LOOK FORWARD TO HKSN CME COURSE AND ASM

On behalf of the Hong Kong Society of Nephrology HKSN, I would like to invite full members to join our CME Course jointly organized with the Asian Pacific Society of Nephrology APSN. Mark your diary on 1 October 2022.

For all Full and Associate members, you are welcome to join the Annual Scientific Meeting on 2 October 2022. Yes, that means a fully packed - but educational – weekend around the National Day.

Please register for the event from the email sent to you. We will follow prevailing measures and hygiene etiquette during the physical meeting. We need your support for the AGM on 2 October 2002 too.

This year, we have dedicated a new session for young fellows and nurses on conducting research. That means not just learning from giants (from named Award Lectures, Keynote Lectures), but learning to be giants – or David, if not Goliath.
What is New in the Treatment of COVID-19?

We have covered the two oral anti-viral drugs, molnupiravir, nirmatrelvir-ritonavir, in the previous Newsletter. The following topics and articles are worth mentioning this time.

Q: How safe is remdesivir treatment in patients with severe kidney dysfunction?
A: We need to be cautious of drug use in patients with kidney disease, and yet be mindful of the concept of potential “renalism.” The term renalism refers to withholding therapy on the basis of the degree of kidney dysfunction. One good example is the dilemma of providing contrast scan or coronary investigation for patients with low glomerular filtration rate (GFR), largely for the fear of contrast-associated acute kidney injury (CA-AKI). On the other hand, avoiding the use of drugs in patients with low GFR is more often “rationalized” from the exclusion of this group of patients from many clinical trials.

Patients with low GFR are also under-represented in COVID-19 vaccine studies as shown in a systematic review (Glenn DA et al. Kidney Int Rep 2021): any chronic kidney disease was explicitly excluded from 16% of trials, whereas “serious renal disease” from 33% of trials. Remdesivir, in particular, was not used in ACTT-1 Study (Beigel JH et al; ACTT-1 Study Group Members. N Engl J Med 2020) where patients with GFR lower than 30 ml/min/1.73 m² were excluded. There has been concern about accumulation of the drug vehicle SBECD (predominantly excreted through glomerular filtration), and hence SBECD related liver necrosis or renal tubule injury.

After a review on safety of remdesivir for patients with acute and chronic kidney disease (Adamsick ML, et al. J Am Soc Nephrol 2020), there have been new studies on this issue. A retrospective chart review study in the United States (Ackley TW, et al. Antimicrob Agents Chemother 2021) previously assessed the safety outcomes of remdesivir treatment among 40 hospitalized patients with Cockcroft-Gault formula estimated creatinine clearance less than 30 ml/min. Compared to matched subjects with creatinine clearance ≥ 30 ml/min, the primary endpoint of acute kidney injury at the end of treatment was not significantly different (5% versus 2.3%; P = 0.28). There was also no significant difference in early remdesivir discontinuation due to abnormal liver function (0% versus 3.9%; P = 0.37).

Another single-centre cohort study (Pettit NN, et al. Clin Infect Dis 2021) reported 20 patients who had creatinine clearance below <30 mL/min (n = 15) or ESRD (n = 5) and had received remdesivir. Compared to others without severe renal impairment, there was no statistically significant difference in the incidence of abnormal liver function test (10% versus 4%; P = 0.28), or acute kidney injury (27% versus 6%; P = 0.02). Furthermore, the abnormal liver function and and serum creatinine elevations were not attributed to remdesivir in either group.

Notably, there is a recently published secondary analysis of the Canadian Treatments for COVID-19 (CATCO) randomized trial. The CATCO, a substudy of the global WHO Solidarity clinical trial, showed treatment benefit for preventing the need for mechanical ventilation.

The secondary analysis was now published, with special attention to those patients with low GFR.

In brief, the Canadian research group reported the data of 59 patients with GFR less than 30 ml/min/1.73 m² who were randomized to remdesivir (n = 34; standard loading dose 200 mg and then daily 100 mg doses for 9 days or until discharge) or standard care (n = 25). There was no increased risk of abnormal liver enzymes or toxic kidney effects. Furthermore, there was no significant difference in the need for new dialysis or mortality. See next page for the details of safety outcomes.
What is New in the Prevention of COVID-19?

Q: What is tixagevimab-cilgavimab (Evusheld)?
A: This is a SARS-CoV-2–neutralizing monoclonal antibody approved by the U.S. Food and Drug Administration FDA in December 2021 as emergency use for the preexposure prophylaxis (prevention) of COVID-19 in those who are moderately to severely compromised and who are 12 years or older and weigh more than 40 kg.

The drug contains 2 fully humanized monoclonal antibodies that target different areas of the SARS-CoV-2 spike protein. Tixagevimab 300 mg and cilgavimab 300 mg as a single dose, in 2 separate syringes consecutively, are to be administered intramuscularly at different injection sites, preferably 1 in each of the gluteal muscles.

