

Highlights from the 20th International Symposium on HIV and Emerging Infectious Diseases (ISHEID) 16–18 May 2018, Marseille, France: from HIV and comorbidities to global health

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Abstract

The 20th International Symposium on HIV and Emerging Infectious Diseases took place in Marseille, France. It had a refreshing European look with reinforced partnerships with the European AIDS Clinical Society and the British HIV Association and with international speakers and participants. Topics included HIV and global health, HIV and hepatitis cure, the microbiome and immunotherapies, clinical research and methodology, as well as chemsex, pre-exposure prophylaxis, sexually transmitted infections and emerging infectious diseases. Novel areas of research were also described, such as electronic technology in order to improve HIV management, and the expert patient.

Introduction

The 20th International Symposium on HIV and Emerging Infectious Diseases (ISHEID) was held in Marseille, France and reinforced partnerships with the European AIDS Clinical Society (EACS) and the British HIV Association (BHIVA). Participants gathered from all over the world for a rich programme on HIV and global health, HIV and hepatitis cure, the microbiome and immunotherapies, clinical research and methodology, as well as chemsex, pre-exposure prophylaxis (PrEP), sexually transmitted infections (STIs), electronic technology and emerging infections. It was an enriching scientific experience thanks to the presence of, and dynamic exchanges between, experts and younger investigators. In this article we summarise the plenary sessions, keynote lectures, and some of the oral presentations.

From HIV to global health

Stefano Vella (Istituto Superiore de la Sanità, Rome, Italy) gave the inaugural presentation and spoke about HIV as a model of global health, in order to fight health inequalities [1]. At least 30 million people die prematurely every year (half of them before the age of 5) in developing countries from lack of adequate access to basic healthcare and from often preventable or treatable diseases. Despite the concept of health as a human right, there still are intolerable global inequalities in terms of access to health and healthcare services, life expectancy, morbidity and mortality from communicable and non-communicable diseases. The persistence of inequalities in terms of health – not only between rich and poor countries, but also between different regions within a country – is also a scientific contradiction given the growing geographic interdependence of biomedical causes and social determinants of health and diseases.

Global health includes the study, research, and actions that place a priority on improving health and achieving health equality for people worldwide, transcending perspectives and concerns of individual nations (Figure 1). It emphasizes transnational health issues, determinants and solutions, and involves many disciplines within and beyond health sciences. It is a synthesis of population-

based prevention with individual-level clinical care and specific attention to the poor, marginalised and underserved.

The way the HIV pandemic has been addressed, despite still being an unfinished job, may be a model to fight wider health inequalities. Indeed, HIV/AIDS drew together, with the common objective of fighting a major health inequality, scientists, clinicians, governments, the United Nations, visionary politicians, economists, international organisations, the pharmaceutical industry, both proprietary and generics, NGOs, faith based- and patient organisations [2]. It has recognised the supranational character of tackling diseases and the fact that no individual country can on its own address diseases in the face of the migration of people, trade, microbes and risks for disease acquisition. It has mobilised innovative drug production, pricing and procurement, both from generic and proprietary manufacturers. It also has recognised that people affected by disease have a crucial role in the advocacy for new types of treatment and prevention and their equitable access [3]. It has based its action on ethical and moral values that recognise that equity and rights are central to the larger goals of preventing and treating diseases worldwide.

What's up in HIV?

Beatriz Mothe Pujadas (Hospital Germans Trias i Pujol, Barcelona, Spain) overviewed current strategies for therapeutic HIV vaccines. Functional HIV cure still seems not immediately achievable. However, recent 'kick and kill' trials such as the BCN 02 study combining a potent T cell vaccine with a latency-reversal agent (LRA), have suggested that viral control may be achieved by an effective redirection of cytotoxic T lymphocytes (CTL) towards conserved regions of the virus in the context of an early treatment intervention with antiretroviral therapy (ART) (>Fiebig stages III–IV) and limited viral reservoir (Figure 2) [4].

Sofie Rutsaert (Ghent University, Ghent, Belgium) presented evidence for total HIV-1 DNA threshold as a guide for treatment simplification strategies [6]. Although triple ART is the recommended initial treatment, therapy simplification with a reduced number of drugs is being explored. Fewer drugs can

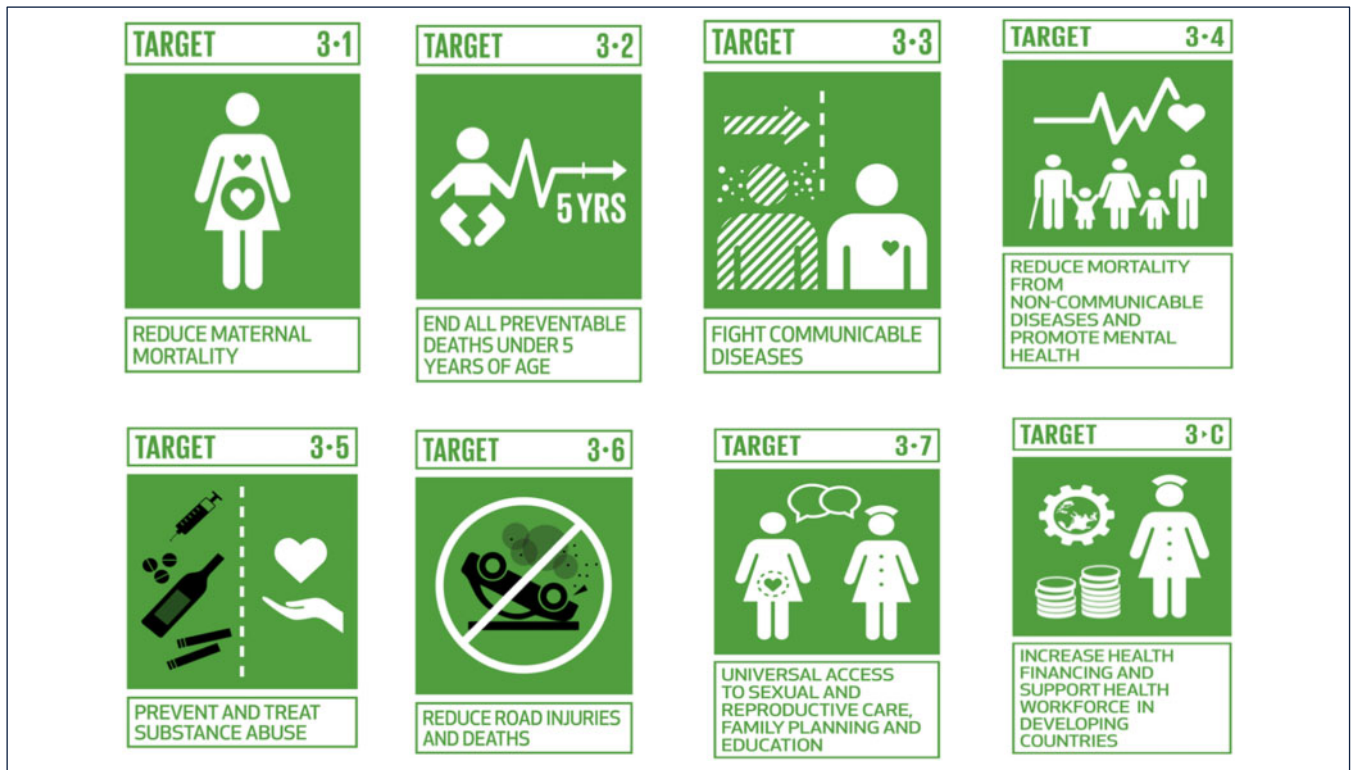


Figure 1. Global health targets

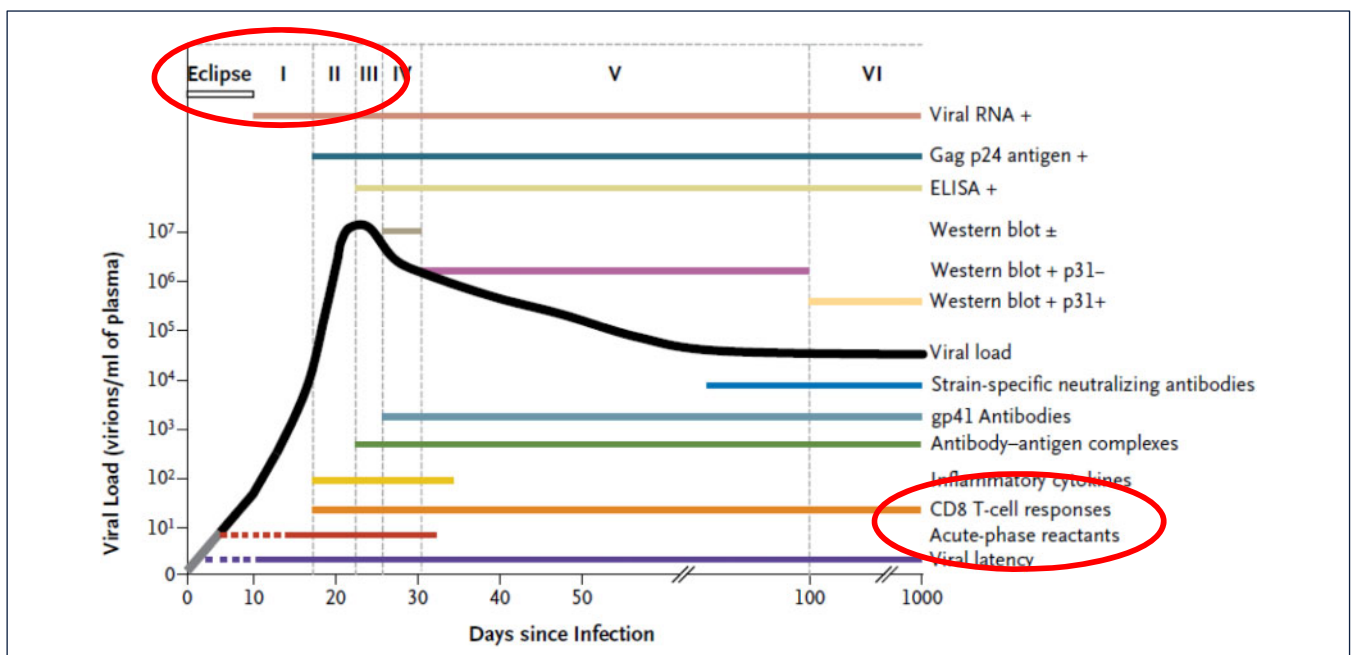


Figure 2. Target population for early phase clinical trials: acute and recent HIV infection. Adapted from [5]

reduce cost, avoid drug–drug interactions, improve tolerability and decrease toxicity in terms of lifelong treatment. Total HIV-1 DNA, which reflects the number of infected cells in treated individuals, can aid in selecting eligible patients. A significantly higher level of HIV-1 DNA is observed in patients whose treatment fails virologically while on a simplified regimen, when compared to patients who maintain an undetectable viral load. This has been observed with various regimens (darunavir/r monotherapy, raltegravir/etravirine) and indicates that total HIV DNA is very informative in terms of treatment strategies, even if its predictive value remains yet to be proven [7] (Rutsaert *et al.*, submitted). However, to be clinically useful, this observation will have to be

confirmed with a long-term follow-up of patients and other regimens, such as dolutegravir/lamivudine, dolutegravir monotherapy (Wijting and Rutsaert, submitted) or dolutegravir/rilpivirine therapy.

