Therefore, intravenous therapy was started again. So far, after 34 months of treatment, patient conditions have improved.
This case shows the challenges in accurately diagnosing and managing Mg disease. Long intravenous antimycobacterial treatment with 3 or 4-drug regimen could be necessary, tedizolid being a good alternative to linezolid in case of poor tolerance.

Basics in viral hepatitis

P 6 COMPARISON OF IMMUNOASSAYS FOR QUANTITATIVE SERUM HBSAG

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Introduction: The characterization of virological profile allows to identify the state of infection, to estimate the risk of evolution and to evaluate the antiviral treatment.
Indeed, during the different state of infection, the HBsAg levels change significantly with a progressive reduction, after the activation of immunological response.
As reported by international studies, quantitative HBsAg is an important predictive biomarker of sustained serological and virological responses. Indeed, all patients with HBeAg positive chronic hepatitis that present, after 12° weeks of therapy, the HBsAg levels <1500 IU/mL, have a higher probability to obtain a positive immunological response. On the contrary, levels >20000 IU/mL seem to correlate with therapeutic failure.
The determination of quantitative HBsAg is also useful to identify the inactive carrier (HBsAg <1000 UI/mL) and to establish the frequency of the patient's follow-up.
The aim of this study was to compare the performance of two different assays for the HBsAg quantification.
Materials/methods: The HBsAg levels were analyzed by HBsAg assay (Architect, Abbott) and Elecsys HBsAg II quant kit (Roche Diagnostics). Two commercial immunoassays approved for HBsAg detection. Abbott assay is considered the reference system for the quantification of HBsAg and it is based on a chemiluminescent reaction. In contrast, the Elecsys HBsAg II quant (Roche Diagnostics) kit uses a chemiluminescent microparticle immunoassay.
The linear ranges stated are different: Roche identifies a range from 0.05 IU/mL to 117000 IU/mL while Abbott detects a 0.05-124925 IU/mL range.
The correlation between quantitative results, was evaluated by using the linear regression analysis and the Bland–Altman plot.
Results: We have selected 110 samples at different concentrations of HBsAg to cover the whole range of values. The samples were contemporarily analyzed by both systems. A good correlation was found between the assays with narrow 95.9% limits of agreement. In contrast, the Bland–Altman test identified a proportional mistake, in particular for values greater than 500 IU/mL.
Conclusions: The study showed that the concentration of HBsAg between the assays was comparable. However, important differences were showed especially at decisional-values level (concentration greater than 500 IU/mL). In conclusion, further studies are necessary to evaluate those discrepancies

Basics in viral hepatitis

P 7 CRYPTIC HBV REPLICATION IS FREQUENTLY REVEALED IN ANTI-HBC POSITIVE/HBSAG NEGATIVE PATIENTS WITH HIV INFECTION BY APPLYING A HIGHLY SENSITIVE DIGITAL DROPLET PCR ASSAY

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Background: Occult HBV infection (OBI) is frequent and associated with poor survival in the setting of HIV infection. Here, we investigate cryptic HBV replication and factors correlated with its detection in anti-HBc positive/HBsAg-negative HIV-infected patients by applying a highly-sensitive (HS) digital droplet (dd) PCR assay for serum HBV-DNA quantification.
Material and Methods: This study includes 81 anti-HBc-positive/HBsAg-negative patients with serum HBV-DNA<10IU/ml by a commercial Real-Time PCR. All patients are HIV-infected, treated with an antiretroviral therapy including >1 anti-HBV drug: TAF/FTC(N=37), TDF/FTC(N=25), or LMV(N=19) (median[IQR] duration: 35[17-61] months). Serum HBV-DNA is quantified by an in-house HS-ddPCR (BioRad) whose linearity, reproducibility and sensitivity are assessed by testing serial dilutions with known concentration. FujiRebio assay is used to quantify anti-HBc titer (proposed to parallel HBV replication). Factors correlated with the detection of cryptic viremia (serum HBV-DNA >1IU/ml) are defined by Fisher exact test. Population-based sequencing of HBsAg major hydrophilic region (MHR, aa 99-169) is used to analyse immune-escape mutations with cryptic HBV viremia.
Results: ddPCR shows excellent linearity in the range of HBV-DNA from 1 to 10,000 IU/ml (R2=0.997), good intra- and inter-run reproducibility (coefficient of variation: 7.8% and 18.6%) and high sensitivity (limit of quantification: 1 IU/ml).
Overall, median (IQR) anti-HBc is 4.2 (2.4-11.6)IU/ml. 29.6% of patients are isolated anti-HBc and 70.4% anti-HBc/anti-HBs positive (median[IQR] anti-HBs titer: 278[90-957]mIU/ml). Median (IQR) HIV-RNA and CD4+ cell count are <20(<20 -38) copies/ml and 541(331-727) cells/ul, respectively.
Notably, by ddPCR, cryptic HBV viremia is detected in 29.6% of patients with a median (IQR) of 4 (1-15) IU/ml, more frequently in in patients an advanced CDC stage (85.7% with cryptic HBV-DNA versus 54% without cryptic HBV-DNA have been diagnosed in B2/3 or C2/3 stage, p=0.01).
No impact of different anti-HBV drugs on cryptic HBV viremia is observed (% of patients with serum HBV-DNA>1 IU/ml: 27% for TAF, 28% for TDF and 37% for LMV, p=0.7). Moreover, a positive correlation is found between serum HBV-DNA and HIV-RNA (Rho:0.26, p=0.02).
By analyzing serological markers, anti-HBs<50mIU/ml combined with Anti-HBc>15IU/ml is predictive of cryptic HBV viremia (63% of patients with anti-HBs<50IU/ml+AntiHBc>15IU/ml have HBV-DNA>1 IU/ml vs 26% without this combination, p=0.046, OR: 4.7[1.1-21.7]). The sequences of HBsAg MHR are obtained for 5/24 patients with cryptic HBV viremia, showing immune-escape mutations in two of them.
Conclusions: ddPCR is a valuable assay for detecting cryptic serum HBV-DNA in the setting of anti-HBc positive/HBsAg-negative patients with HIV infection. The integration of innovative serological and virological markers can help identifying patients with minimal HBV replication, thus optimizing OBI diagnosis

Cancers in HIV

P 8 THE MULTIDISCIPLINARY GROUP FOR HPV RELATED DISEASE AND STD IN AZIENDA OSPEDALIERA UNIVERSITARIA PISANA (AOUP) CISANELLO. AN OPPORTUNITY FOR HIV AND HIV AT RISK PEOPLE

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Background: The recent burden of STD and HPV-related diseases requires a multidisciplinary approach to identify and treat lesions, risk factors, comorbidities, and to prevent recurrences or new infections, mainly in males and in MSM. HPV related not-cervical cancer is on the rise, and HPV need a defeminization to be efficaciously fought.
In our Hospital specialists have joined to offer people a quick and easy way to approach and prevent HPV-RD, centric the patient.
Material and methods: Multidisciplinary visits are held one morning of the month, at the practices of the SOD of Proctology, AOUP Cisanello Pisa. Patients need Basic Physician or Specialist prescription and receive specialist evaluation (proctologic, infectious, dermatologic, urologic, orl) including anoscopy, biological samples and STD-counseling in the same morning or dedicated days. Further investigations and audits are scheduled at the end of the first visit. We record sex, age, HIV serology, Syphilis, other STD, and results by anal pap smear or histologic examination in patients undergoing surgical excision; patients followed according to guidelines (Robert Jr et al. WJGO 2017 15:50 -612017:15:50-61) HPV types is also detected at first and secondary controls. On every Thursday afternoon, a Clinical Microbiologist may take genital samples and processes them in the same week. Patients at risk for ORL HPV-RD (HIV+, presence of HRstrains in other sites, symptomatic, previous cervical lesions)underwent fibroscopy, gargle and brushing for citology and virology. HPV detection and genotyping were carried out in histologic samples by immunohistochemistry (p16) and in situ hybridization (HR and LR), while in cytologic by DNA PCR L1 Clinical Array™. In oral samples and mucosal buffers by two PCR-based methods: L1 Clinical Array, or Anyplex™ II HPV28 (Seegene) (19 HR HPVs and 9 LR HPVs by melting curve analysis). HPV9vaccine and PreP are proposed to eligible patients.
Results: From November 2015 to February 2020, 579 HPV-RD examinations were performed in 363 pts, 258 M and 105 F, av 40.6 + 13.04 ys. 102 pts were HIV+ 28,1% (11 F 91M, av45.235 ys), 193 HIV- (av 36.9 + 13.8 ys), 68 pts unknown or under detection.
Proctology: 218 pts had daysurgery/excision (relapse 16%). Data will be discussed.
Patients HIV+ presented with more and worse dysplasia vs HIV-, and generally have >1 genotype, according to literature. In HIV+ often HPV is detectable in multiple sites, like anal, ORL district and urogenital. Lue is more frequent in HIV+, People born after 1979 showed a decrease in HBV vaccinal protection under the threshold in over 25% of cases.
Conclusions: Multidisciplinary approach is really useful in HPV, mainly if HIV or other STDs coexist; allows early diagnosis and less invasive surgery and follow-up. This approach is an opportunity to offer people screening for other STD and PrEp in a friendly contest, to have counselling about their own risk for other STDs and eventually first or booster vaccination.

Cancers in HIV

P 9 NON-AIDS-DEFINING CANCERS IN A COHORT OF HIV POSITIVE PATIENTS

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cART has significantly reduced HIV morbidity and mortality over the years; in high-income countries, access to early treatment has led to a life expectancy almost comparable to general population. HIV patients have a greater tendency, compared to the general population, to develop cancer. Although this may be partly related to the increase in life expectancy, the complex interaction between immunodeficiency and oncogenic mechanisms, still remains in dark side. The spectrum of cancer diagnosis in the HIV population has therefore shifted from defining AIDS tumors (ADCs) to non-AIDS defining cancers (NADCs).
We conducted a retrospective cohort study from 1985 to 2019 in the Department of clinical infectious diseases of Ancona. We recorded cancers that developed during normal follow-up, both ADCs (Kaposi's sarcoma, cervical cancer, and non-Hodgkin lymphomas) and NADCs. We considered the demographic variables (age and gender), the risk factor for HIV infection (heterosexual, homosexual, IDU) and the presence of co-infections (HCV, HBV) and comorbidities. We assessed the CDC stage and the viro-immunological characteristics of the infection at the time of diagnosis of HIV and their stability in the last two years and, in those who developed cancers, the viro-immunological status at the time of diagnosis. In the oncological subpopulation, we also assessed the days passed since the diagnosis of HIV to the appearance of the neoplasia, the presence of metastases at the time of diagnosis and the onset of relapses. We also analyzed the cART regimen in use at the time of diagnosis of the tumor. Finally, we considered mortality one year after the onset of the tumor and we tried to establish whether the cause of the death was related to the cancer.
Out of a total of 396, 77 patients developed a tumor: 24 were classified as ADCs (31%), 53 as NADCs (69%). At one year of follow-up from the diagnosis of NADCs, 43 patients are alive and 10 are dead. 70% of the deceased patients had HIV-HCV co-infection (p 0.002). As could be expected, the presence of metastasis at the diagnosis of the tumor correlates with a higher mortality (p 0.009). An interesting aspect concerns the stability of CD4 + lymphocytes in the last two years (p 0.04), judged as protective factor against mortality (93% in live patients vs 81% in deceased patients). NADCs were found to be associated with higher mortality in the general HIV population (p <0.001). In contrast, ADCs are linked to a better prognosis and lower mortality for the clinical response of these neoplasia to cART.
Current epidemiology suggests that people who lived with HIV appear to be more predisposed to develop NADCs cancers. The management of the HIV patient continues to evolve, assuming today also a multispecialistic and holistic connotations. Therefore the exclusively infectious approach that was predominant until a few years ago, has now given space to screening, prevention, lifestyle changes in the more complete way.

Cancers in HIV

P 10 CASE REPORT ON ONCOPATHOLOGY IN HIV-INFECTED PATIENTS

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Currently, in the practice of the infectious diseases specialist, the presence of comorbid pathologies increases the number of complications, worsens the prognosis, and requires a non-standard approach in treating patients. Consideration of secondary diseases of non-infectious origin, such as cancer, cardiovascular, renal, hepatic, CNS disorders, and others, are becoming increasingly important for HIV-infected people. The observed mortality from oncopathology in HIV-infected patients for a period of three years did not reveal an increase in oncopathology. The observation of the HIV population revealed an interesting clinical case, which is presented below.

Patient N. born in 1973 Diagnosis. HIV infection stage 4, focal tuberculosis of the right lower lobe (2010), ovarian cancer (2013). Registered in the AIDS center since 2011. Infected sexually from her husband. Has 4 children.

After the registration the following antiretroviral therapy was prescribed : Zidovudine (AZT)+Lamivudine(3TC)+Efavirenz (EFV). The CD4 count was 84 cells / ml. Currently receives Tenofovir(TDF) +Lamivudine (3TC)+Efavirenz (EFV) . CD4 count was following:

2011 CD4 84 cells /ml
2012 CD4 - 174 cells / ml
2013 CD4 - 188 cells / ml
2014 CD4 - 151 cells / ml
2015 CD4 - 191 cells / ml
2016 CD4 -197 cells / ml
2017 CD4 211 cells / ml;
2018 CD4 - 233 cells / ml. Viral load is less than 500 copies / ml.

In 2013 presented with complaints of lower abdominal pain, vaginal discharge, increased weakness, decreased physical performance. After visiting the gynecologist, the patient was referred for consultation with an oncologist. When examined by oncologists, the following diagnosis was established: ovarian cancer T3NXM0 III stage.

Complications: Ascites, Left Ureterohydronephrosis

Concurrent condition: Urolithiasis

The patient was hospitalized in the Department of Oncogynecology.

The abdominal laparacentesis was performed, 6 litres of ascitic fluid were evacuated. Consulted by a chemotherapist; recommended neoadjuvant chemotherapy. Antiretroviral therapy was continued. During the treatment patient's condition has improved. At the present time, in 2019, the patient feels satisfied, has no complaints.

Conclusion: The creation of new diagnostic and treatment algorithms is the basis for the provision of medical care to HIV-infected patients with comorbid pathology.

Cancers in HIV

P 11 PRIMITIVE NHL OF BONE IN AN HIV PATIENT: CASE-REPORT AND REVIEW OF LITERATURE

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Background: Primary non-Hodgkin lymphoma of bone (PLB) is a rare disease in the overall population but its incidence is two times higher in immunodepressed and HIV positive population. [1]
We present the case of an aggressive PLB in a 44 years old HIV-positive patient with persistent pain in the lower-extremities.
Materials and Methods: We reviewed all patient's medical records and the epidemiological and clinical data about PLB using PubMed®.
Results: The patient is a 44 years-old caucasian male that was diagnosed with HIV infection in 2010 but, according to previous guidelines on the management of HIV, was not treated when diagnosed. When diagnosed the patient had 748/mmc CD4+ (29%) and a Viral Load (VL) of 46.000 cp/mL (CDC A1). The patient was lost during follow-up and came back to our attention on February 2019, with persistent bone-pain followed by a radiological diagnosis of a pathological fracture of the femur associated with a visible mass. This mass was subjected to biopsy showing a Non-Hodgkin aggressive B-cell lymphoma of bone (IIE: CD20+, CD3-, CD138-).
It was followed by a PET that showed a high SUV (40) in the proximal third of the right femur and high captation in the inguinal and axillary regions.
The pathological fracture was stabilized with an osteosynthesis (ɣ-nail) and the patient was elected for chemotherapy using R-CHOP (Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone).
When diagnosed with PLB the patient was a CDC-stage C1 (CD4+ 678/mmc), hence he started ART using ABC/3TC/DTG (Triumeq®).
Chemotherapy was conducted from February to August 2019 (for a total of six cycles) and was complicated with the occurrence of upper extremities neuropathy (requiring pregabalin) and neutropenia (requiring G-CSF infusion).
One month after the end of CHT a follow-up PET showed a resolution of the pathological area in the right hip and was followed by consolidation radiotherapy.
The patient is continuing the emathological and virological follow-up, without any sign of relapse and with a good compliance concerning ART.
Conclusions: PLB is a rare disease that accounts for less than 2 percent of all lymphomas in adults [2]. It is estimated that 3-7% of primary bone tumours are PLB [3] and that 3-5% of all extranodal non-Hodgkin lymphomas are lymphomas of the bone [4, 5].
Most of PLB are diffuse large B cell lymphoma (DLBCL) [6]
The mean age at presentation is 44 years and the M:F ratio is 1.8:1. [7]
The most used treatment for PLB is a combination of lymphoma-specific chemotherapy and radiation-therapy. [8] Overall-survival (OS) is improving overtime but data about HIV-positive population are unknown.
Our case-report shows a similar pattern of manifestations with the ones in literature.
Our study also shows that PLB should be considered as a possibility when an HIV-positive patient complains of persistent bone-pain.

Cancers in HIV

P 12 ALEXITHYMIA AND CANCER-RELATED MORTALITY IN HUMAN IMMUNODEFICIENCY VIRUS-INFECTED PATIENTS: AN ITALIAN MULTISITE PROSPECTIVE COHORT STUDY

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Background: The combined effects of HIV and cancer on mortality are incompletely understood. Both diseases can markedly increase mortality, contributing to a particularly elevated risk of death for HIV-infected people diagnosed with cancer. Elevated cancer-related mortality (CRM) in HIV-infected people may be due to several factors including lifestyle and behavioral factors. In this multicenter cohort of HIV-positive patients we investigated longitudinal predictors of CRM, including several psychological factors.

Material and methods: We carried out a prospective study to evaluate clinical predictors of AIDS-defining cancers (ADCs) and non-AIDS-defining cancers (NADCs) mortality during a 10-year follow-up. HIV patients were consecutively enrolled at the Infectious Disease Units of six Italian regions. Patients were characterized for sociodemographic, clinical, viro-immunological and psychological parameters. The 20-item Toronto Alexithymia Scale (TAS-20) was administered to evaluate alexithymia, Beck Depression Inventory-II (BDI-II) for depression, and DS-14 for Distress Personality (Type D). CRM after enrollment was censored at March 2018. Cox proportional hazards analysis was used to calculate the adjusted relative hazards of CRM by each variable. Nelson-Aalen method was used to test for mortality differences and hazards were compared using the log-rank test.

Results: Between 2008-2018, a multicenter cohort of 712 subjects (75.3% males, aged 46.1 ± 10.1 years) was recruited. Of them, 91.4% had been on HAART for 103.3±84.5 months. Mean CD4 T-cell counts at enrollment were 640.5 ±360/mmc. Seventy-two patients (10.7%) had malignancies at baseline, 57.5% of which ADCs, and 42.5% NADCs. The mean follow-up was 4.3 ± 2.6 years. Twenty-two cases (3%) of CRM were recorded during the follow-up. The overall incidence of CRM was 0.67 per 100 person-years. At univariate analyses, AIDS diagnosis at baseline, suboptimal adherence to HAART (less than 95% of the doses), lower CD4 T-cell count, and alexithymia were significantly associated with CRM (all p<.001). In the Cox proportional hazard model, AIDS diagnosis (hazard ratio [HR],6.97; 95% CI, 2.3–21.2; p = .001), suboptimal adherence (HR, 4.61; 95% CI, 1.8–11; p = .002), and alexithymia (HR, 5.23; 95% CI, 1.8–16; p = .004) remained independently associated with CRM. The incidence rate of CRM was 1.52 per 100 person-years in alexithymic patients vs. 0.22 in non-alexithymic. Nelson–Aalen plots of cumulative hazard (Fig.1) showed that CRM incidence was significantly higher in the alexithymic group (log rank test, p < .001).

Conclusions: This is the first study to examine the prospective association between psychological factors and CRM in a multisite cohort of HIV-positive patients. This result provides further evidence of the impact of alexithymia on health outcomes in the context of HIV infection.

Cancers in HIV

P 13 KAPOSI SARCOMA AMONG AIDS-PRESENTERS IN MODENA: COULD IT BE A CLUSTER?

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Background: Kaposi sarcoma (KS) is an AIDS-related tumor associated with HHV8 infection that typically occurs in patients (pts) with low CD4 cell count. The presence of a high number of cases in Modena HIV Clinic during the last two years led us to investigate this phenomenon.

Patients and methods: All new diagnosis of HIV infection during the period 02/2018 to 08/2019 in Modena were collected from Regional HIV Surveillance System. Serum samples of all patients with KS diagnosis were obtained and tested for HHV8 quantitative DNA assay and genotyping. HHV8 genotyping was conducted at the Virology Laboratory of Pitié-Salpêtrière Hospital in Paris by ORF-K1 (or VR1) Sanger sequencing.

Results: During the study period, 10 cases of KS out 75 pts with new diagnosis of HIV infection (13.3%) were reported. In the previous 4 years, 2 cases out of 213 HIV diagnosis were identified (0.94 %).

All pts were Italian MSM, with a mean age of 41 y. o. (range 25 – 60), 3 were excluded from the analysis due to loss of follow up (1 patient) or death for other causes (2 patients). Median CD4 cell count at baseline was 48.0 cells/ml (IQR 25 – 150). INSTI were prescribed in 6, and PI in one. Six showed a rapid viro-immunological response, with sharp decrease HIV RNA in one month and a median increase in CD4 of 82 cells/mmc (IQR 52 – 148), while the median CD4/CD8 ratio remained 0.13 (IQR 0.03 – 0.26).

All 7 patients were diagnosed for cutaneous lesions, 5 patients had mucosal involvement, with gastrointestinal lesions in 3. At baseline a quantitative HHV8 VL was detectable in 5 patients: 2601, 1331, 662, 140, 140 copies/ml, respectively. A1, A4, B1 and C2 HHV8 subtypes were detected using DNA sequencing in 4 viremic patients; in the remaining the assay was not conclusive for low viremia. A clinical worsening of KS lesions occurred in 4 patients, all treated with INSTI regimen, after one month of ARV: new cutaneous lesion onset or extension of the previous (1 patient), nodular progression of mucous lesions (1 patient), or both (2 patients). One of the latest, with ocular and pulmonary involvement, underwent chemotherapy, the other 3 improved spontaneously. In 2 out of the 3 patients with higher baseline HHV8 viremia a significant reduction of VL was not observed at one-month follow-up.

Conclusion: Despite a high number of KS in a short period of time may suggest a cluster of infection, this was not confirmed by either epidemiological or phylogenetical data. IRIS was frequent with progression of the neoplasm, even if only one patient underwent chemotherapy. High HHV8 baseline VL and no spontaneous clearance after ARV initiation seem to be risk factors for KS progression. The role of specific antiretroviral drugs should be evaluated.

Cancers in HIV

P 14 ORAL HUMAN PAPILLOMAVIRUS (HPV) DETECTION IN THE CONTEXT OF THE MULTIDISCIPLINARY HPV GROUP IN AZIENDA OSPEDALIERO-UNIVERSITARIA PISANA (AOUP): A SCREENING OPPORTUNITY FOR HIV+ AND OTHER AT RISK-PATIENTS

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Background: Human papillomavirus (HPV) is recognized as an important risk factor for non-cervical cancer, and in particular, in the field of the head and neck oncology, in oropharyngeal HPV-related squamous cell carcinoma (HPV-OPSCC). Although the natural history of HPV-OPSCC is not clearly delineated, it is presumable that exposure to HPV and HPV oral/oropharyngeal chronic infection could be underexplored risk factors for oncogenesis. Patients with high risk of oral/oropharyngeal HPV positivity, like HIV positive patients, should be individuated and followed more closely than others. Therefore, in our Hospital, patients at high risk exposure for HPV are taken in charge by the ENT specialist and evaluated in a standardized fashion, independently from local signs or symptoms.
Methods: On the basis of the existing literature, we adopted some inclusion criteria to select patients considerable at high risk for oral/oropharyngeal HPV: HIV patients, presence of High Risk strains in other sites, with oral/oropharyngeal symptoms and/or previous cervical lesions. All patients underwent complete ENT fibroscopic evaluation and oral wash (oral gargles) for the individuation of HPV, and demographic data (sex, age, HIV positivity) and some personal information (sexual orientation, smoke exposure, previous tonsillectomy, CD4 cell count, HPV-vaccination status, HAART therapy) were registered. The oral fluid samples were used for DNA extraction and conventional PCR amplification; HPV genotyping was performed by hybridization.
Results: We collected data from a total of 76 patients (19 F; 57 M), of which 27 were HIV-positive and 49 at-risk HIV negative. HPV genotyping revealed 11 samples were positive for HPV DNA; some samples were positive for more than one genotype. The major high-risk HPV types identified were 16, 33, 35, 53, 59, 66.
Conclusion: Our preliminary data show that there was no significant difference between the HIV group and non-HIV HPV-high-risk group. Surely more data are necessary to clarify the natural history of oral HPV infection, that is currently mostly unknown, and to define the use of the oral wash as a potentially diagnostic tool and therapeutic tool

Cancers in HIV

P 15 HCC RECURRENCE 8 YEARS POST LIVER-TRANSPLANT WAS LINKED TO HEPATITIS DELTA REACTIVATION IN A PERSON LIVING WITH HIV

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A 59 years old man, previous IDU was diagnosed with HIV in 1984 and then documented HBV, HDV and HCV co-infection.
In 2012 he was referred to our center to undergo orthotopic liver transplantation (OLT) for decompensated cirrhosis and bifocal hepatocellular carcinoma (HCC). He was treated with tacrolimus immune-suppressive (IS) therapy and TDF/FTC and RAL as ARV, then switched to E/C/F/TAF and TAF/FTC and RAL. After OLT he achieved HCV SVR with no anti-HCV treatment. HBV-HDV relapse was prevented with monthly HBsAb infusion (hepatect) with target of 200 IU. In May 2018 he was found HBsAg positive regardless HBsAb infusion, therefore interrupted. In June 2018 HDV-RNA turned detectable up to 100238 copies/ml in September 2019. HBV-DNA remained undetectable. Hypertransaminasemia (ALT=550 UI/l) occurred in March 2019. Hepatic stiffness was 5,8 kPa, measured with Fibroscan ®, excluding liver fibrosis.
Liver biopsy proved chronic hepatitis with focal areas of necrosis, macrovesicular steatosis in 20% of hepatocytes, occasional presence of glycogenated nucleous, no iron and copper accumulations, immunicytochemistry negative for HBsAg and HBcAg. Moderate activity hepatitis, moderate fibrosis with presence of porto-portal septa. No signs of acute or chronic organ reject. Degree (A) 2+ (B) 1+ (C) 2+ (D); total=7. Stage=3 sec. Ishak. Fibrosis progression was document in one year until stiffness 14 kPa. Abdominal CT scan found a 25 mm adrenal lesion suggestive of cancer. Differential included neuroendocrine tumors or HCC relapse. Tumor was excided in September 2019 and proved undifferentiated HCC. HBV-DNA was found (PCR) in tumor cells; sequences gene excluded HBsAg gene-coding mutations. A rapid HBsAg decay was found after surgery becoming undetectable at week 3, with a parallel HDV-RNA decrease, undetectable at month 2. Transaminasemia reduced as well as liver stiffness measured with Fibroscan® (10,9 kPa at month 4). After the HCC recurrence, IS therapy was switched to everolimus.
Discussion: We described a rare case of a post-OLT HDV-related hepatitis linked to the occurrence of HCC metastasis producing HBsAg. The rapid decay of HBsAg few days after tumorectomy proved that HCC metastasis was the site of HBsAg production. We speculate that HDV replication in the tumor drove HDV-related hepatitis in the transplanted liver.
We formulated two possible explanations to justify why the tumor expressed HBsAg but was unable to replicate HBV: either HBV-DNA was integrated in the HCC metastasis or TAF prevented replicative cycles. We cannot neither prove nor exclude the role of HIV infection and immunologic disarrangements associated with this disease or with IS therapy in the pathogenesis of late occurrence of the secondary tumor 8 years post OLT. Everolimus's immune-suppression, although seldom used in HIV setting is supported by evidence of its efficacy in preventing solid tumors presentation or its recurrence in the post-transplant period in general population.

Cancers in HIV

P 16 EPIDEMIOLOGICAL ANALYSIS FROM A NEWLY ESTABLISHED ANAL HPV SCREENING AMBULATORY

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Background: Sexual behavior, age and alterations of immune response represent the most relevant risk factors for the risk of HPV infection and, ultimately, HPV related malignancies. Almost all cases of Squamous Cell Carcinoma of the Anus (SCCA) are related to anal HPV infection. Italian HIV guidelines recommend screening for anal cancer in high risk subpopulations, particularly Men who have Sex with Men (MSM), through the early diagnosis of HPV related anal dysplasia. Here we report the initial experience of a newly established anal cancer screening ambulatory in Rome.
Materials and methods: Data from 135 HIV+ MSM and 8 HIV+ men to women transgender individuals were included in the present study. Participants underwent thorough evaluation of HPV risk factors, anal swab for HPV detection and genotyping, anal cytology and High Resolution Anoscopy (HRA); anal biopsies were collected if suspected dysplasia were visualized during HRA.
Results: Mean age of enrolled subjects was 43 years old, median of CD4 nadir was 202 cells/mm3, median CD4 at the moment of the screening was 700 cells/mm3. Anal HPV infection was found in 49% of patients. 16.9% of participants showed high risk HPV genotypes, 19.2% showed low risk genotypes, HPV genotypes of undefined risk category were found in 8.6% of patients and infection caused by multiple genotypes was observed in 55.3% of HPV positive subjects. Anal cytology showed squamous intraepithelial lesions of any grade in 47.6% of participants (46% Low Grade Squamous Intraepithelial Lesions-LSIL and 1.6% High Grade Squamous Intraepithelial Lesions-HSIL). HRA guided biopsies showed a LSIL rate of 35% and a HSIL rate of 8%. The prevalence of HPV specific risk factors was similar between participants <45 or 45 years. Multivariate analysis showed previous or actual anal or genital condylomatosis as risk factor for the presence of HSIL (p= 0,008). A lifetime number of sexual partners >500 and any alteration found at digital ano-rectal examination resulted as risk factors for the presence of LSIL (p= 0,012 and 0,05).
Conclusions: Anal HPV infection and HPV related anal dysplasia are common among HIV+ MSM and screening programs should be implemented in order to reduce the risk of SCCA in high risk subgroups.

Gender issues

P 17 BEHAVIOURAL AND AWARENESS CHANGES IN A HIV PREVENTION PROGRAM BASED ON WOMEN EMPOWERMENT IN UGANDA

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Background: Uganda has among the highest women HIV incidence rates worldwide: HIV and STIs infections among <25 years old are 4 times more frequent in women than in men. HIV stigma is still a burden, resulting in low testing and negatively affecting the quality of life. Cultural and gender roles put women at increased HIV risk, so empowerment and behavioural programs are starting being implemented in such areas to boost agency, self-awareness and information about prevention to this vulnerable group.

Material and methods: In a community-outreached cohort of women of a rural area of Gulu, Northern Uganda, a self-reported survey on sociodemographic, sexual activity, HIV/AIDS awareness, stigma and sexual self-determination (110 questions) was offered as well as 4th generation antigen/antibody combination HIV-1/2 immunoassay, serologic test for syphilis (treponemal test), HBV (HBsAg and Anti-HBsAg) at baseline and 6 months apart up to 3 years.

In between timepoints, several prevention and behavioural initiatives about HIV, STIs and sexual empowerment were held on a weekly/monthly basis, performed by same community peer-educated women and dedicated staff. Trajectories of sexual behaviour and awareness across the first time point (baseline to 6 months) within "Pe Atye Kena" study are herein reported. SAS software was used. In addition to descriptive statistics, crosstabs have been done. Statistical association among variables was evaluated by Chi square.

Results: From April to October 2019, data about 427 women aged 18-49 years old were collected. 56% were <30 years old. 50% had primary-level education; 15.6% had experienced sexual assault. In 6 months the working rate has risen from 63,9% to 65,6% and a higher proportion of women were in a stable sexual relationship (76.0% vs 77.8%). Among the high risk behaviours, the alcohol use during sex (30,2% vs 19,7%) (p <0,001) and current relationship with older sexual partner (91% vs 77.8%, p 0,001) decreased over time and consistent use of condom decreased from 32,3% to 21,1% (p 0,002). The proportion of women doing transactional sex increased from 5.4 to 6,6%, with a trend toward an increased use of condom in this subgroup. Conversely, the perception about their sexual partner HIV status changed from 4% of women thinking their partner was HIV positive at baseline to 4,9%. HIV/AIDS awareness changes are summarized in Table 1.

Conclusions: These results showed a positive impact on awareness about HIV transmission and prevention of a short-period intervention, while initial, but still inadequate positive changes on behaviours occurred. A significant reduction in HIV-related stigma was observed. Cohort sexual self-determination is improving: women perception about consent in sexual relationships is shifting, although they are still tangled with their cultural standard. These results highlight how prevention strategies should be long lasting and multifaceted, including both behavioural and cultural intervention.

Gender issues

P 18 THERAPY BURDENS OF ITALIAN WOMEN LIVING WITH HIV - FINDINGS FROM THE POSITIVE PERSPECTIVES 2 STUDY

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Background and Objectives: Women are under-represented in clinical research despite the fact they face specific challenges related to antiretroviral treatment (ART), including difficulties in adherence, management of side effects, treatment preferences. A better understanding of ART-related women's challenges is needed.
Materials and Methods: Positive Perspective 2 is an international survey of PLHIV aged 18+, on ARV conducted between April/August 2019 in North and South America, Europe, Russia and in the Asia Pacific region. In total, 24 countries were represented reaching a total sample size of 2112 interviewed. The Study was run by ViiV Healthcare in collaboration with an international, multi-disciplinary Advisory Committee of experts, which includes PLHIV, patient group representatives and HIV physicians. A multi-mode recruitment approach was used, but subject to quota boosts for three specific cohorts: newly diagnosed, women living with HIV and people aged 50 or over. Here we propose a sub-analysis of the Italian women participants. Data were analysed using descriptive statistics.
Results: 120 PLHIV completed the survey in Italy, that is 5,7% of global respondents. Of these, 20% (n = 24) were women, with a mean age 40,8 (vs. overall 43,4). Sample demographics in Table 1. Mean time since HIV diagnosis was 15,8 years (50% diagnosed before 2006). A relatively high proportion of respondents (38%) reported having a detectable viral load. 45% report very or quite good health overall, only one out of four with no co-morbidities. 38% taking a Single Tablet Regimen (HIV therapy). The most common reasons for having switched medications (multiple-choice allowed) were: reducing severity and frequency of side effects (women vs men: 45% vs 59%), reducing the number of pills (resp. 50% vs 32%) reducing the number of medicines (35% vs 28%), controlling viral load (25% vs 22%), managing drug-drug interaction (20% vs 13%), reducing costs (20% vs 6%). Social aspects which may be associated with women vulnerability are: change of work aspirations because of HIV (women vs men: 67% vs 35%), uncertainty in future planning (resp. 50% vs 20%). Moreover, higher level of stress compared to men if someone founds HIV pills (women vs men: 54 % vs 40%) suggest how diminishing taking medicine burden could play a role for improving the quality of life of this population.
Conclusions: The sample of Italian women participating to the Positive Perspective 2 Study shows awareness about the HIV therapy taken. Next to the well-known need for better tolerability, reducing the number of pills and ARV's both emerge as possible matters to be improved. Interestingly, reducing medicine taking burden could be a specific strategy for this population for improving the quality of life.

Gender issues

P 19 TRANSGENDER PEOPLE AND HIV

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Background: In 2017, WHO included among the priority objectives that of promoting effective actions aimed at protecting the health of transgender people.
In Italy there is no effective planning and health surveillance aimed at the transgender population, in particular those HIV +, nor evidence on elementary data (life expectancy, prevalence and incidence of particular pathologies), in the absence of estimates on the number (it is estimated a total of 400,000 transgender people, no estimate on HIV).
At the 22nd IAS, the need to pay more attention to sex workers and MtF was highlighted, more at risk than the general population.
Material and methods: The project, in partnership with Istituto Superiore di Sanità, SIMIT and CEST, aimed at:

- identifying main issues and evidence starting from the point of view of transgender people;
- identifying the methods of data collection and clinical features in the SSN and infectious diseases field;
- producing an estimate of the prevalence of HIV among transgender people in Italy.

The actions included:
context analysis (gray and regulatory literature), national survey for associations representing transgender people, national survey of infectious disease centers, service design.
Results: The survey addressed to the associations showed that:
there are few information campaigns aimed at prevention (AIDS, IST and testing);
although aware that the transgender population is among the risk groups, there is a strong impact of double stigma;
there is a high percentage of transgender people who are sex workers.
The survey at the infectious disease centers showed that:
there is no homogeneity in the distribution of patients taken in charge by the centers, divided into those who have many (greater than or equal to 100) and those who have few (about 10).
In general, services offered to transgender people are the same as those offered to other patients (there are no specific routes or visits);
most of the transgender people in charge are MtF.
Conclusions: In the social sphere, there is a double stigma, driving a high level of privacy about one's identity and clinical condition; this leads to "migrations" towards clinical centers not related to one's own territory of residence, probably chosen through word of mouth within the community.
Transition pathways influence the decision to test and proceed with treatments: for fear that antiretroviral therapy may interfere with hormonal therapy, the first is preferred to the detriment of the latter, with important consequences in terms of the effectiveness of treatments and public health.
Considering the 90 90 90 objectives, the channels for accessing testing and adherence to therapies are weak; however, retention in care appears excellent.
The lack of a registry that recognizes transgender people is a major obstacle to the knowledge of a vulnerable group, affecting clinical efficacy.

Gender issues

P 20 HIV-POSITIVE TRANSGENDER PEOPLE IN FOLLOW-UP AT AN ITALIAN SINGLE TERTIARY CARE HOSPITAL IN FLORENCE: A CROSS-SECTIONAL STUDY

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Background: According to UNAIDS, Transgender (TG) people are considered as a group that is particularly vulnerable to HIV and frequently lacks adequate access to the health-care service. Complete epidemiological data and antiretroviral therapy (ART) outcomes in the TG population are still scarce in Italy.
Objectives: Bridging the lack of epidemiological data on TG people in our area and assessing some aspects of their vulnerability to HIV/AIDS.
Methods: This is a mono-centric cross-sectional study. We included all transgender-people that live with HIV followed-up on 31/12/2019 at the Department of Infectious and Tropical Diseases, AOU Careggi (Florence, Italy). Demographic, clinical and laboratory data were analyzed. Categorical variables were analyzed with X2/Fisher's exact test and continuous variables with the Wilcoxon signed-rank test for paired data. We defined an "undocumented migrant" as a non-EU citizen without a residence permit and indigent.
Results: Overall, 69 patients were included. All of them were transgender women with a median age of 39 years (IQR 28-50). Forty-five patients (65.2%) reported being sex workers. Fifty-two were foreigners (75.3%) and 35 (50.8%) came from Peru. Among the foreign-born patients, 36 (69.2%) were undocumented migrants and nearly half [24 out 52 (46.2%)] had started ART in the country of origin. However, upon arrival in Italy, they interrupted treatment due to bureaucratic delays to obtain healthcare assistance as a Temporarily Present Foreigner (STP). One third ([22 (31.8%)] are smokers, 5 (7.2%) had a history of intravenous drug use (IVDU). A Previous sexually transmitted disease (STD) was reported in 45 (65.2%). Many [23 (33.3%)] take estrogen-based therapy, hardly ever prescribed by an endocrinologist [(9 out of 23 (39%)] and 24 (34.8%) had a diagnosis of AIDS mostly due to tuberculosis [13 (54.2%)]. All patients except one (who refused therapy) were on ART. At the survey, median CD4 cell count was 633 cells/mm3 [IQR 420-972], and median viral load (cp/mL) was <50 cp/mL in 53 (78.7%). The median CD4 count and viral load at diagnosis were available only for 34 (49.2%) patients. Missed appointments were recorded in the last year for 31 (44.9%). More detailed population characteristics are shown in Table 1.
Conclusions: Most TG people in follow-up at our clinic are made up of Latin Americans especially Peruvians. At arrival in Italy, sex work is widely practiced; foreign-born TG people often lack previous health-care records and they frequently have interrupted ART. Overall, during the follow-up, missed appointments are very common. Made-easy healthcare pathways are desirable for this fragile population.

Gender issues

P 21 HPV AND BACTERIAL VAGINAL INFECTION IMPACT ON IMMUNE SYSTEM IN A COHORT OF HIV FEMALE POPULATION UNDER SUPPRESSIVE ART

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Introduction: Relation between HPV infection and bacterial vaginal infection is not well known.Some data show that these infections are closely interconnected in healthy and HIV female population.Moreover, HPV infection rate is higher in HIV than in healthy women. The first line of defense against HPV is the innate immune system responsible of recognition, persistence and elimination of the virus. The aim of our study is to explore the role of mediators of immune response in a cohort of HIV positive women and healthy donors.

Methods: We enrolled 30 healthy women (HD) and 23 clinically stable, receiving effective ART, HIV women with no statistical differences in terms of age.

We analyzed lymphocyte subpopulation (CD4, CD8) and NK cells on blood samples and IL-1beta on vaginal liquid (VL) and plasm. Moreover we collected vaginal and cervical swabs to detect HPV DNA, common vaginal germs and sexual transmitted bacteria and we performed PAP tests. We compared two populations (HIV vs HD) to each other and these subgroups: HIV/HPV+, HIV/HPV-, HD/HPV+ and HD/HPV- denominated as the "HPV subgroups" and HIV/bacteria+, HIV/bacteria-, HD/bacteria+, HD/bacteria- called as the "Bacteria subgroups". Not parametric test were used for statistical analysis.

Results: No statistically difference in terms of HPV prevalence in HIV and HD is observed (65% vs 40%, p>0.05). Regarding prevalence of bacterial vaginal infection is higher in HIV(78% vs 40%, p=0.005). Even the association of coinfection of HPV and bacteria is statistically different in these populations(p=0.008).

As expected, CD4 counts is higher in HD (p=0,03) and CD8 is higher in HIV (p=0,004). Analyzing CD8 counts in HPV and Bacteria subgroups we observe difference between HIV/HPV- and HD/HPV+ (p=0,03) and between HIV/Bacteria+ and HD/Bacteria+(p=0,03).

NK cells count is higher in HD compared to HIV (p=0.01) and this difference is stressed in comparison HD/Bacteria- with HIV/Bacteria-.

IL-1beta plasma level is higher in HIV than in HD(p=0.001), while in VL a lower trend is observed (p>0.5). Analyzing the HPV subgroup, a higher plasmatic levels is in HIV+/HPV+ compared to HD/HPV+ (p=0.01). No differences in terms of IL -1beta in VL in the HIV women and HD were observed neither in the subgroups.

The PAP tests show HSIL (High grade Squamous Intraepithelial Lesion) in 1 case and 1 with undefined abnormalities in HIV (8,7% of HIV) and 2 cases of LSIL (Low grade)and 1 of ASCUS (Atypical Squamous Cells of Undetermined Significance) in HD (10%).

Conclusions: Higher prevalence of genital HPV and vaginal bacterial infection in HIV women than HD were observed. Even though in HIV a higher plasmatic IL1beta level in plasm was observed, this level does not reflect the level in vaginal environment that is similar to HD. Although HIV population is under suppressive ARV, the driving force seems to be HIV, not HPV neither bacterial infection, probably because at vaginal level not many cytological modifications were observed.

HCV elimination

P 22 QUALITATIVE ANALYSIS OF SIGNIFICANT CLINICAL EVENTS IN A COHORT OF PATIENTS AFTER DAA TREATMENT FOR CHRONIC HCV INFECTION AFTER VIROLOGICAL ERADICATION

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Background: Direct antiviral agents (DAAs) revolutionised treatment outcome of patients chronically infected by Hepatitis C Virus (HCV). Recently, data about metabolic changes after viral eradication have been published, such as cholesterol level increase and weight gain. However long-term data of incident and significance of clinical events in this population are lacking.
Methods: We performed a retrospective, longitudinal evaluation of patients who started treatment with DAAs from March 2014 to March 2018. As for clinical significant events we considered: malignancies (in addition to Hepatocellular Carcinoma, HCC), liver decompensation, ischaemic heart disease, stroke, bleeding (including variceal), and any cause death.
Results: 226 patients were included in our analysis. Seventeen patients were lost to follow-up, so outcomes were assessed for 209 of them. 159 patients did not report any significant clinical events. Overall, 68 clinical significant events were recorded in 50/209 (23.9%) patients. Among these, 33 (66%) were male and mean age was of 71 (standard deviation: 14) years. Fifteen out of 50 (30%) patients reported more than one clinical significant event. These events were: 24 cirrhotic decompensation episodes, 12 hepatocellular carcinoma, 11 non-liver cancer (2 colon, 1 brain, 1 ovarian, 1 breast, 1 non Hodgkin Lymphoma, 1 multiple myeloma, 1 pancreatic, 1 kidney, 1 lung, 1 myelofibrosis), 10 myocardial infarction, 8 deaths, 2 major bleeding, and 1 stroke. Cause of death was end-stage liver in 6/8 (75%) cases, in 1 case myocardial infarction and in 1 case brain cancer complication.
Conclusion: Our study showed that new significant clinical events in patients after DAAs treatment for chronic HCV infection were quite frequent notwithstanding sustained virological response. Continuous surveillance for these patients is needed especially as far as cancers and cardiovascular diseases are concerned.

HCV elimination

P 23 A FAST TRACK CITY MICRO-PROJECT TO ERADICATE HCV INFECTION IN PLWHIV

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Background: HCV co-infection is a frequent diagnosis in HIV infected subjects (PLWHIV). The availability of DAA (direct acting antivirals) for treating HCV infection and the possibility to extend treatment to all patients offer the opportunity to eradicate HCV in this population, however adequate surveillance and monitoring systems have to be implemented to demonstrate that this goal is achieved.
Methods: All HCV-RNA positive subjects in our cohort are offered DAA treatment and all patients are yearly screened for HCV. HCV-Ab (antibodies anti HCV) is performed if they are HCV negative and HCV-RNA if they ever had a HCV infection. All subjects with a previous HCV-RNA negative test who test again HCV-RNA positive are re-screened and re-treated with DAA.
Results: 2769 PLWHIV are actually actively followed in the cohort. Of them 74.5% are males, their median age is 52.8 years (IQR 46.8-57.8) and they are mostly Italian (87.2%) with sub-Saharan Africa and South America being the other more represented backgrounds (6.4% and 2.9%). Most of our patients acquired HIV infection through heterosexual intercourse (48.3%) being IVDU and MSM the other most frequent risk factors (26% and 25%). At the end of 2018 when the eradication project started 190/2589 (7.3%) patients were still HCV-RNA positive. In the first year of the project we screened or re-screened 1113 subjects including all new diagnosis of HIV (see figure). Overall, the new figure is 127/2769 (4.5%) HCV-RNA positive patients. This picture is the result of several factors (see figure):
117 new HCV-Ab patients joined the cohort;
100 known patients did not perform a visit in 2019;
30 known patients died;
9 patients with a previous HCV treatment and actual HCV-RNA negative test joined the cohort;
1 patient with a spontaneous healing of HCV infection joined the cohort;
108 known patients were treated with DAA and obtained SVR;
21 new HCV-RNA subjects joined the cohort;
15 HCV-AB positive subjects joined the cohort (HCV-RNA pending);
5 treated patients relapsed;
6 patients were re-infected.
Overall, more than one third of our current HCV-RNA positive subjects are newly diagnosed or re-infected PLWHIV.
Conclusions: These preliminary results indicate that HCV eradication micro-projects are feasible, but they also stress the necessity of a strict surveillance program to confirm HCV eradication in the PLWHIV population as the rate of new infections or re-infection is rather relevant.

HCV elimination

P 24 A PILOT INTERVENTION FOR HCV ELIMINATION AMONG MSM IN ROME: PRELIMINARY RESULTS

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Background: HCV prevalence among men who have sex with men (MSM) is not negligible. However and information on issue in Italy is scarce, particularly for HIV-uninfected MSM. Up to date, few target interventions have been conducted to identify and treat unaware HCV infected MSM, which represent an important reservoir for secondary infections. Thus, an HCV screening program targeted to MSM in Rome started in the summer 2019 in two hospital settings and in one urban community setting run by a NGO. The program is based on the offer of rapid tests for HCV antibodies and aimed to identify, linking to care and treating with DAA, MSM with undiagnosed HCV infection.

Methods: Adult (>18 years old) males reporting same gender-sex in the previous 12 months attending an HIV counseling and testing site and a STI clinic centers for HIV in Rome and one gay venue, have been invited to undergo, after providing informed consent, a free-of-charge rapid HCV Antibody test (OraQuick HCV®). For all participants, demographic, clinical and behavioral data using an anonymous questionnaire were collected. Free confirmatory standard serology tests were offered for those found as HCV antibodies reactive. Individuals with confirmed chronic HCV-infection, were referred though a dedicated "fast track" pathway for further clinical and laboratory assessment and DAA-treatment according to the national treatment guidelines.

Results: From July 2019, 677 MSM agreed to be screened for HCV infection (89.1% Italians, median age 41 years, interquartile range: 33-50), mostly (578, 85.4%) tested in the two clinical centers. HIV-infection was reported by 216 (31.9%) MSM and 53.0% of all participants of being previously tested for HCV. Overall, 3 MSM (all of them enrolled in clinical centers) were found to be reactive at rapid test, resulting in an overall prevalence of 0.4% (95% Confidence Intervals, CI: 0.1-1.2). Two out of three were HIV-infected: prevalence among HIV-pos was 0.9% (CI: 0.2%-3.0%) and 0.2% among HIV-neg/unknown (CI: 0.0%-1.1%). All cases were newly discovered HCV infection, and all were confirmed been viraemic (range 1.7x106-5.4x106 UI/mL) harboring HCV genotype 1a (2 cases) or 4 (1 case). All of them were linked to care, clinically assessed and started DAA treatment. One of them (HIV-neg, HCV 1a genotype) already ended treatment schedule and reached SVR after 8 weeks protocol with Glecaprevir/Pibrentasvir.

Conclusions: These preliminary data suggest feasibility and potential effectiveness of a program aimed at MSM living in Rome, which combines HCV screening and linkage to care with prevention strategies. Overall, HCV-prevalence in this population is quite low, although it is higher (more than 4 times) in those HIV co-infected. Supported by: Grant Gilead IN-IT- 987-5359, part of the LEGA-C™ program "Local Elimination Programs leading to Global Action in HCV".

HCV elimination

P 25 HCV ERADICATION IN PEOPLE LIVING WITH HIV IN SASSARI: THE FINAL COUNTDOWN?

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Background: with the availability of direct–acting antiviral agents (DAA), according to WHO, five million people with HCV-infection have been treated by the end of 2017. Among people living with HIV (PLWH) it is estimated that 15-30% have HCV coinfection. This population shows a rapid progression of hepatic fibrosis and a high morbidity and mortality. The aim of this study was to follow PLWH with an active HCV infection after 2018 and investigate the critical barriers to the eradication in these patients.
Methods: we performed a prospective study including PLWH with a positive HCV-RNA after 01/01/2018. Main characteristics of the participants at baseline were compared between those who have been treated or not, using chi-square or Mann–Whitney U test, as appropriate. Furthermore, we collected data about the HCV and liver disease. For the PLWH that have been treated we collected clinical data after 2, 4, 8, 12, 24 and 48 weeks after the DAA start.
Result: Seventy-three PLWH had a detectable HCV-RNA, their clinical characteristics are summarized in Table 1. Of these, 61 (83.6%) were eligible to receive DAA's treatment but only 53 (72.6%) were treated. Of these 53 patients, 30 (56.6%) have been treated with the combination Sofosbuvir/Velpatasvir, 16 (30.2%) with Glecaprevir/Pibrentasvir, 4 (7.5%) with Sofosbuvir/Velpatasvir/Voxilaprevir and 3 (5.7%) with the combination Elbasvir/Grazoprevir. At the 01/02/2020, 40 (75.5%) reached the sustained virologic response (SVR), 4 (7.5%) are still in treatment, 6 (11.3%) finished the DAA and are waiting the SVR and three (5.7%) patients failed the therapy. Two of them have been retreated with Sofosbuvir/Velpatasvir/Voxilaprevir. One of them has failed again, the other one has finished the therapy and SVR result is pending.
Over this two year of follow-up, three (4.1%) people died. Two PLWH, not treated for HCV, died for acute liver failure and encephalopathy. For the other patient, the cause of death is unknown.
At the 01/02/2020, 20 patients have not been treated. In 8 cases the treatment has not been started due to patient's choice. In other 8 cases, there is an important psychiatric condition which implicates a poor adherence to HIV treatment. The other 4 patients were difficult to reach and had lacking compliance.
Conclusion: in our center, we currently look after 645 PLWH, of which 242 (37.5%) are HCV-antibody positive. Most of them have been already treated or spontaneously cleared the virus over the years. In the last two years, we treated 53 PLWH meaning that only 8.2% (20 PLWH) still have a detectable HCV-RNA. To treat this kind of patient (psychiatric, people with poor adherence and those difficult to reach) we need to implement new strategies, such as directly observed treatment with the addiction centers' support or in synergy with home caring staff assistance.

HCV elimination

P 26 GLECAPREVIR/PIBRENTASVIR AND SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR FAILURE IN A YOUNG MAN WITH GENOTYPE 1A CONGENITAL HCV INFECTION: A CASE PRESENTATION

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Background: Direct-acting antivirals(DAA)are nowadays the first-line treatment for adult patients with hepatitis C virus infection(HCV). Despite their high efficacy,few cases of failure have been registered in the "real word" in historically difficult to treat populations such as patients with liver cirrhosis or previously exposed to antiviral therapy.Moreover few data are available for children,including those vertically infected. We reported a clinical case of virological failure after Glecaprevir/Pibrentasvir and Sofosbuvir/Velpatasvir/Voxilaprevir treatment in a young man without the common risk factor associated to DAA failure.

Case presentation: We present the case of an Italian 33-year old man born from a mother with HCV infection,without other risk factors for HCV infection,no significant comorbidities reported except for childhood appendicectomy,no chronic pharmacological treatments,no history of Interferon-based HCV treatment.HCV infection has been detected during childhood but patient was lost at follow-up,then admitted to our clinic in January 2018.

We assessed his liver function with standard tests: laboratory tests revealed normal AST/ALT levels,normal platelets level, renal function and glycometabolic profile.HCV RNA 9.669.613 UI/ml with genotype 1a.No viral coinfection.Fibroscan showed F1 fibrosis.Abdominal ultrasound was normal.According to current guidelines we started 8 weeks of Glecaprevir/Pibrentasvir treatment. It has been well tolerated and correctly assumed with a progressive reduction in HCV viral load until HCV RNA <12 IU/ml at the end of treatment (EOT).12 weeks after the EOT he did not achieve sustained virologic response (SVR) with new intense viral replication,same 1a genotype and no risk factors for a new infection.

At resistance analysis with deep sequencing we found a 174S resistance-associated substitution (RAS)associated with a reduced susceptibility to Telaprevir,no significant resistance to DAA was detected.

Then we started a second line 12-week treatment with Sofosbuvir/Velpatasvir/Voxilaprevir. As in the first DAA course, HCV RNA decreased rapidly with HCV RNA < 12 IU/ml after 8 weeks of treatment, at the EOT and 4 weeks after EOT. 12 weeks after EOT the patient relapsed, with a detected intense viral replication. A new resistance test showed the same 174S RAS, no DAA resistance was detected.

Conclusion: We reported a case of Glecaprevir/Pibrentasvir and Sofosbuvir/Velpatasvir/Voxilaprevir treatments failure with 174S RAS and no other DAA resistance mutations. Patient didn't show the common risk factor associated with DAA virological treatment failure and didn't report intake of other interacting drugs/substances.

We speculate that the long duration of HCV infection due to congenital acquisition could have expanded viral reservoir, thus requiring more time to be eradicated, especially for the high pre-treatment viral load. A longer treatment duration of 24 weeks with Velpatasvir/Sofosbuvir is now planned.

HCV elimination

P 27 ACUTE HEPATITIS C TREATMENT WITH DIRECT ANTIVIRAL AGENTS (DAAS) IN PATIENTS WITH SOLID ORGAN CANCER

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Introduction: Acute hepatitis virus C infection is largely asymptomatic with persistent infection developing in 43–86% of the cases. It is not standard practice to treat patients with acute hepatitis C, preferring to defer treatment in case of chronic infection. However in cancer patients, an impaired hepatic metabolism due to acute HCV infection may reduce chemotherapy tolerance and, on the other hand, delaying the start of chemotherapy until the end of the acute phase may worsen the outcome.

In this context we present two clinical cases of patients with solid organ cancer who, shortly before starting chemotherapy, have undergone acute HCV infection due to iatrogenic causes. The oncologists stressed out the need of reducing hypertransaminasemia and not delaying beyond the initiation of chemotherapy, thus these patients have been treated with direct antiviral agents (DAAs) during acute hepatitis C. Given the marked hypertransaminasemia, a Sofosbuvir/Velpatasvir 8 weeks regimen was chosen.

Case 1: A 73-year-old man diagnosed with esophageal squamous cell carcinoma, previously with normal AST and ALT values and negative HCV-Ab, performed oesophageal stent placement followed two months later by an hypertransaminasemia, compatible with acute hepatitis C (AST 233 UI/ml, ALT 446 UI/ml, HCV-RNA 7.480.000 UI/ml, genotype 2). Subsequently, the patient was treated with a Sofosbuvir/Velpatasvir 8 weeks regimen in off label mode and showed a normalization of the transaminases levels and undetectable HCV-RNA within four weeks, enabling a prompt initiation of chemotherapy.

Case 2: A 68-year-old man, diagnosed with adenocarcinoma in descending colon with negative viral hepatitis markers, underwent left hemicolectomy and three months later, prior to initiate adjuvant chemotherapy with Capecitabine, he presented with hypertransaminasemia (>20 ULN) with HCV-RNA 1,600,000 UI/ml, genotype 2, in the absence of further exposure at risk. A Sofosbuvir/Velpatasvir 8 weeks in off-label mode was effective and safe and the patient was able to start adjuvant chemotherapy.

Discussion: Cancer treatment in the setting of acute HCV infection represents a unique challenge for clinicians.

Last EASL recommendations state that DAAs treatment should be considered in acute hepatitis C as it results to be highly cost-effective compared with deferring therapy to the chronic phase; moreover it improves clinical outcomes and prevents the progression to chronic infection.

These two clinical cases demonstrated that an 8 weeks DAAs treatment (Sofosbuvir/Velpatasvir) has excellent tolerability and efficacy even in case of acute hepatitis C, with a sustained virological response (SVR 12) which allows a prompt and safer beginning of chemotherapy.

Conclusion: In our experience, DAAs treatment in oncological patients with acute hepatitis C has proven to be effective and safe, avoiding to delay chemotherapy with potential prognostic improvements.

HCV elimination

P 28 HOW TO ELIMINATE HCV IN PEOPLE WHO INJECT DRUGS? PRELIMINARY RESULTS OF A PROVINCIAL MULTI-TARGETED APPROACH INVOLVING THREE DIFFERENT SETTINGS: ADDICTIONS SERVICES, PRISON, OUTREACH MOBILE UNIT FOR ACTIVE USERS

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Background: People who inject drugs (PWID) are major targets of HCV micro-elimination programs.
Addiction services (SERD) are privileged settings for offering HCV screening, but inconsistent attendance for different reasons (e.g. incarceration or active drug use) could hamper subsequent linkage to care.
Methods: We set up a multi-targeted approach in Monza-Brianza province for offering systematic HCV screening to PWID in 3 different settings: SERD (5 services), prison, and a harm reduction mobile unit. A fast-track referral to Infectious Diseases (ID) Unit was arranged for SERD and mobile unit attendees, while inmates were treated in prison.
Results: Among 1458 PWID followed in external SERD, HCVAb was available for 480 individuals (32.9%) and positive in 238 (49.6%). After excluding 63 subjects (26.5%) with negative HCVRNA (spontaneous clearance or previously treated), 91/175 (52%) have been referred to ID (median time between first contact and first appointment: 17.5 days): 18/91 (19.8%) did not show up at the first appointment. Treatment-by-second-appointment was started in 56/73 (76.7%) PWID after a median of 85 days from the first appointment. The remaining 17 subjects still have forthcoming scheduled 2nd appointment. There were no treatment discontinuations. There were 2 reinfections, one of which with subsequent spontaneous HCV clearance.
In prison, where half of the population is followed by internal SERD, among 722 inmates, 532 (73.7%) have been tested for HCVAb (blood, saliva, or both): 47 were HCVAb positive (8.8%); of these, 12 (25.5%) had already cleared the virus, 6 (12.8%) have been released or transferred, 17 (36.2%) have been treated (including 2 attendees of external SERD who did not show up because of incarceration), for 12 (25.5%) treatment is ongoing.
Overall, glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, grazoprevir/elbasvir were used in 51 (69.9%), 19 (26.0%), 3 (4.1%) patients, respectively.
Outreach mobile unit for harm reduction is delivering sterile needles and distillated water to active users thrice a week since September 24th, 2019: in 4 months of activity there have been 1,237 contacts among 191 single users (6.5 mean contacts per user). Screening with rapid oral HIV/HCV tests will start on February 25th, 2020. Data on test acceptability and HCV prevalence in this marginalized population will be generated soon and presented at forthcoming ICAR (Fig1).
Conclusions: Screening and 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 SERD, and those referred but not linked. Conversely, once enrolled in ID service, PWID have shown a strong adherence to care. A comprehensive integrated network model of linkage to care that includes prison and, innovatively, a mobile unit close to a large open drug scene intercepting active drug users, could speed up the pace of HCV elimination in PWID.

HCV elimination

P 29 INNOVATIVE PROCEDURES FOR MICRO-ELIMINATION OF HCV INFECTION IN PERSONS WHO USE DRUG (PWUD)

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Background: People who use drug (PWUD) population is a key population in the global HCV control To evaluate the efficacy of an innovative model to eliminate HCV infection in a high-risk population of PWUD in a Service for Dependence (SerD)

Methods: between January 2018 and December 2018 a prospective, interventional, before and after study, based on the active and close cooperation between a SerD in Piedimonte Matese and Teano and the corresponding 3rd level units of Infectious Diseases in Caserta, Campania, Southern Italy, was performed. The pre-intervention period was defined as January-December 2017; the post intervention period as January-December 2018

Results: The subjects followed up at the SerD in pre-intervention and in post-intervention periods were 318 and 275. In the two period evaluated 135 (42.4%) and 118 (42.9%), respectively, were people who inject drug (PWID). The majority were males (90.6% and 91.3%, respectively) and young (median age 39 years, range 18-73; and 41, 20-74, respectively). The half of subjects in both observation period has been followed by the SerD from at least 10 years.

The Figure 1 shows the HCV cascade in the two periods considered considering all the PWUD population evaluated. Compared with the pre-intervention period the number of anti-HCV positive subjects tested for HCV-RNA was higher in post-intervention period (91% vs. 27%, p<0.0001). Compared with the pre-intervention period the number of subjects tested for HCV-RNA increased in the post-intervention period (91% vs. 27%, p<0.0001), such as the number who started DAA. In fact, of the 18 HCV RNA-positive subjects in pre-intervention period only 3 (16.6%) started DAA, a percentage decisely lower than that observed after the start of the program, 63 (84%) of 75 subjects (p<0.0001) (Figure 1). Considering only the PWID, at high risk of HCV infection, 135 subjects in pre-intervention and 118 in post-intervention period, the number of subjects tested for anti-HCV incresed in the post-intervention period (89.8% vs. 74.1%, p<0.001), with a higher prevalence of anti-HCV-positive subjects (81.1% vs. 60%, p<0.001) (Figure 2). Moreover, compared with the pre-intervention period the number of subjects tested for HCV-RNA significantly increased in the post-intervention period (94.1% vs. 33.3%, p<0.0001), such as the number who started DAA (Figure 2). In fact, of the 55 HCV RNA-positive subjects in post-intervntation period 45 (87.3%) started DAA, a percentage decisely higher than that observed before the start of the program, only 3 (18.7%) of the 18, (p<0.0001) (Figure 2).

Conclusions: The use eof our innovative model with a close interacton between infectious disease unit and SerD determined a significant increase in HCV-RNA testing, linkage to care and DAA start in PWUD population.

HCV elimination

P 30 SHORT COURSE THERAPY FOR CHRONIC HEPATITIS C INFECTION

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Background: Hepatitis C chronic infection (HCV) therapy reached in recent years surprising sustained virological response (SVR) rate with almost no side effects. Glecaprevir/Pibrentasvir (G/P) and Sofosbuvir velpatasvir are recommended in the EASL guidelines for the treatment of Hepatitis C Chronic Infection (CHC) and have a good pharmacokinetic and pharmacodynamics (PK/PD) profile with a standard treatment ranging from 8 to 12 weeks depending on different immunovirological and patient's features. We describe here the characteristics of patients that underwent short term course therapy for any reason to treat a well known and challenging chronic condition in difficult-to-treat patients.

Materials and methods: In this observational analysis we retrospectively included the features of all patient that did not complete the HCV treatment as scheduled by guidelines and clinician indications between 2017 and 2019 at our institution. Viral and plasma biomarkers and clinical data were routinely available. Data were analyzed and are presented with frequencies and median using SPPS 26.0 for Mac.

Results: We identified 7 patients, all from European ascendency, of whom three (42,8%) were ex IDU. Median age was 53 (47-72). HBV and HIV status tested negative, no history of crioglobulinemia, obesity nor diabetes was recorded, one patient was known to be cirrhotic.

