Newsletter
Hong Kong Society for HIV Medicine
香港愛滋病醫學會

MESSAGE FROM PRESIDENT

Issue 4 November 2018

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Beyond the HIV status

Nineteen eighty-eight witnessed the commemoration of the first World AIDS Day, which marked also the world's first ever "day" devoted to a specific health issue. Thirty years on, and on 1 December 2018, we observe the 31st World AIDS Day. With the increasing importance of a biomedical approach to HIV prevention and control, it's not surprising that the theme this year is "Know your status". One's HIV status, if known, heralds the beginning of the cascade of HIV care. Prompt treatment, continued adherence and the achievement of undetectable viral load form the backbone of effective treatment, and contribute to achieving Treatment-as-Prevention (TasP). HIV medicine is naturally intricately associated with the HIV positive status.

How about an HIV negative status? Unfortunately, knowledge of a person's negative HIV status is often the end of the encounter between the tested and the service provider. Let's not forget that effective prevention begins with the HIV negative status and is founded on keeping the status negative. Pre-exposure prophylaxis (PrEP), the other biomedical intervention is indicated for HIV negative individuals with substantial risk of infection. A modelling study concluded that at 40% coverage of MSM at risk in the United States (US), PrEP could avert one-third of the expected infections. A MMWR report published in October 2018 estimated that as of 2016, only 7% of those indicated were prescribed with (tenofovir disoproxil fumarate/ emtricitabine) TDF/FTC for PrEP in the US. They accounted for half of all PrEP users globally… so the coverage must have been much lower in other parts of the world. To date very few places on earth have more than a few thousand persons on TDF/FTC for PrEP, except US/Canada, Brazil, Australia, some European and African countries. In Asia, this is achieved only in Thailand.

In Hong Kong, we could easily blame the high cost of brand TDF/FTC for the low coverage of PrEP. Like it or not, the number of people needing PrEP are accessing generic TDF/FTC either on internet or from another country, notably Thailand. PrEP does not equate simple distribution of TDF/FTC tablets. Are PrEP users in Hong Kong aware of the benefits and limitations of PrEP? Are they screened for hepatitis B and renal functions? Is risk compensation an issue? Is HIV/ sexually transmitted infection (STI) monitoring provided to PrEP users? Is there effective linkage with HIV/STI care? HIV Medicine is not confined to the prescription of antiretrovirals at a local clinic but the commitment to enabling at risk individuals to achieve HIV prevention. At this year's Annual Scientific Meeting, we are, therefore focusing on PrEP once again. We have invited colleagues from Thailand

and Taiwan to share with us their rich experiences in making PrEP available. Our Society is finalizing the production of a series of videos on PrEP, post-exposure prophylaxis (PEP), HIV/STI screening and STI treatment, which fellow members can use for informing clients in need. A primary care workshop is in the pipeline as we believe that primary care practitioners can be important professional providers of PrEP and related services. Overseas studies reported that PrEP access could be hampered by "purview paradox" – primary care professionals did not see their roles in PrEP contrary to the beliefs of HIV physicians. Can we prove these studies wrong here in Hong Kong?

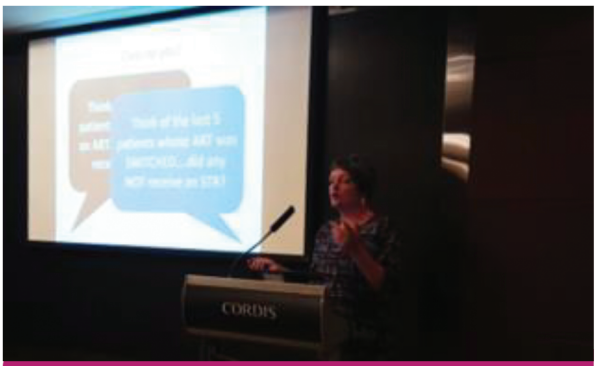
Prof SS Lee

Activities of the Society

HIV symposiums

Symposium on "Impact of recent ART development on HIV treatment paradigm" (May 2018)

On 25th May 2018, at the evening symposium organized by HKSHM, Dr. Laura Waters from Mortimer Market Centre, CNWL NHS Trust shared her opinion on the use of various single tablet regimens (STRs) and the recommendations on their use in the guidelines.