Chloe Orkin (Barts Health NHS Trust, London, UK) argued for two-drug therapy (2DR) as a treatment and management strategy to reduce toxicity and ART exposure, using new agents or different ART formulations. Switching to 2DR in a virologically suppressed patient should be done safely and for a good reason, after review of ART history, genotype, interactions and possible co-infections. There are knowledge gaps regarding 2DR that include a lack of

long-term data, hepatitis B co-infection, high viral loads, low CD4 T cell counts, resistance mutations, HIV viral reservoir measurements, pregnancy and chronic inflammation. Ongoing issues include the adherence level necessary to maintain virological control, frequency of virological monitoring for 2DR, if relevant for those with unclear genotypic history, and options for salvage in the case of virological failure on 2DR treatment.

Emerging infectious diseases

Frederic Bartumeus (Blanes Advanced Study Centre, Girona, Spain) described the organisation of a Platform for the Integrated Control of Arbovirosis in CATalonia (PICAT): Mosquito Alert 2.0 [8]. Traditional methods for tracking disease-carrying mosquitoes are hitting budget constraints because the scale over which they must be implemented is growing exponentially. Citizen science offers a set of innovative tools for public health management, allowing sustained and flexible data collection while facilitating public participation in problem solving [9,10]. There is increasing evidence that combining citizen scientist data with other sources of information significantly improves our knowledge in a given area [11]. In particular, once we adjust for sampling bias, vector data obtained through the Mosquito Alert citizen science programme has almost the same quality and predictive power as that obtained through traditional surveillance. Vector data is now being further integrated with epidemiological and socially relevant data into a digital platform to augment the information already available from public health sources and to provide risk models and key information to public health authorities at near real-time. The scientific exploitation of citizen science programmes and big data solutions should effectively help to reduce the presence of targeted mosquitoes and minimise current health threats.

Jean-Paul Gonzalez (Center of Excellence for Emerging and Zoonotic Animal Diseases, Manhattan, Kansas, USA) gave a passionate talk about climate change, socio-political changes and emerging pandemics [12]. Hippocrates, in his treatise *'On Airs, Waters, and Places'*, written almost 2500 years ago, shows us the links that exist between environment and health. Indeed, many communicable diseases are known to be climate-dependent (e.g. vector-borne diseases, seasonal flu, meningoencephalitis), and certain degenerative diseases can be influenced by climatic factors (e.g. neurodegenerative and rheumatic diseases). Currently, the effects of greenhouse gas emissions and climate change on health can be seen in the resurgence of certain infections. Following on from a 'One Health' approach, some exemplary epidemic events were presented, for example the seasonality of the microbiome [13], which provides the necessary fundamentals for the understanding of climate change, extreme climatic events, their impact on health and, how to be prepared and respond.

What about hepatitis cure?

The liver is one of the major anatomical sites targeted in HIV infection, mostly as result of frequent co-infection with hepatitis viruses and/or hepatotoxicity associated with lifelong ART exposure. In addition, the prevalence of fatty liver disease is rising in this population as successfully treated individuals live longer, while frequently experiencing metabolic complications [14].

Several presentations addressed the current burden of viral and non-viral liver events, comparing trends in those living with HIV and the general population.

Hepatitis A

Hepatitis A virus (HAV) is a small RNA agent predominantly transmitted via the faecal–oral route from contaminated food and water, or from person to person. The mean incubation period is

1 month. Acute HAV is always self-limited, very rarely fatal, and does not progress to chronicity. Acutely infected persons are most likely to transmit the virus before the onset of jaundice, when the concentration of viral particles in stools is highest. Hepatitis A is a vaccine-preventable disease, although universal childhood vaccination is not mandatory in most Western countries. In adults, vaccination is generally recommended for men who have sex with men (MSM) and injecting drug users (IDUs) as well as in travellers to regions where it is endemic such as Latin America, Africa and Asia. In the European Union and North America almost all infections are directly or indirectly imported.

Olga Tsachouridou (AHEPA University Hospital, Thessaloniki, Greece) presented a study on 1210 adults living with HIV who attended hospital during the last decade [15]. Natural immunity to HAV was recognised in 338 (28%) individuals. Vaccination was recommended to those non-immune. Of 203 who received only a single dose, protective antibody titres (>20 IU/mL) were achieved by 71%. It increased to 81% for those who completed the two-dose vaccination schedule. Patients immunised during the peak of the financial crisis in Greece (2010–2015) and IDUs frequently missed the booster dose. Altogether, this data supports testing for HAV antibodies in all individuals living with HIV, acknowledging that 20% may not respond with protective antibodies, even following the second vaccine dose.

Transmission of HAV through sexual contact, particularly in MSM, as well as through sharing of needles and syringes has been the subject of a recent alert in several European countries, with outbreaks among MSM in the UK, Germany, Portugal, Italy and Spain [16]. It highlights the interconnectedness of MSM and the need to increase HAV vaccine coverage within this group. Of note, the recent shortage of HAV vaccine is partially contributing to the lack of control of the ongoing HAV epidemic in Western countries. Although HIV infection does not seem to increase susceptibility to HAV, and liver enzyme elevations tend to be milder in this group, a high rate of concomitant sexually transmitted infections (STIs), including syphilis, chlamydia and gonorrhoea, has been reported. The alarming rising incidence of STIs among MSM occurs regardless of HIV status, as highlighted at ISHEID by French investigators [17].

In summary, MSM are at particular risk for HAV infection and there is a need for proper information and education on safe sexual behaviour, including personal hygiene measures before and after sexual contact. Immunisation rates against HAV should be increased in this population, as well as post-exposure prophylaxis to close contacts (active and passive immunisation is effective if administered within 2 weeks of exposure). Finally, it was noted that it is important to exclude other sexually transmitted diseases in those with acute HAV.

Hepatitis B

The major pandemics caused by chronic viral infections involve HIV, hepatitis C (HCV) and hepatitis B virus (HBV), with estimates of 38, 70 and 250 million affected people worldwide, respectively (Figure 3). In the past few years, the advent of direct-acting oral antivirals for HCV treatment has led to plans for global eradication. These new drugs cure more than 95% of cases of HCV when given for only 2–3 months [18]. This breakthrough has resulted in renewed interest in finding curative strategies for both HIV and HBV. However, important biological differences between these viruses may preclude such rapid success.

Once HCV enters into hepatocytes, its viral genetic material replicates within the cytosol whereas HIV integrates into chromosomes as provirus and HBV is converted into a circular

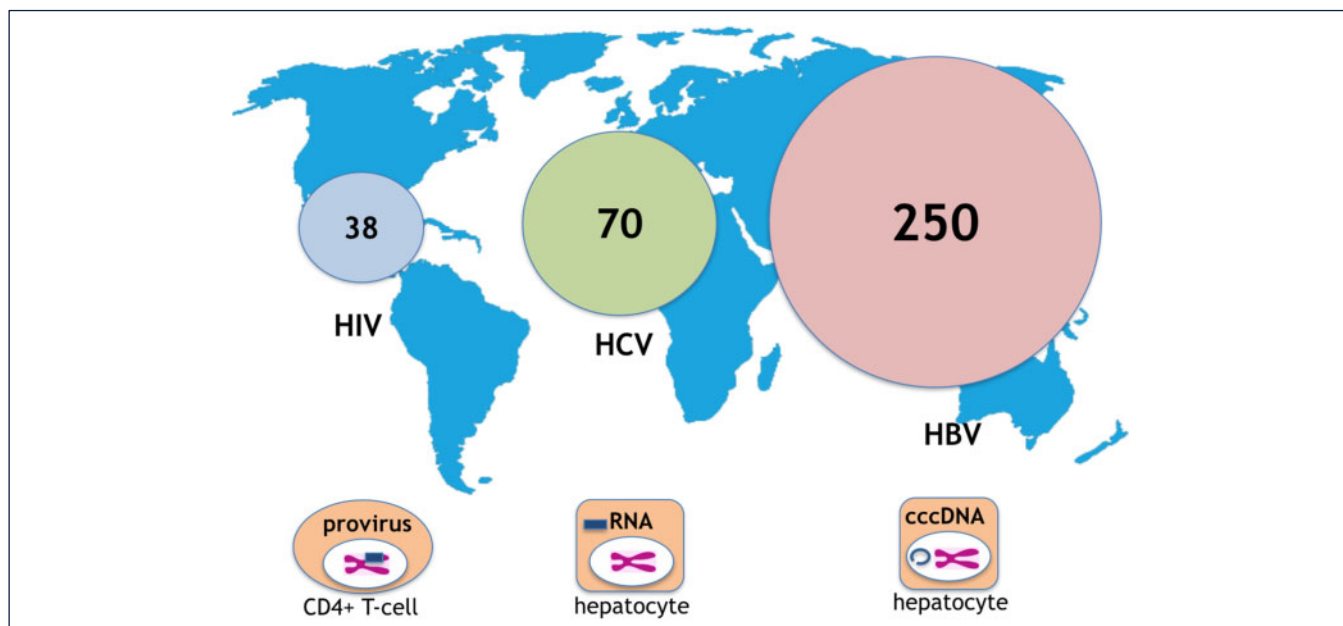


Figure 3. Major chronic viral pandemics

Table 1. The new HBV armamentarium

	Mechanism	Drugs
Antivirals (<i>life cycle</i>)	Entry inhibitors	Myrcludex B
	cccDNA cleavage (gene editing)	CRISPR/cas9, TALENS, ZFNs
	Transcription inhibitors (RNA interference)	ARC-520, ARO-HBV, ARB-1740, AB-729, ALN-HBV, TKM-HBV, RG-7834
	Polymerase inhibitors	TAF, CMX-157, AGX-1009, besifovir, lagociclovir
	Capsid blockers	GLS-4, NVR 3-778, JNJ-379
	Release inhibitors	Rep-2139, Rep-2165
Immune modulators (<i>immunity</i>)	Innate immunity	<ul style="list-style-type: none"> • TLR-agonists (GS-9620) • Anti-PD1 (nivolumab)
	Adaptive immunity	<ul style="list-style-type: none"> • Therapeutic vaccines (GS-4774, TG-1050) • Engineered T cells

