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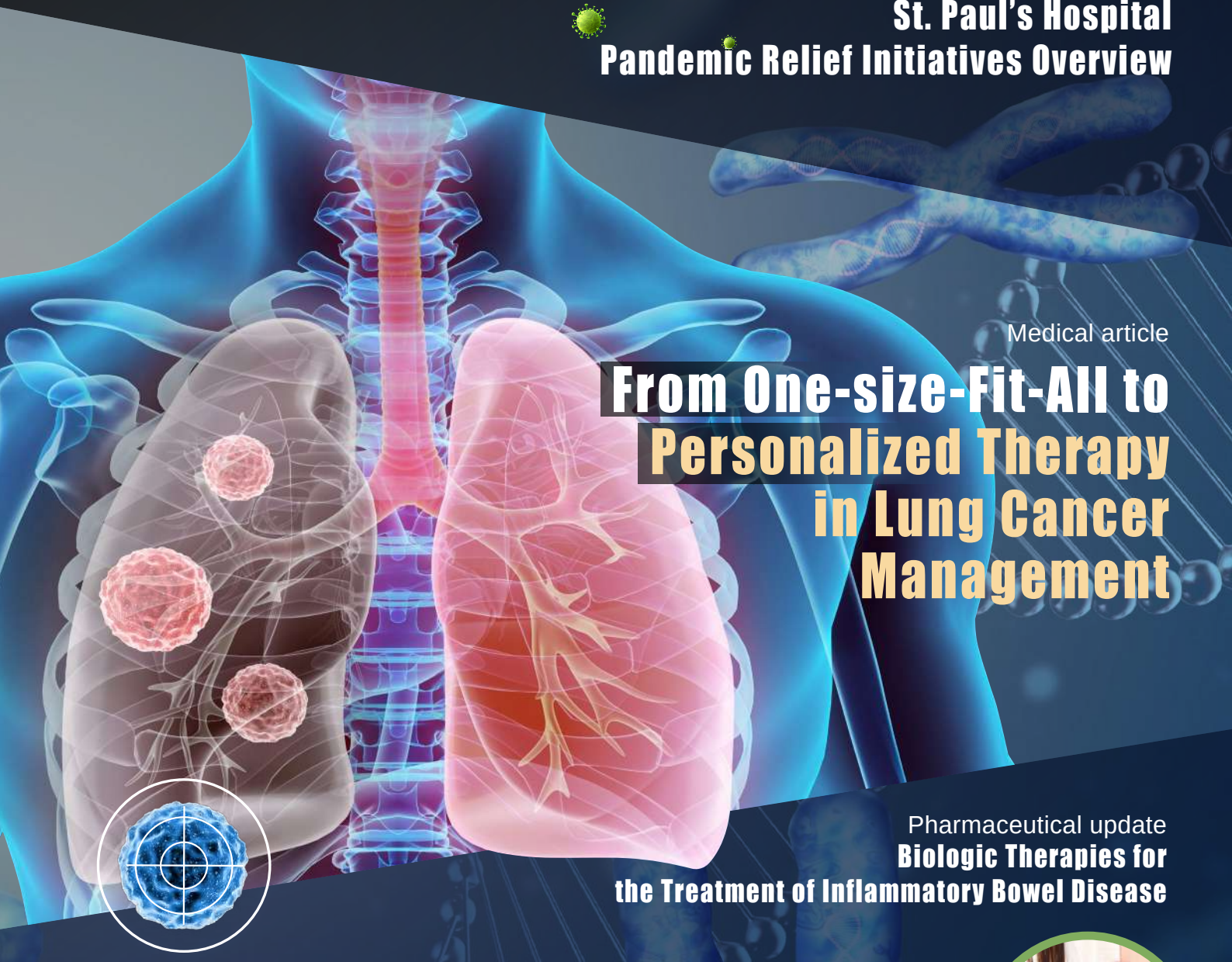
St. Paul's Hospital Pandemic Relief Initiatives Overview



