Conference proceedings from the 22nd Bangkok International Symposium on HIV Medicine

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The Bangkok International Symposium on HIV Medicine is one of the longest running and largest international conferences in the Asia-Pacific, providing healthcare workers with the most up-to-date information pertaining to HIV and coinfections. In the third week of January 2020, 500 HIV researchers and service providers from over 21 countries worldwide gathered in Bangkok to share data and experiences in the treatment and prevention of HIV, TB and sexually transmitted infections. Highlights of the 2020 symposium included a roundtable discussion of pre-exposure prophylaxis, a 1-day forum on TB, the potential for a HBV cure and, for the first time, oral presentations from four young investigators from the region.

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Professor David Cooper Memorial Lecture: future directions for HIV therapies

Anthony Kelleher (The Kirby Institute, UNSW, Sydney, Australia) paid tribute to the late professor David Cooper. Treatments for HIV are advancing. In future, immunotherapy may become an option to treat HIV. The new concept of ‘block and lock’, aims to block HIV from entering the cell and if HIV has already entered, to lock it into a permanently latent state. *In vitro* experiments showed that siPromA and si143 target different areas of 5’ long terminal repeats, causing it to become silent or suppress HIV-1 transcription; shPromA transduced peripheral blood mononuclear cells or CD34 stem cells [1,2], were able to protect the mice from becoming infected with HIV. To achieve a functional cure, a combination of RNA therapeutic targets (e.g., shCCR5 Cal 1 or shPromA1) are needed [2,3]. In mice, PromA + Cal1 increases specific CD4 cells during challenge, ultimately protecting them from becoming infected or have delayed viral rebound. Different delivery mechanisms (i.e., lentiviruses and nanoparticles) of genes (i.e., Env of HIV1 and HIV2, and Vpx) into resting T cells have been studied.

Professor Joep Lange & Ms Jacqueline van Tongeren Memorial Lecture: treatment for all means getting treatment to all: where are we now in the Asia-Pacific?

Giten Khwairakpam (TREAT Asia, Bangkok, Thailand) began his talk using Dr Lange’s quote, “*Nothing is impossible, especially if it is inevitable*”. He reviewed barriers to HIV treatment in Asia-Pacific and discussed how community and civil society were instrumental in creating increased access to HIV treatment. Prices for HIV

drugs have now fallen because of inexpensive and quality generic antiretroviral therapies (ARTs), such as generic dolutegravir, making it possible for all people living with HIV (PLHIV) to be treated. He ended his talk using late Dr Lange's famous quote, *"If we can get cold Coca-Cola and beer to every remote corner of Africa [and Asia], it should not be impossible to do the same with HIV drugs"*.

Pre-exposure prophylaxis (PrEP) Roundtable was chaired by Nittaya Phanuphak (PREVENTION, Thai Red Cross – AIDS Research Centre, Thailand).

Toshibumi Taniguchi (Department of Development Genetics, Chiba University, Japan) provided an overview of multiple global PrEP implementation models.

Taweessap Siraprapasiri (National AIDS Management Center, Ministry of Public Health, Thailand) reviewed the timelines to scale up HIV ART and HIV prevention (PrEP) in the universal coverage program (UC) in Thailand. UC was launched in 2001, ART and PrEP are included in UC since 2006 and 2020, respectively.

Reshmie Ramautarsing (PREVENTION, TRC-ARC, Thailand) talked about the implementation of PrEP in Thailand. The Princess PrEP program is part of the key population-led health services model. Through the program, trained lay providers – who themselves are members of key populations, such as men who have sex with men and transgender women – deliver PrEP and other services in community-based organizations. Both low uptake of PrEP due to risk misperception and suboptimal retention remain a challenge. PrEP-15 is a fee-based program implemented at the Thai Red Cross Anonymous Clinic, through which PrEP and related laboratory monitoring are available for 15 Thai baht per day, or about US\$15 per month. Together, these two programs have contributed to 10,077 cumulative Thai PrEP users (82% of all Thai PrEP users). While being impressive, this represents only 5% of national PrEP targets. Strategies implemented to increase uptake of and retention in PrEP services include service flow optimization, public campaigns using 'gain framed messaging' and partnering with private hospitals and clinics to expand services. Expansion of PrEP services provides an important opportunity to incorporate sexually transmitted infections (STI) testing and treatment, facilitating the engagement of a high STI burden population in services.

Donn Colby (Henry M. Jackson Foundation, Bethesda, USA and the US Military HIV Research Program, USA) reported that condom use was declining and STI rates were increasing prior to the introduction of PrEP. After PrEP, STI rates increased marginally among men who have sex with men in high income countries, where most of the published data originated. The WHO views PrEP as an opportunity for increased attention to STI prevention and control, with the possibility of decreasing both HIV and other STI incidences demonstrated in modeling studies. Antiretroviral drug resistance is a minor risk with PrEP use, but accounts for only 5% of resistance in the community. Transmission of resistant virus is exceedingly rare. The greatest risk is when initiating PrEP during acute HIV infection (AHI), before HIV antibody tests become reactive. Data from the Thai Red Cross Anonymous Clinic found about 1/350 PrEP starters had AHI, of whom 43% developed resistance to emtricitabine and 0% to tenofovir. Therefore, rule out AHI before starting PrEP. If there is any risk for AHI in the previous 30 days, prescribe three drug post-exposure prophylaxis for 1 month, then switch to PrEP if HIV antibody is nonreactive at 1 month.