covalently closed form (cccDNA) [19]. Blocking viral nucleic acid replication for a length of time allows definitive clearance of HCV infection, with degradation of residual cytoplasmic HCV RNA strands. In contrast, given the stability of the HIV provirus and HBV cccDNA, blocking viral replication has only a transient effect as mRNA expression resumes following treatment discontinuation.

Vicente Soriano (Hospital Carlos III, Madrid, Spain) gave an update on the new therapeutic strategies against HBV. The achievement of a functional cure with clearance of serum HBsAg will be the next step in the path to finding a cure. Ultimately this will require the elimination of the reservoirs of cccDNA and chromosomal integrated HBV DNA [20]. Presently, it seems that a combination of antivirals and immune modulators may be the best way forward. Several antivirals that target different steps of the HBV replicative cycle are being tested (Figure 4), including entry inhibitors (e.g. Myrcludex B), transcription inhibitors (RNA interference molecules such as ARO-HBV), capsid assembly inhibitors (e.g. JNJ-379), and nucleic acid polymers (NAPs) that inhibit HBsAg release (e.g. REP 2139). Alongside antivirals, several immunological agents are being evaluated (Table 1).

When considering the pros and cons of novel HBV therapeutic candidates, HBV gene therapies are among the most attractive ones. Several advances have contributed to position gene therapy at the forefront of the experimental HBV armamentarium. First, progress in delivery systems, including the use of polymers and nano formulations, has allowed the development of subcutaneous and monthly treatments that are easier to administer. Synthetic production of oligonucleotide formulations has reduced costs. Their specificity against HBV is higher than other experimental agents: toll-like receptor (TLR) agonists (e.g. GS-9620) or check point inhibitors (e.g. nivolumab) are immune modulators that enhance innate immunity. Significant declines in serum HBsAg are demonstrated during gene therapy that have never been seen using the most potent polymerase inhibitors (e.g. tenofovir or entecavir).

Lastly, unanticipated significant reductions in cccDNA are seen with HBV gene therapy, most likely as a result of an indirect benefit in reducing the immunosuppressive effect of large amounts of HBsAg released by infected hepatocytes that contributes to T cell exhaustion.

Hepatitis C and NASH

The unprecedented success of direct-acting antivirals (DAAs), which achieve an HCV cure in most treated individuals, has shifted the attention to other frequent conditions in this population. There is a need to continue monitoring and screening for hepatocellular carcinoma in patients with cirrhosis who have been cured of HCV [21]. Another frequently associated condition is fatty liver disease. **Laurence Serfaty** (Hautepierre Hospital, Strasbourg, France) addressed this issue, beginning with a review of the interplay between lipids and HCV, and how HCV cure may unveil metabolic abnormalities which, if not managed properly, may lead to progressive liver disease despite HCV elimination. Non-alcoholic liver disease (NAFLD) and steatohepatitis (NASH) are very prevalent and directly associated with overweight/obesity and

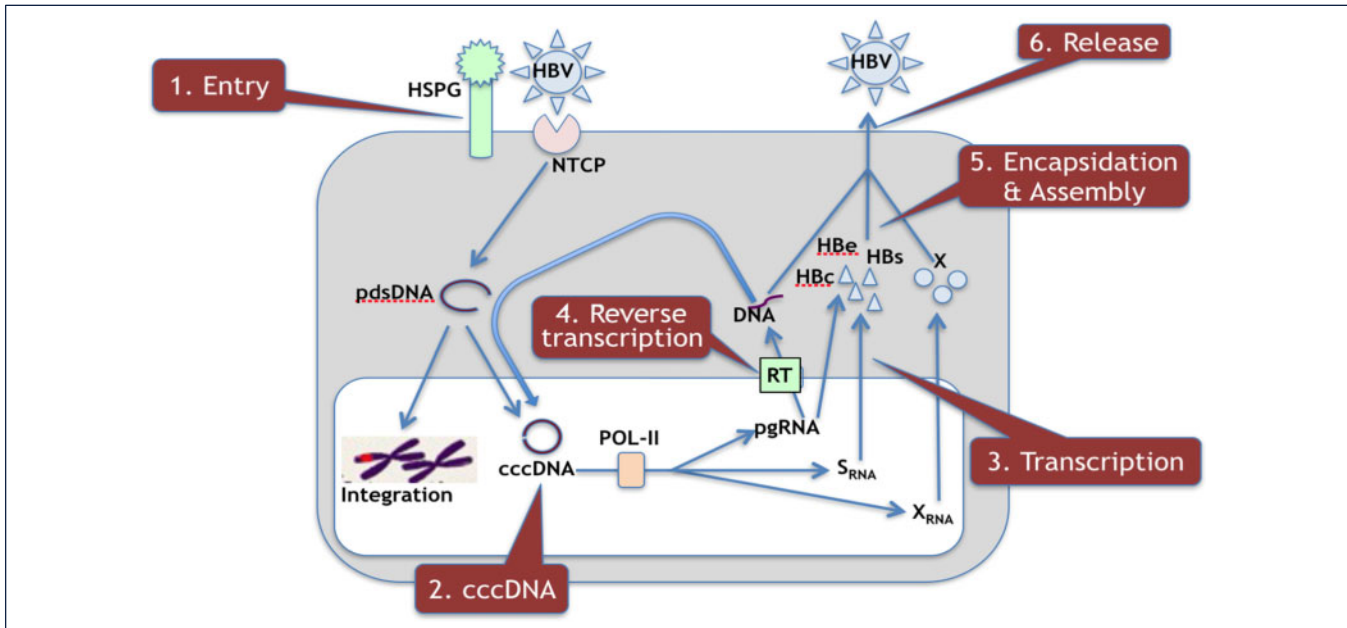


Figure 4. Major HBV therapeutic targets

sedentary life style [22]. To date, there is no good drug therapy to treat NASH, which unfortunately is becoming the predominant cause of cirrhosis, end-stage liver disease and liver transplantation in Western countries.

Hepatitis D

Hepatitis delta virus (HDV) is the smallest pathogenic agent that infects humans. However, it causes the most severe form of viral hepatitis, with frequent progression to cirrhosis and liver cancer [23]. To date there is no efficacious treatment against HDV, although anecdotal cases of benefit using tenofovir have been reported [24] and promising new experimental drugs are in development [25].

To complete its replicative cycle, HDV requires the presence of HBsAg, which is incorporated within the HDV envelope. Acute dual HBV and HDV co-infection may be clinically severe, sometimes presenting with fulminant hepatitis, but generally self-limited with development of antibodies and clearance of both viruses. In contrast, HDV superinfection of HBsAg+ carriers generally progresses to chronicity. Roughly 5% of the 240 million people with chronic HBV worldwide are estimated to be superinfected with HDV [26]. The decline in injection drug use in Western countries has driven a reduction in HDV incidence [27]; however, the growing opioid epidemic in the United States and rising ‘slamsex’ practices in Europe are challenging this trend [28].

The diagnosis of HDV infection is generally based on the demonstration of HDV antibodies (HDV-Ab) in HBsAg+ individuals. Serum HDV-RNA can be found in most chronic HBsAg+ carriers with reactive HDV-Ab, although with frequent significant fluctuations. Information on the rate and clinical relevance of HDV-Ab in persons with markers of resolved HBV infection is rather scarce. Presumably, this population should reflect past acute dual co-infection episodes. However, some of these individuals may present with elevated liver enzymes and/or significant hepatic fibrosis, opening the question of the existence of HBsAg-seronegative occult HDV infections.

Carmen de Mendoza (Puerta de Hierro University Hospital, Madrid, Spain) discussed this topic [29]. In her study, sera from 406 individuals with markers of resolved HBV infection were tested

for HDV-Ab, of which 20 (5%) were reactive. All of them were repeatedly negative for HDV-RNA, despite four displaying elevated liver enzymes. A retrospective investigation showed that three individuals had concomitant chronic HCV and one admitted high alcohol intake. She concluded that active HDV infection is not seen in patients with reactive HDV-Ab and markers of past HBV exposure [24]. These results reinforce the notion of a self-limited outcome following dual acute HBV and HDV co-infection and support the current policy of excluding HDV only in HBsAg+ individuals.

Chemsex

This year the subject of chemsex was covered during the first collaborative symposium between the European AIDS Clinical Society (EACS) and ISHEID.