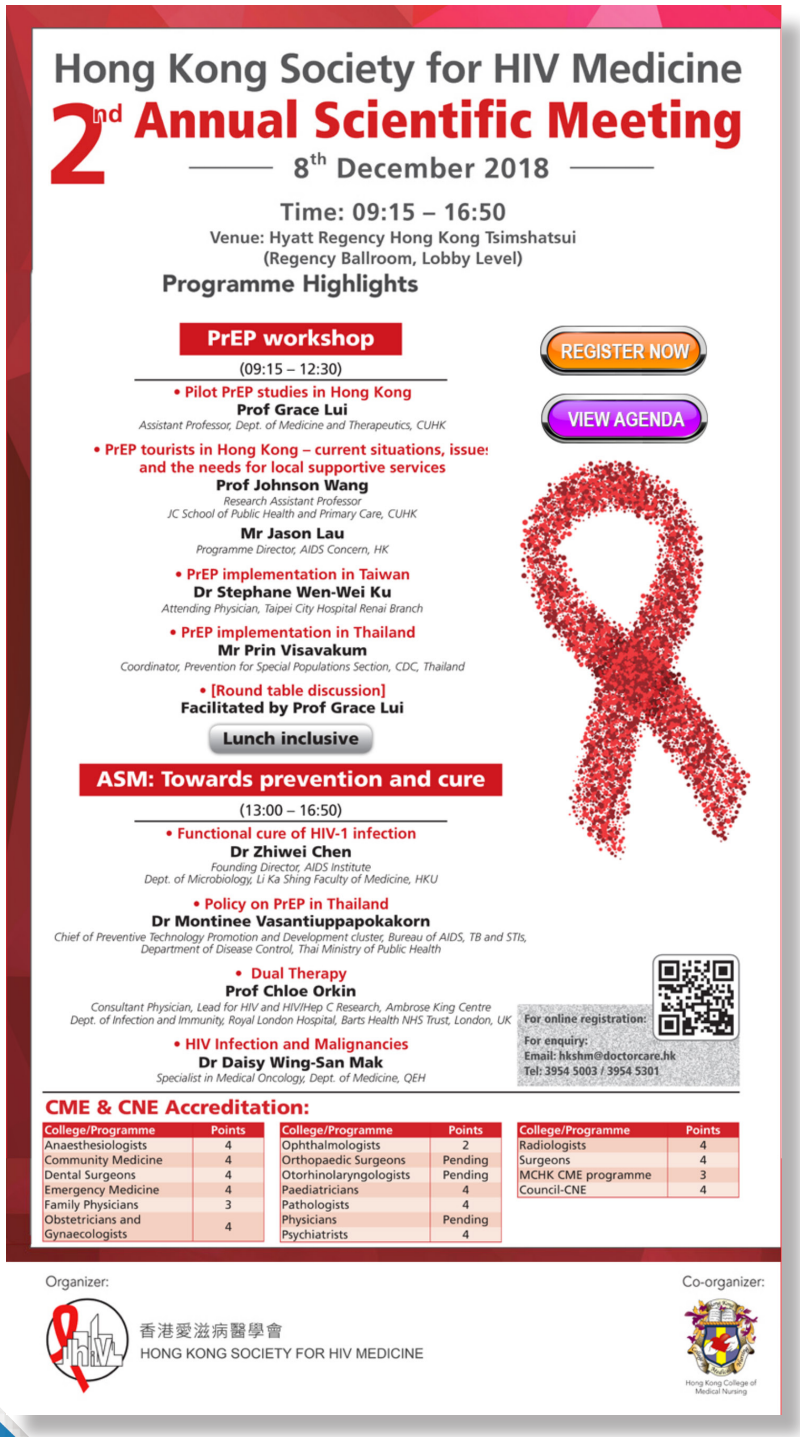
Dr. Waters shared her insights on how to optimise HIV management for individual patients

Symposium on "The Impact of HAART Regimens on HIV-related Comorbidities: the Need for New Alternative Strategies" (September 2018)

The dinner symposium was held on 21st September 2018. After the brief introduction of HIV situation in Hong Kong by Dr. Wai-Shing Leung, Dr. Marta Boffito from Chelsea and Westminster Hospital NHS Foundation Trust delivered the lecture on the screening and management of comorbidities in people living with HIV. She then presented a case to illustrate the challenges in choosing appropriate ART in patients with comorbidities.

