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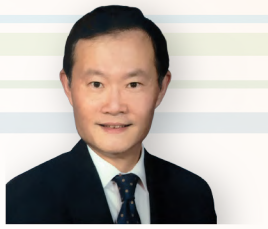
聖保祿醫院
St. Paul's Hospital

NewsLetter
院訊

PET-CT Service Commencing Soon



Dr. William Ho
Medical Superintendent

May Peace Return Soon

For the past few months, Hong Kong has gone through historically unprecedented turmoil, and there is still no end to it. The economy, people's livelihood, as well as Hong Kong's international reputation have greatly suffered. Hospital colleagues at times have difficulties coming to work or going home because of the transport disruption. From the Academy of Medicine, I learned that visiting professors and examiners are refusing to come, thus affecting academic activities and professional examinations of certain specialty Colleges. Mainland tourists, and patients alike, have dwindled. As our hospital is situated in Causeway Bay, not far from frequent protest sites, particular attention is paid to safety and security. Faced with such challenges, we have been constantly assessing the situation and responding appropriately. Through concerted effort, operation is smooth. I would like to thank our dedicated staff for striving to be punctual for work by departing earlier in the morning, our Nursing Administration Department for opening up more night accommodation for staff in need, our security staff for doing much more to ensure safety, and management of all levels for reducing late meetings so that staff members can be released earlier. While out-patient attendance has inevitably dropped, the impact so far on inpatient activities is still within normal fluctuations, although patients now more prefer to come on weekdays than weekends. We are grateful for the continued support of visiting doctors. Let's pray that the political instability will not last long.

On the positive side, our cardiac work keeps going strong. We just had our first TAVI (Transcatheter Aortic Valve Implantation) operation successfully done this month, with fantastic patient outcome. Our new PET-CT suite had been completed with the machines installed and commissioned. Licenses have been obtained, and pending Department of Health's approval, the service will commence any time. Meanwhile, the final phase of hospital reconstruction project is proceeding well. With demolition of the old Block C, construction of a basement at the site is commencing. A number of floors in Block A are being renovated, including a state-of-the-art Auditorium with close to 200 seats for academic meetings, performances, and external links for e.g. live surgical demonstrations. Another floor will be renovated to a Geriatric Day Centre to meet the needs of patients and narrow the existing service gap with long waiting list for such service in the Eastern District.

Many patients and visitors have commented that St. Paul's Hospital really feels like a serene oasis amid the hustle and bustle of Causeway Bay, well suited for body recovery and spiritual rejuvenation. By God's grace, we will continue to uphold our healing mission with unity and professionalism no matter the external environment. May peace return to Hong Kong soon.

聖保祿醫院放射部A座及B座地庫一樓 St. Paul's Hospital, Radiology Department, LG1, Block A & Block B

預備室
Preparation room

放射部即將提供
正電子電腦雙融掃描服務

Provision of Positron Emission Tomography-Computed Tomography Service in Radiology soon

- 先進的診斷儀器檢測腫瘤
  Advanced diagnostic equipment for tumour imaging
- 專業團隊提供優質的醫療服務
  High-quality health care from a professional team
- 環境寬敞舒適
  Spacious calming environment
- 醫院管理局轉介折扣優惠
  Special discount for Hospital Authority's referrals

正電子電腦雙融掃描是現時最先進檢測腫瘤的診斷儀器之一，聖保祿醫院放射部將於**二零二零年一月**為社區提供全面及高質量的診斷服務。

PET-CT is one of the most advanced diagnostic equipment for tumour imaging. By January 2020, Radiology Department of St. Paul's Hospital will provide comprehensive and high quality diagnosis service to the community.

查詢熱線 / ENQUIRY：2830 3786

更多資訊
For more information

INTRODUCTION
Of New Faces

I obtained my medical degree in the Chinese University of Hong Kong and completed specialist radiology training at Pamela Youde Nethersole Eastern Hospital, with subspecialty interest in Breast Radiology, Head and Neck Radiology & Interventional Radiology. In addition, I undertook post-fellowship overseas training at Stanford University in USA, Asan Medical Center in the Republic of Korea and University Hospital Aachen in Germany. After a decade of public service in the Hospital Authority, I have been working as a private radiologist in various private hospitals and imaging centres in Hong Kong, providing diagnostic and interventional radiology services. Moreover, I am a photography, music and football lover. It is my privilege to serve St. Paul's Hospital with my public and private working experience and I look forward to engaging closely with clinicians in providing holistic care to patients.