Dominic Rowley (Saint James Hospital, Dublin, Ireland) presented on the whole new world of synergy between geo-sexual networking and recreational drugs (gammahydroxybutyrate or GHB or G, synthetic cathinones, crystal methamphetamine) that define a syndemic of specific behaviours and STI outbreaks worldwide. Chemsex practices have increased in prevalence over the past decade, especially in the MSM population, and are becoming a real public health problem. The concerns about these practices are not only related to their high toxicity (cardiovascular, psychological), which remain largely unknown and underestimated by consumers, but are also related to the increased prevalence of STIs and the risk of HIV acquisition. Dr Rowley described the new ‘MTV generation’ [30], those using methamphetamine, Truvada and Viagra to enhance sex and stay safe. The MISI (MSM Internet Survey Ireland) 2015 reports that in more than 3000 participants interviewed, 7% used chemsex during the previous year. Drugs used included ketamine, mephedrone, crystal meth and G, and were more often used by men with higher education, HIV seropositive status and aged under 30. In the GMHS, Ireland’s only MSM-specific sexual health clinic, 27% of persons interviewed (486 questionnaires) had engaged in chemsex, and 56% of respondents met their partners for chemsex through phone apps or online. Chemsex was associated with more partners, unprotected anal intercourse, having ever been diagnosed for a STI, and having ever been treated for an STI or HIV. However, 30% asked for help

or advice regarding chemsex. Direct drug-related harm may include polydrug use, injecting drug use, loss of consciousness and potential for addiction. Indirect drug-related harms include sexual risk-taking behaviours, increased risk of STIs and HIV, mental harms (depression, psychotic episodes, suicidal tendencies) as well as a negative impact in their lives (high financial burden, losing sense of time, loss of career, social isolation). These results support international evidence for a growing chemsex culture among MSM and reinforce the need for developing educational programmes/training courses around chemsex, aimed at not only users but also healthcare professionals in order to help manage this underestimated addiction, which is becoming a significant public health issue.

Viken Darakjian (Positive People Armenian Network Social NGO, Yerevan, Armenia) gave an overview of the current status of chemsex practices in Europe and presented chemsex from the community perspective. Chemsex is more common in the gay community, probably more in HIV-infected and younger MSM, with a higher prevalence in major Western European cities (see the European MSM Internet Survey (EMIS) 2016). This practice has appeared more recently in Eastern Europe but may be underestimated owing to stigma and discrimination in some countries. Different surveys carried out in France (25% of Hornet users are engaged in chemsex, of whom 7% engage several times a week), Ukraine and Armenia report that the major reasons for starting chemsex use are environmental and linked to their partner (already using it or in a 'party' context), or through curiosity. The main reason for continuing is related to the improvement (pleasure, potential) in their sexual life. Drug services and healthcare providers across Europe struggle to offer appropriate support because of a lack of expertise around chemsex and social media apps, as well as prejudice around drug use and gay sex. Sexual health professionals should learn to discuss sex and drugs with their MSM patients. Therefore, there is an urgent need for developing a chemsex care plan, involving both social and health professional communities, to help people who want to come out of the chemsex scene, and to work on harm reduction. Data collected during the European MSM Internet Survey (EMIS) 2017 will provide up-to-date information on the prevalence of chemsex across Europe, and will allow identification of priority target groups for interventions.

Zoë Greenwald (L'Actuel Medical Clinic, Montreal, Canada) presented results of a retrospective study carried out in 1881 MSM from their cohort, evaluating chemsex use and STI incidence among PrEP users [31]. Overall, 28% of MSM were chemsex users (most common drugs used were GHB/GBL and ecstasy) and they were significantly younger (35 versus 37.6 years), had more partners within the past 12 months (34 versus 28), a lower education level and an income <€23,000 (35% versus 30%), and using daily more frequently than intermittent PrEP (84% versus 78%) compared to non-chemsex users. Chemsex users experienced significantly higher 12-month cumulative STI risk (44.3% versus 34.6%) and cumulative rate of gonorrhoea (35.7% versus 21.3%) that corresponded to a 48% increased STI risk (RR 1.48, 95%CI 1.20–1.82). In conclusion, this study reported chemsex consumption in a high proportion of PrEP users, which may contribute to increased STI risk and highlights the urgent need for implementing counselling and combined prevention measures to minimise the potential harms associated with its use.

Lyme disease

Christian Perronne (Raymond Poincaré Hospital, Garches, France) gave a thought-provoking overview of Lyme disease, the tick-borne borreliosis infection that was first described more than 30 years

ago in the north-eastern part of the USA as a new rare regional event [32]. However, it is likely to have been present more than 5000 years ago. Professor Perronne described the associated clinical manifestations and stressed the pitfalls in terms of diagnosis and treatment in a context of increased incidence of the infection in many parts of Europe but with a lack of standardised surveillance reporting procedures [33].

The diagnosis of Lyme disease remains difficult as it mimics many other medical conditions and laboratory tests do not always permit confirmation of the diagnosis [34,35]. Furthermore, the initial bite is not always reported by affected individuals and the rash (erythema migrans) can be atypical. Untreated Lyme disease can produce a wide range of symptoms depending on the stage of the disease. Ticks can also spread several other organisms that may cause different types of rash. Stages 2 and 3 of the illness, coming weeks or months later, encompass symptoms such as high-grade fatigue, migrating pain, chronic signs and symptoms, often objective, but not specific, cutaneous, neurological, ophthalmological, psychiatric, articular, musculo-skeletal and cardiac, as well as auto-immune syndromes. Issues remain with commercial diagnostic tests that are not considered totally reliable in establishing the diagnosis and need to be supplemented by clinical data.

Persistence of symptoms after the initial standard antibiotic treatment may require a longer period of treatment. Professor Perronne cited randomised studies published in the *New England Journal of Medicine* with a longer duration of treatment that have brought negative results [36,37]. These have methodological issues and were therefore considered by him as non-conclusive. There is still a lack of trials looking at a very prolonged period of treatment and its impact on symptoms. Professor Perronne urged for urgent research in diagnostics and therapy.

The microbiome

Sergio Serrano (Ramon y Cajal Hospital, Madrid, Spain) gave a presentation on considering the microbiota as an ecosystem [38]. Blood microbiota may play a crucial role in HIV/SIV pathogenesis, and in individuals living with HIV, there is a blood microbiota signature that is linked with immune recovery and inflammation under ART [39], as well as vaccine immunogenicity. Genital microbiota not only influence the risk of HIV acquisition in men and women [40] but may also determine the effectiveness of tenofovir gel against HIV (Figure 5) [41]. The lung microbiome is related to bacterial infection [42] and tuberculosis susceptibility and could affect the risk of pulmonary diseases in HIV, such as chronic obstructive pulmonary disease and lung cancer. He suggested that HIV, HPV and microbiota may be partners in the crime of HPV-related cancers in HIV, because epithelium-adherent microbiota (anal, cervical or oral) may promote HPV malignant transformation [43]. Microbiota-oriented precision medicine may offer an opportunity for personalised medicine, even if results so far have been inconclusive in individuals living with HIV.

New pathways for HIV cure

Ole Schmeltz Søgaard (Aarhus University, Aarhus, Denmark) discussed 'shock and kill' versus 'block and lock' strategies. Although many LRAs have been tested in clinical trials (Table 2), their impact on the size of the reservoir has been disappointing [44,45]. Either the 'shock' has been too weak, reactivating too few infected cells (suggesting the need for LRA combinations), or the 'kill' does not occur *in vivo* owing to inadequate immune responses. Therefore, 'shock and kill' as a strategy for a sterilising HIV cure will be very difficult to achieve with the current portfolio of compounds. The timing of therapeutic interventions relative

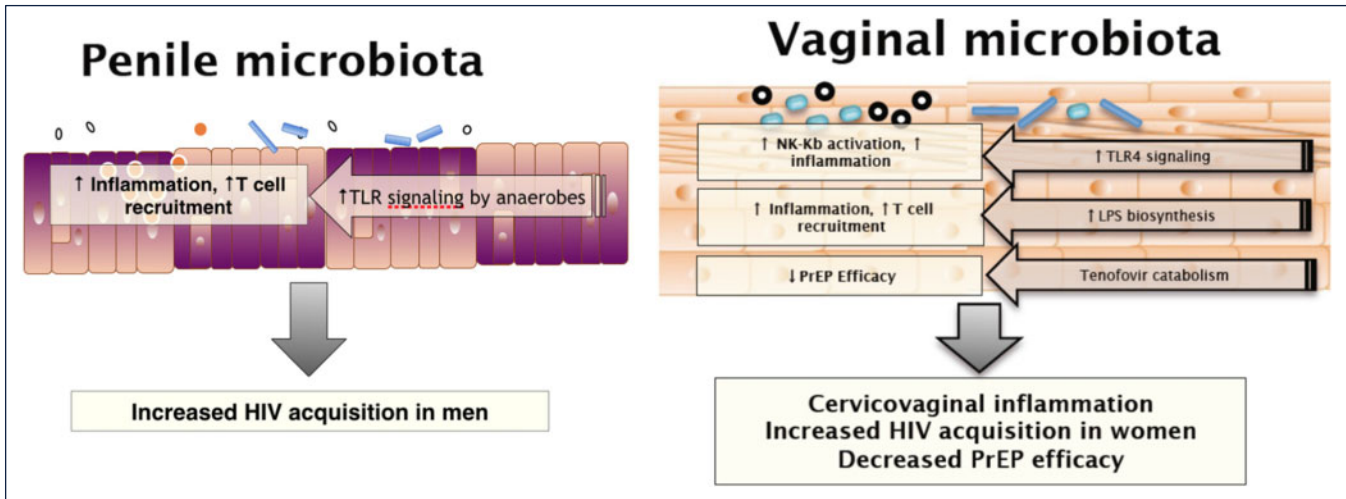


Figure 5. Genital microbiota and HIV transmission

Table 2. LRAs tested in clinical trials

Latency reversing agent	Drug class	Effect on transcription in CD4s	Single or Multi-dose study	US HIV RNA (transcription)	HIV protein expression	Plasma HIV RNA (SCA or TMA)	Plasma HIV RNA (Cobas)	Reference (s)
Vorinostat	HDACi	Direct	S+M	++	+	+	-	Archin et al. 2012, 2014, 2017; Elliott et al. 2015
Panobinostat	HDACi	Direct	M	++	+	+	ND	Rasmussen et al. 2014
Romidepsin	HDACi	Direct	(S)+M	++	ND	++	+	Søgaard et al. 2015; Leth et al. 2016
Disulfiram	Anti-alcohol	Direct	M	+	ND	+	-	Spivak et al. 2014; Elliott et al. 2015
Bryostatins	Protein Kinase C (PKC) activator	Direct	S	-	ND	-	-	Gutiérrez et al. 2016
MGN1703	TLR9 agonist	Via pDCs	M	-	ND	ND	(+)	Vibholm et al. 2017
GS-9620	TLR7 agonist	Via pDCs	M	?	?	?	?	?

