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

# MESSAGE FROM PRESIDENT

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Coronavirus Disease 2019 (COVID-19) is causes by a novel coronavirus. World Health Organization (WHO) announced COVID-19 outbreak as a pandemic on 11 March 2020, with cases reported in more than 180 countries. Hong Kong is facing the third wave of COVID-19 outbreak with significant community spread since early July, leading to government action of tightening social distancing measures.

COVID-19 is a global health emergency posing enormous health and socio-economic challenges. Dr. Jacky Chan, Council Member of the Hong Kong Society for HIV Medicine, enlightens us the impact of COVID-19 on HIV in this issue of Newsletter. The data currently available do not indicate that the disease course of COVID-19 in people with HIV (PLHIV) differs from those without HIV, unless they have other comorbidities or risk factors. Similar to general public, PLHIV are advised to take precautionary measures to minimize the risk of contracting COVID-19 such as maintaining good personal hygiene and following social distancing guidance. It is also important for PLHIV to maintain an on-hand adequate supply of anti-retroviral drugs during the outbreak.

Maintaining HIV care continuum and achieving the 90-90-90 treatment targets during COVID-19 pandemic could be challenging. The implementation of quarantine and different degrees of social-distancing measures might reduce access to HIV testing, timely linkage to HIV care, and viral control due to treatment interruptions. Government, health care providers and community organizations should monitor and evaluate the situation closely and take necessary action accordingly.

In this issue, Ms. Chan Shan and Ms. Pansy Yu also report the conduction of HIV Forum for Elderly Home Staffs in collaboration with Community Geriatric Assessment Teams (CGAT) of two local hospitals. As the aging population among PLHIV is growing, the demand for services for elderly homes is increasing. The forum aimed to provide health care providers the key concepts of caring PLHIV and a platform for sharing ideas. The forums were well attended by elderly home staff, doctors and nurses of CGAT with good feedback.

During COVID-19 pandemic, conducting educational activities through webinars and video conferencing becomes a new norm. Our society has also converted symposia and on-site workshops into webinars at this time to continue bringing updated knowledge of HIV/AIDS management to our members and health care professionals. We are going to co-organize with

Hong Kong Medical Association the HIV/STI Primary Care Workshop via Webinar on 24 October 2020, which targets family physicians and general practitioners. Wide coverage of topics including clinical diagnosis and management of sexually transmitted infections in primary care setting, and updates on HIV prevention workshop.

Wish you enjoy this issue of HKSHM Newsletter!

*Dr MP Lee*

***President, HKSHM***

# Alert

## HIV in the time of COVID-19

**Dr. Jacky Man-Chun Chan**

COVID-19 disease, caused by SARS-CoV-2 virus, is challenging and unique. The virus was first identified in China as the cause of a respiratory disease. In March 2020, the World Health Organization (WHO) declared the outbreak a global pandemic. As of 6 September 2020, more than 26.9 million cases have been reported, resulting in more than 880,000 deaths worldwide. Symptoms of COVID-19 range from fever, cough, sore throat, headache, anosmia to dyspnea, respiratory failure and multi-organ failure. Lymphopenia is one of the prominent features in patients with COVID-19, and at the same time, as a predictor for HIV disease progression. However, the immune response and the role of host immune system in COVID-19 infected patients were not fully understood.

### COVID-19 infection in HIV patients

HIV-infected patients accounted for only 0.8-1.4% of patients hospitalized with COVID-19 in the three large studies in China, the United Kingdom and New York City, USA. One study in France reviewed the attack rate of COVID-19 was similar among HIV-infected patients, clients in PrEP and the general population [1]. In one case control cohort in New York City involving 120 patients, there was no significant difference in the clinical characteristics of COVID-19 among patients with or without HIV infection [2]. The mean CD4 cell count of this patient cohort was 332 cells/ul. Both groups shared similar common presenting symptoms, including fever, cough and dyspnea. The laboratory findings of HIV-infected patients were also similar to the general patients, including lymphocyte counts and inflammatory markers. There was no significant difference on need for invasive mechanical ventilation, length of hospital stay or in-hospital mortality.