Two (28,6%) patients were genotype 4 while five (71,4%) genotype 3 respectively. Four patients (57,2%) had Chronic Kidney disease and were undergoing haemodialysis three times a week. Three (42,8%) patients were on F3, others resulted one each (14,3%) F1, F2 and F4 respectively based on Fibroscan. Four (57,2%) started 12 weeks Glecaprevir/pibrentasvir, three (42,8%) 12 weeks Sofosbuvir/velpatasvir treatment. The median treatment duration resulted in 28 (28-42) days, with an exceptional case of 10 days. For two (28,6%) patients mild adverse events were registered. All reached SVR 12.

Conclusions: Direct acting antiviral (DAA) regimens of 12 weeks result in HCV clearance in vast majority of patients across genotypes. Here we describe 7 cases of short therapy for different reasons resulting in SVR 12. Notably, the majority of these patients were haemodialytic and had moderate-elevated fibrosis. Possible mechanisms rely on PK/PD unique patient variability, renal clearance, complex plasma and tissue immune-viral interactions. These are preliminary data, further studies are need in order to fully understand the characteristics of these patients and the undergoing adjunctive mechanisms that led to viral clearance, with the chance of individuating and tailoring shorter tratment in selected cases.

1. Romani et al. "Peripheral PD-1+ T Cells Co-Expressing Inhibitory Receptors Predict SVR With Ultra Short Duration DAA Therapy in HCV Infection." Frontiers in Immunology 10 (2019): 1470.

HCV elimination

P 31 DAA FAILURE IN HCV GENOTYPE 3: VIROLOGICAL FEATURES AND EFFICACY OF RE-TREATMENT

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Background: direct-acting antivirals (DAA)-regimens are associated with failure in about 5% of the cases. The failure was associated with the emergence of resistance associated substitutions (RASs) within the viral quasispecies. This real-life study characterized the virological patterns in genotype 3 patients failing to DAA and evaluated the efficacy of retreatment.
Methods: all the consecutive 51 HCV patients genotype 3 failed to DAA observed at the laboratory of infectious diseases of University of Campania, Naples were enrolled. All the patients were treated 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: Patients enrolled were mainly males (88,2%) with median age of 55 years (range, 31-80). HCV RNA, IU/ml median value was 1,0 x 106 (range, 1,3x103-2,2x107), 56,8% of patients had a diagnosis of cirrhosis, 80,4% were relapse, 19,6% were non responder.
Out of the 51 patients enrolled, 26 (51%) were re-treated. At failure, 61,5% of patients presented one RAS and 19,2 % had 2 or more RAS. At retreatment 84,6% obtained SVR and 15,4% were relapse. In table 1 we analyze the SVR prevalence according to previous/latest DAA regimen, RASs distribution and Resistance-Guided Therapy (RGT). Patients retreated with the latest DAAs regimen most frequently obtained SVR than patients retreated with previous generation of DAA (94,4% vs 62,5%, $p<0.05$). Patients with SVR most frequently had RGT (77% vs 25%, $p<0.05$).
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. Patients with RGT more frequently obtain SVR. NS3, NS5A and NS5B sequencing seems mandatory in the choice of re-treatment DAAs.

HCV elimination

P 32 THERAPY OF HEPATITIS C IN PRISON: EXPERIENCE OF SYSTEMATIC TREATMENT PROGRAM IN ROME

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Background: In Italian prisons, the HCV-Ab prevalence observed is ranges between 22% and 38%.
Aim of the present study is to describe results of the hepatitis C treatment among prisoners from the two largest prisons in Rome.
Methods: HCV treatment for prisoners started from January 2017.
Inmates tested positive for HCV screening were informed that they might undergo hepatitis C treatment by request. Liver elastography was executed in prison during the weekly visit.
The choice of DAA prescribed to HCV prisoner patients was done following EASL guidelines.
A database of patients was created, including demographic characteristics, nationality, fibrosis score, HCV-genotype, previous treatments, HIV coinfection, type of HCV therapy, outcome of treatment at 12 weeks after EOT (SVR12), interruptions of treatment.
SVR12 and treatment failure, as endpoints, was assessed both for patients who completed DAA therapy and had a HCV-RNA evaluation at 12 weeks after EOT (per-protocol analysis – PP) and for patients who in addition interrupted DAA (intention-to-treat analysis - ITT).
The association with SVR12 (both PP and ITT) was measured with Fisher exact test in univariable analysis and association with DAA failure with logistic regression in multivariable analysis.
Results: Overall, from July 2017 to November 2019, 231 prisoners started DAA treatment: 198 of them (85.7%) completed DAA (194, 84.0% in prison and 4, 1.7% out of prison), 20 patients (8.7%) were still in therapy and 13 (5.3) interrupted therapy for personal decision (2 patients), after transferred to other prison (4) or end of detention (7).
The number of patients evaluable at 12 weeks in PP analysis was 150; 163 patients were else included in the ITT analysis.
Overall, 7/150 patients failed to achieve SVR12 in PP analysis
(SVR12: 95.2%) and 20/163 (7 plus 13 who interrupted treatment) in ITT analysis (SVR12: 87.7%). The proportion of SVR12 in PP was significantly lower in HIV-coinfected patients (88.1% vs. 98.1%, p=0.019). Moreover, in ITT, SVR12 was showed significantly lower among non-Italian patients (77.8% vs. 90.6%, p=0.048) and GT 1a (83.1% vs. 91.9% of other GT, p=0.032).
In multivariable PP analysis, HIV-coinfection (95% CI: 1.57-101.04, p =0.017) and pre-treatment of HCV (95% CI: 1.89 -166.11, p=0.012) were found at significant higher risk of DAA failure. In multivariable ITT analysis, HIV-coinfection (95% CI: 1.07-9.37, p=0.038), pre-treatment for HCV (, 95% CI: 1.13-18.28, p=0.33) and non-Italian nationality (95% CI: 1.60 -16.04, p=0.006) were found associated with DAA failure.
Conclusion: Our data suggest that DAA therapy in prison is feasible with acceptable SVR rates but the continuing changing imprisonment situation (transfers or end of detection) has resulted in loss of adherence thus influencing treatment success.
Key points of treatment in prison are: i) motivation of patients, ii) close collaboration with prison operators, iii) easy accessible follow-up clinic to manage patients out of prison.

HCV elimination

P 33 FIVE YEARS REAL-LIFE EXPERIENCE WITH DIRECT-ACTING ANTIVIRALS FOR HEPATITIS C IN A SUBURBAN SETTING IN ROME: A RETROSPECTIVE ANALYSIS

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Background: Although direct-acting antiviral (DAA) therapy for HCV is highly effective, simple and well-tolerated, to reach the WHO's targets for eliminating hepatitis C it is necessary to scale up the linkage to care of hard-to-reach populations like people who use drugs (PWUD). Aim of this study is to assess the efficacy of DAAs and the rate of retention in care in a suburban setting of Rome.

Methods: All patients starting DAAs from February 2015 to October 2019 in the Infectious Diseases Clinic of Tor Vergata Hospital were included. Data retrospectively analysed came from the Lazio Regional Network for DAAs. Sustained virologic response (SVR) was defined as undetectable HCV-RNA 12 weeks after the end of treatment. Chi-squared test was used for the statistical analysis.

Results: 610 patients (71% males, median age 52 y) with complex viral, clinical and social features received at least one DAAs dose. Most of our cohort was composed of active and former drug users (respectively 46% and 23%). The patients were resident in several areas of Lazio region, and only 39% of them came from the closer area to our hospital (ASL RM-B). Genotype-1a and genotype-3 infections were the most common (40% and 25%); 29.5 % of patients had cirrhosis and 76% were treatment-naïve. Overall, median liver stiffness was 9.5 kPa and median HCV RNA was 879259 UI/ml. 7.6 % and 1.2% of patients was respectively HIV and HBV coinfected, and 9% had more than one comorbidity. The DAA regimens used, stratified according to the year of beginning of the treatment, were reported in Figure 1. The overall proportion of lost to follow-up was 21.8% (133/610). The SVR12 rate was 97.7% (465/477) in per protocol analysis. Twelve patients experienced a virologic failure at week 12 after the end-of-treatment: half of these had prematurely discontinued treatment (3 patients for drug adverse effects). SVR12 rates were lower in patients who discontinued DAAs ($p<0.001$), but independent of HCV genotype, previous treatment, presence of cirrhosis, HIV coinfection and end-stage renal disease. Six active people who use drugs had a HCV reinfection confirmed by phylogenetic analysis; one of them spontaneously cleared the virus.

Conclusions: In a real-life cohort of a suburban setting in Rome, nearly all patients achieved SVR12 regardless of clinical complexity of the population that in the last 5 years has been treated at our clinic, while a deeper attention must be paid to the need to complete treatment. In addition, it emerges that people who use drugs represents a reservoir of constant infection over time: this population must be particularly monitored especially in the follow-up phase where reinfections can emerge. The high number of patients lost to follow-up after the end of treatment highlights the need to improve the retention in care in complex settings, for example through recall strategies or widening the possibility to prescribe DAAs and follow the patients in out-of-hospital settings.

HCV elimination

P 34 ASSOCIATION BETWEEN POLYMORPHISM IN THE ENHANCER GENE AND HEPATITIS C VIRUS-INDUCED HEPATOCELLULAR CANCER RISK

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Background: The main agent of hepatocellular carcinoma (HCC) in the world is the hepatitis C virus. Although surveillance programs for the diagnosis of HCC exist, they are not satisfactory, in fact many tumors are diagnosed in the subsequent, incurable stages. As reported in literature, HCV infection induces epigenetic change at the genomic level that may increase the development of hepatocellular carcinoma (HCC). These changes persist as an epigenetic signature even after DAA (direct-acting antiviral) has eradicated the virus. The genome modifications alter the expression of specific genes that promote carcinogenesis. Reliable prognostic markers needed for the correct follow-up of HCV positive patients. The aim of this work is to analyze patients who develop hepatocellular carcinoma, even if eradicated by virus after effective antiviral therapies and evaluate the relationship between polymorphism in enhancer gene and the risk of developing hepatocellular carcinoma (HCC).

Methods: The present study used "human" Li-7, SNU-387 and HepG2 cells to extract data from HCC patients in the HACER database. The platform-based dataset contained 4375 in Li-7, 4045in SNU-387 and 6095 HepG2. NHGRI-EBI GWAS catalog data (hg19) was downloaded from https://www.ebi.ac.uk/gwas/downloads. GWAS SNPs are assigned if the SNP falls within a central region of the Enhancer. The three different cells were used to predict the target genes of Enhancers in HCV patients. Gene ontology (GO) enrichment analysis using Metascape software. To further investigate the pathogenesis of HCC, a PPI network was constructed using Cytoscape software. Then, the topological structure of the network was analyzed and the degree for each gene was calculated.

Results: To reveal the regulation of genes involved in HCC, the use of bioinformatics has been used to predict single nucleotide mutations at the level of Enhancers involved in HCC, which alters the regulation of the hepatocarcinogenesis-related gene set. 37 altered potentiators have been predicted, regulating 176 genes in HCC patients, which have been mainly enriched in the cell cycle, cell division and biological processes associated with oxidative stress. Significant associations were found for a single SNP chr15-59711691 in the CCNB2 gene, highly involved in HCC. Therefore, a PPI network consisting of eleven hub genes with an interaction degree ≥10: CDK2, CDK1, CCNB2, MAD2L1, CDC20, AURKB, CCNB1, PLK1, NDC80, BUB1.

Conclusions: In conclusion, several SNPs all over the genome are expected to be associated with HCV-related HCC risk. The SNP chr15-59711691 were significantly related to the HCV-related HCC risk. These findings indicate that CCNB2 plays an important role in HCV-related HCC risk, however, additional studies will be helpful in understanding the regulatory patterns of genomic variations related to polymorphism in enhancer gene. These studies are currently being validated in our laboratory.

HCV elimination

P 35 GENOTYPING AND TREATMENT ISSUES WITH UNUSUAL 1E AND 1G HCV SUBTYPES FROM AFRICAN SUBJECTS: REPORT OF TWO CASES

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Background: Unusual HCV genotype 1 (HCV1) subtypes are rare in Europe and more prevalent in Africa. The majority of unusual HCV1 subtypes have natural resistance associate substitutions (RASs) in NS5A region and treatment with first generation DAAs has shown a lower sustained virological response (SVR) rate compared with common HCV1 a/b subtypes.

Material and Methods: We analysed the HCV sequence database at the HIV and Hepatitis unit of the University Hospital of Siena, for unusual non a/b HCV1 subtypes. Genotyping by Sanger sequencing of the NS3/NS5A/NS5B and 5' UTR/core regions was compared with commercially available 2nd generation rapid genotyping assays results. The Geno2pheno[HCV] version 0.92 web system was used to compute genotype/subtype and predict drug resistance based on sequence data.

Results: Of 136 HCV genotype 1 infected patients with complete sequencing of the NS3/NS5A/NS5B and 5'UTR/core regions, 44 harboured subtype 1b (32%), 90 subtype 1a (66%) and 2 unusual non 1a/1b subtypes (1.5%), namely one 1e (ptE) and one 1g (ptG). Both patients were from sub-Saharan Africa (SSA). By commercially available 2nd generation HCV genotyping assays, the 1e virus was classified as 1b (GEN-C 2.0, Nuclear Laser Medicine) or indeterminate (Abbott RealTime HCV Genotype II) and the 1g virus was classified as 1a (ABBOTT RealTime HCV Genotype II). At baseline, the subtype 1e sequence had two NS3 (positions 36, 54) and multiple NS5A (positions 24, 28, 30, 31, 93) polymorphisms and the subtype 1g sequence had two NS5A polymorphisms (positions 24, 30) labelled as substitutions at scored positions by Geno2pheno[HCV]. PtE (75 years old, fibrosis stage F3) failed DAA treatment with the pangenotypic regimen sofosbuvir/velpatasvir for 12 weeks, while SVR 12 was achieved in ptG (62 years old, fibrosis stage F1) after treatment with the same regimen.

Conclusions: Unusual non a/b HCV1 harbour resistance associated natural polymorphisms which may reduce SVR rates compared with more common subtypes. Rapid genotyping assays fail to detect these sequences and treatment with a triple DAA regimen may be a preferred option

HCV elimination

P 36 FEASIBILITY AND IMPACT OF HCV TREATMENT IN A HRS IN MILAN

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Background: People who use drugs (PWID) represent a key population group for the prevention and control of blood-borne viruses, including hepatitis C virus (HCV). PWID are characterised by a high burden of disease and high incidence of new infections, particularly among drug injectors. With the advent of new direct antiviral agents (DAAs) HCV micro-elimination in this setting has become a feasible goal. While access to conventional healthcare services is sub-optimal among PWID, addiction center may offer an effective opportunity for linkage to care. We conducted a prospective evaluation of HCV treatment in a Harm Reduction Service (HRS) in Milan.

Methods: We collected demographic data (sex, age, nationality, drug and alcohol addiction) and clinical data (Syphilis, HIV and HBV prevalence and HCV test and treatment) on all register HRS users who started DAAs therapy from February to December 2019. Data collection was closed on 31 January 2020.

Results: Among the 75 individuals, majority (60, 80%) were males, Italian nationals (68, 90.7%), with median age of 47 years. 25(33,3%) were previously incarcerated. The majority reported consuming drugs (53,70.6% -mostly to heroin), 26 (34,6%) alcohol, and 72(96%) were on opioid substitution treatment. Only 6(8%) had previously undergone Interferon-based HCV therapy.

Out of 72(96%) tested for HBV co-infection, none had chronic infection, 30(41,7%) had positive serology, 20(27,8%) were vaccinated, 22(30,5%) were negative. 74(98,7%) were tested for HIV with 6(8,1%) being positive. Of these, all were current/former PWID and 4 were on ART. Syphilis screening was performed on 73(97,3%), with 4(5,5%) positive results. A psychiatric disease was diagnosed in 8(10.7%). The most frequent HCV genotype was 1a (42.7%), followed by 3a (30.7%).

Fibroscan® was carried out on 56/75: 38(67.9%) were classified as F1 grade, 3(5.4%) as F2, 11(19.6%) as F3, 4(7.1%) as F4. APRI score was calculated for 74/75: values were lower than 1,0 for 56 (75.7%) and higher for the others (24.3%). Sofosbuvir+Velpatasvir was used for 31/75 (41.3%), while Glecaprevir+Pibrentasvir for 44/75 (58.7%). Therapy (58.7%) was mostly administered weekly, 24% daily or bi-weekly and 17.3% every 2 or 3 or 4 weeks. Despite the different methods of administration, adherence to the treatment was high, with one interruption.

At the end of data collection, 56(74.8%) people completed the treatment with negative HCV viremia, for 18(24%) treatment was ongoing and 1(1.2%) was transferred out. SVR24 was available for 34 patients, 1(2.9%) was positive (genotype 1a). The remaining did not reach the time test yet; 2 were transferred to another centre and 3 were missing data.

Conclusion: Our study demonstrate that it is feasible to achieve good efficacy and compliance for HCV treatment among PWUD when decentralising treatment to HRS. To achieve the viral hepatitis elimination agenda goals, HRS-based model of treatment provision needs to be implemented at larger scale

HCV elimination

P 37 AN EFFECTIVE STRATEGY TO ACHIEVE HCV MICRO-ELIMINATION: HCV TEST AND TREATMENT INTO TWO HARM REDUCTION SERVICES IN MILAN

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Background: Most of Harm Reduction Service(HRS) users are individuals from vulnerable and underserved communities, who often have psychiatric disease and imprisonment history. They represent a crucial high-risk population for blood borne infections, including HCV. With the advent of new direct antiviral agents (DAAs), HCV micro-elimination in this setting has become a feasible goal. We evaluated HCV treatment cascade in two HRSs located in Milan.
Methods: We collected data on demographics, substance abuse history, HIV prevalence, HCV prevalence, testing and treatment on all register HRS users on first January 2019. Data collection was closed on first January 2020.
Results: A total of 881 HRS users(732M, 149F) were included, with a median age of 45. The 87.7%(773/881) were Italian. The 28%(247/881) reported current or prior judiciary problems.
The majority was addicted to heroin 67.5%(595/881), 24.1%(212/881) to cocaine, 5.3%(47/881) to THC and 3.1% (27/881) to other substances. Problematic alcohol use prevalence was 39.7%(194/881). 168/881(19.1%) were under psychiatric treatment.
HCV serological screening (HCVAb) was performed for 587/881(66.7%), 113/881(12.8%) were in process, 2/881 (0.2%) refused, 179/881(20.3%) were not HRS user anymore. 364/587(62%) resulted HCV Ab positive, of whom 324 (89.0%) were tested for HCV RNA. Among them 123/324(37.9%) were positive, 165/324(50.9%) were negative, 4/324(1.2%) were in progress, 1/324(0.3%) refused, 31/324(9.5%) were not user of HRS anymore. Among HCVAb positive, 116/364(31.9%) were tested for HIV and 92(79.3%) resulted HIV positive.
Among HCV RNA positive 92/123(74.8%) were initiated on DAAs treatment; 70/92(76.1%) received DAAs in HRS, of the remaining 14/92(15.2%) for whom the information was available, 8 received the treatment in hospital, 5 in prison and 1 started the therapy in HRS and continued it in prison. Compliance to treatment was high, as almost all patients completed their therapy. One treatment failure was registered: the patient admitted very poor adherence.
Individuals tested for HCV and HCVAb positive people had an average age significantly higher than individuals not tested and HCVAb negative people ($p<0.001$).
According to univariate logistic regression people addicted to heroin had a higher likelihood of being tested both for HCVAb($p<0.001$) and for HCV RNA($p<0.001$). The heroin users had also a higher likelihood of being positive to the HCVAb test($p<0.001$).
Conclusion: Our study demonstrate that it is feasible to achieve good efficacy and compliance for HCV treatment among people who use drugs when targeting and locally adapting HCV test-and-treat intervention to HRS. To achieve the viral hepatitis elimination agenda goals, HRS-based model of treatment provision needs to be implemented at larger scale. Young people and people who are addicted to other substance than heroin resulted more difficult to link to HCV care; for this reason, tailored intervention may be needed for these groups

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P 38 LONG FOLLOW UP OF MONOCYTE-MACROPHAGE IMMUNEACTIVATION MARKERS IN HCV MONO-INFECTED PATIENTS UNDERGOING DAA TREATMENT

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Background and aims: Increased levels of chemokine interferon-gamma (IFN-γ)-inducible protein-10 (CXCL-10), soluble CD163 (sCD163) and soluble CD14 (sCD14) have been reported in HCV infection with different extents depending on fibrosis stage. The aim of this study was to monitor the effect of HCV eradication on monocyte-macrophage immuneactivation markers in a cohort of HCV mono-infected patients undergoing DAA treatment.

Methods: Viral RNA reservoir was determined using real time PCR. Abbott real time HCV Genotype II was used to determine the genotype of the virus. Liver fibrosis was measured using Transient elastography Fibroscan. Myeloid (mDCs), plasmacytoid (pDCs) DCs, slan-DC and Mo subsets (intermediates, classical, atypical) were assessed by flow cytometry. sCD163, sCD14 and CXCL-10 were longitudinally measured by ELISA kit (RD system) in plasma samples from 79 subjects, 48 HCV infected subjects, 19 Low Fibrosis (LF), F0-F2 and 29 High fibrosis (HF), F3-F4, undergoing DAA therapy and 31 age and sex matched healthy donors (HD). Different time points were analyzed (T0, T1 at SVR12, T2 at SVR48 T3 from 3 to 5 year after treatment). Non parametric tests were used for statistics.

Results: CXCL-10 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 value 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). Also, there was a positive correlation ($r=0.072$) between the levels of scd163, CXCL-10 and the Fibroscan values stating that they play a major role in determining the extent of fibrosis. They decreased at T1 and T2, significantly ($p<0.04$ and $p<0.01$) but persisted elevated in both population of LF and HF when compared to HD ($p<0.01$). Moreover, sCD14 was higher in LF and HF in respect to HD with higher levels in LF as compared to HF ($p<0.001$). In LF group sCD14 did not decrease at T1 but it started to decrease at T2 and T3 ($p=0.04$) compare to baseline, without level differences at T3 with HD. Also, there was a negative correlation ($r = -0.67$) between the levels of SCD14 and the Fibroscan values. In HF patients in monocytes subclasses, in MDC-8, pDCs, mDCs no differences between T0 and T3 were observed.

Conclusions: During HCV infection there is a monocyte-related inflammatory milieu. The DAA treatment is able to highly reduce this inflammatory process, albeit a complete normalization can be seen only after several years from the HCV eradication. Despite a successful therapy, it seems that, the immune system need time to remodeling itself after a chronic antigen stimulation such as HCV. It is important to monitor patients for HCV extra-hepatic diseases that could derive

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P 39 ERADICHIAMOCI: HCV MICRO-ERADICATION PROJECT AMONG 5 PSYCHOACTIVE SUBSTANCES USER SERVICES USING A DAA DELIVERY STRATEGY

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Background: Treating chronic hepatitis C virus (HCV) infection among PWID is crucial to achieve the WHO goal of HCV eradication, in fact this population is highly affected and carries a high risk of transmission. Many people who inject drugs (PWID) do not have access to treatment for hepatitis C virus (HCV) infection, even if they are receiving opioid agonist therapy (OAT). The aim of our study was to lead HCV treatment among PWID either in opioid agonist treatment (OAT) in five low-threshold access primary care-based addiction medicine institution.
Material and methods: A net between Infectious Disease Unit and 5 SERD was set up in a large region of south Lazio, covering 2.250 Kms. A point of care strategy was chosen with rapid diagnosis and staging followed by DAA delivery at SERD. A 11 items questionnaire regarding the knowledge and perception of HCV infection was self-filled by persons before visit. During visit we collected information about life habits and history of drug addiction. Liver stiffness was evaluated by portable non-invasive transient elastography (Fibroscan) and biochemical index (FIB-4).
Results: 79 pts PWID in opioid agonist treatment (OAT) were enrolled, 69 subjects (87%) male with a median age of 45 yrs (range 19-72 years). Female pts were younger than male. Liver fibrosis was very low in 64% of subjects. We found 49 HCV-RNA positive pts and we start DAA in 27 of them with a median time between enrollment and start therapy of 1 month. Until now, 7 patients finished anti-HCV therapy without side effects and no one left. The most represented HCV genotypes were 1a and 3a (48% and 48% with 1a and 3a vs 2% of other genotypes). Interestingly, 20 pts (74%) were naïve for anti HCV-therapy. Only 58% of subjects that filled questionnaire known right HCV transmission mode and have the perception that they can re-infect themselves.
Conclusions: These preliminary results confirm that PWID can be successfully tested, visited and treated with DAAs therapy using a focussed, integrated health care model. PWID face several barriers and difficult to accessing HCV care and treatment that need to be overcome. Local settings should be taken in account to better joint HCV microelimination.

HCV elimination

P 40 EFFECT OF DIRECT ANTIVIRAL THERAPY AGAINST HCV ON CD4+ T CELL COUNT IN PATIENTS WITH HIV-HCV COINFECTION

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Background: About one-third of patients with HIV infection are coinfected with HCV and HCV- related liver disease is an important cause of morbidity and mortality in patients with HIV infection. It is well-known that the response rates to HCV therapy are similar between HCV-monoinfected patients and HIV- HCV coinfected ones. Aim of this study was to evaluate the impact of HCV eradication on CD4 + T cell count in a population of HIV-HCV coinfected patients.
Materials and methods: We enrolled patients with HIV-HCV coinfection attending the Infectious Diseases Unit of the A. O.U. Federico II of Naples, from January 2016 to February 2019, treated with ART (AntiRetroviral Therapy) and DAAs (Direct Antiviral Agents). For each patient, we evaluated HIV and HCV viral load, and CD4+ T cell count before starting therapy with DAAs, by SVR12 time and by SVR48 time. Fibrosis was evaluated by the mean of Fibroscan ®.
Results: Fifty-two patients were enrolled (40 male, 27 genotype 1 (22 subtype 1a), 3 genotype 2, 17 genotype 3, 5 genotype 4). Fibrosis score were F0 in 6 patients, F1 in 13 patients, F2 in 7 patients, F3 in 15 patients and cirrhosis in the remaining 11 (all in Child-Pugh class A). All had been receiving ART and all but one were virosuppressed (due to non-compliance). All were treated with DAAs (10 with Sofosbuvir-Ledipasvir, 2 with Sofosbuvir-Ribavirin, 13 with Sofosbuvir-Daclatasvir, 17 with Sofosbuvir-Velpatasvir, 9 with Glecaprevir/Pibrentasvir, 1 with Sofosbuvir-Simeprevir) and all but one achieved SVR12 and SVR48. The same patient who had not achieved HIV viral suppression for non-compliance experimented also a relapse of HCV infection after the end of DAAs. In all patients, we observed that the CD4+ T cell count at baseline did not show significant variations compared to by SVR12 and SVR48 time figures (724 vs 684, vs 713, respectively; see Table1). We also assessed CD4 count in relation to HIV categories and stage of liver disease, see Table1. Also based on the assessments of the subclasses considered, there were no significant changes in the CD4 + T cell count.
Conclusions: Our study shows that viral eradication obtained with DAAs in patients with HIV-HCV coinfection is not associated with significant changes in the CD4 + T cell count, regardless of CDC category and stage of liver disease. Further studies with larger sample size are necessary to confirm these data.

HCV elimination

P 41 HCV TREATMENT IN PWID: A LINKAGE TO CARE MODEL IN CAGLIARI

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Introduction: WHO has set an ambitious goal to eliminate HCV as a major public health threat by 2030. Others WHO targets include reducing new HCV infections by 80% and increasing HCV diagnoses up to 90%. The number of eligible persons receiving HCV treatment will grow from <1% to 80%. To reach this goal it's important to treat PWID and prisoners with HCV infection. In Italy, at present, few subjects with HCV belonging to risk groups have been treated with Direct-Acting Antivirals (DAAs), and sometimes they don't know their HCV RNA+ .

Aim: The objective is the development of a treatment integrated model between Liver Unit and SerDs (Servizi per le dipendenze – "Addiction Services") able to facilitate access to HCV treatment for people who inject drugs (PWID) infected with HCV.

Materials and Methods: The first action to be undertaken is screening for HCV in the population at risk. Universal and free-of-charge infective screening is offered to PWID by SerD staff. HCV antibody detection represents the first-line of screening. People with anti HCV positivity access to our Liver Unit where they are evaluated with further testing (i.e., HCV-RNA and genotype, AST, ALT, but also a screening for other liver disease) and by abdominal ultrasound. In HCV RNA + people the medical specialist prescribes DAA. Therapy administration and supervision are planned according to patients'compliance and when possible family support to avoid drop out and incorrect drug intake. During treatment patients were tested monthly (at baseline, after 4, 8 and 12 weeks of therapy) for liver enzymes and HCV RNA. Last evaluation will be done 12 weeks after end of treatment to see if SVR is achieved.

Conclusions: The goal is to create a straightforward care model that take into account the complexity and vulnerability of the patient. It's important an universal screening in a population at risk, a quicker access to treatment, but also surveillance in people with liver disease, that should be optimal if it was made by a liver specialist inside SerDs.

Hepatitis epidemiology

P 42 HEPATITIS A: HAS THE OUTBREAK ENDED?

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Background: Infection with hepatitis A virus (HAV) is the commonest viral cause of liver disease and represents an important public health problem. An outbreak of hepatitis A has already been reported in the past. We aim to define the epidemiology of acute hepatitis A in our District of Pordenone (Friuli Venezia Giulia).
Materials and methods: Between January 1, 2017 and December 31, 2019, patients admitted to our Hospital for hepatitis A were retrospectively identified. Diagnosis of hepatitis A was confirmed by the presence of anti-hepatitis A virus (HAV) IgM and IgG combined with clinical and biochemical features consistent with acute hepatitis and excluding other causes of hepatitis.
Results: In 2017, we registered 18 patients (16 males, 2 females) with acute hepatitis A, 2 male subjects in 2018 and 3 subjects (2 males and one female) in 2019. The average age was 39 years old in 2017, 29 years old in 2018 and 41 years old in 2019. 4 adults were foreigners and 2 were children. The average ALT was 2077 U/L (± SD 931.51), the average total bilirubin 9 mg/dl (± SD 5.12) while the average INR was 1.01 (± SD 0.45). Hepatic encephalopathy was absent in all patients. HIV infection was present in 3 patients and hepatitis B virus was detected in one patient in 2017. HIV and HBV were not reported as comorbidities in 2018 and 2019. HEV testing was negative in all patients. We detected in a 43 years old Italian man with chronic hepatitis B, a biphasic acute hepatitis A while an autoimmune thrombocytopenia as extrahepatic manifestation developed in a 38 years old female. Chronic liver disease was present in 17% (4/23). The majority of patients (73%) were admitted to our Department and the average hospital stay was 5 days while for 6 patients, hospitalization was not necessary. Fecal-oral route was prevalent in 2017, 2018 and 2019. The consumption of raw seafood and travel to an endemic area were usually reported but in 2017, in a total of 18 patients, hepatitis A virus was sexually transmitted in 5 men (27%) who have sex with men (MSM). In 2 adults we did not find a clear risk factor and in 2017 we reported one family outbreak. In all cases, acute hepatitis A resolved spontaneously with supportive care. Even if no fulminant hepatic failure was showed, HAV was the cause of acute on chronic liver failure in a patient with alcoholic liver cirrhosis. The patient with the biphasic hepatitis A recovered completely in 5 months.
Conclusions: Although molecular investigations for HAV were not performed and our data are related to a small area, our results confirm that the outbreak of 2017 is concluded because acute hepatitis A declined in 2018 and 2019. Patients with viral infections (HBV, HCV, HIV), chronic liver disease and risk factors should be checked for HAV immunization because the administration of HAV vaccine is strongly recommended. Strategies to obtain HAV elimination are vaccine, food and water control, adequate hand-washing and hygienic handling.

Hepatitis epidemiology

P 43 RE-TREATMENT OF HCV INFECTION FOLLOWING FAILURE TO DAAS: DATA FROM THE SCOLTA COHORT

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Background: Current evidence on management of virological failure (VF) to HCV direct active agents (DAAs) is scarce. We aimed at reporting the therapeutic strategy and the outcome of these patients.

Material and methods: Multicentric cohort study. All HCV-infected patients who experienced failure to DAAs and received a second-line treatment at one of the participating centers in the SCOLTA cohort were evaluated. The rate of virological failure was calculated. Type of second-line regimens and sustained virological response (SVR) rates were reported.

Results: Since DAAs became available, 3201 HCV-infected patients have been treated at the participating centers. Of them, 62 (1.9%) experienced VF, 40 (64.5%) of whom started a second-line HCV regimens. Of these 40 VF, 22 (55%) re-treatment was guided by HCV resistance testing. Seventeen (42.5%) failed to DAAs regimens still recommended by 2018 European recommendations. Median age at re-treatment was 53 (50.5-56) years; 8 (20%) were females and 38 (955) of Caucasian origin; 26 (65%) were relapser to DAAs and 18 (45%) had Metavir-F4 liver fibrosis according to biopsy or elastography. Child-Pugh score was A5-6 for all but one cirrhotic patients, and 6 (15%) have previously been diagnosed with hepatocellular carcinoma. As second-line DAAs, 19 (47.5%) patients received sofosbuvir/velpatasvir/voxilaprevir, 14 (35%) sofosbuvir/velpatasvir, 5 (12.5%) sofosbuvir/ledipasvir, 1 (2.5%) glecaprevir/pibrentasvir, 1 (2.5%) grazoprevir/elbasvir. Overall, 12 received ribavirin together with second-line DAAs. Virological outcome was available for 33 patients, as follow-up was still ongoing for the others. SVR was 90.9% (30/33), while 1 patient relapsed after treatment, 1 was HCV viremic at the end of treatment and the last was lost to follow up. Table 1 reports on second-line DAAs regimens and outcome of patients with previous virological failure to DAAs recommended by 2018 European guidelines.

Conclusions: First-line DAAs regimens were highly effective in a real-life multicenter cohort. While one third of VF did not receive re-treatment so far, second-line SVR rates are higher than 90% despite a large proportion of re-treatment was not guided by resistance testing.

Hepatitis epidemiology

P 44 HEV IN SOUTHERN ITALY. STILL A CHIMERA?

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Background: Hepatitis E is caused by infection with HEV; this is most largely a zoonotic disease, still underestimated even though widespread, as we now know that HEV is endemic in most high-income countries with pigs as the primary host (20 mln infections worldwide; 70,000 deaths/year). The virus has four genotypes (1- 4), with one shared serotype. Genotypes 1 and 2 infect only humans, whereas genotypes 3 and 4 primarily infect several mammalian animals, with occasional transmission to humans. In Italy, HEV is responsible for only the 2% of the cases of acute viral hepatitis, even if this rate can be influenced by the small number of laboratories that can test the sample, and the number of autochthonous cases is increasing.
Material and methods: Since September 2018 we started to test for HEV all those patients that came to our observation for acute hepatitis, after excluding major hepatitis virus (epidemiological criteria). In 3 cases of 35 acute viral hepatitis hospitalized to our structure we found a positive result for specific IgM and IgG, and we sent to ISS a blood sample that confirmed the presence of HEV RNA.
The first case we observed was a 63yo woman from Morocco, stably resident in Italy since some years, that occasionally went homeland for vacation. At hospitalization she had AST > 100nv, ALT>155nv, spontaneous INR>2. During her staying we found an autoimmune pattern (ANA+ 1:160). In 1 year of follow-up we observed 3 hepatitis flares with the worsening of her liver function, until the last hospitalization (February 2020) when she had cirrhosis.
The second case was a 68yo man, moved to our Hospital for ALF (acute liver failure). He had been admitted with AST>190nv, ALT>185nv, spontaneous INR>2, fV 51%. As report he was a wild boar hunter, alcohol consumer, obese (BMI>35) and suffered for chronic ischemic heart disease. In 3 weeks of observation, the hepatic function was improving, even though he just had an underlying advanced alcoholic liver disease. Unfortunately, he died for heart attack a few days before being discharged.
The third case of HEV infection was a 32 yo Romanian man, living in Italy since he was 29. He lived in an urban area, never had contacts with wild animals. He was admitted to hospital with AST>75nv, ALT>100nv, spontaneous INR>1.5, fV 61%. He reported he had lost almost 50 kg in the previous year, since he had been obese, and during the hospitalization he went on losing weight rapidly. As sometimes reported with HEV infection, he developed a serious immune thyroiditis that needed medication.
Results: Even though it is possible to treat specifically with ribavirin, in none of the cases we used it, as the rapid seroconversion to IgG, with the disappearing of IgM showed us the unnecessary of antiviral therapy.
Conclusions: In southern Italy acute HEV infection still represents an occasional event, even if in some cases (as shown) it can relate to prolonged hospitalization due to overlapping hepatic diseases.

Hepatitis epidemiology

P 45 EVALUATION OF EARLY HCC OCCURRENCE RATE AND ITS RISK FACTORS IN HCV PATIENTS TREATED WITH DIRECT-ACTING ANTIVIRALS

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Background. Hepatocellular carcinoma (HCC) represents one of the most important complications of chronic liver disease, with an incidence rate of the 1–6% per year. Recently, an unexpected increased HCC recurrence and occurrence rate among HCV patients treated with direct-acting antivirals combination has been reported. Aim of the study was the evaluation of early HCC occurrence rate and its risk factors in a HCV infected population, during and after antiviral treatment with direct-acting-antivirals. **Materials and Methods**: According to the Italian ministerial guidelines for direct-acting-antivirals treatment, 1022 consecutive HCV patients treated with direct-acting-antivirals were enrolled. In this real-life population study, patients with either active HCC at imaging or history of previous treated HCC, HBV or HIV co-infection, or liver transplant recipients were excluded. The SVR, defined as the persistent absence of detectable serum HCV-RNA 12 weeks after the end of treatment (SVR12), was assessed for all enrolled patients. An abdominal ultrasound (US) was performed before starting the antiviral therapy and repeated every 6 months. The baseline HCC screening for all patients enrolled was performed according to the European Association for the Study of Liver (EASL) guidelines. Patients with nodular patterns suggestive of HCC or with uncertain dynamic vascular behaviour were excluded from a further follow-up.
Results: Nine hundred and eighty-five patients completed treatment and follow-up. A Sofosbuvir-based regimen was administered in the 74.9% of patients, among whom, the 71.6% underwent a simultaneous Ribavirin administration. A virological response at 12 weeks off treatment was documented in 966 patients (98.2%). During the post-treatment follow-up HCC was detected in 35 patients (3.55%). At multivariate analysis, four variables resulted independently associated with HCC development, both in a cirrhosis based and a class B Child based model, respectively: cirrhosis/class B Child, therapeutic schedule including Sofosbuvir without Ribavirin, liver stiffness values, male gender and presence of diabetes. A multivariate analysis performed on Child A cirrhotic patients, showed that Sofosbuvir based therapeutic treatment without Ribavirin had a HCC occurrence 5.7 higher than Ribavirin-based schedules with or without Sofosbuvir.
Conclusions: Our data suggest that early HCC occurrence appears more frequently related to Sofosbuvir-based therapy without Ribavirin which, indeed, seems to play a protective role on HCC onset. Therefore, a careful follow-up should be mandatory, particularly in patients undergoing a SOF (Sofosbuvir) without RBV (Ribavirin) antiviral regimen.

HIV and COVID

P 46 COVID-19 IN PATIENTS WITH HIV-1 INFECTION: A SINGLE-CENTRE EXPERIENCE IN NORTHERN ITALY

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Background: On February 20, 2020 the first patient with COVID-19 was diagnosed in Lombardy region, in Northern Italy. Since then, the increasing number of cases reported throughout the country led Italy to be the second most affected country in the world, after the United States, as of the end of March 2020. However, clinical data about COVID-19 in HIV -1-infected patients are still lacking.

Case series: Between March 1, 2020 and April 30, 2020, a total of 756 SARS-CoV-2 infections were diagnosed at the S.Orsola Hospital in Bologna. During these two months, 26 cases of SARS-CoV-2 infections were diagnosed in patients with HIV-1 infection. Therefore, the overall prevalence of coinfection of SARS-CoV-2 and HIV-1 among all cases of COVID -19 diagnosed in this period was 3.4%. Overall, 19 (73%) were men, median age was 53.8 years (range, 28-80), all were currently treated with combination antiretroviral therapy, and 22 subjects (85%) had a plasma HIV RNA below 50 copies/mL. Current CD4+ lymphocyte count was above 350 cells/mm3 in 22 individuals (85%), and 19 (73%) had one or more comorbidities, including arterial hypertension in 11 cases (42%), type 2 diabetes mellitus in 4 (15%), and obesity in 4 (15%). Diagnosis of COVID-19 was made by detection of SARS-CoV-2 RNA in oro- and/or naso-pharyngeal swab specimens by real-time RT-PCR targeting regions in the N gene, following the US CDC protocol. Clinical diagnosis was represented by upper respiratory tract infection in 20 cases (77%) and interstitial pneumonia in 6 (23%). At diagnosis, the median duration of symptoms was 4.2 days, and most frequent symptoms were fever >38°C, cough, fatigue, myalgia, and tachypnea. A reduction in O2 saturation <95% in ambient air was present in 7 subjects (27%), but only 2 patients (8%) had an initial respiratory failure with a PaO2/FiO2 ratio <300 at arterial blood gas analysis. No cases of acute respiratory distress syndrome (ARDS) with PaO2/FiO2 ratio <200 were observed at diagnosis and during the following observation period. Only 5 patients (19%) with interstitial pneumonia were hospitalized. All hospitalized patients had current CD4+ lymphocyte count above 350 cells/mm3. At diagnosis, 6 patients (23%) were receiving a PI-based cART, including darunavir-cobicistat in 5 cases and darunavir-ritonavir in one case. A transitional change in cART was made in other 6 patients who were treated with a non-boosted PI-based regimen. Moreover, we prescribed hydroxychloroquine in 13 subjects (50%) and enoxaparin in 6 (23%). Recovery was obtained in 22 patients (85%) and clinical improvement in the remaining 4 (15%), while there were no admissions to ICU and no deaths.

Conclusion: In our experience, SARS-CoV-2 infection seems to have among HIV-1-infected patients a clinical presentation comparable or milder in comparison to general population, do not seem to be more frequent among subjects with low CD4+ lymphocyte count, and is frequently associated with chronic comorbidities.

HIV and COVID

P 47 A CASE OF ACUTE HEPATITIS C IN A PATIENT WITH HIV, OCCULT HBV AND SARS-COV-2 CO-INFECTION

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Background: In Italy, data about HIV and SARS-CoV-2 co-infection are scarse and we report our first experience.
Material and methods. A 25-year-old Nigerian MSM (man having sex with man) presented to our Department for soar throat, fatigue and myalgia without fever or dyspnea. His personal history included HIV infection from 2017 (at the beginning of the disease HIV RNA 42.000 copies/ml and CD4 358/µL) and an occult HBV infection in the absence of other comorbidities. ABC+3TC+DTG was prescribed from November 2017 to January 2020 as a combined antiretroviral therapy, switching to BIC+TAF+FTC because of persistent low viremia achieving later virological suppression and CD4 cell count equal to 768/µL. Screening for HCV and sexually transmitted infections had been regularly performed. Liver function tests had always been normal.
Results: The nasopharyngeal swab was positive for SARS-CoV-2 real-time polymerase chain reaction while dosing immunoglobulin (Ig) M and IgG was not available in our Laboratory at that time. Routine laboratory examination showed acute hepatitis (alanine aminotransferase [ALT] 924 U/L, total bilirubin 1.4 mg/dl, INR 1.2, ammonia 30 µmol/L) while other results are indicated in Table 1. His arterial blood gas showed pO2/FiO2 (21%) ratio equal to 399. Chest X-ray was negative and abdomen ultrasound revealed slight liver steatosis. He denied having used alcohol and illicit drugs use or having been abroad. We planned an additional biochemical investigation that showed negativity of HIV RNA, HBV DNA, HEV RNA, CMV DNA, EBV DNA, HHV-8 DNA and anti-hepatitis A virus IgM while HCV RNA was detected (117 U/L). Genotype was not determined because of very low viral load. Blood markers of autoimmunity were negative, IL28B rs12979860 genotype was C/C. During the hospital stay, intravenous fluid therapy was prescribed, BIC+TAF+FTC was continued but no specific therapy for COVID-19 was started. The patient reported that he was feeling better and after one week he was discharged. At the moment of discharge, LFTs were spontaneously improving: ALT 275 U/L, AST 53 U/L, total bilirubin 0.8 mg/dl, GGT 300 U/L and INR 0.9. A diagnosis of acute hepatitis C in HIV and SARS-CoV-2 co-infection with OBI was made. After 2 weeks, the patient remained well and the second nasopharyngeal swab was negative for SARS-CoV-2; on 4-weeks follow up, HCV RNA was undetectable, ALT 41 U/L, GGT 100 U/L. We still closely continue to monitor him.
Conclusions: The incidence of elevated serum liver biochemistries in hospitalized patients with COVID-19 ranges from 14 -53%. When assessing these patients, it is recommended to consider etiologies unrelated to COVID-19, particularly hepatitis B and C. Genome-wide association studies could be important to predict prognosis of some viral infections. Sexually acquired hepatitis C remains a public health problem with significant disease burden in MSM and major effective health interventions are needed to control this disease.

HIV and COVID

P 48 SARS-COV-2 INFECTION IN A HIGHLY-EXPERIENCED PERSON LIVING WITH HIV

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Introduction: Patients infected by the SARS–CoV–2, the etiological agent of COVID-19, show symptoms of fever, cough and dyspnea, lymphopenia, and interstitial pneumonia in radiological examinations. Given the correlation with lymphopenia, it was thought that people living with HIV could have an increased risk of contracting COVID-19 and manifesting a severe form of the disease, albeit, currently there is no clear evidence of a higher COVID-19 infection rate or different disease course in HIV people than in HIV-negative ones.
Case discussion: We present a case of a 75 years old male patient, with a history of 23 years since HIV diagnosis with no AIDS-defining event in his clinical history, with a nadir CD4+ cell count of 159 cell/mm3; the last determination prior to hospital admission was 709 cell/mm3 with an undetectable HIV-RNA. He had a resolved HBV infection and suffered from high blood pressure and was in treatment with perindopril. On March 21st 2020 he was hospitalized following a 7-days history of high fever, diarrhea and cough; molecular (RT-PCR) assay of nasopharyngeal swab for SARS-CoV-2 was positive. Blood exams showed a C-Reactive Protein value of 45 mg/L, a lactate dehydrogenase of 221 U/L, a d-dimer of 2232 ng/mL and a leukocyte count of 6340/mm3, with a lymphocites count of 1380/mm3. Chest X-rays showed bilateral signs of interstitial pneumonia with ground-glass opacity in the anterior segment of the upper right lobe. Antiretroviral therapy was hence modified, discontinuing the single tablet regimen (STR) of rilpivirine/emtricitabine/tenofovir alafenamide and starting a STR with darunavir/cobicistat/emtricitabine/tenofovir alafenamide. Hydroxycloroquine was also started along with antibiotic therapy with azithromycin. In the days immediately following, clinical conditions worsened, with persistent fever and worsening dyspnea, requiring a progressive increase in oxygen supplementation up to a FiO2 of 0.6. On March 28th, a dose of intravenous sarilumab was administered with a second dose two days later. Following conduction disorder, on April 1st both hydroxycloroquine and azithromycin were discontinued. From April 4th, we observed a progressive improvement in clinical conditions, with the resolution of fever and improvement of respiratory parameters and gas exchange. Oxygen supplementation was rapidly discontinued and after two consecutive negative swab tests performed 24 hours apart the patient was discharged on April 9th in good clinical conditions. One month later in a follow-up visit he tested positive for IgG against COVID-19.
Discussion: Our work describes one of the first reported cases of COVID-19 in a person living with HIV. This case may suggest that the clinical course of the disease could be more insidious in this group of patients and the choice to switch the antiretroviral therapy to a PI-based regimen along with the sarilumab administration could be beneficial. Further studies are necessary to confirm these data.

HIV and COVID

P 49 SARS-COV-2 INFECTION IN A HIV+ PATIENT ON DARUNAVIR-BASED ART MONOTHERAPY: A CASE REPORT

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Background: Despite the pandemic emergency of novel coronavirus disease (COVID-19) and the high number of people living with HIV (PLWH) globally, coinfection has been described in a limited number of cases. We report a severe case of SARS-CoV-2 in a PLWH on ART monotherapy based on protease inhibitor.

Material and methods: In April 2020 K.A., an Ethiopian 42-year-old woman infected with HIV since 1997, on ART monotherapy with darunavir/cobicistat (800/150 mg qd) during the last 6 years, was admitted to our Department for 5-day fever, dry cough and fatigue.

At the admission she was febrile (37,5° C), tachypneic (24 breaths/min), tachycardic (120 beats/min) with 96% on peripheral blood saturation. She had a 15 pack-year history of smoking, no alcohol and no intravenous drug abuse habits. For the past 23 years her HIV status has been immunologically and virologically stable with no reported opportunistic diseases. Laboratory tests revealed: HIV viral load < 50 copies/ml, in line with the past months, CD4+ T-cell count of 242 cells/μL, CD8+ T-cell count of 336 cells/μL and CD4+/CD8+ ratio of 0.72. The patient had lymphocytopenia (610 cells/μL), elevated CRP (15.67 mg/dl), LDH (490 UI/l), interleukin-6 (50.96 pg/ml), D-dimer (920 μg/l), normal PCT (0.09 ng/ml). Arterial blood gas analysis showed: pH 7.48, pCO2 35 mmHg, pO2 70 mmHg, P/F ratio 333 on 21% FiO2. M. pneumoniae IgM and C. pneumoniae IgM on blood test resulted negative, as peripheral blood smear, TB-GOLD Quantiferon and urinary Legionella antigen.

Nasopharyngeal swab resulted positive for PCR amplification of SARS-CoV2 RdRp gene. She, then, performed a lung HRCT that detected multiple peripheral ground-glass areas bilaterally and crazy paving signs suspicious of COVID-19 pneumonia.

Thus, she underwent high flow nasal cannula associated with 7-day therapy based on hydroxycloroquine 200mg bid and enoxaparin 4000 UI bid, maintaining darunavir/cobicistat as baseline ART. At the end of the treatment, on day 7, the patient reported resolution of fever and fatigue and normalization of respiratory rate with improved oxygen pressure on arterial blood gas analysis. Besides, her CPR declined (2.1 mg/dl), lymphocytes increased (800 cells/μL) as D-Dimer did (3454 μg/l). Using multi-parametric flow cytometry, a trend was observed towards a general increase in the immune activation level in both CD4+ and CD8+ T-cell subsets, except for CD4+ naive T-cells. On day 14 the patient interrupted oxygen support and performed two consecutive nasopharyngeal swabs 24 hours apart resulted negative. Laboratory tests revealed lymphocytopenia (810 cells/μL), CD4+ count 528 cells/μL, CD8+ count 533 cells/μL, CD4+/CD8+ ratio 0.99 and slightly reduced D-dimer (3054 μg/l).

Conclusions: The aim of this report is suggesting further investigation on the efficacy of COVID-19 treatment in combined therapy, especially in earlier stages and in the potential prevention of severe forms of the disease associated to SARS-CoV2.

HIV and COVID

P 50 COVID-19 IN PEOPLE LIVING WITH HIV (PLWH): CLINICAL PICTURE, VIRAL CLEARANCE, CELLULAR AND ANTIBODY RESPONSE IN A CASE SERIES OF A REFERENCE HIV/AIDS CENTER IN A COVID HOSPITAL IN ROME

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Background: Currently, few evidences on SARS-CoV2 infection in PLWH are available.
Material and Methods: We identified all HIV+ patients (pts) admitted into the National Institute for Infectious Diseases L.Spallanzani IRCCS, from the 1st of March to the 12th of May 2020 with SARS-CoV-2 infection diagnosed by detection of RT-PCR on nasopharyngeal (NP) swab and/or positive serology. Clinical and virological data and immunological response were reported.
Results: We identified 5 HIV+ pts among the 630 pts admitted to our centre with SARS-CoV-2 infection. Main demographic and clinical characteristics are summarized in Table 1. Briefly, of the 5 HIV+ pts, 2 had relevant comorbidities and 2 had concomitant AIDS-related conditions, all were virologically suppressed on antiretroviral therapy (ART), of whom 2 protease-inhibitors (PI)-based and 3 non-PI-based. Baseline CD4 cell count was below 200/mm3 only in 1 pt. At hospital admission, all 5 pts had radiological evidence of pneumonia without signs of clinical severity and hyperinflammation. 4 pts received hydroxychloroquine for 10 days without changing ART whereas 1 pt underwent to a transitional change of initial ART from a non-PI to a PI-based regimen for 14 days. During hospitalization, none of the pts developed severe respiratory failure or needed invasive/non-invasive ventilation, 2 of 5 pts required oxygen supplement with Venturi mask and in 1 pt immunomodulatory therapy with steroids and intravenous tocilizumab was initiated. In 2 of 5 pts, viral RNA was not detected by RT-PCR from NP swab, and viral clearance occurred in all of 3 pts with positive NP swab on admission within a maximum time of 39 days. All but one pt were discharged within 20 days.
Concerning immune response, SARS-CoV-2 infection elicited IgG response in all pts, and neutralizing antibodies (nAb) production was found in all but 1 pt. A higher immune-activation was found in more immunocompromised pts, and a greater T-cell response against SARS-CoV2 antigens was observed in pts with a more severe COVID-19 presentation. Similarly, in the only pt with severe pneumonia the highest level of IL-6 was detected. Of note, the lack of T cell response in 1 pt was associated to the absence of nAb response.
Conclusions: According with previous reports, our data confirmed the lack of evidence for an increased severity of COVID-19 in HIV+ pts. During the first two months of COVID-19 outbreak, 0.8% of pts admitted with a confirmed SARS-CoV2 infection in our centre were HIV+ and all had a mild-moderate clinical picture. Clinical presentation and antibody response did not seem to be strictly influenced by HIV-related viro-immunological status. A specific T cell response was detected also in an immunocompromised pt, was associated with nAb production and was stronger in pts with a more severe disease, supporting the hypothesis that adaptive immunity could be involved in more serious presentations.

HIV and COVID

P 51 CLINICAL COURSE AND VIROIMMUNOLOGICAL IMPACT OF COVID-19 IN HIV INFECTED PATIENTS: A SINGLE-CENTER REPORT FROM MILAN, ITALY

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on behalf of the HIV-COVID OSR Study Group2 (E. Messina, A. Danise, M. Guffanti, R. dell'Acqua, S. Nozza, N. Gianotti, V. Spagnuolo, L. Fumagalli, H. Hamid, S. Bossolasco, G. Morsica, G. Gaiera, M. Cernuschi, M. Ripa, B. Castiglioni, C. Oltolini, D. Canetti, C. Tassan-Din, A. Andolina, P. Scarpellini, G. Tambussi, C. Uberti-Foppa)

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Background: Since late February, a rapid spreading of SARS-CoV-2, the causing agent of COVID-19, has occurred in Lombardy region. Data on the clinical course and impact of COVID-19 in HIV infected patients are still scanty. Here, we report the characteristics of 7 HIV-COVID-19 co-infected patients referred to the Infectious Diseases Unit of San Raffaele Hospital, Milan.
Material and methods: Clinical charts of either in- and outpatients with HIV infection referred to San Raffaele Hospital due to PCR-confirmed SARS-CoV-2 infection were reviewed. Laboratory and radiological data were collected from clinical database. All patients signed informed consent to be enrolled in the observational cohort of COVID-19 patients at San Raffaele Hospital.
Results: 7 HIV-infected patients developed COVID-19 between February and May 2020; 6 were admitted to San Raffaele Hospital. All were male, median age was 62 years (range: 48-79). All had a complete viroimmunological profile within the 90 days before COVID-19 diagnosis: two (28%) displayed CD4+ T-cell<200 cells/mL and detectable HIV-RNA in plasma (Table 1).
All patients but one experienced fever; 3/7 (43%) had respiratory symptoms on admission, with O2 saturation <94% while breathing on ambient air in two. CT scan revealed diffuse bilateral ground glass opacities in 6/7 patients (85%). Median value of C-reactive protein, LDH and total lymphocytes on admission was 61 mg/dL (range 4-169), 245 U/L (range 162-387) and 1.1 cellsx106/L (range 0.2-1.4), respectively. cART therapy was modified due to COVID-19 in 4/7 (57%) patients (in three cases a protease inhibitor was added to the regimen). Of note, one patient experienced severe COVID-19 despite being on cART with lopinavir/ritonavir.
Neither fatalities nor accesses to intensive care were registered. Overall, three patients (42%) had severe COVID-19 requiring non-invasive mechanical ventilation and immunomodulating agents; all these subjects had a long history of adequate HIV suppression. In these patients with severe disease, the median peak value of IL-6, ferritin and D-dimer was 160 pg/mL (range 42-346), 2589 ng/mL (range 804-4018) and 1.92 µg/mL (range 1.28-3.88), respectively. Four patients had mild disease and included the two with detectable HIV-RNA and lower CD4+ T-cells number, who notably did not require supplemental oxygen and were rapidly discharged. Mild-COVID-19 subjects had median peak value of IL-6, ferritin and D-dimer of 11.9 pg/mL, 789 ng/mL and 0.5 µg/mL, respectively.
Median CD4+ T-cell count decreased markedly during/after COVID-19 (median 651 vs. 361 cells/mL, p=0.04, Wilcoxon signed rank test). No major modifications in HIV viral load were observed.
Conclusions: In this single-center case series of HIV-infected patients with COVID-19, severe disease occurred in patients with well-controlled infection and suppressed viral load. SARS-CoV-2 infection was not associated with increased HIV viral load despite causing a depletion of CD4+ T-cells.

HIV and COVID

P 52 MANAGEMENT OF EMERGENCY COVID-19 IN PRISON, MONZA EXPERIENCE

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In this article we'll explain the procedures adopted by the doctors of the jail of Monza during the Covid-19 emergency. The first step was to identify the suspected cases and interrupt the visits received by the prisoners. We drew up a specific triage form with questions about the symptoms related to the infection and the situations with a transmission risk and with a temperature check. All the prison officers and the employees underwent triage every time they entered the building. We had 13170 forms filled out.

Every new prisoner, wearing the surgical mask, had to udergo the triage in a structure outside the jail. The medical staff has always worn the FFP2 mask. After the triage, the prisoners who were negative were isolated in a section of the jail during 14 days with a daily medical supervision. On the 21st of march we started with the first swabs and we repeated them after 14 days.

The prisoners with respiratory symptoms and high temperature were isolated with their cell mates under a daily supervision until the disappearance of the symptoms. The ones relocated in other structures, under house arrest or hospitalized, got tested for Covid-19 just once.

Between the 21st of March and the 12th of May 86 prisoners performed the Covid-19 swab. 15 of them received only one swab at the beginning of the isolation and two at the end. According to the guidelines, the following 64 prisoners underwent one swab at the beginning and one at the end oft he isolation. 7 prisoners underwent just one swab.

Conclusion: Up to May 12 no Covid-19 positive case has been detected among the prisoners. Thanks to the triage it was possible to identify 5 suspected cases with symptoms and 10 SARS-CoV-2 cases among the employees. During the epidemic we relocated outside the structure 125 out of the 655 convicts.

HIV and COVID

P 53 PSYCHOLOGICAL IMPACT AND AWARENESS OF COVID-19 IN YOUNG PEOPLE WITH HIV

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Background: Public health emergencies may affect the health, safety, and well-being of both individuals and communities. These effects may translate into a range of emotional reactions and unhealthy behaviours. Some people may be more vulnerable than others to the psychosocial effects of pandemics. Young people living with HIV can experience solitude, depression and anxiety as a consequence of the stigma that continues to surround HIV and the daily challenge of living with a chronic infection. We investigated the psychological impact of the current COVID-19 pandemic among a group of HIV-infected young people and assessed their knowledge on HIV and COVID-19 infections.

Materials and Methods: In June 2020, Ospedale Pediatrico Bambino Gesù (OPBG, Rome, Italy) and Penta (Padova, Italy) organized a webinar focused on COVID-19 and HIV infections and the importance of clinical trials in improving knowledge of infectious diseases. Participants were vertically infected HIV patients, aged 15-30 years-old, receiving treatment from the Paediatric HIV Service in OPBG or to the Department of Women's and Children's Health, University of Padova. Each participant was asked to complete a preliminary online anonymous survey on their knowledge of the infections before attending the webinar. Data were collected using Redcap®.

Results: A total of 40 participants attended the webinar, of which 33 completed the survey Participants showed a good knowledge of HIV and COVID-19, with almost all responses related to transmission and prevention of both viruses being correct. Only 3/33 people thought COVID-19 is a bacterium rather than a virus, while 6/33 (18%) respondents thought COVID-19 can be transmitted through the air, not by droplets. A total of 23/33 (70%) people were aware of the correct definition of a clinical trial, while 15% believe a clinical trial is an informative meeting on a specific disease.

Concerning the psychological impact of the current pandemic, 21% of participants stated they experienced a lot of sufferance for social isolation during the lockdown period, while 18% did not suffer at all.

In the 2-months period prior to survey completion, participants stated they had felt tired (79%), worried (91%) and upset (82%). 79% of respondents signaled to have experienced a loss of interest and/or pleasure in their daily activities. 15% of respondents reported some interruption on HIV treatment during the previous 2 months.

Conclusions: Our data highlights that the current COVID-19 pandemic has had a psychological impact on young people living with HIV. Based on these preliminary data, we have created a more comprehensive survey using psychometric validated tests to be distributed across 40 countries across the world - thanks to the Penta ID Network – to investigate the psychosocial impact of the current pandemic and the restrictive measures on HIV infected young people

HIV and COVID

P 54 REVIEW OF LOPINAVIR AND DARUNAVIR USE IN SARS-COV-2 AND HIV CO-INFECTION: IS IT TIME TO FIND ANOTHER ROLE AND ANOTHER ACTOR?

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Background: The knowledge of HIV and SARS-CoV-2 virology allows to identify key molecules for the design of common antiviral drugs. The main difference in HIV protease lies within the divergent spatial structure of the HIV aspartic protease when compared to SARS-CoV-2 3CLpro cysteine protease. Lopinavir and darunavir, two protease inhibitors (PI) used for HIV infection, have been proposed at the beginning of pandemic Coronavirus disease 2019 as suitable treatment for SARS-CoV-2 infected patients. In fact, lopinavir shows activity to inhibit SARS-CoV-2 in vitro and in silico while darunavir in vitro does not. Our aim is to evaluate if the use of lopinavir and darunavir is protective in the outcome of HIV patients infected with SARS-CoV-2, analyzing data literature.

Material and methods: We carried out a systematic literature review using online database of PubMed and we included publications up to September 2, 2020 with results in discussion on use of PI. Single case reports and case series without comments about combined antiretroviral therapy were excluded.

Results: We considered 13 papers (Table 1). Authors stated cART as PI in 17% of co-infected patients with HIV and SARS-CoV-2. Findings of 6 studies showed: SARS-CoV-2 infections may occur during treatment with PI, they did not influence severity of disease, HIV-infected individuals should not be considered to be protected. Huang et al. found cART discontinuation as risk factor for COVID-19 but there was no significant difference in COVID-19 occurrence between people living with HIV infection taking different cART regimens (all P>0.05). In a 12 persons case-series, Hu et al. suggested the value of cART for potential mitigation of COVID-19 co-infection but they registered PI treatment only in 2 patients. Gervasoni et al. documented favourable outcomes in HIV patients treated mainly with integrase inhibitors but not with PI while Sigel et al. argued a correlation between NRTI use and lower mortality, although their analyses were not subject to correction for multiple statistical tests. In a survey of 8 patients for COVID-19 among HIV/AIDS patients in 2 districts of Whuan, use NRTI e NNRTI was associated with COVID-19, so they concluded for a positive role of PI. COVID -19 has improved in patients with cART or HIV suppressed in a case series of 4 patients from Turkey. Finally, Calza et al. defined data about efficacy of HIV-1 PI inconclusive.

