Highlights of the 17th European AIDS Clinical Society (EACS) Conference, 6–9 November 2019, Basel, Switzerland

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Introduction

The 17th European AIDS Conference (EACS) was held in Basel, Switzerland over 4 days in November 2019. The event was co-chaired by Jürgen Rockstroh and Manuel Battegay. The organisers declared that preventing, diagnosing and treating HIV and AIDS was a shared mission and hoped Basel would become a global village for the exchange of knowledge.

Antiretroviral therapy: today and in the future

Tracy R Glass (Swiss Tropical and Public Health Institute, Basel, Switzerland) opened the only session dedicated solely to antiretroviral therapy [1]. Researchers used the Swiss HIV Cohort Study to look into asymptomatic people living with HIV (PLWH) with a preserved immune system who experience life-long antiretroviral therapy (ART) initiation, and at the virological and clinical outcomes of universal Test and Treat between 2003 and 2018. The authors looked at various outcomes, namely non-adherence (any self-reported missed ART doses), viral failure (VF) defined as HIV-1 viral load (VL) >50 copies/mL on two consecutive measurements achieved after viral suppression or >24 weeks of ART, or the development of new resistance mutations. In multivariate logistic regression models, among 7131 individuals, 74% of whom had started ART when asymptomatic. These individuals were more likely to be younger, men who have sex with men (MSM), better educated, having unsafe sex, have a stable HIV-positive partner, have a lower VL, and started ART in later calendar years.

When looking at trends over time regarding the time to ART after an HIV diagnosis, PLWH in the Swiss HIV Cohort Study started ART earlier in recent years, from a median of 66 and 2 weeks in 2000 and 2018, respectively. When considering the CD4 T cell count at ART initiation over time, despite the increase in those periods of time, this trend started to fade away in more recent years with no significant differences between the two groups (time to first treatment interruption after 2009 was 73 weeks for asymptomatic vs 57 weeks for asymptomatic individuals (P=0.28) and length of treatment interruption was 10 and 11 weeks, respectively (P=0.30).

Treatment adherence, assessed by missed doses in the last 4 weeks, was high at 87% which was constant over time in both groups. Multivariate repeated measures models showed no association between an asymptomatic status at ART initiation and missing any ART dose (odds ratio [OR] 1.03; 95% confidence interval [CI] 0.93–1.15).

Asymptomatic PLWH were at decreased risk of confirmed VF (hazard ratio [HR] 0.87, 95% CI 0.76–1.00, P=0.05) during the entire period of the study, including after 2009. The rate of transmitted resistance was relatively similar between the two groups, but newly-acquired resistance was less common in the asymptomatic group. As a whole, results of this cohort study on ART initiation were encouraging as asymptomatic did as well, if not better, as symptomatic individuals.

Marc Underwood (ViiV Healthcare, Research Triangle Park, USA) presented an assessment of differences in very low-level viremias (viral load <40 copies/mL) and ‘target not detected’ (TND) ones between dolutegravir (DTG) + lamivudine (3TC) 2-drug regimen and DTG + tenofovir disoproxil/emtricitabine (TDF/FTC) 3-drug regimen in the GEMINI-1 and GEMINI-2 studies, through week 96 and by baseline (BL) VL and CD4 T cell count [2]. A similar median time to TND (median of 8 weeks) was observed across groups in observed or snapshot analysis, and through week 96, the proportions of participants with TND were similar at all visits in the DTG+3TC and DTG+TDF/FTC groups. At week-96 analysis, proportions of participants with TND were comparable in both groups, regardless of baseline VL, and regardless of CD4 T cell count only in the observed analysis.

Delphine Sculier (Geneva University Hospital, Switzerland) described the 48-week outcomes in the Swiss SIMPL’HIV study of virologically suppressed patients on standard combination antiretroviral therapy (cART) switching to DTG + FTC as compared to those staying on cART [3]. Participants were randomised 1:1:1:1 to switching to DTG+FTC or to continuing on cART and to patient-centred surveillance regimen defined as reduced biological monitoring and an individualised follow-up compared to continuation of a 3-monthly monitoring. The primary objectives were to assess the efficacy of DTG-based maintenance therapy in virologically suppressed individuals who had been randomly switched from standard cART to a DTG+FTC regimen, as well as the costs of a simplified, patient-centred as compared to standard monitoring. The primary endpoint was the proportion of patients maintaining HIV-1 RNA <100 copies/mL throughout 48 weeks. Ninety-three participants were randomised to DTG+FTC and 94 to cART. In the intention-to-treat analysis; the proportion of patients with HIV-RNA <100 copies/mL throughout the 48 weeks was 93.5% (87/93) in the DTG+FTC group and 94.7% (89/94) in the cART group (difference: -1.2%; 95% CI -7.8–5.6; non-inferiority margin: -12.0%). In the week 48 window, the FDA snapshot virological success was 90.3% vs 91.5% (difference: -1.1%; 95% CI -9.3–7.1%). Therefore, criteria for non-inferiority were met for both the FDA snapshot analysis and ITT or PP analysis. Only one confirmed VF was observed in the cART arm (HIV-1 RNA ≥100 copies/mL on two separate occasions through 48 weeks of follow-up) with no emergence of resistance mutations or treatment change. Overall the rates of adverse events, including