Dr. Wan Yu Hon, Alvin
Staff Consultant Radiologist

Hello I am Alan Wong. I graduated from Saba University in the Netherlands-Antilles where I also completed my Master of Science degree in Hyperbaric Medicine. I then went on to do further training in Family Medicine at the University of Minnesota in the United States. I enjoy teaching and have worked as a Lecturer at the University of Melbourne while I was working in Australia. Currently I also teach medical students in Hong Kong as an Honorary Clinical Assistant Professor at the University of Hong Kong. It is my pleasure to meet all of you and to be part of the St. Paul's Family.

Dr. Wong Yan Ho, Alan
Resident Medical Officer

Hello, I'm Dr. Eric MAN. I have my basic and high training in radiology in Pamela Youde Nethersole Eastern Hospital after my graduation from medical school in 2003. I had my overseas training in Toronto Sick Kids Hospital and South Korea's Samsung Medical Centre. My subspecialties are neuroradiology and interventional radiology. I've worked in Hong Kong Sanatorium Hospital for 5 years before joining the family of St. Paul's Hospital. I'm happy to see so many familiar faces and meet new friends here.

Dr. Man Man Wai, Eric
Staff Consultant Radiologist

Hi everyone! My name is Candice and I am really happy to join the St Paul's Hospital. I graduated from HKU in 2005 and went into physician training. I first obtained my fellowship in Respiratory Medicine at the Tuen Mun Hospital in 2012. Subsequently I underwent further training in Critical Care Medicine at the Kwong Wah Hospital Intensive Care Unit. My special interest is in the ventilatory support of critically ill patients, especially those with acute respiratory distress syndrome or severe asthma. I look forward to working with everyone in the St Paul's family; and to serving the Church and the community.

Dr. Lee Yin Yin, Candice
Staff Consultant in Respiratory Medicine

Maviret™ & Vosevi™: The New Cure to Hepatitis C Infection

SPH Pharmacy Department

Hepatitis C infection is a liver infection caused by Hepatitis C virus (HCV). According to the 2016 Hepatitis Surveillance Report from the Centre for Health Protection, Department of Health of Hong Kong, there was a drastic rise in the number of reported cases of HCV infection from 2015 (14 cases) to 2016 (39 cases). The gold standard of treatment for HCV infection was ribavirin plus pegylated-interferon. However, apart from its limited efficacy in most subtypes of HCV, this combination has been associated with severe problems such as thyroid dysfunction, psychosis, hepatotoxicity and bone marrow suppression. Therefore, since 2015, the use of pegylated-interferon was gradually replaced by a new class of antivirals, namely the Direct-Acting Antivirals (DAAs). The first DAA approved by the U.S. Food and Drug Administration (FDA) is Harvoni®(ledipasvir and sofosbuvir). Since then, numerous new DAAs have become available such as Daklinza®(daclatasvir), Epclusa® (sofosbuvir and velpatasvir), Sovaldi®(sofosbuvir), Sunvepra®(asunaprevir), Viekira Pak™(dasabuvir, ombitasvir, paritaprevir and ritonavir), and Zepatier™(elbasvir and grazoprevir). This article covers the new concepts of DAAs and gives an overview of the newest highlights of the two new DAAs approved by FDA in 2017, Maviret™ (glecaprevir and pibrentasvir) and Vosevi™ (sofosbuvir, velpatasvir and voxilaprevir).

Fig. 1 Maviret ™

Fig. 2 Vosevi ™

HOW DO DIRECT-ACTING ANTIVIRALS (DAAs) WORK?