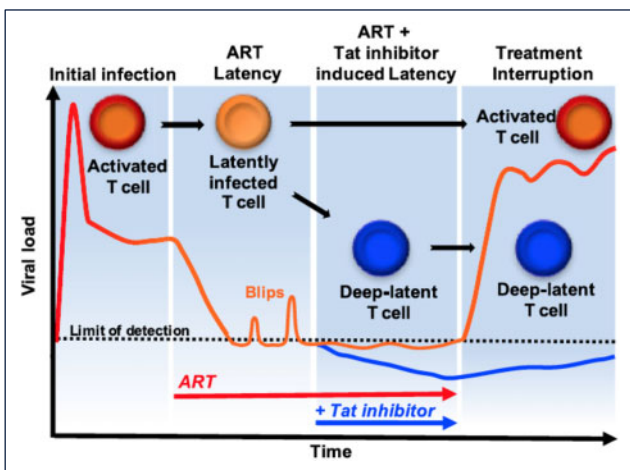


Figure 6. Principles of the block and lock strategy [46]

to ART may impact both the reservoir and immune functions. The ‘block and lock’ strategy (Figure 6) is a more recent development and is currently using a Tat inhibitor (didehydro-cortistatin A or dCA) that has been tested in cell culture and humanised mice; however, the safety profile in humans is unknown [46].

Christina Psomas (European Hospital, Marseille, France) presented perspectives of new markers of HIV latency. The ‘Holy Grail’ of the HIV world is to identify a marker that could characterise latently

infected cells. Indeed, these latently infected long-lived memory CD4+ T cells are the major obstacle for achieving a sterilising cure. They not only remain invisible to the immune system but are also not removed by antiretroviral therapy and cure approaches because of a lack of targeting specificity of ‘shock and kill’ strategies involving reactivation of the dormant virus. In a recent *Nature* article, Descours *et al.* reported that CD32a, the low-affinity receptor for the immunoglobulin G Fc fragment may be a cell surface signature of CD4+ T cells harbouring latent HIV genomes [48]. Since then, the relationship between CD32a expression and HIV persistence has been strongly debated by other groups. Will this biomarker help us address the mystery surrounding *in vivo* latent reservoirs and develop a cure-focused HIV diagnostic in the near future? Will newer biomarkers such as CD30 be less debated and more helpful [49]?

Therapeutic management of comorbid diseases

During this morning session, **Patrick Mallon** (University College Dublin School of Medicine, Dublin, Ireland) gave an overview of bone disorders. Several factors are involved such as the increased number of individuals living with HIV reaching the age at which bone issues occur, the fact that low bone mineral density (BMD) is more prevalent in people living with HIV in comparison to the general population with similar demographic characteristics and the available evidence showing an increased risk of fractures in those living with HIV regardless of age.

With a practical clinical point of view, Dr Mallon structured this topic into three parts: prevention, reversion of BMD loss and some tips for maintaining bone health.

Regarding prevention, he stressed the need for systematic screening for low BMD by performing DEXA scans. The EACS guidelines suggest DEXA scans in high-risk patients: postmenopausal women, men over 50 years of age, those under the age of 50 at high risk for fractures, patients with risk factors for falls, those with past history of low impact fractures, clinical hypogonadism, and those with significant steroid exposure. Initiation of ART is associated with a BMD loss of between 2% and 5%, irrespective of the regimen, and is similar to that observed after menopause. The degree of BMD loss in ART-experienced patients after re-initiation of ART (demonstrated in the Second-Line study) is similar to what is observed with first line treatment.

For reversion of BMD loss, Dr Mallon reviewed the different effects of ART on BMD. Data from several clinical trials demonstrates the negative effects on BMD of tenofovir disoproxil fumarate (TDF) and protease inhibitor-based regimens in ART-naïve patients. Switching from TDF to tenofovir alafenamide (TAF) produces increments in BMD of around 1.5%. Other strategies such as giving calcium and vitamin D supplements or bisphosphonates during ART initiation have proved useful in ameliorating the initial BMD loss. There is less evidence on the effect of switching away from TDF-based regimens in the long term. Data from some cohorts such as the HIV-UPBEAT demonstrate that the initial decay of BMD after ART tended to stabilise in the long term.

Dr Mallon suggested strategies other than pharmacological interventions for maintaining bone health in the long term: strengthening physical exercise, lowering immune activation (future area of research) and in particular, smoking cessation. He explained that in the HIV-UPBEAT cohort the statistically significant association found between bone microarchitecture, measured by trabecular bone score (TBS), and HIV disappeared after adjusting for smoking status, highlighting the importance of this issue.

Rosan van Zoest (Institute for Global Health and Development, Amsterdam, the Netherlands) discussed the new challenges of comorbidities. This topic is directly derived from the happy fact that, as a consequence of effective ART, people living with HIV have a similar life expectancy as those in the general population. A modelling study from the Netherlands shows that 73% of those living with HIV will be over 50 years in 2030. This will imply a high burden of comorbidities and multimorbidity, with this trend likely to increase over time. Recent reports highlight the increased frequency of comorbidities in people living with HIV in comparison with HIV-negative controls, especially with respect to cardiovascular (CV) diseases, some non-AIDS-related cancers and chronic kidney disease. The ultimate cause of this is multifactorial. The higher prevalence of some traditional CV risk factors such as smoking, dyslipidaemia or hypertension is a critical issue. Among these, tobacco use is the one that deserves most attention as several studies have suggested that the relationship between smoking and comorbidities, in particular, CV disease, may be stronger in HIV-positive individuals compared with the general population. Platelet dysfunction, endothelial-cell activation, low-grade immune activation, and inflammation, in spite of effective ART, are likely to be involved in the higher comorbidity burden in people living with HIV. Rosan van Zoest concluded that several strategies could be used to reduce the burden of comorbidities in those living with HIV, including prompt HIV diagnoses and early ART initiation, avoidance of certain HIV agents with some toxic side-effects in both the short and long term, and a more aggressive management of traditional risk factors for comorbidities.

Jean-Pierre Routy (McGill University, Montréal, Canada) reviewed the interplay between HIV infection and lungs, focusing specifically on lung cancer [50]. It is the most frequently diagnosed non-AIDS cancer in people living with HIV and the only increasing one with a non-infectious cause. Several risk factors have been put forward: smoking, history of bacterial pneumonia and a low CD4: CD8 ratio. Lung infections promote some metabolic and epigenetic changes in innate immune cells located in the lungs, which result in enhanced immune responses upon re-infection. This trained innate immunity could inappropriately activate inflammatory pathways in the long term and increase the risk for lung cancer.

Professor Routy also presented data on specific characteristics of lung cancer in people living with HIV. Data from a Canadian study showed an increased mortality in patients with non-small-cell lung cancer in comparison with the general population. A recent systematic review and meta-analysis, including different types of lung cancer, also suggest a higher mortality for patients with HIV and lung cancer [51]. A recent revolution in medicine involves immunotherapy against cancer with anti-PD1/PD-L1 antibodies that have shown high efficacy against different types of cancer. These drugs are promising. Recent data have demonstrated a higher expression of PD-L1 levels with increased immune infiltration in samples from patients with HIV and lung cancer [52]. This should encourage further investigation and the commitment from pharma companies not to systematically exclude people living with HIV from clinical trials testing these new immune therapies. Finally, an intriguing discovery: the gut microbiota influences the response to PD-1-based therapies against different epithelial tumours and could explain resistance to some of these drugs.

After these excellent plenaries, there were two oral presentations on environmental exposures and airflow obstruction, and the impact on the lipid profile of switching to TAF. **Cecilia Costiniuk** (McGill University Health Centre, Chronic Viral Illness Service, Montreal, Canada) [53] underscored the importance of COPD with a prevalence of 11% in people living with HIV according to a recent meta-analysis published in *Lancet Global Health* [54]. Dr Costiniuk presented a cross-sectional study in 508 participants, 95% on ART, and 92% with suppressed HIV viral load.

Spirometry was performed in all participants and an extensive questionnaire about environmental/occupational exposure was completed. The authors found an 11% prevalence of airflow obstruction defined by a FEV1/FVC <70% post-bronchodilator. Smoking and older age were independent predictors of non-reversible airflow obstruction but environmental or occupational exposure was not associated with non-reversible airflow obstruction.

In the final oral presentation **Aoife Lacey** (University College Dublin, School of Medicine, HIV Molecular Research Group, Dublin, Ireland) presented the results of a retrospective study that showed changes in the lipid profile following switch from a TDF- to TAF-containing regimen [55]. They compared pre- and post-switch lipid data in 194 patients. Baseline characteristics of the participants were a median age of 46 years, 70.6% were male and 70% white. Median CD4 T cell count was 621 cells/mm³, 90% had an undetectable viral load (HIV-1 RNA <40 copies/mL), 23.7% were on lipid-lowering drugs, and 87.8% had TAF as a backbone. Significant increases in all lipid fractions were observed (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and TC: HDL ratio). Using the recent definition of dyslipidaemia according to the ATP III guidelines thresholds, a greater proportion of participants met this definition especially for total cholesterol and LDL cholesterol. The authors concluded that further studies are needed to ascertain whether these differences are a consequence of TDF cessation or TAF initiation.