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weight gain, were similar in both groups. Therefore switching to DTG+FTC was non-inferior to cART in maintaining viral suppression through 48 weeks and appears to be a safe maintenance therapy strategy.

The relative risk of failure of a 2-drug regimen compared to 3-drug ones in HIV-1 naïve patients was evaluated via a systematic review and meta-analysis of clinical studies published as full articles from January 2007 to January 2019 [4]. Antonio Russo (Università degli Studi della Campania, Napoli, Italy) described the results of 10 studies including 3495 subjects at 48 weeks. No difference between the two groups was observed in terms of relative risk (RR) of treatment failures (TF) and VF after exclusion of studies using maraviroc, as well as of adverse drug reactions (ADR) leading to regimen discontinuation. The authors have observed a RR of 2.4 for TF in participants with <200 CD4 T cells/mm³ at week 48 in the dual-therapy arm. The week-96 analysis revealed no statistical difference in RR of TF, VF and ADR but data were limited for this analysis. These results suggest that a dual therapy strategy may be used in HIV-1 naïve patients, especially in regimens without maraviroc and in the setting of patients with >200 CD4 T cells/mm³.

Ramon Teira (Hospital de Sierrallana, Torrelavega, Spain) performed a retrospective analysis of the large Spanish VACH cohort study comparing time to discontinuation owing to (TF) and adverse events (AEs) of DTG-based 2-drug combinations (2DC) (DTG+3TC and DTG+rilpivirine (RPV)) versus an integrase inhibitor (INSTI)-based triple-therapy (TT) in a real-world setting [5]. Treatment failure was defined as clinician’s report of VF, immunological failure or disease progression. All patients switching to INSTI-based TT or the above 2DC between 2 May 2016 and 15 May 2019 were included. Altogether 5047 TT and 617 2DC patient regimens were analysed. Baseline patient-regimen characteristics differed between groups with the 2DC one being older and more treatment-experienced but with a higher proportion of virological suppression at switch. Time to discontinuation due to TF was significantly shorter on 2DC versus TT (P<0.0001) but no difference was observed in time to and risk of treatment discontinuation due to AEs.

The hazard ratio (HR) of risk discontinuation due to TF was 2.3 times higher on 2DC vs TT (P=0.0033 after controlling for demographic and clinical characteristics. No difference was observed for time and risk of discontinuation due to AEs (HR 0.8, P=0.488). Results were maintained when looking at discontinuations due to VF (HR 2.236, P=0.024) and when restricted to patients with VL <50 copies/mL at switch. In this real-world setting, the risk of discontinuation due to TF and VF was more than double in patients switching to DTG-based 2DC compared to INSTI-based TT, with no difference in discontinuation due to AEs. Results were similar when restricting the analysis to patients suppressed at the time of switch, when comparing matched samples (by age, gender, number of previous VL and treatment line). Unfortunately no data were presented on viral load, emerging resistance at the time of VF, or archived mutations at baseline.

Jade Ghosn (SMIT CHU Blicth, Paris, France) described HIV-1 RNA kinetics in blood plasma (BP) and in seminal plasma (SP) of men starting a DTG-based regimen at the time of primary HIV-1 infection (PHI) [6]. DOLUPRIM is an open-label, single-arm, prospective study enrolling men diagnosed at the time of PHI (≤3 months) and starting DTG+TDF/FTC. The primary outcome was time to first HIV-RNA below the lower limit of quantification (LOQ) in BP (20 copies/mL) and in SP (60 copies/mL), using the Kaplan–Meier method.