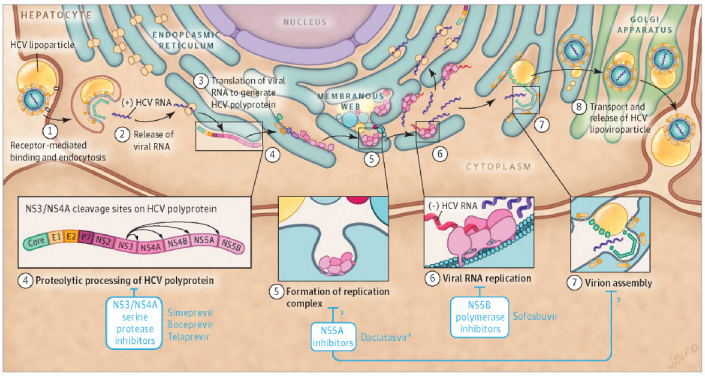


Fig.3 Life-Cycle of Hepatitis C Virus (HCV)

HCV is a ribonucleic acid (RNA) virus. Upon viral entry into host cell, the viral RNA undergoes translation into polyproteins by the host machinery. The polyproteins then undergo a series of processes (post-translational modification, RNA replication, assembling and eventually release of new mature viral protein from the original host cell) involving viral-encoded proteins, which are the major sites of action of DAAs. The fact that these targeted proteins are not present in host cells gives rise to the specificity of killing action of DAAs towards HCV rather than host cells.

NS3/4A protease is one of the HCV-encoded enzymes involved in post-translational modification and replication of HCV. This protease also impairs the induction of interferons, which are the host-signalling protein responsible for the elimination of HCV. NS3/4A protease inhibitors (-previr) inhibit these processes and therefore possess anti-viral activity against HCV. Examples of this class of DAAs include asunaprevir, glecaprevir, grazoprevir, paritaprevir, and voxilaprevir.

NS5A protein is another HCV-encoded enzyme which is targeted by NS5A inhibitors. NS5A protein is believed to be responsible for regulating HCV replication as well as assembling of HCV particles. As a result, inhibition of NS5A protein leads to the disruption of life-cycle of HCV. Examples of NS5A inhibitors (-asvir) include daclatasvir, ledipasvir and pibrentasvir and velpatasvir.

NS5B is an RNA-dependent RNA polymerase encoded by HCV. It is essential to post-translational modification and replication of HCV. Inhibition of the RNA polymerase contributes to the anti-viral activity of NS5B polymerase inhibitors (-buvir). Examples of this class of DAAs include dasabuvir and sofosbuvir.

After understanding the mechanism of actions of the DAAs, we can now learn more about the most recently registered DAAs: Maviret™ and Vosevi™.

MAVIRET™, THE FIRST EVER 8-WEEK-CURE DAA

Maviret™, a combination of glecaprevir and pibrentasvir, is a pan-genotypic drug approved for the treatment of Hepatitis C treatment-naïve patients 12 years and older or weighing at least 45 kg with HCV genotype 1-6 infection. It is also indicated for most treatment-experienced patients with or without compensated cirrhosis. In general, Resistance-Associated Substitution (RAS) testing is recommended prior to the initiation of DAA treatment. In a subset of

patients with HCV infection, viral variants harbouring substitutions associated with resistance to DAAs are detectable prior to antiviral therapy and, particularly in the case of NS5A inhibitor-containing regimens, may negatively impact treatment response. These substitutions are referred to as baseline RASs. Maviret™, unlike some other DAAs, RAS testing is unnecessary prior to the initiation of therapy.

According to the latest practising guideline published by the American Association for the Study of Liver Diseases (AASLD), Maviret™ is listed as the recommended treatment option for almost all subtypes of HCV infection. Some exceptions, where Maviret™ is listed as an alternative agent, include patients with genotype 3 infection who was treated with pegylated-interferon plus ribavirin, and patients with genotype 1 infection who was treated with NS5A inhibitor, with or without compensated cirrhosis. Sustained Virologic Response (SVR12), which is defined as HCV RNA remains undetectable at 12 weeks after the end of treatment, is the major outcome in evaluating the efficacy of Hepatitis C medications. From clinical studies, Maviret™ has shown SVR12 as high as 92% to 100% in different subtypes of HCV infection. Besides, it is noted that for most other available DAAs, the recommended duration of treatment is usually 12-16 weeks and even up to 24 weeks for some subtypes of genotype 2 or 3 infection. The minimum duration of treatment with Maviret™, uniquely, can be as short as 8 weeks for treatment-naïve patients with genotype 1-6 HCV infection without cirrhosis and some treatment-experienced patients without cirrhosis and treated only with (pegylated-) interferon, ribavarin, and/or sofosbuvir. This could be an advantage to patients with poor compliance to long-term therapy. Furthermore, Maviret™ is a generally well-tolerated drug, with the most common side effects being headache and fatigue.