### Highly active antiretroviral therapy (HAART) and COVID-19 infection

Lopinavir-ritonavir, a protease inhibitor as part of HIV backbone treatment for the last decade, has been shown to have activity in vitro against SARS-CoV and MERS-CoV. Triple combination of interferon beta-1b, lopinavir-ritonavir (LPV/r) and ribavirin has been used in locally as a specific therapy for patients with COVID-19 infection. A randomised multicentred, phase 2 trial done in Hong Kong revealed that triple therapy was superior in alleviating symptoms and shortening the duration of viral shedding and with mild to moderate COVID-19, when compared to using LPV/r alone [3]. On the other hand, one randomized control trial in Wuhan revealed that no clinical benefit was observed in severe COVID-19 cases with LPV/r treatment beyond standard care [4]. However, the median symptom onset to study recruitment interval time was 13 days in this cohort, i.e. the patients mostly presented late in their disease. Whether the use of LPV/r as HAART backbone in HIV-infected persons helps alleviate symptoms or protect from COVID-19 infection is unknown. In vitro study also suggested possible inhibition of tenofovir disoproxil against SARS-CoV-2. One retrospective cohort done in Spain, involving 77,590 HIV-infected patients, suggested a lower risk for COVID-19 and related hospitalization in patients receiving tenofovir disoproxil /emtricitabine than those receiving other regimens [5]. However, further

randomized trials are warranted to investigate the protective effect.

### Newly diagnosed HIV during the era of COVID-19

Prior to specific treatment commencement for COVID-19 in Hong Kong, baseline blood tests including hepatitis B, C and HIV serology will be taken. Two patients were eventually diagnosed to have HIV infection in Princess Margaret Hospital, during pre-treatment workup for COVID-19. The CD4 T lymphocyte counts of these patients were 337 and 488 cells/ul respectively. They did not present with any AIDs-defining illness and recovered fully from COVID-19 infection without severe complications. Subsequent follow-ups were arranged and HAART were commenced. It may be interesting to know the overall incidence of HIV infection, diagnosed through this pre-treatment workup protocol. This may serve as a reference for the effectiveness of pre-admission HIV screening in Hong Kong.

### Implication of COVID-19 on HIV care

From an HIV perspective, the efforts to mitigate the pandemic can have major impact on clinical care for HIV-infected patients. The greatest impact was estimated to be from interruption to antiretroviral therapy, which could occur during a period of high health system demand. In Hong Kong, some patients got disturbed on their routine clinic attendance or access to HAART by lockdown policies. Locally, drug refill clinics have been launched for patients who had difficulties in attending clinics or were afraid of acquiring COVID-19 while waiting for doctor consultation in the clinics. Fortunately, the in-patient and out-patient services for HIV-infected patients in Hong Kong have remained sustained since the emergence of SARS-CoV-2 outbreak with the effort of local experts.

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# Action

## HIV Forum for Elderly Home staff
## 安老院舍座談會 - 伴你同行、護理情真


**Ms Pansy Yu, Advanced Practice Nurse**
**Ms Shan Chan, Advanced Practice Nurse**


Aging population of people living with HIV (PLHIV) is growing and there is increasing demand of service for elderly homes in Hong Kong. Currently only a few elderly homes would accept HIV patients. The 2019 HIV forum was co-organized by HKSHM and the Queen Elizabeth Hospital (QEH) HIV Clinical Service. It aimed to raise the public awareness on HIV and to educate elderly home staff on key concepts of caring PLHIV. Two identical sessions of the HIV forum were held in QEH on 18 Oct 2019 and Kwong Wah Hospital (KWH) on 29 Nov 2019, in collaboration with the Community Geriatric Assessment Team (CGAT) in both hospitals.