Nineteen men were enrolled, 4 at Fiebig stage II (F-II), 5 F-III, 1 F-IV, 4 F-V and 5 F-VI. At baseline, median VL was 6.5 (interquartile range [IQR] 3.4–8.6) and 4.5 (IQR 2.7–5.9) log₁₀ copies/mL in BP and SP, respectively. Treatment was started a median of 7 days (IQR 1–43) after diagnosis. A significantly higher proportion of participants achieved a first HIV-1 RNA below LOQ in SP (93.0%) than in BP (84.2%; P=0.008). In addition, the median time to undetectable HIV-1 RNA was shorter in SP (8 weeks; 95%CI 5.6 to 10.4) versus BP (24 weeks; 95%CI 14.1 to 33.9), although not statistically significant. Evolution of HIV-1 RNA (log₁₀) levels in BP and SP throughout the 48-week study period demonstrated a sharp decrease within 2–4 weeks of treatment in both compartments. Total HIV-1 DNA in PBMCs also decreased from 3.68 log₁₀ HIV-1 DNA/10⁶ PBMCs at day 0 to 2.08 log₁₀ HIV-1 DNA/10⁶ PBMC at week 48. Regarding pharmacokinetics, total blood plasma DTG concentrations were >1000 ng/mL in the vast majority (>95%) of participants, which suggest excellent treatment adherence. Despite the DTG high plasma protein binding in BP, free concentrations were higher in SP than BP, suggesting a probable accumulation in semen.

Is the weight gain in individuals living with HIV on integrase inhibitors real?

Andrew Hill (Department of Translational Medicine, University of Liverpool, UK) spoke in a very popular session in favour of the risk of clinical obesity linked to the use of newer antiretroviral agents [7]. While 20 years ago protease inhibitors (Pis) and nucleoside analogues were the main suspects in terms of their role in lipodystrophy, the first reports for integrase Inhibitors (INSTI) came out 3 years ago when there were reports to ViiV of unexplained weight increases which were reversible after stopping treatment. Data from toxicology analysis suggested that DTG had an effect on melanocortin receptors that impact on appetite. Weight gain (WG) was observed while taking DTG in the Phase 2 SPRING-1 trial and in five cohort studies, as well as while on raltegravir (RAL) in the STARTMRK and ACTG trials. Drivers that affect WG include the ‘return to health’ phenomenon (especially for lower CD4 T cell count/high HIV-1 RNA), and some antiretrovirals such as DTG, bictegravir (BIC) and Pis while TDF and efavirenz (EFV) were associated with smaller WG, and gender and race (women and black people). In a recent study, Paul Sax compared the ART effect in terms of WG with the following results: INSTI>P<NNRTI, BIC>DTG>EV/C/<, (tenofovir alafenamide (TAF)>ABC>TDF>AZT, RPV>EFV) [8]. However, body weight increases in individuals of white ethnicity are quite small (1–2 kg).

There remain unanswered questions. The first issue is that unfortunately we cannot use data from the main ViiV Phase 3 trials with almost 6912 participants because weight has often not been measured. The other one is that they underrepresent people at highest risk of AEs. For instance, data from a large US cohort study show that women on INSTI have twice the WG of men, and similarly black people have twice the WG as compared to non-Hispanic white people [9]. We do not know if this WG effect is just an artefact driven by good tolerability of newer treatments. Who has advised on WG via a meta-analysis for the 2019 guide on integrase inhibitors real?
disease, type II diabetes, cardiovascular disease/hypertension, mobility/ability to work, life expectancy) in different populations. Moestrup KS (Righospitalet, CHIP, Department of Infectious Diseases, Copenhagen, Denmark) analysed predisposing factors of weight changes in the START (Strategic Timing of Antiretroviral Treatment) trial [11]. This study has suggested that ART was associated with lower WG [12]. The 4684 HIV-1 positive adults with CD4 T cell counts >500 cells/mm^3 were randomly assigned to initiate ART immediately or defer it until a CD4 T cell count <350 cells/mm^3 was reached or the occurrence of progression to AIDS. While median baseline weight was 74kg (25th, 75th percentile: 64, 83), weight increased by 1.13% (95% CI 0.86 to 1.48) in the immediate and 1.92% (95% CI 1.65 to 2.19) in the deferred groups. The mean treatment difference in percentage weight change was -0.79% (95% CI -1.08 to -0.50; P<0.001). This effect was pronounced among participants with low baseline HIV-1 RNA levels, suggesting that the ART impact among those with high levels was countered by WG due to reduction in viral replication.