Dr. Boffito discussed with participants on the management of HIV patients with comorbidities

2nd HKSHM Annual Scientific Meeting : Towards prevention and cure cum PrEP workshop 8th December 2018



More HIV conference in Hong Kong...

HIV conference tilted "Combination HIV prevention strategy : What are the options for Hong Kong? " will be held on 19th January 2019 at The University of Hong Kong.

Host:
AIDS Concern

Co-host:
Department of Family Medicine and Primary Care; The University for Hong Kong

Date:
19th January 2019 (Saturday)

Time:
0900-1700

Venue:
Yu Chun Keung Tam Shuk Yin Lecture Theatre, 3/F, The Jockey Club Tower, Centennial Campus, The University of Hong Kong

Supporting organization:

- The Hong Kong Society for HIV Medicine
- The Hong Kong Society of Behavioral Health

Other upcoming HIV conferences ...

- **Conference on Retroviruses and Opportunistic Infections (CROI) 2019,** 4-7 March 2019 | Seattle, USA
- **4th Asia Pacific AIDS & Co-infections Conference (APACC) 2019,** 27-29 June 2019 | Hong Kong SAR, China
- **10th IAS Conference on HIV Science (IAS 2019)**, 21-24 July 2019 | Mexico City, Mexico
- **17th European AIDS Conference,** 6-9 November 2019 | Basel, Switzerland

Academic corner

Highlights from AIDS 2018

Wai-Shing Leung

Some 16,000 stakeholders from more than 160 countries gathered together in Amsterdam, the Netherlands, from 23 to 27 July 2018 for the 22nd International AIDS Conference (AIDS 2018), where leaders focused on the major new investments, science-based policies and the political will needed to put the HIV response back on track. With the theme, "Breaking Barriers, Building Bridges," AIDS 2018 serves as a platform to highlight innovative and evidence-based approaches to reach those at greatest risk for HIV with treatment and prevention. Some of the studies and policies presented at the conference are summarized below.

Potential safety signal of neural tube defects with preconception dolutegravir (DTG) exposure

- Dr. Rebecca Zash presented the data on "Surveillance for Neural Tube Defects following Antiretroviral Exposure from Conception, the Tsepamo study (Botswana)" at the conference. The study started in August 2014 in Botswana to look at birth outcomes by HIV status and ART regimen and to see if there is an increased risk of neural tube defects (NTDs) in infants exposed to efavirenz (EFV) from conception.
- The original plan was a four-year analysis (to August 2018) to compare the prevalence of NTDs in infants born to women on EFV at conception vs other ART regimens. The sample size of 94,000 births was based on ability to detect a 2-fold increase in NTDs with the assumption of 0.1% prevalence.
- Mid-2016 Botswana changed first-line ART from an EFV-based to a DTG-based regimen. Recently published data from women who started DTG during pregnancy showed no difference in adverse birth outcomes compared with those who started EFV. There was no increased risk of birth defects among 280 women who started DTG in the first trimester.
- The Tsepamo group were asked to provide any preliminary data on outcomes for women who started DTG before conception for WHO guidelines committee in May 2018. At the time of analysis there had been 89,064 births at eight surveillance hospitals: 21,955 among HIV positive mothers; 11,726 of these who received ART from conception; and 426 (3.3%) of these were on a DTG-based regimen. Of the remaining 11,300 mothers on ART from conception, 5,787 received EFV.
- Overall, 86 NTDs were identified among 88,755 births: 0.1% (95% CI: 0.08 to 0.12).

There were 4/426 NTDs in infants born to women receiving DTG at conception: 0.94% (95% CI: 0.37 to 2.4). This compared with 14/11,300 among non-DTG at conception exposures: 0.12% (95% CI: 0.07 to 0.21), and 3/5787 EFV at conception exposures: 0.05% (95% CI: 0.02 to 0.15).