The forum was targeted at elderly home staff, doctors, nurses and allied health professionals of CGAT. Content of the forum included the introduction and updates on HIV, infection control for caring PLHIV as well as a sharing session. In preparation for the sharing session, we interviewed the son of one of our patients to share his experience and challenges while searching for an elderly home for his HIV positive father. Similarly, we interviewed the staff of the elderly home where the patient was eventually admitted to share their feelings towards caring for HIV patients. We had summarized the comments of both sides and prepared the real story scenario for sharing in the forum. We were glad to see many positive responses from the elderly home staff and health care workers in the forum.

The prognosis of PLHIV has improved dramatically over the past 20 years, but the rates of co-morbidities as well as geriatric syndromes increase significantly. To improve the understanding and acceptance on PLHIV among elderly home staff is one of our goal. The forum has provided a good platform for interaction and mutual communication.

# Activities of the Society

## HIV Live Webinar

### Live Webinar on "Redefining HIV treatment Goals to Enhance Patient Care" (June 2020)

During the COVID-19 pandemic, live webinar becomes a popular platform to share up-to-date information. HKSHM co-organized our first live webinar with the HKSID on 22 June 2020. In this webinar, Dr. Laura Waters from United Kingdom illustrated the unmet needs of our current antiretroviral regimens with case studies. She also discussed the current evidence and international guidelines on the use of dolutegravir and lamivudine dual therapy.


Dr. Kenny Chan chaired the webinar


After the lecture, Dr. Kenny Chan discussed with Dr. Laura Water on the use of dual therapy in the discussion session.

***More HIV webinars –***

- **The Game Changer of HIV Management,** Dr. Vincente Estrada – October 2020
- **A strong return of NNRTI class**, Prof. Chloe Orkin – November 2020

**and**


***Upcoming HIV conferences...***

- **HIV Drug Therapy Glasgow 2020,** 5-8 October 2020 | Virtual event
- **Asia Pacific AIDS & Co-infections Conference (APACC) 2020,** 15-17 October 2020 | Virtual event

# Academic corner

## When CROI 2020 met COVID-19


**Dr. Helen Chan Shuk-Ying**

The world is seven months into the COVID-19 pandemic and it has touched everyone's life in some way. Schools and restaurants are closed, while exams and trips are forced to postpone. Healthcare workers need to work behind masks for long hours, families and friends were asked to limit face-to-face contacts with others. Situation seems under controlled initially, however, different countries were experiencing new wave of infection after easing of these restrictions. The 27th Conference on Retroviruses and Opportunistic Infections (CROI) was held, in the middle of the COVID-19 crisis, from 8 to 11 March 2020. The conference eventually turned virtual but was still able to fulfill its aims to "brings top basic, translational, and clinical researchers from around the world to share the latest studies, important developments, and best research methods in the ongoing battle against HIV/AIDS and related infectious diseases".

- **DTG and pregnancy**

Since August 2014, a national-wide observation birth outcomes surveillance study was conducted in 8 government obstetric centers by the Botswana Harvard AIDS Institute Partnership. In 2018, a possible link between dolutegrevir (DTG) and neural-tube defects (NTDs) in infants with its exposure at conception was reported from this study. Among 426 infants born to HIV-positive mother from August 2014 to June 2018 who were on DTG-based antiretroviral therapy (ART) before conception, four NTDs were identified [1]. Subsequently, a full report from this Tsepamo Study (adding 10 additional sites between July 2018 and March 2019, making the coverage to approximately 72% of all births) was published which revealed a lower risk (5 of 1683 exposures) than previously mentioned, yet still significant statistically. In this report, the prevalence of NTDs among HIV-positive women who were on non-DTG ART and efavirenz (EFV) at conception were 1 per 1000 deliveries and 0.4 per deliveries respectively [2]. Though World Health Organization (WHO) gave affirmative recommendation of using DTG as preferred first-line and second-line treatment for reproductive-age women and pregnant ladies, it is necessary to have more data provided to help women make an informed choice.