A Cochrane meta-analysis (Hirsch C, et al. Cochrane Database Syst Rev 2022) confirmed a decrease in development of clinical COVID-19 symptoms (high certainty), infection with SARS-CoV-2 (moderate certainty), and admission to hospital (low certainty) with tixagevimab-cilgavimab.

Q: How long should we wait after COVID-19 vaccine to give tixagevimab-cilgavimab (Evusheld)?
A: Tixagevimab-cilgavimab should not be given for at least 2 weeks after vaccine administration. The reason is a theoretical concern that the presence of antibody may impair antigen presentation to immunocytes, thus impairing the body’s immune response to the vaccine. There is, on the other hand, no minimum interval from tixagevimab-cilgavimab to the subsequent COVID-19 vaccine dose administration.

Q: What is tixagevimab-cilgavimab (Evusheld) not used for?
A: It is not intended as a substitute for vaccination. Patients should be advised to receive a full vaccine series, including booster doses in addition to receiving tixagevimab-cilgavimab, unless full vaccination is not possible because of a history of severe allergic reaction to the COVID-19 vaccine.

Q: How may kidney transplant recipients (or patients with B-cell depletion for immunological disease) benefit from tixagevimab-cilgavimab (Evusheld)?
A: The evidence first came from the landmark PROVENT (Phase III Double-blind, Placebo-controlled Study of AZD7442 for Pre-exposure Prophylaxis of COVID-19 in Adult) trial, which was conducted before the emergence of the Omicron variant and subvariants.
The study involved over 5000 adults who had not received COVID-19 vaccination, had no history of prior SARS-CoV-2 infection (negative serologic test result) but were at increased risk for inadequate vaccine response or for SARS-CoV-2 exposure. Since only 4% of study subjects in the PROVENT study had an immunocompromising condition, the results might not be easily extrapolated to kidney transplant recipients (who are vaccinated, as is often the case nowadays). As such, the relevant question is whether we have real-world data of tixagevimab-cilgavimab in kidney transplant recipients during the Omicron period.

A recent retrospective cohort study from France reported the efficacy of tixagevimab-cilgavimab in 222 solid organ transplant recipients and 222 vaccine-matched solid organ transplant recipients without monoclonal antibody pre-exposure prophylaxis during the Omicron period. More than half were kidney transplant recipients.

The use of tixagevimab-cilgavimab was shown to be associated with a significantly lower risk of SARS-CoV-2 breakthrough infection (5% versus 14%; P < 0.001) after a mean follow-up period of 3 months.
Their analysis showed no significant difference in the incidence of breakthrough in the subgroup of organ transplant recipients who had prior SARS-CoV-2 infection. In other words, kidney transplant recipients with no prior SARS-CoV-2 infection or those with low anti-spike antibody responses to vaccination may benefit most from tixagevimab-cilgavimab pre-exposure prophylaxis. However, their study was conducted before the emergence of BA.4 and BA.5 lineages.

Q: How long can tixagevimab-cilgavimab (Evusheld) protect kidney transplant recipients?
A: According to the PROVENT study, the efficacy of tixagevimab-cilgavimab lasted for at least 6 months (before the Omicron era).

The kinetics of anti-receptor-binding domain RBD of the SARS-CoV-2 spike protein had been investigated in kidney transplant recipients (who received 150 mg tixagevimab and 150 mg cilgavimab, lower dose than the current recommendation). The French study group (Benotmane I, et al. Kidney Int 2022) demonstrated a significant decrease of the anti-RBD IgG 4 to 5 months after the administration of tixagevimab-cilgavimab.

That would make sense if we follow the latest advice to give the tixagevimab-cilgavimab every 6 months.

- Tixagevimab-cilgavimab are not eliminated intact in the urine. Renal impairment is not expected to significantly affect the exposure of tixagevimab and cilgavimab. Similarly, dialysis is not expected to impact the pharmacokinetics of tixagevimab and cilgavimab.
During the Educational Symposium on 30 April 2022, we dedicated a half day zoom meeting for a timely topic: COVID-19. The overwhelming registration (502) this year, with 373 turn-up rate, speaks for the importance to equip ourselves with updated knowledge in our battleground of fighting COVID-19.

My gratitude to the speakers and the organizing committee led by Dr. Yuen SK, and efforts of Dr. John Chan (Education Committee), Dr. Jack Ng and Gary Chan (Young Nephrologists Committee).

In addition to the knowledge about prevention and treatment of COVID-19 infection from local and overseas speakers, we learned about liver involvement, electrolyte disorder, rehabilitation and ethics of COVID-19.