Conclusions: Althought the size of samples is limited, PI are not protective in the outcome HIV and SARS-CoV-2 co-infection. ART regimen should not be changed to include a PI to prevent or treat COVID-19 in the co-infection with HIV, except in clinical trials. For example, in our opinion, it could be speculate a role of PI in the context of pre-exposure prophylaxis. Since the low incidence (1-2%) of COVID-19 in PLWH, future studies focused in key proteins involved in the co-infection are needed to identify the protective factor for SARS-CoV-2 infection

HIV and COVID

P 55 SEROPREVALENCE OF SARS-COV2 ANTIBODIES IN PAEDIATRIC HIV PATIENTS

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The seroprevalence of SARS-CoV2 antibodies allows to define a better picture of the spread of SARS-CoV2 infection in the population, being many people asymptomatic carriers. Researching SARS-CoV2-antibodies can help detecting the asymptomatic infected people and subsequently allows to define a better picture of the overall spread of SARS-CoV2 infection in the population. HIV-infected patients are at increased risk of contracting a wide range of viral infections.
We analized the overall seroprevalence of SARS-CoV2 antibodies in 76 HIV infected aged between 3 months and 32 years old in follow up at Bambino Gesu' Children's Hospital from May to July 2020 .All of the patients were regularly assuming their ART.All of the patients were tested for SARS-CoV2 antibodies, specifically for IgG using the CLIA method. (Architect ABBOT).7 patients showed a detectable HIV viral load (M 430 copie/ml) but a CD4 cell count > 20%,. A SARS-CoV 2 IgG positive value was considered over the range of >15.0 AU/mL and in this condition a nasopharyngeal swab To detect SARS COV 2 was needed.Out of the 76 tested patients, 3 proved to be positive for SARS-CoV2 antibodies (IgG) and in 1 was detected a borderline value (12,7 AU/ml).
The 4 patients were all regularly taking ART, none of them had a detectable viral load and their CD4 count was ranging in between 35% and 40% .The 4 positive patients were then subjected to a nasopharyngeal swab to confirm or exclude via PCR the presence of SARS-CoV2 in their upper respiratory tract and underwent a second serological assay as well to detect SARS-CoV2 antibodies once again.
In all 4 cases, nasopharyngeal swabs were negative and the second assay for SARS-CoV antibodies proved to be negative as well. HIV patients are known to have a lower ability in building and maintaining an optimal immune response compared to non HIV-patients. This feature varies according to the stage of infection.
In our court of patients only 4 persons proved to be positive/borderline for SARS-CoV2 IgG and the antibodies were then measured once again proving not be detectable anymore. The nasopharyngeal swab that was performed after the positive results to confirm or exclude the infection proved to be negative in all 4 cases and the anamnestical recall brought no elements of suspicion for a past SARS-CoV2 infection.
Our study means to leave the discussion on the prevalence and the impact of SARS-CoV2 infection on HIV patients open. No differences could be stated between HIV patients and the general population. It is significant to underline thought that the 4 patients were in a good state of control of the infection. The reliability of serologic testing for IgG anti-SARS-CoV2 remains debated . These data need to be reviewed according to further evidences also during the time

HIV and nervous system

P 56 STUDY OF THE TYPES OF THE NERVOUS SYSTEM BASED ON TEMPERAMENTS OF HIV-INFECTED PATIENTS

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Relevance: In the nerve centers of the cortex of the human brain, two opposing active processes proceed in a complex interaction: excitation and inhibition. The type of nervous system is determined by the compatibility of strength, balance and mobility of the processes of excitation and inhibition

Methods: A study of 100 HIV-infected patients. All subjects were registered with the AIDS Center, with a confirmed diagnosis. The control group consisted of 22 healthy people. All patients underwent a consultation with an infectious disease specialist, a general practitioner, a neurologist and a psychologist. All examined were tested by special questionnaires to determine the type of temperament, stress resistance and psychological state at the time of the study. All subjects gave voluntary consent to the study. The study was conducted in 2016 and 2019.

Results and discussion: An analysis of the results showed that in 93% of cases, HIV-infected people are dominated by a state of anxiety, fear, stress, frustration, and disbelief in one's abilities. The stress test showed low-stress tolerance in 86% of patients with HIV infection.

A study of types of temperament based on types of the nervous system revealed that among HIV-infected patients, choleric temperament prevailed (35.7%) in a study in 2019, in 2016 it was found in 42.4%. The melancholic type was more defined in 2016 and reached 45.5%. It is indicated by the weakness of the processes of excitation and inhibition. Even with a slight overstrain, in the case of solving a difficult task or a life situation, a breakdown occurs in melancholic type. A melancholic has a weak nervous system that is unstable under circumstances requiring overcoming or severe excitation of the nervous system.

Among patients with extraversion there was a slower disease progression, and greater adherence to treatment. In the group of healthy individuals who were students of medical universities, a strong, balanced, mobile sanguine temperament prevailed in 54.5% of cases, phlegmatic in 22.7%, choleric in 13.6%, melancholic in 9%. Pavlov I.P. correlated the selected types of nervous systems with the psychological types of temperaments and discovered their similarity.

Conclusion: Thus, the study showed that HIV-infected patients had a choleric and melancholic type of temperament, which was correlated with the type of nervous system, and was reflected in the patient's activity and behaviour. The brain and the immune system are the two leading adaptive systems in humans, and therefore the type of nervous system of HIV-infected people affects the violation of regulatory psychological functions and modifies the individual responses of the immune system to stressors and stress resistance of the body, which affects patients' adherence to treatment. In this regard, the need for neurovegetative regulation in the formation of PNI relationships in HIV/AIDS disease has been determined.

HIV and nervous system

P 57 PERSISTENT ACTIVATION OF CXCL13 AXIS IN THE CEREBROSPINAL FLUID OF PEOPLE LIVING WITH HIV DESPITE CENTRAL NERVOUS SYSTEM VIRAL SUPPRESSION

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Background: CXCL13 is a chemokine secreted by follicular T-helpers to attract B cells to germinal centres. Plasma CXCL13 seems to predict the neutralization breadth of humoral responses to HIV vaccines in people living with HIV (PLWH). Data on cerebrospinal fluid (CSF) CXCL13 is missing, but central nervous system (CNS) represents one of the reservoirs threatening eradication strategies. Therefore, we evaluated whether CXCL13 can be detected in CSF and associate with local phenomena among cART-treated PLWH.

Material and methods: Retrospective cross-sectional study. Inclusion criteria: cART-treated adult PLWH undergoing lumbar puncture for clinical/research reasons with plasma HIV-RNA<200 cp/mL. Exclusion criteria: spirochetal infections, lymphoproliferative disorders, infective or inflammatory CNS disorders unrelated to HIV. Eight CSF biomarkers were measured by ELISA (including CXCL13, limit of quantification 7 pg/mL) or immunoturbidimetry. Data were analysed through non-parametric tests.

Results: 103 patients were included. 96 were Caucasian (93.2%), 70 male (68.0%), 83 (80.5%) and 78 (75.7%) had plasma and CSF HIV-RNA<20 cp/mL, respectively. Median age, nadir and current CD4 count were 49 years (42-56), 153 (47-245) and 444 cells/mmc (281-693). Plasma and CSF HIV-RNA among non-suppressed patients were 40 (32-84) and 88 (46-128) cp/mL. 22 patients underwent lumbar puncture due to research purposes (21.4%), 37 due to HIV-associated neurocognitive disorders (35.9%), 11 due to isolated brain MRI abnormalities (10.7%), 19 due to control in previous CSF viral escape or encephalitis (18.4%) and 14 due to other clinical indications (13.6%). CSF CXCL13 was detectable in 12 patients with CSF HIV-RNA<20 cp/mL (15.4%; 10.01 pg/mL [8.05-14.25]) and in 8 patients with low-level replicating CSF virus (32%; 8.89 pg/mL [7.92-19.7]), without significant difference according to the amount of CSF HIV-RNA (as shown in the figure). Patients with vs without detectable CSF CXCL13 differed only for CSF neopterin (1.4 [0.81-2.40] vs 0.56 ng/mL [0.41-0.98], p<.01) and CSF proteins level (52 [38-63] vs 39 mg/dL [32-48], p.034). CSF CXCL13 did not correlate with any peripheral parameter, while weakly correlated with intrathecal synthesis (r.24, p.016), CSF HIV-RNA (r.20, p.042), neopterin (r.33, p<.01) and proteins (r.26, p.012). At multivariable analysis, only intrathecal synthesis (β.22, p.026) and CSF neopterin (β.36, p<.01) resulted associated with CSF CXCL13, regardless of CSF HIV-RNA and CSF proteins.

Conclusion: About one fifth of cART-treated PLWH showed detectable CSF CXCL13 levels despite acceptable or optimal CSF viral suppression. This CSF chemokine correlated with the magnitude of compartmentalized immune-activation, inflammation and intrathecal synthesis. Further studies are required to clarify the stimuli underlying CSF CXCL13 production as well as the consequences of the chronic activation of CXCL13 axis in on cART PLWH.

HIV and nervous system

P 58 LIMITED HEALTH LITERACY (HL) ABILITY AND LOW AWARENESS OF HL DIFFICULTIES IN PEOPLE LIVING WITH HIV

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Background: Health literacy (HL) is an individual's ability to process basic health information needed for appropriate health decisions. It's an important determinant of patient centered care and a key component in managing chronic illnesses, such as HIV. Our aim was to better explore HL in person living with HIV (PLWH).

Material and Methods: We performed a cross-sectional single cohort study by consecutively enrolling during routine visits 38 PLWH on antiretroviral therapy (ART) and 16 age-and-education matched healthy controls (HC).

Exclusion criteria were: age<18 years, active/past central nervous system opportunistic infections, history of neurological disorders, active psychiatric disorders, alcoholism or drug abuse.

PLWH underwent a comprehensive neuropsychological assessment (NPA). Global performance was measured by transforming raw scores at each task into standardized Z-scores and averaging to calculate a composite total and for each domain score. To measure HL, both groups underwent the Newest Vital Sign (NVS) and the Brief Health Literacy Scale (BHLS), an objective and subjective measurement respectively. HL was compared in PLWH vs HC and factors associated to HL in the PLWH were explored.

Results: PLWH were 71,1% male with a median age of 52 yrs (IQR 47-59) and a median education of 13 yrs (IQR 11 -17).Median time from HIV diagnosis and first ART were 17(IQR 4-26) and 14(IQR 4-21) yrs, respectively. Overall 20% of PLWH were past injecting drug users, 17% HCV coinfected, 23% with past AIDS-defining events and 97% showed HIV-RNA <50 copies/mL, with a median CD4 cell count of 194 cells/µL (IQR 41-462) at nadir and 701 cells/µL (IQR 529 -918) at the time of NPA.

PLWH were cognitive asymptomatic and, on NPA, the total mean Z-score was 0.42 (SD 0.62).The mean NVS total score was significantly worse in HIV+ group when compared to HC [mean 3.79 (SD 1.5) vs 4.69 (SD 1.07); p=0.039] resulting patients' lower objective HL ability.On the other side, PLWH significantly differed from HC in mean BHLS total score, showing lower subjective judgments of HL difficulties [mean 1,87 (SD 1,9) vs 3,69 (SD 1,4); p=0.002].

In PLWH, better performance at NVS was associated to higher attention scores (β 7.47; 95% CI 0.11-1.3; p=0.022) after adjusting for education (β 1.11; 95% CI -0.62/0.28; p=0.202) and gender (β 4.59; 95% CI -0.59/1.51; p=0.383). Furthermore, higher judgment of HL difficulties at BHLS was independently associated to longer time from first ART (β -0.28; 95% CI -0.05/-0.005; p=0.021) and to CDC stage C (β 14.5; 95% CI 0.62/2.85; p=0.041).

Conclusion: PLWH seemed to show limited objective HL ability jointly to lower subjective judgment of HL difficulties than HC. Furthermore good attention abilities seem to support better HL skills, and longer time on therapy or AIDS event experience seemed to promote higher awareness of HL difficulties.

HIV and nervous system

P 59 EVOLUTION OF COGNITIVE PERFORMANCE AT A 2 YEARS FOLLOW-UP IN A GROUP OF HIV-INFECTED PATIENTS

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Background: Although the introduction of combined antiretroviral therapy (cART) milder forms of HIV-Associated Neurocognitve Disorders (HAND) remain common.Cognitive functions are reported to improve after cART initiation.Our aim was investigated cognitive change over a two-year period in a group of person living with HIV (PLWH).
Method: We performed a retrospective,longitudinal analysis of a monocenter dataset including 146 PLWH on cART who underwent,during routine clinical care between November 2008 and February 2019, two comprehensive neuropsychological assessments (NPA) exploring memory,attention,language,executive functions and fine motor abilities, with a median follow-up interval of 18 months (IQR 11-42).Global performance (GCP) was measured by transforming raw scores at each task into standardized Z-scores and averaging to calculate a composite total score.A repeated-measure analysis was performed to compare the cognitive performance at follow-up in comparison to baseline.Factors associated to GPC change were also explored.
Results: PLWH were 65% (n=95) male and the baseline demographic and clinical characteristics were as follows:a median age of 45 yrs (IQR 41-52),a median education of 11 yrs (IQR 5-16),median time from HIV diagnosis and first ART of 11 (IQR 5-16) and 9 yrs (IQR 4-12),respectively.Overall 14%(n=21)of PLWH were past injecting drug users,15,8% (n=22) HCV coinfected, 26,7%(n=39)with past AIDS-defining events and 93%(n=133)showed HIV-RNA <50 copies/mL, with a median CD4 cell count of 162 cells/µL (IQR 52-178)at nadir and 581 cells/µL(IQR 454-758)at the baseline.CD4 cell count at the time of NPA significantly improved at follow-up(p <0.001).All patients were cognitive asymptomatic and PLWH with asymptomatic neurocognitive impairment(ANI)decreased, although not significantly, at follow-up than at baseline [19% (n=28) vs 17% (n=25); p 0.119].GPC was significantly improved at follow-up than at baseline[mean -0.10 (SD 0.56) vs 0.03 (SD 0.73); p 0.013].PLWH showed up a significantly better performance at follow-up than at baseline for the memory[mean -0.78 (SD1) vs -0.31 (SD 1.2); p<0.000],attention [mean -0.2 (SD 0.6) vs -0.10(SD 0.7); p 0.003] and language[mean 0.32 (SD 1.11) vs 0.65 (SD 1.42); p 0.002]domains.On the other hand, executive function domain significantly got worse[media 0.34 (SD 0.64) vs 0.13 (SD 0.79); p 0.002]and motor abilities didn't significantly change at follow-up (p 0.480).Higher GCP improvement was associated to reaching HIV-RNA <50 copies/mL(undetectable status) at follow-up with a trend toward significance (β 0.388; 95% CI 0.01/0.78; p 0.056).
Conclusions: In our population, GCP in HIV+ patients was significantly improved at a 2 years follow-up, in particular regarding memory, attention and language domains, and seemed to be associated to reaching HIV-RNA <50 copies/mL at follow-up.Therefore GPC improvement in PLWH appears to be driven also by therapeutic success of cART, that is reaching undetectable status.

HIV and nervous system

P 60 CEREBROSPINAL FLUID VIRAL REPLICATION AND BURDEN OF RESISTANCE IN HIV-1-INFECTED PEOPLE WITH MULTIDRUG RESISTANCE TREATED WITH IBALIZUMAB

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Background: Ibalizumab (IBA) has demonstrated to be effective in the setting of multidrug resistant HIV-1 infection in combination with an optimized background therapy; up to now, no data are available on viral replication in cerebrospinal fluid (CSF) during a treatment regimen including IBA.
Aim of the study was to evaluate viral load (VL) and resistance tests in CSF in HIV-1-infected people with multidrug resistance treated with IBA.
Methods: Case-series analysis of HIV-1 infected adults who received intravenous IBA every two weeks as a salvage therapy in patients with no other options at IRCCS San Raffaele Hospital from March 2019 who performed lumbar puncture (LP) and collected paired CSF and blood samples at a single time point. All the participants underwent CT scan before LP. HIV-1 RNA was quantified by polimerase chain (PCR) (Cobas® HIV-1 Test on 6800 Systems, Roche Diagnostics). Co-receptor tropism was inferred with the geno2pheno (G2P) algorithm. Genotypic resistance tests were performed on HIV-1 RNA and results were interpreted according to the Stanford HIVdb Program.
Results: Three male individuals with no fully active drugs from all the antiretroviral classes were evaluated.
Case 1: 23 years old, with a vertical transmission of HIV-1 infection (CDC C3). Before starting IBA, HIV-1 RNA was 21966 copies/mL and CD4+ 278 cells/μL (13.6%); from week 2 HIV-1 RNA remained stably below 200 copies/mL. LP was performed at week 46: CSF analysis showed glucose 53 mg/dL (72 mg/dL on plasma), protein 35 mg/dL and 3 white blood cells (WBC)/μL; CSF viral load (VL) was undetectable. Plasma VL was 59 copies/mL and CD4+ 432 cells/μL (14.4%).
Case 2: 61 years old heterosexual men, known for HIV-1 infection since 1986 (CDC C3). IBA was started when HIV-1 RNA was 275000 copies/mL and CD4+ 9 cells/μL (0.9%). At week 43, he underwent LP: glucose was 56 mg/dL (74 mg/dL on plasma), protein 27 mg/dL and WBC 3/μL; CSF VL was 108 copies/mL. Plasma VL was 249 copies/mL and CD4+ 23 cells/μL (1.5%)
Case 3: 55 years old heterosexual man with HIV-1 infection since 1992 (CDC C3). Prior to start IBA, HIV-1 RNA was 62600 copies/mL and CD4+ 5 cells/μL (0.7%). CSF was collected at week 30: glucose was reported 72 mg/dL (147 mg/dL on plasma) protein 31 mg/dL and WBC 13/μL; CSF VL was 63 copies/mL, plasma VL 3690 copies/mL and CD4+ 8 cells/μL (1.2%).
Cumulative resistance mutations (2010-2019) on plasma and current resistance mutations to protease inhibitor, nucleoside reverse transcriptase inhibitor, non-nucleoside transcriptase inhibitor, integrase strand inhibitor and co-receptor tropism were tested on plasma and on CSF as reported in Table 1.
Conclusions: In all the three HIV-1-infected people with multidrug resistance treated with IBA, low levels of viral replication were described in CSF and no discordance between plasma and CSF viremia were observed. The available tests showed a similar pattern of HIV-1 drug resistance in plasma and CSF.

HIV and nervous system

P 61 IN VITRO EFFECT OF EFAVIRENZ ON CULTURED PRIMARY ASTROCYTES: ANALYSIS OF NEUROTOXICITY AND MATRIX METALLOPROTEINASE INHIBITION

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Background: Efavirenz (EFV) is a non-nucleoside reverse transcriptase inhibitor, used in the past as a first-line regimen for the treatment of HIV-1 infection.
Despite proven efficacy as antiretroviral drug, currently WHO recommend the use of EFV, as an alternative first-line ART regimen only in certain clinical conditions*.
Therefore, the therapeutic role of EFV, at low doses, is being re-evaluated also for its implications in the improvement of some CNS pathologies, also through its direct action on extravirologic factors involved in neurodegenerative diseases.
The aim of our research is to evaluate, in an in vitro study, the efficacy of EFV to exert extravirologic effects on the levels and expression of matrix metalloproteinases (MMPs), identified as important pathogenetic factors in various diseases associated with HIV infection, including neurological damage.
Material and methods: Primary cultures of rat astrocytes were activated with 10 µg/ml of LPS (positive control) and treated with EFV at doses ranging between 0,05-50 µM which included the concentrations detected in the CSF (0,05 µM) and serum (7 µM) of HIV-positive subjects. After incubation for 20h at 37°C, 5% CO2, supernatants were collected and subjected to gelatin-zymography for the detection of MMP-2 and MMP-9 levels whereas the cells were assayed for cell viability by the MTT test. The highest concentration of EFV that determined a cell viability above 60% was considered as the maximum non-toxic concentration (MNTC).
In addition, the intracellular free oxygen radicals (ROS) were detected by 2',7'-dichlorofluorescein diacetate (DCFH-DA) in astrocytes pre-treated with EFV.
In another set of experiments, the effect of EFV on MMP mRNA expression was detected by RT-PCR in LPS-activated astrocytes. In order to study the molecular mechanisms of MMP modulation by EFV, ERK 1/2 were detected by immunoblot analysis, in cell lysates from LPS-activated astrocytes.
Results: Our results indicated that EFV was toxic for astrocytes at concentrations higher than 10 µM, which was considered as the MNTC, and induced a statistically significant production of ROS only at doses higher than MNTC. Furthermore, our results indicated that EFV, at the concentration measured in serum of HIV-infected, was able to inhibit levels and expression of MMP-9 in LPS-activated astrocytes whereas a statistically significant inhibition of both MMP-2 and MMP-9 was detected at the MNTC.
The immunoblot highlighted that EFV exerted its action on the expression of MMPs by inhibiting the activation of ERK1/2, which is the main signaling transduction pathway involved in the regulation of MMP gene expression in LPS-activated astrocytes.
Conclusions: Our results indicate that EFV, used in low concentrations, inhibits MMP levels without toxic effects, suggesting its possible use in the treatment of HIV-associated neurological diseases.

*WHO.Update of recommendations on first and second line antiretroviral regimens.HIV treatment. 2019

HIV and nervous system

P 62 EVALUATION OF PATIENT-REPORTED OUTCOMES (PROS) AND COGNITIVE PERFORMANCE IN HIV NAÏVE PATIENTS WITH ADVANCED DISEASE: RESULTS FROM THE PRO-ADVANCE STUDY

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Background: Aim of this study was a) to evaluate the quality of life and sleep, the perception of mental health status, the anxiety and depression symptoms in HIV-naïve patients with advanced disease, assessed by PROs at the time of HIV diagnosis, and b) to compare PROs with the patients' cognitive performance.
Material and methods: PRO-Advance is an observational, prospective, monocentric study. We enrolled pts aged >18 years, with a new diagnosis of HIV infection and advanced disease. Naïve pts were divided into: group 1) pts with an AIDS defining event, group 2) pts with CD4<200 cells/mm3 without AIDS defining events and group 3) asymptomatic pts with CD4>350 cells/mm3. PROs were collected at diagnosis of HIV (BL) by the following questionnaires (qst): Instrumental Activities of Daily Living (IADL), Beck depression inventory-II (BDI-II), Beck anxiety inventory (BAI), Pittsburg sleep quality Index (PSQI), state of health qst -Short form (SF-12). At BL, pts also underwent a neuropsychological assessment (NPA) through a standardized battery of 12 tests. Pts with confounding factors (opportunistic infections/neoplasia involving the CNS, major depression, not Italian speaking, physical and cognitive disabilities) were excluded. Kruskall Wallis test was used for statistical comparison of PROs, NPZ12 and 5 cognitive domains among groups.
Results: 70 pts were enrolled: 95.7% male, 50% MSM, 12.9% with a diagnosis of HAND (22.9% group 1, 41.4% group 2, 35.7% group 3), median age of 41 yrs (IQR 32-53), median nadir CD4+ count 187 cells/mm3, median years of education 13 (IQR 9-16). NPA was assessed on 56 pts, 8 (14.3%) group 1, 26 (46.4%) group 2 and 25 (39.3%) group 3. Nine (12.9%) pts were classified as HAND (8 ANI and 1 MND). At BL, the three groups did not show any difference in the perception of mental health status, anxiety and depression symptoms, quality of life and sleep (Table 1). A higher proportion of pts from group 1 (62.5%) had a pathological perception of physical health status than pts from group 2 and 3 (34.5% and 20%, respectively; p=0.021). As regarding cognitive performance, NPZ12 score (p=0.011) and the attention/working memory domain (p=0.030) were significantly lower in group 1 versus groups 2 and 3 (Table 2). No correlation was found between the PROs qst and overall cognitive performance (NPZ12).
Conclusions: Our findings showed that an AIDS defining event at diagnosis of HIV infection, is associated with a worsen perception of the state of physical health and a worsen cognitive performance. However, these preliminary results represent the starting point of this evaluation as we expect additional information from the ongoing longitudinal analysis

HIV and nervous system

P 63 CEREBROSPINAL FLUID ANTI-EBV VIRAL CAPSID ANTIGEN IGG PRODUCTION ASSOCIATES WITH POORER PERFORMANCE IN ATTENTION, MEMORY AND EXECUTIVE FUNCTIONS DOMAINS AMONG PEOPLE LIVING WITH HIV

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Background: Blood CMV IgG titers but not blood/cerebrospinal fluid (CSF) CMV-DNA correlated with neurocognitive performance in people living with HIV (PLWH). Even EBV may reactivate boosting chronic immune-activation and infecting blood-brain barrier endothelial cells, but scarce data are available on its possible role in HIV-related neuropathogenesis. We assessed whether CSF EBV replication and the associated humoral response may link to different type of central nervous system (CNS) injuries and neurocognition in PLWH.

Methods: Retrospective cross-sectional study on adult PLWH undergoing lumbar puncture for clinical/research reasons. Exclusion criteria: negative plasma anti-EBV Viral Capsid Antigen IgG (aVCA), CNS disorders unrelated to HIV. Plasma/CSF aVCA were quantified by ELISA, ten CSF biomarkers were measured by ELISA or immunoturbidimetry. The neurocognitive assessment was composed by 16 tests covering 9 cognitive domains. Data were analysed through non-parametric tests.

Results: 91 patients were included: 36 (39.5%) and 55 (60.4%) with CSF HIV-RNA below and above 20 cp/mL. 68 male (74.7%), 81 Caucasian (89.0%), 39 (42.8%) with plasma HIV-RNA<20 cp/mL; median age, nadir and current CD4 count were 48 years (41-53), 74 (21-197) and 170 cells/mmc (48-550), respectively. Plasma and CSH HIV-RNA among non-suppressed patients were 5.3 (4.8-5.8) and 3.5 Log10 cp/mL (2.2-4.6). CSF EBV-DNA and aVCA were detectable in 22.2% (192 cp/ml [74-535]) and 16.5% (16 IU/mL [16.0-36.1]) of patients. Median plasma aVCA level was 652 IU/ml (270-1435). CSF aVCA concentrations were similar in those with or without detectable CSF EBV-DNA (p.085). Higher CSF aVCA levels associated with higher CSF-serum albumin ratio (CSAR, r.31, p<.01), CSF CXCL13 (r.31, p<.01), CSF EBV-DNA (r.25, p.022), serum aVCA (r.34, p<.01) and CSF proteins (r.34, p<.01). Multivariate linear regression model identified that higher CSF aVCA levels independently associated with CSAR (p<.01), plasma aVCA (p.014) and CSF EBV-DNA only (p.042; R2 0.31, p<.01). 40 patients underwent full neurocognitive examination. CSF aVCA correlated with the age/sex/education-adjusted scores of several neurocognitive tests, as shown in the table. The same association between high CSF aVCA and poor neurocognitive performance in similar subsets of the same tests was confirmed both in patients with and without CSF HIV-RNA<20 cp/mL (data not shown). On the contrary, CSF EBV-DNA and plasma aVCA did not correlate with any neurocognitive test score.

Conclusion: Rather than the CSF low-level replicating EBV per se, the amount of intrathecal synthesis of aVCA may influence neurocognitive performances in both CSF suppressed and non-suppressed PLWH. CSF aVCA associated with blood-brain barrier impairment and poorer performance in memory, attention and executive functioning tasks. Further studies are required to understand the role of CSF anti-EBV humoral response in PLWH suffering from neurocognitive disorders

HIV and nervous system

P 64 CRYPTOCOCCAL MENINGITIS IN A YOUNG WOMAN HIV LATE PRESENTER: A CASE REPORT

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Background: Cryptococcus neoformans is a very important cause of fungal meningitis in immunosuppressed patients
Objective: Describe a case of cryptococcal meningo-encephalitis in an HIV/AIDS late-presenter patient.
Methods: An 44-year -old Bulgarian female, presented with a last 30 days weight loss and a last 7 days story of headache and fever. Physical examination revealed oral thrush, no neurological focal deficits. She was clinically assessed and performed LP. Results showed: 30 cells; 47 total protein, 40 mg/dl glucose, Pandy:+ Culture on Sabouraud dextrose agar showed the growth of Cryptococcus.
Laboratory examination showed an absolute CD4 of 51 cell/cmm, a VL of 614000 c/mL, a CD4/CD8 ratio 0.10. She was initiated on conventional amphotericin B 5 mg/kg/daily and fluconazol 400 mg bid for 3 weeks (induction) On day 21, the remission of fever and headache and the negative CSF cultures suggested stopping amphotericin and fluconazole, continued high fluconazol 400 mg daily for 6 weeks (consolidation phase). On 35 days HAART (FTC/TDF+DTG) was introduced. On day 63 the clinical deterioration associated with India Ink positive on CSF recommended to reintroduce Amphotericina and high-dose fluconazole for 2 weeks before transition to maintenance therapy. At the end of the induction phase, the recurrence of fever, headache, neurological bladder and no sterilization of CSF, suggested the reintroduction of amphotericin, fluconazole and desamethasone for 4 weeks and then fluconazole 400 mg daily.
Results: After the first induction phase, with clinical remission and negative CSF culture, and after the introduction of HAART, she had a worsening of neurological symptoms WITH India ink positive on CSF, and then the total remission after the reintroduction of the new induction phase.
Conclusion: A persistently positive CSF at 2 weeks after treatment is associated with morbidity and mortality, higher risk for treatment failure at 10 weeks, relapse, and paradoxical IRIS. Relapse is defined as a recurrence of symptoms, after an initial resolution, with a positive CSF culture after ≥4 weeks of treatment.This may be secondary to several possible etiology: disease relapse, paradoxical IRIS, new opportunistic conditions, drug toxicity, or a combination of them. Patients who received inadequate induction treatment and/or had poor adherence to consolidation/maintenance therapy are also at high risk for disease relapse. Relapse was more frequent in cohorts using induction therapy with only fluconazole monotherapy . Among patients without these clues, discriminating between disease relapse and IRIS is difficult.
It is recommended by several experts that a CSF culture at 2 weeks should be sent to determine CSF sterility after induction phase .It is crucial to determine the etiology, as each requires a distinct management strategy although it is difficult to distinguish by clinical signs and symptoms of the patients alone

HIV cure

P 65 A MULTIDISCIPLINARY APPROACH TO IMPRINT A SUCCESSFUL LONG TERM ADHERENCE SKILL TO ANTIRETROVIRAL THERAPY IN NAIVE PATIENTS: BACKGROUND AND PRELIMINARY DATA OF A PILOT PROJECT OF THE GLAD GROUP

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Background: The pilot project for a multidisciplinary intervention to sustain adherence to Antiretroviral Therapy (ART) started in September 2019. The project is focused on naïve patients because clinical and epidemiological data state that the first therapy is the most important for the subsequent clinical history of the patient, especially for advanced-naïve patients. Our goal is also to collect data on adherence to recent ART regimens. The multidisciplinary group is working on shared strategies to show if an early educational intervention could have an impact on the three phases of adherence process, according to Espacomp Medication Adherence Reporting Guidelines (Emerge): initiation, implementation and persistence.

Material and methods: The project is based on multidisciplinary approach and the team is formed by specialists in HIV disease, psychologists, nurses and pharmacists in Amedeo di Savoia Hospital in Turin. We focused on our strategies with naive patient to build a unique "GLAD protocol" that includes: Educational information about HIV/AIDS infection; Information about the patient journey from diagnosis onwards; Special focus on importance of adherence to ART; Easy and quick contact with specialists.

Results: We included so far in our project 24 patients: 10 (42%) received the "GLAD educational intervention", 14 (48%) the standard of care and were used as control group in this proof of concept preliminary study. Among the 10 GLAD patients, there were 9 male patients (90%), and 1 female (10%), with a mean age of 45.8 years; CDC classification: 5 (50%) A, 5 (50%)C; 5 MSM (50%), 1 (10%) drug user, 4 (40%) heterosexual. At the baseline, mean HIV-RNA was 1212500 cp/ml (23000–9750000) and mean CD4 count was 367,4 cell/mmc (8-693). ART regimens: 7 STR (70%), 3 triteraphy (not STR). 6 patients (60%) started psychological follow-up. All patients came easily into contact with the hospital pharmacy and withdrew the therapy correctly (data from pharmacy refill). Among the standard of care patients, there were 12 male (86%), 2 female (14%), with a mean age of 41,43 years; CDC classification: 11 (79%) A, 2 (14%) B, 1 (7%) C; 9 (64%) MSM, 1 (7%) drug user, 4 (29%) heterosexual. At the baseline, mean HIV-RNA was 868810,29 cp/ml (104-10200000) and mean CD4 count was 438,5 cell/mmc (43-856). ART regimes: 11 STR (79%), 2 (14%) dual therapy, 1 (7%) 2 triteraphy (not STR). 3 patients started psychological follow-up. All patients came easily into contact with the hospital pharmacy and withdrew the therapy correctly. At week 12 (reached by 2 and 5 patients respectively), in both group patients obtained virological outcome as expected and pharmacy refill was similar.

Conclusions: Our preliminary data show a good acceptability of this GLAD protocol by patients and multidisciplinary team. Our primary goal is the empowerment of the patient which leads to a long-lasting adherence. This requires a longer observation period and a larger number of patients involved.

HIV cure

P 66 SWITCHING DOLUTEGRAVIR/ABACAVIR/LAMIVUDINE SINGLE TABLET REGIMEN (STR) TO A LESS-COSTLY MULTI-TABLET REGIMEN OF DOLUTEGRAVIR+ABACAVIR/LAMIVUDINE (GENERIC) IN THE SETTING OF VIROLOGIC SUPPRESSION: DATA AT 48 WEEKS

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Introduction: The cost for lifelong anti-retroviral therapy (ART) is of increasing concern worldwide. Recently available generic regimens are associated with cost-saving and the debate on their optimal use is still open. The objective of the study is to evaluate efficacy and safety of a cost saving switch from a branded ART STR (Dolutegravir/Abacavir/Lamivudine) to the equivalent multi-tablet regimen (Abacavir/Lamivudine plus Dolutegravir) in selected voluntary HIV patients attending the outpatient clinic of The Infectious Diseases Division of Padova.
Methods: Between January and June 2019, all consecutive virologically suppressed HIV-positive patients were asked to switch from the branded STR Triumeq® (Dolutegravir/Abacavir/Lamivudine) to the equivalent multi-tablet regimen (2 pills taken together once a day) composed of the generic drug Abacavir/Lamivudine plus Tivicay® (Dolutegravir). Physicians widely discussed with the patients all the reasons, including costs, for the de-simplification they were offering, and the patients could freely decide to remain in their STR or not. Data on socio-demographic and clinical characteristics of the patients were collected. Viro-immunological and safety outcomes, baseline and trimestral self-reported adherence and VAS Quality of Life (QoL) scores were registered during a 48 weeks follow-up for all the patients who switched regimen. Cost calculations were performed.
Results: At the beginning of the study period, 149 patients with HIV-RNA <40 copies/ml for >6 months were taking Triumeq®. 127 patients (85%) agreed on the regimen de-simplification. Most patients were male (91%), the mean age was 47.0 years (range 22-77). 81% were Italians, 19% from non EU-countries. 64% were homosexuals, 34% heterosexuals and 2% IDUs. The mean time since ART initiation was 6.58 years (95%CI:2.60–8.80), 12% were ART-naive.114 and 63 patients completed 24 and 48 weeks of follow-up, respectively. 11 patients (8.6%) reintroduced the branded STR because of patient or clinician's decision, often due to reported toxicity. 2 patients were lost to follow up. Baseline mean CD4 count was 673 cells/μL (95%CI:78-1588) and no significant change was observed at week 48 (mean CD4 count:678 cell/μL; 95%CI:120-1346; p=0.5). HIV-RNA remained undetectable in all patients but 3. No significant differences in adherence and QoL VAS scores were observed. Measured cost savings in the first 24 weeks ranged between 84132-93726 €, with annual projected savings of 168264-187452 €.
Conclusion: The study shows that the change from the STR DTG/ABC/3TC to the generic multi-tablet co-formulation ABC/3TC plus DTG is safe, effective and acceptable. Incidence of discontinuation is low and there are no significant changes in viro-immunological outcomes and QoL perception. The results suggest that the choice for ARV generic drugs could be cost-effective in selected patients and could contribute to lower the economic burden on health care institutions

HIV cure

P 67 COMPLEMENTARY-ALTERNATIVE MEDICINES AND SELF PRESCRIBED DRUGS USE IN WOMEN LIVING WITH HIV

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Background: The use of complementary-alternative medicines (CAM) and self-prescribed pharmaceutical drugs (SP-PD) is well recognized among people living with HIV, as well as in patients with chronic conditions. Data and studies are lacking regarding the use of those additional therapies among HIV women, especially in relation with psychophysical changes related to age.The objective of the study is to explore prevalence, patterns and reasons for the use of CAM and SP-PD and correlations with socio-demographics variables and therapeutic outcomes among female patients receiving anti-retroviral therapy (ART).
Methods: This descriptive study was conducted between November 1, 2018 and May 31, 2019, among a cross-sectional convenience sample of attendees of three HIV clinics in North-East Italy. Face-to-face interviews on the use of CAM and SP-PD in the last 90 days were conducted. Socio-demographics and clinical data were collected. Descriptive statistics and logistic regression analysis were performed to describe the use of CAM and SP-PD among women.
Results: The sample includes189 female patients. Mean age is 48.3 years, 58.3% are above 50 years. 45.5% declares the use of any CAM and/or SP-PD. Females above 50 years were more likely to use CAM and/or SP-PD (54.3%) compared to younger women (38.6%, p=0.03).The reason for the use of adjunctive medications is “fatigue, improvement of general well-being” in more than 75% of the women, followed by “psychological” issues such as anxiety, insomnia and depression (21%) and “ostheoarticular” problems (19%). The adjunctive medications were vitamins and dietary supplements (34.9%), herbal (14.8%) and homeopathic products (5.3%). In 87.2% of the cases the use followed a self-prescription, in 16.2% the indication of a health professional and in 4% of a non-health professional (chiropractor, homeopath, iridologist). Besides the correlation with age, the multivariate analysis do not show correlations with the use of CAMS and/or SP-PD with socio-demographic variables, quality of life VAS score, smoking, alcohol intake, ART class, adherence to ART, CD4 count, viral suppression, CDC class, number of comorbidities and pill burden.
Conclusions: The study shows that the use of CAM and SP-PD is common among women on ART, it increases with age and seems to be transversal and homogeneous among the patient population. The impact of HIV on physical and emotional health may be worse in certain vulnerable group of patients, such as women in older age, and there is likely to be a burden of unmet health needs among this growing population. CAMS are often used to address these complex health issues. Better data are required to inform optimal care delivery and health providers should incorporate routine assessment of adjunctive therapy use in order to provide instruction regarding the potential risks, avert potential adherence problems, and maximize the benefits of conventional care

HIV epidemiology and retention in care

P 68 AVAILABILITY OF RAPID HIV SELF-TEST IN ITALIAN PHARMACIES: A SURVEY

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Background: Starting from Dec 2016, HIV self-tests (HIVST) are sold in pharmacies in Italy. However, data on the availability HIVST in pharmacies are not currently available. We conducted a survey on a random sample of pharmacies to investigate availability of HIVST, services offered with HIVST and number of tests sold.
Methods: From the official list of 7032 active pharmacies in 16 Italian provinces with higher incidence of new HIV cases (official 2018 data, source ISS) we extracted for each province (8 from Northern, 4 Central and 4 Southern Italy) a 5% stratified random sample of pharmacies (total n=357) accounting for the different distribution of pharmacies within the capital vs. the rest of the province (ranging from 68% in Rome to <20% in Brescia). Project staff invited pharmacies personnel to participate to a short survey conducted by telephone. Pharmacies not willing to participate were replaced with others from a further random sample extracted among those not already included, to fulfill 100% respondents.
Results: We herein report results from 346/357 (96.9%) respondents (175 in the North, 81 Centre and 90 in the South). Overall 174 (50.3%) reported HIVST immediately available (>90% Mylan HIV Autotest) with no need to order it in advance, with significant differences between pharmacies in province capitals vs. rest of the province (68% vs. 38%). While in province capitals HIVST selling pharmacies were constantly >60% all over Italy, differences were observed according to geographical area (see Fig.1). In less than 10% of cases tests are directly available on the shelf or sold through automatic vending machines. Specific training received on HIVST use was scarcely reported by respondents (4.6%, mostly delivered by the company agent of the test), but among those who didn't receive a specific training 42.2% are willing to receive it. Three quarters of selling pharmacies reported they received questions from customers, mainly on instructions for use, reliability of the test and what to do in case of reactive result. Regarding 2018 sales, median number of reported tests sold was 3 (interquartile range: 1-7), only 9.8% reported >20 tests sold in a year and 14.4% referred they sold none. A clear gradient North-South on test sold in 2018 was evident as well as differences within the province capital and the rest of province (see Fig. 2).
Conclusions: Rapid HIVST are not readily available in many Italian retail pharmacies, especially outside province capitals and in South Italy. To further increase the contribution of HIVST as tool to address timely HIV diagnosis, concerted public health activities should be implemented actively involving public pharmacies. Project funded by 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].

HIV epidemiology and retention in care

P 69 REDUCING LATE PRESENTERS PATIENTS RATE IN MILAN AREA (RELAPP STUDY): PRELIMINARY RESULTS

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Background: Almost one-third of HIV infected individuals in Europe do not receive healthcare services until diagnosis. In Italy, this phenomenon is evident, considering the high number of late presenter (LP) patients. During the years in which the infection is not diagnosed, it may not be completely silent: several pathologies can occur and, if correctly interpreted by General Practitioners (GPs) or by hospital specialists, an "alert" can be raised to advise the need to perform the HIV test. Starting from this assumption, the primary objective of the study "ReLaPP 2019" is to investigate the burden of LPs in Milan Area and to identify a list of behaviors and clinical events which can encourage HIV testing at a primary care level.
Materials and Methods: To identify relevant clinical events of LP patients, a cohort of LPs in charge at Sacco Hospital was selected. All consecutives cases in the previous 8 years were selected, among patient resident within the hospital catchment area (from 2011/01/01 to 2018/12/31 and a CD4 count ≤ 350 cells/mm3). Medical records were analyzed to identify the clinical events or risks factors likely to be related to HIV infection in the five years before diagnosis. Statistical analysis was performed using STATA 16.0 (StataCorp Collge Station TX USA 2019).
Results: Among the 653 new diagnoses reported at Sacco Hospital between 2011 and 2018, 45.9% were LP, of whom 295 (98.3%) were residing within Sacco Hospital catchment area and 243 (82.4%) were males. 196 patients were Italian (66.4%) and 74.6% were Caucasian. The most representative risk factors were MSM (52.2%) and Heterosexuals (43.2%) with a mean age at diagnosis of 40.5, with a statistically significant difference between groups, as determined by one-way ANOVA (F(2,283) = 7.05, p = .001). Before HIV diagnosis, HIV test was prescribed only for 38.6% of patients at risk. 110 patients (37.3%) had an AIDS diagnosis with 50-250 cells/µL and 64 (21.7%) were diagnosed with <50 cells/µL. 150 patients (50.8%) had pre-diagnosis symptoms and pathologies (95% CI .45-.57) (Figure 1): unexplained weight loss (17.2% [95% CI .13– .22]) and unexplained lymphadenopathy (7.5% [95% CI .08 – .11]) were the most frequent ones. Medical examinations were performed in more than 90% of cases (91.1%).
Conclusions: These preliminary findings show that HIV test was prescribed only to 38.6% of patients at risk, even though risk factors were present or pre-diagnostic symptoms/pathologies occurred. The results confirmed the need to implement training activities for GPs concerning the epidemiology and early symptoms of HIV infection, and to develop a tool indicating risk factors and clinical pathologies closely linked to HIV infection to be monitored at a local level to optimize early access to care and treatment.

HIV epidemiology and retention in care

P 70 MAY ADMINISTERING ROUTINE HIV TEST BE USEFUL TO UNCOVER THE ICEBERG IN A UNIVERSITY HOSPITAL SETTING? OUR EXPERIENCE

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Background: About 50%of new HIV cases in Europe are late diagnosis and these patients represent the major source of contagion. Starting from experiences of routine HIV testing in several European and Italian Healthcare settings demonstrating the utility in revealing the submerged seropositivity, the aim of this study was to assess the feasibility of this diagnostic approach in the setting of our University Hospital.
Material and Methods: We selected all new HIV diagnosis from 2013 to 2019 (recorded by informatic database); for each patient all the accesses to different services of our University hospital occurred prior to the HIV diagnosis were traceable in hospital informatic system. All the patients whose1st access to the hospital was concurrent or within40days from HIV diagnosis were not included. A descriptive analysis of the population at the time of 1st HIV positive test was performed. We considered the cumulative number of accesses, where and when the various accesses occurred, the type of symptoms registered/exams performed (when available)classifying them between suspicious of underlying HIV infection (low platelet count, leukopenia, leukocytosis, recurrent infections, FUO, STIs, mononucleosis-like symptoms, diarrhea)or not suspicious. We calculated a cumulative time between HIV diagnosis and each access.
Results: Of 512 new HIV diagnosis, 202had at least1 access to our hospital before HIV diagnosis and 94 had accessed prior to 40days from HIV diagnosis. Of those, 68(72%) were males, median age was 40y (IQR 33-51), 41(44%) were MSM; median CD4 cell count was228/mmc (IQR 55-436); CDC HIV stage at diagnosis was: A for35 patients (37%), B for11 (12%) and C for 24(25%); for24 patients (25%)data were missing. Median number of accesses was 2(IQR 1-8) (Table1). Considering the cumulative accesses (N=486), the majority was registered in analysis laboratories (N=206,42.4%) and in Emergency Department(N=88, 18.1%)(Figure 1). 27 patients(28.4%)presented with at least one suspicious exam. Any statistically significant differences were found neither in the population with or without a suspicious exam or in cumulative time between positive HIV test and suspicious/not suspicious exam performed (p=0.667). According to CDC HIV stage no differences were found neither in median number of accesses nor in the proportion of patients with or without suspicious analysis and HIV diagnosis.
Conclusions: Considering the limits of this study (few patients, poor availability of exams performed, no information about comorbidities preexisting to HIV test administration), these data do not consent to support a major indication to routine administering HIV test in the various services of our University Hospital, even though this strategy has proved to be a valid instrument to uncover the iceberg of HIV seropositivity in other Healthcare settings. Moreover, to have a suspicious exam does not seem to be related to a prompt decision to perform a HIV test in our experience.

HIV epidemiology and retention in care

P 71 HIGH RATES OF LOST-TO-FOLLOW-UP AMONG NAIVE HIV+ FEMALE POPULATION: REAL-LIFE DATA FROM UOC "IMMUNODEFICIENZE E MALATTIE INFETTIVE DI GENERE", D. COTUGNO HOSPITAL, NAPLES, 2017 -19

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Background: Despite worldwide about 50% of subjects affected by HIV are female, women are usually under-reported in clinical trials. Compared to men, women have different physiological, psychological and social characteristics, which may affect treatment response and safety. Moreover, real-life data have shown that women living with HIV (WLWH) receive a later diagnosis, at an older age and with a higher risk of treatment discontinuation. Therefore, real-life data about epidemiological and clinical features of HIV infection among women are still needed, in order to optimize the management.

Methods: We conducted a retrospective observational study including all newly diagnosed WLWH in the period 2017-19 in the UOC "Immunodeficienze e Malattie Infettive di Genere" at Cotugno Hospital, in Naples. Data source was represented by clinical electronic database. Aims of the study are: (i) to describe epidemiological and clinical characteristics of WLWH at diagnosis; (ii) to describe clinicians' attitude in the choice of ART; (iii) to investigate the rates of virological suppression, immunological recovery, safety, treatment discontinuation for any reason and lost-to-follow-up (LTFU) at 48 weeks (± 1 month).

Results: In the study period we enrolled 45 newly-diagnosed WLWH. Demographic and clinical characteristics are shown in Table 1. Median age was 37 years (range 18-65); 76% of population study was not italian, with 62% coming from Africa. Advanced naïve (CD4<200) were 55% and 42% showed an opportunistic infection. In 5 cases, diagnosis was established during pregnancy, while 2 women became pregnant during the study period. The most frequent comorbidities were cardiovascular diseases (hypertension and dyslipidaemia) and psychiatric disorders.

Initial ART regimens are summarized in Table2. Of note, 15% of WLWH showed at least one major mutation at the diagnosis. Triple regimens including INSTI represented the preferred option (52%).

Main clinical outcomes are shown in Table3. Rate of LTFU is 22% at week 24 and 24% at week 48. Including those LTFU, only 53% of patients achieved the viral suppression at week 48. Rates of treatment discontinuation were stable, but reasons for switching were different at 24 and 48 weeks (fig 1), with proactive/simplification switch increasing at week 48, due to the approval of TAF-including regimens.

Discussion: In this population of WLWH, clinical outcomes were poor. The high rates of LTFU may be due to demographic characteristics, with most of patients being immigrants. Most of LTFU were already not retained in care at week 24. On the other hand, those retained in care showed a good immunological recovery and a satisfying rate of viral suppression.

These data suggest the need for focused interventions on retention in care and adherence, favouring high-barrier-to-resistance regimens, and on vulnerability of this population, thanks to tailored social and psychological paths, in order to improve clinical outcomes.

HIV epidemiology and retention in care

P 72 RISK FACTORS FOR LATE HIV PRESENTATION IN A TERTIARY CARE UNIVERSITY HOSPITAL

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Background: Late Presenters (LPs) are defined as patients (pts) who are diagnosed with HIV with CD4 <350 cells/µL or an AIDS-defining illness (at any CD4). Among these pts, those who are diagnosed with CD4 <200 cells/µL or an AIDS-defining illness (at any CD4) are defined as LPs with Advanced Disease.
Late presentation has many consequences, such as poorer clinical outcomes, increased risk of transmission to others and higher economic impact.
Materials and methods: In our study, we included all the pts newly diagnosed with HIV during the period 2010-2018 at ASST Sette Laghi (Varese, Italy). We evaluated their clinical characteristics with one-year follow up.
Statistical analysis of data was performed using Kruskal-Wallis test, Mann-Whitney test and Chi-squared test. The significant results were expressed with the p-value set to 0,05.
Results: From January 2010 to December 2018, a total of 214 new HIV diagnosis was made at ASST Sette Laghi; 153 (71.5%) pts were male.
We evaluated the risk factors for HIV infection: 111 (51.9%) were heterosexuals, 80 (37.4%) were MSM, 7 (3.3%) were injecting drug users. At HIV diagnosis, the median age was 41.5 (17-80) years and the median CD4 cells count was 222.5 (1-1293) cells/µL.
One hundred thirty-six (63.6%) pts had <350 cells/µL or developed an AIDS-defining illness within 6 months from HIV diagnosis: 108 (79.4%) were LPs with Advanced Disease. Among the clinical characteristics analyzed, we found that late presentation was linked to older age (44±12.7 vs 39.1±11.1; p=0.007) and to a different reason to get tested for HIV (p<0.0001): the majority of LPs underwent HIV test during other clinical assessments (84%, p=0.0062) while non-LPs decided to get HIV tested after they had risky behaviors (25.6% vs 11%).
During the 6 months following the HIV diagnosis, 68/136 (50%) pts developed an AIDS-defining illness (8 were LPs and 60 were LPs with Advanced Disease). The most frequent AIDS-defining illness observed was Pneumocystis jirovecii pneumonia (17/68, 25%), whereas 14 (20.6%) had two or more AIDS defining conditions.
Twenty-two out of 136 (16.2%) pts were from African Countries and, compared to others, they were younger (36.6± vs 45.4±12.8, p=0.0034), the majority was heterosexual (95.4%, p=0.0028), they showed the lowest compliance to therapy (59.9% vs 12.2%, p<0.0001) and a higher mortality rate (13.4% vs 11.4%, p=0.031).
In the 12 months after the HIV diagnosis, 16/214 (7.5%) pts died: all of them were LPs (4/16, 25%) or LPs with Advanced Disease (12/16, 75%).
Conclusion: More than sixty percent of our pts were diagnosed with a late HIV infection. In our population, LPs were older and discovered their HIV infection while doing diagnostic investigations for other reasons. During the six months after diagnosis, 50% of the LPs developed an AIDS-defining disease.
Our study suggests the necessity of an implementation of HIV screening programs to increase early diagnosis and treatment of HIV infection.

HIV epidemiology and retention in care

P 73 EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF HIV/AIDS AMONG FOREIGN IN CAMPANIA REGION, 2008-19: WHICH DIFFERENCES WITH ITALIAN POPULATION?

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Background: Epidemiology of HIV/AIDS in Italy is continuously evolving. Foreign patients represent a significant part of incident cases in last years, increasing from 28,6% in 2010 to 34,4% in 2017. At national level, this increasing proportion is due to the decrease of cases among Italians, and not to a real increase among foreigners. This population have peculiar epidemiological and clinical characteristics. We briefly describe the epidemiological and clinical characteristics of newly diagnosed cases of HIV/AIDS among foreign people at "D.Cotugno" hospital, Naples, in 2008-2019, as a representative sample Campania Region.

Methods: Data about newly diagnosed HIV/AIDS cases among Italian and foreigners in 2008-19, derived from Forms sent yearly to Italian National HIV Surveillance system, were extracted and analysed. "D.Cotugno" hospital is a Infectious Diseases specialistic hospital, accounting for the most part of all HIV/AIDS new diagnoses in Campania Region.

Results: In the study period, a total of 1676 HIV/AIDS cases were diagnosed at "D.Cotugno" hospital, being about 70% of total cases in the Campania Region. Foreign patients were 560 (33,4%). The proportion of foreigners is stable over years (figure 1). Most of them come from Africa (68%) and Europe (21,8%). Among foreigners, female population is more represented (51,8% vs 13,8, p<0,0001), and median age is lower (36 vs 39 years-old). Risk factors strongly differ among Italian and not-Italian population, with homosexual intercourse and use of injective drugs being significantly higher among Italians, and heterosexual contacts being higher among not-Italians (p<000,1; table 1). Reasons for HIV testing are different, also, with tests performed for suggestive symptoms and pregnancy services significantly higher among foreigners (figure 2).

Clinical picture at diagnosis is more severe among foreigners: CD4 mean is lower (256 vs 339), as well as prevalence of AIDS cases is higher (31,3% vs 18,5%, p<0,0001). Prevalence of foreign patients with CD4 <350 and <200 across years is shown in figure 3: these categories stably represented more than 50% of cases. The prevalence of foreigners with HIV-RNA higher than 100.000 copies at first diagnosis significantly increases over years, ranging from 34% in 2008 to 71% in 2019 (p for correlation <0,0017).

Discussion: Data from foreign patients newly diagnosed at "D. Cotugno" hospital in 2009-19 do not substantially differ from national data in the same population. Indeed, at National level too, foreigners have different epidemiological characteristics, being the female heterosexual population the most represented, and showing a more severe clinical picture. In our population, the severity of disease at diagnosis is much more evident than National data, with more than 50% of patients with CD4<200 at diagnosis. Targeted interventions and campaigns should be developed in order to fill the gap between Italian and not-Italian HIV/AIDS patients.

HIV epidemiology and retention in care

P 74 THE EFFICACY OF CART REGIMENS AND RETENTION IN CARE IN AN HIV-INFECTED COHORT OF NAÏVE PATIENTS

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The guideline panels recommend antiretroviral therapy (ART) be offered to all HIV-infected patients, including asymptomatic individuals, regardless of their immune status. Initiating therapy at the initial visit can improve virologic outcomes and retention in care. Early ART is particularly important in patients with a CD4 count ≤200 cells/μL and for patients with comorbid conditions directly resulting from HIV infection.
The aim of this study is to analyze the HIV-infected naive population at S. Orsola-Malpighi Polyclinic of Bologna defining the epidemiological, therapeutic and adherence aspects of ART. The patients were divided into 5 groups based on the class of antiretrovirals prescribed. For each group, the parameters assessed were the percentage of patients with suppressed viral level and the mean of the CD4 + count at 1 and 3 months from the start of therapy and the number of patients lost to follow-up and therapeutic changes. Virological data and cART regimes were collected from our medical records and tracked in an Excel database. This analysis concerns naïve patients under treatment since January 2018 to December 2019.
The study involved 159 patients (22 female and 137 male) with a mean age of 42 years (range 19-78). Of these, 39 patients were foreigners.
N=37 (23%) received ABC/3TC+INI, N=43 (27%) TAF/FTC+INI, N=27 (17%) TDF/FTC+INI, N=40 (25%) TAF/FTC +NNRTI, N=12 (8%) other regimens.
GROUP 1=basal viral level 164373 cp, basal CD4+ count 310 cells. After 1 month, 38% of patients had HIV-RNA<50 cp/ml and CD4+ count 479. After 3 months 88% HIV-RNA <50 cp/ml and the CD4+ count 544. N=7 patients were lost in follow-up and 5 needed a switch of therapy (4 for ADR).
GROUP 2=basal viral level 865143 cp, basal CD4+ count 269 cells. After 1 month, 29% of patients had HIV-RNA<50 cp/ml and CD4+ count 474. After 3 months 88% HIV-RNA <50 cp/ml and the CD4+ count 490. N=2 patients were lost in follow-up and 9 needed a switch of therapy (3 for ADR).
GROUP 3=basal viral level 952161 cp, basal CD4+ count 331 cells. After 1 month, 52% of patients had HIV-RNA<50 cp/ml and CD4+ count 531. After 3 months 68% HIV-RNA <50 cp/ml and the CD4+ count 621. N=7 patients were lost in follow-up and 6 needed a switch of therapy (1 for ADR).
GROUP 4=basal viral level 47809 cp, basal CD4+ count 522 cells. After 1 month, 42% of patients had HIV-RNA<50 cp/ml and CD4+ count 701. After 3 months 85% HIV-RNA <50 cp/ml and the CD4+ count 799. N=3 patients were lost in follow-up and 6 needed a switch of therapy (1 for ADR).
Adherence to therapy assessed through drug picking was optimal in all patients.
By evaluating the clinical outcomes, all the groups allowed to have more than 50% of the patients with suppressed viral level and to reach a CD4+ count that allowed immunocompetence. However 12% of patients lost to follow-up and 16% needed a therapeutic switch. Therefore the naive are configured as a group of patients who need adequate support from a multidisciplinary team.

HIV epidemiology and retention in care

P 75 CHARACTERIZATION OF HIV-1 TRANSMISSION DYNAMICS IN NORTH AND CENTRAL ITALY OVER THE YEARS 2012-2019

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Background: To evaluate the dynamics and phylogenetic relationships of HIV-1 strains recently circulating in Northern and Central Italy.

Material and Methods: HIV-1 pol sequences were obtained from 1770 naïve individuals (1 per patient) diagnosed in different Italian centres in 2012-2019. The phylogenetic tree was built using HIV-TRACE and confirmed by a maximum likelihood approach implemented in FastTree 2.1.4 with automatic selection of the best fit evolutionary model of DNA substitution (GTR+G+I). Sequences linked with at least one other sequence with a bootstrap ≥0.90 and a mean pairwise distance ≤0.015 were considered genetically linked and classified as either pairs (2 members) or transmission-clusters (TCs, ≥3 members). Factors associated with TCs were evaluated by multivariate logistic regression (MLR).

Results: Most individuals were men (83.6%) and Italian (69.3%), with a median age of 39 (IQR:31-48) years. Of them, 83.1% were diagnosed in Central and 16.9% in Northern Italy. Men having sex with men (MSM) represented 44.1%, heterosexuals 32.4%. Individuals were infected mostly by B (63.5%), CRF02_AG (7.3%) or BF recombinant forms (6.9%). Compared to Central Italy, diagnoses in Northern Italy presented a lower proportion of MSM (32.0 vs 47.3%, p<0.001), a higher proportion of non-Europeans (28.7 vs 13.8%, p=0.001), higher CD4 cell counts (364 cells/mm3 [141-534] vs 301 [133-481], p=0.028), and lower viral load (4.86 log10 copies/mL [IQR: 4.14-5.50] vs 5.06 [4.50-5.59], p<0.001). Non-B subtypes, particularly recombinant forms, were more represented in Northern than in Central Italy (39.0 vs 35.9% and 24.3 vs 17.2%, respectively, p=0.168 and 0.003). No differences were found in transmitted drug resistance prevalence (13.7 vs 14.1%, p=0.468).

Regarding TCs, 80 pairs and 43 TCs were observed, corresponding to 15.0% and 21.1% of Northern and Central sequences (45.9% in pairs and 54.1% in TCs). Northern TCs were characterized by a lower prevalence of Italians (64.4% vs. 81.1%, p=0.003), MSM (37.8 vs. 63.2%, p=0.013), and a higher prevalence of non-B subtypes (55.6 vs. 36.4%, p=0.012). Sequences from Northern and Central Italy rarely intermingled: 31 mixed in 9 pairs and 3 TCs. Two of the 3 mixed TCs involved non-B subtypes (02_AG and 20_BG) and MSM individuals (85.7%), spanning over >5 years.

By MLR, infection by non-B subtype was the only factor significantly associated with being in TCs both in Northern and Central Italy (adjusted odds ratio: 7.87 [2.57-24.06] and 1.67 [1.17-2.40]).

Conclusions: Overall results highlight the existence of different profiles characterizing new HIV-1 diagnoses and transmission groups in Italy, that in absence of an adequate geographical coverage would be underestimated. Compared to Central Italy, Northern Italy is characterized by a higher number of non-B subtypes and non-European infected individuals, actively spreading among TCs, and participating in the epidemiological shift from B to non-B subtypes in Italy.

HIV epidemiology and retention in care

P 76 "EXTERNA": QOL PERCEPTION IN PLWHIV DURING ID CHECKUP

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Background: Since 2010, EXTERNA is a free of charge service offered - in partnership with ASA Milano - to PLWHIV undertaken by San Luigi ID Center (HSR), Milan. From EXTERNA we obtain key parameters concerning Linkage to care and Retention in care. Since 2018, following 2017 QoL guidelines, ASA's psychologists support of patients with treatment failure risk(10%), low adherence and multifactor vulnerability.
Aim: to assess QoL impact on psychological and clinical aspects during meeting with PLWHIV, ID doctor and psychologist.
Methods: A cross-sectional study on a random sample on 2018-19 questionnaires includes median (IQR) or frequency (%) by chi-square test/Fisher exact test or Wilcoxon rank-sum test. After check up by ID doctor, psychologists fill, in accord with PLWHIV, a semi-open grid questionnaire, based on variables emerging from preceding investigations.
Results: 41 PLWHIV(29 M, 11 F, 1 M2F)average age 52.8 MSM 48.7%, heterosexuals46,2%, bisex5.1%, otherwise classified as aging59%, foreigners15.4%, on chemsex 12.8%. Housing difficulties 14.6%, job problems 26.8%, alcohol addiction 22.5%, illegal drugs addiction30.8%. 24 persons remain in care by the same ID doctor and 17 persons change their ID doctor. 38 persons on 41 receive a modified therapy. 43.9% have no psychological support, 39% have been suggested a psychological support, 12.2% request by themselves support, 4.9% are taking support. Adherence: very high (92.7%)with only 3 persons not adherent (1 decease). 71% have perception of a low QoL, 29% of a good one. LowQoL when occurs only one ART simplification change(41.4% P<0.0001), betterQoL when changes are 2 or more(33.3% P<0.0001). Same significance referred to changes due to treatment failure, 1 change(lowQoL 37.9% P<0.0001) and 2 or more changes(good QoL 25% P<0.0001). When HPV is absent(12.2% of sample) goodQoL (25%), the opposite when HPV is present(29.3% of the sample)bad QoL(31% P<0.0001). All categories -aging64.3%, chemsex14.3%, foreigners 10.7% P<0.0001– show a lowQoL, of which better aging 45.5% and foreigners 27.3. No mention of safesex(56.8%) means lowQoL(66.7%) compared to safesex practice(40.5%) with 70% QoL P<0.0001. Positive correlation to QoL whether no psychological support is mentioned(75%) or it is suggested(16.7%)PLWHIV who perceive themselves sick (75.6%) have a lowQoL, 96.6% P<0.0001. Concern about the doctor or bad doctor/patient relationship lead to lowQoL85.7%. No connection shown among QoL and Hiv-rna, CD4 and sexual orientation.
Discussion: Being both reduced sample and inhomogeneous distribution, we can say adherence in itself is not sufficient to get a good Qol, which is influenced by at least 2 changes - in ARTsimplification and after TreatmentFailure-, no HPV, safesex practice and no need of psychological support. Concerns, doctor/patient difficulties and the perception of being a sick person play negatively on QoL. ASAwas supportedbyViivhealthcare

HIV epidemiology and retention in care

P 77 HIV SCREENING IN MIGRANT POPULATION LIVING IN "GHETTI" IN APULIA

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Introduction: Despite the universal health system and laws on protection of the migrant health, around 10,000 foreigners in Italy have limited or no access to essential assets and medical care. In Apulia, migrants form a large proportion of the low-cost labour force in the agricultural sector, often living in conditions of extreme marginalization in informal settlements called "ghetti". Since 2015, Doctors with Africa CUAMM, offers basic health care to migrants, reaching some settlements through a mobile clinic. A screening campaign for HIV has been conducted in this population using rapid tests.

Methods: From June 2019 to January 2020, a screening campaign for HIV–diabetes–hypertension was conducted, involving migrants living in 2 Apulian establishments: ghetto Pista in Borgo Mezzanone and Casa Sankara in San Severo, where, according to unofficial data, 2000 people usually stay during the tomato crops in summer. These sites were reached by a team of doctors, cultural mediators and volunteers with the use of a mobile clinic, given by the Apulian Region. A socio-demographic questionnaire was administered to all participants. Blood pressure was measured (high pressure defined as BP greater than 140/90 mmHg), and random glycemia was assessed using a cut-off of 200 mg/dl. After informed consent, a 3rd generation capillary HIV blood rapid test was used (Alere Determine, Abbott) for HIV testing.

Results: A total of 287 people (92% males) were screened, 96% from West Africa, 2% from East Africa and 2% from Middle East (most represented countries were Senegal, Gambia and Nigeria); median age was 28 years (IQR 24-34); subjects had been in Italy for a median of 48 months (IQR 36-60) and had lived in the "ghetto" for a median of 12 months (IQR 4-24). 42% of them did not have regular documents; however, 40% had had regular residency permission in the past; most of them (89%) did not have a family doctor.

41% of the population was married, but in most cases (78%) partners were in the country of origin; 76% had knowledge of sexually transmitted diseases, but only 22% had previously undergone HIV testing and only 38% had used the condom during the last sexual intercourse. However, none of subjects resulted HIV positive.

During the visit, 33% of subjects complained of other health problems, in most cases (61%) probably work-linked troubles (myalgia, arthralgia, asthenia, headache) and dental problems (11%). Less than 10% of subjects had hypertension and only 2% hyperglycaemia.