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聖保祿醫院
St. Paul's Hospital

MESSAGE
From The Chief Medical Executive

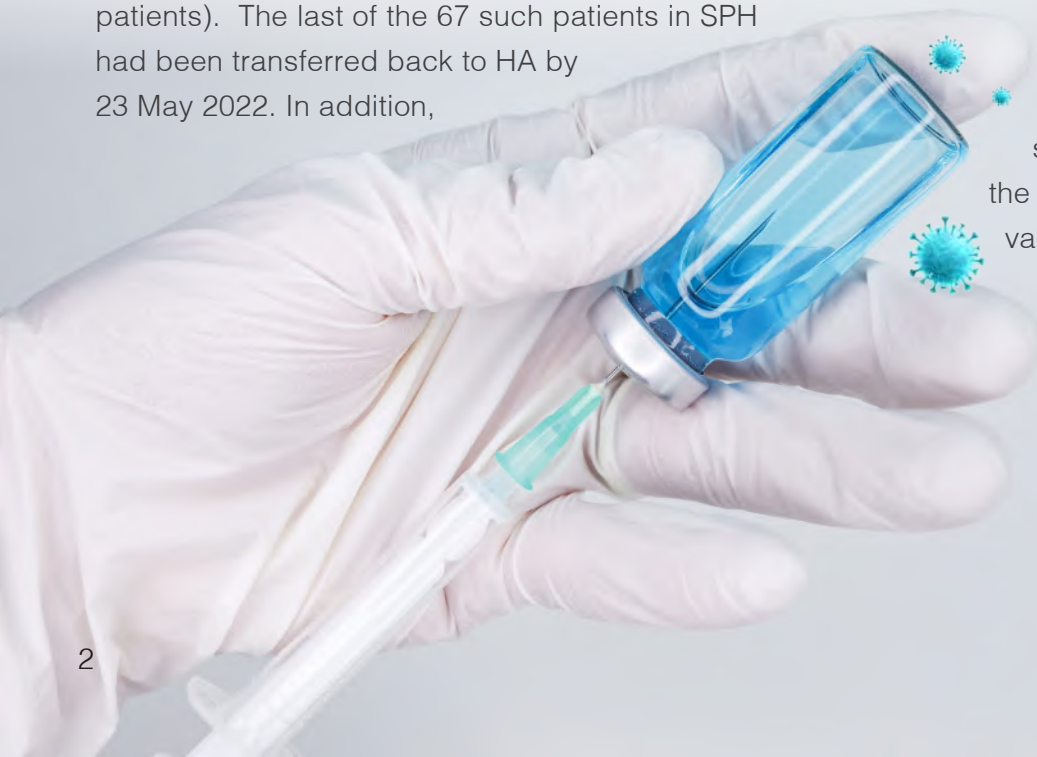
Dr. William Ho
Chief Medical Executive

The New Normal?

At the time of writing, the number of COVID cases in Hong Kong hovers around 3,000 with no sign of abating. The new Secretary for Health Prof. C M Lo is warning a surge, and actively planning with the Hospital Authority on the bed reservation and usage strategy for different scenarios. Strengthened public health measures including real name LeaveHomeSafe registration with color coding, and re-introduction of electronic wrist bands for overseas arrivals, are being mulled.

In parallel, the Hong Kong Private Hospitals Association is actively discussing with the HA on mechanisms to restart the PPP Inpatient Transfer program should there be a need. Looking back, the combined effort of private hospitals benefited more than 1,300 public patients so transferred, with more than 12,000 bed days occupied. St. Paul's Hospital was the first to pilot such transfers starting on February 24, and the patients we received had an even longer average length of stay of 21 days (cf. <2.5 days for our own private patients). The last of the 67 such patients in SPH had been transferred back to HA by 23 May 2022. In addition, we provided medical support in the Harbour Road community Isolation Facility and treated 96 COVID positive elderly patients with stable conditions. A total of 511 COVID positive out-patient with mild symptoms were managed in our 24-hour OPD. And 14 COVID positive inpatients with difficulty to be transferred to HA for various reasons were treated in our negative pressure rooms. Our effort in providing COVID vaccination tallied more than 380,000 shots given to citizens.

While the 13 private hospitals had pledged 1,000 beds to support the HA-transferred patients, in reality the actual total private beds used by such patients peaked at 266 on 1 April 2022, which then tapered off following subsidence of the fifth wave. So a repeat should be more than adequate to cater for any possible sixth wave, given that the availability of more isolation facilities recently built could have rendered the public sector better equipped, and elderly homes that accounted for the major outbreaks last time should have been better guarded.



As the WHO Director-General Dr. Tedros recently emphasized, COVID is not leaving us any time soon. We should brace ourselves to the new normal of periodic repeated vaccinations, tightening of public health measures whenever the epidemic curve ticks up, and collaborate with the public sector to help patients in need. May God help us pull through these difficult times.

St. Paul's Hospital

Pandemic relief initiatives overview

Relieving the Hospital Authority by taking non-COVID patients

Since the outbreak of COVID-19, St. Paul's Hospital has actively participated in various public private partnership projects of the Hospital Authority (HA). The Hospital has provided computed tomography (CT) and magnetic resonance imaging (MRI) to more than 5,000 referred patients, and performed surgeries on more than 250 public patients.

When the fifth wave of the epidemic broke out in early 2022, St. Paul's Hospital was the first to allocated 20 adult beds, 12 paediatric beds and additional renal dialysis sessions to take in non-COVID public patients to relieve HA hospitals. As the epidemic develops, the number of beds allocated increased to 66, out of a total commitment of up to 100. As at end of May 2022, 67 convalescent/ rehabilitation patients transferred from 11 different public hospitals with a combined length of stay of more than 1,400 bed days had been successfully treated in St. Paul's Hospital. All patients were discharged or transferred back to HA by 23 May 2022. Another 9 HA patients with chronic renal failure are receiving ongoing renal dialysis service in our hospital.

Treating COVID-19 patients

To date, St. Paul's Hospital has treated 511 outpatients with mild COVID-19 disease and 14 inpatients with COVID-19 needing hospitalization. In addition, St. Paul's Hospital was the first private hospital to support Community Isolation Facility for elderly patients with COVID-19. Such service commenced operation on 16 March 2022 in the Harbour Road Sports Centre. A total of 96 COVID-positive elderly patients had been treated, and the last patient had been discharged on 30 April 2022.

Participating in community testing and vaccination programs

The Hospital participated in the Government's Universal Community Testing Program in September 2020 and collected more than 10,000 samples. From March 2021 onwards, the Hospital dedicated a whole floor in our Main Block to operate a Community Vaccination Center for COVID-19 vaccination, and has delivered more than 380,000 doses of vaccine.

31 March 2022

Allocated a total of 66 beds to receive non-COVID patients referred by the Hospital Authority.

21 March 2022


Special arrangement was made in the Out Patient Department to cater for consultation for patients with mild COVID-19 symptoms.