TB lectures from the preconference TB research forum & the symposium

Frank Cobelens (Amsterdam Institute of Global Health and Development, The Netherlands) talked about advances and challenges in developing new diagnostic tests and biomarkers. In 2020, Truenat MTB Plus was approved for diagnosis of TB and rifampicin resistance by WHO. Fuji lipoarabinomannan urine test performed better than WHO's approved Alere lipoarabinomannan test [4]. He introduced several novel host biomarkers which can be used to predict progression to disease (i.e., HLA-DR, CD27, CD38, Ki67 and CD8). Immunoactive proteins can distinguish TB from nonTB samples (e.g., IFN- γ , IP-10, CRP and complement q1 ([Cq1]). RNA transcription signatures can be used to monitor disease, predict treatment failure and predict progression to disease. Circulating cell counts (e.g., monocyte/lymphocyte ratio) can predict progression to disease. The monocyte/lymphocyte ratio at baseline predicted TB incidence in 1,862 PLHIV starting ART in South Africa and has the potential to diagnose incipient/early TB in PLHIV [5,6]. Small circulating molecules (e.g., Inosine and kynurenine) can distinguish active TB from latent TB infection (LTBI) and healthy individuals [7]. Indoleamine 2,3-dioxygenase (IDO) activity (kynurenine/tryptophan ratio) can discriminate TB disease from healthy controls, and pneumonia and predict TB disease progression over a 6-month interval [8]. Biomarkers may 'behave' differently in populations that vary by characteristics including comorbidities or geographical regions. There is a need to translate biomarkers and

signatures to field-feasible platforms that require limited staff skills, minimum lab requirements, are inexpensive and noninvasive (e.g., saliva and breath).

Richard Chaisson (Johns Hopkins University Center for Tuberculosis Research; and Hopkins Center for AIDS Research [CFAR], USA) reviewed TB treatment, management of LBTI and treatment guidelines [9]. There is a need to improve treatment and prevention for both drug susceptible and multi-drug resistant TB. There are options for treating drug resistant TB: new (bedaquiline, delamanid and pretomanid) versus repurposed (linezolid, imipenem/cilastin + clavunate and clofazimine) products. He discussed global multi-drug resistant treatment outcomes, survival of extensively drug-resistant TB patients in South Africa [10] and the 'Bangladesh' regimen. He discussed current options for TB preventative therapy and the results of BRIEF TB/A5279 1HP (1 month of INH and rifapentine) versus 9H (9 months of INH) short course preventative therapy in PLHIV and the 4r9 trial (4 months daily of rifampin [4R] versus 9 months daily of isonicotinic acid hydrazide [INH] to prevent TB in high risk nonHIV-infected patients). There is also a Phase IIb controlled trial of M72/AS01 vaccine for TB prevention [11].

Management of LTBI was the focus of his symposium presentation and is a key element of the WHO end TB strategy. The Thrio study showed that people who were treated with isoniazid preventive therapy for 6 months were protected from getting TB for 7 years [12]. Characteristics of different LTBI treatment regimens (1HP, 3HP [3 months of INH and rifapentine] and 9H), were discussed. 3HP had fewer hepatic adverse effects compared with other regimens [13]. For pregnant women, isoniazid preventive therapy should start in the second or third trimester of pregnancy or 6 weeks after delivery [14].

Strategies for a cure for chronic HBV

Sharon Lewin (Doherty Institute for Infection and Immunity, University of Melbourne, Victoria, Australia) briefly reviewed the natural history and current treatment of chronic HBV. A cure for HBV would accelerate declines in HBV incidence and reduce costs because it is a life-long treatment and for some, can progress to hepatocellular carcinoma. Only 25–30% of the patients with Hepatitis B surface antigen (HBsAg) positive can be treated and lifelong treatment can result in poor adherence and/or cumulative toxicity. Covalently closed circular DNA (cccDNA), persistent high levels of HBsAg and ongoing immune dysfunction are major barriers to cure HBV. HBsAg inhibits innate and adaptive immunity through Toll-like receptor 2 and 9, IFN- α and myeloid dendritic cells [15,16]. Different clinical strategies that can be used to achieve HBV cure by reducing HBV replication and HBsAg include capsid allosteric modulator (i.e., ABI-H0731), siRNA or translational inhibitors that block HBsAg synthesis (i.e., JNJ-3989) and sAg inhibitors that block HBsAg synthesis or block subviral particles. Immunotherapy with Toll-like receptor 8 agonist GS-9688 and anti-PD1 (nivolumab) can boost the immune system but can exacerbate liver disease. A combination of interventions that inhibit replication, reduce antigen and stimulate the immune response is necessary to cure HBV.

The next symposium, 23rd Bangkok International Symposium on HIV Medicine, will be held on 13–15 January 2021.

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