- There were 0/2,812 NTDs in infants born to mothers who started DTG during pregnancy: 0% (95% CI: 0 to 0.13), and 61/66,057 among those born to HIV negative mothers: 0.09% (95% CI: 0.07 to 0.12).
- The four defects in the preconception DTG-exposured infants were: encephalocele, anencephaly, myelomeningocele, and iniencephaly. None of the women were reported to be on folate supplementation before pregnancy – this was similar across exposure groups.
- Review of maternal data found no other risk factor for NTDs and there was no clustering by site. A sensitivity analysis, restricted to births occurring after the rollout of DTG, showed there was no increase in NTDs overall.
- Dr. Zash emphasised that, although statistically significant, the signal is based on only four cases and the absolute prevalence difference of about 0.8% is small. She also noted the occurrence of 4 different defects among infants exposed to DTG at conception is unusual.
- This preliminary signal for NTDs needs further data to confirm or refute. Tsepamo has plans in place to expand the study from 8 to 18 sites, increasing from 45% to 72% of births in the Botswana, and continues to collect data on neural tube defects and also evaluate all major malformations and other adverse birth outcomes (stillbirth, preterm, small for gestational age and neonatal death). They will also include women already exposed to DTG from conception before the recent guideline change. The investigators hope to have over 1200 births with DTG exposure from conception to report in the next formal analysis which will occur after 31 March 2019.
- It is uncertain what will happen with this signal between now and March 2019. Dr. Zash explained that with no more neural tube defects, the total prevalence will be 0.33% and the lower CI of 0.13% will overlap with the upper CI for other ART at conception (0.21%), EFV at conception (0.15%) and with HIV negative (0.13%). Results from the expanded surveillance, in March 2019, will be critical to better understanding the safety signal.

GEMINI studies - dual therapy with DTG/3TC was non-inferior to the triple antiretroviral therapy, DTG+TDF/FTC

- Both GEMIMI 1 and 2 are identically designed, international phase 3 studies, and each randomised treatment-naive participants to either DTG+3TC (2-drug arm) or DTG+TDF/FTC (3-drug arm).
- GEMINI 1 and 2 randomised 714 and 719 treatment-naive participants respectively with screening viral load of 1000 to 500,000 copies/mL. Participants could have no more than 10 days of antiretroviral experience, and anyone who had HIV infection with any pre-existing major resistance mutations, HBV infection, or a need for HCV therapy was excluded. The primary endpoint was the proportion of participants with plasma viral load <50 copies/mL at week-48 (using ITT snapshot analysis).
- Baseline characteristics included median CD4 and viral load of 432 cells/mm^3 (range: 19 to 1497) and 4.4 log copies/mL (range: 1.6 to 6.4) respectively. Less than 10% of participants in each arm had baseline CD4 counts <200 cells/mm^3. Approximately 2% of participants in each arm were later reported as having viral load above entry

criteria threshold of 500,000 copies/mL. 85% of the participants were men; 70% were white, 12% African-American, 10% Asian and 10% other ethnicity.

- At week-48, viral load was <50 copies/mL in the 2- vs 3-drug arms in 90% (320/356) vs 93% (332/358) in GEMINI 1 and 93% (335/360) vs 94% (337/359) in GEMINI 2. The adjusted between-arm difference was well within the predefined non-inferiority margin of –10%: –2.6 (95% CI: –6.7 to +1.5) and –0.7 (–4.3 to +2.9), in GEMINI 1 and 2 respectively. In a pooled analysis, although the adjusted treatment differences favoured the triple therapy arm, non-inferiority was also met : –1.7 (–4.4 to +1.1).
- In a pooled snapshot analysis, the 48-week response rate proved lower with DTG/3TC than with triple therapy in people with a pretreatment CD4 count below 200 (79% versus 93%), but results did not differ by pretreatment viral load in the snapshot analysis. However, in an analysis in which treatment-related discontinuations equaled failure, similar proportions in the pooled dual-therapy and triple-therapy arms had a week-48 viral load <50 copies regardless of pretreatment viral load (above or below 100,000 copies/mL) or CD4 count (above or below 200).
- Across both studies, six participants on DTG+3TC vs four on DTG+TDF/FTC met the protocol-defined virologic failure but none of them developed new primary mutations associated with INSTI or NRTI drug resistance.
- Overall rates of side effects were similar between the two arms. Serious adverse events were rare with dual and triple therapy (7% and 8%), as were adverse events leading to withdrawal from the study (2% and 2%). Drug-related adverse events were somewhat less frequent with DTG+3TC than with DTG+TDF/FTC (18% versus 24%).
- Changes in renal and bone biomarkers significantly favoured the dual-therapy group, similar to other TDF vs non-TDF comparing studies.