16 March 2022


St. Paul's Hospital supported a Community Isolation Facility for the elderly at Harbour Road which holds 130 beds. The center receives COVID-19 patients originating from elderly homes who are in stable conditions after triage in Accident and Emergency departments of public hospitals. They will be treated till recovery and sent back to elderly homes, thus sparing beds in HA.

16 November 2021


St. Paul's Hospital launched SARS-CoV-2 Serology Antibody Test.

16 March 2021

2019冠狀病毒病 疫苗接種計劃 COVID-19 Vaccination Programme

St. Paul's Hospital operated a Community Vaccination Centre (CVC) in Hospital Main Block to provide BioNTech vaccination service. More than 380,000 doses of vaccine had been given to citizens.

1 September 2020


Staff from various departments in St. Paul's Hospital participated in the Universal Community Testing Scheme for COVID-19, over 10,000 samples were collected.

16 March 2020

St. Paul's Hospital launched COVID-19 PCR tests for the public.

Recognized on 29 October 2020 by the Government as one of the COVID-19 nucleic acid testing institutions to issue health certificates.

Dr. Chan Siu Hong
Hon. Director of Oncology Services

From One-size-Fit-All to Personalized Therapy in Lung Cancer Management

Have you ever thought of the treatment and prognosis of patients suffering from stage IV lung cancer 20 years ago compared to now? In a landmark study ECOG1594 that compared 4 different chemotherapy regimes in over 1100 late-stage lung cancer patients published in 2001, the median survival was only 7.9 months.[1] Besides, the response rate (tumor shrinkage more than 30%) was only 19%. Only 11% patients can remain alive for 2 years. At that time, the diagnosis of stage IV lung cancer was equivalent to hopelessness and gloominess.

Stage IV lung cancer therapy used to be a one-size-fit-all treatment. Chemotherapy is the only systemic treatment option for patients. And only those young and fit will be eligible. In the past 2 decades we are fortunate to witness the rapid therapeutic and diagnostic advancement in lung cancer. Lung cancer is no longer a single entity disease. Instead, different genetic aberrations that causes lung cancers are identified. And more importantly, specific therapies known as target therapies, have been developed. They specifically target on different subtypes, leading to a higher response rate, longer survival and less toxicity compared to conventional chemotherapy. Most of the target therapies are in oral forms, and thus the administration is much convenient compared to conventional chemotherapy that requires intravenous infusion.

EGFR (epidermal growth factor receptor) tyrosine kinase inhibitor (TKI) is the first lung cancer target therapy. The development of EGFR TKI has completely revolutionized the management paradigm of lung cancer. Initially EGFR TKI was found more effective in females, younger patients, never smokers, adenocarcinoma and in patients with eastern Asia ethnicity. However, these clinical parameters are not specific enough. In the landmark IPASS study, it was found that tumor harboring EGFR mutations was predictive of treatment response.[2] Since then, more and more oncogenic drivers are identified, including ALK, ROS1, BRAF, MET, RET etc. And clinicians have to try their best to look for the genotypes of every single patient and treat accordingly. The diagnostic and genotyping procedures are getting more complicated and time consuming, but at the same time, the treatment outcomes are getting better and better.

Take EGFR as an example, it is a cell-surface receptor that triggers cellular cascade for growth, after the binding of growth factors onto the receptor. Once mutated, it becomes constitutively active and leads to continuous downstream signaling and hence tumor growth, even without the presence of growth factor. EGFR TKI specifically blocks the receptor and halts the downstream signaling, leading to cell death and tumor control. Compared to conventional chemotherapy that can only give 20-30% response rate, the tumor response rate of EGFR TKI reaches 70%. Nearly 90% tumor will be brought under control. In addition, the progression free survivals are much prolonged, with a lesser toxicity and a more convenient route of administration. Nowadays, EGFR TKI evolves to the third generation. And the latest 3rd generation EGFR TKI has a better tolerability and is brain penetrant. It can also give a longer median progression free survival up to 19 months.[3] Median overall survival generally exceeds 3 years. Common side effects include skin rash, diarrhoea, xerosis, deranged liver functions and paronychia. Around 1% patients may suffer from drug induced pneumonitis, and it can sometimes be fatal.

ALK rearrangement is the second genetic alteration that can be controlled by oral drugs. Since the initial discovery in 2007, there are now multiple types and generations of treatment.[4] In general, 2nd and 3rd generation ALK inhibitors can effectively control the tumor more than 30 months, and the median overall survival in patients having this type of lung cancer usually exceeds 5 years.

Interesting, certain genetic alterations have different ethnic preponderance. For example, EGFR is more commonly found in east Asian than in the White population. The prevalence can reach 40-50% in east Asian patients with adenocarcinoma but is only 10% in Whites.[5] On the contrary, KRAS is a more common mutation in the White population than Asians.[6]

The development of lung cancer therapy does not restrict only in target therapy. In recent years, immunotherapy becomes a novel and important armaments for cancer treatment. In essence, immunotherapy refers to the harnessing of patients' own immune system to fight against cancer. The most-commonly used immunotherapy in lung cancer is termed immune checkpoint inhibitors (ICIs). PDL1 is a cellular surface protein on cancer cells, and lung cancer inhibits immune T-lymphocytes by combining PDL1 with the PD1 molecules on T lymphocytes. ICIs are monoclonal antibodies that blocks either PDL1 or PD1, preventing the "communication" between cancer cells and T-lymphocytes. Thus, the function of T lymphocytes (tumor cell identification and eradication) can be restored and thus renders cancer control. In general, the abundance of the PDL1 molecules on cancer cells correlates with the chance of cancer control. The higher the PDL1 it is, the higher chance that ICIs work. ICIs are initially used to treat stage IV lung cancer, but now its application is extended to earlier stage of lung cancer. For example, it can be used as maintenance therapy after chemoradiotherapy in stage III disease, and as adjunctive therapy after surgery in stage II-III disease.[7]

