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Infectious Diseases - Vaccines

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References: 1. Prevenar 20 (Pneumococcal polysaccharide conjugate, 20-valent adsorbed) Prescription Information. Pfizer Corporation Hong Kong Limited: Version December 2022. **2.** Prevenar 13 (Pneumococcal polysaccharide conjugate, 13-valent adsorbed) Prescription Information. Pfizer Corporation Hong Kong Limited: Version January 2021.

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The Cover Shot

An annular solar eclipse occurred on 21 June 2020. A solar eclipse occurs when the Moon passes between Earth and the Sun, thereby obscuring the image of the Sun for a viewer on Earth. Annular solar eclipse occurs when the Moon's apparent diameter is smaller than the Sun's, blocking most of the Sun's light and causing the Sun to look like an annular (ring). However, the annular eclipse on 21 June 2020 appeared as a partial solar eclipse over a region of the Earth thousands of kilometres wide.

This photo of the partial solar eclipse was taken between some clouds at 16:08 on 21 June 2020 in Hong Kong. The Moon obscured 89 % of the Sun's diameter at that moment. If you missed the partial solar eclipse on 21 June 2020, you could find a similar partial solar eclipse 50 years later (i.e. in 2070) in Hong Kong.

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Editorial

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Specialist in Infectious Disease

Issue Editor

Dr CHAN Kai-ming

It is my honour to be the issue editor of the Hong Kong Medical Diary. 2023 is a very special year for me and probably for everyone in Hong Kong. It is the thirtieth year of my medical practice in Hong Kong. As a physician in the field of infectious disease, I am privileged to have direct personal experience working with my colleagues to fight against very important infections. I was diagnosed with my first Avian flu in 1997, from which, 18 people died in this year. The epidemic was stopped by large scale poultry culling. At that time, only antiviral oseltamivir was available, and there was no effective avian flu vaccine available for high risk groups. Luckily, the source of avian flu was recognised, and the spread was halted.

2023 is the twentieth anniversary of SARS 2003 epidemic that claimed 298 lives among the 1,755 infected in Hong Kong. We strongly bonded with each other and formed our Centre for Health Protection. Our preparedness against pandemic infection is greatly enhanced. The appearance of crises like MERS and other avian flu were well handled. We showed our unity in facing the five waves of COVID-19 pandemic. In 2023, the COVID-19 pandemic was over, and we are returning to normalisation. Vaccine played a very important and determining role in ending this pandemic. The great challenge is to develop a safe vaccine for all people, whether they are sick or healthy within the shortest time. China is the very first country in the world to have an effective COVID-19 vaccine produced.

In this very special 2023, we decided to put "Vaccine" as the theme in this September issue of Medical Dairy. First of all, I would like to walk through the story of vaccines. Thank you to Prof Ivan Hung and his colleague Dr Khong for telling us more about the current advances in COVID-19 vaccines. Dr Jacky Chan gives us a review of the invasive pneumococcal infection and the use of pneumococcal vaccines. Dr Ho King Man will share with us the details of the human papillomavirus and the use of HPV vaccine to prevent cervical cancers, head and neck cancer and genital warts. By using the newly launched recombinant adjuvant zoster vaccine, the morbidity in the old age and immunocompromised people will be protected against the herpes zoster infection and related complications. However, even though we may have the most effective vaccine available, the vaccine hesitancy and misunderstanding will jeopardise the power of vaccines to save lives. Dr Philip Li and his colleague Dr Gordon Chu will discuss the myths of vaccine allergy on an expert level.

Practising in the medical field is always challenging, no matter we are in the private or public sector. A work life balance is necessary. Dr Jonpaul Zee would like to share his cool leisure sport - kayaking.

Finally, I would like to express my gratitude to the editorial board, and the authors for contributing their valuable time in sharing with us their expert views on the contemporary new and safe use of vaccines to make this September issue a reality.

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The Story of Vaccines

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 September 2023.

INTRODUCTION

Antibiotics and vaccines are the two most important medical advances in history that by save lives from infection. Antibiotics protect human killing the pathogenic microorganisms, whereas by vaccine save lives by preventing infection from occurring by injection (most of the time) to healthy individuals. This article gives a brief account of the journey of vaccine development in contemporary medicine and Hong Kong.

MIASMA THEORY

In the old days of Western medicine, people believed in the miasma theory[1] that epidemics were caused by poisonous air called miasma. The rotting organic matter produced smelly air. Through this poisonous vapour which originated from the decomposed matter, it caused disease development, including the infamous diseases cholera, chlamydia and the Black Death.

THE EARLIEST DOCUMENTATION OF VACCINATION IN ANCIENT CHINA

Smallpox entered ancient China during the Jin Dynasty. In the era of the Qing dynasty, four (順治(1638 - 1661年)、康熙(1654 - 1722年)、咸豐(1831 - 1861年)、同治(1856 - 1875年) of the 10 Qing emperors got smallpox and only two (康熙 and 咸豐) survived from smallpox[2]. Noted that the documented mortality of variant of smallpox variola minor & major (smallpox) was 1 - 2 % & 20 - 45 %, respectively[3].

The very earliest documentation of vaccination is by variolation in China[2, 4]. Variolation is derived from the word variola, the smallpox. In the old days, people found survivors of smallpox remained in good health and never get it again after recovery. The "ancient vaccine" was produced from the smallpox scabs or liquid collected smallpox patient. A healthy child who received this "vaccine" was mildly infected and produced antibodies. In this way, the invasion, as well as the infection of variola virus was prevented. The mortality of variolation itself is significant even though the ancient vaccine was processed with secret methods hoping that the virulence was attenuated.