Conclusions:No cases of HIV infection were registered in the screened migrant population living in 2 large settlement in Apulia. Our experience suggests that the health conditions of this population are mainly linked to specific working activities in the agricultural fields, as well as to living conditions.

The screening campaign in difficult environments is an opportunity to take care of people who live on the fringes of society for whom it is difficult to access the healthcare system.

HIV epidemiology and retention in care

P 78 GEOGRAPHIC DISTRIBUTION OF DELAYED PRESENTATION OF HIV INFECTION IN HIV EMILIA ROMAGNA SURVEILLANCE SYSTEM

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Background: Late presentation of persons with HIV infection remains an obstacle to viral eradication. Age, male sex and being immigrants related to late presentation, but usually the role of geographical distribution was not considered. Our aim was to explore if geographical factors could play a role in the delay of HIV diagnosis.
Material and methods: We used data on new HIV diagnoses from the Emilia Romagna Regional HIV Surveillance, 2006-2018, linked through the anonymous identification code to local data of Parma, Reggio Emilia, Modena, Ferrara and Rimini Infectious Diseases Clinics. To identify similar profiles, epidemiological characteristics, CD4 cell count and AIDS at diagnosis were entered in a cluster analysis (Latent Class Analysis-LCA). To investigate HIV delayed presentation, we estimated a multinomial logistic regression (MLR) on the obtained cluster, with the geographical features of municipalities of residence as explanatory factors.
Results: We linked 2090 out of 2534 persons resident in the municipalities of the 5 provinces during the study period. Most persons were male (71%), median age at diagnosis was 39 yrs (interquartile range (IQR) 31-48), 34% were immigrants; 56% reported heterosexual contacts and 33% were men who have sex with men (MSM). Median CD4 count was 320 cells/mmc (IQR 128-550) and median HIV RNA 4.8 log (IQR 4.2–5.5). After LCA, we identified three groups that we labelled according to the characteristics most relevant in the group and that best differentiate groups (Figure 1). Group 1: Italian Male Late Presenters (IM-LP), 709 persons, mostly male, older, born in Italy, heterosexually-infected, CD4 count <350 cell/mmc; group 2: Foreign-born LP (FB-LP), 729 persons, mostly female, younger, foreign-born, heterosexually-infected, CD4 count <350 cell/mmc; group 3: Italian MSM Early Presenters (IM–EP), 652 persons, predominantly male, younger, born in Italy, MSM with a CD4 count >500 cells/mmc. Compared to IM-EP (Table 1), the risk of being in the IM-LP group was higher for persons who lived in small municipalities (<10,000 inhabitants Relative risk ratio (RRR) 1.9, 95%CI 1.3-2.6) or in lowland/mid-mountain municipalities (RRR: 2.3, 95%CI 1.3-3.9; RRR 2.6, 95%CI 1.3 -5.4). The risk of being in the FB-LP group was higher for persons who lived in municipalities located less than 30 km away from county seats/HIV clinics (RRR 1.9, 95%CI 1.3-2.8), or in lowland/mountain municipalities (RRR 2.1, 95%CI 1.1-3.8; RRR 3.5, 95%CI 1.6-7.6), and lower for persons who lived in medium-size cities (10-100,000 inhabitants RRR 0.7, 95%CI 0.6-0.9).
Conclusions: Although the HIV population considered comes mainly from large municipalities, this study suggests that subpopulations with a higher risk of delayed presentation could be identified in specific geographical contexts.

HIV epidemiology and retention in care

P 79 IMMUNOLOGICAL EVOLUTION OF A COHORT OF HIV-2 INFECTED PATIENTS: PECULIARITIES OF AN UNDERESTIMATED INFECTION

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Methods: We retrospectively analyzed all HIV-2 and HIV-1/HIV-2 positive patients followed in a large Italian clinic devoted to HIV care, from January 1987 to December 2018. We recorded demographic, viro-immunological, clinical and therapeutic data. We performed a descriptive analysis followed by a longitudinal analysis to explore the factors associated with CD4+ evolution; lastly, we studied in a multivariable model the possible predictors of death and AIDS in our cohort.

Results: 36 subjects were enrolled, 20 (55.6%) HIV-2 infected and 16 (44.4%) HIV-1/HIV-2 dual-infected. During observation, 16 patients were lost to follow up, while 4 died. Baseline characteristics of the population in study are summarized in Table 1. We found a lack of HIV-2 viremia in 20/36 subjects, however the major part of patients at baseline had a good viro-immunological profile with HIV-2 RNA <200 copies/ml and CD4+ >200 cell.

Median CD4+/CD8+ ratio at baseline were significantly higher in females than in males [CD4+/CD8+ ratio 0.85 (IQR 0.65 – 1.39) vs. 0.4 (IQR 0.15 – 0.6), p=0.03].

We found a CD4+ improvement overtime (beta regression coefficient - BRC- 462.63, p<0.001); in particular, patients aged >30 years had a worse CD4+ recovery (BRC 617.17, p<0.001).

Nevertheless, subjects taking ART had CD4+% increase overtime regardless of year of ART initiation (before or after 2007) and this trend appeared significantly better than in those who did not receive therapy (BRC 34.15, p<0.001)

Lastly, in multivariable model CD4+ T-cell count increase was negatively associated to death or AIDS (HR 0.40 95%CI 0.17-0.95, p=0.037 and HR 0.37 95%CI 0.18-0.75, p=0.006 respectively).

Conclusion: In our cohort, we found a higher prevalence of HIV-1/2 dual infection in respect of previous observations. Subjects with HIV-2 infection showed a favorable immunological condition at diagnosis; although some patients did not receive any treatment due to the high CD4+ and undetectable viremia, benefits of ART in those who received treatment are undiscussed. Moreover, our data suggest a different disease course based on age at diagnosis as happened in HIV-1 infections. We encourage starting ART at diagnosis in HIV-2 patients, regardless of CD4+, because even in new ART era, CD4+ decrease remains the strongest predictor of death and AIDS also in this population.

HIV epidemiology and retention in care

P 80 HIV TESTING OFFER AND SERVICES TO IMPROVE LINKAGE TO CARE IN PUBLIC SERVICES FOR HIV TEST: A SURVEY

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Background: Interventions aimed at promoting timely diagnosis, prompt access to and maintenance in clinical care for people diagnosed with HIV infection are relevant both for the single patient and for limiting HIV transmissions in the community. We conducted a survey on public centers offering HIV test investigating characteristics of their services focusing on activities aimed at promoting Linkage to Care (LtC) of people newly diagnosed with HIV.
Methods: We invited all public services offering HIV testing (excluding transfusional centers or services for drug consumers) in 16 Italian provinces (8 from Northern, 4 Central and 4 Southern Italy) with higher HIV incidence in 2018 (source ISS) to participate to an on-line survey.
Results: Among 171 services identified (92 clinical care centers - CC and 79 testing points - TP), 101 participated to the survey (59%) among which 59 CC (64%) and 42 TP (53%), less frequently in Southern Italy (44% vs. 68% in Northern and 61% Central Italy). A confirmatory test after a positive result at the screening test is performed in 89% of services, but in 62% of these cases, a second blood sample is needed. Rapid tests are available in 13% of services (17% in CC, 7% in TP). In 86% of cases test prescription is not required (95% in CC, 74% in TP). HIV test can be performed anonymously always or upon request in 81.2% of cases and is offered free of charge in 72.3%, while a payment is requested always (n=18) or in some cases (n=10; e.g. absence of a prescription when required, to perform the test in anonymity, screening people at risk or when counseling is requested but not standardly offered). In 40% of these 28 centers, the cost for HIV-testing was >10€. Pre-test counseling is not available at all in 57% of PT and 5% of CC. Post-test counseling is performed always in 45.5% of services (75% in CC, 5% in TP) or only in case of HIV-positivity (43.6% overall, 78% in TP). Communication of an HIV positive result is generally given during a post-test counselling (91/101) when indications are given on how to be linked to care in the same center where test was performed (n=40) or in other local centers, but in this case only 16/58 services have a concerted protocol for linking patients to a specific center(s). Many centers also offer other support activities for people who tested positive for HIV (e.g. psychological support, assistance for LtC) also in collaboration with NGOs. The median number of reported HIV tests performed in 2018 was 1500 (IQR: 300-5460, 4620 in TP, 680 in CC). HIV prevalence in 2018 was by far higher in CC than TP (median 1.6% vs 0.2%) as well as the reported proportion of HIV positive cases effectively linked to care (median 100% vs. 88%).
Conclusions: The results of this survey showed big differences in HIV testing offer and services for LtC people with a new HIV diagnosis, deserving further considerations to improve LtC. Project funded by Minister of Health (ref 4023/P.G.1)

HIV epidemiology and retention in care

P 81 GAP IN CARE AND LOSS TO FOLLOW UP DUE TO ADMINISTRATIVE BARRIERS AMONG MIGRANTS LIVING WITH HIV IN THE CITY OF PADOVA

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Continuum of care is essential in HIV to ensure good clinical outcome and reduce transmission. National estimates report loss to follow up (LTFU) from 30 to 20%, with significantly higher rates among migrants, for reasons hard to investigate. HIV care is offered free of charge in Italy, and the supply of antiretroviral therapy (ART) is hospital based. Both documented and undocumented migrants have the right to access the National Health System and to benefit from essential and preventive services, included HIV care. However, migrants can occur in administrative delays or impasses, especially during the renewal procedures of personal documents. Aim of the study is to evaluate gap in care and LTFU due to administrative reasons in the cohort of migrant followed at the HIV clinic of Padova.

Methods: This cross-sectional observational study was conducted through the review of clinical files of all HIV foreign patients on ART in the years 2018-2019. The analysis refers to the period 01/2016-01/2020. Socio-demographic and clinical data (last viral load and CD4 count) were collected. Any interruptions of visits or ART supply (≥3 months), occurring contextually to the expiration or delays in the renewal of the health insurance card, were registered. LTFU was considered for interruptions ≥12 months.

Results: The total number of HIV patients followed at the clinic is 1676. 372 (22.2%) are migrants, 52.4% male, mean age 44 years. 52.3% are from Sub-Saharan Africa (SSA), 14% from South America, 10.9% from EU-countries, 10.1% from Eastern Europe and 7.6% from Asia. 94% are regularly documented. We registered 27 therapeutic interruptions for 26 patients (7%), 23 from SSA and 3 from East Europe. 14 the females. The mean period since the first arrival in Italy is 7.4 years, and 5.1 years since HIV diagnosis. 20 patients had treatment adherence >90% and 19/25 were virologically suppressed before the interruption. 50% were re-engaged in care and the mean duration of interruption was 7.4 months (range 3-25). The mean time since the health insurance card renewal to the return to the clinic was 5.8 days. 10 patients presented a detectable viral load at re-engagement. 15 gaps occurred in 2019, 10 in 2018, 1 in both 2017 and 2016. Patients experiencing gaps have no significant differences in CD4 count and viral load compared to the others. The univariate analysis shows that older patients (OR 0.90, p=0.02), those with a longer diagnosis of HIV (OR 0.90, p=0.02) and coming from region other than SSA (OR=0.21, p=0.003) were less likely to experience interruptions; at the multivariate analysis only the provenience resulted significantly associated (aOR=0.20, p=0.003).

Conclusions: For a remarkable quote of migrant patients retention in care could be hampered by administrative problems, with clinical consequences and losses to follow up. These issues hit a population already particularly vulnerable and awareness and regional based surveillance appears to be necessary

HIV epidemiology and retention in care

P 82 LONG-TERM SURVIVORS IN A COHORT OF HIV+ PATIENTS DIAGNOSED BETWEEN 1985 AND 1994: PREDICTIVE FACTORS ASSOCIATED WITH MORE THAN 25 YEARS OF SURVIVAL

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Background: HIV remains a serious public health challenge. By the end of 2018, 32.0 million people are estimated died from HIV-related causes since the start of epidemic. Although the mortality rate among patients diagnosed during the pre-HAART era has been dramatic, a considerable number of them is still alive. Aim of this study was to evaluate the percentage of HIV long term survivors (LTS) in a cohort of HIV+ subjects diagnosed between 1985 and 1994 speculating on potential predictive factors associated to long survival.

Material and methods: Single-centre retrospective study. Epidemiological and clinical data registered at the time of HIV diagnosis were collected from medical records. Longitudinal observation was stopped on 31 Dec 2019. Subjects surviving more than 300 months from HIV diagnosis were defined LTS. Chi-square and Mann Whitney U test were used when appropriate to compare the two groups. Identified variables in the univariate analysis with a p value <0.05 were included in a logistic regression model. Globally 224 subjects were enrolled; 169 (75,4%) males, 109 (48.7%) IVDUs, 43 (19.2%) MSMs, 54 (24.1%) heterosexuals. Median age 29 (IQR 25-34) years, median CD4+ 239 (IQR 58-456) cells/µl, median CD4+ nadir 51 (21-169) cells/µl; 72 (32%) were AIDS presenters, 124 (55%) had any AIDS diagnosis (ADI), 110 (49%) were anti HCV+. 132 (59%) were treated with suboptimal pre-HAART treatment, 128 (57%) with HAART regimen.

Results: 99 (44.2%) subjects were LTS (all but 7 still alive at the end of follow up) with a median (IQR) survival of 363 (330-402) months. 125 (55.8%) subjects died before 25 years (NLTS) with a median survival of 35 (14-112) months. The main cause of dead was an HIV associated event.

At univariate analysis to be LTS vs NLTS was associated with the following conditions: female sex (37.3% vs 14.4%, p<0,0001), median age [27 vs 30 years, p=0,0003], HCV coinfection (57,6% vs 42,4% p=0,034), AIDS presentation (3% vs 55.2% p < 0,0001) any AIDS defining illness (23.2% vs 80.8%, p<0,0001), median CD4 count [378 vs 78 cells/µl, p<0,0001], CD4 nadir [163 vs 33 cells/µl, p<0,0001] and CD4/CD8 ratio [0,4 vs 0,24, p<0,0001]. Finally, during the follow up 75.7% and 100% of LTS were respectively exposed to suboptimal ARV treatment or HAART vs 45.6% and 23.2% of NLTS (p<0,0001). At multivariate analysis CD4 nadir, HCV coinfection, lack of ADI during the follow up and to be treated with HAART remain significantly associated with LTS.

Conclusions: Surprisingly 44% of patient survived more than 25 years from HIV diagnosis. Conditions traditionally associated with late presentation as male sex, older age, low CD4, AIDS and lack of ARV treatment were associated to bad prognosis. In accord with multivariate analysis, only CD4 nadir, HCV coinfection and lacking of clinical progression towards AIDS could be considered the main favourable condition driving to ARV treatment that has to be considered the stronger predictor of long-term survival.

HIV epidemiology and retention in care

P 83 NEW DIAGNOSES OF HIV INFECTION: WHAT HAS CHANGED IN 10 YEARS

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Background: Despite effective prevention measures and therapeutic regimens are available, the annual number of new HIV diagnoses remained stable.
The aim of this study was to evaluate baseline characteristics, clinical course and treatment of patients with a new diagnosis of HIV infection referred in the last ten years to the Infectious Disease Unit, Foggia. Italy.
Methods: In this retrospective study. all newly consecutive HIV-diagnosed patients observed from January 1, 2010, to December 31, 2019 were enrolled. For each patient demographic characteristics, mode of HIV transmission, timing of HIV diagnosis. antiretroviral (ART) prescription, CD4 cells counts and plasma HIV-RNA viral load (VL) at the time of diagnosis were collected. During follow-up, retention in care, proportion of undetectable VL and reason for switch ART were evaluated.
Patients were classified as lost to follow up (LTFU) if they were more than six consecutive months without visit and/or drug intake.
Statistical analysis was performed by the $\chi 2$ test (or by Fisher's exact test) for categorical variables.
Results: Overall. 170 newly diagnosed HIV-infected patients were enrolled in 10 years. During the observation period, the number of new HIV diagnoses has slightly increased, but it remained stable in the last 3 years.
Demographic, epidemiological, clinical and therapeutic aspects were shoved in table 1. Most of patients were Italians, median age at diagnosis was 35 years (3–78), 78.8% of patients were male; foreign patients were 63 (37.1%). A total of 74 patients (43.5%) were advanced naives (CD4 <200 cell/mmc). Patients who started ART within one month of diagnosis have significantly increased in the last two years. At the end of the study period, 21.8% patients (34/170) were LTFU, and 10 had died because of AIDS related disease. Overall, 74% of participants were retained in care in whole period, of whom 95.7% achieved and maintained viral suppression over ten years, with an increasing significative trend from 2010 to 2019. Starting cART within 30 days from diagnosis showed a significant association with retention in care. Being foreign-born patients, being advanced naives and baseline HIVRNA >100000 cp/ml was statistically significant for failed retention in care (Table2)
Conclusions: Early ART initiation reduces loss to follow-up and increases viral suppression. Even though this analysis was limited to one site and could not be representative of all HIV patients in Italy, it could be crucial identifying categories of patients at greater risk of not being retained in care. Intercepting these vulnerable population and rapid ART initiation could have the potential to improve linkage and retention in HIV and facilitate the achievement of the UNAIDS goal.

HIV immunology and immune-based therapies

P 84 ACNE VULGARIS AS POSSIBLE IMMUNE RECOVERY FOLLICULITIS DRIVEN BY THE LYMPHOCYTE T CD8+ IMMUNOLOGICAL RECOVERY IN NAÏVE AND EXPERIENCED PATIENTS

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Background: Since the introduction of the antiretroviral therapy (ART), we assisted to a reduction of incidence of eosinophilic folliculitis and ART-related skin effects, as maculopapular rash with regimens containing NVP or EFV. Whereas Immune Recovery Folliculitis (IRF) have increased.
As for the Herpes Zoster reactivation, the rapid reconstitution of lymphocyte T CD8+ was recognized as the main pathogenic factor of the phenomenon. Patients with dermatologic diseases can experience significant psychological morbidity.
Material and methods: We report two cases of possible IRF diagnosed at the HIV clinic of the INMI L- Spallanzani in Rome: the first occurred in a patient ART experienced with good immune status and stable virological suppression after a treatment simplification; the second occurred in Primary HIV Infection (PHI) after the ART starts.
Results: CASE REPORT 1. A 26-year-old Argentinian woman was diagnosed as HIV-1 positive on July 2016 during the w8 of her pregnancy. At diagnosis she had a CD4+ count of 1045 cells/μL and a viral load (VL) of 1.620,000 cp/mL (CDC A1). She started ART with TDF/FTC + LPV/r, simplified to TAF /FTC + DRV/c in March 2018. 12 weeks after the switch a pruritic papular-pustular facial eruption appeared. She received the clinical diagnosis of acne vulgaris. She had no previous history of acne vulgaris. She was treated with oral doxycicline during 1 month plus a topical retinoid, without improvement. So the was put on oral contraceptive with a decrease of lesions but a lowering of the mood. At the start of TAF/FTC+ DRV/c her CD4+ was 1151 cells/μL, CD8+ 630 cells/μL and CD4/CD8 was 1.82. 20w after the cART simplification, the CD8+ count increased until 1006 cells/μL and ratio CD4/CD8 decreased to 1.00. 1y after the switch, CD4+ was 1272 cells/μL; CD8+ 961 cells/μL and CD4/CD8 1.32.
CASE REPORT 2. A 24-year-old Caucasian man was diagnosed with acute infection (Fiebig score V). Within 4 days he started a 4-drug regimen with DRV/c+ RAL+TDF/FTC. At the diagnosis CD4+ was 324 cells/μL, CD8+ 440 cells/μL and CD4/CD8 ratio 0.73 and with a VL of 6.889 cp/ml. 3w after therapy start, patient developed few facial comedons, papules and pustules, and immunological parameters revealed CD4 635, CD8+ 827 cells/μL, CD4/CD8 0.76. After 8w, therapy was simplified to E/C/F/TAF and the lesions persisted. He recalled past history of acne. Clinical diagnosis of acne vulgaris was made and was started treatment with topical retinoid during 4 months plus oral Doxicicline during 40 days with a mild reduction of lesions. For both cases was not performed a cutaneous biopsy.
Conclusions: The skin manifestations caused by immune recovery should be ruled out by clinicians, even in experienced-ART patients in simplification switch. IRF needs to be considered in differential diagnosis from antiretroviral drug-related skin effects. Further studies are necessary on pathogenic, diagnostic and treatment of uncommon IRIS manifestation.

HIV immunology and immune-based therapies

P 85 INFLUENCE OF HLA HAPLOTYPE ON IMMUNOLOGICAL RECOVERY IN HIV-INFECTED PATIENTS

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Introduction: Overall, almost one third of HIV patients have insufficient CD4/CD8 ratio recovery despite prolonged suppression of HIV replication. Indeed, immunological recovery is also influenced by host related factors. In particular, the HLA haplotypes are involved in the activation of immune response and have been linked to the progression of disease in HIV-infected people not on antiretroviral therapy (ART). Herein, we evaluated the influence of different class I HLA haplotypes on immunological recovery in HIV positive patients who, after initiating ART, had achieved viral suppression.
Materials and methods: A total of 306 patients, with available HLA haplotypes, were retrospectively analysed. Epidemiological and clinical data, including HBV/HCV coinfections, comorbidities, CMV serostatus were retrieved. Immunological recovery was defined as the achievement of a CD4/CD8 ratio >0.9 within 3 years of follow up after viral suppression. Patient follow-up was censored in case of viral failure (HIV-RNA>200 copies/ml, twice consecutively).
Results: With respect to their counterparts, 129/306 (42%) patients who had achieved immunological recovery were younger (mean±SD: 46±11 vs 50±10 years, p<0.001), had higher basal CD4 cells (467±272 vs 277±225 cell/mmc3, p<0.001), higher CD4/CD8 ratio (0.63±0.38 vs 0.31±0.28, p<0.001) and lower viral load (5.36±6 vs 5.34±5.8 log10 copies/ml, p<0.001). Moreover, they were less likely to have HCV coinfection (16% vs 30%, p=0.005), AIDS diagnosis (9% vs 24%, p<0.001) and comorbidities (46% vs 70%, p<0.001); finally, they had been treated with newer HIV drug classes (p<0.001) as a first ART regimen. Overall, HLA A2 was the most frequent allele (41%), followed by HLA B35 (27%) and HLA A24 (25%). The remaining ones were observed in less than 20% of cases. At univariable analysis no HLA haplotype was significantly associated with immunological recovery. Similarly, Kaplan-Maier curves did not show any significant difference in terms of immunological recovery according to various HLA groups. Using a multivariable logistic regression model, comorbidities [adjusted odds ratio (aOR)= 0.39, 95% confidence interval (CI)= 0.20-0.74], older ART regimens (aOR= 0.22, 95% CI= 0.07-0.68) and HLA-A24 (aOR= 0.48, 95% CI=0.24-0.97) predicted persistent immunological impairment (Table 1). Conversely, the only predictor of immune recovery was a higher baseline CD4/CD8 ratio (aOR= 31.5, 95% CI=7.1-138.8).
Conclusions: In our analysis, while baseline CD4/CD8 ratio predicted immunological recovery, comorbidities, use of older ART regimen and HLA A24 were associated with persistent immunological impairment. This finding, obtained in subjects successfully treated with ART, is consistent with previous studies demonstrating a correlation between HLA-A24 and a faster disease progression, thereby confirming the detrimental impact of HLA-A24 on HIV infection in the absence of therapy.

HIV pathogenesis

P 86 OXIDATIVE STRESS AND GUT MICROBIOTA COMPOSITION IN PRIMARY HIV INFECTION

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Background: HIV induces oxidative stress by deregulation of oxidative stress balance with increased reactive oxygen species (ROS) production and mitochondrial dysfunction. ROS are known to affect both the composition of mucosa-associated microbiota and the integrity of gut epithelial barrier. Given that a marked gut dysbiosis has been described in both early and chronic HIV infection, we hypothesize a role of ROS in promoting gut dysbiosis, possibly linked to persistent inflammation, with differences according to HIV infection phase/stage.
Methods: We enrolled 10 HIV+ cART naïve patients (pts): 5 chronically infected HIV (CHI) and 5 in primary HIV infection (PHI), according to Fiebig stage. Reactive oxygen species (ROS) and C reactive protein (CRP) were assessed by ELISA. Fecal microbiota composition (relative abundance, α-/β-diversity) was evaluated by MiSeq Illumina®). Statistical analyses: Mann-Whitney U, Chi-squared, Linear regression as appropriate.
Results: Epidemiological, clinical and HIV-related featured were comparable between the two study groups, except for HIV infection duration that is longer in CHI (p=0.05).
CHI showed higher circulating ROS (p= 0.03) (Fig.1a), yet no differences in CRP were observed.
While Observed and Chao1 indexes were comparable in PHI and CHI patients, Shannon and Simpson indexes resulted higher in PHI group (p<0.01 both) (Fig.1b). In the Beta-diversity analysis, patients cluster together (Fig.1c), and the LEfSe analysis showed slight differences between the two study groups, with higher prevalence of Bacteroides in PHI, and Clostridia and Gammaproteobacteria in CHI (Fig.1d). No major differences were observed in the relative abundance. Nelle figure dovete usare sempre le diciture CHI e PHI. Aggiungere la legenda anche ad 1c
Interestingly, we observed a positive association between plasma levels of ROS and Lactobacillaceae family (p=.038) and a negative trend with Veillonellaceae family (p=.093) (Fig.1e). Furthermore, plasma CRP levels positively correlate with Bacteroidaceae (p=.028), Bifidobacteriaceae (p=.0009), Lactobacillaceae families (p=.002) and negatively with both CD4 and CD8 T-cell count (p=.058, p=.029, respectively).
Conclusions: In our cohort of naïve HIV-infected patients, PHI and CHI featured different microbiota composition, with loss of bacterial taxonomic richness in CHI, suggesting a detrimental effect of HIV infection on the human gut microbiota as the infection advances.
Interestingly, the associations of certain bacteria taxa with both circulating levels of ROS and CRP, support our hypothesis of an interplay between oxidative stress, inflammation and dysbiosis in the setting of acute/early HIV infection, whom causal-effect relationship needs to be further deciphered

HIV prevention (PrEP and PEP)

P 87 PrEP awareness and attitudes in a survey among Italian clinicians

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Background: Following the results of trials assessing the safety and efficacy of daily oral antiretroviral preexposure prophylaxis (PrEP) for the prevention of HIV infection, international guidelines suggested the use of emtricitabine/tenofovir disoproxile fumarate in selected populations at risk of contracting HIV infection. We aimed to understand the evolution of knowledge of, and attitudes toward, PrEP among Italian infectious diseases specialists.

Methods: Physicians from 13 centers located in differente Italian regions were surveyed to assess their awareness of PrEP and PrEP-related guidance, willingness to prescribe PrEP and concerns about its use. We also collected data on eventual PrEP failures and/or other sexually transmitted diseases (STDs) occurred during follow-up. Descriptive statistics were computed for physicians' attitude-related and PrEP-related questions.

Results: Awareness of PrEP was high, as all clinicians were aware of the indications of PrEP in national and international guidelines. Fifty-four percent prescribed PrEP at least once, 23% have never prescribed it but they assisted patients on PrEP while 23% physicians told that no patients were on PrEP in their clinical centers. No cases of PrEP failure were reported, while 26% of patients contracted another STD while on PrEP. When asked to which patients they would prescribe PrEP, most clinicians identified patients at increased risk in accordance with CDC guidelines: MSM with inconsistent condom use during receptive anal sex (77%), MSM with inconsistent condom use during insertive anal sex (54%) and women with an HIV+ male partner (67%). Considering also populations not specifically identified as an eligible target, 61% would prescribe to sex workers and 54% to male-to-female transwomen. When asked how likely they were to prescribe PrEP to an adult patient with ongoing risk of HIV and no medical contraindications, 77% were definitely or very likely to do so. Most frequently reported concerns include: increased risk of contracting other STDs (92%), toxicity (46%), correlation between PrEP and ARV resistance (38%), increased costs for the national health system (38%).

Conclusions: In Italy access to PrEP is not uniform for different problems (cost, reduced drug availability, difficulty in having it accepted by local ethics committees), and also the offer of PrEP differs between hospitals. It is important to continue monitoring clinicians' attitudes and practices as the use of PrEP increases.

HIV prevention (PrEP and PEP)

P 88 PREP: THE STORIES ABOUT WHO USED THE THERAPY

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Context: The project "PrEP: the stories about who used it" completes the trilogy started in 2016 with the project "Long-term-survivors" and continued in 2017 with the project "Serodiscordant partner: exception or normality?".
In 2017 ASA gave birth to the help desk PrEP-Prophylaxis Pre-Exposure HIV. Twice a month, in the headquarters of the association, a team of experts was available to give advice to people and clarify doubts and concerns regarding this new treatment.
During the meetings in the headquarter, the experts of ASA met and advised people about the correct use of PrEP. Thanks to the interviews a lot of data about people who used PrEP have been collected to understand the reasons which brought them to assume PrEP and what changed in their life thanks to the treatment. This project has been carried out within a few months and the interviews will be published on the special number EssePiù, the magazine of the Association.
Methodology: The methodology which has been used was the one of direct interviews or interviews through questionnaires which were distributed to people who started the treatment after the meetings in ASA. People chose to remain anonymous, in fact, in the interviews a fake name was used.
The questionnaire has been realized under the supervision of a psychologist.
Results: 31 interviews have been realized: 28 homosexual, 2 bisexual and 1 transgender, aged between 28 and 64. The majority is between 40 (14 people) and 50 (6), nine are between twenty (2) and thirty (7), two exceed the sixty years old.
Among the respondents, 20 people are single, 8 are in a couple in which one is serodiscordant and three are in a complex relationship.
Most of them live in Lombardy, mainly in Milan (16) or in the provinces (14) and one in Catanzaro.
21 of them chose the continued therapy while 8 used the on demand one and eventually 2 started with a continued assumption to end up with the on demand one.
Conclusions: From the interviews it appears that PrEP changed for the better the quality of life of people. The therapy supported not only who lives casual relationships, but also the couple's life in order to be more serene.
HIV is still very scary and knowing that PrEP eliminate the possibility of contagion make people quieter and more relaxed during their sexual relations. Concerning the side effects, the majority of respondents didn't have particular problems with the assumption of therapy.
Moreover, respondents don't have problem at talking about PrEP with occasional partners and with friends, in some cases from consumers they became promoters of PrEP.
They are very satisfied with the meetings organized by ASA for the preparation of PrEP, especially they appreciated the know how, kindness and willingness of doctors, psychologists and volunteers.
Asa was supported by Gilead.

HIV prevention (PrEP and PEP)

P 89 YOUNG PEOPLE INFORM YOUNG PEOPLE - SPEAK TO THE STUDENTS WITH THE PEER SECTION OF THE SCHOOL PROJECT

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Background: Peer Education is a methodology based on the activation of learning paths and knowledge, able to affect in cascading in the social reference environment through the abilities and skills developed by the student leaders trained. Taking on the role of "experts", student leaders try to inspire a change in knowledge, attitudes, rules, beliefs and behaviors of their peers.Anlaids Lazio, in partnership with INMI Spallanzani, organizes activities of peer education for students of Second Grade Schools in the Lazio Region, with age between 14 and 20 years, as a joint section of School Project since 2006, to:
- Spread correct information on HIV/AIDS/STI
- Train Opinion Leaders
- Support the realization of PEER Projects, such as events and/or products for actions on prevention among the entire in school/young population
- Create awareness and encourage access to HIV/STI Tests

Steps:
- Presentation Meeting of the project in the participating schools and selection of Peer Educators (each peer group is composed of 15/20 students).
- Conduction of a survey to evaluate knowledge of students related to the subject matters.
- Educational path of information/education with peer groups.
- Information/education workshops (maximum 40 hours) for in-depth analysis of scientific contents, to improve the perception of self effectiveness, self -esteem and self confidence, to work on a final project.
- Final seminar with all the classes of each Institute, managed by opinion leaders with the supervision of tutors and informants.

Each peer group for the realization of the final project, has at its disposal its own qualified tutor – infectious diseases specialists, psychologists and experts.
Every meeting is based on an active methodology, with interactive techniques (circle time, brainstorming, role playing, etc...).

Results: From 2008 to 2019 adhered to the School Peer Education Project:
A) 21 Schools for a total of 432 peer students trained as opinion leaders, able to inform more than 10.000/year.
This Methodology allowed to:
- Inform/educate on HIV/AIDS/IST
- Rise more self-consciousness and the ability to work in groups
- Be active key players and not inactive audience
- Intensify the process of self - empowerment
- Collect data on knowledge of the young population

B) 21 PEER Projects (such Video, Gadget, Brochure, theatrical performances, etc...) were realized with and for the young people

Conclusions: We have observed a welcome interest and intense participation to the activities by the students, with a growing enthusiasm for the given opportunity to be put in the game as protagonists. The peer education not only carry out training purposes for the individuals involved, but turns out to be a real empowerment, since peer educators are called to engage the recipient population in learning participatory processes.

HIV prevention (PrEP and PEP)

P 90 PROBLEMS AND DIFFICULTIES IN THE MANAGEMENT OF A PREP CLINIC

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Background: Hiv Pre-Exposure prophylaxis (PrEP) is a practice that, along with the use of condoms, can reduce the risk of contracting HIV+ by over 90%.
As established by the ministerial guidelines, the drug for PrEP (Tenofovir Disoproxil + Emtricitabine) can be bought by patients with a special prescription (Group C), while a follow-up is provided by the hospital.
Since May 2019 our hospital founded 4 centers dedicated to PrEP, active every day from Monday to Friday. In this study the activities of one of these centers will be described, along with the difficulties we came across.
Material and Methods: from May 2019 to January 2020, in 9 months of activity, a total of 28 people (27M + 1F) have come to the hospital, 24 (28%) of which have been deemed fit for PrEP (Tenofovir Deisoproxil + Emtricitabina) after a detailed clinical evaluation and bioumoral tests (clinical chemistry, virology and kidney functionality). Of the 24 patients (23M+1F; average age 41.6), 8 have come multiple times to the center (second and third prescription of the drug) for a total of 38 visits. All (100%) of the 23 males enrolled were men who have sex with men (MSM), 20 of which reported at-risk behaviours (occasional unprotected sex, many partners, erectile disfunctions and difficulties with wearing condoms etc.) while 3 of them were partners of HIV+ patients with non suppressed viral load.
The only female enrolled was the partner of a HIV+ patient with non suppressed viral load (discordant couple).
All patients had pre-therapy counselling and signed a consent form (see Fig.1) (not suggested by guidelines, made ad hoc and given to the patient) which highlighted PrEP strategy, its risks and benefits and the different possible methods of use (day by day or on demand).
Results: Of the 24 patients enrolled none reported collateral symptoms caused by the drug; these participated in the follow-up in different times in relation to the type of PrEP (day-by-day or on demand). The difficulties have been many and, in particular, related with the 1) lacking promotion of the service on the hospital's website; 2) inadequate level of privacy that the procedures garantee to the patients (necessity to consult the family doctor both for the first visit and for the laboratoty tests); 3) expensive procedure for the patient (tickets for visits and laboratory tests, drug's cost); 4) initial difficulty with finding the drug in city pharmacies; 5) competition with the Internet (the drug is acquirable from other countries at very low prices with no follow-ups required).

HIV prevention (PrEP and PEP)

P 91 POST-EXPOSURE PROPHYLAXIS IN REAL LIFE

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Background: The ANLAIDS FORUM is a large database suitable to evaluate the real life awareness of post-exposure prophylaxis (PEP) as an intervention to respond to HIV potential exposure. Despite national guidelines (GL) on when and how to administer PEP, there is large variability on its use according to health care provider opinion.
Materials And Methods: We evaluated 4,258 messages of people about potential transmission of HIV in the 2015 -2019 period, focusing our attention on questions about PEP. Data on sex, risk factor, sexual practices, time of PEP initiation and completion of treatment were collected in each case in which PEP was requested. The accordance with the subsequent editions of GL on PEP was assessed in each case. Time trends and correlates of PEP administration were analyzed by Cochran-Armitage and Chi squared tests.
Results: Questions regarding PEP increased significantly from 1.5% (9/606) in 2015, to 1.1% (8/734), 1.7% (16/953), 2.8% (27/990) and 4.9% (46/975) (p=0.0002) in the following years. People entering the forum after having requested PEP for professional exposure were only three out of 106. Of the remaining 103, 91.5% were men, 46.2% identified themselves as heterosexuals (HEs), 41.5% as men having sex with men (MSM). The type of sexual intercourse concerned was vaginal in 31.7%, anal in 29.1%, not defined in 19.1%, to be considered not at risk in 12.3% and active oral sex in 7.8% of cases. One-hundred-one out of 106 individuals (95.3%) were recommended PEP of whom 77 (76.2%) assumed the drugs within 48 hours. Interestingly, 58.5% of subjects (62/106) obtained the prescription although it was not strictly recommended by GL. Among PEP users 44.5% of cases (45/101) self-reported a complete treatment cycle.
Sex, risk factor, type of sexual intercourse, time of administration and completion of PEP did not change over the course of the study. Similarly, the proportions of individuals taking PEP regardless of GL did not vary over time. PEP was more often prescribed regardless of GL to men rather than women (65.2% vs 22.2%, p=0.012), HEs rather than MSM (77.8% vs 58.1%, p=<0.001) and those reporting vaginal rather than anal intercourse (86.2% vs 42.9%, p=0.02).
Conclusions: The results of a real-life experience of PEP suggest that information about PEP has grown among people that experience a risk of HIV transmission because of unprotected vaginal or anal sexual intercourses and active oral sex. Moreover, Infectious Diseases physicians seem to be open to prescribe PEP even though the criteria of GL were not always fulfilled, probably because the risk reported was not clearly assessable. Our data show that individuals seeking PEP are mainly heterosexual men who had an unprotected vaginal intercourse. Nevertheless, prevention strategies should be implemented to reduce the risk of HIV transmission and the subsequent reduction in PEP requests.

HIV prevention (PrEP and PEP)

P 92 DETERMINANTS OF DRUG START, SCHEDULE CHANGE AND DISCONTINUATION IN PREP USERS

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Background: Italian guidelines recommend offering pre-exposure prophylaxis (PrEP) to men who have sex with men (MSM) who recently engaged in condomless anal sex, had a diagnosis of sexually transmitted infection (STI), required post-exposure prophylaxis (PEP) or used chemsex. Aims of present study are: describe the agreement with guidelines recommendation in subjects starting PrEP; assess proportion and reasons for schedule change between continuative and event-driven (ED) administration; define the determinants for drug discontinuation.
Methods: This monocentric, retrospective analysis included all subjects who started PrEP between January 2018 and January 2020. Demographic, behavioral and clinical features were collected. Descriptive statistics and non-parametric (Chi-square and Mann Whitney U, as appropriate) tests were used. Odd Ratios (ORs) were calculated to describe potential risk factors for drug discontinuation. Incidence of sexual acts per 100 person/years (PY) was evaluated in those who continued PrEP and in those who discontinued; differences among groups were estimated with the conditional maximum-likelihood estimate Rate Ratio.
Results: 80 subjects were included in the analysis: they were mainly MSM (95%), Italian (85%), with a median age of 35 (IQR 30-42) years and with a high level of education (61.3% had a University degree). 86.2% showed at least one condition that would recommend PrEP while 55% had a combination of more than one unsafe behavior; 5 subjects (6.3%) resulted at highest risk showing all risky deeds (Figure 1).
The majority (67.5%) chose the ED administration, while 13.8% changed the schedule over time (mainly for increased sexual activity or because they wanted to test drug tolerability).
PrEP was discontinued by 13 subjects (13.3%) above all for loss to follow up (7.5%). Those engaging in receptive anal intercourses showed a OR of 3.75 (95%CI 1.08-13.02, p=0.031) to remain on treatment. Those who persisted in PrEP showed a higher rate of sexual acts (6045 versus 3167 x100PY, p<0.001) and of condomless sex (2439 versus 1300 x100PY, p<0.001).
Conclusions: PrEP was generally prescribed according to guidelines recommendations and with ED administration. The rate of discontinuation was similar to what reported in published literature: subjects who decided to remain on PrEP showed to be at higher risk engaging in more sexual acts – especially condomless – and in receptive anal intercourses.

HIV prevention (PrEP and PEP)

P 93 NO INCREASED RISK OF ADVERSE EVENTS AND SEXUALLY TRANSMITTED INFECTIONS IN PREP USERS DESPITE THE RISE IN CONDOMLESS SEX

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Background: Pre-exposure prophylaxis (PrEP) demonstrated to be highly effective in reducing the risk of acquiring HIV infection. Nevertheless, several critics started about its toxicity – especially in terms of renal tubulopathy – and the expected rise in condomless sex with a potential consequent increase in sexually transmitted infections (STIs). Aim of present study is to describe the outcomes in terms of clinical adverse events (AE) and laboratory alterations, number of sexual acts, condomless anal sex and STI acquisition in PrEP users.
Methods: This monocentric, retrospective analysis included all subjects who started PrEP between January 2018 and January 2020. Demographic, behavioral and clinical features were collected. Descriptive statistics and non-parametric (Chi-square and Kruskall-Wallis, as appropriate) tests were used.
Results: 80 subjects were included in the analysis: they were mainly MSM (95%), Italians (85%), with a median age of 35 (IQR 30-42) years and with a high level of education (61.3% took a University degree). The vast majority had a previous STI diagnosis (68.8%), mainly syphilis (31.3%) and anal condylomas (20.1%). Chemsex was performed by 13.8% subjects. A large part (67.5%) chose the event-driven administration.
The median follow-up was 124 (IQR 53-207) days. Figure 1 shows clinical and laboratory trends over time: no difference in terms of tubular function and liver parameters was observed. AEs (especially gastro-intestinal) were mentioned by 40.9% of subjects at the first visit after PrEP start, but these complaints significantly decreased over time (at the last visit, they dropped to 15.4% and none was drug-related, p=0.048).
The mean number of sexual acts did not increase over time, while condomless sex passed from 39.4% to 54.4% (p<0.001). STIs at baseline visit were 27.5% (50.0% if including pathogens not clinically relevant as Ureaplasmas and M. hominis) and remained permanently very common throughout the study period (p=0.092). Chlamydia (15.0% at baseline) and gonorrhea (11.3%) were the most common; the diagnoses of these STIs showed an increasing trend over time but without reaching the threshold of significance (p=0.056). Of note, syphilis persisted always below 2%.
Conclusions: PrEP was generally well tolerated and did not show any lab toxicity concern. The median number of sexual intercourses did not change, while condomless sex increased strengthening that PrEP might modify sexual habits. Nevertheless, the presence of STIs was high at baseline visit and remained stable over time, thus confirming that this population was already at high risk of HIV acquisition before PrEP prescription. As already published, syphilis in PrEP users was uncommon probably because the treatment of other STIs have an impact on treponemal infection. These data confirm that PrEP could have an essential role against the HIV epidemic and for a better sexual health.

HIV prevention (PrEP and PEP)

P 94 PREP: PSYCHOLOGICAL AND EMOTIONAL ASPECTS

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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 ASA offers a service on appointment aimed to counteract DOIY 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 1st 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, after service's merging into Milano Checkpoint_ct and ng rapid tests are also offered at the same time.The psychologist faces motivations leading to PrEP,sexual behavior (also chemsex),attitude towards Hiv,thoughts and expectations regarding medication,giving opportunity to reflect over themselves.Both specialists stress that PrEP cannot substitute condoms.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 December 2019 have been analyzed by descriptive statistics.Bio-psycho-social and medical features,sexual habits and risk behaviors are observed.Qualitative analysis on interviews with the psychologist have been conducted.

Results: 189 users(M 97,8%;26-40 49,2%;homosexual 85,2%;graduated 59,2%;Italians 84,6%;using Chems 36,3%;STI and/or PEP before 69%).During the 1st 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 2nd appointment we talk about eventual difficulties of having safe sex.Following appointments are devoted to their own relationship with PrEP taking and changes in sexual life.

Conclusions: Contrarily to common PrEP preconceptions, more than half of the sample take PrEP as "precaution, supplementary care". Only 32% of the users always have safe sex. To take PrEP is easy for everybody and produces positive fallout on sex emotional aspects. Particularly in beginning months, persons on PrEP develop better sexual activity. During the subsequent meetings, along with their sexuality, they talk over themselves, their relationships and how they face Hiv. At baseline, 36% of them are scared by stigma and, during the process, aware of U=U and of PrEP successful results, they appear less scared. Half of the users who did not show for the follow-up, had engaged in new relationships.PrEP is confirmed as a valid tool for prevention,as well as for fight against stigma and for a better self-consciousness.

HIV prevention (PrEP and PEP)

P 95 PREP USE AMONGST MSM IN ITALY: DATA FROM THE EMIS 2017 SURVEY

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Background: Whilst the WHO and the ECDC recommend that countries integrate PrEP into HIV prevention programmes for key populations to reach the goal of ending the AIDS epidemic by 2030, in 2019 only 14 European and Central Asian countries provided and reimbursed PrEP within their national health system. In Italy generic PrEP became available in pharmacies in October 2017 at a reasonable cost. EMIS 2017 provides an opportunity to analyse the need for PrEP in Italy, since the data indicates the proportion of PrEP uptake amongst respondents, and allows the possibility to estimate the gap between PrEP access and expressed need in Italian MSM at the time of the survey.
Methods: EMIS 2017 is an Internet based self-completion survey funded by the EU Health
Programme 2014-2020. It enrolled 127,000 MSM from 47 European and Central Asian countries between October 2017 and January 2018. The Italian dataset comprised 11,025 respondents; data was analysed using STATA V13.0 adopting a descriptive approach to generate estimates and related confidence intervals.
Results: 8.172 respondents (74.15%; CI: 73.32-74.95) defined themselves as gay or homosexual, whilst 1.940 (17.60%; CI: 16.90-18.32) identified as bisexual. Mean age was 38.78 (St Dev: 12.36), with a minimum of 14 and a maximum of 84 years of age. Considering PrEP as a preventive option, 6.080 respondents declared they had heard of it (56.07%; IC: 55.13-57.00), whereas 2.67% (IC: 2.39-2.98) reported they had tried to get PrEP since its introduction as a preventive measure. Considering PrEP use, only 70 MSM (0.64%; IC: 0.51-0.80) reported having ever used it and only 42 (0.40%; IC: 0.29-0.53) confirmed that they were either taking PrEP daily or 'on demand' at the time of the survey. When asked about potential PrEP use, 4.136 respondents (42%; IC: 41.34-43.30) declared they would be quite likely or very likely to use it if PrEP was made available and affordable.
Conclusions: Based on the Italian national dataset of EMIS 2017, at the end of 2017/beginning of 2018 PrEP use was still quite rare in Italy despite the potential benefits that could derive from PrEP implementation at individual and community level. Almost half of respondents had never heard of PrEP, and almost half would have been willing to use it but could not access it. Such data are striking and suggest that significant efforts are required to speed-up the introduction of a national Italian strategy for PrEP promotion and implementation.

HIV prevention (PrEP and PEP)

P 96 PRE-EXPOSURE PROPHYLAXIS (PREP): THE ONE-YEAR EXPERIENCE OF THE FIRST DEDICATED SERVICE OF TUSCANY REGION IN S.M.ANNUNZIATA HOSPITAL, FLORENCE

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Background: Pre-Exposure Prophylaxis (PrEP) is currently an approved strategy for prevention of HIV infection in high-risk populations. In January 2019 the Infectious Diseases Unit of S.M.Annunziata Hospital (Azienda USL Toscana Centro), Florence, set up the first PrEP service of Tuscany Region.

Methods: Azienda USL Toscana Centro created a new dedicated e-mail account for people requiring PrEP information (profilassipreesposizione.firenze@uslcentro.toscana.it), that was published on www.prepinfo.it website (Plus association) and on Facebook.

The account was daily managed by three dedicated medical doctors of the Infectious Diseases Unit of S.M. Annunziata Hospital, and a visit was offered to all people asking for a contact.

Users performed a baseline screening for renal function, HIV, HAV, HBV, HCV, Syphilis and other sexually transmitted infections (STIs), and received a counseling for PrEP evaluation. Smith Score was applied for MSM.

For those beginning PrEP, follow-up exams and visits were planned every three months.

Epidemiological and clinical data were collected.

Results: From January 2019 to January 2020 43 people contacted us; of these, 9 didn't further reply to our e-mail, while 34 performed the first visit and baseline screening. They were all males, median age 41.7 yrs, 85.3% MSM, 35.3% coming from other Tuscan cities or other regions; 76.5% had a high-level instruction (degree), 32.4% reported at least one previous episode of post-exposure prophylaxis (PEP) and 38.3% a previously diagnosed STI.

At baseline, one patient had a first diagnosis of HIV infection showing a recent seroconversion, and 4 cases of undiagnosed STIs were identified, with an overall rate of newly detected and untreated infections of 14.7%.

The 29.4% of users was susceptible to HBV and 44.1% to HAV; all of them were sent to the dedicated vaccination service of our Unit. Complete baseline characteristics are shown in Tables 1-2.

PrEP was prescribed in 30 cases (35.3% on-demand); 5 users were lost-to-follow-up after the first prescription, while 83.3% is regularly on follow-up (Fig.1-2).

No adverse events were reported, and no acute HIV, HBV, HCV and HAV infections were observed.

During follow-up, 7 cases of STIs were diagnosed and treated (3 C.trachomatis, 2 Syphilis, 1 N.gonorrhoeae, 1 U. urealyticum).

Conclusions: The first Tuscany Region experience of a PrEP service performed by our Unit with the collaboration of HIV associations, received a high interest among high-risk populations; the availability of a dedicated e-mail account was a strategy that allowed a quick access to visits.

In our experience PrEP confirmed effectiveness in HIV prevention; moreover, the required baseline and follow-up screenings proved to be an important instrument for the identification of people susceptible for vaccinations, and for the quick diagnosis and treatment of STIs. A dedicated service was organized in our Unit twice a month to immediately refer people requiring vaccinations.

HIV prevention (PrEP and PEP)

P 97 IN VITRO EFFECT OF CASTANEA SATIVA MILL. BARK EXTRACT (ENC®) ON HIV-1 INFECTION: A POTENTIAL MICROBICIDE

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Background: Unprotected sexual intercourse is the first route for sustaining the global spread of human immunodeficiency virus type 1 (HIV-1), responsible for 85% of new HIV-1 infections in the world. The development of topical treatments might be crucial to prevent or reduce the transmission of HIV at the level of the genital and rectal mucosa.
Natural molecules, containing tannins and related compounds, have shown an interesting antimicrobial activity: we analysed the antiviral activity of the partially purified Castanea Sativa Mill. bark extract (ENC®), consisted of over 78% hydrolysable tannins, in cell cultures infected with different HIV-1 strains.
Material and methods: HIV-1Bal and HIV-1IIIb (5ng/ml HIV-1 gag p24), R5 and X4 laboratory strains respectively, were pre-incubated with scalar concentrations (0, 1, 5, 10 and 20 micrograms/ml) of ENC®, then added to activated PBMCs and seeded at 1x10^6 cells/ml into fresh medium at 37°C: the antiviral effect of ENC® was determined measuring HIV-1 p24 HIV level in cell supernatants at 5 dpi using an ELISA kit (Biomerieux). In the next experiments, attachment, pre-attachment and post-attachment assays were carried out to investigate the ENC® related antiviral mechanisms. In addition, in a dilution assay, the compound was pre-incubated with the two viral strains and diluted 50-fold to reduce ENC® concentration below the concentration capable of preventing HIV infection; after that, the diluted mixtures were added to the activated PBMCs. Finally, the cytotoxicity of ENC® was assessed using the CCK-8 viability assay (Merck), followed by analysis of the lactate dehydrogenase (LDH) levels.
Results: In the first set of experiments, the R5-tropic HIV-1Bal or X4-tropic HIV-1IIIb (5 ng/ml of HIV-1 gag p24) were pre-incubated with scalar concentrations of ENC®: a significant decrease in the p24 protein ($p<0.05$; Mann Whitney test) was detected in ENC® concentration-dependent way respect to untreated control. Time-binding assays with HIV-1IIIb and HIV -1Bal (pre and post attachment assay) were performed to determine the stage of the viral replication cycle at which ENC® interferes with the infection. No inhibition was observed by these experimental approaches, but the p24 levels revealed a significantly reduction of HIV-1 infection at 5 dpi in dilution assay, suggesting that the antiviral effect might be related to a direct interaction between the virus and compound during extracellular phase. Finally, ENC® was not cytotoxic and no statistical differences in the release of the cytoplasmic enzyme LDH were observed between treated and untreated cells.
Conclusions: Castanea Sativa Mill. bark extract (ENC®) could be an attractive candidate microbicide against HIV-1 infection: it is safe and free of side effects, with a significant antiviral activity. In future, we also would like to examine its role in preventing the HIV-1 infection using a biologically organotypic model of cervicovaginal epithelial tissue.

HIV virology

P 98 UNDETECTABLE VERSUS LOW LEVEL HIV VIREMIA ON PATIENTS TAKING ANTIRETROVIRAL THERAPY

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Background: The persistence of Low levels of viremia (LLV) continues to be a challenge for Infectious Diseases physicians even in age of highly effective and tolerable treatments. The basal immuno-virologic condition, the viral subtype and the co-infections are factors that may impact on this results.
The aim of our study is to compare the demographic and clinical characteristics between patients with viremia from 20 through 100 copies/mL (LLV), viremic blips (viremia >20 copies/mL preceded and followed by undetectability), viremia under 20 copies/mL (VLLV) and undetectable HIV RNA (U).
Materials and Methods: observational retrospective study including people living with HIV who have had access to Infectious Diseases ambulatory of Perugia from January 1ST to December 31ST 2018. Exclusion criteria were poor compliance, diagnosis of HIV from less than 12 months and presence of primary mutations of resistance. Data were extrapolated from clinical files and analyzed through one way ANOVA and Chi Square test.
Results: Overall 356 patients were examined, the majority of which were male (273/356), Italians (258/356), heterosexual (178/356) divided in: 64 (18%) LLV, 83 (23%) blip, 109 (31%) VLLV and 100 (28%) U. The mean age and the age at HIV diagnosis were respectively 50 and 37.6 years without significant differences between the groups. Epidemiological and clinical characteristics of each group are shown in table 1. We have found no relation between co-infection with syphilis and detectable HIV viremia; co-infection with HBV was significantly related with U group. The U group showed high level of nadir CD4 cells count compared with VLLV (p=0.039) and LLV (p=0.0008) and lower HIV RNA zenith compared to LLV (p=0.0133) and blips (p=0.0138).
Conclusions: This study shows that U group has, as expected, the best immuno-virologic condition at the HIV diagnosis. As a matter of fact, CD4 cells nadir is lower in LLV and VLLV patients while HIV RNA zenith is significantly higher in LLV and blips group. Further studies with a wider sample are needed to confirm these findings.

HIV virology

P 99 QUANTIFICATION OF TOTAL HIV-1 DNA IN THE PERIPHERAL BLOOD OF NAÏVE AND TREATED PATIENTS

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Background: Despite the suppression of plasma HIV-1 RNA to undetectable levels obtained by effective antiretroviral therapy, HIV-1 DNA can persist in host cells, establishing a reservoir from which replication can resume in case of therapy interruption. HIV-DNA quantification allows the evaluation of the global residual HIV burden in blood and tissues and can guide possible therapy simplification. The study is aimed to quantify total HIV-1 DNA in a cohort of patients either naïve or chronically infected using a totally validated protocol for HIV-1 proviral DNA.

Material and methods: A total of 128 samples, whole blood or PBMCs as available, from a cohort of HIV-1 patients, either naïve or chronically infected, were analysed. Whole blood specimens were collected and PBMCs were separated by Ficoll density gradient centrifugation. DNA was extracted on Abbott m2000sp instrument. Results were interpolated on a master calibration curve generated from 2 standards extracted and amplified as clinical samples. HIV-1 DNA results were normalised on both Lymphocytes and CD4+ cells using human telomerase reverse transcriptase (hTERT) as reference gene. Results obtained for blood samples and PBMCs from the same patient were compared when both specimens were available. Spearman correlation, Mann Whitney U-test and Wilcoxon's rank sum test were performed using GraphPad Prism software.

Results: HIV-DNA was significantly higher ($p<0,0001$) in drug naïve than chronically treated patients. Proviral loads correlated with lymphocytes and CD4+ counts only in naïve patients ($p=0,0002$ and $p<0,0001$, respectively). Both naïve and treated patients displayed a significant inverse correlation between CD4+ nadir and proviral loads. Considering only naïve patients, a significant correlation between HIV-RNA and proviral reservoir, measured on the same day, was observed. Correlation between therapy duration and proviral loads was investigated in chronically infected patients. No significant difference was obtained from the comparison between proviral loads on whole blood and PBMCs from the same patient.

Conclusions: A consistent variability in proviral loads was found probably due to differences in disease stage and progression among patients. The significantly wider HIV-1 DNA reservoir in naïve than in chronically infected patients confirms that viral reservoir reduction could be linked to therapeutic effectiveness. Our results confirm HIV-1 DNA as marker of disease progression and highlight its value as a predictive factor of therapy success, supporting the relationship between the width of latent reservoir and the immunological status of patient.

HIV virology

P 100 HIV2-VPX MODULATION OF MDDCS-CD4+ T CELLS HIV-1 TRANS INFECTION

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Dendritic Cells (DCs) are professional Antigen Presenting Cells (APC) that serve as a bridge between innate immune sensing of pathogens and adaptive immune responses, especially in the mucosal tissues.
By capturing the virus and presenting it to CD4+ T cells, DCs are believed to play a pivotal role in the cellular spreading of Human Immunodeficiency Virus (HIV) infection: this mechanism has been termed Trans Infection. Notably, the receptors required for HIV-1 entry are present on DCs cell membrane but HIV-1 infection of DCs is blocked at the level of reverse transcription by the host cell restriction factor SAM domain and HD domain-containing protein 1 (SAMHD1). In addition, HIV-1 is not sensed by DCs and does not induce an antiviral type-I Interferon (IFN) response, at least in vitro. On the contrary, HIV-2 efficiently infects DCs by inducing SAMHD1 degradation through interaction with the viral accessory protein Vpx, absent in HIV-1. The efficient infection of DCs by HIV-2 results in a robust antiviral response.
In this study, we want to investigate whether circumventing SAMHD1 restriction by ectopic expression of Vpx could alter their ability to Trans-Infect CD4+T cells.
In order to analyze the effect of Vpx on HIV-1 infection of DCs, we purified CD14+ cells from buffy coats of healthy donors and differentiated them into Monocyte-Derived Dendritic Cells (MDDCs) by adding Interleukin-4 (IL-4) and Granulocyte-macrophage colony-stimulating factor (GMCS-F). MDDCs were infected with HIV-1-GFP in the presence and in the absence of Vpx. MDDCs RNA was collected at different time points post infection and expression of different ISGs was determined by Real-Time PCR. Levels of infection of MDDCs were monitored by Flow Cytometry.
We observed that adding viral particles containing Vpx during HIV-1 infection of DCs dramatically increased infection and expression of Interferon Stimulated Genes (ISGs) in 3 different donors, as previously reported by other groups (Manel et al., 2010 Nature, Yoh et al., Cell 2015). In order to analyze how this antiviral state influences DC-T cell Trans Infection, we pulsed MDDCs with HIV-1 with or without Vpx for 6 hours and added resting CD4+ T cells from the same donor. Levels of infection of CD4+ T cells was monitored by Flow Cytometry.
We observed that the antiviral state induced by HIV-1 in the presence of Vpx did not alter the ability of DCs to Trans-Infect resting CD4+ T cells added 6 hours after pulsing.
Taken together, these data suggest that CD4+ T cells might be resistant to IFN antiviral signaling elicited by DCs, or that DC-T Trans Infection is more rapid than the IFN signaling.

HIV virology

P 101 NEW POTENTIAL ANTI-HIV AGENTS: THE ANTIMICROBIAL PEPTIDE TEMPORIN L

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Background: Temporins are small (8-17 amino acid residues), C-terminally alpha-amidated peptides with a weak cationic charge that are widely distributed in frogs belonging to the Ranidae family. They represent the largest family of antimicrobial peptides (AMP) with over 100 different isoforms. Most of these peptides adopt an amphipathic helical-like conformation in a hydrophobic environment. The first isolated and well-characterized are the isoforms A (TA), B (TB) and L (TL). They are principally active against Gram-positive bacteria, and only weakly active against Gram-negative bacterial strains, with the exception of Temporin L. TL is the strongest antimicrobial peptide, but it is toxic on human erythrocytes and for this reason, it's possible to design new synthetic analogues with a higher therapeutic index vital. Several interesting TL derived peptides have been identified, called TL34, TL48 and TL49, which preserved yet the antimicrobial activity albeit with reduced cytolytic effects in vitro. Therefore, the aim of this work is to evaluate their potential as anti-Human Immunodeficiency Virus type 1 (HIV-1).
Materials and Methods: The cytotoxic activity of TL34, TL48 and TL49 on TZM-bl and peripheral blood mononuclear cells (PBMCs), cell lines suitable for HIV-1 infection, was evaluated through 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) assay. Then, we evaluated TL derived peptides' activity to inhibit HIV-1 infection in pre-treatment and post-treatment assays on the same cellular models. Finally, to determine the infectivity, the enzyme-linked immunosorbent assay (ELISA) HIV p24gag was used.
Results: In order to determine a not cytotoxic concentration useful to the antiviral tests, a MTT assay was performed. TZM-bl cells resulted more sensitive than PBMCs to the treatment with the three peptides after 48 hours. The peptides showed a relevant antiviral effect against HIV-1. In detail, TL49 was able to reduce more than half of the viral infectivity at 5 micromolar in post-treatment assay on PBMCs. On the other hand, TL48 could inhibit HIV entry at 10 micromolar in pre-treatment assay on TZM-bl. **Conclusions:** Recently, we found that some TL analogous peptides had high anti-herpetic activity, both against HSV-1 and HSV-2. It is well known that HSV-2 is associated with incident HIV infection facilitating its transmission. Therefore we analysed the anti-HIV potential of TL34, TL48 and TL49. The results seem to be an attractive topic for future research with the aim of discovering a drug with a dual antiviral potential.

HIV virology

P 102 FAST AND SENSITIVE QPCR ASSAY FOR THE CONCOMITANT QUANTIFICATION OF BACTERIAL 16S RDNA AND HIV-1 DNA: PRELIMINARY DATA FROM BLOOD SAMPLES OF HIV-1 INFECTED PATIENTS

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Background: Chronic HIV infection is characterized by persistent microbial translocation, higher immune activation and latent viral reservoirs. Given the role of microbial translocation and HIV reservoirs in promoting diseases progression and CD4 loss, we investigated the feasibility of concomitant measurement of both DNA sequences encoding bacterial ribosomal 16S RNA (16S rDNA,as marker of MT) and total HIV-DNA levels in blood samples of HIV-infected subjects.
Material/Methods: Cellular DNA of 5 HIV-1 infected patients and 5 healthy donors was extracted from blood cells following the pretreatment step for gram-positive bacteria. We used primers spanning the hypervariable region V1-V2 of the 16S rDNA in order to detect the majority of bacteria. To evaluate the false-positive signals from contaminating bacterial DNA we included various negative controls in each DNA extraction section. The 16S rDNA, total HIV-DNA levels and a selected endogenous genes (internal control, IQ), were quantified by Sybr-Green PCR based assay. The quantity of targets was interpolated using a specific standard curve. Results for 16S rDNA levels were obtained applying a correction factor of 1.24, taking into account the contamination of bacterial DNA and 16S rDNA levels in the HIV negative subjects. The final data were reported as 16S rDNA and HIV DNA copy number per µg of cellular DNA or mL of blood.
Results: The method validation was performed by evaluating a series of parameter characteristics. The limit of detection (LOD) and quantification (LOQ) were 1 and 2 copies of each target/PCR reaction, the linearity range was >5-log and reproducibility were within 20%. High (95%-100%) and similar (delta slope <0.1) efficiency of amplification was obtained for all targets, allowing an accurate comparison of the data. We have successfully obtained the concurrent measurement of 16S rDNA and HIV DNA in 100% of a preliminary series of samples. The mean levels of 16S rDNA and HIV DNA were: 23337 vs 12407 and 1493 vs 792 cp/mL in Off-ART and On-ART patients, respectively. The levels of 16S rDNA were lower in cART-treated persons with undetectable viremia (8957 cp/mL) than in those with viremia <40 cp (14131 cp/mL). HIV-negative persons had detectable 16S rDNA levels of 36 ± 10 cp/PCR reaction.
Conclusion: To our knowledge, the developed qPCR format the we describe here, was the first method for the concomitant measurement of 16S rDNA (marker of MT) and total HIV-DNA in a single PCR run, starting from few volume of blood and using an internal control for procedure and sample variations normalization. Preliminary results showed that cART naive subjects had detectable 16S rDNA in the blood twice as high as cART treated patients, while the HIV-DNA levels were 2-4 fold higher in untreated. Further studies on larger sample size are needed to confirm the feasibility of the developed assay and the results, in order to apply this method in the clinical practice.