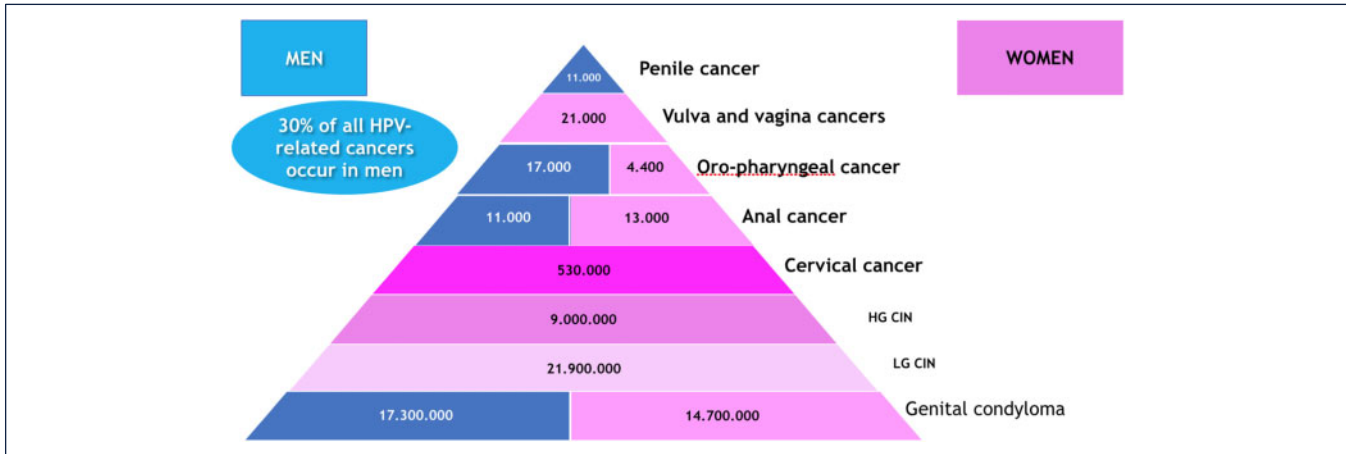


Figure 7. Estimate of number of HPV-related lesions/year worldwide

Immunotherapies and immune check-points

Jean-Philippe Spano (Pitié-Salpêtrière Hospital, Paris, France) gave an overview of this very fast emerging new therapeutic approach in oncology [56]. For a wide spectrum of malignancies, the use of PD-1 or PD-L1 and/or CTL-4 immune-checkpoint-inhibitor antibody (ICI) that restores antitumor immunity by disrupting PD-1/PD-L1 or CTL-4-mediated signalling has demonstrated efficacy compared with conventional chemotherapy but also a significant toxicity profile. Since several Phase 3 studies show a significant impact upon overall survival compared with conventional chemotherapy, some ICIs (ipilimumab, nivolumab, pembrolizumab, atezolizumab, darvelumab) have already received FDA and/or EMA approval, providing a new standard of care for some cancer patients. PD-1 receptor for example, which is expressed on activated T cells, in link with ligands PD-L1 and PD-L2 expressed in tumour cells, remains the cornerstone for the rational for the development of such drugs. In the HIV setting, PD-1 expression on HIV-specific T cells is associated with T cell exhaustion and some preclinical studies have suggested that blocking the PD-1/PD-L1 axis with monoclonal antibodies would be of interest in HIV-associated lymphoma and possibly other cancers.

Workshop on STIs

Dominique Tessier (PEP Clinic, Centre Hospitalier de l'Université de Montréal, Montreal, Canada) presented results of PrEP consultations at L'Actuel/CMUQL. Over 1500 patients have already been enrolled in their PrEP programme. The entire team is committed to standardised follow-up, prescription and data collection. Until recently, only Quebec had offered public reimbursement for PrEP. Elsewhere, individuals wishing to use PrEP had been limited to coverage via private third-party insurance, or through use of so-called 'buyers' clubs, which promote access via online pharmacies. Positive PrEP consequences principally include a 90% decrease in HIV incidence, after a discouraging increase in new HIV cases in 2015. Negative PrEP consequences include failures (HIV seroconversion at the beginning of PrEP or after it has been stopped), 'pretend to be on PrEP' issues, and an increase in STI diagnoses and treatment. This last point still requires analysis to see whether it involves a net increase in acquired STIs or early diagnosis in the context of PrEP programmes.

Deborah Konopnicki (Saint Pierre University Hospital, Brussels, Belgium) discussed HPV vaccination in prevention and cure [57]. Human papillomaviruses (HPV) are responsible for the development of condyloma and cancer in the ano-genital and oropharyngeal areas (Figure 7). These lesions are more frequent and more difficult to

treat in HIV-positive persons. Preventative vaccines against HPV have been available for a decade. They are safe and efficacious and their use in primary and secondary prophylaxis should be suggested to HIV-positive patients, where suppressed HIV viral load is associated with a higher level of antibodies induced by vaccination. Until further data are available for HIV-positive patients, a three-dose schedule is recommended for both adults and children. Meanwhile, other therapeutic vaccines are in development. In future, they could contribute to less aggressive ablative therapy for HPV-associated lesions.

Clinical research and methodology

In the first of two methodological talks, **Rodolphe Thiebaut** (Research Center 'Bordeaux Population Health' U1219, Bordeaux, France) described how *in silico* clinical trials could add value to existing drug development programmes. This computer-simulation approach could be used in the development or evaluation of a new drug, device or intervention, allowing efficiencies in the selection and design of subsequent clinical trials. The approach requires investigators to define a mathematical model that will reasonably approximate the underlying mechanisms of interest, which is then parameterised using existing information from a variety of sources. These models also incorporate unmeasured inter-individual variability. As a first example, he described how models of viral dynamics could be used in the assessment of novel ART strategies that would reduce the amount of individual drug exposure, thus potentially reducing toxicity risk and costs. The model findings suggested that while ART strategies that treated individuals for 4 or 5 days out of every 7 may provide adequate drug coverage to ensure maintenance of viral suppression (with the ART regimens based on EFV/3TC plus a second NRTI), further reduction in the number of days of treatment is likely to lead to viral rebound. His second example illustrated how *in silico* models could be used to identify the impact of different frequencies of IL-7 administration on CD4 cell survival and proliferation. He concluded by emphasising that while no model was ever perfectly defined, some may provide useful information that could be used to guide the design of future strategic treatment trials.

Caroline Sabin (University College London, London, UK) next described the benefits and possible disadvantages of cohort studies [58]. While randomised controlled trials are generally felt to be the study design that provides the highest level of evidence, these are not always feasible or practical. In such cases when it is impossible to conduct a randomised trial (for example, when assessing the impact of a lifestyle or behavioural exposure), cohort studies may offer a good alternative design. These studies follow a group of

individuals over time, identifying those who are and are not exposed to a factor of interest and relating this exposure to outcomes. However, whilst cohort studies are commonly reported in the literature, they do have several limitations, particularly around the possible presence of bias. Confounding, in particular, may have a strong impact on the estimated association between exposure and outcome. To illustrate this point, she provided examples of situations where associations between HIV infection and a comorbidity or biomarker have been confounded by age and cytomegalovirus (CMV) infection, respectively. In both cases, an apparent association between HIV status and the outcome was attenuated after adjustment for the confounder. These examples emphasise the importance of consideration of the possibility that bias may have been introduced as part of the study design, analysis or publication process. She also noted that while appropriate statistical methods may sometimes reduce the impact of bias, they may not always be successful.

How to measure HIV-1 reservoirs

Alexander Pasternak (Laboratory of Experimental Virology, Department of Medical Microbiology, Academic Medical Center, Amsterdam, the Netherlands) discussed the important issue of how to measure HIV-1 reservoirs and predict the outcome of ART interruptions. He described the ideal assay that would include the following characteristics: high sensitivity as it must be able to detect rare events in a high background of uninfected cells; high specificity; potential to distinguish replication-competent from non-replication-competent reservoir; high precision with a large dynamic range with the possibility to detect small changes in the reservoir when monitoring *in vivo* curative interventions.

Dr Pasternak then reviewed the various methods that are available to measure the HIV reservoir. The PCR-based methods for HIV DNA (total or integrated) cannot distinguish replication-competent from non-replication-competent virus, bearing in mind that the majority (>90%) of the proviruses detected are defective and therefore the size of the replication-competent reservoir is overestimated. The quantitative viral outgrowth assay (qVOA) is able to distinguish replication-competent from non-replication-competent virus but underestimates the size of the latent reservoir [59]. The murine viral outgrowth assay (mVOA) which uses *in vivo* amplification of replication-competent HIV may be more sensitive than qVOA but is long, laborious, requires laboratory animals, and is not quantitative (unless multiple mice are xenografted in the LDA) [60]. Another type of assay, which includes the inducible RNA transcription assays (i.e. TILDA, iCARED, and others), still overestimate the true size of the replication-competent reservoir and partly detect defective provirus [61]. The HIV translation-competent reservoir might be more specific than cell-associated RNA alone but is laborious, requires many cells and still overestimates the reservoir as gag expression is necessary but not sufficient for replication-competence [62].

When looking at the results of a clinical randomised study of early and temporary antiretroviral treatment in primary HIV infection in the Netherlands, cell-associated HIV-1 unspliced RNA level independently predicted both time to virological suppression and time to virological rebound in patients treated with temporary early ART [63]. Unspliced RNA, total viral DNA and the CD4+ T cell count were measured before ART interruption. Unspliced RNA was associated to time to viral rebound and warrants further exploration as a predictor of post-treatment control in large-scale clinical trials aimed at functional cure. Cell-associated HIV-1 multiply spliced (MS) RNA level independently predicted disease progression (CD4+ T-cell loss) after interruption of early ART, while unspliced RNA was not.

In conclusion when looking at reservoirs, HIV DNA represents a marker of total reservoir that is mostly defective. Unspliced RNA is a marker of the active reservoir (cells transcribing viral RNA). It overestimates the latter but may correlate with functional reservoir (cells that produce virus or can become reactivated upon latency reversal). Multiply spliced (MS) RNA, a marker of the 'hyperactive reservoir' (cells with high MS RNA levels, a subset of active reservoir). The relative size of this 'hyperactive reservoir' may drive HIV pathogenesis, determining the rate of CD4+ T cell loss.

COREVIH session: the pathway of care for people living with HIV

Guillaume Gras (CeGIDD 37, President of COREVIH Centre Val de Loire, France) inaugurated this session explaining that the chronicity of HIV infection combined with medical demographic changes contribute to improvement of the care pathway.

A cooperation agreement between healthcare workers could lead to changes in activity patterns. For example, consultations every 6 months alternately with a doctor and a nurse could be implemented. The nurse could perform blood tests, clinical measures, vaccinations, counselling, evaluation of risk factors (cardiovascular, neurological, bones, tobacco use), prescriptions and appointments, as well as record the visit. It is important to notice that a high level of acceptability from patients is expected, even if healthcare workers express some fears.