Monitoring and treatment of immunotherapy related side effects are in general more difficult than conventional chemotherapy and target therapy. Immunotherapy can theoretically trigger inflammation of any organs, although the incidence is usually low (<5%). The most common side effects are fatigue and skin rash. Endocrine dysfunction is another common side effects. Pneumonitis, hepatitis and enteritis can also occur though in low single digit incidence. However, the time of onset can be quite variable, ranging from weeks to months after commencement of treatment. Therefore, both the doctors and patients need to be vigilant to be aware of the occurrence of these side effects.

In summary, there has been tremendous improvement in the treatment of lung cancer in the past two decades. With the novel therapies, lung cancers patients now live longer and can enjoy a better quality of life. More and more actionable targets will be identified, and more potent targe therapies are expected in the near future. In addition, novel generation of immunotherapy targeting not only PDL1 are under active research. The days of hopelessness and gloominess after the diagnosis of lung cancer are gone. A bigger leap in lung cancer therapeutics and diagnostics will soon materialize. Let's stay tuned!

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Evusheld: The Medication for Pre-exposure Prophylaxis of COVID-19

SPH Pharmacy Department

Evusheld, developed by AstraZeneca, is the first pre-exposure prophylaxis product for COVID-19 apart from vaccines. Evusheld has been authorized for use in the United States, United Kingdom, European Union and Canada.[1-4] In Hong Kong, it is conditionally approved with limited safety, efficacy and quality data for public health emergency and can only be supplied to institutions or registered medical practitioners.[5] As of 23 April 2022, approximately 190 doses of Evusheld have arrived in Hong Kong. The Hospital Authority (HA) stated that it would order a suitable number of doses of Evusheld based on the number of immunocompromised patients in Hong Kong.[6]

[N.B. Evusheld is currently unavailable in all private hospitals including SPH.]

Evusheld contains two active substances, tixagevimab and cilgavimab, which are both human immunoglobulin G1 (IgG1κ) monoclonal antibodies, that act as SARS-CoV-2 spike protein-directed attachment inhibitors. Tixagevimab and cilgavimab are able to persist in the body for months due to their long half-lives of around 85 days.[7]

On 8 December 2021, the U.S. Food and Drug Administration (FDA) approved the emergency use authorization (EUA) of Evusheld for the pre-exposure prophylaxis of COVID-19 in adults and pediatric individuals (12 years of age and older weighing at least 40 kg) who either have moderate to severe immune compromise or cannot receive any COVID-19 vaccines due to a history of severe adverse reaction to the vaccines.[1,8,9] Evusheld is not indicated for the treatment of COVID-19 or the post-exposure prophylaxis of COVID-19 in individuals exposed to infected person. Also, Evusheld is not a substitute for COVID-19 vaccination in individuals for whom vaccination is indicated. For individuals who have received COVID-19 vaccination, Evusheld should be administered at least 2 weeks after vaccination.[7] Due to risks of hypersensitivity reactions, clinical monitoring is required for at least 1 hour after administration of Evusheld.[7]

The FDA authorized dosing of Evusheld is 300mg tixagevimab and 300mg cilgavimab as separate consecutive IM injections.[8] Furthermore, no renal or hepatic dose adjustments are recommended.[7] There is currently insufficient data for Evusheld regarding the risks of its use in pregnant or breastfeeding women. Therefore, Evusheld should only be used in pregnancy provided that the potential benefits outweigh the risks to the mother and the fetus.[7]

The PROVENT trial, a Phase III, double-blind ongoing clinical trial has shown benefit in reducing the risk of symptomatic COVID-19 before exposure. Evusheld was associated with a 77% relative risk reduction in symptomatic COVID-19 illness and a 69% relative risk reduction in the incidence of symptomatic COVID-19 illness or death from any cause.[7] The most common adverse events, besides injection site reactions, were headaches (6%), fatigue (4%), and cough (3%).[7] Serious cardiovascular events, such as myocardial infarction, heart failure and arrhythmia, occurred at a higher rate in the Evusheld arm (0.6%), compared with placebo arm (0.2%).[7] The STORM CHASER trial, which investigated the use of Evusheld for the post-exposure prophylaxis of COVID-19, found no statistically significant difference between the treatment arm and placebo arm.[7]

Based on the results from the PROVENT trial, Evusheld shows effectiveness in reducing the risk of symptomatic COVID-19 before exposure to the SARS-CoV-2 virus, with protection lasting for at least 6 months.[9] Physicians should exercise caution especially when prescribing Evusheld for patients who are at risk of cardiovascular events or have a history of cardiovascular disease. Additionally, Evusheld does not replace COVID-19 vaccines and COVID-19 vaccination is still the most effective method in preventing COVID-19 infection and minimizing COVID-19 related hospitalizations and death.

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Biologic Therapies for the Treatment of Inflammatory Bowel Disease

SPH Pharmacy Department

Introduction to Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a spectrum of chronic, relapsing inflammatory disorders involving the gastrointestinal (GI) system. It is comprised of two major types, namely, ulcerative colitis (UC) and Crohn's disease (CD). In Hong Kong, the prevalence of IBD has increased about thirty times over the past three decades.[1] Patients with UC usually have inflammation of the colon mucosa in a continuous pattern, beginning from the distal rectum and extending proximally to a variable extent. CD is characterized by transmural inflammation of any part of the GI tract in a discontinuous manner.[2] Both conditions can lead to significant impact on quality of life and heavy burden on the healthcare system.