HIV virology

P 103 HIV-DNA QUANTIFICATION IN PBMC: EVALUATION OF TWO NEW REAL-TIME PCR COMMERCIAL TEST

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Introduction: Quantification of total HIV-1 DNA from peripheral blood mononuclear cells (PBMC) of patients via polymerase chain reaction (PCR) provides a useful tool to monitor the size of the viral reservoir. Total HIV-DNA (integrated and unintegrated forms) is a marker of disease progression and survival, a potential indicator for the initiation of antiretrovirals in treatment-naïve patients, a predictor of virological rebounds in treatment-patients, and could be a predictor of the presence and severity of some HIV-1 associate disorders. Standardized methods for the total HIV-DNA quantification are currently lacking and several discordant results are still present in different studies.
Aim of this work was to analyze the performances of two commercial total HIV-DNA kit based on real-time PCR (qPCR) for the measurement of total HIV-DNA in PBMCs samples from HIV positive patients.
Materials and Methods: Ten plasma samples derived from 10 HIV-1 patients (2 naïve patients and 8 patients with viraemia below 20 copies/ml) were tested with two commercial total HIV-DNA quantitative assays, the HIV-1 DNA quantitative kit (HIV-DNA Q, Diatheva, Italy) and the Realquality RQ-HIV DNA (RQ-HIV DNA, AB Analitica, Italy) and compared with the "in house" qPCR test routinely used in our laboratory. All the two commercial methods allow the detection and quantification of total HIV-1 DNA, M group, in PBMC. The "in house" HIV-DNA quantitative assay is a qPCR test designed to target LTR regions (Viard et al., AIDS 2004) and that use as standard curve a serial pNL4-3 HIV-1 plasmid dilution (from 105 to 10 copies/reaction). PBMCs were obtained with separation of lymphocytes and peripheral mononuclear cells by using the Leucosep tubes (Greiner Bio-one, RM, Italy).
Results: All the three tests were able to detect and quantify total HIV-DNA of 9 patients while for 1 patients HIV-DNA resulted undetectable with all the assays. Correlation between RQ-HIV DNA and HIV-DNA Q, RQ-HIV DNA and the in-house test, and HIV-DNA Q and in-house assay, were respectively, 0.95, 0.79 and 0.7 (Spearman rank test). Comparing the two commercial test with the in-house method, we observed a quite difference: with the Bland-Altman analysis the mean difference between in-house test and RQ-HIV DNA and HIV-DNA Q were, respectively, 0.71 and 0.81. The two commercial tests with a Bland-Altman analysis, reported a close quantification of all samples since the mean of difference was -0.05.
Conclusions: In this study, the two commercial test for total HIV-DNA quantification, showed a good performance in the quantification of total HIV-DNA from PBMC derived from HIV positive patients and reported an high correlation. Therefore, these commercial assays could be interesting in the standardization method for total HIV-DNA quantification and to better understand clinical implication of this marker.

HIV virology

P 104 INFLUENCE OF HIV-1 V2 DOMAIN CHARACTERISTICS ON IMMUNOLOGICAL RECOVERY UNDER ART

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Introduction: The V2 domain of HIV-1 plays many functions, especially in early phases of infection; however, its role in chronic phase of disease and immune response is still debated. In previous studies, elongation of the V2 sequence was a predictor of slow disease progression as it was a lower net charge of the V2 domain. No data are available regarding the influence of specific V2 sites on immune recovery under ART. Herein, we aim to investigate if some properties of V2 may influence the immune recovery in course of a successful antiretroviral therapy (ART).
Methods: V2 sequences were obtained from 249 naïve patients with newly diagnosed HIV infection who initiated a successful ART regimen. V2 sequences were analyzed in terms of length, net charge (NC), N-linked glycosylation sites (PNGs) and 179-181tripeptide. Clinical and immuno-virologic data at the start of therapy (baseline) and at 6 months, 1 and 2 years after the first undetectable viral load were retrieved from our internal database. Predictors of CD4/CD8 ratio increase, defined as the difference between the last and first available CD4/CD8 ratio, were assessed by univariable and multivariable linear regression model.
Results: Patients were mostly males (n. 213; 86%), with a mean age (±SD) of 36.9 (±11.7) years. An acute HIV infection was diagnosed in 6.8% of subjects, while 13% of patients had an AIDS diagnosis at presentation. Mean baseline CD4 cells count was 387 (±256) cells/μL, mean CD4/CD8 ratio was 0.45 (±0.33), and mean HIV viral load (VL) was 4.70 (±0.89) log10 cp/ml. In the majority of patients (55%), the first line ART regimen was a protease inhibitor (PI)-based regimen, whereas 25% of patients received an integrase inhibitor-based regimen.
Mean length of V2 sequences was 42 (±3.7) base pair, mean number of PNGs was 2.4 (±0.79), and mean NC was 0.63 (±1.4). Among different V2 179-181tripeptide, the LDV mimotope was the most frequently detected (99 cases, 40%), followed by LDI (66, 26.5%).
After 2 years of viral load suppression, 52,6% of patients achieved a complete immune recovery (CD4/CD8 >0.9), with a mean increase of 0.45 (±0.47) of CD4/CD8 ratio.
By performing a linear regression model, acute HIV infection was associated with a CD4/CD8 ratio increase (r2= 0.258 p=0.031). A higher baseline CD4/CD8 ratio (r2= -0.45 p<0.001), a PI-based ART (r2= -0.17 p=0.037), AIDS diagnosis (r2= -0.21 p=0.027), and the presence of the LDV 179-181tripeptide (r2= -0.155 p=0.033) were inversely correlated with the CD4/CD8 ratio gain (Table 1).
Conclusions: Our study appears to suggest a potential participation of some properties of V2 in influencing the CD4/CD8 ratio after obtaining viral load suppression in patients who receive effective ART

HIV virology

P 105 SUSCEPTIBILITY TO HIV-1 INTEGRASE INHIBITORS IN HIV-1 SUB-SUBTYPE A6 ISOLATES

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Background: Regimens based on second generation integrase inhibitors (INSTIs) such as dolutegravir (DTG) and bictegravir (BIC) are currently recommended as the preferred first-line HIV-1 therapy. Considering the recent introduction of second generation INSTIs in the Russian Federation, this study aimed to evaluate the natural susceptibility of INSTIs in viral strains belonging to sub-subtype A6, which is the most prevalent genetic variant circulating in Russia and surrounding countries.

Materials and methods: The identification of plasma samples harboring viral strains belonging to sub-subtype A6 was carried out through phylogenetic analysis of HIV-1 sequences generated during routine HIV-1 drug resistance testing. Viral sequences assigned to subtype A according to sequence homology were aligned with representative sequences of each subtype including A6 retrieved from the HIV Database of the Los Alamos National Laboratory. Phylogenetic analysis was performed with Mega 7 software. Plasma samples harboring viral strains assigned to sub-subtype A6 were used for the generation of NL4-3 based recombinant viruses carrying patient derived integrase coding region. In vitro susceptibility to the INSTIs raltegravir (RAL), DTG, BIC and cabotegravir (CAB) was determined through a TZM-bl cell line based phenotypic assay and fold-change (FC) values were calculated with respect to the IC50 value obtained with the wild-type NL4-3 strain.

Results: Twenty out of eighty-one (24.7%) viral sequences originally labelled as subtype A were assigned to sub-subtype A6. Residual plasma available in eight cases was successfully used for the construction of recombinant viruses. Seven additional recombinant viruses were created from plasma samples obtained from the Institute of Virology in Cologne, Germany (n=2), and from the Gamaleya National Research Center in Moscow, Russia (n=5). None of the fifteen A6 sequences harbored major INSTIs RAMs while 14/15 (93%) sequences harbored the L74I variant, which is the consensus aminoacid in subtype A and found to be weakly selected in patient under INSTI therapy with no impact on INSTIs susceptibility when alone. Median FC values for RAL, DTG, BIC and CAB were 0.9 (IQR 0.8-1.1), 1.3 (IQR 0.9-1.7), 1.0 (IQR 0.8-1.2), and 0.9 (IQR 0.6-1.4), respectively. According to the available biological or clinical FC cut-offs established by the reference Phenosense Assay, all FC values calculated for RAL and DTG were below the FC threshold associated with reduced susceptibility.

Conclusions: The A6 sub-subtype strains, including the L74I variant, appeared to be naturally susceptible to INSTIs. The A6 consensus L74I variant does not contribute to INSTI resistance. In addition to analyzing a larger number of samples for phenotypic susceptibility, also the genetic barrier to resistance to INSTIs in sub-subtype A6 isolates should also be investigated in order to give a firm support to a safe use of second generation INSTIs in Russian Federation countries

HIV virology

P 106 RESIDUAL PHENOTYPIC SUSCEPTIBILITY TO SECOND GENERATION NNRTI IN MULTIDRUG RESISTANT HIV -1 FROM THE PRESTIGIO REGISTRY

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Background: The recently approved NNRTI doravirine (DOR) has a partially distinct resistance profile within the NNRTI class. In order to explore the possible use of second generation NNRTI as salvage therapy, this study evaluated the residual phenotypic susceptibility to DOR, rilpivirine (RPV) and etravirine (ETR) in a panel of multidrug resistant HIV-1 isolates collected from patients enrolled in the PRESTIGIO Registry.
Materials and methods: Recombinant viruses expressing patient derived PR-RT were generated from plasma samples from 22 patients at virological failure (VF) and documented resistance to PIs, NRTI, NNRTI and INSTIs. In vitro susceptibility to DOR, RPV and ETR was assessed through a TZM-bl cell based phenotypic assay measuring fold-change (FC) values with respect to the reference NL4-3 virus. Genotypic susceptibility was computed by the Stanford HIVdb algorithm 8.9-1. Patient demographics and laboratory data were described as median (Q1-Q3) or frequency (%).
Results: Twenty (91%) patients were male, median age 55 years (50-58), time since HIV-1 diagnosis 27 years (23-31), time on ART 23 years (22-26), 12 (55%) with a previous AIDS diagnosis, median viral load (VL) 4.30 log10 copies/mL (3.35-5.14) and median CD4+ cell count 195 cells/μL (80-279); 11 patients (50%) were receiving an NNRTI (ETR=10, RPV=1), while 9 (41%), 5 (23%), 8 (36%) patients had been exposed to 1, 2 and 3 NNRTI, respectively, with a median time of exposure to NNRTI of 1,414 days (298-2158). Median DOR, ETR and RPV FC were 9.8 (2.9-40.4), 42.9 (3.1 -100) and 100 (17.9-100), respectively. Median FC values were higher in patients exposed to NNRTI at VF (DOR 17.9 [7.4-80.1] vs. 4.4 [0.9-27.1], p=0.145; ETR 100 [48-100] vs. 4.0 [0.5-26], p=0.004; RPV 100 [100-100] vs. 30.6 [3.9 -100], p=0.029). According to clinical or biological FC cut-offs, only 1/22 (5%) viruses was still susceptible to RPV, while 4 (18%), 3 (14%) and 15 (68%) viruses had susceptibility, partial susceptibility and resistance to ETR, respectively. Agreement between phenotypic and genotypic susceptibility was observed in 9 (41%) cases for ETR and 19 (86%) for RPV, with phenotypic ETR activity underestimated by genotype in 9 (41%) cases. Intermediate to high-level resistance to DOR was predicted by genotype in 14 (64%) cases. While DOR FC biological and clinical cut-offs are not available, DOR FC values correlated with predicted susceptibility levels (r=0.746; p=0.0001). Median DOR FC values were significantly higher in viruses harboring major DOR RAMs according to both HIVdb (FC 100 [41.9-100] vs. 6.2 [1.3-18.9], p=0.003) and IAS-USA lists (FC 100 [38.4-100] vs. 6.2 [1.3-22.1], p=0.007).
Conclusions: This panel of multidrug resistant HIV-1 showed limited residual susceptibility to second generation NNRTI. DOR and RPV activity appears to be inferred with fair accuracy by HIVdb algorithm, while ETR activity is underestimated in nearly half of cases

HIV virology

P 107 IN VITRO ACTIVITY OF ISLATRAVIR AGAINST HIV-1 MUTANTS HARBORING MULTIPLE NRTI RESISTANCE MUTATIONS

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Background: Islatravir (ISL, formerly EFdA or MK-8591) is a first-in-class nucleoside reverse transcriptase translocation inhibitor (NRTTI) currently under phase II clinical evaluation. In vitro testing on NRTI resistant viruses revealed that the M184V/I mutation alone or in combination with other NRTI resistance mutations is associated with a variably reduced susceptibility to ISL. This study aimed to evaluate the antiviral activity of ISL on a panel of HIV-1 viruses harboring different NRTI mutational patterns.

Materials and methods: Recombinant viruses, harboring patient-derived PR-RT, were generated from 20 samples of patients enrolled in the Italian PRESTIGIO Registry having different combinations of NRTI mutations. In vitro susceptibility to ISL was determined through 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. Patients' demographics were described by median (Q1-Q3) or frequency (%); FC data were described by mean±SD and compared by the Mann-Whitney test.

Results: Eighteen (90%) patients were male, median age 54 years (48-58), time since HIV-1 diagnosis 27 years (23-31), time on ART 24 years (22-26), 11 (55%) with a previous AIDS diagnosis, median viral load 4.30 log10 copies/mL (3.32 -5.16) and median CD4+ cell count 145 cells/μL (69-280). At sample collection, 13/20 (65%) viruses harbored the M184V mutation. Overall, mean ISL FC value was 6.0±5.1 and higher mean FC values were observed in viruses harboring M184V (7.9±5.2 vs. 2.6±2.6, p=0.006). According to the Stanford HIVdb NRTI mutation list, viruses harboring TAM type 1 (TAM1, n=2) only and TAM1 only plus M184V (n=3) had a mean FC values of 2.3±0.4 and 13.1±4.6, respectively, while the pattern TAM1 only plus M184V and L74V (n=2) appeared to reduce ISL resistance (mean FC 4.0 ±0.2). Similarly, viruses with TAM2 only (n=2) and TAM2 only plus M184V (n=3) had FC values of 2.1±1.1 and 10.8 ±6.0, respectively. Viruses with both TAM1 and TAM2 mutations plus either M184V (n=3) or insertion at codon 69 (n=1), or L74V (n=1) had FC values of 4.5±1.9, 8.1 and 0.7, respectively.

Conclusions: This study confirms that M184V and aminoacidic insertions at codon 69 in addition to TAMs are associated with a reduced susceptibility to ISL in vitro. The presence of L74V appears to decrease TAMs+M184V driven resistance. Data from in vivo activity are awaited to define the clinical role of ISL in patients harboring NRTI mutations

HIV virology

P 108 DOES HLA-C BINDING STABILITY AFFECT HIV-1 INFECTION?

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MHC-I complex consists of HLA, β2microglobulin and a peptide. Differently from HLA-A and -B, HLA-C molecules are less expressed on the cell surface and generally less stable complexes. HLA-C is crucial in the modulation of HIV-1 infection. It has been demonstrated that higher HLA-C expression level correlates with a better HIV-1 control, instead its lower expression leads to a rapid AIDS progression.
We recently reported that, following the HLA-C/β2microglobulin dissociation, HIV-1 Env interacts with HLA-C free chains, highlighting the involvement of the different HLA-C variants in controlling viral infectivity and spreading. In addition, HIV-1 infected patients who developed AIDS dementia complex (ADC), a very severe neurological HIV-1 related condition, showed high level of β2microglobulin in the cerebrospinal fluid. Accordingly, we observed that ADC patients presented a higher frequency of HLA-C unstable variants. We propose that the different HLA-C allotypes differ in their stability, and that the HIV-1 infection progression can be modulated by both the HLA-C surface expression and HLA-C stability.
We aimed to investigate the contribution of each HLA-C variant in controlling HIV-1 infection. To address the role of the different HLA-C allotypes in HIV-1 infection progression, we used the CRISPR/Cas9 technique to generate a 293T HLA-C KO packaging cell line. The different HLA-C variants were then restored, producing cell lines each stably expressing a specific HLA-C allotype. To study the HLA-C binding stability, we performed an acid wash time course treatment to follow the β2microglobulin dissociation kinetic and to determine the binding stability of each HLA-C variant. Besides, to assess how each HLA-C molecule affects HIV-1 infectivity, the different 293T HLA-C expressing cell lines were used to produce HIV-1 pseudotyped viruses and their infectivity tested through the TZm-bl infectivity assay.
In agreement with our hypothesis, we observed that HIV-1 pseudotyped viruses produced in the CRISPR/Cas9 293T HLA-C KO cell line resulted significantly less infectious than those produced in HLA-C expressing cells. Furthermore our preliminary results showed differences in the stability among HLA-C allotypes and that each variant differently modulates HIV-1 infection. Taken together, our preliminary results show that our new cell model, developed using CRISPR/Cas9, is suitable to stratify the different HLA-C variants based on their stability and to evaluate the involvement of each HLA-C allotype in modulating HIV-1 infectivity. Our system will allow us to define the specific contribution of each HLA-C allotype in HIV-1 infection progression

HIV virology

P 109 GENOTIPIC RESISTANCE TEST IN RAPID ART ERA

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Background: Transmitted Drug Resistance (TDR) is an emerging and growing problem worldwide and, particularly, it affects viral subtypes B carriers. But, according to the ARCA database, TDR's prevalence in ART naive HIV-1 infected patients in Italy, is went down over the last few years (data update to 2016).
Objectives: The aim of this study is the evaluation of the proportion of primary mutations and the role of resistance test in the first ART regiment prescription.
Methods: The profile of mutations and polymorphism in PI, NRTI, NNRTI, INSTI, was examined in newly diagnosed patients of the "Infectious Deseases Department of Foggia", from the 1st Jan 2017 to 31 Dec 2019, in order to identify subtypes and circulating drug resistant genotypes. About Reverse Transcriptase codons: the region was sequenced succesfully and cover codons 1-386; about Protease codons: the region was sequenced succesfully and cover codons 1-99; about Integrase codons: the region was sequenced succesfully and cover codons 1-288. The report of resistance test is generated by Vela Genomics using HIV drug resistant variants reported by Sentosa SQ Reporter. The drug resistance is interpreted by Stanford HIV db software. After the results of resistance test, we evalueted if the therapy was changed.
Results: 68 patients were enrolled in the study: 43 (63,2%) Italians, 52 (77,6%) men, 36 (51,5%) aged < 45 years. 9 samples were not analysed; 28 were classified as subtype B and 31 as non-B. 6 samples showed primary resistance mutations (D67N and V179D; M184V and E92Q; T215F and N384I; A62V; K103N; I54S); 1 sample presented resistance mutations to PI, 1 to INSTI, 4 to NRTI and 3 to NNRTI.
42 patients had begun HAART before testing drug resistance; 22 patients were treated after the report of test resistance. The mean time to obtain the report was 29 days from the confirmation test of HIV.3 patients had begun therapy with NRTI + PI; 58 with NRTI + INSTI; 2 with NRTI + NNRTI. After the Genotipic resistance test , there was no change of therapy.
Conclusions: A long period of time is required for the report of the test of resistance and, in rapid ART era, we cannot ever expect it to start therapy; altough the test of resistance remains an essential test for the futures therapeutic choices.
The proportion of primary mutations for all ARV classes is very small. There are not informations about the role of accesories mutations in subtype non-B carriers.

HIV-associated tuberculosis

P 110 TUBERCULOUS AND NON TUBERCULOUS MYCOBACTERIAL EXTRA-PULMONARY INFECTIONS IN HIV

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Background: Opportunistic bacterial infections amongst HIV-infected individuals contribute significantly to HIV-associated mortality. The role of HIV-mediated modulation of innate mechanisms helps the survival of pathogenic Mycobacterium tuberculosis (Mtb) and Non-Tuberculous Mycobacterial strains (NTMs).
MTB and NTM are mostly isolated by pulmonary infection but, compromised host-immune system (e.g. due to synergism of HIV and Mycobacterial infections), increases the risk of more serious manifestations such as concurrent extra-pulmonary MTB/NTM that are also responsible to infections in other district as lymph node, gastrointestinal, central nervous systems, bone and joints and urogenital.
Extra pulmonary diseases may emerge at one particular body site or at multiple body sites even with no sign of PTB-concurrency (e.g due to re-activation of previous TB infection).
Is very challenging at diagnosis and treatment, albeit of its lower infectious potential. Hence, investigating the main risk factors associated with clinical phenotype is a crucial step towards speeding up diagnosis process and improving overall clinical experience for patients.
Several studies have found a significant impact of gender and age on the development of extra-pulmonary MTB/NTM among active TB patients.
This was suspected to be due to weaker immune status, hormonal changes, nutritional status, socio-economic and cultural factors experienced by older women
Material and methods: We analyzed all HIV patient followed in our ambulatory and recovered in our yard since 2010 to 2019. We selected only extra pulmonary mycobacterial infections caused by Mtb and NTM and divided by gender, age, immunological status, adherence to cART, type of cART and timing of it.
We made also a difference between an opportunistic infection diagnosed at beginning or arosed during cART.
Results: 12 subject presented extra-pulmonary Mycobacterial infections localized on skin, bone, heart, lymph nodes, central nervous system.
Lots of them were not positive to tine-test or igra, mostly due to their immunosuppression. The diagnosys was made principally isolating the bacteria from the biologic material.
Conclusions: Our study has shown an incident MTB and NTM also in patients on ART. It clearly demonstrates that despite ART scale-up and improving life expectancy of HIV positive patients, sizeable proportion of individuals remain susceptible to incident TB. Starting ART early in treatment naïve individuals, close monitoring for incident MTB and NTM in patients with low baseline and time updated CD4 count, routine virologic monitoring of all patients on ART and routine use of ART with IPT are important takeaways from our study.

Issues on antiretroviral therapy

P 111 SHORT-CYCLE THERAPY COMPRISING A LAMIVUDINE AND DOLUTEGRAVIR REGIMEN OF 5 DAYS ON AND 2 OFF IN A SMALL COHORT OF SUPPRESSED HIV-INFECTED PATIENTS

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Background: Short-cycle therapy (SCT) has proven to be a safe and effective alternative to the standard every-day regimen for HIV-1 infected patients, as demonstrated in several previous studies both in high- and in low-income countries. By reducing the number of doses taken by the patient,short cycle antiretroviral therapy has the advantage of improving tolerability and quality of life, as well as reducing the cost of antiretroviral therapy (ART). While many previous studies on SCTs focused on combinations containing efavirenz, in this study we focused only on combination containing lamivudine and dolutegravir , which are known to be better tolerated. Primary aim of the study was to monitor virological suppression (viral load <50 copies/ml) 24 weeks after the deintesification to five days on therapy (from Monday to Friday) and two days (Saturday and Sunday) off.

Materials and Methods: 22 Patients included in the study were adults with HIV-1 infection, in ART for more than 12 months, with at least 12 months of virological suppression (<50 copies/ml) and a CD4 cell count> 200/µl for more than 6 months) and no evidence of drug resistances or failures with their regimens before the beginning of SCT. Routine tests including HIV viral load at week 4, 8, 12 and then every other 12 weeks. A pharmacokinetics analysis was performed to see how much dolutegravir was still present after two days without taking it in the first three months after deintensification for every patients.The results are in progress.

Results: 22 patients were included in the study and their mean age was 47,8 years (range 25-63 years). 7 of them were female. All the patients were on therapy with lamivudine and dolutegravir . At the last visit ,after a mean time of follow-up of 5,2 months (1-24 months) on this short cycle antiretroviral strategy no virological failure and viral blips were observed.All the patients reported to prefer the SCT over the past standard daily treatment regimen.

Conclusions: SCT with three-drugs ART containing rilpivirine could be a feasible option for optimization of ART in selected HIV patients. The advantages of SCT, combined with its effectiveness, could make it a good option especially in low-resource settings.

Issues on antiretroviral therapy

P 112 ARE 2-DRUG REGIMENS WITH LAMIVUDINE PLUS BOOSTED-PI STILL A FEASIBLE OPTION IN THE ERA OF INTEGRASE INHIBITORS? A MULTICENTER ANALYSIS

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Background: Dual therapies (DT) with lamivudine (3TC) plus a boosted protease inhibitors (bPI), have for a long time represented the preferred choice for treatment simplification in virologically suppressed people living with HIV (PLWHIV). In the last 5 years, however, the introduction of dolutegravir (DTG) has shifted this paradigm, reducing the use of 3TC+bPI strategies. In this study we aim to assess how many patients, in our multicenter cohort, still maintain a 3TC+bPI strategy and their viro-immunological outcome.

Methods: We performed an observational, retrospective analysis on a multicentre cohort of PLWHIV currently on a DT strategy with 3TC plus either boosted-atazanavir or boosted-darunavir. We collected patients' characteristics, clinical history and viroimmunological parameters. Parametric and non-parametric tests were used to compare variables, as appropriate.

Results: Considering all four participating clinical centers, 771 patients are currently on a DT: 551 (71.5%) with 3TC +DTG and 220 (28.5%) with bPI, of whom 89 (40.5%) with atazanavir and 131 (59.5%) with darunavir.

Considering patients on bPI: 165 (25%) were males, with a median age of 49 years (IQR 43-56); main risk factor for HIV infection was sexual intercourse (MSM in 47.7% of cases, heterosexual in 34.1%). Patients were highly experienced with a median time from HIV diagnosis of 12 years (IQR 6-18) and a median of 8 years (IQR 5-14) of ARV exposure. Peak HIV-RNA was 5.05 log10 copies/mL (IQR 4.56-5.49) while nadir CD4+ cell count was 216 cell/mm3 (IQR 108-315); seventy-five patients (34.1%) experienced at least one previous virological failure. Forty-two patients (19.4%) had HCV-coinfection while 19 (8.6% of patients with available genotypic test) had the M184V resistance mutation. As to previous ARV regimens, the majority of patients switched from a 3-drug regimen with 2 NRTIs plus a bPI (91, 41.4%), 82 (37.3%) came from another 3TC-based DT, 23 (10.5%) from a non-3TC-based DT, 19 (8.6%) from 2NRTIs plus a NNRTI and 5 (2.3%) from a 3-drug regimen with 2NRTIs plus an INI. Median observation time was 2.5 years (IQR 1.8-3.8). During observational period, we registered 7 VF, with an overall incidence of 1.03 per 100 PYFU. All patients quickly regained virological suppression without discontinuing DT and with no evidence of developed resistance mutations.

Conclusions: In our multicenter cohort, DT with 3TC and a bPI are still used in a high proportion of patients, representing more than 25% of DT. This simplification strategy, even after almost a decade from the first studies analizing its feasibility, maintains appeal in heavily experienced patients, given its high efficacy in maintaining virological suppression and overall good tolerability. In conclusion, even with the ongoing widespread use of INI-based DT, PI-based simplification strategies are still a feasible alternative.

Issues on antiretroviral therapy

P 113 HIV-DNA DECAY IN ART-NAÏVE PATIENTS STARTING A DTG-BASED DUAL VS TRIPLE THERAPY

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Background: No information is available regarding the HIV-DNA decay in ART-naïve patients (patients) starting a dolutegravir(DTG)-based dual regimen (2DR). Our aim was to compare both HIV-DNA and HIV-RNA decay in ART-naïve patients starting a DTG-triple regimen (3DR) or 2DR.

Methods: This was a retrospective study on patients starting three different regimens: 6 patients with lamivudine (3TC) and DTG (2DR), 17 patients emtricitabine (FTC)/tenofovir alafenamide (TAF) and DTG (3DR-TAF) and 13 patients abacavir/3TC/DTG (3DR-ABC). We quantified the blood-associated total HIV-DNA by droplet digital PCR (detection limit of 32copies/106CD4+) using a home-made protocol targeting the HIV-1 LTR region, before starting therapy (baseline, BL) at virological success (VS, HIV-RNA <50 copies/mL) and, for 81% of patients, 6 months after VS (6mVS). Results were expressed as log10 HIV-1 DNA copies/106CD4+. Non parametric tests were used to compare the medians among the 3 groups and to assess the change of log10 HIV-DNA and log10 HIV-RNA at the different time points. Linear regression analyses explored predictors of HIV-DNA and HIV-RNA change at VS.

Results: We included 36 ART-naïve patients, mostly males (89%), with homosexual transmission as the main risk factor (53%), a median age of 35 (IQR 28-47) years with an equal distribution of subtype B and non-B (48 and 48%); the main BL characteristics were balanced among the 3 groups, albeit 3DR-TAF group, likely due to AIDS event occurred in 23% of patients, showed a higher BL HIV-RNA and lower CD4+ count. Overall there was a direct correlation between BL HIV-RNA and BL HIV-DNA levels (p=0.001).

Among the 3 groups, the proportions of patients reaching the undetectable viremia, and at VS, the CD4/CD8 ratio improvement was similar. At VS, HIV-RNA significantly decreased in all 3 groups to a comparable level, albeit with a different delta change: both 2DR and 3DR-ABC showed a similar less sharp decay, while, in the 3DR-TAF group the decay was more pronounced, even if the time to reach the VS was longer (Fig1). BL HIV-DNA levels were similar among groups. At VS there was a significantly reduction with a comparable delta change with all the groups (Fig1); although this reduction resulted more marked in both triple therapies (3DR-TAF p<0.001 and 3DR-ABC p=0.004) as compared to 2DR (p=0.046). Higher BL HIV-DNA levels predicted a more pronounced decay of HIV-DNA (1 log increase: -0.564; 95%CI -0.994/-0.280, p=0.012). For patients whose samples were available at 6mVS, HIV-RNA levels remained stable as compared to VS, without any difference among the groups, while HIV-DNA levels resulted more reduced in 3DR-ABC.

Conclusion: In ART-naïve patients all three DTG-based regimens determined a significant HIV-DNA decay at VS; however 2DR resulted in a less marked decline when compared to both 3DR DTG-based therapies. A larger sample size is needed to confirm these results.

Issues on antiretroviral therapy

P 114 SIDE EFFECTS DETECTED IN HIV-POSITIVE PATIENTS DEPENDING ON THE ART REGIMEN

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With the advent of highly active antiretroviral therapy (HAART), morbidity and mortality among HIV-positive patients have been significantly reduced. However, there are many side effects associated with ART and impairing the quality of life of patients.

Materials and methods: 153 patients with HIV infection were observed. 82 (53.6%) were male patients and 71 (46.4%) were female. All patients were registered in the AIDS Center with confirmed HIV-infection.

Results and discussion: 74 patients took the AZT + 3TC + EFV regimen. 61 (82.43%) patients of those felt various side effects of ART, 3 of those had anemia of severe level. 13 (17.57%) patients did not feel adverse reactions to this ART regimen. In the group of individuals taking ABC + 3TC + LPV/r, 22 (70.97%) experienced side effects in the form of nausea, vomiting, and diarrhea. 9 (29.03%) patients did not feel adverse events. One patient had severe gastrointestinal disturbances. Among patients taking the ABC+3TC+NVP regimen, 10 (90.91%) reported side effects in the form of erythema multiforme, rash, nausea, and abdominal pain. 1 patient did not have adverse effects. 80.0% (8) patients taking the combination of TDF+3TC+EFV felt adverse effects (skin itching, rash), 2 (20.0%) patients do not have side effects. All 15 patients (100%) who received a combination of ABC+3TC+EFV felt various side effects. 10 of 12 patients taking AZT + 3TC + NVP (83.33%) had various adverse reactions. There was 1 case with a severe allergic reaction in the form of Stevens-Johnson syndrome. The incidence of anemia (20%) and dizziness (31%) prevailed in patients who took the AZT +3TC+EFV regimen. People who took a combination of ABC+3TC+LPV/r were more likely to experience gastrointestinal side effects such as nausea (36%), vomiting (8.1%), diarrhea (15%), and abdominal pain (15%). Rash and itching were most often determined in patients taking ART regimens containing nevirapine (ABC + 3TC + NVP, AZT + 3TC + NVP). 9% of patients in the group of people taking ABC+3TC+NVP had a skin rash and 4% of the patients noted itching. In patients taking AZT + 3TC + NVP: anemia was noted in 21% of them. Skin rash and itching occurred in 10% of patients.

Conclusion: Side effects of ART were equally found in both men and women. Patients taking 6 different ART regimens had the following groups of side effects: Gastrointestinal disorders: nausea, vomiting, diarrhea, abdominal pain, loss of appetite. Neurological disorders: dizziness, sleep disturbance. Allergic reactions: rash and itching of the skin. Mental disorders: depression and drowsiness. Myelosuppression: anemia.

The study has shown that all ART regimens have various adverse effects. Those must be taken into account when prescribing therapy taking into consideration the concomitant diseases in patients at the time of ART administration.

Issues on antiretroviral therapy

P 115 SAFETY AND TOLERABILITY OF TENOFOVIR ALAFENAMIDE (TAF) ON BONE MINERALIZATION AND RENAL FUNCTION IN A COHORT OF YOUNG ADULTS WITH HIV INFECTION

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Background: The adverse effects of tenofovir disoproxil fumarate (TDF) on renal function and bone mineralization have been reported in several studies. This study aimed to evaluate renal and bone safety in a cohort of young adults after switching from a TDF-based antiretroviral regimen to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide fumarate (EVG/c/FTC/TAF).

Material and methods: HIV-positive young adults treated with efavirenz (EFV)/FTC/TDF, with a mean treatment duration of 10 years, were enrolled in our study. Patients affected by chronic kidney disease were excluded.

We evaluated serum and urinary creatinine, calcium and phosphorus, proteinuria, eGFR, alkaline phosphatase (ALP), 25-hydroxy-vitamin D (25-OH-D), and parathyroid hormone (PTH) at baseline and after 3, 6 and 12 months of EVG/c/FTC/TAF therapy. We also measured bone mineral density (BMD), bone mineral content (BMC), and bone area (BA) by dual-energy x-ray absorptiometry before and 12 months after switching. BMD, BMC and BA were measured at the lumbar spine and the whole skeleton. The changes in laboratory and radiological findings after 12 months were evaluated by means paired t-test.

Results: We enrolled 18 HIV-positive young adults (9 females), with a median age of 23 (range 17-32) years.

Mean CD4 count was 804 n/µl (SD 187.3) at baseline and 837.9 n/µl (SD 196.6) after 12 months of EVG/c/FTC/TAF. At month 3, mean creatinine value increased by 0.07 mg/dl (p=0.005; 95%CI: 0.03;0.12) and mean eGFR decreased by 8.71 ml/min/1.73m2 (p=0.01; 95%CI: 14.94;2.48), remaining nearly stable until month 12. Mean ALP activity changed from 89 U/L (SD 29) at baseline to 72 U/L (SD 19) after 12 months (p=0.003). PTH and 25-OH-D changes were clinically insignificant.

Whole body BMD z-score increased significantly from an initial average of 0.4 (SD 1.2) to 0.8 (SD 1.3) after 12 months on the new regimen (p=0.001; 95%CI: 0.20;0.66); lumbar BMD z-score changes were clinically insignificant. Both BMC and BA whole skeleton and lumbar spine measurements did not change markedly during the 12 months of study.

Conclusions: Our study indicates that switching from a TDF-based regimen to EVG/c/FTC/TAF has a positive impact on bone mineralization in young adults. EVG/c/FTC/TAF is effective and safe for the treatment of HIV infection in this population. The increase in creatinine values and the corresponding reduction of eGFR could be explained by the known effect of cobicistat on tubular excretion of creatinine, which does not affect glomerular function.

Issues on antiretroviral therapy

P 116 A RARE CASE OF ACUTE TUBULAR NECROSIS TENOFOVIR ALAFENAMIDE-RELATED

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A 56-year-old Caucasian heterosexual woman with chronic HIV infection, first diagnosed in 2011, had started cART based on TDF/FTC/ATV/r. The patient's comorbidities included metabolic disorders, diabetes, GERD, depressive syndrome, and hypovitaminosis D. Additional medications: clonazepam, cardioaspirin, ranitidine, cholecalciferol, insulin glargine, and linagliptin.

In May 2018, she had a rise in serum creatinine levels (1.6 mg/dl, and eGFR of 44 ml/min/1.73 m2), thus the therapy was modified by replacing TDF with TAF. After one month of therapy due to the further deterioration (creatinine 6.6 mg/dl, eGFR 11 ml/min/1.73 m2), the cART was modified with replacement of ATV/r by DTG. However, despite this change, there was a worsening of renal function, with serum creatinine values up to 7.48 mg/dl and eGFR 9 ml/min/1.73 m2. Therefore, the patient underwent renal needle biopsy that showed an acute tubular necrosis associated with tubular and interstitial infiltrate. The cART was modified again to the advantage of RAL + ETV, with good tolerability and excellent viro-immunological parameters. A serum creatinine control after one month showed values of 5.6 mg/dl, eGFR 13 ml/min/1.73 m2.

One year after the acute episode, creatinine value is 3 mg/dl, eGFR 23 ml/min/1.73 m2.

Discussion: In case of renal failure alleged to TDF, as reported in numerous cohort studies and case reports since its market approval, it is common switch therapy to TAF, because pharmacokinetics and pharmacodynamics support an improved renal safe- profile of TAF compared with TDF.

Instead, high plasma TDF exposure correlates with the development of proximal renal tubulopathy.

The expected better renal tolerance of TAF is related to its higher plasma stability and lower administered dose, both generating less plasma TFV than when TDF is used.

In effect, regardless the administered prodrug is TAF or TDF, the end product is TFV. This molecule is excreted in urine by tubular secretion and by glomerular filtration.16 TFV enters the proximal tubular epithelial cells (PTEC) at their basolateral pole through the human organic anion transporters 1-3, and it is secreted in urine by the multidrug resistance-associated protein 4 at the apical pole of PTEC. Evidence from clinical studies, suggests that TFV may cause nephrotoxicity due to a dose-dependent accumulation in the cytoplasm of PTECs, which results in mitochondrial DNA polymerase dysfunction.

So, when nephrotoxicity is induced by TFV accumulation (derived by TDF metabolism), the TAF therapy switch does not seem able to restore renal function. This occurs because the TFV, generated by the metabolism of TAF, although in smaller concentrations, accumulates to that generated by the metabolism of TDF.

Conclusion: Although the risk of long-term toxicity and the best cost-benefit ratio have often justified switching from TDF to TAF, caution is advisable in case of prescription of TAF to patients who experienced a TDF-induced renal adverse event.

Issues on antiretroviral therapy

P 117 NEW CASES OF DIABETES DOLUTEGRAVIR-ASSOCIATED IN HIV PATIENTS: A CASE SERIES

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Background: Integrase strand transfer inhibitors (INSTIs), in particular dolutegravir, have become first line agents of antiretroviral therapy, because of their high efficacy and lack of signature side-effects. However, very recently, in an American cohort, use of INSTI among antiretroviral naïve patients has been associated by higher rates of diabetes than NNRTI-based treatments. Moreover, a few cases of new onset of diabetes and hyperglycemia after INSTI introduction have been reported in the literature. The frequency of this side effect and the mechanism by which INSTI may induce diabetes are largely unknown.
Methods: We reviewed our case history and we identified three cases of HIV patients who developed diabetes right after switching from a stable antiretroviral treatment to a dolutegravir-containing regimen.
Results: Case report 1: a 46-years-old Caucasian man, with history of hypertension and mild dyslipidemia developed diabetes four months after switching from abacavir/lamivudine and efavirenz to dolutegravir and lamivudine. The patient presented elevated fasting glucose (up to 300mg/dl) and his glycated hemoglobin (HbA1c) was 75; he started metformin and switched HAART to emtricitabine/tenofovir alafenamide, rilpivirine. After a month, HbA1c was reduced (56) and glycemia was 95mg/dl. Anti-GAD autoantibody tested positive at the diagnosis of diabetes but were found to be already positive on a stored plasma sample, drawn before the switch to dolutegravir, when he was euglycemic.
Case report 2: a 39-years-old overeweight African woman with a history of hypertension, dyslipidemia, HBV coinfection and a past diagnosis of Castelman's disease switched from emtricitabine/tenofovir alafenamide, darunavir and ritonavir to emtricitabine/tenofovir alafenamide and dolutegravir to improve metabolic profile. After six months, she had developed diabetes (glycemia 445mg/dl, HbA1c 111). Following the introduction of metformin and dolutegravir discontinuation, her glycemic values steadly improved (glycemia 107mg/dl, HbA1c 55).
Case report 3: a 57-years-old Caucasian man with HCV coinfection and metabolic syndrome experienced hyperglycemia (342mg/dl) and glycosuria nine months after switching from emtricitabine/tenofovir alafenamide, atazanavir, cobicistat to emtricitabine/tenofovir disoproxil fumarate and dolutegravir. He introduced metformin. Follow-up and further investigations are on the way
Conclusion: INSTIs often represent a therapeutic choice in patients with metabolic disorders. However, the possible association between dolutegravir introduction and new-onset of diabetes in predisposed patients merit attention. Further studies are necessary to understand the real incidence of diabetes among patients switching to INSTI and to elucidate its pathogenesis.

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P 118 REDUCED BONE CATABOLISM AND INFLAMMATION IN PATIENTS SWITCHING TO TAF-CONTAINING CART

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Background: By reducing tenofovir plasma levels, tenofovir alafenamide (TAF) preserves bone mineral density (BMD). Changes in bone composition appear to be multi–factorial and can be affected by HIV reservoir, probably through the effects of immune dysregulation associated with a persistent low–grade inflammatory state. The impact of switch to TAF-containing regimens on osteo-immunity, inflammation and HIV-DNA has been poorly investigated. Thus, we investigated changes in bone turnover, inflammatory markers and HIV-DNA in patients (pts) switching from tenofovir disoproxil fumarate (TDF) to TAF.

Methods: We enrolled ART-treated HIV+ pts within Icona (HIV-RNA<50 cp/ml) switching from TDF to TAF regimens. Samples were available pre-switch (T0) and 12 months post-switch (T1). Lab analyses: (a) sCD14, C-reactive protein (CRP), IL-6 and vascular cell adhesion molecule 1 (VCAM-1) (Luminex), (b) C-terminal telopeptide-1 (CTX-1), procollagen type I N-terminal propeptide (P1NP) (Elisa), (c) osteoclast precursors (OCP:CD14+CD16+CD51/61+), osteoblast precursors (OBP:CD15-OC+AP+), CD8+CD38+HLA-DR+ (Cytometry), (d) HIV-DNA (LTR5' ddPCR assay, normalized by cps/106 CD4+). Pearson correlation and univariable and linear regression models using the markers variation over T0-T1 as outcome were used. Variable selection for inclusion in multivariable models was performed using a best subset approach with manual addition of known confounders.

Results: We enrolled 146 pts: median (IQR) CD4 and age at switch were 672/mm3 (475-879), 48 years (40-55). All pts maintained virologic suppression through 12 months. In the unadjusted model, at T1 we observed a reduction in activation (-1.8 p<0.01), inflammatory markers (sCD14: -0.5 p<0.01, IL-6:-0.8 p<0.01),VCAM-1: -0.1 p<.01, with no changes in HIV-DNA (+12.5, p=0.85). Among bone markers, only CTX-1 showed a non-significant decreasing trend (-4.9 p=0.06), with no differences in OBP, OCP, P1NP (Fig 1a). Having shown a trend for reduced resorption marker CTX-1, we performed a multivariable model to identify the factors associated with change in osteoclastogenesis. While this model showed no association between bone resorption and inflammation, we found a positive association between OCP change and T0 CD8 +, independent of potential confounders, including CD38+ (0.10 increase in OCP per 100 CD8+/mm3 higher p=.004, Fig 1b)

Conclusions: In virologically suppressed HIV+ pts switching from TDF to TAF regimens, we describe an early decrease in pro-inflammatory markers and free osteoclast-derived collagen (CTX-1) suggesting a containment in bone resorption. This finding, together with the independent association between reduced post-switch osteoclast progenitors and high pre-switch CD8+, known osteoclastogenesis inhibitor in murines, might indicate a mechanistic pathway behind the greater bone safety of TAF

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Issues on antiretroviral therapy

P 119 VIRAL OUTCOME ON TAILORED TREATMENT STRATEGYUSING COST SAVING ANTIRETROVIRAL (ARV)

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Background: Simulation studies showed that cost saving ARV utilization lead to significant cost reduction of treatment in developed world. This studyaims to evaluate the viral and cost impact of tailored treatment strategythat takes into account patient needs and usescost saving ARV.

Materials and Methods: From January to September 2019,1470 HIV positive patients(pts)took up medication at the pharmacy service of A.O.U. Careggi, a tertiary hospital in Florence Italy. They were divided bygender, age (20-40,41-60, >60) and treatments that werelayered in 4 groups:alternative therapy (AT) (4 drug combinations),classic triple therapy (CT), dual therapy (DT) and mono-therapy (MT).Gender and age differences between the groups have been valued.For those in CT and DT, therapy price have been calculated and viral loads were observed for 9 months before and 3 months after the pharmacy uptake. Viral outcomeswere defined as: undetected if viral load <50copies/ml, not available if pts took medication but not followed at the center /skipped exams, detected (≥50cp/ml). Viral detection was layered as viral failure (VF)if 2 consecutive detections ≥50 or 1 detection≥200 copies/ml, detected but not failed(blip) if one viral detection <200 copies/ml, and not suppressed yet (NS).

Continuous data were expressed by median and inter quartile range (IQR), categorical data as percentages whom differences were analyzed using the χ-squared test.

Results: Overall median age was 53 IQR (59_44),335 (22.9%) females and 1135(77.7%) males, 35(2,45%) pts were in AT, 1074(73,06%) in CT, 310(21,09%) in DT, 51(3,47%) in MT. Gender differences have been observed in every therapy group and in every age range P<0.0001 (Tab1).

Female and maleaged 20-40 were more likely treated in CT than in DT, with statistically significant difference, respectively P=0.0377 and P<0.0001.There was not statistically significant difference for those aged 41-60 both in male P=0.1457 and female P=0.0618, nor in female >60. There was statistically significant difference in male aged >60, that were mostly in DT than in CT P<0.0001 (Tab2).

There was a quite significant difference on viral suppression P=0.0450.There was not a statistically significant difference on viral detection P=0.5209 even when was layered as VF P=0.8270, BLIP P = 0.4536 and NS P=0.1542(Tab3).

For CT 83 different ARV combination prices have been found depending on daily dose and if booster was used with 7.237 € as median wage per patient/per year while for DT 36 with 6.694€(Tab 4).

Conclusions: In tailored HAART treatment, pts aged 20-40 were mostly in CT in both genders. Statistically significant viralsuppression difference may be due to switching pts from CT to DT only when viral suppression occurs according to patient therapy compliance and patients' clinical needs. Cost saving treatment strategy in CT vs in DT lead to a median money saving of 543 €/patient/year with no statistically significant difference on VF nor on BLIPs.

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P 120 THE NEED FOR REDUCING BOTH ARV AND MEDICINE-TAKING BURDENS AMONG ITALIAN PLHIV - FINDINGS FROM THE POSITIVE PERSPECTIVES 2 STUDY

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Background and Objectives: Daily antiretroviral treatment (ART) has immense clinical benefit, but may pose some specific challenges related to the dosing, pill burden, number of medications, side effects, modes of administration and others. All these therapy-related burdens generate a Patients' lived experience with medicine that should be explored in order to try to improve ART effectiveness.

Materials and Methods: Positive Perspective 2 is an international survey of PLHIV aged 18+, on ARV conducted between April/August 2019 in North and South America, Europe, Russia and in the Asia Pacific region. In total, 24 countries were represented reaching a total sample size of 2112 interviewed. The Study was run by ViiV Healthcare in collaboration with an international, multi-disciplinary Advisory Committee of experts, which includes PLHIV, patient group representatives and HIV physicians. A multi-mode recruitment approach was used, but subject to quota boosts for three specific cohorts: newly diagnosed, women living with HIV and aged 50 or over. Here we propose a sub-analysis of the Italian participants. Data were analysed using descriptive statistics.

Results: 120 PLHIV completed the survey in Italy, that is 5,7% of global respondents. Sample demographics in Table 1. With a mean age of 43,4 years, average time since HIV diagnosis is 11 years, with one third of respondents having been diagnosed before 2006. 21% of respondents report having a detectable viral load. 3 out of 5 PLHIV report very or quite good health overall. 42% of male and 25% of female respondents report having no co-morbidity. 46% take a Single Tablet Regimen (HIV therapy). The most common reasons for having switched medications (multiple-choice allowed) were: reducing severity and frequency of side effects (56%), reducing the number of pills (35%), the number of medicines (29%), controlling viral load (23%), managing drug-drug interactions (15%), reducing costs (9%). Although overall treatment satisfaction was high (73%), 47% of the sample foresee room for improvement for their current HIV treatment, with 47% concerning about reducing long-term impact/side effects and 31% for reducing both the number of ARV's (that is 'ARV burden') and medicine-taking burden.

Conclusions: Italian participants to the Positive Perspective 2 Survey show awareness and high level of satisfaction concerning the ART they are taking. A large proportion foresee room for improvement, mainly to reduce long-term side effects as expected. ARV burden and medicine-taking burden both emerge as matters to be improved. Next generation ARVs must be designed to address these challenges.

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P 121 SWITCH TO DARUNAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR ALAFENAMIDE IN HIV-INFECTED PATIENTS NOT RECEIVING PROTEASE INHIBITORS-BASED REGIMENS

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Background: The primary aim of this study was to estimate the proportion of patients who switched from a non-protease inhibitors(PI)-based regimen (integrase strand transfer inhibitor[InSTI]-based or non-nucleoside reverse transcriptase inhibitor[NNRTI]-based regimen) to darunavir, cobicistat, mtricitabine, tenofovir alafenamide(D/C/F/TAF). Secondary objectives included the evaluation of the reasons leading to switch to D/C/F/TAF and changes in laboratory parameters during such treatment.

Methods: This is a retrospective analysis on the CSLHIV Cohort Study of the Infectious Diseases (Milan, Italy). We included HIV-infected adults, on treatment with a non-PI regimen on January 2017, who switched to D/C/F/TAF or to another ART regimen for any reason within November 2019.

The analyses estimated the incidence rate of switch and time to switch to D/C/F/TAF; follow-up was censored at the date of switch to D/C/F/TAF or to another antiretroviral therapy (ART) or at last available visit.

Virological failure (VF) was defined as 2 consecutive HIV-RNA values >50 copies/mL.

The time to switch to D/C/F/TAF was estimated by Kaplan-Meier curve.

Changes in laboratory parameters during D/C/F/TAF were assessed by univariate mixed linear models; in these analyses, follow up accrued from the date of start of D/C/F/TAF until the last available visit or discontinuation for any reason of this regimen.

Results: Overall, 3076 patients (on ART since 5.2 [IQR: 0.3-13] years) were included; 83% were males and the median baseline age was 50 (42-56) years. During 17099 person-years of follow-up (median follow-up: 4.76 [IQR: 3.70-6.38] years), 423/3076 (14%) patients discontinued the non-PI-based regimen and 106/423 (25%) patients switched to D/C/F/TAF for an overall incidence rate of switch to D/C/F/TAF of 6.2 per 1000-PYFU (95%CI: 5.02-7.38). Among patients who switched to D/C/F/TAF, the ongoing regimen was based on NNRTIs in 37 (35%), on InSTIs in 69 (65%).

The time to switch to D/C/F/TAF is shown in Figure. Main reasons leading to switch to D/C/F/TAF included central nervous system/neurological adverse events (37%, Figure), VF (26%) and Kaposi sarcoma progression (5%).

During treatment with D/C/F/TAF (median follow-up: 10.6 [3.8–26.8] months), VF occurred in 11 (10%; 95%CI: 5.7% -17.8%) patients. Significant mean changes per year [95%CI] were observed in: CD4/CD8 ratio (0.03 [0.001,0.060]; p=0.041), platelet count (8.19 [3.91,12.47] 109U/L; p=0.0002), eGFR (-2.81 [-4.16,-1.46] mL/min/1.73 m2; p<0.0001), homeostatic model assessment for insulin resistance (HOMA-IR) index (0.48 [0.01,0.95]; p=0.044), LDL-cholesterol (9.04 [4.20,13.88] mg/dL; p=0.0003), alkaline phosphatase (-8.6 [-16.9,-0.26] U/L; p=0.043), indirect bilirubin (0.01 [0.005,0.2] mg/dL; p=0.003).

Conclusions: In the last years, a non-negligible proportion of patients on an NNRTI- or an InSTI-based regimen switched to D/C/F/TAF, mainly because of neuropsychiatric toxicity and virological failure.

Issues on antiretroviral therapy

P 122 NEVIRAPINE-BASED THERAPY IN THE TWENTY-FIRST CENTURY: STILL AN EFFECTIVE AND SAFE LONG-TERM CHOICE

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Background: Nevirapine (NVP) was the first non-nucleoside reverse transcriptase inhibitor approved for the treatment of HIV infection. Since it entered the market in 1991, many other therapeutic options have been licensed, addressing the need to improve efficacy, safety and durability of antiretroviral therapy, but also resulting in increased costs. Because of the potential occurrence of hypersensitivity reactions (either skin rash or liver enzymes elevation) in the first 3 months after initiation requiring close follow up, NVP is being used less and less, although its favourable lipid profile and well-documented penetration into sanctuaries. In this context, the aim of the study was to evaluate the potential role NVP could play in current antiretroviral treatment in a real-life cohort of HIV-positive patients

Material and methods: We conducted a retrospective study including all HIV-positive patients followed at our Infectious Diseases Unit receiving NVP-based regimen for at least three months. For each patient we collected demographic characteristics, HIV-related informations at baseline, immunological and biochemical parameters before starting NVP and at the last clinical visit. Wilcoxon signed-rank test was used to compare variables.

Results: We analysed 121 patients (66% male, median age 57 years). Baseline characteristics are shown in Table 1. The median duration of NVP-based regimen was 120 months (range, 5-247). The CD4 cells count significantly increased ($p<0.001$) over time. Globally, median values of ALT (p 0.03), creatinine ($p<0.001$) and LDL cholesterol ($p<0.001$) remained within the standard normal range throughout follow-up (Figure 1).

Conclusions: In our cohort, long-term exposure to NVP was associated with fully suppressed HIV viral load, significant immunological recovery and favourable metabolic profile. Furthermore, NVP prolonged use resulted in good liver function evolution even in coinfected HCV patients.

Our data suggest that this low-cost drug still represents an effective, safe and durable option in current HIV management.

Issues on antiretroviral therapy

P 123 SWITCH TO DUAL THERAPY (3TC+DTG OR RPV+DTG) IN A COHORT OF PEOPLE LIVING WITH HIV: EXPERIENCE FROM REAL LIFE

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Introduction: Dolutegravir (DTG) based dual-therapy represents a valid therapeutic choice in both, treatment experienced HIV infected patients (PLWH) with over 6 months of undetectable viral load (VL) and in the naïve ones with both CD4+ T cells >200 cells and a VL < 500.000 cp/ml. However, an increase in body weight related to the use of recent integrase inibitors (INSTI) has already been observed. Aim of our study was to compare the immunovirological and metabolic parameters as well as the body weight of PLWH before and after starting a DTG based dual therapy.
Methods: An observational study on PLWH attending the DH of Infectious Diseases Clinic of Perugia from 2018 to 2019 and starting or switching to a dual therapy with lamivudine (3TC) or rilpivirine (RPV) plus DTG was carried out. Data regarding demographic and clinical characteristics as well as the reasons for the switch were collected for 30 patients. We compared immuno-virologic (HIV-RNA, CD4 cells count) and metabolic parameters (total cholesterol, HDL-c,LDL-c, triglycerides), BMI and body weight before and 2 months after starting dual-therapy.
Results: A sample of thirty PLWH who started a DTG based dual therapy: 15 with 3TC and 15 with RPV, twenty-nine switching from a previous ART, 1 starting the dual therapy as naive. Male gender (77%) and Caucasian ethnicity (83%) were mainly represented, the median age was 52.5(30-80). Among the overall population, current smoking rate as well as hypertension rate were 33%. A history of diabetes (all from the 3TC group) and of cardiovascular diseases were present in 10% of PLWH. Seven patients had a history of AIDS (2 in 3TC group, 5 in RPV group). The 29 pre-dual ART were: NRTI +INI in 8, NRTI + NNRTI in 7, NRTI+PI in 10, INSTI + PI in 4 patients. The switch was motivated by simplification in 12 (40%), by pro-active action in 9 (30%), by toxicity (mainly due to PI) in 8 (27%) PLWH. In Table 1, immuno-virological and glico-metabolic parameters are reported. No changes were observed in the immunovirological parameters as well as in BMI ($p>0.05$) and in the body weight ($p>0.05$). A significant amelioration in total cholesterol (p0.001), LDL-cholesterol (p0.001) and tryglicerides ($p<0.05$) within 2 months was observed. The decrease of glycemia was observed only in the RPV+DTG group, where diabetes was absent (data not shown).
Conclusions: Despite the limitations given by the small size of the sample and the short duration of observation, also in our study a DTG based dual regimen is an excellent therapeutic choice in the real life, maintaining unchanged the immunovirological and improving the metabolic balance of the patients observed. A larger number of cases and a longer observation period may provide further information.

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P 124 CHANGES IN LIPID PROFILE AND SUBCLINICAL ATHEROSCLEROSIS AFTER SWITCHING TO TENOFOVIR ALAFENAMIDE (TAF) CONTAINING ANTIRETROVIRAL REGIMENS IN PEOPLE LIVING WITH HIV

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Background: In the antiretroviral treatment (ART) of human immunodeficiency virus (HIV), tenofovir disoproxil fumarate (TDF) has shown a lipid lowering effect and, therefore, switching from TDF to tenofovir alafenamide (TAF) may cause increases in all cholesterol subgroups. The impact of these lipid changes on atherosclerosis, fat deposition and effective cardiovascular disease (CVD) risk is still unclear.

Material and Methods: We conducted a prospective study on 59 consecutive HIV-positive ART-treated subjects; 44 were randomized to switch to TAF-containing regimens whereas 15 subjects continued current ART. Total cholesterol (TC), low-density lipoprotein cholesterol (LDLc), high-density lipoprotein cholesterol (HDLc) levels, waist circumference (WC), body mass index (BMI) and CVD risk scores (5 and 10 years-Framingham Risk, D:A:D and ASCVD scores) were assessed at baseline and after 48 weeks (T1). Furthermore, transthoracic echocardiogram (TE) and supra-aortic trunks ultrasound were performed at baseline and T1 in order to measure epicardial adipose tissue (EAT) and carotid intima media thickness (cIMT), markers of visceral fat deposition and subclinical atherosclerosis, respectively.

Results: At T1, subjects in the switching arm experienced a significant increase in TC, LDLc and HDLc levels (all p<0.001), whereas triglycerides values, TC:HDLc and LDL:HDLc ratios remained unchanged. In this arm, the prevalence of subjects with total (TC>200mg/dL) or LDL hypercholesterolaemia (LDLc>130 mg/dL) significantly increased over the study period (20.4% vs 45.4%, p=0.03 and 18.2% vs 40.9%, p=0.003, respectively). No significant changes in lipid profile were documented among controls, except for an HDLc levels increase (p=0.012) (Fig. 1)

No modifications of EAT thickness were registered at TE between baseline and T1 neither in TAF (6.7±0.2 vs 6.5±0.2 mm, p=0.852) or control group (7.2±2.2 vs 7.1±2.2 mm, p=0.45), whereas a significant increase in T1 cIMT was documented at supra-aortic trunks ultrasound compared to baseline for subjects enrolled in the switching arm (0.709±0.020 vs 0.727 ±0.019 mm, p=0.008). In the switching arm a significant increase in BMI occurred over time (24.0±3.6 vs 25.1± 4.0 Kg/m2, p=0.002), whereas no changes in WC were registered (90.1±14.0 vs 88.2±16.0 cm, p=0.231). No significant changes regarding BMI, WC, cIMT, EAT thickness were documented in the control group.

The assessed CVD risk scores did not change from baseline to T1 nor in the switching arm nor in the control group.

Conclusions: In conclusion, our study suggests that switching to TAF-containing regimens may impact not only on lipid metabolism, but also on subclinical atherosclerosis. Interestingly, these modifications are not detected by main CVD risk scores. Furthermore, BMI but not indirect measurements of visceral adipose tissue (WC and EAT) seems to worsen with TAF introduction. These preliminary results need to be confirmed by larger randomized studies.

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P 125 AN EARLY PROACTIVE SWITCH TO ELVITEGRAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (E/C/T/TAF) IS EFFECTIVE IN MAINTAINING VIROLOGIC CONTROL, REDUCING LOW LEVEL VIRAL REPLICATION AND CONTINUING IMMUNOLOGICAL RECOVERY IN PATIENTS WITH A PRIMARY HIV-1 INFECTION (PHI). AN INTERIM ANALYSIS OF A PHASE IV CLINICAL TRIAL (ESTER STUDY)

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Background: The aim of this study was to evaluate the evolution of virologic response, patient-reported outcomes (PROs) and neurocognitive performance (NP) after an early switch to single-tablet regimen in HIV+ patients (pts) starting an intensified ART during PHI.
Material and methods: ESTER is a pilot 96-week (w) single-arm trial enrolling HIV+ pts who achieved virologic suppression (at least 1 viral load [VL]<40cp/mL) on a 4-drug regimen of boosted darunavir qd + raltegravir bid + tenofovir disoproxil fumarate/emtricitabine started during PHI. Pts included in the study were switched to E/C/F/TAF. The following virologic outcomes were evaluated: proportion of pts experiencing virologic failure (VF), defined as confirmed VL≥ 40 cp/ml, evolution from baseline (BL) to w48 of residual viremia assessed by ultrasensitive HIV-RNA (with detection limits of ≤5 cp/mL,95% confidence interval [CI] and of not-detected HIV-1 RNA) and viral reservoir assessed by HIV-DNA. NP was evaluated by comparing the means in total cognitive performance consisting of 12 tests (NPZ12) and in the 5 cognitive individual domains. Adherence and health perception were assessed by a visual analogue scale; QoL was assessed by the 30-item version MOS-HIV Health Survey score. Here we reported the interim analysis at 48w.
Results: 30 pts were enrolled: 28 completed 48 weeks of the study, 1 withdrew consent and 1 was lost to follow-up (FU). The main BL characteristics were: 97% male, 87% MSM, median age 34 yrs, BL CD4 count 667 cells/mm3, median time from HIV diagnosis 6.5 months. Over the FU, 2/30 (6.6%) pts experienced VF, of whom none developed drug resistance mutations and all achieved re-suppression without ART changes. At 48w a significantly higher proportion of pts achieved HIV-RNA≤5cp/ml and HIV-RNA not-detected compared to BL (89.3% vs 64.3%, p=0.027 and 53.6% vs 10.7%, p=0.001, respectively). Mean HIV-DNA showed a stable trend from BL to 48w (3.3 vs 3.2 log10 cp/106 PBMC, p=0.090) (Table1). At 48w both CD4 count (667 cells/mm3 vs 766 cells/mm3, p=0.009) and CD4/CD8 ratio (1.00 vs 1.14, p=0.007) significantly improved compared to BL (Table 1). Although total cognitive performance did not change over the FU, significant improvements in speed of information processing and attention and working memory were observed (Table 2). There were no significant improvements in health perception and adherence over time (Table 3). Health distress significantly increased from BL to w48 (Table 4).
Conclusions: Although not recommended in guidelines, starting ART with an intensified regimen in pts with PHI has been common clinical practice in recent years. In those pts an early switch to E/C/F/TAF was effective in maintaining virologic control, reducing low level viral replication, and continuing immunological recovery. There were no significant changes in PROs and total cognitive performance, although the small population size could have led to misestimations.

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P 126 EFFICACY OF DOLUTEGRAVIR VERSUS DARUNAVIR IN FIRST-LINE REGIMENS ACCORDING TO RESISTANCE MUTATIONS AND VIRAL SUBTYPE

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Background: Dolutegravir (DTG)-based first line regimens have shown superior efficacy versus darunavir (DRV)-based ones in randomized trials. We compared these two strategies in clinical practice, particularly considering the role of transmitted drug resistance mutations (TDRMs) to study drugs and of HIV-1 subtype.

Material and methods: The multicentre Antiviral Response Cohort Analysis (ARCA) database was queried to identify HIV-1-positive patients (pts) starting a first line-therapy with 2NRTIs (ABC, 3TC/FTC or TDF/TAF) plus either DTG or DRV between 2013 and 2019. Only adults (≥18 years) pts with a genotypic resistance test (GRT) prior to therapy and with HIV -1 RNA≥1000 copies/mL were selected. Through multivariable Cox regressions we compared DTG versus DRV-based regimens in the time to virological failure (VF, as identified by the first HIV-1 RNA≥50 copies/mL after 3 months from therapy start), by stratifying for TDRMs and viral subtype (B versus non-B).

Results: Six hundred and forty-nine pts were enrolled, 359 (55.3%) and 290 (44.7) starting DRV and DTG, respectively. Main characteristics of study groups are reported in table 1. In 12 months of median follow-up time, there were 41 VF (0.7 per 100 pts-years follow-up, PYFU) and 15 VF (0.4 per 100 PYFU) in the DRV and DTG groups, respectively (p=0.067). After adjusting for age, gender, baseline CD4 count and concurrent AIDS diagnosis, DTG was associated with a reduced risk of VF (versus DRV, aHR 0.51, 95% CI 0.27-0.98; p=0.043). Non-B viral subtypes (particularly, C vs B: aHR 2.96, p=0.044 and circulating recombinant forms vs B: aHR 2.07, p=0.044), a higher baseline HIV-1 RNA (versus ≤100k cps/mL: >100k up to 500k cps/mL, aHR 3.84, p<0.001; >500k cps/mL, 5.22, p<0.001), and a longer time since HIV-1 diagnosis (>1 versus ≤1 month, aHR 2.89, p=0.015) were predictors of VF. After adjusting for the same variables, a second Cox model was performed to compare DTG and DRV-based regimens according to the presence of TDRM. Compared with a fully active DTG regimen, the risk of VF was confirmed to be higher with DRV compared with DTG (aHR 2.30, p=0.017), as well as in patients on a DTG-containing regimen in the presence of TDRM to study drugs (aHR 14.14, p=0.001). The effect of DTG (with and without TDRM) on the outcome was similar in the subgroup of pts harbouring an HIV-1 B-subtype, whereas no protective effect was shown in the subgroup with non-B subtypes. Of note, in the latter the use of DTG plus ABC/3TC was associated with VF when compared with DTG plus TDF(TAF)/FTC (aHR 7.69, p=0.024) after adjusting for confounders. No comparison could be done between DTG and DRV-based regimens in the setting of TDRM, due to the lack of VF in the latter group.