Nevertheless, as with the majority of DAAs, drug interaction has to be taken into consideration when prescribing Maviret™. For example, when warfarin is co-administered, close monitoring of INR values is recommended due to potential fluctuation in INR values. Moreover, Maviret™ is a p-glycoprotein (p-gp) substrate and inhibitor. When co-administered with p-gp substrates such as dabigatran, Maviret™ may lead to a rise in the concentration of dabigatran. Dose modification of dabigatran may be needed in renally impaired patients. As Maviret™ may also increases plasma concentration of digoxin when both drugs are used concomitantly, monitoring of signs and symptoms of toxicity and therapeutic drug monitoring of digoxin may be warranted. Additionally, Maviret™ may increase the concentration of statins, hence concurrent use with atorvastatin, lovastatin or simvastatin is not recommended. On the other hand, co-administration of Maviret™ with CYP3A inducer such as rifampicin and carbamazepine could decrease Maviret™ plasma concentrations and may lead to reduced therapeutic effect of Maviret™ or loss of virologic response. Details of drug interactions and other prescribing information are summarized in Table 4.

Table 1. Indications and duration of treatment of Maviret™ for treatment-naïve patients

HCV Genotype	Treatment Duration	
1-6	No Cirrhosis	Compensated Cirrhosis (Child-Pugh A)
	8 weeks	12 weeks

Table 2. Indications and duration of treatment of Maviret™ for treatment-experienced patients

		Treatment Duration	
HCV Genotype	*Previous Treatment*	*No Cirrhosis*	*Compensated Cirrhosis (Child-Pugh A)*
1	An NS5A inhibitor without prior treatment with an NS3/4A protease inhibitor	16 weeks	16 weeks
	An NS3/4A protease inhibitor without prior treatment with an NS5A inhibitor	12 weeks	12 weeks
1, 2, 4, 5 or 6	Regimens containing (pegylated-) interferon, ribavirin, and/or sofosbuvir, PLUS no prior treatment experience with an HCV NS3/4A protease inhibitor or NS5A inhibitor.	8 weeks	12 weeks
3		16 weeks	16 weeks

VOSEVI™, THE RECOMMENDED CURE FOR HEPATITIS C INFECTION REFRACTORY TO NS5A-INHIBITOR

Vosevi™, a combination of sofosbuvir, velpatasvir and voxilaprevir, is approved for the treatment of Hepatitis C treatment-experienced adult patients with chronic HCV infection with cirrhosis or without compensated cirrhosis. Same as Maviret™, no RAS testing is required prior to the initiation of Vosevi™.

According to the POLARIS studies, the SVR12 of Vosevi™ for treating the approved indications range from 91% to 100%. Vosevi™, valuably, is the only option suggested by the AASLD guideline for sofosbuvir and NS5A-experienced genotype 2 patients, and DAA-experienced (including NS5A Inhibitors) genotype 3-6 patients with or without compensated cirrhosis. The launch of Vosevi™ would definitely be a silver-lining for the aforementioned patient groups who did not have any well-established pharmacological treatment options in the past. Additionally, Vosevi™ is a well-tolerated drug with the most common side effects being headache, fatigue, diarrhoea, and nausea.

Nonetheless, Vosevi™ appears to have more potentially significant drug interactions with concomitant drugs. Apart from the potential fluctuation of INR values when co-administered with warfarin and elevation of statin concentration, Vosevi™ is prone to drug interaction with p-gp inducers or CYP3A4 inducers which may reduce the therapeutic effect of Vosevi™. As a p-gp inhibitor, Vosevi™ may also increase the level of co-administered p-gp substrate including dabigatran and digoxin. Additionally, co-administration of Vosevi™ with amiodarone may lead to serious symptomatic bradycardia, particularly in patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or liver disease. As a result, alternative anti-arrhythmic treatments should be considered unless they are not tolerated or are contraindicated. If the concomitant use of amiodarone and Vosevi™ is necessary, patients should be counselled about the risk of symptomatic bradycardia and the importance of self-monitoring of heart rate. Moreover, the solubility of Vosevi™ (specifically velpatasvir) decreases as pH increases. Therefore, special consideration is required when co-administering with acid-reducing medications. For details, please refer to the summary in Table 4.