Reference:

Cahn P, Madero JS, Arribas JR, et al. Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials. Lancet. 2018 Nov 9. pii: S0140-6736(18)32462-0. doi: 10.1016/S0140-6736(18)32462-0. [Epub ahead of print]

WHO updated the Consolidated ARV guidelines

- At AIDS 2018, WHO presented the highlights of recent updates to the Consolidated ARV guidelines, focusing on the role of dolutegravir (DTG) based regimens in first and second line treatment.
- WHO launched new interim guidance on HIV treatment recommending dolutegravir (DTG) for HIV infected individuals aged six years and above as WHO has recently updated its ART systematic review and meta-analysis. The review confirmed the 2016 review findings, showing a regimen with two nucleoside reverse-transcriptase inhibitors (NRTIs) plus DTG to be more effective, with better viral suppression, CD4 count recovery and lower risk of treatment discontinuation compared with EFV-based ART in treatment-naive adults.
- However, there are safety concerns with women and adolescent girls using DTG at conception. For women and adolescent girls of childbearing potential who do not wish to become pregnant, and are fully informed of the benefits and risks, DTG is recommended with consistent

contraception. If consistent and reliable contraception cannot be assured or if a woman wishes to become pregnant, WHO recommends women and adolescent girls of child-bearing potential receive EFV or protease inhibitor (PI)-based regimens.

- WHO also recommends DTG for children six years and above and notes that raltegravir (RAL) could be an effective integrase inhibitor for younger children for whom approved DTG dosing is not yet available.
- For second-line treatment, WHO recommends DTG for people who have failed an NNRTI or PI-based first-line, with the same preconception safety caveats for women. PI-based treatment with an atazanavir/ritonavir (ATV/r) or lopinavir/ritonavir (LPV/r)-based regimen is recommended for people who receive DTG first-line.

Summary of WHO treatment guideline on options for first-, second- and third-line ART regimens for adults (including pregnant women and adolescents) and children:

Population	First-line	Second-line	Third-line
Adults and adolescents (including women and adolescent girls of child bearing potential or pregnant)	2 NRTIs + DTG	2 NRTIs + ATV/r or LPV/r	DRV/r + DTG + 1–2 NRTIs if possible, consider optimization using genotyping)
	2 NRTIs + EFV	2 NRTIs + DTG	
Children	2 NRTIs + DTG	2 NRTIs + ATV/r or LPV/r	
	2 NRTIs + LPV/r	2 NRTIs + DTG	
	2 NRTIs + NNRTIs	2 NRTIs + DTG	

Key: ATV/r, atazanavir/ritonavir; DTG, dolutegravir; DRV/r, darunavir/ritonavir; EFV, efavirenz; LPV/r, lopinavir/r; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleos/tide reverse transcriptase inhibitor

Reference:

Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: interim guidance. 2018; World Health Organization.

香港愛滋病醫學會
HONG KONG SOCIETY FOR HIV MEDICINE

Membership registration form

Personal details

Prof/Dr/Mr/Mrs/Miss/Ms Surname: _____ First name: _____

Present appointment: _____

Institution: _____

Postal address: _____

_____

Email address: _____@_____Phone number: _____

Relevant HIV experience or work: _____

_____

Membership category

Ordinary member: HKD200 per year or HKD2000 life membership ☐

Eligibility: Medical practitioners who practices or are interested in HIV medicine.
Privilege: entitlement to vote, to hold office and to take part in all Society functions.

Associate member: HKD150 per year (no life membership) ☐

Eligibility: Healthcare professionals other than doctors including nurses, pharmacists, medical laboratory technologists, occupational therapists, physiotherapists, clinical psychologists, dietitians who are involved or are interested in HIV medicine.
Privilege: entitlement to take part in all Society functions.

Affiliate member: no fees required ☐

Eligibility: Non-healthcare professionals who are interested in HIV medicine
Privilege: receive news and updates from the Society, and participation in selected activities as decided by the council of the Society

Application proposed by HKSHM member: Name _____ Signature _____

Application seconded by HKSHM member: Name _____ Signature _____

Comments and suggestions

What do you expect from the Society (e.g. benefits, meetings, courses, education fund)?

Any other comments or suggestions for us to work on?

Date: _____

Please email the completed form to Dr Wilson Lam, Hon, Secretary, HKSHM at lwzz04@ha.org.hk

Data protection: Personal data provided by you will be used by the Hong Kong Society for HIV Medicine (HKSHM) only for the purposes of handling your application and activities related to HKSHM. Personal data in the application form, or copies of which, will be disclosed or transferred to parties relevant and necessary for the purposes as stated above only.