High CD4 T cell counts, female gender and living in mid-low-income regions were associated with smaller WG in the immediate ART group (P-values of interaction of difference between treatment groups of CD4, gender and geographical region were P<0.001, P=0.048, P=0.019, respectively). Chloe Orkin (Ambrose King Centre, Royal London Hospital, UK) compared the effects of doravirine (DOR), ritanavir-boosted darunavir (DRV+r) and EFV on body weight (BW) and body mass index (BMI) using data from the Phase 2b (PO07) and Phase 3 trials (DRIVE-FORWARD and DRIVE-AHEAD) through 96 weeks of therapy in HIV-1 positive treatment-naive adults [13]. This was a post hoc, pooled data analysis, and as such needs to be interpreted with caution. The change in BW from baseline (BL), WG ≥10% (adjusted for differences in BL characteristics) and BMI class increase (change from underweight/normal to overweight/obese or from overweight to obese) were assessed using generalised linear models. At 48 and 96 weeks, median weight change from BL was comparable between arms (1.5 kg for DOR, 0.7 kg for DRV/r and 1 kg for EFV groups). Looking at the estimated proportion of participants with ≥10% WG or BMI class increase using a model which adjusted for differences in BL characteristics, similar values were observed among the three treatment arms (≥10% WG observed in 15.8% in DOR, 16.9% in DRV/r, and 13% in EFV groups while BMI class increase in 15.8% in DOR, 15.3 in DRV/r and 14.2% in EFV groups). Only a low CD4 T cell count and high VL affected WG at both timepoints. Overall change in BMI class (excluding obese patients at BL) concluded that 7% on DOR, 6% on DRV/R and 5% on EFV became obese over the course of the study, and that the EFV arm had more participants than the other two arms remaining in the normal BMI class. In conclusion, WG over 96 weeks was low and similar to the average yearly change in adults without HIV-1.

The dual-energy X-ray absorptiometry (DXA)-assessed body composition changes in the ADVANCE clinical trial were presented by Michelle Moorhouse (Wits Reproductive Health and HIV Institute, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa) in order to determine the type of treatment emergent metabolic syndromes across all three arms at both weeks 48 and 96, with statistically significant differences only between TAF/FTC-DTG and TDF/FTC/EFV.

Katrina Mugglin (Department of Infectious Diseases, Bern University, Switzerland) assessed weight and BMI changes after switching to DTG-containing regimens in virologically suppressed participants among the Swiss HIV Cohort Study to identify risk factors for disproportionate weight change [15]. Among the 2186 participants included in the analysis, median age of 51 years (IQR 44–56), 81% were white, median BMI was 24.0 (IQR 21.7–26.8), and time on ART 11 years (IQR 6–17). Slopes in weight change were analysed in the pre-switch and the post-switch period using interrupted time series. Overall switching to DTG was associated with a modest increase of 0.72 kg per year (95% CI 0.58 to 0.86, P=0.029 when compared to pre-switch value) as compared to the time-period before switch (0.47 kg/year; 95% CI 0.34–0.61). Weight change was statistically significant in male gender and black ethnicity. Patients switching to TAF and DTG gained an average of 1.4 kg per year after switch but the sample size was small. There were 477 patients who experienced ≥5% WG after the switch. Females, participants of black ethnicity and current smokers were more likely to experience ≥5% WG after the DTG switch, while obese people at switch had lower odds of getting ≥5% WG after the switch.

Sebastiaan Verboeket (Amsterdam University Medical Centers, Department of Global Health and Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands) argued that switching to an INSTI-containing ART within the AGEhiV study was not associated with above-average WG in middle-aged PLWH on long-term suppressive ART [16] when compared to HIV-positive virally suppressed non-switching and HIV-negative participants. In total, 119 HIV-positive participants switched to an INSTI-containing regimen (53% dolutegravir; 35% elvitegravir; 13% raltegravir), mainly for simplification of regimen or side effects. For the efV arm, there was no increase in lean mass as seen in the other two treatment arms by week 96. There were treatment emergent metabolic syndromes across all three arms at both weeks 48 and 96. While median baseline weight was 74kg (25th, 75th percentile: 64, 83), weight increased by 1.13% (95% CI 0.86 to 1.48) in the immediate and 1.92% (95% CI 1.65 to 2.19) in the deferred groups. The mean treatment difference in percentage weight change was -0.79% (95% CI -1.08 to -0.50; P<0.001). This effect was pronounced among participants with low baseline HIV-1 RNA levels, suggesting that the ART impact among those with high levels was countered by WG due to reduction in viral replication.