Table 3. Indications and duration of treatment of Vosevi™

HCV Genotype	Previous Treatment	Treatment Duration
1-6	An NS5A inhibitor	12 weeks
1a or 3	Sofosbuvir without an NS5A inhibitor	12 weeks

PHARMACIST'S POINT OF VIEW:

Both newly marketed DAAs, Maviret™ and Vosevi™ have shown promising efficacies with high SVR12 range from 91% to 100% in different subtypes of HCV infection. Maviret™ features a short treatment duration of 8 weeks for treatment-naïve patients with genotype 1-6 HCV infection without cirrhosis would be a benefit to patients who are reluctant to long-term therapy. Vosevi™ targets patients who have previously been treated with other Hepatitis C regimens containing an NS5A inhibitor but have not been cured. This new drug provides a treatment option for those special patient populations. Despite their good side effect profiles, it is worth to note that both drugs involve certain significant drug-drug interactions. Careful consideration should be made when initiating both drugs. Moreover, in late August 2019 the FDA announced that there were reports regarding the use of Maviret™ and Vosevi™ in patients with moderate to severe liver impairment has resulted in rare cases of worsening liver function or liver failure. In most patients, symptoms resolved or new onset worsening of liver function improved after stopping the medicine. Health care professionals should continue to prescribe Maviret™ and Vosevi™ to patients without liver impairment or with mild liver impairment (Child-Pugh A). It is recommended to assess severity of liver disease at baseline and closely monitor for signs and symptoms of worsening liver function. Maviret™ and Vosevi™ are registered in Hong Kong and available on request in St. Paul's Hospital.

TABLE 4. COMPARISON OF PRESCRIBING INFORMATION FOR MAVIRET™ & VOSEVI™

Brand	Maviret™	Vosevi™
Active Ingredients	· Glecaprevir 100mg · Pibrentasvir 40mg	· Sofosbuvir 400mg · Velpatasvir 100mg · Voxilaprevir 100mg
Adult & Geriatric Dose	· Three tablets once daily	· One tablet once daily
Renal Dose	· No adjustment required	· No adjustment required for mild/ moderate impairment · Safety and efficacy not established for eGFR <30mL/min/1.73m^2 or ESRD requiring hemodialysis
Hepatic Dose	· No adjustment required in Child-Pugh A · Not recommended in Child-Pugh B · Contraindicated in Child-Pugh C	· No adjustment required for Child-Pugh A · Not recommended in Child-Pugh B or C
Paediatric Dose	· ≥12 years or ≥45 kg: refer to adult dose · Safety and efficacy not established in ≤12 years	· Safety and efficacy not established
Administration	· Orally with food	· Orally with food · Separate with antacid by 4 hours
Contraindication	· Severe hepatic impairment (Child-Pugh C) · Co-administration with atazanavir or rifampin	· Co-administration with rifampin
Common S/E	· Headache and fatigue	· Headache, fatigue, diarrhea and nausea
Special Warning and Precaution	· Risk of Hepatitis B Virus (HBV) reactivation in patients co-infected with HCV and HBV	
Pregnancy & Lactation Use	· Not well-established	
Major Mechanisms Of Drug Interaction	Substrate of · P-glycoprotein (p-gp) · Breast cancer resistance protein (BCRP) · OATP1B1/3	Substrate of · P-glycoprotein (p-gp) · Breast cancer resistance protein (BCRP) · OATP1B1/3 · CYP2B6, CYP2C8, CYP3A4
	Inhibitor of · P-glycoprotein (p-gp) · Breast cancer resistance protein (BCRP) · Organic anion transporting polypeptide (OATP)	
Drug Interaction with Statins	Co-administration not recommended with: · Atorvastatin, lovastatin and simvastatin Specific considerations · Rosuvastatin: not exceed 10mg · Pravastatin: reduce dose by 50% · Fluvastatin/ Pitavastatin: lowest effective dose	Co-administration not recommended with: · Rousuvastatin and pitavastatin Specific considerations · Pravastatin: not exceed 40mg · Atorvastatin, simvastatin, lovastatin and fluvastatin: lowest effective dose
Key Examples of Drug Interaction	Maviret™ increase concentration of · Digoxin, dabigatran, statins The following increase concentration of Maviret™ · Darunavir, lopinavir, ritonavir and cyclosporine; atazanavir (a contraindication) The following decrease concentration of Maviret™ · St. John's wort, carbamazepine, efavirenz; rifampin (a contraindication)	Amiodarone · Serious symptomatic bradycardia when co-administered Solubility of Vosevi™ decreases as pH increases · H2RA: not exceed famotidine 40mg BD equivalent · PPI: omeprazole ≤20mg (the only studied option) Vosevi™ increase concentration of · Digoxin, dabigatran, statins and tenofovir The following increase concentration of Vosevi™ · Atazanavir, lopinavir and cyclosporine The following decrease concentration of Vosevi™ · St. John's wort, carbamazepine, phenytoin, phenobarbital, oxcarbazepine, tipranavir/ritonavir, efavirenz, rifabutin and rifapentine; rifampin (a contraindication)
	· Fluctuations in INR values may occur in patients concomitantly receiving warfarin. Frequent monitoring of INR values is recommended during treatment and post-treatment follow-up	