Results from IMPAACT 2010 trial was presented on 11 March 2020 in CROI [4]. IMPAACT 2010 trial was a three-arm randomized open-label study to assess the safety and efficacy of DTG + emtricitabine / tenofovir disoproxil fumarate (FTC/TDF) vs DTG + FTC / tenofovir alafenamide (TAF) vs EFV/FTC/TDF in pregnant ladies and breastfeeding women. 643 women (88% were from Africa) with median age of 27 years were randomized to the above regimens at an average of 22 weeks of gestation and were followed-up for a median of 17 weeks before delivery. More than 80% of the participants were on ART for a median of 6 days prior study entry and 16% of the total study population have HIV viral load (VL) < 50 copies/ml at entry. In the intention-to-treat analysis, 97.5% of combined DTG-arm achieved HIV VL < 200 copies/ml at delivery, which was significantly higher than those in EFV-arm (91%, risk difference 6.5%, 95% confident interval (CI) = 2% to 10.7%, p=0.005). DTG/FTC/TAF combination demonstrated significantly fewer (24.1%, p = 0.047) adverse pregnancy outcomes (composite: preterm delivery, small for gestational age or still birth) than DTG/FTC/TDF arm (32.9%) and EFV-arm (32.7%). When looking particularly into preterm delivery, DTG/FTC/TAF performed better with only 5.8% of preterm delivery, compared to 9.4% in DTG/FTC/TDF and 12.1% in EFV-arm (p = 0.023). Near 5% of infants born to HIV-positive women who were on EFV-arm died during the study period, compared to 1.5% in DTG/FTC/TAF and 1% DTG/FTC/TDF arm (p = 0.019).

The findings in IMPAACT 2010 echoed the WHO recommendations of DTG as preferred treatment for

all populations including women of child-bearing potential and TAF is more preferable choice than TDF.

- **Long-acting / extended-release (LA/ER) formulations and treatment pipelines**

We all know that poor drug adherence to ART can lead to treatment failure and drug resistance, simplification of ART by reducing intake frequency or pill burden may improve drug adherence and treatment outcome. LA/ER ARTs are developed to provide more options for physicians and patients.

Cabotegravir/rilpivirine (CAB/RPV) are the long-acting candidate drugs under active evaluation. Two multi-center randomized phase 3 studies (ATLAS and FLAIR) involving more than 1100 subjects demonstrated non-inferiority of this LA injectable combination in term of viral suppression when compared with standard 3-drug oral therapy or abacavir/lamivudine/DTG (ABC/3TC/DTG). Week 48 results of these two studies were presented in CROI last year and the investigators provided updates in CROI 2020.

As a recap, FLAIR is a randomized, open label, multi-center trial to assess the efficacy of monthly intramuscular CAB/RPV (with 4 weeks oral CAB and RPV as lead-in) versus ABC/3TC/DTG to maintain viral suppression after 20 weeks of induction of ABC/3TC/DTG [5]. After 48 weeks, 2.1% of patients in CAB/RPV and 2.5% of patients in oral therapy had HIV RNA level ≥ 50 copies/ml (non-inferiority margin 6%) [5]. Week 96 results were presented in CROI 2020: 3.2% of study subjects in both arms met the primary endpoint of plasma HIV RNA ≥ 50 copies/ml (adjusted difference: 0.0%, 95% CI: -2.9 to 2.9) [6]. The study design of ATLAS was similar as FLAIR except the subjects in control arm were required to continue with their current 3-drug oral ART [7]. At week 48, 1.6% in study arm and 1.0% in CAR arm had measured plasma HIV-1 RNA ≥ 50 copies/ml (adjusted difference: 0.6%, 95% CI: -1.2 to 2.5, non-inferiority margin 6%) [7].