Treatment of IBD mainly involves two phases: remission induction and maintenance phase. Drugs conventionally used in IBD include aminosalicylates (mesalamine and sulfasalazine), corticosteroids (prednisolone and budesonide), immunomodulators (thiopurines such as azathioprine and 6-mercaptopurine, methotrexate, and cyclosporine), as well as antibiotics.[2] Rectal or oral mesalamine may be sufficient to induce remission in patients with mild UC or CD, depending on the site of inflammation. For more severe cases, systemic corticosteroids and/or immunomodulators, together with biologics are likely required. Biologics are relatively newer pharmaceutical agents used in the treatment of IBD. They include the tumor necrosis factor-alpha (TNFα) inhibitors infliximab, adalimumab, golimumab and certolizumab pegol. Other biologic agents licensed for IBD treatment are the integrin receptor antagonists vedolizumab and natalizumab, and the interleukin (IL)-12/23 inhibitor ustekinumab.[2] Biologics previously reserved for more severe cases are now introduced sooner with a step-down approach to improve outcomes and prevent complications.[3]

How Do Biologic Agents Work?

TNFα Inhibitors (infliximab, adalimumab, golimumab and certolizumab pegol)[4-7]

TNFα is an endogenous pro-inflammatory cytokine that has a critical role in normal inflammatory and immune processes. The cytokine causes induction of other pro-inflammatory cytokines such as IL-1 and IL-6. It also facilitates migration of leukocytes through enhancing endothelial layer permeability and upregulating expression of adhesion molecules. TNFα inhibitors (infliximab, adalimumab, golimumab and certolizumab pegol) are monoclonal antibodies that bind specifically to TNFα with high affinity. They prevent TNFα from interacting with its receptors, thereby neutralizing the biological activities mediated by the cytokine.

Integrin Receptor Antagonists (vedolizumab, natalizumab)

Integrin receptor antagonists mainly target the α4β7 integrin, a transmembrane receptor expressed mostly on the gut-selective memory T-cells.[8] α4β7 integrin interacts with mucosal addressin cell adhesion molecule-1 (MAdCAM-1), an adhesion molecule predominantly expressed on vascular endothelial cells within the GI tract.[9] Subsequently, memory T-lymphocytes from the peripheral circulation can migrate across the gut endothelial barrier into the inflamed GI parenchymal tissue.[9] Specific binding of vedolizumab to the α4β7 integrin prevents it from interacting with MAdCAM-1, hence blocking the release of leukocytes into the gut.[10] Natalizumab disrupts interactions of α4β7 integrin with MAdCAM-1 as well as that of α4β1 integrin with vascular cell adhesion molecule-1 (VCAM-1).

Interleukin-12/23 Inhibitors (ustekinumab)

Like TNFα, IL-12 and IL-23 are endogenous cytokines with an essential role in mediating inflammatory and immune responses. Examples of immune processes include differentiation of naive CD4+ T-cells into Th1 cells and expansion of Th17 cells.[9] Ustekinumab selectively binds to the p40 protein subunit of both cytokines, thereby blocking interaction of the cytokines with their receptors on T-cells. IL-12 and IL-23-mediated signaling cascades that contribute to the inflammatory nature of IBD are thus disrupted.[12]

Role of Biologic Agents in the Treatment of Inflammatory Bowel Disease

The role of biologics is more profound in the management of IBD of greater severity. They are licensed for inducing and maintaining clinical remission or response in patients with moderately to severely active IBD. Table 1 summarizes the FDA approved indications, dosing and administration methods of individual agents.

Table 1. Licensed Indications, Dosing and Administration of Biologic Agents for IBD[4-7, 10-12]

Class	Ingredient (Brand name of original biologic)	Licensed IBD Indication	Administration	Adult Dosing	
				Induction	Maintenance
TNFα Inhibitors	Infliximab (Remicade®)	Pediatric (≥6 years) and Adult UC & CD	IV infusion over ≥ 2 hours	5 mg/kg at Weeks 0, 2 and 6	5 mg/kg every 8 weeks
	Adalimumab (Humira®)	Pediatric (≥6 years) UC Adult UC & CD	Subcutaneous injection	160 mg given over 1-2 days then 80 mg on Day 15	40 mg every other week starting from Day 29
	Golimumab (Simponi®)	Adult UC	Subcutaneous injection	200 mg at Week 0, then 100 mg at Week 2	100 mg every 4 weeks
	Certolizumab Pegol (Cimzia®)	Adult CD	Subcutaneous injection	400 mg at Weeks 0, 2 and 4	400 mg every 4 weeks
Integrin Receptor Antagonists	Vedolizumab (Entyvio®)	Adult UC & CD	IV infusion over 30 minutes	300 mg at Weeks 0, 2 and 6	300 mg every 8 weeks
	Natalizumab (Tysabri®)	Adult CD	IV infusion over 1 hour	300 mg every 4 weeks	
Interleukin -12/23 Inhibitor	Ustekinumab (Stelara®)	Adult UC & CD	Induction: IV infusion over ≥ 1 hour Maintenance: Subcutaneous injection	≤55kg: 260 mg >55-85kg: 390 mg >85kg: 520 mg For single dose only	90 mg given 8 weeks after IV dose then every 8 weeks

Some of the above agents may not be stocked by St. Paul's Hospital.