Conclusions: In line with randomized trials, DTG-based first line regimens show overall superior efficacy compared with DRV-based regimens. GRT may still play a role in identifying pts more at risk of VF and in guiding the choice of antiretroviral backbone

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P 127 SWITCH TO DOLUTEGRAVIR-BASED DUAL THERAPY: OUTCOMES IN ART-EXPERIENCED PATIENTS

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Background: The use of dual therapies (DT) in HIV positive patients can improve adherence and can reduce drug-drug interactions, toxicities and costs. Among DT regimens, dolutegravir (DTG)-based ones are known to have the same efficacy of three-drugs-regimens, both in naive and experienced patients. The objective of our study is to analyse the use of DTG-based DT in our cohort of cART experienced patients and to evaluate efficacy and tolerability.
Material and methods: All antiretroviral therapy (cART) experienced patients that started a DTG-based DT (DTG/3TC or DTG/RPV) from January 2015 to January 2020 at San Paolo Hospital's Clinic of Infectious Diseases (Milan) were included. We analysed the probability of virological failure (two subsequent viral loads >50 cp/ml) and of therapeutic failure (defined as the first of two events: virological failure or interruption of therapy for any reason) using Kaplan-Meier curves. Median and interquartile range was used for quantitative variables. Variables with $p<0.05$ were considered significant.
Results: 112 experienced patients (77 DTG/3TC, 35 DTG/RPV) were included, with the following clinical characteristics: median age of 53 (45-58) years, 26.8% females, 84.8% italian, 42.2% MSM. Immune-virological characteristics were: CD4 nadir 216 cells/ul (111-308), viral load zenith 137269 copies/ml (68286-319000). Patients had a median ART exposure of 12.3 years (7.6-17.5). Cumulative TAMS at genotype analysis were detected in 37.8% and M184V mutation in 27.6%. Previous ART regimens were PI-based in 9%, NNRTI-based in 27%, INSTI-based in 21%, other DT in 37%. Reasons of switch to DT were toxicities in 43.5%, simplification in 37%, drug-drug interactions in 11.1%, virological failure in 3.7%. At switch time (baseline) CD4 lymphocytes count was 691 cells/ul (533-837), HIV-RNA was <50 cp/ml in 86.6% of the patients. After a mean observation time of 12 months (IC95% 1-20), the probability of therapeutic failure was 7% at 6 months and 11.5% at 12 months, with no difference according to the type of DT regimen. The probability of virological failure at 12 months was 1.2% with no differences according to the type of regimen; in the sub-population with drug resistance (TAMS or M184V) at cumulative genotype the probability of virological failure at 12 months increased to 5%.
Conclusions: In our cohort of ART-experienced patients, DTG-based DT was offered to ART long-exposure patients in order to reduce toxicities and drug-drug interactions and to promote a therapy simplification. These regimens resulted well tolerated and associated with an high probability of virological success in patients with no documented drug resistance at cumulative genotype

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P 128 EVALUATION OF EFFICACY AND DURABILITY OF RALTEGRAVIR ONCE-DAILY: REAL-LIFE DATA FROM AN ITALIAN CENTER

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Background: Non-inferiority of RAL 600 versus RAL 400 in terms of efficacy and tolerability has been shown by ONCEMRK trial in HIV+ treatment naïve patients (pts). The aim of our study is to evaluate efficacy and durability of RAL 600 in clinical practice, as first line treatment and as switch strategy in virologically suppressed pts.
Material and methods: In this monocentric, retrospective study we enrolled all HIV-infected patients that started RAL 600 as first line therapy or as a switch strategy from April 2018 to November 2019 in our Clinic of Infectious Diseases. We collected viro-immunological, renal and metabolic parameters at baseline (BL) and at 3, 6 and 12 months of follow up. Survival function were used to evaluate the percentage of patients free from treatment discontinuation (TD) and virological failure (VF); Cox regressions were used to evaluate factors associated with TD and VF. The Student's T test for paired samples were used to evaluate the changes in viro-immunological and metabolic parameters.
Results: We enrolled 130 patients, with a median time of follow up of 9.8 months (IQR range 4.3-19.8). Eighty-nine pts (67.7%) were males, with a median age of 53.3 years (IQR 45.8-58.3), a median time of HIV infection of 17.2 yrs (IQR 6.1-23.5) and of virological suppression of 12.9 yrs (IQR 2.6-18.1): 12 pts (9.3%) were treatment naïve. Characteristics of patients at BL are shown in table n.1. Seventy-five patients (56.9%) came from a therapy with RAL 400 mg and 25 (19.2%) from a dual therapy (of which 14 with a boosted PI). The main reasons for switch to RAL 600 were therapeutic optimization (73), drug-drug interactions (6) and toxicity (16, of which 4 for neurological toxicity from a DTG-based therapy). 120 patients start a 2NRTI+RAL regimen, 9 a PI/b regimen and 1 a regimen with more than 3 drugs. We registered 34 treatment discontinuations: 15 of them for simplification, 6 for toxicity (4 GI toxicity), 4 for VF and 7 for other reasons. Among TD for optimization, 12 pts switch to a single tablet regimen, most of them (10) to FTC/TDF/BIC. Overall, we observed 4 VF: among them, 1 patient failing a DRV/r+RAL regimen showed a major mutation in PI region at HIV genotypic-resistence test. At multivariable analysis, only drug addiction as HIV risk factor were predictor of TD (HR 7.65, IC 95% 1.05-55.7, p 0.045). No predictors were found for VF. Analyzing only patients switching to RAL 600, we found a median increase of CD4/CD8 ratio at 6 months of follow up of +0.07 (IC 95% 0.01-0.13, p 0.023). No other changes were observed for CD4 cells count and metabolic parameters.
Conclusions: Our results showed an overall good efficacy and tolerability of RAL 600 in both treatment naïve and experienced patients, with a neutral effect on metabolic profile. Compared to the previous formulation, RAL 600 seems to show a higher gastrointestinal toxicity that rarely can lead to TD, but further data are needed to confirm this result

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P 129 IMPACT ON CD4 COUNT AND CD4/CD8 RATIO OF 3 DIFFERENT INTEGRASE INHIBITOR-BASED REGIMENS IN NAÏVE AND EXPERIENCED PATIENTS

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Background: INSTI-based regimens use has increased, due to rapid effect on HIV RNA decay and immune restoration. We analyse the different impact in achieving immunological recovery between Raltegravir (RAL), Dolutegravir (DTG) and Elvitegravir/Cobicistat (EVG/c) based regimens.
Methods: We performed a longitudinal retrospective study on 128 (35.1%) naïve and 237 (64.9%) experienced patients starting their first INSTI regimen from year 2009 to 2018, median follow up 96 weeks. Patients treated with a salvage or a less-drug regimen triple therapy were excluded. A CD4 cell count ≥500 cells/μL was considered normal.
Results: 365 patients were included; 168 (46%) received DTG, 130 (35.6%) RAL and 67 (18.4%) EVG/c. Baseline median (IQR) CD4 count was 491 (320-684) cells/μL. 139 (38.1%) patients had a CD4 count ≤350 cells/μL (median 232 (142-296) cells/μL), 226 (61.9%) had a CD4 count >350 cells/μL (median 580 (471-786) cells/μL).
25 (18%) patients with a baseline CD4 count ≤350 cells/μL had a normal CD4 count at week 96th (5 EVG/c, 9 RAL, 11 DTG), 68 (48.9%) reached normality at least once during the follow up. The mean time to reach a CD4 count >500 cells/μL was 49 weeks.
During the follow-up only the CD4 cell count median trend of EVG/c based regimens patients (starting treatment with ≤350 cells/μL) reaches 500 cells/μL. However, although a different rate, each INSTIs has a significant effect on CD4 count (RAL p=0.0030; EVG/c p=0.0080; DTG p<0.0001).
Patients with CD4 count >350 cells/μL showed a significant CD4 improvement (RAL p<0.0001; EVG/c p=0.0078; DTG p=0.0002). The slope value was higher in patients treated with RAL. Baseline median CD4/CD8 ratio was 0.62 (0.33 -0.91). 207 (56,7%) had a ratio >0.5. Out of 158 patients with a ratio ≤0.5, 74,6% obtained a ratio >0.5 at week 96th (13 EVG/c, 39 RAL, 66 DTG). Moreover, 52 (32,9%) patients reached and maintained a ratio >0.5 since week 4th (13 RAL, 8 EVG/c and 31 DTG). Overall, 135 (85,4%) patients with a baseline ratio ≤0.5 reached a value >0.5 at least once within the follow up. The mean time to reach a 0.5 ratio was 24 weeks. 61 out 127 patients with a ratio >0.5 but <1.0, reached a value >1.0 at least once in a mean time of 39 weeks.
In patients with a ratio ≤0.5, RAL (p<0.0001) and DTG (p<0.0001) have a significant effect of improvement. In patients with a baseline ratio ≤0.5, RAL fails to normalize median ratio; EVG/c acted the quickest but failed to maintain normal values. In patients with a ratio >0.5, the 3 INSTIs showed a statistically significant improvement on the ratio (RAL p=0.0064; EVG/c p=0.0045; DTG p<0.0001).
Conclusions: Although INSTIs showed a no significant different impact on immunological recovery, we were able to establish a rank of effectiveness between patients with ≤350 cells/μL (EVG/c>DTG>RAL) and patients with >350 cells/μL (RAL>DTG>EVG/c) and between patients with a ratio ≤0.5 (DTG>RAL>EVG/c) and patients with a ratio >0.5 (DTG>EVG/c>RAL)

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P 130 ALTERATION OF SERUM LIPID PROFILES IN HIV/HCV CO-INFECTED PATIENTS UNDER TREATMENT WITH HAART/DAAS COMBINED THERAPY

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Background: Highly Active Anti-Retroviral Therapy (HAART) and Direct Acting Antiviral (DAA), are currently the main options for the treatment of patients HIV/HCV co-infected. Hepatitis C virus promote changes in serum lipid profiles and can influence lipid metabolism, also HAART is known to change lipidic profile. Aim of our study was to evaluate, in real life, lipid alterations occurring in HIV/HCV co-infected patients undergoing an effective HAART/DAAs combined therapy.
Materials and methods: we conducted a prospective study, including HIV/HCV co-infected patients receiving HAART/DAAs treatment during a 4-year period. Inclusion criteria were: adulthood, accomplishment of DAA cycle along with completion of 12 weeks post treatment follow up, virological suppression on HAART therapy and during follow-up. Exclusion criteria were: early discontinuation of DAA/HAART therapy, relapse or non-response to a complete cycle of DAA treatment, any lipid modulating therapy. We completed a case report form for each patient, including sex, age, HAART/DAAs schedule, HCV genotype, immune profile and HIV-RNA viral load recorded at the start of HCV therapy and after treatment, plasma HCV-RNA at baseline, after 4 weeks of treatment and at the end of therapy. We collected and analysed variations in lipid profile in terms of total cholesterol (TC), LDL-C, high-density lipoprotein (HDL-C) and triglycerides (TG), during and after the DAA therapy (until 12 weeks of follow-up). Descriptive statistics were expressed as mean, median, IQR, and standard deviation or as percentage, for categorical variables, as appropriate. Statistical analysis was performed as appropriate.
Results: Fifty-four HIV/HCV patients met the inclusion criteria for the study. Thirty-four (68%) patients were male, median age was 56 yrs (range 32-78). All patients were naïve to HCV therapy and received HAART. HCV genotyping highlighted genotype 1 in 30 (55%), genotype 3 in 16 (29%), and genotype 2 or 4 in the remaining cases. Hypercholesterolemia (>200 mg/dl) was reported in 12/54 (22%) at baseline and in 23/54 (42%) at the end of therapy(p=0.02), instead LDL-cholesterol >130 mg/dl was reported in 5/54 (9%) at baseline and in 18/54 (33%) at the end of therapy(p=0.002). No significant changes were observed in triglycerides and HDL concentrations. Similar findings was retrieved after 12 weeks of post-treatment follow-up. No difference was reported when we performed a separate analysis on different HCV genotypes.
Conclusion: Patients living with HIV report a higher incidence of cardiovascular events, associated to HAART and HIV action itself. Changes in lipid profile after DAA/HAART treatment can be an important clue, as an elevated concentration of LDL-C is a risk factor for cardiovascular events in general population including those with HIV infection. This population has to be targeted for prevention strategies including anti-platelets agents and Cholesterol lowering drugs to reduce cardiovascular risk

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P 131 PLASMA VIRAL LOAD DECAY IN FIRST-TIME INSTI-USERS. A COMPARISON BETWEEN RALTEGRAVIR, ELVITEGRAVIR/COBICISTAT AND DOLUTEGRAVIR

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Background and aim: Since the introduction of integrase strand transfer inhibitors (INSTIs)-based regimens, we assisted to a revolution in HIV-RNA plasma viral load (pVL) decay. It is an established fact that INSTI, as a class, decrease the pVL more rapidly than the previously available drugs. Here, we wanted to compare the effect of different INSTI-based regimens [raltegravir (RAL), elvitegravir/cobicistat (EVG/c), dolutegravir (DTG)] on pVL decay.
Patients and methods: We anonymously collected and analyzed data about 365 patients who started combined Anti-Retroviral Therapy with an INSTI (RAL, EVG/c, DTG) during the period January 1st, 2009 and October 31st, 2018. Follow-up data were collected until December 31st, 2019. pVL lower limit of detection was 20 cps/mL. Absolute number, percentages, median and interquartile ranges (IQR) were used to describe the variables studied. t-student test and linear regression were used to determine any statistically significant difference between treatments. A p value <0.05 was considered significant. Confidence interval (CI) was 95%.
Results: Overall, 124 patients (34%) had a baseline undetectable (target not detected, TND) pVL. 156 patients (42.7%) reached TND during the period of the study, while 85 (23.3%) patients never reached TND. Among viremic patients at baseline, 45 (56.2%) treated with RAL, 29 (69.1%) with EVG/c and 82 (68.9%) with DTG reached TND. This difference is not significant (p = 0.3040). Of 116 individuals showing a baseline pVL ≤ 100,000 cps/mL (median (IQR) 8,427 (115 -31,964) cps/mL), 70 (60.3%) reach TND after only 4 weeks of treatment. Among the 40 patients showing a baseline pVL ≥ 100,000 cps/mL (median (IQR) 347931 (168,850-722,682) cps/mL), only 7 (17.5%) reaches TND at 4 weeks, while 19 patients (47.5%) show TND at 16 weeks (figure 1). However, baseline pVL do not determine differences in time to TND between the INSTIs (p = 0.3040 in patients with a baseline pVL 100,000 cps/mL; p = 0.3657 in patients with a baseline pVL >100,000 cps/mL) (figure 2).
Discussion: One third of the patients included in our study were switched to an INSTI-based regimen with an undetectable pVL. In addition, more than the 40% of the patients reached undetectability during the INSTI-based treatment. Despite a different pVL trend showed by RAL-treated patients compared to EVG/c and DTG, the time to TND does not differ between the treatments in a statistically significant manner. Moreover, the three INSTI-based treatments are not significantly different with regards to the number of patients reaching TND within a 2-year time frame.
Conclusion: INSTI-based treatments are all effective in durably suppressing pVL. Although the only factor influencing time to TND was the zenith pVL, we were not able to show any differences in time to TND between the different arms of treatment

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P 132 METABOLIC PROFILE CHANGES AFTER SWITCHING FROM A PI- TO AN INI-BASED REGIMEN IN THE MAINTENANCE TREATMENT OF HIV INFECTION

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Several clinical studies have reported a lower impact on the metabolic profile by integrase inhibitors (INI) compared to protease inhibitors (PI). However, in clinical practice, many factors affect the lipid profile and, in this setting, the impact of the therapeutic regimen could be less relevant.
The aim of our study is to evaluate the changes over time (at three, six, 12 and 24 months) of the total cholesterol, LDL, triglycerides, ACC score and weight in patients who have switched from a PI-based regimen to an INI- based.
In this prospective multicenter study (5 clinical centers of 3 Italian tertiary hospitals) we enrolled all the patients who switch their regimen from a PI-based to a INI-based starting from June 2015.
Currently a total of 83 patients were enrolled, of these 48 completed the 24-month follow-up while for 35 it is still ongoing. The average age was 51.6 years and most of the patients were male (M 69%).
At the time of the switch 49% received a regime with DRV, 45% one with ATV and 6% one with LPV. The median of CD4 was 682 cells / uL (440 - 519), of total cholesterol was 219 (189 - 251), of LDL was 144 (128 - 165) and of triglycerides 140 (99 - 189). The main reason for the switch was simplification of the regimen (39%) followed by metabolic reasons (33%), interaction with other drugs (6%) and the lack of virological control (4%). Sixteen patients were on statin therapy at the time of the switch and none of them stopped it during the observation period.
In 67% of cases a regimen with DTG was started, in 24% with ELV and in 9% with RAL.
The data collected at three, six, 12 and 24 months were analyzed using the Wilcoxon Signed-Rank Test.
The results show a reduction in the median values of triglycerides, cholesterol and LDL at each time point. This reduction is statistically significant with regard to triglycerides at three months (- 23 mg / dl, p <0.01), six months (-21.5 mg / dl, p 0.01) and 12 months (-25.5 mg / dl, p <0.01); for total cholesterol at three months (-26.0 mg / dl, p <0.01) and 12 months (-9.0 mg / dl, p 0.01) and for LDL at three months (-17.0 mg / dl, p <0.01) and 12 months (-10.0 mg / dl, p 0.02).
On the other hand the ACC score shows only a slight drop, between 0.1% and 0.5%, not statistically significant and the weight does not show any significant variations.
In conclusion these data confirm the lower impact on the metabolic profile of INI compared to PI, even if this reduction does not seem to significantly affect the cardiovascular risk

Issues on antiretroviral therapy

P 133 EVALUATION OF LIPID PROFILE IN HIV NAIVE PATIENTS, TREATED BY TAF-BASED REGIMENS

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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,270 patients with HIV infection at the time of the start of ART and with a follow-up of at least 48 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 significant 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 evaluate the factors associated to hypercholesterolemia at T1 and T2 (tab.3): at T1 only age was related to hypercholesterolemia, while at T2 this condition appeared related only to group of patients treated by TAF/FTC/EVT/Cobi.

Conclusions: Our preliminary data from a real-life multicentric study show that, in HIV naïve patients, TAF, if associated to INI with 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 with longer follow-up 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.

Management and treatment of viral hepatitis

P 134 YOUNGER AGE, MALE GENDER AND HCC PRESENCE ARE ASSOCIATED TO ANTI HCV-DAA FAILURE

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Background and Aims: Sustained Virological Responses (SVR) are nowaday obtained in real life settings, in almost 98 -99% of HCV-infected patients using 8 or 12W schedules and 2nd generation DAAs (glecaprevir/pibrentasvir, sofosbuvir/velpatasvir and elbasvir/gazoprevir). Clinical and virological predictors of viral failures (VF) with both 1st and 2nd generation DAAs are poorly understood.

Methods: Between April 2015 and April 2019, 2508 patient received DAAs for HCV at our Institution. A retrospective analysis of the Virology Laboratory Database was performed to identify all the patients who completed their first DAA treatment schedule, having HCV-RNA detectable 12 or 24 weeks after end-of treatment (EOT). Such cases were considered as VF. Second line DAA treatments were excluded.

Several clinical and virology parameters (age, gender, HCV genotype, HIV status, Metavir stage, type of DAA and HCC diagnosis before DAA start) were compared between subjects with VF or SVR. This latter group included 780 consecutive subjects with SVR, treated with DAA at our Unit during the same time interval. Uni and Multivariate analysis was performed to identify factors associated to VF.

Results: The global SVR24 rate at our Institution was 97.1% (72/2508). Fifty-nine patients experienced failure with first generation DAA, and 13 with 2nd generation DAAs. HCC was diagnosed in 84 subjects (TABLE 1)

Viral relapses occurred in 48.6% of the cases already at PTW4 (n.35), 37.0% between PTW4 and PTW12 (n.27), 6.8% between PTW12 and PTW24 (n.5) and 6.8% (n.5) after PTW24. Sixty out of the 72 subjects with viral relapse where submitted to a second DAA course with 98.3%% of SVR12.

At univariate analysis virological failure to DAA was associated to Male gender, age <60 yrs, 1st generation DAA, Metavir F4 stage, Genotype 3, and pre DAA HCC diagnosis (Table 2). Statistical significance persisted at multivariate analysis only for age, gender and HCC presence (Table 3)

Conclusions: Although affected by possible bias, our study shows that age below 60 yrs, male gender and pre- or post-treatment HCC, independently increase the risk of viral failure with DAAs.

Management and treatment of viral hepatitis

P 135 REACTIVATION OF OCCULT HBV INFECTION IN HIV PATIENTS TREATED WITH DIRECT-ACTING ANTIVIRALS FOR CHRONIC HEPATITIS C: A RETROSPECTIVE STUDY

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Background: Reactivation of occult hepatitis B virus infection (OBI) is a condition that was widely studied in subjects with compromised immune systems, such as those receiving immunosuppressive therapies or cytotoxic drugs for neoplastic, autoimmune diseases or those who receive a solid organ transplant However, reactivations of OBI have been described also with anti-HCV direct-acting antivirals. According to international guidelines, all HIV-infected and HBsAg-positive patients should be treated with antiretroviral therapy (ART) containing nucleoside reverse transcriptase inhibitors (NRTI) dually active against HBV and HIV. However, there are not precise indications regarding HBsAg-negative and HBcAb-positive individuals with HIV infection and to date the risk of HBV reactivation in patients with HIV and OBI, treated with NRTI-sparing ARV regimens, and exposed to DAAs regimen, is unknown.

Aims: The aim of this study was to determine HBV reactivation risk in HCV-HIV patients with occult HBV infection, treated for HCV.

Methods: We retrospectively included HCV-HIV individuals with occult HBV infection (HBsAg-/HBcAb+), treated for HCV, not receiving antiretroviral drugs simultaneously active against HIV and HBV. We defined HBV reactivation as an increase in HBV DNA and aminotransferases. HBV DNA levels (together with HBsAg) were promptly measured if any ALT and/or AST increase was detected at routine blood samples.

Results: Two of the 24 enrolled subjects (8%) developed HBV reactivation (Table 1). Both patients had AIDS history and CD4+ T-cells nadir<50/mm3. CD4+ T-cells nadir was significantly lower in those who had HBV reactivation compared to those who did not (P=0.013). One patient had HBV reactivation with signs of liver decompensation and the other one experienced asymptomatic reactivation. Both patients were switched to a Tenofovir-containing antiretroviral regimen with virological response.

Conclusions: This is the first study analyzing the risk for occult HBV infection reactivation in HCV-HIV population treated with new antivirals for HCV. Our findings suggest AIDS events and low CD4+ T-cells nadir as potential risk factors. Despite the small sample size, the remarkable rate of HBV reactivation might suggest that HIV patients with negative HBsAg and positive HBcAb would require antiretroviral drugs dually-active for HIV/HBV in, during anti-HCV treatment.

Management and treatment of viral hepatitis

P 136 DAA FAILURE IN HCV GENOTYPE NOT 1: VIROLOGICAL FEATURES AND EFFICACY OF RE-TREATMENT

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Background: Despite the excellent efficacy, direct-acting antivirals (DAA)-regimens are associated with failure in about 5% of cases. The failure to DAAs was associated with 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 90 HCV patients with failure to IFN-free regimen observed at the laboratory of infectious diseases of University of Campania, Naples were enrolled. All the patients had been treated with DAA-regimens 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 enrolled were mainly males (80%) with median age 57,5 years (range 31-86). HCV RNA, IU/ml median value was 6,48 x 10e5 IU/ml (range: (1,3 x 103 IU/ml – 3,8 x 108 IU/ml), 62,2% of patients had a diagnosis of cirrhosis. 29 patients were HCV genotype 2a/2c, 55 were genotype 3 and 6 were genotype 4.

The prevalence of RASs in NS5A region were more frequently detected in genotype 3(60%) and genotype 4 (50 %) than in genotype 2a/2c (37,9%) with no statistical meaning. RAS in the NS5B region were identified only in genotype 3 (12,7%) and genotype 2a/2c (3,4%). Out of the 90 patients enrolled, 47 (52,2 %) patients were re-treated.

Table 2 shows the epidemiological, clinical and virological characteristics of the 47 retreated patients genotype not-1. According to therapeutic outcome, 12,8% were relapse and 2,1 % were non-responder at retreatment.

The 17 patients re-treated with genotype 2 less frequently (88,2%) showed an SVR than the 27 patients with genotype 3 (96%) with no statistical meaning.

In table 3 we analyze the SVR prevalence according to genotype, previous/latest DAA regimen, RASs distribution and Resistance-Guided Therapy (RGT).

11,8 % of patients with genotype 2, 11,1% with genotype 3 and 66,6% with genotype 4 without SVR show RASs.

According to therapeutic regimen, SVR was more frequent in patients HCV genotype 2 treated with the latest DAAs regimen (76,5% vs 11,8%, p=0.0001); also for patients with HCV genotype 3 treated with the latest generation DAAs (79,1% vs 18,5%) SVR was more frequent.

Only one HCV genotype 4 patient reached SVR.

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 2 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.

Management and treatment of viral hepatitis

P 137 VIROLOGICAL FEATURES AND EFFICACY OF RE-TREATMENT IN HCV PATIENTS: A REAL EXPERIENCE IN SOUTHERN ITALY

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Background: direct-acting antivirals (DAA)-regimens are associated with failure in about 5%. The failure was associated with the emergence of resistance associated substitutions (RASs). This real-life study characterized the virological patterns in patient failing to DAA and evaluated the efficacy of retreatment.

Materials/methods: all the consecutive 207 HCV patients failed to DAA observed at the laboratory of infectious diseases of University of Campania, Naples were enrolled. All the patients were treated 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: Patients enrolled were mainly males (68.1%) with median age 65(31-89). 86% were Relapse, 8,7% no Responder,5.3% Breakthrough, 35 (17% %) were re-treated. Table 2 shows the epidemiological, clinical and virological characteristics of the 35 retreated patients. At failure, 68,5% of patients presented one RAS and 42,8 % had 2 or more RAS. 17 (48,6%) obtained SVR. The 17 re-treated patients with genotype 3 most frequently (41,2%) showed SVR than the patients with genotype 1 (29,4%), 2 (23,6%) and 4 (5,8) but without statistical significance.

We analyze the SVR prevalence according to previous/latest DAA regimen, RASs distribution and Resistance-Guided Therapy (RGT). Patients retreated with the latest DAAs regimen most frequently obtained SVR than patients retreated with previous generation of DAA (76.6% vs 13.3%, $p<0.05$). Patients with SVR most frequently had RGT (63.4% vs 26.6%, $p<0.05$).

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. Patients with RGT more frequently obtain SVR. NS3, NS5A and NS5B sequencing seems mandatory in the choice of re-treatment DAAs.

Management and treatment of viral hepatitis

P 138 OVERALL SURVIVAL AT 3, 5 AND 10 YEARS OF HIV-POSITIVE PATIENTS WHO UNDERWENT LIVER TRANSPLANTATION AT THE UNIVERSITY HOSPITAL OF ANCONA

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Liver Transplantation (LT) is the only life-saving treatment option in patients with end-stage liver disease (ESLD). HIV/AIDS patients only recently could access to LT programs thanks to HAART. For many years HIV-HCV co-infected liver candidate patients had a worse prognosis respect to mono-infected HIV-patients as the sudden HCV graft reinfection after LT was associated with quick onset of ESDL. Here we describe the clinical characteristics and overall survival of HIV-positive patients who underwent LT from 2007 to 2019 at the University Hospital of Ancona. Among the 29 patients who underwent LT, 26 (90%) were male and 3 (10%) were female; a total of 30 LT was performed as one patient underwent a re-transplant. In 22 cases (73%) the indication to perform the procedure was HCV infection, in 5 cases (17%) HBV-HCV-HDV co-infection, in 1 case (3%) HBV-HCV co-infection, in 1 case (3%) by HBV-HDV co-infection. The re-transplantion (1 case, 3%) was due to Primary Non-Function (PNF). Hepatocellular carcinoma was detected in 13 (45%) patients. HIV viremia and CD4+ count were not available for 3 and 2 patients, respectively. For 26 (96%) patients HIV viremia was not detectable or lower than instrument detection limit; in 2 (7%) cases the CD4+ cells before the transplant were less than 100/mmc, in 6 cases (21%) they were between 100 and 200 and in 20 cases (71%) they were higher than 200. In 9 (30%) cases the MELD score when the patient got on the national transplant waiting list less than 15, in 12 (40%) cases it was between 15 and 25 and in 9 (30%) cases it was greater than 25. The MELD score at liver allocation, in 4 (13%) cases was less than 15, in 17 (57%) cases it was between 15 and 25 and in 9 (30%) cases it was greater than 25. The average age of the donors was 52y; in 5 (17%) cases the donor was younger than 30y, in 10 (33%) cases donor's age was between 30y and 50y and in 15 (50%) cases it was over 50y. A total of 30 transplants were performed; 27 (90%) were whole liver transplants and 3 cases (10%) split liver transplantation. The average ICU hospital stay was 5,7 days, three patients' length of stay was not available. The study population overall mortality rate was 55,2% (16 dead, 13 alive). The calculated post-transplant 3-years overall survival was 58% (15 patients alive out of 26 patients during a 3-years follow-up), the 5-years one (60 months) was 43% (10 patients alive out of 23 patients during a 5-years follow-up), the 10-years one (120 months) was 25% (2 patients alive out of su 8 patients during a 10-years follow-up). The estimated post-transplant survival is reported in Figure 1. Causes of death include recurrence of HCV infection (6 cases), sepsis and septic shock (2 cases), cerebral hemorrhage (2 cases), recurrence of hepatocellular carcinoma (2 cases), hemolytic-uremic syndrome (1 case), massive hemorrhage of the tracheobronchial tree (1 case), heart attack (1 case), PTLD (1 case).

Management and treatment of viral hepatitis

P 139 VIRO-IMMUNOLOGICAL AND HISTOLOGICAL CHARACTERIZATION OF A CASE OF HBV-RELATED HEPATITIS WITH IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME AFTER TREATMENT INITIATION FOR HBV/HIV-1 CO-INFECTION WITH BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE

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The prevalence of chronic HBV infection is about 2-8% in Mediterranean countries. HIV and HBV infections share the same transmission ways and co-infection is common. Hepatotoxicity after antiretroviral (ARV) initiation is increased in HBV co-infected individuals. The distinction between immune reconstitution inflammatory syndrome (IRIS) and drug liver toxicity is essential for the clinical management of these cases. Here we describe clinical, viro-immunological and histological aspects of a case of HBV-related hepatitis in an HIV infected patient after ARV initiation.

Liver enzymes (AST, ALT), white blood cell, CD4 and CD8 cell counts, HBV-DNA, HIV-RNA were routinely assessed. T- and B-cell phenotypes were assessed with flow cytometry. Histological examination after hematoxylin and eosin, core and surface HBV antigen staining was performed on a liver biopsy. Intrahepatic HBV DNA (ihHBV DNA), covalently closed circular DNA (cccDNA), HBV pregenomic RNA (pgRNA) were assessed trough digital droplet PCR on a liver biopsy.

A 50-year-old Caucasian man was hospitalised because of pancytopenia, and squamous cell carcinoma. HIV-1 (subtype B) and HBV (genotype A) co-infection was diagnosed. CD4 cell count was 9/mmc with a CD4/CD8 ratio of 0.04. HIV-RNA was 3.3x105 copies/ml and HBV-DNA was 2.94x108 IU/ml. ARV therapy was started with bictegravir/emtricitabine/tenofovir alafenamide, which was also active for HBV infection. Pre-ARV liver enzymes were altered (ALT/AST: 67/89 IU/ml) and improved during the first month of treatment (43/39 IU/ml). Despite a decrease in HIV-RNA and HBV-DNA, the patient experienced a 20-fold increase of ALT and AST (1010/927 IU/ml), more than 6 weeks after ARV initiation. CD4 cell count and CD4/CD8 ratio had increased to 100/mmc and 0.23, respectively (fig 1A). A liver biopsy was performed and histological examination showed chronic inflammation with piecemeal necrosis, HBcAg+ staining of hepatocyte nuclei and lymphocyte infiltration of porto-biliary spaces. Drug toxicity was excluded. Furthermore, ihHBV DNA, cccDNA and pgRNA were 324, 141 and 3,3x106 copies/1000cells, highlighting an extensive burden and transcriptional activity of intrahepatic reservoir. Peripheral blood T- and B-cell phenotype showed a strong increase in activated CD4+ and CD8+ T-cells, immunosenescent CD8+ T-cells and plasma cells, when compared to a healthy donor (fig 1B). Despite liver enzyme elevation, ARV treatment was continued and ALT and AST decreased. Importantly, HBV e antigen seroconvertion was observed.

IRIS is a self-limiting inflammatory response, occurring 2-8 weeks after initiation of ARV. Both HBV-specific and nonspecific CD8+ T cells seem to be involved in hepatocyte damage, with the recruitment of monocytes and CD8+ T cells to the liver. In our case, histological and viro-immunological studies confirmed the diagnosis of HBV-related IRIS hepatitis, and supported the role of activated CD8+ T cells in the pathogenesis of liver necro-inflammation.

Management and treatment of viral hepatitis

P 140 INDIRECT HYPERBILIRUBINEMIA AND JAUNDICE DURING CHRONIC HEPATITIS C IN AN HIV-INFECTED PATIENT TREATED WITH GLECAPREVIR/PIBRENTASVIR (GLE/PIB) AND ANTIRETROVIRAL THERAPY (ART). THE FIRST REPORTED CASE IN ITALY

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Real-world evidence indicates that GLE/PIB is a well-tolerated and highly effective pangenotypic treatment for a broad range of HCV-infected patients. We report the first case of serious indirect hyperbilirubinemia and jaundice observed in Italy in an HIV-infected patient treated with GLE/PIB and ART.

A 55-year-old man with a history of HIV infection in ART (Elvitegravir 150 mg/cobicistat 150 mg/emtricitabina 200 mg/tenofovir alafenamide 10 mg) and compensated liver disease (without cirrhosis), due to chronic hepatitis C virus (HCV) genotypes 4 has been admitted to our hospital because of jaundice. At 10 weeks following treatment with GLE/PIB, this patient showed evidence of severe hyperbilirubinemia (Total bilirubin 12.76 mg/dL, direct bilirubin 7.14 mg/dL). The ALT and AST levels were within the normal range. At baseline: Cd4+ cells count 374, HIV-RNA < 20 copie/mL, HCV-RNA 1.490.000 UI/mL. Fibrosis stage: F3. Plasma samples for determination of GLE and PIB concentrations were collected at weeks 11 and 12 and were characterized at the Laboratory of Clinical Pharmacology and Pharmacogenetics, University of Turin.Plasma levels of GLE and PIB were 2472 ng/mL and PIB 92 ng/mL, respectively (for GLE more higher than the drug concentration in healthy adults).The patient completed GLE/PIB treatment, maintaining an excellent virological response. Completed 12 weeks after the end of the treatment, total bilirubin has returned to normal values.

Yoon JH et al. reported the first known case of severe jaundice after medication with GLE/PIB in a patient with compensated liver cirrhosis, with a plasma drug concentration level of GLE more than 15 times higher than the drug concentration level verified in normal adults. (Medicine,2019).High level of GLE derived from low activity of CYP3A. In a Taiwanese investigation on the profile of GLE/PIB, 3 (2%) patients had Grade 3 elevation of total bilirubin level (Hsu SJ et al., J. Form Med Ass 2019). Higher GLE and/or PIB exposures may be expected in HCV-infected patients with Child-pugh-B and CP-C hepatic impairment than in HCV-infected subjects with compensated cirrhosis (Kosloski MP et al., Eur J Clin Pharmacol 2018). GLE exposures were increased by ritonavir boosted protease inhibitors and cobicistat boosted elvitegravir (Kosloski MP et al., J Infect Dis 2019). Cobicistat is metabolised by CYP3A CYP2D6 (minor), (Inducer on CYP2C9, CYP2C19, and UGT1A1 is unknown but is expected to be low; inhibitor of CYP3A, CYP2D6, P-gb, BCRP, MATE1, OATP1B1, OATP1B3). Grade 3 transient elevations in indirect bilirubin occurred in 1% of patients from clinical trials, and most of these patients had preexisting indirect bilirubin elevations, consistent with the known mechanism that glecaprevir can impact bilirubin transport and conjugation. All of these mechanisms may contribute in part to observed increases in indirect bilirubin and jaundice in our patient.

Management and treatment of viral hepatitis

P 141 CURRENT MANAGEMENT OF HEPATITIS B IN SCLEROSIS PATIENTS TREATED WITH DISEASE-MODIFY THERAPIES

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Background: In 2015, 257 million people were living with hepatitis B virus (HBV) infection and 887.000 deaths are related to HBV infection, mostly from cirrhosis and hepatocellular carcinoma (1). Current multiple sclerosis (MS) treatments consist on immunomodulatory agents, immunosuppressants or selective immunosuppressants and could impact on immune system. These disease-modify therapies (DMTs) may result in high, moderate and low risk of reactivation of HBV. Current guidelines advice two different approach of management of HBV infection in patients undergoing immunosuppressive therapy or chemotherapy: HBV prophylaxis with antiviral drugs or a preemptive strategy of monitoring HBV-DNA, usually every 3 months (2).

Materials/methods: At the Neuroinfectious Unit of Policlinico Umberto I (Rome), for all MS patients candidate for DMTs treatment, HBV screening by serologic tests (HBsAg, anti-HBs, anti-HBc), liver enzymes was carried out. Following screening, HBV infection diagnosis was based on medical history, physical examination, and exclusion of acute hepatitis B. All MS patients with HBsAg negative, HBsAb and anti-HBc positive were monthly monitored with assessment of liver enzymes, HBsAg and HBV-DNA, due to potential risk for HBV flares or reactivation.

Results: Before started DMTs treatment, 133 MS patients (74 females, 59 males) with a median age [interquartile range (IQR)] of 48.0 (39.8-56.0), median years of disease (IQR) of 9 (3-18.3) and median Expanded Disability Status Scale (IQR) of 4 (2-6), were enrolled. At baseline, the 9.8% (13/133) of MS patients showed HBV surface and core antigens (HBsAb and HBcAb, respectively) positive and HBsAg and HBV-DNA negative. To date, nine patients are at least six months of ocrelizumab (anti-CD20 monoclonal antibody) treatment, three patients at seven months of teriflunomide (oral DMT immunomodulator) treatment, one patient at five months of dimethyl fumarate (oral DMT immunomodulator) treatment. Among MS patients under ocrelizumab treatment, one patient showed a reactivation of HBV after 13 weeks from DMT starting. The patient showed a mutation in the major hydrophilic HBsAg region that it is known to act as immune-escape mutations. He started antiviral specific treatment and HBV-DNA rapidly was undetectable. The patient received the scheduled dose of ocrelizumab and remained asymptomatic. The patient is currently under follow-up.

Conclusions: The evaluation of HBV infection in MS patients candidates to DMTs treatment, must be considered standard care in MS management. The use of preemptive strategy or prophylaxis must be chosen based on patient and her/his compliance, and on DMTs.

In our cohort, reactivation monitoring can prevent ocrelizumab discontinuation and the choice of preemptive strategy allowed to spare HBV prophylaxis in unnecessary cases.

Management of HIV infection

P 142 EFFECT OF 12-WEEK PHYSICAL ACTIVITY PROGRAM ON SARCOPENIA MEASURES IN PEOPLE LIVING WITH HIV

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Background: Sarcopenia is defined by the progressive reduction of muscle mass, strength and function occurring in the elderly and in people with chronic conditions and is an emerging health issue in people living with HIV (PLWH). No study has specifically addressed the benefits of physical activity on sarcopenia in PLWH. Therefore, the aim of this study was to investigate the effects of moderate intensity exercise on physical function and muscle mass by total body dual energy absorptiometry (DEXA).

Material and methods: Twenty-five PLWH [20 M, 5 F, age: 51 (47-55) years, 96% with VL <40 copies/mL; CD4: 576 (462-701); nadir CD4: 144 (37-197)] were enrolled in a 12-week pilot study consisting of 3 sessions per week of 60-min brisk walking at 65-75% of HRmax with ("walk-strength" group) or without ("walk" group) 30-min circuit training at 65% of 1RM. Assessment of sarcopenia measures at baseline (BL) and week 12 (W12) included physical function evaluation by 6MWT, 1RM test in the walk-strength group and body composition by DEXA. Appendicular Skeletal Muscle Mass (ASMM) and ASMM Index (ASMMI) were also calculated according to the cut-off points for low muscle quantity (ASMM: <20 kg male, <15 kg female; ASMMI: <7.0 kg/m2 male, <5.5 kg/m2 female). Changes between BL and W12 were assessed by Wilcoxon matched-pairs signed rank test, and percent change differences between groups by Mann–Whitney test.

Results: Fifteen participants were enrolled in the walk group and 10 in the walk-strength group. All completed the 12-week program with a median adherence of 64% (59%-75%). At BL, 8 participants (32%) were diagnosed with sarcopenia with both the ASMM and ASMMI values below the cut-off point for definition of sarcopenia. At W12, there was a significant improvement of speed of 6MWT ($p<0.0001$) in both groups, and of 1RM in all strength exercises in the walk-strength group (crunch $p=0.004$, lat machine $p=0.002$, chest press $p=0.002$, leg extension $p=0.004$, sitting calf $p=0.006$, leg press $p=0.004$). Significant W12 reductions were observed of BMI ($p=0.001$), total body mass ($p=0.001$) and total fat mass ($p=0.048$) in the walk group. Significant W12 increases were observed of lean mass of total body ($p=0.002$), arms ($p=0.002$), and legs ($p=0.002$), and of both ASMM ($p=0.002$) and ASMMI ($p=0.002$) in the walk-strength group. Significant percent change difference between the walk and the strength-walk group were observed in lean mass of total body ($p=0.025$), arms ($p=0.004$), and legs ($p=0.0298$), and of both ASMM ($p=0.003$) and ASMMI ($p=0.003$).

Conclusions: This pilot study indicates that a 12-week program of brisk walking was effective to improve physical function in both training groups. However, it was only the association of walking with resistance training effective to improve muscle strength and mass by DEXA. This information could be relevant in order to prescribe effective exercise interventions that focus specifically on prevention and treatment of sarcopenia in PLWH.

Management of HIV infection

P 143 REASONS FOR STARTING D/C/F/TAF AND CHARACTERISTICS OF PATIENTS ENROLLED IN AN ITALIAN NON-INTERVENTIONAL STUDY: THE DIAMANTE (TMC114FD1HTX4011) STUDY

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Background: Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) is a single-tablet regimen (STR) based on a protease inhibitor, developed to reduce the pill burden and avoid the mistakes in drug intaking in PLWH; this formulation allows the adherence improvement, which is a critical factor contributing to treatment success.
Material and methods: DIAMANTE is a retrospective and prospective non-interventional study carried on HIV-positive adult outpatients treated with D/C/F/TAF as per clinical practice, in eighteen Italian centers. Three groups of patients were included in the study: patients who have always been treated by boosted-DRV (bDRV)-based ART (Group1); patients switching to D/C/F/TAF from a non bDRV-based ART (Group2) and patients starting D/C/F/TAF as first-line therapy at least one month before enrollment (Group3). Study endpoints include effectiveness of D/C/F/TAF based treatment, measured as virological suppression at week 48; safety and tolerability; QoL. Demographic characteristics of patients enrolled in this study and the reasons for starting D/C/F/TAF are described here.
Results: Two-hundred-forty-six patients have been enrolled; 81 in Group1, 44 in Group2 and 121 in Group3; 45/246 (18,4%) were females. Median(Q1-Q3) age was 43(34-50) years in Group1, 39,5(34-44,5) in Group2 and 39(31,5-46) in Group3.The majority of patients were of Caucasian ethnicity (82,5%).Main way of infection was unprotected homosexual intercourses in Group1 (52%) and Group3 (47%), whilst in Group2 was heterosexual intercourses (52%).
At enrollment, median CD4 cell count was 704(502;836) cells/mm3 in Group1, 582 (401,5;780,5) in Group2 and 481 (295;716) in Group3; VL was<50cp/mL in75% of patients in Group1, 63% in Group2 and 35,5% in Group3.
Considering the ARV history, in Group1, most of patients (96,3%), came from a triple therapy DRV-based, while only 3 patients were in a dual regimen. In Group2, 63% of patients came from an INSTI-based regimen, 35% from a PI-based regimen and 2% from RPV-based one. The reasons for switching are shown in Figure1.
Considering the risk of CVD, 28,4% in Group1, 29,6% in Group2 and 27,3% in Group3 declared lack of familiarity.
The median waist circumference at baseline was 89,5 (80;98) cm in Group1, 87(76;93) cm in Group2 and 87,5 (78;97) cm in Group3. The median BMI was 23,8 (21,6;25,8) Kg/m2, 23,1(21,4;27) Kg/m2, 23,7 (21,9; 25,7) Kg/m2 over the three groups, respectively. 44,4% in Group1, 31,8% in Group2 and 43% in Group3 were smokers.
Conclusions: In this study, half of enrolled patients (49%) started their ART with D/C/F/TAF as naïve (Group3); this regimen is considered as a valuable simplification strategy: 96% of Group1 patients, always treated with bDRV, came from a triple, multiple-tablet regimen. The main reason for switching from other PI-based regimens is simplification as well, while switching from INSTIs is mainly due to AE/tolerability. Baseline characteristics show no particular issues.

Management of HIV infection

P 144 HIV-1 DNA QUANTIFICATION: COMPARATIVE ANALYSIS AND VALIDATION OF TWO COMMERCIAL QPCR ASSAYS

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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. "HIV-1 DNA Test" (Diatheva srl) is a real-time PCR (qPCR) showing reliable quantification results of HIV-1 DNA. The kit contains an exogenous Internal Control to detect sample inhibitors and requires DNA quantification. The "HIV-1 DNA Test PRO" is a new kit, containing HIV primers/probe set of "HIV-1 DNA Test", that allows the simultaneous amplification of HIV DNA and human Telomerase Reverse Transcriptase (hTERT). The endogenous gene allows to verify DNA extraction success, to determine the presence of PCR inhibitors, and to obtain HIV DNA copies quantification without cellular DNA measurement.
Aims of study: validation of "HIV-1 DNA Test PRO" amplification performances; comparison between the two kits; analytical specificity determination; "HIV-1 DNA Test PRO" robustness analyzing different DNA quantities.
Material and methods: "HIV-1 DNA Test PRO" standard curves were amplified to study its calibration functions. DNA from 16 blood samples collected from HIV+ patients were analyzed using both kits to check their correlation using the Pearson Coefficient with a 95% CI. Seventy-two PBMC samples of HIV+ patients (subtype group M) were evaluated using both qPCR tests to verify the analytical specificity. The "HIV-1 DNA Test PRO" robustness was obtained amplifying 3, 5, 10 and 20 µl of 6 HIV+ samples.
Results: Testing the "HIV-1 DNA Test PRO", efficiency and R2 of HIV standard curve were 99.1%±0.04 and 0.997 ±0.001 respectively, and for hTERT were 108.5%±0.03 and 0.997±0.002. Positive samples ranged from 24.6 to 555.0 HIV cps/106 cells by "HIV-1 DNA Test PRO" and from 16.7 to 982.0 HIV cps/106 cells by "HIV-1 DNA Test". The median [IQR] value was 121.2 [78.7-229.4] cps/106 cells and 169.7 [102.2-271.7] cps/106 cells, respectively. Pearson Coefficient was 0.863 (P<0.0001). DNAs of HIV+ PBMC samples were amplified. HIV-1 DNA quantification was similar by analyzing quantities ranging from 0.1 to 3.2 µg DNA/reaction.
Conclusions: "HIV-1 DNA Test PRO" showed good amplification performances ensuring reliable quantification in comparison with the validated "HIV-1 DNA Test". HIV DNA and hTERT co-amplification, testing different DNA quantities, has no side effect in HIV DNA quantification.

Management of HIV infection

P 145 INTESTINAL ALKALINE PHOSPHATASE LEVELS IN HIV INFECTED PATIENTS

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Introduction: Alkaline phosphatases (AP) are hydrolase enzymes that catalyze the breakdown of monophosphate esters by removing their phosphatic groups. AP are grouped into two classes: the tissue non-specific alkaline phosphatases (expressed in bone, liver and kidney) and the tissue specific enzymes such as placental alkaline phosphatase (PLAP) and intestinal alkaline phosphatase (IAP) 1.
IAP plays an essential role in intestinal homeostasis through interactions with the microbiota, diet and intestinal flora. In addition, it is a mucosal defense factor that limits bacterial translocation across the mucosal barrier into the mesenteric lymph nodes2.
IAP is expressed by enterocytes in the duodenum, jejunum, ileum and colon and it is absent in the stomach1,2.
The altered expression of IAP is implicated in many chronic inflammatory diseases such as IBD, celiac disease and obesity. The expression of the ALPI gene encoding IAP is reduced in inflamed tissues1.
HIV enteropathy is an enteric disorder characterized by diarrhea and malabsorption that occurs in advanced HIV infection. It may be due to direct and indirect effects of the virus on the enteric mucosa. It is characterized by villous atrophy, lymphocytic infiltration of the epithelium, hyperplasia of the crypts and absence of well-defined pathogens3.
Scientific rationale: The altered expression of IAP is implicated in several chronic inflammatory diseases that cause epithelial damage of enterocytes. HIV enteropathy may be mentioned in this category.
Aim of the study: The aim of this study is to evaluate IAP levels in HIV infected patients and the possible correlation with intestinal disorders.
Methods:
-Recruitment of HIV + subjects with intestinal disorders afferent to our clinic;
- study of IAP levels at time 0, 6 months, 12 months.
Expected outcomes: FAI levels could be indicative of enteropathy in HIV + subjects and be related to epithelial damage caused by direct and indirect effects of the virus.

Management of HIV infection

P 146 DIAGNOSTIC PERFORMANCE OF DIFFERENT SCREENING STRATEGIES FOR THE PREVENTION OF HPV-RELATED ANAL CANCER

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Background: Anal cancer is strongly related to anal HPV infection. HPV 16, 18 and few more high-risk genotypes (HR-HPV) account for almost all anal cancer cases. Although this neoplasm is rare among general population, the incidence in MSM and HIV+ MSM is as high as colon cancer and prostate cancer in seronegative men respectively. Guidelines indicate High Resolution Anoscopy (HRA) guided biopsies as the suitable screening method to identify anal potentially precancerous lesions (high grade-squamous intraepithelial lesion, HSIL), but this procedure requires a specific equipment, trained physicians and a long learning curve and its availability is limited to a small number of facilities.
Material and Methods: Results obtained from 60 MSM, that subsequently underwent anal cancer screening with the combination of anal HPV test, anal HPV genotype, anal cytology and HRA driven biopsies, were retrospectively evaluated. Histology findings were considered as gold standard to evaluate diagnostic performance of anal HPV test, anal HPV genotype and anal cytology, alone or in combination.
Results: 8 HIV- MSM and 52 HIV+ MSM were included in the analysis. Mean age of the population was 45 (IQR: 35 -53). Mean CD4 nadir of HIV+ participants was 209 cells/uL (IQR: 114-302) and mean CD4 count was 779 cells/uL (IQR: 562-900). All HIV+ subjects were on stable and effective antiretroviral treatment. Histology results showed squamous intraepithelial lesions of any grade in 88.4% of subjects, with an HSIL rate of 15.1%. No HSILs were found on cytology; on the other hand, low grade-squamous intraepithelial lesion (LSIL) or atypical squamous cells of undetermined significance were observed in 81.7% of participants. Anal HPV test was positive in 48 individuals (20 HR-HPV, 23 LR-HPV, 5 undefined). HPV 16 or 18 were found in 12 out of 20 HR-HPV isolates. ROC curve analysis showed that nor anal cytology, HPV test or HR-HPV identification alone are useful to identify patients harboring HSIL. By contrast, diagnostic performance of the combination of anal cytology and HR-HPV was consistent with HRA driven histology findings (p=0.029; AUC 0.803; SE 0.73; 95% CI 0.660-0.945).
Conclusions: Combination of anal cytology and HR-HPV test could be useful as a triage method in those settings where access to HRA is limited. HRA driven biopsies are still the reference method for HSIL diagnosis and should be performed in high risk patients. The identification of LR-HPV does not improve anal cancer screening strategies

Management of HIV infection

P 147 SYPHILIS IN NEWLY HIV-1 DIAGNOSED FROM 2010 TO 2019: A SINGLE CENTER REPORT

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Background: In the past decade in high income countries, incidence of syphilis and other Sexual Transmitted diseases (STD) are growing up expecially among men who have sex with men (MSM), particularly those with coexistent HIV infection. The aim of our study is to evaluate the proportion of syphilis in naive HIV patients diagnosed in the last ten years at the Infectious Disease Department of Foggia.
Methods: In this retrospective, observational study, we analyzed newly diagnosed HIV + individuals from 1 january 2010 to 31 december 2019 at the Infectious Desease Department of Foggia. We collect data about age, sex, nationality, route of HIV transmission, viro-immunological and clinical data. We performed odds ratio and chi-square analysis (with Yates correction) of following variables: nationality (foreigner/italian) ,age, heterosexual/MSM, HIV-RNA viral load; CD4 + cell count.
Results: 172 patients were enrolled: 136 (79,07%) men; 109 (63,37%) italians. 107/172 (62,20%) individuals aged <40 years. 74 (43%) individuals with CD4+ count < 200 cells/mL; 104 (60,5%) individuals with HIV-RNA >100.000 copies/mL. About the overall sample, 31 (18%) individuals had been a diagnosis of syphilis: 25/31 (80,6%) were co-infected at the time of HIV diagnosis, 6/31 (19.35%) got infection later. 4 patients had primary syphilis; 5 had secondary; 22 had latent infection. 25/31 (80,6%) had been treated with Long Acting Benzathine Penicillin G or Ceftriaxone or Doxicycline. Among these patients, 7 (22.5%) had reinfection from two to three times (all patients were MSM), carrying out several cycles of therapy. About route of HIV transmission patients with syphilis 24/31 (77,4%) were MSM, 7/31 (22.6%) heterosexual. Statistical analysis showed that MSM have a higher risk of infection/reinfection of 7 times than heterosexuals (p value< 0.00001; p< 0.05). Patients aged < 40 years (25/31) presented a higher infection risk of 3.05 times than newly HIV+ diagnosed aged > 40 years (p-value 0.029716, p< 0.05). Italian HIV-syphilis infected represented the majority compared to foreigners in our study population (respectively 27/31 VS 4/31) with a significant higher infection risk 8 times (p-value 0.024727, p < 0.05).
Conclusions: In our cohort, young (<40 years) Italian, MSM represented the major syphilis infection/reinfection risk group. In the "Undetectable = Untransmittable" (U=U #UequalsU) era, in this kind of population, sierological monitoring for STD and counseling has to be more frequent. A screening and testing risk population is mandatory to increase the number of diagnosed infections, which can lead to control transmission. Frequent screening are recommended in this population and expecially among MSM, which have an higher risk for syphilis infection.

Non infectious comorbidities in HIV

P 148 3TC+DTG VERSUS FTC/TAF PLUS AN INTEGRASE INHIBITOR: COMPARING CHANGES IN BONE MINERAL DENSITY

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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).

Methods: We analyzed a multicenter cohort of HIV-1 infected, virologically suppressed patients (pts) 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, vitamin D supplementation and smoking status whether or not significant at univariable analyses.

Results: We enrolled 53 pts, 20 in the DT group and 30 in the TAF group; thirty-five (58%) were males, with a median age of 54 years (IQR 48-63), a median time from HIV diagnosis of 17 years (IQR 7-23) and a median time of TDF-exposure of 68 months (IQR 25-116). At baseline, 42 pts (79% of our population) presented a pathologic BMD value: sixteen (27%) were diagnosed with osteoporosis at BL (8 in the DT group and 8 in the TAF group), while 26 (43%, 7 in DT and 19 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, pts in the DT group presented a significant improvement in spine BMD (+0.03 g/cm2, p=0.023), as well as in spine T-score (+0.30, p=0.027) and spine Z-score (+0.01, p=0.020). In this group we also registered an improvement in femur BMD, but it was not significant (+0.02 gr/cm2, p=0.064). In the TAF group, we recorded a significant improvement in femur BMD (+0.03 gr/cm2, p=0.014) and non-significant changes in spine BMD (-0.001 gr/cm2, p=0.476) after 48 weeks. At a multivariate analysis, no predictors of change were found.

In the TAF group, changes in femur BMD were significant in pts without osteoporosis (p=0.028), and not in osteoporotic ones (p=0.285), as well as in pts over 50 years of age (p=0.042) but not in younger pts (p=0.180).

Changes in spine BMD (p=0.029), spine T-score (p=0.035) and spine T-score (p=0.013) were significantly different between groups.

Conclusions: In our cohort, 3TC+DTG showed an overall favorable effect on BMD. TAF-based regimens led to an improvement in femur BMD, although only in a selected proportion of pts.

Non infectious comorbidities in HIV

P 149 HTA ANALYSIS OF GLATIRAMER AND NEUROPROTECTION IN HIV-RELATED COMORBIDITIES

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Background: The literature shows how the HIV virus correlates significantly with multiple sclerosis(MS) and can also be the cause of the onset of numerous neurological pathologies. In fact, it is confirmed by clinical data that antiretroviral therapies improve the outcome of MS. In this sense, glatiramer, which was widely used in the early days of MS, could promote neuroprotection and positively correlate with HIV related comorbidities. The growing demand for resources to ensure optimal levels of health care increasingly requires that the task of the NHS pharmacist must be to carry out a strict control of the prescriptive appropriateness in each therapeutic area. The inclusion of Glatiramer in the AIFA Transparency List allows automatic therapeutic substitutability and represents an important opportunity to contain healthcare costs.
Materials and methods: In USL Umbria 2 the data of the year 2018 and of the year 2019 were extrapolated to verify the prescriptive trend of the glatiramer and observe the trend of the expenditure generated after the placing on the market of the equivalent drug. In the Umbria region, the cost of the annual therapy of the originator drug was compared with that of the equivalent drug which allows a saving of 40.76%. On the basis of complete therapeutic equivalence, the possibility of immediately shifting all patients towards the use of the equivalent drug alone would make it possible to obtain significant savings that can be readily invested in other healthcare goods.
Results: In 2019, 37 patients were treated with glatiramer compared to 40 in 2018, generating an expense that was €219,482 in 2018 and €170,459 in 2019 with a reduction in spending of almost €50 thousand due both to the reduction in patients and both thanks to the phenomenon of drug generation. However, only 7 patients in 2019 have been directed towards the treatment with the equivalent drug generating a normalized saving between the two years of only 17%. The analysis shows how the overall enrollment of all patients present with the equivalent glatiramer would allow savings of 46.6% with a reduced expenditure of almost 80 thousand euros.
Comments: In recent years, chronic therapies, both in HIV and MS, have evolved considerably and the placing on the market of new high-cost drugs and the generation of some standard therapies require careful analysis of appropriateness so as not to generate waste and, at the same time, allow to free up resources to reinvest in innovation and ensure sustainability. The careful application of the principles of substitutability is synonymous with correct health governance that must actively involve clinicians and patients in order to ensure the sustainability of the NHS in an increasingly increasing healthcare spending context. The pathogenesis of MS has been linked to several viruses including HIV. Antiretroviral therapy assisted with that of MS with the use of glatiramer could coincidentally treat or prevent the progression of MS.

Non infectious comorbidities in HIV

P 150 LOW VITAMIN D CONCENTRATION IS ASSOCIATED WITH NAFLD AND METABOLIC SYNDROME IN HIV-1-INFECTED PATIENTS ON COMBINATION ANTIRETROVIRAL THERAPY

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Background: Vitamin D insufficiency was found to be associated with non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome (MetS) in the general population, but data among HIV-infected patients are lacking still today.
Patients and methods: A cross-sectional study was performed to investigate correlation between serum level of 25 (OH) vitamin D and presence of NAFLD and metabolic syndrome (MetS) in adult HIV-infected patients on stable antiretroviral therapy, with age>40 years, and with abdominal ultrasonography performed in the last 12 months. Vitamin D insufficiency was defined as serum level <30 ng/mL, NAFLD as liver steatosis involving >10% of hepatocytes without alcohol abuse, and MetS as the presence of >3 of the following criteria: waist circumference >80 cm (women) or 94 cm (men), triglycerides >150 mg/dL, HDL <50 mg/dL, blood pressure >130/85 mmHg, and glucose >100 mg/dL.
Results: On the whole, 412 patients were enrolled: 88% were men, 91% Caucasian, and the mean age was 49.2 years (range, 40-79). The mean CD4 T lymphocyte count was 588 cells/mm3, 176 (93.6%) had plasma HIV RNA <20 copies/mL, 54% were smoker, 18% had hypertension, 72% triglycerides >150 mg/dL, 67% HDL cholesterol <50 mg/dL, 32% BMI >25 Kg/m2, and the mean 10-year cardiovascular disease risk (by the 2013 ACC/AHA equation) was 8.4%. The mean serum concentration of vitamin D was 33.6 ng/mL, and 211 (51.2%) patients had a vitamin D insufficiency. NAFLD was reported in 147 (35.7%) subjects and MetS in 128 (31.1%). The mean vitamin D concentration was significantly lower among patients with NAFLD or MetS than among those without these conditions (NAFLD: 15.5 vs 38.2 ng/mL, p<0.001; MetS: 12.6 vs 37.8 ng/mL, p<0.001). In the multivariate linear regression analysis adjusted by confounding factors, vitamin D insufficiency was significantly associated with NAFLD (OR 2.55, 95% CI 1.88-3.49), MetS (OR 2.87, 95% CI 1.98-3.79), central obesity (OR 2.23, 95% CI 1.54-2.91), hypertension (OR 1.87, 95% CI 1.22-2.41), high triglycerides (OR 1.66, 95% CI 1.19-2.08), and low HDL cholesterol (OR 1.58, 95% CI 1.08-1.97). Moreover, the mean vitamin D concentration decreased with increasing number of MetS components (p=0.019).
Conclusions: In our study, HIV-infected patients with vitamin D insufficiency had a significantly higher risk of NAFLD and MetS than those with adequate levels, suggesting a central role of vitamin D in the pathogenesis of these metabolic disturbances.

Non infectious comorbidities in HIV

P 151 CARDIOVASCULAR DISEASE RISK MARKERS IN A SMALL COHORT OF HIV-INFETCTED PATIETNS SWITCHED FROM ABACAVIR/LAMIVUDINE/DOLUTEGRAVIR TO LAMIVUDINE PLUS DOLUTEGRAVIR

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Background: D:A:D cohort group linked the recent use of abacavir to an increased risk of cardiovascular events in 2008.However this correlation was not found in other more recent studies. Recently, we observed that the deintensification of highly active antiretroviral therapy (HAART) from ABC/3TC/DTG to 3TC/DTG effectively controls HIV-1 replication and does not induce any significant variations of total HIV-1 DNA content. The goal of this study was to verify whether abacavir removal might affect several markers of inflammation (IL-6), coagulation (D-Dimero) and lipid metabolism linked to cardiovascular disease.

Materials and Methods: Data of 17 HIV+ patients ,naive to HAART, were analyzed (12 men and 5 women). The plasma samples were collected before starting ABC/3TC/DGT (group 1),at the deintensification to lamivudine plus dolutegravir (after 12 months of viral suppression) (group 2)and after 12 months of dual antiretroviral therapy (group 3). IL-6, D-dimer and plasmatic lipids (total cholesterol, HDL, LDL, triglycerides) were analyzed in plasma samples with specific commercial kits. The data were evaluated by non-parametric statistical procedures (i.e. Wilcoxon test).

Results: No notable changes were observed when group 1 was compared with the group 2 and 3, respectively.For IL-6 group 1 had a mean 0.8+0.37 pg/ml, median 0.77 pg/ml; group 2 had a mean 0.96 +0.82 pg/ml; median 0.675 pg/ml and group 3 had a mean 0.90 + 0.69 pg/ml, median 0.84 pg/ml(group 1 vs 2 p=0.83; group 1 vs 3 p=0.65; group 2 vs 3 p=0.97.For D-dimer group 1 had a mean 209.3 + 33.4 ng/ml, median 221 ng/ml; group 2: mean 217.8 +34.9 ng/ml; median 232.5 ng/ml and group 3 a mean 220.7 + 20.64 ng/ml, median 229 ng/ml (group 1 vs 2 p=0.32; group 1 vs 3 p=0.38; group 2 vs 3 p=0.69).Regarding plasmatic total cholesterol, HDL, LDL, triglycerides the analyses of these data indicated that all these parameters did not show any significant variation (Total cholesterol: group 1 vs 2 p=0.07; group 1 vs 3 p=0.65; group 2 vs 3 p=0.41; HDL: group 1 vs 2 p=0.92; group 1 vs 3 p=0.88; group 2 vs 3 p=0.58; LDL: group 1 vs 2 p=0.09; group 1 vs 3 p=0.87; group 2 vs 3 p=0.36; Triglycerides: group 1 vs 2 p=0.57; group 1 vs 3 p=0.39; group 2 vs 3 p=0.93).