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reviewing AIDS-defining cancers (ADCs), non-AIDS-defining cancers (NADCs) and temporal changes in the ADCs/NADCs ratio [17]. Among 5411 HIV-1 positive participants followed-up between 1986 and 2018, there were 643 patients diagnosed with at least one malignancy. Comparative analysis between participants with ADCs or NADCs revealed that those with NADCs were about 10 years older, predominantly male, with a history of IDU HIV-1 transmission and having more frequently chronic hepatitis co-infection. NADCs occurred later after the time of HIV-1 diagnosis (15.1 years for NADCs versus 4.1 years for ADCs, P=0.001), mostly because of a greater rate of participants simultaneously diagnosed with HIV-1 and ADCs (81% vs 19% for NADCs). While the ADC prevalence clearly decreased over time, that of NADC was slightly increased, resulting in a reversion of the ADCs/NADCs ratio by the end of the follow-up. The most frequent cancers were: cervical cancer (n=134, 20.8%), Kaposi sarcoma (n=132, 20.53%), non-Hodgkin lymphoma (n=52, 8.09%), Hodgkin lymphoma (n=43, 6.7%), hepatocellular carcinoma (n=32, 4.9%), anal cancer (n=30, 4.7%), head and neck (n=27, 4.2%) and lung cancers (n=25, 3.9%). Overall 13.3% were diagnosed at an advance stage (T4 stage or metastatic), while 67% of diagnosed cancers were virally associated (54% herpes viruses, 39% human papilloma virus, 7% hepatitis viruses). There were 57 (9%) participants who presented with more than one cancer. The overall mortality was 18%, with a significantly higher mortality in participants with NADCs (25% in NADCs vs 11% in ADCs, P<0.001).

Ricky Hsu (NYU Langone Medical Center, New York, USA) assessed the incidence of chronic kidney disease (CKD) with TDF and non-TDF-containing antiretroviral regimens stratified by baseline D:A:D CKD risk score and boosted or unboosted regimens in PLWH participating in the OPERA prospective cohort study [18]. The study population involved ART-naive adults initiating ART by June 2018 and having a normal eGFR within 12 months of treatment initiation, calculated with the CKD-EPI equation. Incident CKD was defined by the standard nephrology guidelines, namely a drop of 2 consecutive eGFR<60 ml/min/1.73 m² test results that were separated by >90 days. The associations between TDF use, baseline D:A:D CKD risk, and incident CKD were assessed with unadjusted incidence rates (IR, Poisson regression) and adjusted survival analyses (pooled logistic regression). Sensitivity analysis attributed a correction factor for each ART responsible of an eGFR decrease in clinical trials (DTG, EVG/c, PI/c, RAL, RPV). Of 9802 PLWH included in the study, 6222 initiated TDF (76% low-risk D:A:D CKD score, 16% medium-risk, 8% high-risk) and 3580 did not (79% low-risk, 13% medium-risk, 8% high-risk); 40–47% initiated a boosted regimen. Among participants, a great majority had a considerably low D:A:D CKD risk score both in TDF and no TDF based regimens (76% and 79% respectively). Regardless of TDF use, participants with a medium or high CKD-risk BL score were more likely to be older, female, having started ART earlier and to be introduced to nephrotoxic medications, those minimising proteinuria and to develop comorbid conditions such as HCV co-infection, diabetes and hypertension. Participants in the low BL D:A:D CKD risk strata on TDF compared to the one not on TDF were also more likely to be female and having started ART earlier. Overall, 125 incident CKD events occurred over 24,382 person-years of follow-up. Within strata of D:A:D CKD risk score, incident ratios were similar by TDF exposure, with high BL CKD risk associated with highest incidence of CKD regardless of TDF use. Interestingly, there was no difference in unadjusted incident CKD events before and after the eGFR correction in participants with low BL CKD risk score, whether they were on a TDF regimen or not. Roughly half of the patients in both arms were started on boosted versus unboosted regimens. Even if no difference was seen in adjusted analysis looking for associations between CKD events and TDF/boosting either in the TDF or non-TDF arms, the adjusted analysis corrected for eGFR effects, the authors could see a general trend for boosted regimens to have a higher CKD incidence rate as compared to non-boosted ones, even if this difference was not significant. Altogether there was a low CKD incidence after ART initiation in ART-naive PLWH and CKD progression was strongly associated with BL D:A:D CKD risk score. In this cohort participants had mostly a low BL D:A:D CKD risk score, that did not worsen even with TDF use. The incident CKD was a rare outcome, limiting the power to detect differences and the authors did not observe any association between CKD and TDF or boosted regimens, except after eGFR correction, where increased CKD incidence rates were associated with TDF and with higher BL D:A:D CKD risk.