Ulcerative Colitis

For UC management, TNFα inhibitors (adalimumab, golimumab, or infliximab) as well as vedolizumab are recommended by the American College of Gastroenterology (ACG) for induction of remission in patients with moderately to severely active disease.[13] Vedolizumab is also recommended for patients who failed anti-TNF therapy previously.[13] The American Gastroenterological Association (AGA) recommends using ustekinumab or the above biologics in adult patients with moderate to severe UC or who have not responded to other UC therapies.[14] While biologic monotherapy has been proven superior to placebo for induction of remission in UC[15-17], biologic agents combined with thiopurines or methotrexate is preferred for remission induction for moderately to severely active disease.[14] Of the treatment options, infliximab with thiopurines is the only combination

supported by robust clinical evidence.[13] For patients who achieved remission with anti-TNF agents, vedolizumab or ustekinumab, it is recommended to continue use of the biologic agents for remission maintenance.[13, 14] In the case of acute severe ulcerative colitis that requires hospitalization, infliximab, as an alternative to IV cyclosporin, is recommended after treatment failure with IV corticosteroids.[13] Infliximab is also recommended for maintenance therapy in patients who achieved remission with it.[13]

Crohn's disease

Regarding management of moderate to severe/high-risk CD, the ACG recommends use of anti-TNF agents (infliximab, adalimumab and certolizumab pegol) for CD resistant to corticosteroids, thiopurines or methotrexate.[18] Similar to UC, infliximab combined with thiopurines is more effective than either agents alone in patients who are naive to these medications.[18] Vedolizumab (with or without immunomodulator) and natalizumab are superior to placebo in patients with active CD and should be considered for remission induction.[18] Ustekinumab is recommended in patients with moderate to severe CD who have experienced treatment failure with immunosuppressants or TNFα inhibitors, or are naive to TNFα inhibitors.[18] For treatment of perianal, enterocutaneous or rectovaginal fistulas in CD, infliximab should be considered and treatment is more effective when combined with antibiotics.[18] Adalimumab and certolizumab may also be used for perianal fistulas.[18] For patients in remission induced by anti-TNF agents, anti-integrins or ustekinumab, treatment with these agents should be continued in the maintenance phase. Owing to the possible risk of immunogenicity and loss of response, combination of anti-TNF agents with thiopurines or methotrexate should be considered.

Precautions and Safety Considerations[4-7, 10-12, 18]

Due to the affect on the immune system, the increased risk of infection is one of the major concerns with biologic therapy, especially when TNFα inhibitors are used or in combination with another immunosuppressant. TNFα inhibitors have a boxed warning of serious infections, including tuberculosis (TB), invasive fungal infections (aspergillosis, blastomycosis, candidiasis, etc.), opportunistic bacterial and viral infections. These infections may be disseminated and may lead to hospitalization or fatality. Caution should be exercised when prescribing anti-TNF agents for patients with advanced age (over 65 years), co-morbid conditions or concomitant immunosuppression therapy due to the increased risk of infection. Anti-TNF agents should not be initiated in patients with active infection. After the start of therapy, patients should be closely monitored for the signs and symptoms of infection. Prompt diagnosis is warranted if infection is suspected and biologic treatment should be discontinued in case of serious infection or sepsis.

As active TB infection or reactivation of latent TB is associated with biologics, particularly TNFα inhibitors, screening of TB should be performed. TB risk factors should be evaluated and assessment for latent TB with a tuberculin skin test should be done before and regularly during therapy. Latent TB treatment should be started before initiation of biologics. The presence of viral hepatitis should also be assessed prior to initiation of TNFα inhibitors. Vaccination for hepatitis B should be given if the patient is seronegative. For those who are chronic carriers, treatment with antiviral agents should be initiated to prevent reactivation of hepatitis B and liver failure. Apart from hepatitis B vaccine, a patient's immunization (especially pneumococcal and influenza vaccination) should be reviewed and brought up to date prior to use of biologics. Live attenuated vaccines should not be administered to patients on immunomodulators or biologic therapy unless the benefits outweigh the risks.

Another warning for TNFα inhibitors and interleukin inhibitors is malignancy. Reported malignancies included hepatosplenic T-cell lymphoma and other lymphomas, non-melanoma skin cancer, melanoma and some solid tumors. Benefits should be weighed against risks when considering biologic use in patients with known malignancy or in those who develop a malignancy during treatment.

Due to the risk of severe infections and malignancy associated with TNFα inhibitors, vedolizumab is the preferred agent for initial therapy in patients with increased risk of infection or cancer. Vedolizumab is a gut-selective biologic, making it less associated with an increased infection or malignancy risk. For other potentially significant adverse effects associated with biologic treatment, please refer to Table 2.