Conclusions: These results indicate that the switch from ABC/3TC/DTG to 3TC/DTG, did not significantly vary the levels of some inflammation markers and lipids in plasma samples in this small cohort of patients. Although abacavir has been linked to the increased risk of cardiovascular disease, these data show that abacavir is not able to affect the levels of these markers, as reported in recent studies. These observations suggest that the abacavir-mediated mechanisms inducing cardiovascular risk may be unrelated to the impairment of these markers.

Non infectious comorbidities in HIV

P 152 PREVALENCE AND INCIDENCE OF HEPATIC STEATOSIS IN SCOLTA COHORT

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Background: Hepatic steatosis (HS) prevalence and incidence are reported to be high in people living with HIV (PLWH). Treatment with Dolutegravir (DTG) has been recently associated with weight gain. Because of known effect of increased BMI on HS development, we aimed to evaluate the prevalence and incidence of HS in a cohort of PLWH on a DTG-containing regimen.

Methods: HS was defined as a Hepatic Steatosis Index [8×(ALT/AST ratio) + BMI (+2, if female; +2, if diabetes mellitus)] >36. Consecutive patients with HIV infection enrolled in SCOLTA project on a DTG containing regimen and backbone including TDF/FTC or TAF/FTC or 3TC/ABC or on dual treatment were included. Patients with hepatic infections were excluded, as well as those missing any variables needed to calculate HSI. Groups were compared using chi-square for categorical variables and uni- and multivariate analysis of variance for continuous variables. Prevalence was expressed as percentage (95% confidence interval, CI) and incidence as rate (events/100 patient years (PY), 95% CI).

Results: At baseline (T0), 545 PLWH were selected. They were mostly males (73.9%), Caucasian (88.8%) and on CDC stage A (55.4%). See Table 1 for patients' details at baseline. Prevalence of HS was 30.3% (95% CI 26.4-34.3%) and was associated with hypertension (p=0.0004) and partially with diabetes (P=0.08) . Apart from variables used to calculate HSI, hypertension, higher total cholesterol and triglycerides were associated with HS at baseline. 331 PLWH with HSI ≤36 at T0 had at least one follow-up visit; 245 (74.1%) were males and 298 were Caucasian (90.1%). See Table 1 for patients' details at baseline.

Over the follow-up period, 24 (7.3%, 95% CI 4.7-10.6%) developed HS (median observation 29 months, interquartile range 11-40), with an incidence rate of 3.28/100 PY (95% CI 2.15-4.80%). They were mostly males (9% vs 2.3% F, p=0.04), with hypertension (14.6% vs 6.2% without HT, p=0.05), and with BMI>25.0 at T0 (20.6% vs 3.5% BMI≤25.0, p<0.0001). They had also higher ALT at T0 (23 vs 19 U/L, p=0.04). There was no association with ART regimen, detectable HIV-VL, CDC stage, ethnicity and diabetes.

Conclusions: The prevalence of HS in this cohort of PLWH treated with DTG containing regimens is high and comparable with people with diabetes. Incidence was related to classical risk factor for HS. We need further studies to clarify if the antiretroviral treatment can play a role in the pathogenesis of HS in PLWH.

Non infectious comorbidities in HIV

P 153 FACTORS ASSOCIATED WITH IMMUNOSENESCENCE DURING EARLY ADULTHOOD IN HIV-INFECTED PATIENTS AFTER DURABLE EFFICIENT CART

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Background: Perinatally HIV-infected patients face the consequences of both chronic infection effects per se and long-term antiretroviral therapy (ART) on immunosenescence. Aims of our study were to evaluate which factors independently contribute to immunesenescence in HIV-infected young adults with a very different HIV infection duration (perinatally HIV-infected young individuals -pHIVy- and age-matched non perinatally HIV-infected youths –npHIVy), after a long period on efficient ART.

Methods: In this cross-sectional study we included all perinatally HIV-1-infected patients in active follow-up at our Department at December 2018 and a group of age-matched npHIVy with HIV infection duration >12 months. All patients were treated according to current guidelines for HIV management. We evaluated T-cell receptor excision circles (TRECs), K-deleting recombination excision circles (KRECs) and telomeres lenght (TL) as markers of immunosenescence. The associations between variables (including age, gender, years living with HIV, number of previous AIDS diagnosis, ART regimen, CD4+ and CD8+ cell counts and chronic viral coinfections as CMV) were assessed using linear regression univariate and multivariate models.

Results: We included 21 pHIVy and 19 age-matched npHIVy, sexually infected in the last 3-8 years prior to the enrollment in our study. Mean age was 27 years for both groups. All participants were receiving an efficient ART at the time of study, with plasmatic viremia <50 copies/mL. Mean duration of last period with HIV suppression before the enrollment in our study was 1533.6+1079.6 days for pHIVy and 1085.8+434 days for npHIVy. For pHIVy, total mean time without ART since birth was 3836.3 days (SD: 2783.5). npHIVy after initiating their first ART regimen never spent time without therapy. No differences between pHIVy and npHIVy were observed for CD4+ cells, CD4+/CD8+ ratio, TRECs number, KRECs number or TL levels. Only CD8+ percentage was significantly higher in pHIVy than in npHIVy (42% vs 33.9%, p = 0.015). CD4+ cell quartile increase (coef 4882.10; 95%CI 2061.7;7702.5) and CD4+/CD8+ quartile (coef 3174.0; 95%CI 249.6;6098.3) were associated with TRECs number. CD4+ quartile increase (coef 0.14; 95%CI 0.01;0.2) and CD4+/CD8+ quartile (coef 0.11; 95%CI 0.03;0.2) were also associated with TL, while no association where found for any variables and KRECs number. In particular, CMV chronic infection was not associated with TRECs, KRECs or TL. In adjusted models, only CD4+ quartile increase was associated with TRECs and TL (coef. 4829.1; 95%CI 1988.7;7669.5 and coef. 0.16; 95%CI 0.1;0.2, respectively).

Conclusions: pHIVy individuals on long-term successful ART show immune patterns similar to those of coetaneous patients infected with HIV during early adulthood, suggesting that a good level of thymic activity can compensate the deleterious effects of past periods without ART, if HIV replication is suppressed for a sufficient time.

Non infectious comorbidities in HIV

P 154 METABOLIC CHANGES IN HIV-INFECTED PATIENTS WHO CONTINUE A TWO-DRUG REGIMEN WITH DOLUTEGRAVIR PLUS ONE REVERSE TRANSCRIPTASE INHIBITOR OR SWITCH TO ELVITEGRAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR ALAFENAMIDE: A RANDOMIZED STUDY (BE-ONE STUDY)

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Background: Primary aim: to evaluate changes in metabolic parameters in virologically suppressed patients receiving 2 different integrase strand transfer inhibitor [InSTI]-based regimens (DTG+1RTI and E/C/F/TAF). The secondary objective was to evaluate changes in carotid ultrasound (CUS) in the 2 arms and correlations with metabolic changes.
Methods: Be-OnE (NCT03493568) is a randomized, single-center, open-label, 96-week study, primarily aimed at assessing residual viremia in virologically suppressed HIV-infected patients randomized to continue DTG+1RTI (lamivudine or rilpivirine) or to switch to E/C/F/TAF. Weight, BMI, abdominal circumference (AC), fasting HOMA-IR index, glucose, total (TC), LDL- (LDL-C) and HDL-cholesterol (HDL-C), TC/HDL-cholesterol (TC/HDL-C), triglycerides where measured at baseline (BL) and during follow up (96 weeks). Common carotid artery (CCA) intimal media thickness (IMT) and significant stenosis were measured by color-doppler ultrasonography at BL and at week 96. Patients withdrawn from the study before week 96 were not included in this analysis (per-protocol analysis). Comparisons within and between arms were performed by the Wilcoxon signed-rank test and the Mann-Whitney test or Fisher's exact test, respectively. Spearman correlation coefficients were used to assess linear relationship between continuous variables.
Results: This analysis considered 44/50 patients, enrolled in the study, who successfully completed 96-week follow-up, 22 randomized to switch to E/C/F/TAF and 22 to continue DTG+1RTI. Overall at BL 88% were males; medians age 51 years (IQR=43-55), CD4+ 743 cells/μL, HIV since 11.3 years with HIV-RNA<50 copies/mL since 6 years and on DTG+1RTI since 0.9 years. Trends in metabolic and sonography features are reported in figure. Significant differences between arms were observed for changes at week 96 from BL in TC (p=0.006) and LDL-C (p=0.002). No significant difference between arms was observed for changes in HDL-C, TC/HDL-C, triglycerides, glucose, HOMA-IR, weight, BMI, AC. However, a significant reduction in AC was observed in patients switched to E/C/F/TAF. No significant difference between arms was observed also comparing changes in CUS at week 96 from BL. Furthermore, we did not find any significant correlation between changes in CUS and changes in weight, BMI, AC, fasting HOMA-IR index, glucose, cholesterol profile and triglycerides.
Conclusions: Switching from DTG+lamivudine or rilpivirine to E/C/F/TAF resulted in a limited, but statistically significant increase in total and LDL-cholesterol and in a reduction in abdominal circumference; further study is necessary to define whether these increases are linked to TAF, to cobicistat or to the association of the two or to a different metabolic impact of the 2 InSTIs. We found no significant difference between arms for changes in other metabolic parameters or in CUS characteristics and no correlation between metabolic changes and CUS changes.

Non infectious comorbidities in HIV

P 155 A STRUCTURED SMOKING CESSATION INTERVENTION IN A SINGLE CENTRE IN PATIENTS LIVING WITH HIV

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Background: Due to effectiveness of antiretroviral therapy, HIV-related mortality has dramatically fallen. In this context smoking may have a severe effect on the quality of life of patients living with HIV (PLWHIV) so well treated PLWH may lose more life years through smoking than through HIV.
Design: Single-center cohort study assessing a comprehensive program of implementation the smoking cessation clinical practice guidelines in PLWHIV to assist patients who wanted to quit smoking by means active structured intervention.
Methods: From August 2019 to January 2020 a short active intervention (1'-2') was performed on all identified smokers, smoking habit data were collected by administering a questionnaire; the subjects who showed interest on it received a further intervention (3'-10') which then led, if they wanted to start this way, to the choice of the most appropriate intervention. The proposed intervention provides for counselling and prescription of Varenicline +/- nicotine replacement devices. The outcome evaluation was the smoking abstinence at 30 days. The degree of willingness to quit smoking (i.e. the stages of change) was assessed using the trans-theoretical model of Prochaska.
Results: A total of 653 patients are referred to our clinic in study time. We found 241 (36.8%) current smokers, 387 (59.2%) non-smokers and 25 patients in whom the data are unknown. Overall the mean age of smokers was 50±10.8 years, men were 75.5% and predominantly of Caucasian ethnicity (86.7%). The degree of study saw that 15% attended elementary or lower secondary school, 21.5% in high school and 5% graduated; the 28.6% are workers while 15% are unemployed. The average age at which patients started smoking is 17±5 years, the average length of time they smoked is 33±13.6 years and the average pack-years is 28±22.8.
The stages of change was evaluated in 47.3% of patients: 7.8% of patients have never considered quitting smoking, 30.7% are in the pre-contemplation phase, 18.4% are in contemplation, 22% are in the process of determining while 21% have reached the stage of action and have given consensus for an active intervention.
In the last group, consisting of the 24 patients who accepted the pharmacological intervention, the outcome (30 days smoking abstinence) was achieved in 9 patients (37.5%), 7 of whom also maintained at least 3-month abstinence. In 6 patients (25%), however, no interruption of habit occurred and 9 patients (37.5%) were lost to follow-up.
Conclusions: The comprehensive intervention performed on smoking cessation, containing counseling and pharmacological therapy, resulted in a outcome 30-day success in 37.9% of patients who accepted help to quit smoking. Our findings underscore the value of a comprehensive cessation intervention targeting PLWH in the HIV ambulatory. A repeated and constant intervention who stably improve clinical practice impact significantly the cessation intervention of the smoking habit.

Non infectious comorbidities in HIV

P 156 PHYSICAL ACTIVITY LEVELS IN HIV+ COHORT OF PAVIA

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Background: Since the arrival of highly active antiretroviral therapy (ART) the natural history of HIV infection is dramatically changed and people living with HIV (PLWH) can enjoy longer and healthier lives.
Currently, the management of the comorbidities and age-associated chronic conditions, as cardiovascular diseases (CVD), is one the main topic in the PLWH caring. It is essential to act on modifiable risk factors, as smoking, unhealthy diet and sedentary lifestyle.
The effects of physical activity (PA) on reducing diabetes, hypertension, obesity, and CVD events are indisputable, both in PLWH and in general population.
This study looks to assess the level of PA self-reported among all the HIV patients of Pavia cohort and to examine the factors associated with different level of PA, in order to be able to attend a behavior correction intervention and, therefore, to improve the patient's health and life expectancy.
Material and methods: A cross sectional study started from February 2020. All the HIV+ patients afferent to the Infectious Diseases outpatient clinic for scheduled control were consequentially enrolled. Exclusion criteria were being < 18 years old, ART starting less than 6 months, physical impossibility to make PA.
The short form of International Physical Activity Questionnaire (IPAQ) was administered to assess self-reported level of physical activity of the participants and all the following date were collected: CD4 cell count and HIV-RNA, BMI, gender, age, triglycerides, HDL cholesterol, smoking habits, comorbidities (hypertension, cardiac diseases, diabetes, dyslipidemia, IRC, liver diseases) and ART treatment.
Results: Here we reported the results of the first 100 recruited patients. The median age of patients was 52 years, 80% were males, the mean CD4+ T cells count was 726/ul, 92% of the patients was virological suppressed. The mean BMI was 25,85, triglycerides were > 150 mg/dl in 36 patients and HDL cholesterol was < 50 in 47, a total of 40 patients had dyslipidemia and 21% presented diabetes or impaired fasting glucose. According to the IPAQ scoring protocol, the questionnaire analysis showed the following results: 26% of patients were inactive, 32% reported moderate PA and 42 % high level of PA. Through statistical analysis none correlation was pointed out between different level of PA and different antiretroviral regimes (with or without integrase inhibitors) or the presence of comorbidities.
Conclusions: Identification of modifiable risk factors is a main topic in PLWH management. The analysis of the first 100 patients enrolled of our study showed a self-reported inactivity in 26% of the patients, and adequate level of PA in 64%, comparable to available data on general population. It will be interesting observe if preliminary data of our study will be confirmed or not by next recruitment in the following months.

Non infectious comorbidities in HIV

P 157 MACHINE LEARNING VS KNOWLEDGE BASED APPROACH IN HEALTH OUTCOMES' PREDICTION IN HIV

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Background: WHO suggests to measure healthy aging through intrinsic capacity (IC) that explores 5 health domains: locomotion, vitality, sensory, cognition and psychosocial factors. However, such a tool does not exist, encountering the difficulty in analysing large pool of IC variables collected in daily living. Machine learning overperforms traditional data analysis approach due to the ability to extract knowledge from voluminous raw data. We aimed to compare a knowledge based and a machine learning approach to build an IC index in the prediction of quality of life (QoL) and functional ability in older adults living with HIV (OALWH) enrolled in a multi-centre prospective study (MySAwH).

Methods: My Smart Age with HIV (MySAwH) aims to empower OALWH to achieve healthy aging. A mobile application (MySAwH app) integrates patient-related outcomes randomly collected twice a week and daily physical function data assessing steps count and sleeping hours using a smartwatch. Outcome measures were QoL assessed with EQ-5D-5L and functional ability assessed with short performance physical battery (SPPB) at 9-months follow up.

IC derived from a knowledge based approach (IC-KB) that aggregated 27 health variables through a conceptual association with IC domains. Monthly generated IC-KB was used to test association with outcome measures.

IC-machine learning (IC-ML) derived from artificial intelligence algorithms, fed with 131 700 items, together with the a SHAP (SHapley Additive exPlanations) method to interpret predictions. This allowed to identify cut-off values and customize positive and negative contribution of each variable to outcomes through a tuning approach. Performance of IC-KB and IC-ML of outcomes' prediction was assessed by mean error discrimination after correction for baseline variables.

Results: We analysed 261 OALWH from Italy (128), Australia (100) and Hong Kong (33). Mean age was 56.9 years; 88% were men. Median CD4 was 657 c/μL (480-817 IQR) and 98% had undetectable HIV RNA. Median QoL at 9-months follow-up was 0.90 (0.83-1 IQR), impaired SPPB (≤10) was observed in 54 (21%) patients at follow-up. The mean error of predictive performance of IC-KB and IC-ML for impaired QoL was 10 and 4.5% respectively and for impaired SPPB was 9.3 and 5%.

Conclusions: IC-ML better than IC-KB predicts QoL and physical function in OALWH. Machine learning suits a precision medicine approach to depict domains which contribute to relevant health outcomes.

Non infectious comorbidities in HIV

P 158 USE OF TWO DRUGS REGIMENS (2DR) IN A COHORT OF HIV-INFECTED GERIATRIC PATIENTS (GEPPO COHORT)

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Background: Two drugs regimens (2DR) doultegravir-based have a high genetic barrier to HIV resistance and are an intriguing antiretroviral therapy in elder HIV population with a high rate of polypharmacy (PP) and multi-morbidity (MM). The aim of the study is to assess the use of 2 DR in a cohort of people living with HIV (PLWH) more than 65 years old (GEPPO cohort).

Materials and methods: Multicenter, non-interventional, observational, retrospective, single arm study of geriatric PLWH. We enrolled patients in antiretroviral therapy and we considered the last registered HIVRNA.

Patients' characteristics were described by median (quartiles) or frequency (%). Antiretroviral regimens were compared by Mann-Whitney test or chi-square test. Multimorbidity (MM) was defined as the presence of at least three comorbidities; polypharmacy (PP) was defined as the use of at least five drugs

Results: 1721 HIV-positive patients aged more than 65 years old were included in GEPPO cohort, 246 (14%) in 2DR. In Table 1 we show demographic, immunovirological, comorbidities and concomitant drugs characteristics of patients treated with dual DTG and other ART regimens. MM was less present in patients receiving 2DR regimens in respect of other regimens ($p<0.001$) while PP was similar in the two groups. Interestingly, viral load was undetectable (HIV <50 copies(ml)) in 210 (88.2%) patients in dual DTG vs 42 (93.3%) patients in other (p-value = 0.315).

Dual DTG were NNRTI+DTG in 69 (28%), 3TC+ DTG in 105 (42.7%) and PI+DTG in 21 (8.5%).

We tested the association between time to deprescription of 2DR and being in MM and PP depending on the year of deprescription. We saw a significant increase of the risk of deprescription (HR 4.42, CI 1.02-19.04, p=0.046) of 2DR for subject with both MM and PP during the first years of follow up (2015-2017) and an increased probability of deprescription during the last years of follow-up (2018-2019) (HR 7.41, CI 160-34.46 p=0.011).

Conclusions: Presence of both MM and PP in a strong driver of 2DR. Moreover the increased habitude to deprescription to 2DR in 2018-2019 could be related to the overall convenience of this choice. Therefore, not only patients with MM and PP could receive this innovative strategy. 2DR could save options and toxicity in patients with long ARV experience regardless of MM and PP. Clinician seem to be confident with 2DR as deprescription strategy and as pre-emptive switch also in patients not viro-suppressed.

Non infectious comorbidities in HIV

P 159 POOR CONCORDANCE BETWEEN LIVER STIFFNESS AND NON-INVASIVE FIBROSIS SCORES IN HIV-1 MONOINFECTED VIROLOGICALLY SUPPRESSED PATIENTS

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Background: Severe liver fibrosis (LF) is associated with poor long-term liver-related outcomes and mortality and people living with HIV (PLWH) are at higher risk of multifactorial liver damage than HIV- people. The study aimed to describe liver fibrosis in PLWH, to explore the concordance of fibrosis estimated by different non-invasive methods and to investigate its predictors.

Material and methods: In this multicentric cross-sectional study we enrolled HIV-1 monoinfected patients with HIV-RNA (VL)<50 cps/mL for >12 months referred to two tertiary care hospitals in central and northern Italy. Pts with viral hepatitis and alcohol abuse were excluded. At baseline liver fibrosis was contemporary assessed by Transient Elastography (TE) (significant >6.65 kPa), Fibrosis-4 (FIB-4) (low and high cut-offs <1.30 and >2.67) and AST to Platelet Ratio Index (APRI) (low and high cut-offs <0.5 and >1.5). The correlation between TE/FIB-4 and TE/APRI, was evaluated by non-parametric Spearman correlation and kappa statistic. Predictors of liver fibrosis were analyzed by linear regression models.

Results: We included 154 pts: 109 males (79.8%), with a median age of 51 years (IQR 41-57), 56 pts (43%) reported alcohol consumption (<2 unit/day). 43 (28%) were HbcAb positive, 13 (8%) had diabetes and qualitative ultrasound steatosis was documented in 48 pts (31%). The median time of HIV infection was 13 years (IQR 7-20.25), at baseline 55 (48%) were on treatment with INSTI-based antiretroviral regimens and 41 (27%) pts were on dual or mono-therapy. At TE 30 (19%) had ≥F2, stage, FIB-4 score was >1.5 in 17 (13%) and APRI >0.5 in 9 (6%). The baseline characteristics of the population are summarized in table. At the multivariate analysis, a higher BMI (per 1 unit more, mean change +0.10, 95% CI 0.02-0.18, p=0.02), diabetes (+1.67, 0.37-2.97, p=0.01), VL detectable (vs undetectable +0,97, 0.31-1.63, p<0.01), ALT levels (per 1 unit more, +0.03, 0.01-0.05, p<0.01), dual or mono-therapy (vs 3-drugs ART +1.15, 0.26-1.80, p=0.01) and atazanavir exposure (+1.35, 0.45-2.25, p<0.01) were associated with higher liver stiffness at TE. Factors associated with higher APRI score were CDC stage C (+0.084; 0.05-0.12, p<0.01), DDC exposure (+0.17; 0.00-0.34; p=0.045), while EFV exposure resulted a protective factor (-0.09; -1.80/- 0.01, p=0.04). The CDC stage C was the only predictor of higher FIB4 scores (+0.15, 0.06 - 0.24, p<0.001), adjusting for confounders factor. Qualitative agreement was poor between FIB-4 and TE (r= 0.06 and k=0.04), APRI and TE (r=0.16 and k= 0.08)

Conclusions: In our study in PLWH without viral hepatitis different non-invasive methods were discordant to predict liver fibrosis. A better understanding of liver disease beyond viral hepatitis coinfection is needed in PLWH and early detection of liver fibrosis is extremely important.

Non infectious comorbidities in HIV

P 160 OBESITY AND OVERWEIGHT AMONG PEOPLE LIVING WITH HIV IN THE PROVINCE OF PAVIA: A CROSS-SECTIONAL STUDY

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Introduction: HIV infection is historically associated with weight loss and wasting. As the life expectancy of people living with HIV has matched that of the general population, weight gain and obesity are increasingly being observed in the HIV population. Overweight is defined as having a Body Mass Index (BMI) greater than or equal to 25.0 kg/m2 and lower than 30.0. Obesity, on the other hand, is defined as a BMI greater than or equal to 30.0. Obesity is further divided in three classes: Class 1 if BMI is 30.0 to <35.0. Class 2 if BMI is 35.0 to <40.0. Class 3 if BMI is equal to or greater than 40.0. A recent survey showed that, in 2015, over one third of the adult Italian population was overweight (35,3%), while one tenth was obese (9,8%). Weight excess is a relevant public health problem and has been linked with a heightened risk of several debilitating diseases, such as type 2 diabetes, coronary heart disease and cancer, and all-cause mortality. We describe the prevalence rate of overweight and obesity in a cohort of HIV-infected adults attending our outpatient clinic.

Materials and methods: We collected data on weight, height, sex, CD4+ count, HIV viral load and current antiretroviral therapy regimen in a cohort of 100 HIV patients, starting from February 2020. We then calculated the BMI and applied the cut-offs to assess overweight and obesity. Exclusion criteria were age less than 18, HIV infection diagnosis made less than 6 months before and pregnancy.

Results: One-hundred HIV-patients were enrolled for the study. 80 (80%) patients were male, median age was 65,5 years, 75 (75%) patients had CD4+≥500 cell/mm3, with a median CD4+ count of 727 cell/mm3, 92 (92%) had undetectable viral loads. 61 of all patients (61%) are currently receiving an integrase inhibitor (InI)-containing antiretroviral regimen. Median weight and height were respectively 77,3 kgs and 172,36 cm. 44 (44%) patients had normal weight, 34 (34%) were overweight, 17 (17%) had grade 1 obesity, 3 (3%) had grade 2 obesity; only 2 (2%) patients were underweight, while no patient had grade 3 obesity. Of the 80 male patients, 33 (41,25%) patients had normal weight, 29 (36,25%) were overweight, 17 (18,75%) had grade 1 obesity, and 3 (3,75%) had grade 2 obesity. Of the 20 female patients, 11 (55,00%) patients had normal weight, 5 (25,00%) were overweight, 2 (10%) had grade 1 obesity, and 2 (10,00%) were underweight.

Conclusions: The prevalence rate of overweight in our HIV cohort, especially in male patients, is comparable to that of the general population, while the prevalence of obesity is fairly higher in our cohort compared to the general population. Further data is required to identify the risk factors associated with weight gain in HIV patients and formulate appropriate interventions. Enrollment for this study will continue in the following months

Non infectious comorbidities in HIV

P 161 EVALUATION OF RESTING ENERGY EXPENDITURE AND BODY MASS COMPOSITION IN A COHORT OF HIV INFECTED PATIENTS ON ANTIRETROVIRAL TREATMENT

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Background: There is a growing evidence that use of new antiretroviral (ARV) treatments may lead to a statistically increase of body weight and even clinical obesy. Intake of integrase inhibitors (INI), in particular dolutegravir (DTG) and tenofovir alafenamide (TAF) seem to be the main responsible of this phenomenon.
Here we report the experience of an outpatient clinic aimed to start a dietary intervention in a cohort of HIV infected patients (pts) with overweight or obesity. At baseline resting energy expenditure (REE) and body mass composition (BMC) of the pts were studied.
Materials and methods: from April 2019 to January 2020,HIV infected pts followed up at at San Gerardo Hospital in Monza were referred to a nutritional intervention according to the presence of a BMI>25. At the first visit anthropometric data (weight, height, waist circumference) were collected, REE was measured by indirect calorimetry (Cosmed Fitmate Canopy) and BMC by bioimpedance analyser (Bodystat model).
Results: 32 patients were studied; 24 pts performed an indirect calorimetry and 27 a bioimpedance analysis. Patients' characteristics are shown in table 1. No signs of lipodistrophy were observed in the whole population. 31/32 practised a mild physical activity. At indirect calorimetry, 17/24 pts (11 on INI, 4 on NNRTIs, 2 on PIs) showed a normal, 3/24 pts (2 on INI, 1 on NNRTIs) a slow and 4/24 pts (3 on INI, 0 on NNRTIs, 1 on PIs) a fast REE, (chi squared among the 3 different classes: p= 0.73) compared to the general population.
Patients were grouped according to the intake of TAF, INI (DTG, EVG/cobi, RAL), NNRTIs and PIs; data are shown in table 2.
In a subanalysis which considered the third drug, we found that 13 pts out of 19 got a weight gain >10% along a mean time of 47 months (p=0.36): 7/13 were on INI, 4/13 on NNRTIs, 2/13 on PIs (p=0.41). REE of these 13 pts was normal in 7, slow in 2 and fast in 1 pt (p=0.52).
Pts on TAF as backbone drug, were analysed according to the achievement or not of a weight gain >10%(data are reported in table3).13 out of 19 pts on TAF got a weight gain>10% over time. On DTG a Weight gain > 10% was achieved in 3/11 pts.
Conclusions: From the analised data we can conclude that there is no significant difference in body composition and resting metabolism among pts taking different classes of ARV drugs. REE of pts on ARV treatment is comparable to the general population's one. We observed a weight gain > 10% in 2/3 of pts on TAF along time. On the contrary, no significant weight gain was observed according to the intake of a different third drug. In particular there was no significant weight gain > 10% with intake of INI class, which is actually targeted as one of the main responsibles of this phenomenon. Differently on what suspected, pts on DTG showed a significant increase of fat free mass index and as a consequence, an increase of REE, although that was not statistically significant

Non infectious comorbidities in HIV

P 162 ARCHI-PREVALEAT PROJECT. A NATIONAL REGISTER OF COLOR-DOPPLER ULTRASONOGRAPHY OF THE EPI-AORTIC VESSELS IN PATIENTS LIVING WITH HIV

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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 273 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 >1 has been 22,6% at left carotid bulb,13.6% at right carotid bulb, 17.3 % at left carotid and 11.7% at right carotid (Fig.A). In our preliminary data IMT appears, as expected, associated above all to higher lipids levels, to CDC C stage and to adoption of PI-based regimens.(Fig. B)

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 to extend the investigation to all patients, to proactively prevent CVD, that, in association to aging, inflammation and dyslipidemia, will have a negative impact on good prognosis conquered by the advent of safer antiretroviral drugs.

Pediatric, adolescent, maternal, fetal aspects

P 163 RETHINKING THE NECESSITY OF INTRAPARTUM ZIDOVUDINE ADMINISTRATION. A SMALL CASE SERIES FROM A SINGLE CENTRE IN THE NORTH OF ITALY

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Background: Intrapartum intravenous zidovudine (ZDV) in no longer necessary for pregnant women undergoing antiretroviral therapy (ART) with stable undetectable HIV RNA (≤50 copies/ml) through the late stages of pregnancy and near delivery, although current guidelines do not achieve a strong level of recommendation (BII).
Patients and methods: In February 2018, a multidisciplinary team of a large tertiary acute-care teaching hospital, developed an internal guideline for the management of HIV infected women during pregnancy. Patients were stratified into three categories, with different mother-to-child transmission (MTCT) risk profiles. Risk stratification was made upon the timing of HIV diagnosis, CD4+ cell count, HIV-RNA load over the last four weeks of pregnancy, adherence to ART and follow-up controls, socio-economic context, number of pregnancies and previous C-section deliveries.
Women with uncomplicated pregnancies, known HIV status at time of pregnancy, undergoing effective ART, with stable undetectable HIV-RNA (≤ 50 copies/ml) and CD4+ cell count > 200/mmc for at least four weeks before delivery were considered as low risk. Administration of intravenous pre- and intrapartum ZDV was not recommended in this setting.
Results: Since the guideline's implementation 11 pregnant women were followed-up by our Hospital until the end of pregnancy (Table 1). All patients were classified as low risk for MTCT; 10 of them did not receive pre- and intrapartum ZDV prophylaxis, while 1 did. Infants received post-exposure prophylaxis (PEP) with ZDV for four weeks as recommended by international guidelines. None of them tested positive for HIV infection. Only one patient received intrapartum ZDV despite being classified as low risk for MTCT. Reasons for administering ZDV prophylaxis were obstetrical risk factors secondary to numerous surgical interventions for vaginal and anal condylomas.
Conclusions: In light of U=U concept, no pregnant HIV infected women should receive ZDV prophylaxis if undergoing ART and with stable HIV-RNA suppression, especially if no obstetrical risk factor is present. The possibility of not having to undergo any unnecessary medical procedure during pregnancy is going to represent a further reduction in HIV related stigma, therefore improving maternal health and encouraging rapid HIV testing while planning pregnancy.

Pharmacology, pharmacogenomics and drug interactions

P 164 ANTIVIRAL ACTIVITY OF 1-(41-CHLOROPHENYL)-4-(42-METHYLPHENYL)-5,6,7,8-TETRAHYDRO-2A,4A-DIAZACYCLOPENTA[CD]AZULENE-2-CARBOXYLIC ACID DERIVATIVES

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Background: The H1N1 virus strain, which is influenza A virus subtype, caused the epidemic of Spanish flu in 1918, became the reason of influenza outbreak in 2005-2006 and 2009-2010 seasons. According to the data of the Ministry of Health of Ukraine, just only within the period of influenza and acute respiratory viral infections epidemic (as from October 2009 until May 2010) more than 7,7 millions of people or 16,87% of population contracted the disease in Ukraine. The level of hospitalization in children during influenza epidemic is significantly higher (84%-93%) than in adults. According to the evaluation of the WHO's experts the pandemic of 2009/2010 years led to the death of more than 500 thousands people. During this period, 1128 of those lethal cases were registered in Ukraine. Over 80% deaths from influenza were registered in age category 18-50 years, which characterizes Californian strain.

Material and Methods: Determination of the antiviral activity of 1-(41-chlorophenyl)-4-(42-methylphenyl)-5,6,7,8-tetrahydro-2a,4a-diazacyclopenta[cd]azulene-2-carboxylic acid derivatives was performed at the Southern Research Institute (SRI, Birmingham, Alabama). The efficacy of this compound was expressed by EC50, IC50 and SI, which was determined in vitro by the action of compounds previously dissolved in DMSO at a concentration range of 0.1 to 100 µg / ml. Ribavirin antiviral agent and the active substance Amizon - 4-(N-benzyl)aminocarbonyl-1-methylpyridinium iodide were used as the standard for action.

Results: Antiviral activity of amide (43-methoxyphenyl)-1-(41-chlorophenyl)-4-(42-methylphenyl)-5,6,7,8-tetrahydro-2a,4a-diazacyclopenta[cd]azulene-2-carboxylic acid (I) against Flu A H1N1 California/07/2009, is observed in dose 2.56 times lower, compared to Ribavirin and in 13.8 times lower compared to Amizon. Selectivity index of the researched compound is SI>29 in IC50 >100 mkg/ml. At the same time, selectivity index of compared compound is SI>37 in IC50 >320 mkg/ml. It should be noted, that if IC50 for those two compounds was the same, then SI for amide (I) would be three times higher and would be equal to SI>92.8.

Conclusions: A series of new 1-(41-chlorophenyl)-4-(42-methylphenyl)-5,6,7,8-tetrahydro-2a,4a-diazacyclopenta[cd] azulene-2-carboxylic acid arylamides have been synthesized. The high level of the antiviral activity for amide (43-methoxyphenyl)-1-(41-chlorophenyl)-4-(42-methylphenyl)-5,6,7,8-tetrahydro-2a,4a-diazacyclopenta[cd]azulene-2-carboxylic acid against Flu A H1N1 California/ 07/2009 virus strain (Southern American Research Institute, Birmingham, Alabama) has been found.

Pharmacology, pharmacogenomics and drug interactions

P 165 ANTIVIRAL ACTIVITY OF OF 6-(4-METHYLBENZYL)-3-ARYLAMINO-4H-[1,2,4]TRIAZIN-5-ONE DERIVATIVES AGAINST YELLOW FEVER

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Background: Yellow Fever is an acute arbovirus natural-focal disease from the group of haemorrhagic fever. It is an endemic disease because it is widespread in countries with tropical and subtropical climates with more than 900 million inhabitants. Extensive preventive and anti-epidemic measures, including vaccination, regulate the incidence of the disease. According to the World Health Organization (WHO), there are an estimated 200,000 cases of Yellow Fever each year, 30,000 of which end in death. In general, up to 50% of people who have developed severe form die. The Yellow Fever outbreak in Angola was stopped in 2016 due to active vaccination of the population (over 15 million people). During this period, 3818 cases and 369 deaths were reported.
Material and Methods: Determination of the antiviral activity of 6-(41-methylbenzyl)-3-arylamino-4H-[1,2,4]triazin-5-one derivatives was performed at the Southern Research Institute (SRI, Birmingham, Alabama). The efficacy of this compound was expressed by EC50, IC50 and SI, which was determined in vitro by the action of compounds previously dissolved in DMSO at a concentration range of 0.1 to 100 µg / ml. Infergen_x000 B_(Interferon Alphacon) was used as the standard for action.
Results: It was found that compounds with substituents in the third position of the arylamino group of 6-(41-methylbenzyl) -3-arylamino-4H-[1,2,4]triazin-5-one derivatives are more active than compounds with substituents in the second or fourth positions of the heterocyclic system **более активны**. For 6-(41-methylbenzyl)-(32-fluorophenyl)amino-4H-[1,2,4]triazin-5-one EC50=0.88 µg/ml and IC50=330 µg/ml at SI=380. For 6-(41-met¬hylbenzyl)-(42-fluorophenyl)amino-4H-[1,2,4] triazin-5-one EC50=4.3 and IC50=120 µg/ml at SI=28. For 6-(41-methylbenzyl)-(22-fluorophenyl)amino-4H-[1,2,4]triazin -5-one EC50=5.4 µg/ml and IC50=110 µg/ml at SI=20. For 6-(41-methylbenzyl)-(32-methylphenyl)amino-4H-[1,2,4]triazin -5-one EC50=0.48 µg/ml and IC50=230 µg/ml at SI=480. The base structure 6-(41-methylbenzyl)-3-phenylamino-4H-[1,2,4]triazin-5-one shows EC50=6.2 µg/ml and IC50=130 µg/ml at SI=20.
Conclusions: A series of new 6-(41-methylbenzyl)-3-arylamino-4H-[1,2,4]triazin-5-one derivatives have been synthesized. The high level of the antiviral activity for 6-(41-methylbenzyl)-3-(32-methylphenyl)amino-4H-[1,2,4]triazin-5-one and 6-(41-methylbenzyl)-3-(32-fluorophenyl) amino-4H-[1,2,4]triazin-5-one against Yellow Fever virus strain (Southern American Research In-stitute, Birmingham, Alabama) has been found.

Pharmacology, pharmacogenomics and drug interactions

P 166 DOLUTEGRAVIR, EMTRICITABINE/TENOFOVIR ALAFENAMIDE FUMARATE ABSORPTION IN A GASTRECTOMIZED HIV-POSITIVE PATIENT

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Background: the absorption of orally delivered antiretroviral (ARV) drugs depends on several factors such as gastrointestinal motility and gastric pH [1]. Limited data are available in literature about the absorption of ARV agents, when gastric surface is widely reduced because of gastric surgery as gastrectomy [2].
Thus, aim of our study was to investigate Dolutegravir (DTG)+Emtricitabine/Tenofovir alafenamide fumarate (F/TAF) plasma exposure in a gastrectomized HIV-patient due to gastric adenocarcinoma.
Material and methods: we report a case of a 59-year-old HIV positive man followed in our Outpatient Clinic since 1989, with a good immunovirological profile (CD4+ T cells : 889/mcl; 35.5%, ratio 0.8; HIV-RNA undetectable). He was affected by an infiltrative and ulcerated adenocarcinoma of the stomach and for this reason switched to DTG+F/TAF due to lack of drug-drug interactions (DDIs) with chemotherapy. The patient underwent a 4/5 gastrectomy with consequent total parenteral nutrition and parenteral medication for few days and nasogastric tube positioned for about a week. Ten days after nasogastric tube removal, with natural resumption of feeding and oral intake of antiretroviral therapy, the patient was monitored with determination of 12 hours-plasmatic DTG(plDTG), FTC (plFTC), tenofovir (plTFV) and TAF (plTAF) concentrations (C12) using mass spectrometry (UHPLC-MS/MS) FDA and EMA validated method.
Results: plDTG, plFTC, plTFV and plTAF C12 resulted to be respectively 3051 ng/mL, 210 ng/mL, 5 ng/mL and 1 ng/mL, comparable to those reported in literature [3-5]. No other comorbidities were reported: normal liver function, BMI 25 kg/m2 and normal renal function (eGFR:97.8 mL/min/1.73 m^2 according to CKD-EPI calculator). Moreover, no potential DDIs between ARVs and his concomitant medication (Rosuvastatin, Ramipril, Aspirin, Bisoprolol) were observed. After one month, viral load was still undetectable with good tolerability of ARV regimen.
Conclusions: In patients with gastrectomy, ARVs absorption could be unpredictable. This is the first DTG and F/TAF evaluation of in the context of gastrectomy due to an oncological disease. ARVs plasma exposure was adequate to maintain an immunovirological response. More data are needed to better investigate other ARV regimens recently available in combined fixed dose, not only in the oncological setting, but also in other conditions affecting gastric absorption (i.e. bariatric surgery).

Social and behavioural science, marginalized groups, community aspects and community surveys

P 167 A SURVEY AS A CHANCE OF EDUCATION ON U=U IN ITALIAN GENERAL POPULATION

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Background: Launched in 2016, the U=U slogan has been endorsed by many HIV organisations worldwide, including IAS and UNAIDS.
Up until the end of December 2019, in the scientific literature there is only one Italian study into U=U and its impact on PLWHIV on a national basis: the survey we presented at the Italian National Conference on AIDS 2019, which received the prize for best in social sciences paper.
The aim of the research is to examine the knowledge of U=U, its meaning and its possible effects on the general Italian population; the survey administration itself is intended as a chance to inform people about U=U, and so stimulate responders to seek further information about this issue.
Methods: An anonymous questionnaire had been administered to presenters at HIV rapid testing in the main square in Torino (on 1st December 2019).
The questionnaire is composed by 21 questions; yes/no, multiple choice and open answers. It starts with general data such as age, education, gender and sexual orientation.
Part two consists of 4 items about testing; part three consists of 5 items about knowledge/perception of HIV transmission and prevention; part four consists of 2 items about U=U knowledge: do you know the meaning of "U=U"? And do you know that a PLWHIV, on ART and with constantly undetectable viral load, does not infect another person through sexual intercourses without condom?
During pre-test counselling the presenters receive information about U=U.
Another anonymous questionnaire is administered online, published on the Arcobaleno AIDS ODV web and Facebook pages, on other community web pages, and on other relevant web pages from 10 january to 10 april 2020.
The questionnaire comprises 10 questions: yes/no, multiple choice and open answers.
It starts with general data such as age, education, gender and sexual orientation, serostatus. Question eight is about HIV transmission; question nine concerns awarness of the "U=U" slogan; question ten regards knowledge of the significance of U=U. All responders are Italians or Italian speakers.
Results: Up until 09/01/2020, 146 questionnaires have been completed. We cannot estimate the number of responders to the online questionnaire (260 until today).
Conclusions: Unknown up to 09/01/2020, as the study is ongoing.

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P 168 DEVELOPMENT AND MANAGEMENT OF A WEB-BASED SYSTEM ABLE TO COLLECT AND ANALYSE DATA ABOUT SELF-DIAGNOSTICS HIV TEST - ULISSE

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The availability in the Italian Pharmacies of an HIV self-test which, in full respect of privacy, attracted the attention of many people who perhaps would never have taken into consideration to be tested. The Pharmacy has proved to be the most suitable health structure because it is widespread and capable of communicating every day with its 4 million users of the pharmaceutical service and establish a relationship of trust. The self-test is a very useful tool, which everyone can buy in the Pharmacy, with their general practitioner, with a trusted person or even alone.
The amount and usefulness of the data and information that we are risking to lose is enormous, especially given the numbers that the self-diagnostic test is recording. It is therefore necessary to develop a stem that is easy to consult and that in full respect of anonymity and privacy is able to collect this data and make it available to the scientific community. In this sense, the project aims to evaluate the impact and spread of the self-test available in the Pharmacy and to involve pharmacies more with a Corporate Social Responsibility project.
The project's overall goal is to collect data and information on self-diagnostic HIV tests that are not currently recorded. In addition, the almost total lack of support from the citizen who decide to use of the auto-test.
The goals of the project:
1. Creation of a network of Italian Pharmacies that, once sensitized on the importance of the project and the collection of data, host a desk display containing postcards with all the information for the customer who has used or will use the test
2. Development of a website in 5 languages (Italian, English, French, Spanish and Chinese) hosting a simple method of data collection used by the test user (eg. Gender, age, geographical area, last test offered and outcome)
3. Set-up of an help-line to provide the pre and post test counselling to all subjects who will carry out the self-diagnostic test of HIV
4. Development of information materials to promote the project: desk display, postcards with all the information on the project and the importance of entering data on the web platform
5. Organization of an awareness campaign to stress the importance of the project
Ongoing results
1. Creation of a network of 150 pharmacies. Over 15.000 postcards distributed
2. Development of the website www.autotesthiv.eu:
a) "All about STIs" (what are, how they are transmitted, possible treatments / prophylaxis and false myths)
b) "Self test and outpatient test" section: to have information on why it is useful to do the test, how it works, main differences, etc
c) "Where to take the tests" it will be possible to search for IST clinics in the area with direct access where it is possible to perform the test anonymously and free of charge
d) "Register your test" it will be possible to send the test result and providing very little information about the user

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P 169 HIV prescriptive trend 2018 vs 2019 in a teaching hospital in Rome

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Introduction: With Lazio Region's Decree in 2017 "rationalization of the use of drugs for HIV therapy", regional guidelines have been updated, based as well on the new Guidelines approved by the Ministry of Health in 2016.
ART today is based on a wide choice of drugs and regimens, ranging from new molecules generation to equivalent drugs after the patent expiry,drugs already in use.
Looking to recommendations highlighted in the regional document, we want to analyze the prescriptive trend in a Teaching Hospital in Rome with particular focus on 2018vs2019, based on File F and SSN datas
Materials and methods: Epidemiological datas were analyzed.Attention was focused on therapies with generics and switch to more expensive branded therapies was monitored. For naive patients we monitored cost/therapy combinations and percentages of low-cost therapies'prescription.
Results: In 2018,3,451 new diagnoses of HIV infection were reported, equal to an incidence of 5.7 new cases of HIV infection per 100,000 residents.
Among European nations, Italy and Greece are iat the 13th place in terms of incidence in new HIV diagnoses. After Portugal, Italy has the highest incidence of AIDS among Western European countries in 2018.
In 2018, regions with HIV highest incidence were Lazio, Marche, Tuscany and Lombardy. In 2018 Italy's proportion of foreigners HIV newly diagnosed was 35.8%.
We noticed substantial adherence to strongly and moderately recommended regional guidelines therapies, with a prescriptions'moderate shift towards new and better tolerated therapies in monotherapy (Rezolsta, Evotaz). 30% of patients treated with Prezista800, Norvir, Tenofovir passed to Rezolsta, Tenofovir. 20% of patients with Reyataz, Norvir, Tenofovir moved to Evotaz, Tenofovir. 40% of patients maintained therapy during 2018 and 2019,10% changed therapy. Analysis showed a switch towards high cost therapies(700euro per month),due to developed resistances.
There was a simplification of therapy in 15%of patients in 2018vs2019, with a switch to monotherapy drugs, more expensive but ensuring patient compliance. The switch to generics, after regional tenders, was respected in 100%of cases. Naive patients(5% in 2019vs2018) were first adressed towards less expensive treatment regimens recommended in the first line (Tenofovir, Rezolsta35% or Tenofovir, Evotaz20%)
Conclusions: Datas show a substantial adherence to Lazio Region's recommendations,with an increase in the naive patient in the use of the best drugs cost/therapy, and in large part thanks to the simplification strategies that guarantee quality of care and assistance with a view to sustainable spending
Results show that high adherence patients take less expensive therapy with better control of the infection,thus leading to lower health and social costs.
In the context of a sustainable economic development, in future perspectives, however, clinical governance system has to consider accessibility, sustainability and appropriateness of antiretroviral treatments.

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P 170 HAARTISTICAMENTE AN UNUSUAL FASHION SHOW

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HAARTsticamente is a three-year project by Angela Infante, who works in the UOC of Infectious Diseases and DH of the Policlinico Tor Vergata Roma. HAARTistically, it plays on the phonetic similarity of the word ART and the acronym HAART, antiretroviral therapy. Participants are serocoinvolved people, interested in knowing, discussing, deepening, comparing themselves on seropositivity. The trilogy is three cycles of annual workshops: the first, in 2017, consists of artcounseling workshops, on a monthly basis, in 4 hours the participants worked, trying their hand at different artistic techniques to explore the world of HIV-positive. The topics covered were many: contagion, fear of others and of themselves, care. The second cycle of 2018 was a theater-counseling experiment. The actors were asked to investigate and deepen the issues of incommunicability, the care of themselves and of the other, the couple, to find a key to understanding the world of HIV-positive, individual, introspective and critical, far from stereotypes. The assiduous participation, a management of the interior and scenic space brought an interesting experiment on the stage "Anchovies and Cornices, taking as a canvas the book Alice in Wonderland. The theater was a concrete space and place to dream together, not only construction, but a space that belongs to the community and the imagination. The theater offered a safe framework within which to explore dangerous extremes. "We act to communicate with ourselves, as when we sleep, the theater cannot die before the last dream has been dreamed."
This highlighted the passage by Carroll, the visionary author of Alice in wonderland, the answer to our efforts to always feel up to it, not to feel guilty. In this laboratory you can design, with personal style, an authentic frame for a mental representation of your own serocoinvolvement. In the last cycle of 2019, all participants, old and new, were asked to design and create a catwalk look, the same theme, with two key concepts: Contagion and Care. No limits to imagination. On December 1st of this year, the World AIDS Day, an unusual fashion show was held, an HIV-themed fashion show, an event unique in its kind. The unusual parade was a guest of the MuCiv - Museums of Civilizations, EUR, took place in the Hall of Honor Arts and Popular Traditions and makes use of numerous important sponsorships, among these stand out, for the theme related to health, the SIMIT, Italian Society of Infectious and Tropical Diseases and the PTV - Policlinico Tor Vergata Foundation in Rome.

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P 171 "LA PREVENZIONE VA IN TOURNÉE" A SOCIAL EXPERIMENT AND ON THE FIELD EXPERIENCE ON HIV/STIS AND SOCIAL INTEGRATION

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Background: HIV and STIs are not well-known by the general population. Some deny their existence, others ignore risks and routes of transmission. PLHIV continue to be socially discriminated and stigmatized. Traditional awareness-raising campaigns are generally didactical, with a lack of sexual/prevention education in schools, where often are considered as a taboo. TrinArt ONLUS privilege non-formal communication on HIV, intermediating between clinicians and public, approach used during "La prevenzione va in tournée" (Prevention goes on tour) project. Prevention and risk reduction messages were disseminated using visual and experiential methods, focusing on PLHIV social integration. Another objective was to create and strengthen partnerships between organizations and institutions.

Material and methods: A red Piaggio Ape car travelled from south to north Italy, raising awareness on HIV/STIs, offering rapid HIV testing, carrying out interactive artistic activities, dispelling superstitions on HIV. The choice of the transport, the route and its duration are charge of symbolisms that will be explained in the poster. The project was entirely top-down, interactively involving collaborators in planning, with dissemination through social media. Cities visited, starting from Palermo: Naples, Rome, Florence, Pesaro, Ravenna and Milan. The project was implemented through brochures, video documentaries, workshops, testimonials, with artists performances facilitating communication with audience.

Results: 35 subjects involved, including associations, public institutions, media and shopkeepers. Fundraising was done through Facebook, support from CeSVoP, donations from artists and associations, info stalls, collecting €5850. An orchestra, a music band and 16 artists collaborated. 13 paintings were produced, with photos of the tour exhibited at NPS headquarters in Milan during the 11th ICAR conference. The Ape car was painted/had signatures placed on it by people involved in the activities, becoming itself an artistic installation. About 2100 leaflets, condoms and gadgets were distributed, with about 100 citizens involved per city. Four clinicians performed 15 rapid tests in Palermo, 15 in Naples and 25 in Ravenna. Detailed results will be exposed in the poster.

Conclusions: The project was completed on schedule, despite little experience by TrinArt and short period for planning. Positive feedback from institutions, associations, media and citizens, allowed to expand the scope of the project, achieving unexpected results. The number of artists and institutions reached was greater than expected. New synergies emerge, leading to the sharing of experiences on various themes, opening up the possibility for future collaborations. This project can be replicated adapting activities to the needs of other cities and statute of host associations. More time should be devoted to coordination with partner associations to better modulate activities.

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P 172 MONO-SYMPTOMATIC THERAPEUTICAL GROUP FOR CHEMSEX USERS - AN ONGOING EXPERIENCE

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Chemsex has become a widespread phenomenon in the Milan gay scene, and whilst, at some extent, counselling and information are available to manage the use reducing harm, a call for help starts rising from those who would like to quit. Chemsex is for now a a niche phenomenon, specific of the MSM community, and public services are not yet ready to offer specific tratments.
To address this need our group was created to offer Chemsex users a place of cure, inside the Milan MSM community. The group is hosted by a a professional psychotherapist and a volunteer.
It is weekly semi-open group, composed of a varying number of participants, (generally between 5 and 8) aimed mainly but not exclusively to HIV+ population; it has been advertised on the association magazine and website, fliers in gay venues in the Milan area, in HIV clinics, and on apps. The project had such an echo outside the community that local and national tv and press talked about it and spread the news. The structure mimics the psychoanalytic mono symptomatic therapeutical group used of other addictions such as eating disorders or gambling: through peer confrontation, where common experiences are shared, the participant create a bound that can be summarized in the phrase “I’m like you”. This bound brings them back to the experience of interpersonal relationships that are lost with the abuse of Chemsex. From this bound stems the newly found sense of unicity of each single participant, who focuses his personal and specific problems that caused the abuse.
Among the many lessons learnt, we noticed that MDPV abuse causes enormous and extremely frequent psychotic and paranoidal episodes, group confrontation appears to be a much more effective tool to control and normalize these feeling, rather than individual therapy.
The synergy between professional figure and a member of the MSM community (although not technically a peer, as not a chemsex user) has turned out to be fundamental to bridge potential cultural gap between users and therapist.
The setting within an established and historical organization in the Milan MSM scene, helped create a friendly environment that helps participants talk freely, without fear of being judged or stigmatised.

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P 173 HIV RAPID TESTING OUTSIDE HEALTHCARE FACILITIES: DIAGNOSTIC AND EDUCATIONAL TOOL

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Background: Treatment as prevention (TasP) is a cornerstone in the attempt to reduce the HIV epidemic. To be effective this measure should be expanded at the maximum, that is include and retain most PLWHIV in the cascade of care and treat them effectively. Current experiences in Italy indicate that a week knot of the care cascade is still the proportion of PLWHIV that ignore to be infected.

Methods: A year ago, our township joined the Fast Track City Initiative (FTCI). One of the goal of our project was to expand the accessibility of HIV test outside the healthcare structures. While waiting for the independent city Check Point (recently opened) a place for test, audit, counseling and self-help for PLWHIV and their relatives, we concentrated on spot events were HIV tests were performed in an anonymously and without any copay. In all cases, a rapid blood test combining both antibodies and antigens for a more sensitive diagnosis was used. Events were both directed toward the general population of our area or specifically designed for target populations. All persons that decided to perform a test were asked for a written inform consent and were invited to complete a 13 item standard questionnaire previously agreed among all partners in the FTCI that was used to drive the counseling.

Results: At January 2020, according to our calculation thel estimated number of PLWHIV was 3314 of whom 207 (6.5%) unaware of their infection. Although the yearly rate of new infections lowered in the last years (figure), the epidemic relevance of these 6.5% of PLWHIV should not be underestimated. In the last year, we performed 700 HIV test in 28 different spot events. Four of these were directed toward the general population, while 22 were specifically oriented to well defined targets such as University students, young people frequenting social centers, young people at recreational facilities, gay men frequenting saunas or cruising venues, intravenous drug users at their gathering points. Overall 70% of test were performed on men. Fifty percent of subjects defined themselves as straight, 40 % as gay or lesbian and 10% as bi-sexual. Interesting, for most of people performing the test the reason to perform it was curiosity (33.8%), followed by the need to perform secure sex (15%) (figure), while a perceived risk was a reason far less reported (only 6.7%). This seems quite in contrast with the described sexual behaviors, if we consider that 17% of tested people reported to have had, in the past year more than 10 different sexual partner either males or females (figure). The rate of positive tests was 0.28%.

Conclusions: These preliminary data, based exclusively on spot events, indicate that curiosity is the strongest driver for people to be tested. Differently the perceived risk for HIV infection seems rather low. The test, performed under these circumstances acquires therefore a strong connotation as vehicle of information and appears as a possible educational tool.

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P 174 CHANGES IN CAUSES OF DEATH OF PEOPLE LIVING WITH HIV IN A LARGE TEACHING HOSPITAL IN ROME

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Background: The introduction of combination antiretroviral therapy has dramatically improved life expectancy in people living with HIV (PLWHIV), reducing the cases of fatal AIDS-related events. In this study, we aimed to analyse the causes of PLWHIV in our cohort and describe the changes observed over the last decades.
Methods: We analysed clinical and virological characteristics of HIV-infected patients who died in our clinical centre between 1985 and 2019. We used non-parametric tests to compare variables.
Results: We analysed 915 patients: 719 (78.6%) of them were males, with a median age of 38 years (IQR 33-45) and a median time from HIV diagnosis of 4 years (IQR 1-11). Median nadir of CD4+ lymphocyte was 44 cells/mm3 (IQR 12 -107) while the median peak HIV-RNA was 5.2 log10 copies/mL (IQR 4.5-5.6). Five hundred thirty-five patients (36.7%) had at least one AIDS-defining event.
As to causes of death, 392 (42.9%) patients died for an AIDS-defining event, 228 (24.9%) patients died following a non-HIV related infection, 87 (9.5%) patients had a liver disease, 51 (5.6%) had a heart disease, 38 (4.2%) for non-HIV related malignancies while 6 (0.7%) died because of drugs or traumas. Regarding the other 113 patients (12.3%), we were unable to collect the causes of death.
We divided the analysed patients in seven time groups, each of a 5-year frame: 26 (2.8%) patients died between 1985 and 1989, 325 (35.5%) between 1990 and 1994, 333 (36.4%) between 1995 and 1999, 98 (10.7%) patients died between 2000 and 2004, 24 (2.6%) patients between 2005 and 2009, 50 (5.5%) between 2010 and 2014, while the remaining 59 (6.4%) died between 2015 and 2019. Details are shown in table 1.
In our analysis, we observed a significant correlation between causes of death and time from HIV diagnosis ($p<0.001$), with a lower time in patients dying for AIDS-related events and non-AIDS-defining infections, and between causes of death and CD4+ cells nadir count ($p=0.002$), similarly lower in PLWHIV dying for AIDS-related events and non-AIDS-defining infections.
As to the year of death, we found significant correlations with age ($p<0.001$), time from HIV diagnosis ($p>0.001$) and with CD4+ cell count nadir ($p=0.049$), with PLWHIV dying in the last decade having a higher nadir compared to PLWHIV in the first time groups. Details are shown in tables 2 and 3.
Median age of death resulted increased over years, from 32 years (IQR 28-38) between 1985 and 1989 to 56 years (IQR 51-65) between 2015 and 2019. In the same way median time from HIV diagnosis increased from 0.7 years (IQR 0.4-1.0) to 15.4 years (IQR 0.8-22.7).
Conclusions: In our cohort we observed a decrease over the last decades in deaths related to AIDS-defining events while we registered an increased rate of deaths due to non-AIDS malignancies, which represent the main cause of death nowadays. As expected, we found significant correlation between causes of death and time from HIV diagnosis and CD4+ cell nadir.

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P 175 THE PLWH PERCEPTION OF LONG ACTING INJECTABLE THERAPY

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Background: Lifelong ARV therapy is a major factor influencing QoL of PLWH and on the long period adherence and side effects can be a factor to lose control of health, mainly for those who have to take different medications due to aging or co-pathologies. Nadir decided to investigate if a long acting ARV could be an added value for the QoL of PLWH, taking into consideration the no-need to assume day by day pills in public in front of strangers who might discriminate the person living with a life threatening disease received by sexual behaviors or drug use.
Material and methods: We addressed a questionnaire only to people already taking ARV and we launched it at the Nadir Seminar in September 2019 to 25 HIV Organizations coming from different regions of the country. It was sent out also through our media and in particular through our www.nadironlus.org. Nadir received spontaneous answers during the following 60 days from 34 towns in the country. The sample was quite homogeneous with a median age of 51, long experience of ARVs, 2 or more ARV strategies changed along the years. We investigated adherence, difficulties in assuming the therapy, their expectation, information and perception of the QoL improvement through a long lasting injectable dual therapy, also relating the answers with the age and length of ARV.
Results: The sample, composed by 178 spontaneous PLWH with a median age of 51, mostly males with a high school education. 57% of them are in treatment for more than 10 years thus experienced at least 2 different treatment. Side effects are declared by half of the sample and only 70% confirmed their ability to be adherent. The lack of adherence is defined as "I forgot" and as "being in public" by 20%. Almost 50% of the sample declares they are to take more treatment for different pathologies due to lab results or CV problems (14%). The 83% declared their motivation to receive intramuscular ARV every 2 months and this innovation would improve their QoL. 59% declares they would choose to have it injected in a space different from the hospital. Almost nobody was aware that switching from intramuscular to oral can be feasible and flexible in the case of need (no acceptation of the needle, pain on the injection site...).
Conclusions: The survey Nadir elaborated shows a good motivation of the sample to accept a long acting treatment once every two months due to the commitment most of the participants have to other pathologies medication intake, by consequence aimed at improving their QoL and preventing their lack of adherence linked to the day by day administration. Further studies will be able to understand possible external factors that may become an obstacle to implement correctly this innovative intramuscular treatment.

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P 176 COHORT OBSERVATIONAL STUDY AND HIV BROCHURE IN A TEACHING HOSPITAL IN ROME

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Introduction: In 2019 a training stage was made by a colleague from the United Arab Emirates, in order to optimize a profitable cultural and professional Exchange and as part of the collaboration of our Structure with the PNU College of Pharmacy University.
We want to illustrate the results deriving from the training stage carried out at our Pharmacy Direct Distribution Service, with a focus on the management of HIV positive patients.
Materials and methods: A cohort study on the afferent population was organized, with particular regard to ethnicity and average age. An information brochure on how to manage sieropositivity in daily life was also given to users, with particular suggestions for the managing of possible comorbidities. The brochure was produced in Italian and English, given the cosmopolitan users. and a satisfaction questionnaire was given to be fullfilled by any user.
Results: The afferent population is composed as follows:
Of 3,500 patients followed from January to December 2019:
20 percent of African descent
10 percent non-EU Caucasian origin
10 percent of Asian descent
Of all the foreign population, 45 percent are women, 55 percent are men.
60 percent of the population is under the age of 40.
Patients with STP code(strangers temporarly in Italy) are the 3 percent of the total population.
70 percent of patients consider the brochure useful for managing disease as a chronic comorbidity.
60 percent of patients find information on managing any minor side effects very helpful.
80 percent of patients find information on where to turn in case of illness is important.
90 percent of patients consider useful services such as brochures or dedicated apps (anonymous and renamed, with passwords or privacy screens) for the management of side effects or forgotten doses.
Conclusions: The observational study, the administration of the questionnaire and the brochure highlighted an HIV-positive population increasingly cosmopolitan and attentive to the more aware management of their pathology. The interest shown in bruchure indicates the patient's need to interpret seropositivity as a chronic pathology similar to others.
The brochures were particularly appreciated, datas from the questionnaire demonstrate the need for serum positive patients in understanding their pathology as a chronic morbidity.

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P 177 HIV SELF-TESTING IN ITALY: A USABILITY SURVEY OF CLIENTS USING SELF-TESTS AT TWO COMMUNITY ORGANISATIONS

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Background: In Italy, HIV Self-Tests became available in pharmacies on 1st December 2016. Despite National AIDS Plan having included HIVST in the national strategy, there is a lack of Italian data on its usability. Our survey aimed to investigate HIVST users' experience and related difficulties.

Materials and methods: The use of Mylan HIVST, the most widely available in Italy, was observed. Twenty-eight clients were asked to perform an HIVST under the supervision of a community health worker (CHW) in 2 community organisations, ARCIGAY and LILA. Inclusion criteria were:

- 18+
- Fluent in Italian
- Never used an HIVST before

Both the users and CHWs completed a questionnaire after the HIVST was carried out, to evaluate the experience and assess need for additional support. The study was done in collaboration with Public Health England as part of the European project INTEGRATE.

Results: Demographic details of users (gender, age, sexual partners, education) are shown in Table 1.

CHWs reported that 10/28 users failed at least one step when performing the HIVST and needed assistance to complete it (Figure 1): 7 users failed the blood collection step and 6 had problems in understanding how to put the test in the cap.

The main reported reasons for using an HIVST in the future were: rapid result (n=19), no need for medical prescription (n=10) and privacy (n=6). Reasons for not using the test in the future were: lack of counselling (n=14), worried about reading result alone (n=9) and cost (n=8) (Figures 2 and 3).

When using HIVST, users would like to receive contact details of NGOs (n=18), counselling (n=14), testing for other STIs (n=10). Furthermore, 15/28 users would prefer to take the test with a CHW, while 13/28 would prefer to take it alone.

Conclusions: In this small sample, 10/28 users (36%) failed one or more steps while performing an HIVST, despite most having a good level of education (n=12 High school and n=16 University degree). From these findings, some suggestions may be made to improve the HIVST kits and make them more user-friendly, including:

- improving the information leaflet. Mylan provides a demonstration video online. Nonetheless, although users were free to use their mobile device to help them complete the HIVST and some of them were in doubt about how to proceed, none of them accessed the video
- providing additional lancets in the test kits, to give another chance to obtain blood. Currently, only one lancet is provided and if users fail to collect the right amount of blood (e.g. due to pricking the finger in the wrong place or vasoconstriction), they cannot try again
- providing links with NGOs - by listing their helpline numbers on the information sheet - for support, for assistance in performing the test, interpreting the result, and linkage to confirmatory testing in case of reactive HIVST results.