Michelle Moorhouse (Wits Reproductive Health and HIV Institute, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa) presented DXA-assessed bone mineral density (BMD) and renal outcomes of the ADVANCE trial in HIV-1 positive persons taking TDF-containing regimens versus those taking TAF-containing ones [19]. The ADVANCE trial was a 96-week, open-label randomised trial in 1053 treatment-naive patients in South Africa, comparing TAF/FTC+DTG, TDF/FTC+DTG and TDF/FTC/EFV after 48 and 96 weeks of treatment. All participants showed a similar decline in whole body BMD using bone DXA-scan with no significant difference between arms. The TDF-containing arms had most impact on hip and spine BMD and renal markers. Treatment emergent osteopenia for hip was lowest in the TAF/FTC+DTG arm (6.3% versus 11.1% in the TDF/FTC+DTG and 30% in the TDF/FTC/EFV arms (P<0.001 EFV arm versus TAF arm). Similarly, treatment emergent osteopenia for spine was lowest in the TAF/FTC+DTG arm (21%) versus 23% and 30% in the TDF/FTC+DTG and TDF/FTC/EFV arms respectively. However, there was no statistical difference seen between arms. Using the FRAX equation (even if it is not a validated tool in this population) the predicted 10-year risk of major fractures was 0.2% lower in the TAF/FTC+DTG arm compared with the TDF/FTC+DTG arm, and no difference was observed between TAF/FTC+DTG and TDF/FTC/EFV. Authors described no observed differences in bone fractures between the arms. They also pointed out that there were no consistent differences between TAF and TDF arms regarding elevation of renal markers above the normal range and grade 3 or 4 renal clinical adverse events. A longer-term follow-up is needed to balance the risks of clinical obesity for TAF-containing treatment versus changes in bone and renal markers for TDF.

Andreas Dehlbaek Knudsen (Righospitalet, Copenhagen University Hospital, Denmark) presented highlights of the Copenhagen Comorbidity in HIV infection (COCOMO) study on pericardial adipose tissue (PAT) volume in PLWH aged ≥40 years and matched 1:1 for age and sex to uninfected controls from the Copenhagen General Population Study (CGPS) [20]. The objective of the study was to determine if HIV status was independently associated with PAT volume by CT scanning, as well as to investigate associations between PAT volume, cardiovascular disease risk factors and HIV-1 specific factors. A total of 587 PLWH and 587 controls were included. Mean (SD) PAT volume was similar in PLWH and uninfected controls (185 mL vs 184 mL respectively, P=0.546). After stratifying according to BMI researchers found that PAT volume was 22 mL larger in PLWH with a normal weight compared to uninfected controls with a normal weight. This difference was not observed when PLWH who were overweight or obese were compared to corresponding uninfected controls. In linear regression analysis, adjusted for BMI, age, sex, hypertension, diabetes, smoking, dyslipidaemia and physical activity, HIV-1 status
was associated with 17 mL (95% CI 10–23.4) larger PAT volume (P<0.001) compared to uninfected controls. Apart from HIV-1, the PAT volume was associated with age, male sex, BMI, smoking status, dyslipidaemia and sedentary lifestyle. Among the HIV-1 specific factors only the CD4 T cell nadir<200 cells/mm³ and prior use of thymidine analogues and/or didanosine were both associated with approximately a 10 mL larger PAT volume. However prior exposure to thymidine analogues and/or didanosine modified the effect of CART duration with a larger PAT volume among those exposed to these compounds and lower PAT volume among the unexposed ones.

Davide de Francesco (Institute for Global Health, UCL London) described the development of a comorbidity burden index (CBI) using information on 65 comorbidities collected in PLWH enrolled in the POPPY cohort of 1073 PLWH and compared its performance against the comorbidity count and the VACS index in the AgeHIV of 598 PLWH cohort [21]. Of the three indices, correlation of the CBI with self-reported physical and mental health was better than the correlation of the comorbidity count with physical and mental health (P = 0.08 and P = 0.16 respectively), and significantly better than the correlation of the VACS index (P<0.001 and P<0.001 respectively).