Table 2. Additional Warnings and Precautions for Individual Biologic Agents[4-7, 10-12]

Ingredient (Brand name of original biologic)	Warnings and Precautions
Infliximab (Remicade®) Adalimumab (Humira®) Golimumab (Simponi®) Certolizumab Pegol (Cimzia®)	For TNFα inhibitors in general: • Associated with adverse outcomes in heart failure patients ➢ Closely monitor heart failure patients during therapy and discontinue in patients with new onset or worsening symptoms • Blood dyscrasias has been reported For infliximab: • Severe hepatic reactions have been reported ➢ Discontinue in patients with jaundice or marked elevation in hepatic enzymes (≥5 times the upper limit of normal) • Hypersensitivity/infusion reactions may occur ➢ Pretreatment with antihistamines, paracetamol and/or corticosteroids may be considered
Vedolizumab (Entyvio®)	• Risk of progressive multifocal leukoencephalopathy (PML) cannot be ruled out ➢ Monitor neurological signs and symptoms, withhold drug if PML is suspected, permanently discontinue drug if confirmed • Increased transaminase and/or bilirubin has been reported ➢ Discontinue in patients with jaundice or other evidence of significant liver injury
Natalizumab (Tysabri®)	• Greater risk of PML [US Boxed Warning] ➢ Monitor signs and symptoms, withhold natalizumab if symptoms suggest PML ➢ Perform prompt diagnostic evaluation • Increased risk of acute retinal necrosis, herpes encephalitis and meningitis • Clinically significant hepatic injury has been reported ➢ Discontinue in patients with jaundice or other evidence of significant liver injury • Should not be used with concomitant immunosuppressants or TNF-α inhibitors
Ustekinumab (Stelara®)	• Reversible posterior leukoencephalopathy syndrome (RPLS) was observed in clinical studies • Noninfectious pneumonia has been reported

With no cure, UC and CD may often be progressive and debilitating. The introduction of biologic therapies provided a great leap in the therapeutic advance of IBD treatment with their potency and precision in targeting the affected pathophysiological pathways. The latest treatment guidelines establish the key role of biologic treatments in the indicated UC and CD patient groups. Healthcare professionals should stay up to date with the treatment recommendations, especially with the expanding field of biologic therapies, while staying vigilant on their precautions and safety concerns.

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NEW DRUG APPROVAL

At the Drug and Therapeutics Committee (DTC) meeting in May 2022, the following drugs have been approved and added to the formulary at SPH:

Drugs	Indication (s)	Usual dosage	Remarks
MEZAVANT XL (MESALAZINE) <PR> TABLET 1200MG	• For the induction of clinical and endoscopic remission in patients with mild to moderate, active ulcerative colitis • For maintenance of remission	For induction of remission in adult: • 2.4 g to 4.8 g (two to four tablets) once daily For maintenance of remission in adult: • 2.4 g (two tablets) once daily	• ***Available by request only.*** • Should be taken with food; swallow whole, do not crush/chew
G-NIIB IMMUNITY PRO POWDER	• Restore gut microbiome balance • Boost immunity and expedite the symptom resolution in novel virus patients • Relieve GI symptoms (constipation, diarrhoea, gastrointestinal discomfort, etc.) and skin irritation	For children > 2 years old and adults: • 1 sachet (10 billion CFU/sachet) once daily	• Consume directly, or may be mixed in water, non-fizzy or non-alcoholic drinks or food (below 45°C).

Ms Ip Sek Lan, Iris
RN, RNM, IBCLC, Trainer (WHO BF Course)

Management of Breast Engorgement in the Early Postpartum Period

SPH Nursery Department

As a part-time lactation consultant in a private hospital, my priority is to support mothers with lactation needs after delivery. Challenges I face are different from those in the public sector, my previous workplace, in terms of expectations of the clients and their infant feeding plans, hospital policies and staff support.

Case history

On a sunny day in December 2021, as usual, I walked around the nursery to look for my clients. Mrs. Chan, a first-time mother, came to me asking for help. She was worried as attempts with a hospital-grade electric pump to express breastmilk failed. Her breasts were getting harder with increasing pain. She asked if anything could be done to stop them from worsening into stony breasts (石頭胸).

Mrs. Chan had given birth to her baby boy at 38 weeks of gestation by Caesarean Section 3 days before. She visited the nursery frequently during daytime to breastfeed her baby directly since Day 2 postpartum when the drip-set and foley catheter had been taken off. She did not breastfeed her baby at night as she believed getting good sleep after delivery was important. Her baby was supplemented with formula milk during the day as well as at night.

Walking with the Client through the Early Postpartum Journey

At the first encounter, I explored with Mrs. Chan her infant feeding plan and concerns. She was most distressed by the brief suckling of her sleepy baby. Due to the COVID pandemic, she had not attended any talks on infant feeding during pregnancy. She had some vague ideas about milk coming-in, expressing breastmilk as well as breastfeeding positioning and attachment through scanning the social media. I thought extra patience would be needed to boost her knowledge, skills as well as confidence in breastfeeding.

Observing Mrs. Chan's breastfeeding confirmed her positioning and attachment difficulties. Proper ways were demonstrated but return demonstration was less than satisfactory. Her baby often slipped out from her breast. Mrs. Chan looked disappointed. With all skills, practice makes perfect. I therefore encouraged her to continue practicing, which was as important for her baby.

To normalize her experience, I explained that the difficulties she encountered were not at all uncommon. When the milk came-in, the breast brought together all necessary components to produce milk, including increased vascularization, fluid retention as well as increasing milk storage in the milk sacs and ducts, leading to congestion and discomfort. Such discomfort was indeed a good sign of the breast starting to work, though the extent varied among individuals. However, if such congestion did not resolve, they might progress to painful, stony hard breasts or even result in mastitis. To ease the "traffic jam", frequent milk removal would be paramount. As the baby might take time to improve

his suckling, frequent hand-expression, especially in the early postpartum period, would be a good alternative measure to remove milk. Mrs. Chan showed understanding and was keen to learn hand-expression. She was excited when she hand-expressed a few drops of breastmilk successfully. She promised to hand-express every 3 hours.