Unprecedented rapid advances have been made in the management of COVID-19, most of which are covered in pre-printed or medRxiv format before formal peer review. The upshot of our Educational Symposium is not just giving our members better coverage of the knowledge, but to spark the collaboration between different centres. And, for the first time, we have come up with two articles jointly authored by different chairpersons and speakers of this Educational Symposium: one on the local epidemiology and mortality of kidney disease patients during the Omicron wave, and another on hyponatraemia of COVID-19 patients across the territory.

Stay tuned for the publication of these two articles.
This year, our ceremony has a sharing session on the theme of health literacy, for the community at large, patients and organisation. In brief, health literacy refers to the degree to which individuals have the capacity to obtain, process, and understand basic health information needed to make appropriate health decisions. This has been the common thread through usual discussion on the topic of health literacy. On top of that, we stress the key role of healthcare professionals to play: to provide guidance for patients to navigate a complex health care system, to be culturally competent and speak their language (so they can make informed health care choices) and identify patients' specific health literacy levels and make simple communication adjustments.

Low health literacy has now been shown to be associated with the onset of chronic kidney disease. Based on a prospective cohort study of 93,885 community-dwelling adults living in The Netherlands, low health literacy was associated with the onset of CKD in older adults. Moreover, individuals with worse renal function were more likely to have low health literacy.

The two slides (shown above), as shared by Dr. KM Chow and Desmond Yap during the World Kidney Day ceremony, highlight the impact of health literacy on the kidney health, as well as kidney transplant access.
A drama session by the patient group during the World Kidney Day ceremony demonstrated the need to tackle low health literacy, a highly prevalent problem worldwide. This is definitely a worthwhile effort because low literacy has also been associated with higher hospitalization and mortality rates, with similar effects on chronic kidney disease.

To measure the health literacy and the kidney disease patients’ perspective to obtain information to improve their complex disease management skills across different age groups, the Hong Kong Kidney Foundation and Hong Kong Society of Nephrology presented the survey result during the ceremony. Our thanks to Dr. SF Lui, Jack Ng and YL Cheng.
In some aspects, health literacy is like a whiteboard, to be written on by healthcare professionals like us using marker but not permanent markers. That means it will be wiped clean – well, almost clean - after each session, after new knowledge has come up. The gist is not to give lecture note for patients to copy, and not to aim for rote memorisation. We should provide tools for patients to find the knowledge and develop skills to make health decision. That health decision has no model answer. We are aiming for each and every patient to make health decision appropriate to himself or herself.

This year, the activity was co-organized with the Hong Kong Association of Renal Nurses (HKARN). As a matter of fact, renal nurses are the best to empower patients, to work on improving health literacy.
The patients’ voices are always the focus, as we wish to have better patient-oriented care in health care. We have to admit that patient participation group are slow to take off in Hong Kong. One reason for the unmet need might be that the fittest patients to run the groups are not the most frequent visitors to doctors. With that in mind, our patient group has decided to address the need of patients in the consultation waiting room. Their storytelling is powerful to contextualize and humanize the doctor-patient and nurse-patient relationship. The drama story reminds us the need of patients and the way to improve communication (on top of heavy workload of healthcare workers).

Last but not least, we thank our sponsorship partners to make the event happen.
Musical Appreciation for Renal Patients – HKSN and IACN

Congratulations to Professor Philip Li who received the Oreopoulos Award 2022

We are glad to share the good news: Prof. Philip Li, our HKSN Co-Opt Council member and previous HKSN Chairman, has been presented the Oreopoulos Award to recognize his lifetime PD achievements in terms of delivering care to patients, research, teaching and advocacy.

Becoming a doctor or a renal nurse is the best way to teach us about health and humanity.

The World Kidney Day inspires many to live well with kidney disease. Over the last two years of pandemic, many of us are plagued with loneliness and social isolation. This is even worse for patients suffering from chronic illness.

We believe that patient rehabilitation is one of the keys to better health. With that in mind, the Hong Kong Society of Nephrology and the International Association of Chinese Nephrologists (IACN) have organized a musical appreciation activity on 25 September 2022. We will sponsor patients from renal units across the Hospital Authority to appreciate this musical (see opposite): *The Impossible Trial*. The performance venue of this musical, Grand Theatre, Xiqu Centre at West Kowloon Cultural District, is a cultural site of interest.

Patients will benefit not just the free tickets to appreciate the musical; HKSN and IACN will make good use of the event to educate patients on their need to have vaccine protection. In other words, the patients should learn the appropriate way to protect themselves. We are not asking patients to self-isolate at home for fear of immunocompromised state. We are advising them to take proper precaution including vaccination, which provides strong protection against serious illness, hospitalization and death from COVID-19.

We also take this opportunity to thank the organizing committee: Dr. Terence Yip, Lorraine Kwan, Jack Ng, KM Chow, Prof. Philip Li, Anita Wong and Alice Tin. We remain indebted to the generous sponsorship from different companies and donors. Finally, thank you, our renal unit nurses and staff, for helping with ticket distribution. Let’s all work together to help our patients to live well with kidney disease.