The investigator expanded the study to evaluate the potential for dosing every 2 months in the ATLAS-2M trial by recruiting more patients who were treatment naïve or on standard-of-care treatment (n=654). After combining the new group of subjects with those from ALTAS (n=391), the investigators randomized all the subjects to receive either CAB 600mg plus RPV 900mg once every 8 weeks (n=522) or CAB 400mg plus RPV 600mg once every 4 weeks (n=523) [8]. Using the same primary end point as ATLAS, the proportion of subjects with HIV RNA ≥ 50 copies/ml were similar in both arms (1.7% vs 1.0%, risk difference 0.8, 95% CI: -0.6 to 2.2, non-inferiority margin 4%). However, virologic failure, defined as two consecutive HIV RNA > 200 copies/ml, occurred in 8 patients who took CAB/RPV every 2 months (1.5%) while only two patients in the monthly-arm (0.4%) [8]. The FLAIR and ATLAS/ATLAS-2M demonstrated the potential of using long-acting injectable as therapeutic options for treatment-naïve and experienced patients.

Data of another long acting agent (also a new class of ART) was also presented in CROI 2020. The first-in-class capsid inhibitor, lenacapavir (formerly known as GS-6207), shown potent antiviral activity over 10 days after a single dose ranged from 20 to 750mg [9]. In this phase 1b, dose-ranging study, 39 treatment-experienced patients but naïve to capsid inhibitors or integrase inhibitors, with HIV RNA 5000 to 400,000 copies/ml were randomized to receive one single dose of lenacapavir (20, 50, 150, 450 or 750mg) or placebo. Lenacapavir achieved substantial HIV RNA reduction from 1.3 $\log_{10}$copies/ml to 2.3 $\log_{10}$copies/ml over 10 days, compared to 0.2 $\log_{10}$copies/ml with placebo. Adverse events were generally well tolerated with mild to moderate injection site reactions which were self-limiting. Two phase 2 clinical trials are now on-going to evaluate its efficacy, with a 6-month dosing interval, in treatment-naïve and -experienced patients.

- **HIV and Co-morbidities**

The early initiation of ART and multi-disciplinary management cascade improve the outcome of people living with HIV (PLHIV). The latest data in CROI 2020 revealed PLHIV can now live longer

with overall life expectancy increased from 38 years remaining in 2000-2003 to 56 years remaining in 2014-2016 at the age of 21 years [10]. For those who started ART at a CD4 count of $\geq 500$ cells/mm$^3$ had similar overall life expectancy compared with those without HIV (59 vs 63 in 2014-2016). However, PLHIV still had shorter comorbidity-free life expectancy at age 21 than those without HIV (13 vs 29 years remaining in 2014-2016), especially on chronic liver disease, chronic kidney disease, chronic lung disease and diabetes [10].

As PLHIV can now live longer, more efforts are needed to prevent the development of comorbidities and monitor their outcomes. A retrospective cohort study was conducted in US to determine why PLHIV had a higher cardiovascular disease (CVD) mortality rate than those without HIV, based on data from CDC between 1999 and 2013. The cohort study included 1,125,126 subjects who were admitted to hospitals for acute coronary syndrome (ACS), with over 6600 of PLHIV and 1,118,500 were HIV negative [11, 12]. PLHIV were younger than those without HIV (57 vs 67 years, $p < 0.0001$), they also presented with higher rates of substance abuse, smoking and medical conditions including diabetes (51% vs 47%), chronic lung disease (55% vs 41%), liver disease (36% vs 12%), history of hepatitis C infection (18% vs 1.3%), chronic kidney disease (36% vs 26%) [11, 12]. The rates of obesity and hypertension were similar in both groups. The types of ACS were similar in both groups [11, 12]. Compared to those without HIV, PLHIV had significantly higher in-patient mortality (5.5% vs 5.3%, Odd Ratio (OR) 1.28, 95% CI: 1.15 to 1.43) [12], were likely to readmit to hospitals at 30 days (14.3% vs 9.4%, OR = 1.23, 95% CI: 1.14 to 1.33) and die at 12 months (5.6% vs 5.1%, OR = 1.34; 95% CI: 1.2 to 1.5) [11]. In term of CVD management, 31.6% of HIV-positive patients received coronary angiogram [12], 67.9% prescribed with beta-blockers, 66.8% with statins and 46.8% with anti-platelet agents 12 months after discharge [11], all were significantly lower than those without HIV (all categories $p < 0.0001$). The authors of this study alerted the importance of optimization of risk factors in high-risk patients.

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