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P 178 COUNSELLING AND HIV RAPID TEST FOR MARGINALIZED GROUPS: DATA FROM AN EMILIA-ROMAGNA REGION PROJECT*

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*Regional project DGR 1698/2015

Background: Epidemiological data show that more than 50% of HIV diagnosis are at an advanced stage of infection. Marginalized groups (drug users , migrants, homless) experience obstacles in accessing HIV hospital centers and are at a major risk to be undiagnosed or diagnosed late.
Aim of this project is to offer counselling and HIV rapid test in unconventional settings, in order to favour the access of more vulnerable people. The project was funded by an Emilia-Romagna region grant.
Methods: From January 2016 to December 2019 counselling and oral HIV test (Oraquick;Orasure techologies) were offered to clients of services for marginalized people in 3 cities (Ferrara, Parma, Reggio Emilia) of Emilia Romagna Region. Services involved were: reception centre for migrants, drug-treatment services, drop-ins, mobile uniti. Before the test was carried out an interview about HIV transmission; demographic, sexual behaviors and drug use data were collected during counselling sessions with consent of client. In case of reactive results, individuals were offered accompainment to the HIV hospital for confirmation and linkage to care .
Results: 1812 clients were tested; 1081 (59,6%) questionnaires were completed and data analyzed.
Of 1081 clients, 863 (81,6%) were men, aged from 15 to 72 years; most represented age groups were the 20-30 year-olds (325/1081-30,6%) and the 31-40 year-olds (297/1081-27,47%)
578/1081 (53,6%) were Italians, 330/1081 (30,6%) were Africans.
333/1081 (31,2%) were active intravenous drug users.
367/1081 (34,3%) had never tested before for HIV and they aprreciated the opportunity to take an HIV test in a place other than an hospital centre. Among those who referred previous testing (660), 18 (2,7%) didn't know the result.
Only 219/1081 (20,9%) usually had sex with condom, thus indicating high risk exposure. 54/1081 (5%) had an HIV partner.
2/1812 (0,11) patients were tested HIV positive. The first was a 25 years old male from Costa d'Avorio, he lived in Italy for 1 month; the second was a 28 years old female from Nigeria, she lived in Italy for 2 years. They were referred to local HIV unit and linked to care
The majority of clients considered the initiative useful and the acceptance rate of oral-fluid HIV test was high.
Conclusion: Our data showed that an high percentage of clients in marginalized groups are at risk for HIV transmission and are never tested. HIV infection in migrants could be investigated also in people lived in Italy for years .
Testing services in nonconventional setting is an efficacy strategy to reduce barriers to health servecis and to spread awareness about HIV transmission in hard to reach populations.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 179 SCHOOL AND HIV. COGNITIVE AND EMOTIONAL ASPECTS FOR EFFECTIVE COMMUNICATION

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Background: Since 1985, ASA - AIDS Solidarity Association - is a voluntary association which has been active in the field of prevention of HIV infection and in providing support to HIV-positive people. ASA's activity is focused especially on the MSM, but from the beginning it has also addressed the problem of providing the general population with correct information on HIV-AIDS. Teenagers are a vulnerable population to inform, so ASA has a special program for them, at high school in Milan.
Methodology: Some professional institutes and high schools have been contacted in Milan. At the request of the school it was organized the meeting between ASA and students. Each meeting, lasting for two hours, was held by two volunteers with training of counseling in the field of hiv-related problems. One of the two volunteers is a psychologist who holds aspects properly health: definition of HIV and AIDS, modalities of transmission, epidemiological data, prevention, diagnostic tests; and the emotional and social aspects that pose a challenge to HIV-positive people. Ample space has been given to the theme of discrimination and social stigma. The other volunteer, HIV positive, shares his experience. Every meeting took place ended with student questions. From January to December 2019 there were meetings in 8 schools: two high schools and six professional institutes, with the participation of about 500 students attending the second class of high school.
Results: Observation by the psychologist and the volunteer during the two hours of the meeting, students' questions, the feed-back provided by the teachers highlighted the following points:
- knowledge of HIV-AIDS is weak and often affected by beliefs based on prejudices;
- the level of attention of the students was discreet, the peak of interest was during the story of the volunteer;
- the questions asked by the students in the final part of each meeting have shown interest in knowing better the HIV-AIDS topic;
some students, following the meetings, contacted ASA to take the HIV test accompanied by parents.
Conclusions: The meetings with the students have reached the aim of providing correct knowledge of the HIV-AIDS. The presence of the HIV positive volunteer was important because with his narration he spoke to the emotional sphere of students arousing interest and attention. For the future it is useful prepare and administer two short self-report questionnaires anonymous, one before the other after the meeting. Purpose of the questionnaires is to provide data:
- to better organize and calibrate the two moments
of the meeting: that of the psychologist and that
narrative of the HIV positive volunteer;
- for a more accurate evaluation of the ASA initiative.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 180 SARDINIA, FIRST EVER INSTITUTIONAL HIV TESTING AND TASP PROMOTION CAMPAIGN: THE COMMUNICATION STRATEGY OF LILA CAGLIARI TEAM

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Lila Cagliari, Cagliari

Background: In 2019 – 2020 LILA Cagliari (Italian League for the Fight against AIDS) has developed a multi channels communication campaign on TasP (Treatment as Prevention) and on traditional prevention means (condom use and HIV testing). The campaign has been implemented in the whole of the Region of Sardinia through regional funding. This is the first regional communication campaign on HIV prevention, HIV testing promotion and TasP ever implemented in Sardinia.
Material and methods: The images chosen to promote classic means of prevention are simple yet of strong visual impact particularly due to the colours chosen. One version depicts a young girl on a vivid yellow background who mimics the 'stop' gesture with her hand. The image and the colour are aimed at reinforcing the accompanying text: 'We can stop it by using condoms and getting tested, HIV concerns everyone'. An second version of the above shows an adult man on a mauve background, colour intentionally complementary of the female version. The combination of the images, texts and colours makes the message strong, clear and relevant to the general population. With regard to TasP, we chose to launch the message through the image of a couple – a man and a woman, who are looking at each other and smile in an intimate manner. The complicity that they transmit is tangible, captivating and engaging. The image is accompanied by the message 'One of us has HIV: is undergoing treatment and cannot transmit it'. This is a positive message, based on scientific evidence and innovative for our society. It is aimed to tear down the fear against people with HIV. The message is enhanced by a bright blue that highlights and reinforces the serenity of the couple. To disseminate these different messages, we chose to launch the campaign through street advertising, traditional advertising and social media. The campaign started with very large billpostings, ads in local newspapers (paper and online versions), TV and web ads, and images of the campaign on city buses. The combination on the means chosen to disseminate the campaign, together with a social contest, has amplified the strength and reach of the messages and has promoted interactions and sharing among the recipients of the campaign.
Results: Thus far, the campaign has been quite successful. It has been praised by professionals and organizations that work on these issues. To date, there are 100,743 records of interactions on these themes on social media. The campaign has also been transmitted by local media and it was translate in english too.
Conclusions: The creativity and simplicity of the messages have generated an effective communication campaign. This has allowed to promote essential concepts that should be commonly known (yet they are not) by the general population. Public funding and the support of local authorities remains essential to support and sustain the very important action of civil society organizations at local level.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 181 "TEST WITH THE STAR": A PRE-COUNSELLING "DOG ASSISTANCE" PILOT PROJECT DURING HIV-HCV SCREENING CAMPAIGN "1ST DECEMBER WORLD AIDS DAY. COMMUNITIES MAKE THE DIFFERENCE. UNION MAKES THE DIFFERENCE! HIV LATINA CHALLENGE 2019. U = U"

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Background: Animal Assisted Interventions (AAIs), known as "Pet Therapy", have recently been included by the Italian Ministry of Health as valuable educational activities and complementary treatments in various health-care settings. [1] AAIs with the dog have been used with success in various related care issues (e.g. reduction of anxiety and stress-related to blood sampling [2]; teenagers with social and behavioral problems [3]). In HIV long term care showed benefits for the reduction of stigma related to HIV positivity in daily life [4,5,6] We propose a dog-mediated approach to test and counseling.

Material And Methods: A team made up of two golden retrievers, two dog co-adjutors and an AAI activity manager joined the healthcare staff dedicated to MST counseling and HIV blood-HCV salivary test offer, without interfering with the normal test practice. The initiative took place on 1 December 2019 in Latina city center.

A claim for the initiative "Test with The Star" was exposed on a stand and instant camera pictures were taken during human-animal interactions (with previous informed consent). People waiting to enter in bloodmobile for the test were invited to actively interact with dogs guided by co-adjutors. Feedbacks were collected anonymous and voluntary questionnaire.

Results: AAI related 47 questionnaires were collected (65,3% of participants on a total of 72 tests performed), mean age was 31 (22-74 years), 31 (66%) female and 16 (34%) male. 35 (74%) interviewees had been familiar with dogs, 44 (94%) had some basic knowledge of "pet therapy". In the questionnaire were proposed 6 dogs images to link with the theme of the initiative and the more chosen were a Snoopy cartoon saying "It's exciting to know that you've done something revolutionary" (21; 44,7%) and a representation of a dog as a watchful protector on person lying in bed (19; 40,4%). Similarly, the proverb more chosen to identify the sense of dog during the campaign was "As loyal as a dog" (37; 78,7%).

About the personal role of relation with the dog during the testing initiative, 22 (46,8%) interviewed answered they were enticed and intrigued by their presence, 21 (44,6%) claimed that their presence defuse the wait for the test and 8 (17%) that have some role also to reject fear of test result.

30 (64%) participants answered "yes" and argue for a possible utility of AAIs in HIV subjects' care. The proposals may lead to three areas of intervention: a beneficial effect as emotional support (11; 36,5%); difficulties specifically connected to HIV positivity and illness (11; 36,5 %); stigma and sense of loneliness related to HIV diagnosis (8; 27%). Only one of the participants expressed doubt about the major risks of zoonosis dog related with HIV + subjects.

Conclusions: To our knowledge, this is the first experience of dog-based AAI as a useful means to attract and ease street STD and HIV testing initiatives. Our little survey shows that in common thought the dog as a companion animal may be a key to overcome stigma and illness-related problems. The hope is that in the future structured AAIs programs will be part of multidisciplinary efforts for HIV + subjects' inclusion and maintenance in care.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 182 TEST, CONDOM AND CHEMS: HOW THE HABITS OF PEOPLE IN MILAN CHANGE. A TEST EXPERIENCE IN A PREMISE

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Background: ASA-Associazione Solidarietà Aids-since 1985 is an association active in Hiv-Aids prevention and supporting PLWHIV, particularly focused on MSM population. Since 2012,once a month, ASA provides in its premises a Rapid Hiv Test,anonymous & free of charge,to encourage mass screening. A questionnaire and an informed consent form are handed out to the incoming people. Before the test is carried out, an Hiv specialist counselor conducts an informal interview in accordance with the law. The test is performed by an ID doctor who returns the result. Being the test's result positive a psychologist can assist the person.Individuals that result Hiv+ are directed to the confirmation test,eventually lead in hospital by the same Rapid Hiv Test doc,to facilitate the retention in care. The test is part of the association's prevention/early detection programs. Since October 2016 ASA carries out the Rapid Hiv Test also in MSM bars. Moreover, since February 2019 ASA participates in the prevenction activities of Milan Checkpoint.
Methodology: self-administered questionnaires (April 2019-January 2020) 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.
Results: 131 users(M 78%; age range 31-40; heterosexual & homo-43% and 43%-, graduated 41%; Hiv already tested 82%; employees 40%; 87,6% Italians; 12,9% using Chems; no.of partner:3 & more). None turned to be positive. Here some variables that have been crossed:
-Gender (G)by: Use of Condom By Partner Type(CPT), Use of Condom by Sex Activities(CSA), Use of Chems(UOC)
-SO by: CPT, CSA, UOC
-Sex Under D&A by G by: CPT,CSA
-UOC by Sex Under D&A
-Test already taken by last test
Conclusions: Due to the offering of tests in MSM venues and at the Checkpoint, the no. of tests at ASA premises has lowered.In particular, the no. of women has lowered by 10% (possibly because they prefer a "neutral" site) while the no. of homosexuals has increased(2/3 among men).As shown by preceding analysis,the sample is generally careful, wearing condoms during casual penetrative intercourses.As in the past,30% in equal measure M&W, has made sex under the influence of D&A; under these circumstances the no. of protected sexual intercourses has lowered to 40%, while the no. of casual sexual intercourses has increased to 70%. In particular,almost 13% practises chemsex: MSMs 4 times more than heterosexuals. Both M&W tend not to use condom when engaged,trusting one another. The high no. of users already tested in the last 6 months, along with the absence of positive results (in line with the national and regional trend of reduction of new diagnoses), underlines the power of the test,together with TasP, U=U and PrEP, in order to pursue the goal of 90-90-90. ASA was supported by ViivHealthcare.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 183 COMING OUT SURREALISTA

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Coming out, also serological, is a path, a choice; coming out is telling about yourself. There is no definite time, there are no packaged words, there is no coming out better than another,you are never in a coming out without being yourself. Coming out is a clock that snaps inside you, that wraps you, that can be frightening, that bets on the yes and that takes away the no. Coming out is as you expected, or the opposite of what you thought;coming out is an infinite, deep breath that accompanies you, it is a never closed parenthesis. Coming out is a pride,it crushes stereotypes and does not allow you to hide.These words accompanied the staging of "Surrealist Coming Out", the final product of a theatrical counseling workshop from a project by Angela Infante, promoted by Difference Lesbian Rome.A laboratory for only lesbian women involved,a show for everyone,a guest of a small historical theater in the heart of Testaccio, the Teatro di Documenti,with a memorable sold out. The performance made use of ten talented, non-professional actresses who narrated themselves with dedication, passion and courage.A one-of-a-kind performance, an act of love for yourself and your own difference. The performance is dedicated to aour friend Delia Vaccarello, journalist, writer, without whom we will feel more alone after her untimely death. Our answer is dramatized counselling workshop where one can draw, by using their own personal style, an authentic frame of a mental representation of their own HIV status.The project is inspired by theatrical referential models which are, each, based on the theoretical and practical aspects: Stanislavskij's technique of affective memory, which proposes the identification between the actor and the role; Brecht's estrangement effect, which proposes the separation between thought and action; Artaud's technique of the theatre of cruelty, which conceives theater in cathartic terms. The project envisages a cycle of 9 pre-arranged themed meetings of three hours, on a monthly basis plus a theatrical performance. The project is intended for HIV negative and HIV positive women who seek a debate on the issues related to HIV, through the experience of theatrical workshops. The workshops are conducted by a counselor specialised in expressive-drama.The result still measured the constant participative dimension and the intense involvement of the women, not taken for granted, who experience their own reality in a different light and allow each other to communicate without the stigma that HIV has always carried. The performance went on stage on the 11st of october 2019. The elements of the theatrical mediation process stimulate the imaginative skills. On the other hand, developing these skills increases the cognitive processes and the individual's potential to affect reality and make changes.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 184 APP AS TOOL FOR PREVENTION AMONG STUDENTS: THE LAUNCH OF A NEW COUNSELLING SERVICE ABOUT HIV/STIS PROMOTED BY ANLAIDS ONLUS

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Background: The data of the Italian AIDS operation centre (COA) referring to 2018 report the highest incidence of new diagnosis of HIV infection among the 25-29 age group (11.8 new cases per 100,000 residents).
Prevention initiatives among young people are acquiring importance again. The National School Project (Progetto Scuola Nazionale-PSN) of Anlaids Onlus reached thousands of students since 2013.
Nevertheless, web is the most common reference to search for information regarding the sexual sphere. Global Digital Report 2019 highlights that WhatsApp is the most popular app in Italy for messaging among people, across every age groups.
Material and methods: PSN aims to raise awareness among Middle and High School students (age group 13-19) through trainings and activities focused on HIV and STIs prevention.
In July 2019, during the launch of the Smemoranda 2020 diary (sold on average to about 500,000 Italian students), Anlaids created a web page dedicated to HIV/AIDS awareness. On the diary, in addition to a crossword with questions about HIV and IST, a counselling service through a WhatsApp number dedicated to adolescents was promoted: privately and anonymously, young people can access WhatsApp and ask questions related to HIV/AIDS and STIs. In order to implement the service across the Italian territory, a sim card was activated and a working team was formed on the use of social media with minors.
Moreover, from October 2019, following the purpose of supporting a continuity to the informative process, PSN working group began to share the number of WhatsApp counselling to the students trained after the meetings carried out within the PSN activities.
Results: From September 2019 to January 2020 we received a total of 65 contacts on the Counselling service for WhatsApp. Among them, 38% were female and the remaining 62% were male.
The types of questions we received can be categorised as the following:

- 43,3% on the diary crossword (i.e. “What is the answer to question number x?”)
- 22,4% on HIV/AIDS/STIs (i.e. “How can I catch HIV?”, “Which are the other STIs?”)
- 14,9% on sexual intercourses (i.e. “How does a condom work?”)
- 19,4% on other issues (i.e. “Which are the areas of competence of Anlaids?”).

The answers to the questions focussed on giving the right information the person wanted, while also suggesting a personal reflections on the risky behaviours they might have had and which services available on the territory they might need to access.
Conclusions: After a few months of activation, the WhatsApp counselling might represent a new way for associations to interconnect and communicate with young people and might give students the opportunity to ask for information about STIs and sexuality problems.
The finality of the service is to be improved and spread among not only the schools and students involved in PNS but also to a diverse audiences in need of this information on the Italian territory.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 185 PREP BETWEEN DESIRE AND NEEDING: 2020 UPDATE

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Background: In 2017, Arcigay Modena "Matthew Shepard" (ODV) conducted the internet survey entitled "PrEP between desire and real needing" that clearly showed that there was no correlation between PrEP demand and PrEP need according to Smith Score in local population, and that there was too much lack of information about the topic.
Since then, many PrEP facilities have been created in our country (especially in our region) and awareness on the issue has greatly increased.
We then decided to re-administer our former survey to investigate the effect of our intervention.
Material and methods: This year Arcigay Modena configured an update of the former internet survey destined for LGBT+ community. The survey was divided into three parts: general information (age, sex, gender, residence); prevention strategies evaluation; HIV risk assessment (in this last part questions were taken from the Smith Score publicated in National HIV Guidelines 2017).
The survey was administered mainly by social media and mailing lists, with the support of PrEP outpatients' clinic of Modena Infectious Diseases Ward.
Results: We collected 297 answers from 1/2020 to 2/2020.
Most of respondents were homosexual cis-males, mainly aging between 29 and 40 y.o., 51% of them living in Emilia-Romagna and 23% in Lombardia.
Smith Score was ten to fifteen in 17% of all respondents and higher than fifteen in 39%.
25% of interviewed were in PrEP, 35% could use PrEP in future, 39% would not and 1% suspended PrEP.
Among PrEP users, 85% had a Smith Score higher than fifteen; 50% of the respondents that could use PrEP in future were not at risk (Smith Score lower than ten), and 50% were at risk or high risk (Smith Score higher than ten). 68% of respondents that would never use PrEP were not at risk.
On the other side, 58% of respondents that were not at risk of acquiring HIV would not use PrEP and 37% could use it in future.
49% of respondents with a Smith Score from ten to fifteen would not use PrEP and 36% could use it in future; 56% of respondents with high Smith Score already use PrEP and 31% would use it.
Conclusions: Since 2017 we witnessed some great changes, especially in MSM community: people now know better about PrEP and a quarter of our sample actually use it to prevent HIV. Most important, 85% PrEP users had a Smith Score higher than fifteen, which makes PrEP cost-effective.
However, there are still some issues concerning the easiness of getting PrEP, especially for people at risk/high risk: 17% of them would use it but still don't. Our data suggest that the main reasons are lack of facilities and high costs.
Medical institutions and MSM communities should cooperate in order to spread further knowledge about PrEP in the general population (not only MSM), and more PrEP facilities should be implemented in every city in order to give everybody the concrete opportunity to adopt PrEP as a prevention strategy against HIV.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 186 FREE ANONYMOUS HIV TESTING AND LINKAGE TO CARE ACTIVITIES: DATA FROM THE MILANO CHECK POINT

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Background: Milano Check Point (MCKP) is a community-based center offering HIV rapid tests and PrEP services, active since Feb 2019 as a joint initiative of 5 well established Milanese HIV associations. The present analysis aims to report outcomes of HIV and syphilis testing/linkage to care activities, and to evaluate clients' knowledge of PrEP and Chemsex.
Materials and methods: Data collected retrace 1-year activity from Feb 2019 to Jan 2020. 4th generation rapid capillary tests or 3rd generation capillary tests combined with syphilis were used. Tests were delivered during Milan Pride 2019, Niguarda Hospital 80th anniversary, Milan Festa dell'Unità and Corriere della Sera Time for Health events, besides weekly openings at MCKP premises. Data were anonymously collected through the COBATEST platform, a European network of community-based centers. A logistic regression model was used to describe factors associated with never being tested for HIV before.
Results: 1.493 people were tested: 829 (55.5%) during weekly openings at MCKP and 391 (26%) during Milan Pride events. The age of clients attending MCKP and Milan Pride was significant (29% and 23% <25, respectively) while for other 3 external events avg age was higher (p<0.001). Analogously, gender distribution was similar at MCKP and Milan Pride (30% and 32% females, respectively) while a larger proportion of females tested during other events (47%, p<.001). Proportion of foreigners was almost the same across all events (12%, p=0.895). 8.4% of clients reported to have had at least one STI in previous year; 2.4% were sex-workers. 531 clients had never tested for HIV before (34% MCKP; 32% Pride; 44.3% events). Factors associated with having never been tested before were being heterosexual, other/unknown risky behaviour and being teenager/young adult (Table 1). 13 clients (3.2 %) tested positive for syphilis. 45.8% reported to have heard about PrEP, reaching 53% during Pride; only 3.2% had previously taken PrEP. 3.7% reported chemsex use.
15 clients were reactive to HIV rapid tests (1%), mainly diagnosed during the Milan Pride (Figure). 60% of them were aged between 24 and 35; all were males. Risk factors were in 14 cases being MSM and condomless sex; one case referred intravenous drug use.10 clients (67%) were linked to care, 100% of those detected at MCKP; to date, 9 are already undetectable (Table 2).
Conclusions: In 1-year MCKP performed a considerable number of HIV tests intercepting a many young clients, who are at greater risk for HIV given their scarce awareness of sexual health and uneasiness in attending healthcare settings. Linkage to HIV units and related support was ensured to all clients with reactive tests at MCKP premises. Outreach testing services during the Pride Week demonstrate that targeting key populations proves very effective. These data show that the service is essential for reaching UNAIDS 90-90-90 targets in the Fast Track City of Milan. MCKP received support by Gilead and ViiV.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 187 PLEASURE AND SOCIALITY AS DRIVERS OF CHEMSEX AMONG ITALIAN GAY MEN LIVING WITH HIV

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Background. The paper presents some of the results from different research projects concerning the living choices of gay men living with HIV in several European cities (Barcelona; Rome; Milan; Bologne; Manchester; Leicester; London). Chemsex has emerged as a widespread practice (59 participants out of the 83 interviewed practicing it) despite not being indicated among the recruitment criteria. The paper focuses on the chemsex experiences of the Italian cohort of participants practicing chemsex (total number: 36). The main aim of the paper is to understand how the participants frame their experience of chemsex.
Material and methods: The paper is based on biographic interviews. Participants were recruited through online ads, community gatekeepers (e.g. NGOs working on HIV) and snowballing. The age of Italian participants varied from 21 to 62. Interviews were realized in venues of choice by participants; they lasted between 31 and 244 minutes. Participants were asked about the different stages of their lives. Interviews have been transcribed, catalogued and coded according to the main life events narrated by participants (e.g. 'coming out', 'relocation', 'HIV diagnosis').
Results: When analysing the narratives of participants in regard to chemsex (and sexual practices more generally), the quest for pleasure and sociality emerges as a key-factor leading to the use of recreational drugs to meet new people and have sex. However, sexual intercourse is described as the non-primary scope/activity of these events in the narratives of several participants (13). The quest for pleasure and sociality is often associated with travel and tourism, specific 'gay' cities abroad (e.g. Amsterdam, Barcelona, Berlin, London) occupying a central role in sexual fantasies and experimentation. The narratives show how sexual practices go beyond hegemonic models and discourses around isolation and masculinities. Moreover, the use of recreational drugs appears to differ according to place and other relational factors, the participants describing how their choice to use specific drugs is due to several contextual and relational factors.
Conclusions: The qualitative approach proposed offers the possibility to explore the complex negotiations between sexual practices, identity and desire, going beyond pathologizing discourses and practices as well as criminal/punitive approaches. The research findings may support service providers in better understanding the role of desire, pleasure and the quest for sociality as drivers of chemsex, helping them facilitate behavioral interventions centered around the wellbeing of people seeking support. Finally, the results reveal the need for more qualitative in-depth research on how different recreational drugs shape sexual practices and being with others.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 188 THE MULTIDISCIPLINARY (MD) HPV GROUP IN AZIENDA OSPEDALIERA UNIVERSITARIA PISANA (AOUP). IMPACT OF HIV-HPV SINERGY. PRELIMINARY DATA ANALYSIS

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Background: Human Papillomavirus (HPV) is the most common sexually transmitted agent worldwide. Despite ART therapy, HPV-related diseases have an important impact in HIV positive (HIV+) population. Several studies have shown that HPV infection is more common in subjects with HIV infection than in general population and is statistically associated with anal cancer. The aim of this cross-sectional study was to estimate the prevalence of HPV genotypes in a group of HIV +/HIV- patients.

Material and methods: A total of 109 patients were enrolled during the MD visits in AOUP in 2019. At the time of visit, sex, age HIV serostatus, and CD4 cell count were recorded. The average age was 44.8, (range 22-70). Biological samples (anal, cervix, swabs) were collected during one year and used for genotyping analysis using Multiplex qPCR (Seegene, Anyplex II HPV28). This system comprises automated DNA isolation and qPCR set up (Microlab Nimbus), HPV testing with CFX96 PCR instrument (BioRad) and data analysis with Seegene Viewer (Seegene). The Multiplex qPCR system allows the simultaneous identification of 19 high-risk (HR) HPV and 9 low-risk (LR) HPV types in a single run.

Results: Patients were divided in 3 different study groups: HIV+/HPV+ (n=42, 39%), HIV-/HPV+ (n= 55, 50%), HIV +/HPV- (n=12, 11%) and were distributed by gender in other 3 sub-groups, which including, HIV+/HPV+ 37 M (34%), 12 F (5%); HIV-/HPV+ 30M (27%) 25F (23%); HIV+/HPV- 11M (10%), 1F (1%). Gender analysis showed that males were predominant in our preliminary study. HPV6 was the most frequent LR-HPV in both HPV+ groups with a percentage of 26 and 29 %, respectively. In the HIV+/HPV+ male fraction, HPV6 had a prevalence of 27 % and was detected in (11/24, 45%) anal swabs, whereas in female fraction the most frequently detected in cervical swabs was the HR-HPV31. In the HIV-/HPV group, 23% males presented HPV53 compared to female in which HPV 16 and 6 were the most detectable types in cervical swabs. In general, HIV+ male patients, with a CD4 cell count < 200 cells/mm3 had a higher HR-HPV types prevalence (16,51,53) in the anal swabs compared to HIV+ patients with CD4 count > 500 cells/mm3, in whom LR-HPV types were identified more frequently.

Conclusions: Our data, collected in one year (2019), revealed HPV6, as the most detected type in both HPV+ group of HIV+/- patients, with no obvious differences in prevalence. HPV31 was the most frequent (60%) in HIV+/HPV+ female fraction, showing that immunodeficiency may contribute to increase the susceptibility to HPV31 infection. The association between HR-HPV types and CD4 count <200 confirmed the importance of monitoring HIV/HPV co-infected patients. In HIV-/HPV+ patients, HPV53 was detected in 22% subjects (SOPRA ERA 23%), against which the vaccine (9vHPV) does not afford protection. Our preliminary data show the importance of a multidisciplinary approach for early detection, follow up and health education, mainly in risk populations.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 189 HIV AND STIS AMONGST MSM IN ITALY: DATA FROM THE EMIS 2017 SURVEY

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Background: Reliable data on HIV prevalence and sexually transmitted infections (STIs) amongst men who have sex with men (MSM) in Italy is limited, mainly due to the lack of data on the size of the national MSM population. Information regarding the extent to which MSM are affected by HIV and STIs is essential in order to shape public health initiatives including effective HIV/STI prevention programmes.

Methods: EMIS 2017 was an internet based self-completion survey funded by the EU Health Programme 2014-2020. It enrolled 127,000 MSM from 47 European and Central Asian countries between October 2017 and January 2018. The Italian dataset comprised 11,025 respondents; data was analysed using STATA V13.0 adopting a descriptive approach to generate estimates and related confidence intervals.

Results: 74.15% of respondents (CI: 73.32-74.95) identified defined themselves as gay or homosexual, whilst 17.60% (CI: 16.90-18.32) identified as bisexual. Mean age was 38.78 (St Dev: 12.36; range 14-84). In terms of HIV testing, one in five respondents (20.14%; CI: 19.39-20.89) had never tested, ranging from 16.81% in Central Italy to 28.72% in Southern Italy. 1,100 respondents had been diagnosed with HIV giving a prevalence estimate of 9.98% (CI: 9.43-10.55) in our sample. Amongst those who declared to be HIV+, the vast majority (99.62%; CI: 0.99-1.00) reported being on antiretroviral treatment. In terms of syphilis, 1.717 MSM (15.65%; CI: 14.97-16.33) reported that they had diagnosed with syphilis at least once, and 405 (3.73%; IC: 3.38-4.09) declared they had been diagnosed in the last 12 months. As for other STIs, 641 participants (5.85%; IC: 5.42-6.30) reporting being diagnosed (lifetime) with Chlamydia or LGV, 219 with Hepatitis C (1.99%; CI: 1.74-2.26), and 1,915 with anal/genital warts (17.41%; IC: 16.71-18.13). 13.63% of respondents were not vaccinated for Hepatitis A (CI: 13.00-14.28) and 9.86% (IC: 9.31-10.42) were not vaccinated for HBV; both due to being natural acquired. A high proportion of respondents (36.80%; IC: 35.90-37.70) did not complete their course of vaccination against hepatitis B.

Conclusions: Self-reported data from EMIS 2017 survey show a high prevalence of HIV infection which is in line estimates from other sources. Of particular concern however, is the large proportion of those having never tested (1 out of 5). Also, although no prevalence studies are available for STIs amongst MSM in Italy, distribution of STIs diagnoses is in line with data from the Italian National Institute of Health. There is a need for improving vaccination programmes for hepatitis A and especially B and for targeted programmes for improving HIV and STIs testing practices amongst MSM.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 190 NEVER INFECTED. PERCEPTION OF THE RISK OF HIV INFECTION IN CASE OF UNDETECTABLE VIRUS

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The conclusions of the PARTNER studies (2019) have provided scientific evidence on the principle Undetectable=Untrasmittable: people with ART treatment with HIV, with undetectable viral load, do not transmit the virus. Starting from this assumption, this research has two objectives. First, it aims to provide an analysis of the state of the most recent knowledge of the infection in the population; the second objective is to assess the risk perception associated with HIV infection in the event of an undetectable viral load.
The research aims to answer these questions:
- Are there differences among people regarding the perception of the risk of HIV infection?
- The evolution of the treatments ensued an evolution of the general perception of the disease?
- How does the perception of early awareness of the infection change?

The study, still under way, is made by the Dept. of Social Sciences of the Univ. of Naples Federico II in collaboration with UOC Infectious Diseases AOU Federico II, and is conducted through the administration, from Jan. to March 2020, of papers and on line questionnaires, on a self-selected sample of 300 people living in Naples, and a focus group with health workers and HIV experts.
The data emerging from the analysis of the first 62 questionnaires collected (25 of which were people with HIV) outlines a bias between a group that relies on medicals and perceives the infection and their own health solely under the "being cured" lens (we define them "hiv+ in cure"), and a group that is more open to the evolution of of the infection and in taking care of themselves ("hiv+ in care").
Among the "hiv+ in cure" there are people who declare they are not aware of the viral load. One in four HIV+ respondents in the sample responded negatively to this "control question". They define the virus «like a monster», «evil». Among "hiv+ in care", there are people who declare they are aware of their viral load, and define the virus as «totally controllable. More than a physical, a social disease». HIV- respondents present variable opinions more oriented towards the "hiv+ in care" in case of: higher educational qualification, independent profession, origin from metropolitan city.
The "hiv+ in cure" generally show less agreement with the statement "If the virus is undetectable it cannot be transmitted" (Tab.5 of attachment) or the statement "If the virus is not detectable in the mother, natural breastfeeding does not involve any risk of contagion" (Tab.4). There is greater agreement on the other statements.
The study suggests that a new stage in the history of the infection has started but this must go through a wider recognition of the citizenship rights of people with HIV+. The concept of treatment can no longer be associated with antiretroviral therapies only, but it must be part of the overall experience of care relationships (Corbisiero,2018). Only in this way is it possible to prevent naive (Maraolo, Cotugno,2018) or late presentation behaviors

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P 191 LINKAGE TO CARE IN HIV: THE POINT OF VIEW OF PEOPLE WITH RECENT DIAGNOSIS

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Background and Methods: Little is known about the duration of the time from HIV diagnosis to the first prescription of ARV and difficulties/opportunities encountered. An exploratory survey was conducted between June and Oct. 2019 among people with a recent diagnosis of HIV infection (after 1/1/2016) on individual experiences from HIV diagnosis to ARV initiation, as part of the Linkage to care in HIV project. A further step towards the analysis of the continuum of care in HIV in Italy. An anonymous investigation was conducted through a web-based, self-completion questionnaire. The survey was advertised using leaflets and in several social networks and organisations' websites.

Results: In total, 244 valid questionnaires were collected. Median age was 39 years (IQR: 33-46), 87.5% males, 91.8% Italians. More than 80% had a high education level (high school diploma or above), have a stable job and live in their own house. Most of the participants (71.3%) report they acquired HIV through sex with same-sex partners. 86 live in Northwestern regions 34 in the North East, 80 in the Center, 44 in the South. 84/244 found they acquired HIV after performing a rapid test or self-test (15.5%), mostly in people <30 years. 35/244 (14.3%) people had the venous sampling for HIV diagnosis at a private laboratory.

The positive test result was communicated during a counseling interview in 81.2% of cases. 56.5% said they had symptoms or other conditions before or at the time of diagnosis that made them think of a potential HIV infection. 218/244 (89.3%) were provided with information at the time of diagnosis; among the latter, an appointment for the first visit at the ID centre was provided in 64.7% of cases. Twelve people (4.9%) had their first appointment at the ID centre 30 or more days after the confirmatory test (Fig.1A). Twenty people (8.2%) reported having started therapy more than 60 days after completing the full tests (Fig.1B). When asked about which aspects in their life were influenced the most by the diagnosis of HIV infection in the first 6 months, only 7% said they did not have a particular area. In the remaining 93% of cases, affectivity and/or sexuality and psychological balance are the most affected aspects (Fig.2). When asked if they ever felt unjustly treated or discriminated against for having HIV, 30.3% said this happened at least once (12% did not want to answer the question) (Fig.3).

Conclusions: Our sample is not highly representative of the recently diagnosed people with HIV in Italy: almost half of the respondents live in Lombardy and Lazio and are mainly represented by men who said they contracted HIV by having sex with other men. Nonetheless, the period following diagnosis is a source of great stress. In this population, there seems to be a progressive reduction in the time for accessing treatment services. Further investigation is needed, especially among more socially vulnerable populations. Funded by Minister of Health (ref 4023/P.G.1)

Social and behavioural science, marginalized groups, community aspects and community surveys

P 192 AIDS AND OTHER SEXUALLY TRANSMITTED DISEASES: WHAT DO YOUNG PEOPLE KNOW? – A CROSS SECTIONAL STUDY

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Background: According to World Health Organization, more than one million of Sexually Transmitted Diseases (STDs) are contracted daily. The average number of partners of an Italian before 40 years old is increased in the last twenty years. More than 50% of the subjects between 18 and 40 years has had unprotected sexual intercourses. This study aims to understand how much young people know about STDs and risky behaviors and how they perceive the importance of being informed about this topic.

Methods: This cross-sectional study enrolled 427 subjects, aged from 18 to 35 years living in an Italian medium-sized Northeastern town or nearby. Data have been collected by means of an online questionnaire consisting in three sections: demographic data, "knowledges" and "behaviors". Each correct answer in the knowledge section counted as 1 point, for a maximum of 30 points. Statistical analysis was performed in order to assess relations between knowledge section scores and subjects' characteristics (i.e. age, gender, address, education, current employment, sexual orientation, marital status, faith), and the answers provided in the "behavior" section.

Results: Several lacks in knowledge of STDs can be pointed out and a significant percentage of young people has behaviors that increase the risk of contracting STDs. The "knowledge" section is not influenced by education level ($p=0,47$) or by risky sexual behaviors ($p=0,63$). However sexual risky behavior seems to be related to sexual orientation ($p=0,0023$) - in particular heterosexuals are less informed than non-heterosexuals - to current employment ($p<0,001$) - showing that people that work in health care environment are better informed - and faith ($p=0,0005$) pointing out the gap of knowledge between atheists and Catholics, being the latter less educated. Young people actually would like to be more informed and consider to be appropriate a proper education about STDs involving all population.

Conclusions: Having potentially risky sexual behaviors, young people are not enough informed or educated about STDs and how they are transmitted. It should be noticed that education level does not have an impact on STDs knowledge. It appears however that some groups could be less informed, like heterosexuals and practicing Catholics. These facts may suggest that nurses, as well as other healthcare professionals, educators and teachers, should provide proper sexual education. A good knowledge about STDs could improve healthy behaviors and help to fight the stigma that often involves people who contracted STDs.

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P 193 PREVALENCE AND RISK FACTORS ASSOCIATED WITH NEW DIAGNOSIS OF STI IN INDIVIDUALS ATTENDING AN IN-HOSPITAL STI CLINIC

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Introduction: Epidemiological reports suggest an increasing incidence of sexually transmitted infections (STIs) in Europe. It is important to identify high-risk populations to tailor intervention strategies in terms of prevention and treatment. We analyzed the characteristics of individuals attending our in-hospital STI clinic, the prevalence of STIs and the associated risk factors.
Methods: From November 2018 to September 2019, information about educational level and sexual behaviour were obtained from individuals attending for the first time our STI clinic at San Paolo Hospital, Milan. Every subject received a visit by an infectious diseases physician, performed serological testing for HIV, HAV, HBV, HCV and syphilis, as well as urethral, pharyngeal and rectal swabs for cultural examination of N. gonorrhoeae and NAAT on urines and rectal swab for C. trachomatis. We defined STIs as follows: i) new serological diagnosis of HIV, any acute or chronic hepatitis or syphilis, and ii) culture or NAAT positivity for C. trachomatis or N. gonorrhoeae. Risk factors for STIs were evaluated by uni- and multi-variate logistic regression analysis. Only variables with $p < 0.05$ were considered statistically significant.
Results: During the specified period we enrolled 139 patients. Demographic characteristics and sexual habits are showed in table 1.
97/139 (70%) underwent screening by swabs and NAAT: 9/97 (9%) resulted positive for gonorrhea, (2 at urethral, 1 at vaginal, and 7 at rectal site, with a single case of infection at two sites); 15/97 (15%) resulted positive for Chlamydia (6 at urethral and 9 at rectal site). Infection by both bacteria were detected in 3/97 (3%). Only 40/139 (28.7%) patients were symptomatic at presentation. No difference in the prevalence of swab or NAAT positivity was observed according to presence of symptom at presentation (21.8% in symptomatic vs. 18% in asymptomatic).
By serological screening, we identified 9 cases of syphilis (5 early and 2 late latent, 2 secondary syphilis), 1 case of acute HBV infection and 1 new HIV diagnosis.
At univariate analysis bisexual habit [OR 7.2 (1.7-30), p=0.007], receptive anal sex [OR 6.4 (1.4-30), p=0.02], and any STI during the previous year [OR 3.7 (1.5-9.5), p=0.009] were associated with an increased risk of a new STI. At multivariate analysis, receptive anal sex [aOR 5.9 (1-35), p=0.04] and any STI during the previous year [aOR 7 (2-24.6), p=0.002] were confirmed as risk factors associated with an increased risk of a new STI (Table 2).
Discussion and conclusions: History of receptive anal sex and previous STI were risk factors for new STIs in our population. The increased risk of bisexual subjects is consistent with data from other studies concerning high risk population, as seen also for transgender people. The absence of a predictive role of symptoms on STI positivity underlines the importance of more frequent screening, particularly in high risk population, to limit STI spread

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P 194 SRHR SENSITIZATION AND EDUCATION ACTIVITIES FROM MEDICAL STUDENTS

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SRHR Sensitization and Education activities from Medical Students
SISM is a volunteering Association, member of IFMSA.
It's active in 39 Local Committees all over Italy, covering almost all the Medicine and Surgery Faculties. It's involved in effective sensitization, information and education activities targeting general population, Medical students, health professionals and several stakeholders.
Background: SISM is a no-profit Association of the International Federation of Medical Students' Associations, recognized as a NGO within the UN and the WHO.
Since 1970 it has been acting, training and advocating for SRHR with several parteners.
Material, methods: SISM uses Non Formal Education methods to train its members and make them prepared to manage activities at different levels.
Trained Peer Educators manage Comprehensive Sexuality Education Activities in Middle and High Italian Schools through explanations, games, exchange of understandable information; always in a precise way, following a nationally standardized agenda. Every session is preceded and followed by the administration to children of an 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.
SISM volunteers also organize sensitization and information conferences and activities all over the year, dedicated to different targets and places.
SISM continues evolving and growing up with its volunteers Advocacy and External Representation skills, approaching important stakeholders nationally and internationally: Italian Parliament, AMEE Conference, National Dean's Council, HIV Coalition, Anlaids, Intercultura, UNAIDS and so on.
Results: SISM's Peer Education Project involves circa 160 classes of Italian schools every year, approaching approximately 1600 students. This project also comprehend a CSE program managed in Italian and in English with Intercultura, that involves 25 different Italian cities every year.
SISM's sensitization activities, during Thematic days such as WAD and Candlelight Memorial, but also during the rest of the year, involve 39 Italian cities and an incalculable number of people. They're organized in hospital, streets and public places. They comprehend structured and nationally defined social campaigns, based on reliable and official sources, in order to reach as many people as possible.
Conclusions: SISM activities are great opportunities for the growth and education of the population, especially regarding HIV, STIs and SRHR.
Medical Students can be able to communicate important health topics to the population in a more effective way: as students, they can understand the topics and explain them to the population, by whom are still considered peer.
In this way, Italian medical students hope to contribute in building a world in which every citizen is informed about their own sexuality, including risks, possibilities, rights and duties

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P 195 "SENZA LA C" - HCV DIAGNOSIS AND TREATMENT FOR PEOPLE WHO INJECT DRUGS IN A COMMUNITY-BASED SETTING: RESULTS FROM AN EXPERIENCE IN BOLOGNA

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Background: Eradication of HCV infection is still a challenge in specific groups of people such as people who inject drugs (PWID). Previous data show poor access to HCV treatment, delay in HCV treatment initiation and problems for retention in care in hospitals.
The aim of this study is to evaluate retention in care for PWIDs diagnosed and treated for HCV infection in a community-based setting.
Material and Methods: "Senza la C" project started in January 2019 and involved screening for HCV infection and offer of HCV treatment for PWIDs diagnosed in shelters, services for PWIDs and on the street in Bologna.
Individuals were screened using saliva rapid tests (OraQuick® Rapid HCV Antibody by OraSure Technologies); pre-test peer counseling was offered by educators from OpenGroup, a community-based service for harm reduction; standard blood tests for HIV-Ab, HBsAg and HBsAb were also offered.
In case of reactive saliva HCV-Ab test, a point of care HCV-RNA test on whole blood (Xpert® HCV VL Fingerstick by Cepheid), a transient elastography (Fibroscan®) and a liver echography were performed; those who resulted HCV-RNA positive were tested through standard blood test for liver and kidney function and HCV genotype and started HCV treatment within 4 weeks.
All diagnostic procedures, drug supplying, treatment monitoring and post-treatment follow-up were conducted in a low-threshold, extra hospital setting by a team of peer educators, medical doctors and trained nurses. This study was funded by research grants from AbbVie srl and Gilead sciences.
Results: 343 PWIDs were screened for HCV using saliva test; 67 (19.5%) had a reactive result; 45/67 (67.2%) were linked to the extra-hospital service.
29/45 (64.4%) were HCV-RNA positive.
Median liver stiffness at the baseline was 6.5 kPa [range 5.4-8.3]; 13.8% had cirrhosis, 3/29 were HIV/HCV coinfected.
26/29 (89.7%) are retained in care nowadays; 21/29 (72.4%) completed the treatment. 19 persons reached 12 weeks of follow-up and 18/19 (90.9%) achieved SVR12, while 1 person had reinfection at week 12 of follow-up. The project was stopped in November 2019 because funding is no longer available.
Conclusions: HCV counselling, testing and treatment in an extra-hospital setting is feasible and can lead to high retention in care rates in our cohort of PWIDs.
Longer follow-up will provide more data about HCV treatment efficacy in this population.

Social and behavioural science, marginalized groups, community aspects and community surveys

P 196 WE TEST - NATIONAL COMMUNITY-BASED HIV PREVENTION PROGRAM

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Background: ARCO is a non-profit association created in 2018 by the historical network of LGBTI clubs in Italy, which are in the 90% of cases attended by men.
We Test is the first countrywide and community-based HIV prevention program in Italy and is promoted by: Arcigay – Associazione LGBTI+ Italiana, ARCO – Associazione Ricreativa Circoli Omosessuali, Associazione Culturale e di Volontariato ARC Onlus, ASA – Associazione Solidarietà AIDS Milano, Circolo di Cultura Omosessuale Mario Mieli, Ireos – Centro Servizi Autogestito Comunità Queer, NPS – Network Persone Sieropositive Onlus, NUDI – Nessuno Uguale Diversi Insieme, Plus – Persone Lgbt Sieropositive Onlus
Materials and methods: On the occasion of the World AIDS Day 2018, the partnership decided to extend the testing activities, usually organized in December, to the whole year.
A common website and a facebook page were created to promote We Test "events" through the same communication channels. Four kinds of locations were individuated to reach the LGBTI community: Gay Saunas, Bars & Discos, Associations and Mobile Units.
More than 10 local partners and Italian media Gaynews supported the initiative. The testing activities joined different expertise: the hosting entities and the partners providing know how, volunteers and medical staff. Locations were previously verified to warrant adequate places for testing and separate spaces to ensure privacy.
Two kinds of test have been used: the INSTI TEST HIV, from Screen Italia, and the Alere HIV Combo, from Abbot.
Results: Between December 2018 and November 2019, 100 We Test events were organized and 3727 people were tested in over 15 cities: Torino, Milano, Padova, Verona, Desenzano del Garda, Bologna, Firenze, Roma, Napoli, Bari, Pescara, Senigallia, Catania, Cagliari, Palermo and Sassari. 40 people were found positive. Furthermore, five training days were organized targeting personnel and volunteers of the hosting places with a capacity building activity to improve their approach with the people and give information about the project in the most appropriate way.
The partnership considered this first year of the project as a pilot action to implement the collection of new data in 2020. All partners signed a data collection agreement in order to obtain homogeneous information from each partner's monitoring questionnaires.
Conclusions: Positive feedback came from 90% of the testing venues. Most of the population reached had a scarce awareness of sexual health and uneasiness in attending healthcare settings. The partnership agreed to continue the project in 2020. The data collection agreement will allow to gather information about age, gender, sexual orientation, nationality, when a person had the last HIV test, whether a person has ever been tested for HIV and whether a person used a condom during the last sexual intercourse.

Vaccines

P 197 ANTI-BODY RESPONSE TO PNEUMOCOCCICAL VACCINATION IN HIV PATIENT AFTER SUPPLEMENTATION WITH PROBIOTIC

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Background: HIV infection causes an increased risk of infections, but also a chronic inflammation, with visible signs intestine, where a change in microflora is observed (Ziberman-Schapira et al., 2016). Some studies have shown that probiotic use may improve these symptoms in patients receiving cART, favoring the reconstitution of the intestinal mucosa (D'Ettorre G. et al, Immunity,Inflammation & Disease, 2017; Falasca K. et al, Nutrient,2015).
Immune system impairment in HIV+ patient is an additional risk factor for Invasive Pneumoccoccal Disease (25 times greater risk than the general population).
Both National Plan of Vaccinal Prevention 2012-2014 and the most recent EACS Guidelines strongly recommended pneumococcal vaccination is in HIV-positive patients due to the high incidence of invasive pathologies. These advise administration of one dose of PCV-13, without booster dose.
Material And Methods: The primary objective is the evaluation of patients' antibody response to S.pneumoniae, by measuring specific IgG after 1 month from administration of the pneumococcal polysaccharide conjugate vaccine Prevenar -13.
We have enrolled 40 HIV + patients followed by the DH of Infectious Diseases of the University D'Annunzio in Chieti, homogeneous by gender, age and CDC classification. Randomization will take place according to the block method. Patients will be assigned to one of the two groups with probability of 0.5 for each group.
The first group will take probiotic supplementation (2 + 2 sachets per day of Vivomixx / Visbiome, containing the De Simone formulation) administered via oral and a second group will take. Both groups will take supplementation for 4 weeks before vaccination and 4 weeks after vaccination.
Results: Dosages of Ig are in progress and we expected that probiotic supplementation in HIV + subjects before and after antipneumococcal vaccination can improve the antibody response.
Conclusions: Probiotic supplementation is a common practice to control dysbiosis in many chronic inflammatory conditions, such as inflammatory bowel disease with positive effects on the clinical outcome (Shen et al., 2014). Probiotics modulate the composition
of microbiota, carrying out immunomodulatory effects through action on the NF-kB, expression of costimulatory molecules by antigen-presenting cells (APC). Some lactobacilli induce the maturation of dendritic cells and modulate the T lymphocyte response and cytokine production. We had use a mixture of strains selected for their specific characteristics
in order to increase the immunostimulating activity on both B lymphocytes, T lymphocytes, phagocytic cells.
Many studies have shown that the administration of probiotic improves antiboby response in the elderly (Borge T et al. Vaccine 2009). Consequently, the administration of probiotics to HIV patients finds its rationale in improving immune defenses.

Vaccines

P 198 ADHERENCE TO THE INFLUENZA VACCINATION CAMPAIGN: EXPERIENCE OF A LARGE CLINICAL CENTER

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Background: HIV infection is associated with a higher risk of influenza acquisition and an increased risk for complications and consequently higher rates of hospitalizations and mortality. Although ART has shown to reduce the concomitant infection with transmittable diseases, the risk of severe outcomes in people living with HIV has been proved to be the same as other vulnerable populations where influenza vaccine is recommended.
Materials and methods: We retrospectively analyzed people living with HIV who attended their routine visits at the Department of Infectious Diseases at "Agostino Gemelli" University Polyclinic of Rome from mid-October to the end of December 2019. All of them were offered free anti-influenza vaccination. Adherence to the program as well as clinical and viro-immunological features of the population were collected.
Results: 679 routine follow-up visits were held for HIV positive patients over the last two and a half months of 2019. As indicated in local guidelines, anti-influenza vaccination with either a trivalent, surface antigen, inactivated influenza vaccine adjuvanted with MF59C (Fluad®) or a surface antigen, inactivated, influenza vaccine prepared in cell cultures (Flucelvax®) was offered. Surprisingly among those proposed with vaccination, only 277 patients (40,7%) underwent the vaccination. Women (n=221) appeared to be less willing to undergo vaccination when compared to men (n=458) as only 82 women (37,1%) accepted to be vaccinated versus 195 (42.5%) for their male counterparts. On the other hand, elder patients (>50 years of age, n=424) were not found to be more eagerly vaccinated (40,5%, n=172) when compared to younger patients (<50 years of age, n=255) who got vaccinated in the 41,1% (n=105) of cases. Patients' clinical and viro-immunological features are shown in Table 1.
Although detection of delayed adverse effects has not been conducted yet, no immediate adverse or anaphylactic reaction has been witnessed at vaccine administration.
Conclusions: Although a concurrent free influenza vaccination strategy was offered to patients at the time of routine visits in our seasonal anti-influenza campaign, patients appeared to be not eager to undergo this vaccination. The lack of a vaccination record (transversal between specialists and family doctors), the spread of the no-vax movement, the common belief that influenza is a harmless condition and misinformation through the mass media may be the causes of such a reluctance to get vaccinated even in vulnerable categories.
Since compliance was sub-optimal with a rate of adherence of only 40.7%, an active educational and promulgation campaign is to be considered in order to implement future adherence to the vaccination program.

Vaccines

P 199 HPV ORAL INFECTION AND CLEARANCE IN MEN WHO HAVE SEX WITH MEN AND TRANSGENDER WOMEN UNDERGOING NONAVALENT VACCINATION: PRELIMINARY RESULTS FROM AN INTERVENTIONAL STUDY

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Background: HPV infection is common in men who have sex with men (MSM) and has been identified as causative agent for anal cancer in more than 90% of cases and for oral cavity cancer in 22.4%. A recent Italian study reported that around 20% of HIV+ subjects showed HPV oral infection: they generally carried only one viral strain; half had a high-risk genotype (hrHPV) but only 26.6% would benefit from nonavalent vaccination (NvV). Aim of present study is to describe HPV oral new infection and clearance of previous contaminations after NvV in a cohort of MSM and transgender women (TGW).

Methods: This monocentric, prospective analysis included all MSM and TGW who started NvV from May 2019. Previous vaccination was the only exclusion criteria, while subjects older than 45 years were eligible. Enrolled subjects collected oral rinse when they received the first NvV dose, at the second (T2) and third (T6) dose and then after six months of follow up (T+6). Cellular pellet was extracted through an automatic easymag platform and analyzed with reverse in situ hybridisation. INNO-LiPA HPV Genotyping Extra II assay identified 13 hrHPV (16,18,31,33,35,39,45,51,52,56,58,59,68) and other 19 intermediate and low risk genotypes. Demographic, behavioral and clinical features were collected. Descriptive statistics and non-parametric (Chi-square and Mann-Whitney U, as appropriate) tests were used. Local Ethics Committee approved the study protocol. All subjects provided written informed consent. Enrollment is still ongoing to reach the planned sample size of 140 individuals.

Results: So far, 90 subjects were included in the analysis: they were mainly MSM (94.4%), Italian (83.3%) and with a median age of 42 (IQR 32-50) years. HIV+ subjects were 60% and 32.2% reported recreational drugs use during sex. A large majority (80%) had at least one previous STI; 27.8% had one earlier episode of anal condylomas: for those who had genotyping data available, hrHPV were extremely common (48.8% had genotype 16).

At baseline, 13% had a positive oral rinse: they generally showed a single, low-risk genotype not covered by NvV. A concomitant sexually transmitted infection was uncommon (6.7% had gonorrhoeae, 5.6% chlamydial urethritis and 3.3% syphilis). No difference was observed among those who tested positive and negative: in particular, HIV infection was similar (57.1% versus 68.1% respectively, p=0.603).

Forty subjects reached the T2 time point, 12 T6 and none T+6. Nobody acquired a new oral infection. Oral rinse tested positive in 7.3% at T2 and in no sample at T6 but HPV decline after NvV was not statistically significant (Figure 1, p=0.474).

Conclusions: Our data confirm that HPV in oral rinse is uncommon and scantily covered by NvV. These results suggest that NvV might have a role in protecting from new oral infections, while it weakly affects the clearance of previous contaminations.

Vaccines

P 200 IMMUNIZATION STATUS IN A PEDIATRIC TRANSPLANTED COHORT: THE FEDERICO II TEACHING HOSPITAL EXPERIENCE

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Background: Ortotopic liver transplant (OLT) at an early age is a lifesaving procedure in children with a heterogeneous group of diseases. Transplanted patients (PTNs) are subjects at high risk of acquiring infections and, because of the immunosuppressants, their risk of developing complications is higher. Moreover, attenuated vaccines can't be given to those PTNs, due to the risk of viral reactivation and its consequences.

Materials & Methods: We reviewed medical charts of OLT PTNs in regular follow-up at the Federico II teaching hospital till December 2019, searching for data on both vaccines injected and serological status of PTNs underwent an OLT. Attention was focused on 2 informations: the administration of measles-mumps-rubella (MMR) and varicella (VZV) vaccines; the durability of the immune response against hepatitis B vaccine (HBV). The first because both the vaccines can't be performed in immunosuppressed PTNs; the second in order to understand if the immunosuppression can compromise the serological title against HBV s antigen (HBsAb).

Results: 31 on 43 PTNs analyzed had complete documentation (16 males). The most frequent cause of OLT was biliary atresia (22 PTNs, 8 males). In OLT PTNs, mean and median age (months) at OLT were 17.5 and 8 [1-84], standard deviation (SD) and 95% confidence interval (CI) were 19.3 & 10.44-24.59; mean and median age (years) at the time of last follow-up were 11 and 12 [1-18], SD and 95%CI were 4.9 & 9.2-12.8. In atresic PTNs, mean and median age (months) at OLT were and 16.2 and 8 months [5-72], SD and 95%CI were 16 & 9.1-23.3; mean and median age (years) at the time of the last follow-up were both 11 [1-18], SD and 95%CI were 4.8 & 8.8-13.1.

MMR vaccine was performed in 54.8% in OLT PTNs and in 31.8% cases in the atresic subset; VZV vaccine was done in 19.4% overall PTNs and in 22.7% atresic PTNs. The difference in vaccinations between the 2 groups wasn't statistically significant (p=0.09). Not enough data were available to evaluate the trend of serological response to those vaccinations in time.

In OLT PTNs, HBsAb after OLT was positive in 29% cases, negative despite boosting doses in 35.5% cases, in 19.4% cases became positive after a boosting dose but then return negative, in 16.1% cases was never performed.

Conclusions: While the small number of cases prevent conclusive statements to be done, we observed challenges in performing the attenuated vaccines mainly due to the age at the OLT, in particular for atresic patients. These findings underscore the high-risk status of these PTNs. The discrepancy observed between MMR and VZV vaccinations is highly likely due to the not mandatory administration of the VZV vaccine at the time of vaccination of the oldest PTNs. The possibility of an earlier administration of both MMR and VZV vaccines to elicit an immune response should be investigated. Studies should be conducted in order to fathom if a regular boost should be given to PTNs with a negative HBsAb status.

Vaccines

P 201 VACCINATION KNOWLEDGE, ATTITUDES AND PRACTICES IN PATIENTS WITH HIV: A CROSS-SECTIONAL SURVEY

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Background: HIV patients present more frequent and serious infectious diseases, thus vaccination is very important and effective for this specific subgroup of the population. 5 years ago a strong implementation of vaccination policy started in our centre. HIV patients show different response to vaccines and a diminished protection. It is therefore very important to assess knowledge and attitudes towards vaccination in people with HIV, since precise vaccination coverage and vaccine hesitancy are not well established in this subgroup of patients.
Methods: A total of 119 patients with HIV completed a cross-sectional survey. The study received the approval of Ethics Committee. Patients were recruited during their routine medical examination at the infectious diseases clinic in Turin. The survey explored these main areas: demographics and history of HIV infection, vaccination history, attitudes towards vaccination, confidence in the public health system, disease seriousness and contagion risk perception. Descriptive analysis were conducted in this preliminary phase.
Results: Preliminary data show that 20% of the participants were females. The mean age was 49.51 years. The median CD4 count was 762.50 cells/mm3, plasma HIV-RNA was undetectable in 99 % of cases while the median of HIV infection duration was 10 years. All subjects were receiving antiretroviral therapy.
The disease with the highest seriousness perception was HBV (95.3%), which also has one of the highest vaccination coverage (81%). Nevertheless, only 21.62% of the non-vaccinated patients expressed the willingness to undergo vaccination.
Rubella and measles also had a low vaccination coverage (33.7% and 35.6% respectively) and a low willingness to undergo vaccination among the non-vaccinated patients (14.06% and 17.54% respectively); this is consistent with the low or very low risk perception regarding these two diseases (89.2% and 90.3% respectively).
The disease with the lowest seriousness perception was flu (53.4%), with the risk of infection considered low or very low by the majority of patients (51.9%). This is consistent with a low vaccination rate (48%) and a scarce willingness to undergo vaccination (21.57%).
On the other hand, 90.2% of the participants stated that health care workers do not have economic interests in vaccines and 78.8% did not think that vaccines are an imposition rather than a free choice.
Conclusions: In the HIV patients there is still some misperception regarding certain diseases which are thought to be infrequent or not serious, so vaccination coverage cannot be considered fully satisfactory yet. However, the fact that the majority of the participants did not think that vaccines represent an economic interest for health care professionals or an imposition leads to the conclusion that there is concrete possibility to implement informative and operative strategies about vaccination for this particular subgroup of the population.

Vaccines

P 202 SUCCESS RATE AND EVOLUTION OF IMMUNOLOGICAL PARAMETER OVER FIRST VACCINATION AGAINST HBV WITH FENDRIX© IN PEOPLE LIVING WITH HIV

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Background: PLWH have an increased risk of acquiring HBV and are also at high risk of developing liver-related disease. Vaccination is strongly recommended by all current guidelines. However standard vaccination strategies provide PLWH with protective response with low and variable rates (18-71%). Trials on efficacy of re-vaccination with adjuvated vaccines showed higher efficacy compared to standard strategies.
Methods: Due to the lack of standard vaccine (Engerix©) in Italy, from July 2018 to November 2019, we performed the first line vaccination against HBV with the adjuvated vaccine (Fendrix©), and monitored protective titre of HBsAb and immunological response (lymphocyte count, CD4+ T cell count, CD4/CD8 ratio) over time.
Results: The study included 16 PLWH who were vaccinated during 2018/2019, 75% were males and 25% were females and the mean age was 49.3 years (SD: 9.1). Mean time from HIV diagnosis was 11.8 years (SD: 9.1). No patients developed adverse events over the vaccination route. Median values (and IQR) of immunological parameters before and after vaccination are reported in Table 1. A mild increase was found in CD4/CD8 ratio, even if not statistically significant, while a statistically significant decrease was observed in lymphocyte count (p=0.009). Response to vaccination (i.e., HBsAb titres> 10 IU/ml) was observed in all patients. After vaccination route, median HBsAb titre was of 633 IU/ml (IQR: 76-709).
Conclusion: Our study showed that using adjuvated vaccine as a first line strategy for HBV vaccination is safe and effective. It seems also to have not an impact on immunological parameters. Possible effect on lymphocytes needs to be explored. Lastly, it is important to monitor HBsAb titres over time to check if it allows obtaining a higher long lasting immunization.

Vaccines

P 203 ORGANIZATION OF A DEDICATED VACCINATION SERVICE FOR HIV-POSITIVE PATIENTS, PRE-EXPOSURE PROPHYLAXIS (PREP) USERS, AND PATIENTS IN CARE FOR SEXUALLY TRANSMITTED INFECTIONS (STIS): THE EXPERIENCE OF S.M.ANNUNZIATA HOSPITAL, FLORENCE

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Background: Vaccinations represent a primary strategy for health promotion in HIV patients and for prevention of sexually transmitted infections (STIs) in high-risk populations, as indicated by national and international guidelines.
In February 2019, Tuscany Region published the update of the vaccination schedule recommended in immunocompromised patients.
Material and methods: In July 2019 the Infectious Diseases Unit of S.M.Annunziata Hospital (Azienda USL Toscana Centro), Florence, set up a dedicated vaccination service. The aims were: 1- to promote a quick access to vaccinations for HIV patients, Pre-Exposure Prophylaxis (PrEP) users, and patients who access the service for STIs at our Unit; 2- to assess the effectiveness and adverse events.
The service was active twice a month, and was managed by an healthcare assistant with a medical-nursing supervision.
Before being evaluated for vaccinations, all patients performed a baseline viroimmunological assessment (HIV-RNA, CD4) and a serological screening.
Informed consent was acquired.
The vaccination offer included: anti-meningococcus B (MenB) and ACWY (MenACWY), anti-pneumococcal 13 and 23 valent vaccine (anti-Pneumo), anti-papillomavirus (HPV), anti-hepatitis A (HAV) and B (HBV), anti-flu (H1N1/H3N2/B Colorado/B Phuket), anti-Haemophilus (HiB), anti-measles/pertussis/rubella (MPR), anti-diphtheria/antipertussis/tetanus (DTP), and anti-chicken pox (VZV).
Results: From July 2019 to December 2019, 73 patients received one or more vaccinations: 95.9% HIV positive; 4.1% on PrEP, 82.2% M, median age 49.4 (range 21-79 yrs). Among HIV positive patients, risk factor was MSM 51.4%, heterosexual 21.4%, drug use 20%, bisexual 5.7%, not known 1.5%.
At baseline serological screening, 43.9% was susceptible to HBV (chronic hepatitis B 4.1%, previous infection 28.7%, already vaccinated 23.3%), and 64.4% to HAV (previous infection 28.8%, already vaccinated 6.8%).
For patients susceptible to multiple agents, viral hepatitis vaccination was considered a priority, and administered to all people at risk.
Furthermore, 1 anti-MenB, 38 anti-MenACWY, 26 anti-Pneumo, 31 anti-HPV, 30 anti-DTP and 1 anti-VZV were done.
Only one patient refused the proposed vaccination offer; no adverse events were observed.
Conclusions: The institution of a vaccination service received a high interest in HIV patients, PreP users and patients in care for STIs at our Unit; the availability of a dedicated healthcare assistant twice a month, allowed a rapid access to the service for these high-risk populations. Compliance and tolerability rates were high.

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