Roland Landman (Hôpital Bichat Claude Bernard SMIT IMEA, INSERM U 1137, Paris, France) talked about therapeutic alleviation or decreasing the pill burden in order to reduce toxicities, drug-drug interactions, as well as health costs. Although many studies are yet to report, dual-therapy is already recommended in European and French guidelines for some combinations (protease inhibitors/ritonavir+3TC, DTG + RPV) in virologically suppressed patients (<50 copies/mL) for at least 6–24 months respectively, with particular caution needed for monitoring HIV-1 DNA, archived genotypic mutations and patients' adherence. Results of pilot studies of discontinued regimens are rather encouraging (90% success in 53 patients in the FOTO study, 87% success in 113 patients in a Ugandan study, 100% success in ICCARRE study). QUATUOR is an on-going multicentric French ANRS study evaluating non-inferiority at week 48 between a 4 versus 7 day 3 drug ART regimen in virologically suppressed patients.

Jean-Daniel Matthieu (Réseau Santé Marseille Sud, France) concluded this session explaining his journey as a person living with HIV and the help he had from the community network. He talked about the impact of arguing with medical doctors and healthcare workers and described how he fought for his life. He highlighted the fact that patients should be actors in healthcare.

Electronic technology to improve HIV management

Lynn Fiellin (Yale Center for Health and Learning Games, New Haven, CT, USA) presented her original research about the future of digital games for HIV prevention and care [64]. The purpose of her presentation was to share two digital games that have been developed and evaluated by the play2PREVENT Lab at Yale to focus on risk reduction and HIV prevention, and HIV testing and counselling. The first game, PlayForward: Elm City Stories (PlayForward), is a 2-D graphic novel-style interactive videogame that focuses on adolescents acquiring and practising skills to reduce risk behaviours and gain knowledge and healthier attitudes and intentions with the ultimate goal of HIV prevention. The impact

of PlayForward on at-risk adolescents was recently rigorously evaluated through a full-scale randomised controlled trial and demonstrated a significant and persistent positive effect on behavioural antecedents/health outcomes that are critical for HIV prevention. A follow-up game, PlayForward: Test! was adapted from the original game to have a greater focus on HIV testing and counselling. This game has been pilot-tested and is undergoing further expansion and will then be evaluated through a randomised clinical trial.

What's up in PrEP

The subject of PrEP was covered during the first collaborative symposium between the British HIV Association (BHIVA) and ISHEID.

Rosalind Coleman (Joint United Nations Programme on HIV/AIDS, Geneva, Switzerland) covered a regional review of PrEP regulatory status and activity [65]. She explained that the differences in the specific form of PrEP that is available to a national level depends on international considerations, such as active patents or the existence of national legislation that enables TRIPS flexibilities to be exploited. This is why some programmes may use originator TDF/FTC, some generic TDF/FTC and others generic forms of TDX/FTC. The PrEP provision is handled differently in each country. Only six countries have it reimbursed/free at the point of delivery (Scotland, Wales, Sweden, France, Belgium and Norway). In England, Portugal and the Netherlands it is provided as part of a trial. In other countries, provision is less co-ordinated. EACS recommendations include daily PrEP and, for MSM, event driven PrEP is also an option. Dr Coleman reported that the majority of individuals in Europe use it daily. Owing to low rates of PrEP provision within national programmes, she described high rates of internet purchasing. Internet purchasing is well supported by a large community of activists who are highly motivated and provide very useful materials and advice. She cautions that this situation nonetheless may result in a lack of follow-up, potential for resistance, side-effects and inadequate dosing leading to new infections. 'Generic access via the internet is not a strategy'. She commended the high-level, targeted and rapid roll-out of PrEP in New South Wales which led to a 35% decline in state-wide HIV diagnoses in MSM, and a 44% decline in early HIV infections in this population within one year of enrolment. She noted that in a concentrated epidemic with high testing and treatment coverage, PrEP scale-up has led to a rapid decline in HIV transmission at the population level. She concluded that while there is widespread PrEP demand, provision and access across Europe are highly variable and often inadequate. She identified PrEP as a contributor to the control of the HIV epidemic where it is part of comprehensive and accessible HIV prevention provision, including testing and treatment to viral suppression. She urged countries to use all means possible to provide access to affordable PrEP for people and populations at substantial risk of HIV infection.

The second speaker, **Brooke Nichols** (Johannesburg, South Africa) spoke on the cost-effectiveness of PrEP in the European context [66]. She started by stating that when an infection is prevented, there is saving of the associated lifetime costs of HIV infection. This is estimated to equate to a ~€320,000 lifetime cost. Effectiveness is reported as: quality-adjusted life years (QALYs) gained or infections averted. These are generally calculated using dynamic HIV transmission modelling, that is when PrEP is given to a certain number of people, how many infections can we expect to prevent? How many QALYs can we expect to gain? These measures are affected by adherence and exposure risk which are derived from PrEP trials. While widely debated, an intervention

is considered highly cost-effective if it is below the threshold of GDP per capita per QALY gained. However, it also depends on the willingness of a country to pay and on a country-specific QALY threshold set. She cited the example of the Netherlands that may be willing to spend €20,000/QALY gained, whereas Belgium may be willing to pay €50,000/QALY gained. Dr Nichols reported that PrEP cost-effectiveness has been demonstrated for MSM in European countries with good treatment coverage. The majority of studies on the MSM epidemic show cost-savings are possible with generic pricing. She calls for more information on the epidemic in IVDUs. To the question of whether PrEP is affordable in Europe, she replied that it will depend on healthcare systems structure, financing and resource constraints at the country level but will be more likely with generic pricing.

In summary, this lively symposium re-iterated the importance and cost-effectiveness of PrEP and that more political will is needed across most of Europe to implement this crucial and cost-effective intervention and make it available to all who need it.

The expert patient

During this session, the experience of two individuals living with HIV was shared with the audience. **Xavier Rey Coquais** (Association ACTIF Santé, Université des Patients, Paris) elaborated on the following question: 'Is research more efficient while involving expert patients? Or is it just political correctness?'

In a context where volunteers and healthcare providers are alone with information circulating with delay, the action of creating groups and generating expertise may be an efficient solution for a better dissemination of information among health providers, rapid and accurate feedback on adverse events, faster recruitment into trials and as a result an improved access to therapy. Patient communities may help enhance quality and security of care at reduced cost for the healthcare system.

The second topic was entitled: 'From activism to research: the experience of a patient who became expert.' **Fabienne Hejoaka** (Marseille, France) described her life journey from the fear of dying to the lessons that she drew from other people's HIV experience. In 2012, she graduated with a PhD in social anthropology with a thesis entitled: 'Children and secrecy: living and growing up with HIV in Burkina Faso'. In 2017, she went back to university to study for a certificate in therapeutic education, a course founded by Catherine Tourette-Turgis and a multidisciplinary team in 2009. The purpose of her research was to include 50% of expert patients with a recognition of experiential knowledge of patients, a validation of competencies with a diploma. She showed the importance of narration and testimonies leading to reflexivity, taking distance from YOUR illness, to be able to communicate, disclosing oneself and sharing experience, hearing others, and giving advice to others. The paradox of the 'healthy expert patient' is a real engagement, a will to work with and to support other patients.

Extracts from the movie '*120 Beats per minute*', by **Robin Campillo**, which tells the story of activists from ACT-UP Paris before ART introduction, were shown.

This session closed the Conference with a poignant moment. All participants, community members and healthcare providers, shared together the certainty of the common battle for people living with HIV, with those of us who are still here remembering those who have left us prematurely.