At BL, 11.4% of PLWH were frail. The frailty incidence and death rate were 19.5/1000 and 12.0/1000 person-years, respectively. Cross-sectionally, the CBI showed a stronger association with frailty than the VACS index (P = 0.02) or the comorbidity count (P = 0.27). Whilst prospective associations with frailty development and mortality were strongest for the comorbidity count, the difference between CMI and the comorbidity count in terms of prospective associations with frailty development and mortality were not significant (P = 0.55 and P = 0.24, respectively). In summary, the CBI showed strong associations with quality of life, frailty and mortality, supporting its validity. Comparison with existing indices generally shows better correlation of CMI with physical health, mental health and frailty, with mixed results for predictive associations with frailty development and mortality. More work is needed to further validate and improve the practicality of the CBI, relying for instance on a smaller list of comorbidities.

Jasmin Alagaratnam (Imperial College London, UK) assessed correlation between cerebrospinal fluid (CSF) and plasma concentrations of the neurofilament light protein (NFL) in ART-treated PLWH (n = 32) in the COMorBidity in Relation to AIDS (COBRA) cohort study versus lifestyle-similar HIV-negative controls (n = 79), and determined factors associated with plasma and CSF NFL in PLWH [22]. All PLWH had suppressed plasma viral load, but two of them had detectable CSF HIV RNA. The majority of participants were on tenofovir-D4-based ART regimen and a fifth of participants were on atazanavir. In terms of clinical parameters the CSF to plasma albumin ratio, a surrogate marker of blood-brain barrier dysfunction, was very similar between the 2 groups. While different biological parameters tested (CSF albumin, serum albumin, CSF/serum albumin ratio) were similar between PLWH and HIV-negative participants, only renal function and global cognitive function were significantly poorer in PLWH. Neither the CSF (570 vs 568 pg/mL, P = 0.38) nor the plasma (10.7 vs 9.9 pg/mL, P = 0.15) NFL levels differed significantly between the two groups. CSF and plasma NFL correlated moderately in the COBRA cohort participants, with no significant difference seen by study arm (PWHL: correlation coefficient ρ=0.52 (95% CI 0.38–0.64) P<0.001; HIV-negative controls: ρ=0.47 (95% CI 0.27–0.62), P<0.001, P-value for interaction=0.63).

In multivariate linear regression, older age and lower weight were each associated with higher plasma and CSF NFL Z-scores in PLWH. Whereas lower plasma albumin and higher serum creatinine were associated with higher plasma NFL Z-scores, higher CSF protein was associated with higher CSF NFL Z-score. In conclusion, in PLWH on suppressive ART, the correlation between CSF and plasma NFL is weaker than previously described in untreated PLWH but similar to that observed in lifestyle-similar controls. Consideration of renal function and body composition may be required when using plasma NFL.

Barbara Rossetti (University Hospital of Siena, Italy) presented the impact of INSTI resistance in the real-life setting of the INTEGRATE retrospective and observational study within the EuResist multi-cohort study [23]. This study is a large European collaboration which has enrolled 13,358 patients who had started INSTI-based regimens from 01 January 2012. The authors enrolled 2459 ART-naïve participants (group G1), 3744 ART-experienced INSTI-naïve and aviremic participants (G2a), 1470 ART-experienced INSTI-naïve and viremic participants (G2b), 4068 ART-experienced INSTI-experienced aviremic participants (G3a) and 1,617 ART-experienced, INSTI-experienced and viremic (G3b) participants. When considering the type of INSTI used, a majority of DTG-based regimens were used in all groups with 3-drug ART ones more frequently prescribed in all groups. The probability of VF at 1 year was 6% in G1, 4% in G2a, 20% in G2b, 7% in G3a and 17% in G3b. The probability of VF at 1 year was 5% for DTG-based, 6% for elvitegravir-based and 10% for raltegravir-based regimens. Predictors of VF in the naive group were a lower BL CD4 T cell count and higher VL when using multivariate Cox models. Among virologically-suppressed participants, previous VF predicted a new VF, and in G2a a shorter time of viral suppression, non-white ethnicity and intravenous drug use predicted VF. Among treatment-experienced viremic patients, previous VF, EVG vs DTG use and a lower BL CD4 T cell count were associated to VF; in group 2B a higher BL VL and a younger age were associated to VF. In conclusion INSTI resistance remains uncommon without previous exposure to this class of drugs. Detection of INSTI resistance after InNStI failure supports mandatory genotypic testing for INSTI-experienced patients. Higher BL VL and lower CD4 T cell count were associated with VF in viremic patients. Previous VF and duration of VL suppression before the treatment switch were independent predictors of VF.