References:
1. American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA). 2018. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C.
2. Package Insert: Maviret™
3. Package Insert: Vosevi™
4. Special Prevention Programme, Centre for Health Protection, Department of Health. 2017. Surveillance of Viral Hepatitis in Hong Kong -2016 Update Report
5. Up-to-date. 2019. Overview of the management of chronic hepatitis C virus infection. Retrieved from https://www.uptodate.com/contents/overview-of-the-management-of-chronic-hepatitis-c-virus-infection?search=hepatitis%20c&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

Following Drug and Therapeutics Committee meeting in August 2019, the following drugs have been approved and added to the SPH formulary:

Drugs	Indication	Usual dosage	Remarks
Repatha (evolocumab) solution for injection 140mg/mL	· Adjunct to diet and maximum-tolerated statin for adults with heterozygous familial hyperlipidaemia (HeFH), or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C level. · Patients with homozygous familial hypercholesterolemia (HoFH) on other lipid-lowering therapy.	· Subcutaneous injection into thigh, abdomen, or upper arm. · HeFH or prevention of CV events: 140mg every 2 weeks or 420mg once monthly. · HoFH (for years 12 or above): 140mg once monthly.	On request only. Please contact Pharmacy Department if you would want to prescribe Repatha.
Activon Tube gel 100% [25G] (medical grade Manuka honey)	· For wound dressing or as wound filler for sloughy wounds, pressure ulcers, surgical wounds, burns graft sites and malodorous wounds.	· Single patient use only product. · To apply liberally to the wound bed and cover with a secondary wound dressing.	Once opened use within 90 days.

Mailing Option & Personal Contact Details Update

Mailing Option Update

Should you wish to receive upcoming St. Paul's Hospital Doctors' Newsletters by post, please inform us by ticking the box below. If a reply is not received, an electronic copy of upcoming St. Paul's Hospital Doctors' Newsletters will be emailed to the email address recorded by the Hospital. Please refer to the below for personal contact update, if needed.

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To ensure you receive important updates from St. Paul's Hospital, please complete and return the following form to us (Email: vmo@stpaul.org.hk; Fax: 2837 5241) if you have updated or changed any of your previous information. Information collected will be used for Hospital communications only. Please note that it takes about ten working days to update your contact information in our system.

Personal Particulars

Name of Physician: (IN FULL NAME)

English: _____ Chinese: _____ Physician Code: _____

Correspondence (Please write down changed items only)

Address: _____

Phone: _____ Pager: _____ Mobile: _____

Fax: _____ Email: _____ Effective Date: _____

Others: _____

Signature: _____

Please return the completed form by

1) Fax: 2837 5241 2) Email: vmo@stpaul.org.hk

3) Post: 2 Eastern Hospital Road, Causeway Bay, Hong Kong (Attn: Hospital Management Department)

Thank you!