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References

- Vella S. From HIV to Global Health. *J Virus Erad* 2018; **4**(Suppl 1): abstract S1.
- Vella S, Wilson D. From Durban to Durban: end of AIDS further than hoped. *Lancet HIV* 2016; **3**: e403–405.
- Vella S, Wilson D. Access to medicines: lessons from the HIV response. *Lancet HIV* 2017; e147–e149.
- Mothe B, Molto J, Manzardo C *et al*. Viral control induced by HIVCONSV vaccines and romidepsin in early treated individuals. *Conference on Retroviruses and Opportunistic Infections*. February 2017. Seattle, WA, USA. Abstract 119LB.
- Cohen MS, Shaw GM, McMichael AJ, Haynes BF. Acute HIV-1 infection. *N Engl J Med* 2011; **364**: 1943–1954.
- Rutsaert S. Total HIV DNA as guidance for simplification strategies. *J Virus Erad* 2018; **4**(Suppl 1): abstract S2.
- Marcelin AG. Virological Factors Associated with Outcome of Dual ETR/RAL Therapy (ANRS-163 Trial). *European AIDS Conference*. October 2017. Milan, Italy.
- Bartumeus F, Israel M. Platform for the Integrated Control of Arbovirosis in Catalonia (PICAT): Mosquito Alert 2.0. *J Virus Erad* 2018; **4**(Suppl 1): abstract S3.
- Palmer JRB, Oltra A, Collantes F *et al*. Citizen science provides a reliable and scalable tool to track disease-carrying mosquitoes. *Nat Commun* 2017; **8**: 916.
- Bartumeus F, Oltra A, Palmer JRB. Citizen science: a gateway for innovation in disease-carrying mosquito management? *Trends Parasitol* 2018 (Epub ahead of print).
- Eritja R, Palmer JRB, Roiz D *et al*. Direct evidence of adult *Aedes albopictus* dispersal by Car. *Sci Rep* 2017 **24**; **7**: 14399.
- Gonzalez JP. Climate change, socio-political changes and emerging pandemics. *J Virus Erad* 2018; **4**(Suppl 1): abstract S4.
- Smits SA, Leach J, Sonnenburg ED *et al*. Seasonal cycling in the gut microbiome of the Hadza hunter-gatherers of Tanzania. *Science* 2017; **357**: 802–806.
- Soriano V, Barreiro P, Sherman K. The changing epidemiology of liver disease in HIV patients. *AIDS Rev* 2013; **15**: 25–31.
- Tsachouridou O, Papagianni M, Pilalas D *et al*. Sero-epidemiological study of adherence to vaccine and humoral response against hepatitis A virus in HIV patients. *J Virus Erad* 2018; **4**(Suppl 1): abstract O4.
- Barreiro P, Soriano V. Hepatitis A outbreaks in European homosexual men. *AIDS Rev* 2017; **19**: 113–114.
- Philibert P, Penaranda G, Chiche L *et al*. High incidence of sexually transmitted infections in HIV-negative MSM patients: a real-life prospective cohort study. *J Virus Erad* 2018; **4**(Suppl 1): abstract O9.
- Soriano V, Tefferi A. Prevention of liver cancer with new curative hepatitis C antivirals: real-world challenges. *Cancer* 2018; **124**: 1647–1649.
- Soriano V, Barreiro P, Benitez L *et al*. New antivirals for the treatment of chronic hepatitis B. *Expert Opin Investig Drugs* 2017; **26**: 843–851.
- Soriano V. New antivirals for hepatitis B. *J Virus Erad* 2018; **4**(Suppl 1): abstract S5.
- Soriano V, Benitez L, Arias A *et al*. Need to face liver cirrhosis after HCV cure with antivirals. *EBioMedicine* 2017; **24**: 24–25.
- Serfaty L. Emerging of NASH issues after cure of hepatitis C. *J Virus Erad* 2018; **4**(Suppl 1): abstract S6.
- Fernandez-Montero JV, Vispo E, Barreiro P *et al*. Hepatitis delta is a major determinant of liver decompensation events and death in HIV-infected patients. *Clin Infect Dis* 2014; **58**: 1549–1553.
- Soriano V, Vispo E, Sierra-Enguita R *et al*. Efficacy of prolonged tenofovir therapy on hepatitis delta in HIV-infected patients. *AIDS* 2014; **28**: 2389–2394.
- Soriano V, Aguilera A. Hepatitis delta enters a new therapeutic era. *J Infect Dis* 2018; **217**: 1173–1176.
- Soriano V, Sherman K, Barreiro P. Hepatitis delta and HIV infection. *AIDS* 2017; **31**: 875–884.
- Aguilera A, Soriano V, Rodriguez-Trastoy R *et al*. Prevalence and incidence of hepatitis delta in chronic hepatitis B patients in Spain. *J Virus Erad* 2018; **4** (Suppl 1): abstract O3.
- Soriano V, Ramos JM, Barreiro P, Fernandez-Montero JV. AIDS clinical research in Spain - Large HIV population, geniality of doctors, and missing opportunities. *Viruses* 2018; **10**: E293.
- Aguilera A, Soriano V, Rodriguez-Calviño J, de Mendoza C. Hepatitis delta in patients with resolved hepatitis B virus infection. *J Virus Erad* 2018; **4** (Suppl 1): abstract P22.
- Hammoud MA, Vaccher S, Jin F *et al*. The new MTV generation: Using methamphetamine, Truvada, and Viagra to enhance sex and stay safe. *Int J Drug Policy* 2018; **55**: 197–204.
- Greenwald Z, Beauchemin M, Longpré D *et al*. Chemsex on PrEP: risk behaviours and STI incidence among PrEP patients using illicit substances. *J Virus Erad* 2018; **4**(Suppl 1): abstract O6.
- Perronne C. Diagnosis, treatment and controversy. *J Virus Erad* 2018; **4** (Suppl 1): abstract S7.
- Van den Wijngaard CC, Hofhuis A, Simoes M *et al*. Surveillance perspective on Lyme borreliosis across the European Union and European Economic Area. *Euro Surveill* 2017; **22**: 30569.
- Cook MJ, Puri BK. Commercial test kits for detection of Lyme borreliosis: a meta-analysis of test accuracy. *Int J Gen Med* 2016; **9**: 427–440.
- European Centre for Disease Prevention and Control. A systematic literature review on the diagnostic accuracy of serological tests for Lyme borreliosis. Stockholm: ECDC, 2016. Available at: ecdc.europa.eu/en/publications/Publications/Lyme-borreliosis-diagnostic-accuracy-serological-tests-systematic-review.pdf (accessed June 2018).
- Klempner MS, Hu LT, Evans J *et al*. Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. *N Engl J Med* 2001; **345**: 85–92.
- Berende A, Ter Hofstede HJM, Vos FJ *et al*. Randomized trial of longer-term therapy for symptoms attributed to Lyme disease. *N Engl J Med* 2016; **374**: 1209–1220.
- Serrano-Villar S, Moreno S, Ferrer M. The functional consequences of the microbiome in HIV: insights from metabolomic studies. *Curr Opin HIV AIDS* 2018; **13**: 88–94.
- Serrano-Villar S, Rojo D, Martínez-Martínez M *et al*. Gut bacteria metabolism impacts immune recovery in HIV-infected individuals. *EBioMedicine* 2016; **8**: 203–216.
- Anahtar MN, Byrne EH, Doherty KE *et al*. Cervicovaginal bacteria are a major modulator of host inflammatory responses in the female genital tract. *Immunity* 2015; **42**: 965–976.
- Klatt NR, Cheu R, Birse K *et al*. Vaginal bacteria modify HIV tenofovir microbicide efficacy in African women. *Science* 2017 Jun 2; **356**: 938–945.
- Cribbs SK, Uppal K, Li S, *et al*. Correlation of the lung microbiota with metabolic profiles in bronchoalveolar lavage fluid in HIV infection. *Microbiome* 2016; **4**: 3.
- Serrano-Villar S, Moreno S, Ferrer M. The functional consequences of the microbiome in HIV: insights from metabolomic studies. *Curr Opin HIV AIDS* 2018; **13**: 88–94.
- Rasmussen TA, Tolstrup M, Brinkmann CR *et al*. Panobinostat, a histone deacetylase inhibitor, for latent-virus reactivation in HIV-infected patients on suppressive antiretroviral therapy: a phase 1/2, single group, clinical trial. *Lancet HIV* 2014; **1**: e13–21.
- Winckelmann A, Barton K, Hiener B *et al*. Romidepsin-induced HIV-1 viremia during effective antiretroviral therapy contains identical viral sequences with few deleterious mutations. *AIDS* 2017; **31**: 771–779.
- Kessing CF, Nixon CC, Li C *et al*. In vivo suppression of HIV rebound by didehydrocortistatin A, a 'block-and-lock' strategy for HIV-1 Treatment. *Cell Rep* 2017; **21**: 600–611.
- Psomas C. What's up in HIV latency and cure? *J Virus Erad* 2018; **4** (Suppl 1): abstract S9.
- Descours B, Petitjean G, López-Zaragoza JL *et al*. CD32a is a marker of a CD4 T-cell HIV reservoir harbouring replication-competent proviruses. *Nature* 2017; **543**: 564–567.
- Hogan LE, Vasquez J, Hobbs KS *et al*. Increased HIV-1 transcriptional activity and infectious burden in peripheral blood and gut-associated CD4+ T cells expressing CD30. *PLoS Pathog* 2018; **14**: e1006856.
- Routy JP. HIV and lungs at the time of effective ART. *J Virus Erad* 2018; **4** (Suppl 1): abstract S8.
- Wang YH, Shen XD. Human immunodeficiency virus infection and mortality risk among lung cancer patients: A systematic review and meta-analysis. *Medicine* 2018; **97**: e0361.
- Domblides C, Antoine M, Hamard C. Non-small cell lung cancer from HIV-infected patients expressed programmed cell death-ligand 1 with marked inflammatory infiltrates. *AIDS* 2018; **32**: 461–468.
- Costiniuk C, Nitulescu R, Sanezi Z *et al*. Environmental and occupational exposures as predictors of airflow obstruction in an HIV tertiary care clinic. *J Virus Erad* 2018; **4**(Suppl 1): abstract O16.
- Bigna JJ, Kenne AM, Asangbeh SL *et al*. Prevalence of chronic obstructive pulmonary disease in the global population with HIV: a systematic review and meta-analysis. *Lancet Glob Health* 2018; **6**: e193–e202.
- Lacey A, Tinago W, Power NR *et al*. Investigating the effect of antiretroviral switch to tenofovir alafenamide on lipid profiles in PLWHIV within the UCD ID cohort. *J Virus Erad* 2018; **4**(Suppl 1): abstract O17.
- Spano JP. Immunotherapies and immune check-points. *J Virus Erad* 2018; **4**(Suppl 1): abstract S10.
- Konopnicki D. HPV Vaccination: use in prevention and in cure. *J Virus Erad* 2018; **4**(Suppl 1): abstract S11.
- Sabin C. Cohorts. *J Virus Erad* 2018; **4**(Suppl 1): abstract S12.
- Laird GM, Eisele EE, Alireza Rabi S *et al*. Rapid quantification of the latent reservoir for HIV-1 using a viral outgrowth assay. *PLoS Path* 2013; **9**: e1003398.
- Metcalf Pate KA, Pohlmeier CW, Walker-Sperling VE *et al*. A murine viral outgrowth assay to detect residual HIV type 1 in patients with undetectable viral loads. *J Infect Dis* 2015; **212**: 1387–96.
- Procopio FA, Fromentin R, Kulpa DA *et al*. A novel assay to measure the magnitude of the inducible viral reservoir in HIV-infected individuals. *EBioMedicine* 2015; **2**: 874–83.
- Baxter AE, Niessi J, Fromentin R *et al*. Single-cell characterization of viral translation-competent reservoirs in HIV-1 infected individuals. *Cell Host Microbe* 2016; **20**: 368–380.
- Grjsen ML, Steingrover R, Wit FWNM *et al*. No treatment versus 24 or 60 weeks of antiretroviral treatment during primary HIV infection: the randomized Primo-SHM Trial. *PLoS Med* 2012; **9**: e1001196.
- Fiellin L. The future of digital games for HIV prevention and care. *J Virus Erad* 2018; **4**(Suppl 1): abstract S13.
- Coleman R. PrEP in Europe, where are we? *J Virus Erad* 2018; **4**(Suppl 1): abstract S14.
- Nichols B. Cost effectiveness of PrEPs in Europe. *J Virus Erad* 2018; **4**(Suppl 1): abstract S15.