Early next morning, I visited Mrs. Chan. She was upset because her breasts were more painful and tender. She could not hand-express as her breasts were too painful even with a light touch. She added that she had not expressed milk after 8 pm the night before as she was engaged with visitors. Besides, she thought the congestion could be resolved by massaging alone with which she felt soothing. When I examined her, she was afebrile but the breasts were swollen, with shiny and tight overlying skin. While showing my understanding for her difficulty in milk removal at night, I explained patiently that the engorgement was mainly caused by infrequent and ineffective milk removal. This was worsened by increased milk production due to a higher nocturnal prolactin level. I explained to her the treatment plan (table 1)[1] and how augmenting the milk ejection reflex could activate the myoepithelial cells, small muscle pumps inside the breast, to widen the milk ducts, squeeze the breastmilk from the milk sacs to the ducts and eject it. She realized the need for immediate action.

Table 1

Treating Engorgement:

A. Reduce swelling

1. Apply cold pack for 15-20 minutes between feeds
2. Take anti-inflammatory medication, if indicated

B. Keep milk flowing

1. Augment the milk ejection reflex

- Skin-to-skin contact with the baby
- Apply warm pack up to 2 minutes just before milk removal
- Gentle breast massage before and during milk removal
- Take an analgesic, if painful

2. Frequent milk removal

- Give the baby unrestricted direct breastfeeding, at least 8-12 times in 24 hours
- Ensure the baby is well positioned and attached with effective suckling. If not, remove milk by hand-expression or electric pump

After Mrs. Chan had taken an analgesic and a cold pack had been applied for around 20 minutes, I came over again. Among many breast massage maneuvers, I found shaking the breast useful and simple to do. I asked Mrs. Chan to bend forward with the breasts suspended from her chest, allowing gravity to help the milk flow. Then, I started shaking one side of her breasts gently, making sure she could relax and without any pain. I gradually increased the force of shaking, titrating it against her level of pain. After shaking for a few minutes, milk was leaking from both breasts. I quickly let her baby attach on her breast. However, the baby came off only after a few suckles.

As the baby failed to assist in milk removal, I switched to using an electric single pump, starting with a massage mode to ensure gentle suction pressure. About every 5 minutes or when the milk flow slowed down, I shifted to pumping the other breast to match the pulsatile oxytocin release pattern[2]. In between the pumping, I continued shaking the non-pumped breast. Mrs. Chan reflected she felt soothed and relaxed during breast shaking. I further suggested her husband to work as a team and help shaking the breast. Finally, we collected 8 ml of breastmilk after 30 minutes and the engorgement improved slightly. I reassured her the yield of 8 ml of breastmilk was a good start as the congestion would gradually resolve with continuous drainage. I encouraged her to pump every 3 hours throughout the day and night and reminded her of the importance of taking an analgesic until pain free. I further advised her to do some upper limb stretching, aiming to improve the lymphatic flow and hence alleviating the oedema around the arm pit.

Before I left, I encouraged Mrs. Chan to breastfeed her baby as frequently as possible while keeping regular expression. However, she expressed her worry of not having adequate rest. After being informed of the potential risk of formula milk supplementation, she agreed to compromise by attempting direct breastfeeding and pumping 6 - 8 times a day in the subsequent 2 days, while keeping the duration per feed / pumping session within an hour. Her baby would be supplemented, if needed. Mrs. Chan became more confident after further practices and she could express 20 ml at the third session.

In the morning of Day 5 postpartum when Mrs. Chan was about to be discharged, I met her in the nursery again. She was cheerful and shared that her breasts were not engorged nor painful. She had been practicing the agreed regime of breastfeeding and expression. I complimented the couple's commitment to and joint effort in continuing breastfeeding and reminded Mrs. Chan to refocus on her baby's positioning and attachment as this would be a critical factor contributing to the success or otherwise of combating milk stasis should it happen again.

Key messages:

1. Early and frequent milk removal is important in alleviating breast engorgement in the early postpartum period.
   儘早頻密地排出乳汁，對舒緩產後早期乳房腫脹尤為重要。
2. Hand expression is usually more effective than using a pump when breastmilk is low in supply.
   當乳汁不多時，用手擠奶一般會較奶泵有效。
3. Shaking the breast as one of the many breast massage maneuvers is simple and useful.
   在眾多按摩乳房的方法中，搖晃乳房既簡單又有效。

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INTRODUCTION
Of New Faces

It is my great pleasure to join the St. Paul's family in April this year. I graduated from The University of Hong Kong and completed my residency in Princess Margaret Hospital. My subspecialty interest is in dermatopathology and I underwent overseas training at the Institute of Pathology under Professor Boštjan Luzar in the University of Ljubljana, Slovenia. Clinicopathological correlation is one of the many aspects I enjoy being a pathologist and I look forward to collaborating with all of you in the future to provide the best care for our patients!

Dr. Chung Ivy Ah-yu
Specialist in Pathology

Dr. Chan Kin Wing, Yvonne
Resident Medical Officer

Hello, I am Yvonne, the new OPD night shift doctor. Medicine is my second career. I got bored after several years in a global bank. One day I thought medicine might be interesting and so I packed my bags and went to Ireland. After I graduated, I practised in Singapore for two years before I returned to Hong Kong in 2015 and start anew in Accident and Emergency. I am excited to write a new chapter in St Paul's. I joined at the peak of the 5th wave of Covid and was assigned to support the Community Isolation Facility for the Elderly in Harbour Road Sports Centre. It was quite a new experience. With the mission completed, I am back at SPH and I look forward to meeting many of you in the days to come.