Where do we stand with HIV prevention today?

Claudia Estcourt (University College London, UK) introduced the session on HIV prevention with an overview of what is being done in Europe in terms of combination prevention interventions [24]. Among 160,000 transmissions in 2017 in the WHO European Region, over 80% occurred in the Eastern area and approximately half of them were late diagnoses with a CD4 T cell count <350 cells/mm³. Even though we are proud of a 20% decline in new HIV diagnoses mostly among MSM of the EU/EEA, HIV rates are increasing in a third of countries. Implications of these key facts are that: (a) significant transmission continues and therefore prevention remains a priority; (b) we need to be looking beyond MSM to groups that we are not reaching, such as migrants, persons who inject drugs and transgender or non-binary people. Effective HIV prevention programmes require a combination of behavioural, biomedical and structural interventions that are key to success and need to be tailored to each country and risk group.

Dominique Costagliola (Sorbonne Université, INSERM, Institut Pierre Louis d’Épidémiologie et de Santé Publique, Paris, France) presented results of a sub-analysis of the ANRS Prevenir study, an open-label, prospective cohort study conducted since May
2017 in the Paris area [25]. The objective was to understand PrEP persistence and factors associated with its discontinuation. Out of 3057 participants, 2699 fulfilled the inclusion criteria with a median age of 36 years (IQR: 29–43), 84% were born in France, 73% with over 2 years of university degree, 50% already on PrEP at BL (median: IQR 9–1 months) and 51% using on-demand PrEP. Overall 358 participants discontinued PrEP, including 258 being lost to follow-up and 100 stopping PrEP, mainly for no longer feeling at risk and 4 for AEs (1 HCV infection, 1 grade 3 AE with vomiting, 2 grade 1 AEs with diarrhea, and nausea/headache/dizziness). The 30-month discontinuation rate was estimated at 32% (95% CI 29–35). Factors independently associated with PrEP discontinuation included younger age, lower educational level and not being on PrEP at enrolment (new PrEP users) as already observed in previous studies.

Andrew Carr (St Vincent’s Hospital, Sydney, Australia) presented longitudinal cohort data on changes in BMD over 2 years in men who have sex with men (MSM) on TDF-based HIV pre-exposure prophylaxis [26]. The MSM initiating daily TDF–FTC PrEP through a PrEP demonstration project were offered BMD assessment using DXA at BL and after completing 1 and 2 years of PrEP. Of 185 men with BL scans, 118 (64%) and 51 (43%) men were assessed at a median of 420 (IQR 391–449) and 824 (IQR 776–885) days on PrEP, respectively. Significant numbers of MSM on daily TDF-based PrEP lost ≥3% BMD at all measured sites over 24 months. There may be a plateau BMD loss after 12 months, as is observed in adults initiating TDF-based ART. Therefore, long-term studies of TDF-based PrEP in MSM are warranted.

Eve Plenel (Ves Paris sans sida, Paris, France) described interventions in Paris to decrease HIV diagnoses among MSM, in terms of PrEP effect, testing and political support to communities [27]. Paris Fast-Track Blueprint was based on research and epidemiological surveillance, political support for community engagement and resource mobilisation, with an implementation of combined prevention in an inclusive approach to sexual health. Its objective was to tackle the gap at the first step of the HIV cascade of care, fighting against long delays to diagnosis and high levels of undiagnosed HIV prevalence among key affected populations (MSM and sub-Saharan African migrants). Between 2015 and 2018, new HIV diagnoses have fallen overall by 16% in Paris, and by 28% among France-born MSM. The speaker linked this positive result to an increase in PrEP coverage and testing with a 10–15% increase in HIV testing alongside an investment in self-testing, STI clinics and community-based testing, as well as daily communication promoting HIV testing. PrEP uptake is expanding rapidly among MSM in Paris and has been promoted by the ANRS Prevenir study and the political support given to PrEP early adopters by City officials and public campaigns.

Conclusions

These highlights have focused on some of the developments in HIV prevention and treatment with ongoing issues in terms of metabolic changes, which will need further insight in the future.

Conflicts of interest

The authors declare no conflicts of interest.

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All abstracts are from the 17th European AIDS Clinical Society (EACS) Conference, 6–9 November 2019, Basel, Switzerland unless otherwise stated.

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