THE FIRST SUCCESSFUL VACCINATION

Some of the experiments carried out for the vaccine development were not ethically acceptable in modern medicine. In 1796, an English physician, Dr Edward Jenner administered an inoculation to 8-year-old James Phipps by using material obtained from a cowpox sore found on the hand of a milkmaid. Having a local reaction and being unwell for a few days, the boy fully recovered. Two months later, Phipps was inoculated with matter from a human smallpox sore and did not develop the disease. Phipps was the first human to be vaccinated against smallpox. In 1806, French Emperor Napolean Bonaparte & US President Thomas Jefferson endorsed the smallpox vaccine. Dr Edward Jenner is the father of vaccines.

KOCH'S POSTULATES

In 1872, Louis Pasteur, a famous French chemist who developed the method of pasteurisation that ssterilised dairy milk, made the first laboratory produced vaccine: the vaccine for fowl cholera in chickens. The virulence of pathogenic bacteria was reduced by serial passage under certain raised temperature intervals in the presence of oxygen, and a live attenuated vaccine was produced. This revolutionary technology developed the successful vaccines against anthrax in 1881 and rabies in 1885.

In 1882, Robert Koch identified Mycobacterium tuberculosis as the causative agent of tuberculosis[5]. In 1884, Koch and Friedrich Loeffler formulated the Koch's postulates and published in the report of the discovery of diphtheria bacillus[6]. This leads to the germ theory miasma theory become obsoleted. Koch's postulates became the basis of studies of all infectious diseases afterwards. In 1905, Koch was awarded the Nobel Prize in Physiology or Medicine for "his investigations and discoveries in relation to tuberculosis" [7].

In 1885, Pasteur successfully demonstrated the post-exposure prophylaxis by rabies vaccine injections. It was because the long incubation period from the site of viral inoculation allowed the possibility of achieving adequately high sneutralising antibodies by using a very high attenuated virion vaccine. By giving a total of 13 injections in three weeks of a strong dosage of the rabies virus, Joseph Meister was saved who in return served as "a concierge at the Institu Pasteur" [8].

In 1913, the first Diphtheria vaccine was developed by Emil von Behring, who was awarded Nobel Prize in Physiology or Medicine in 1901 on the work on serum therapy. The breakthrough was brought about by the successful use of mixtures of toxin-antitoxin to immunise people against Diphtheria[9].

In 1937, Max Theiler used a weakened Yellow Fever variant virus, named "17D" to protect a million people from infection. He then became the first and the only scientist awarded Nobel Prize in 1951 because of development of a vaccine against viral infection the yellow fever vaccine[10].

However, the blooming of vaccine development was probably nurtured by Maurice Hilleman, named the creator of vaccines that changed the world. Hilleman developed the vaccines against the Asian flu 1957, the Hong Kong flu (1957), the Japanese encephalitis (1944), the Hong Kong flu pandemic (1968), the measles (1963), the mumps (1967), the rubella (1969), the use of combination vaccines like MMR (1969), the polysaccharide meningococcal vaccine (1974), the polyvalent pneumococcal vaccine (1977); the finding of hepatitis B subunits (1981) and vaccine production of a later yeast base genetically engineered DNA recombinant hepatitis B vaccine (1986), the first varicella-chickenpox vaccine (1981), the hepatitis A vaccine (1995)[10].

SMALLPOX ERADICATION

It was then human mankind who tasted the victory of our battle against the deadly virus - smallpox. In 1980 the World Health Assembly announced the eradication of the smallpox and recommended all countries stop vaccination: "The world and all its people have won freedom from smallpox, which was the most devastating disease sweeping in epidemic form through many countries since earliest times, leaving death, blindness and disfigurement in its wake[11]." Hong Kong reported the last case of smallpox in 1952 and declared free of smallpox from 1979, and the smallpox vaccination programme stopped in 1981[12].

POLIO VACCINE

The story of polio is special. Once reported an infection rate 11 per hundred thousand population in Hong Kong (1962), not all infected got sick; one clinical case of polio represents 100 community infection[13]. The first polio vaccine - the Salk vaccine (1955) was a formadehyde treated inactivated polio vaccine (IPV) that achieved > 99 % in protection against all three types of polio related paralysis. It was named after its developer Jonas Salk. Administered intramuscularly, IPV could induced very high neutralising antibodies in the serum BUT no IgA in the mucosa to prevent infection. Therefore, polio virus is still circulating and transmitting throughout the community. Then came the Sabin vaccine (1960) which was an attenuated poliovirus type 1, 2, 3 by Albert Sabin. This very low cost vaccine virus can spread through oral-fecal route to household contact and induce our gut immunity simultaneously. This oral polio vaccine (OPV) resulted in the elimination of polio from United States by 1979, from Hong Kong by 1984, from Americas by 1994, from China by 2000[13]. In 2021, wild type polio type 2, 3 were gone, only wild type 1 poliovirus were still reported in two countries, Afghanistan and Pakistan. However the oral polio vaccine is not perfect, rarely it causes vaccine-associated paralytic polio (3.8 per million vaccination, mostly related to type 2) Hong Kong has switched to use IPV since 2007. From 2016, only bivalent OPV(against polio 1 & 3) are recommended by World Health Organization (WHO)[14].

MEASLES VACCINE - THE CHALLENGE OF VACCINE HESITANCY AND DROPS IN UPTAKE RATES OF VACCINE

The highly infective airborne measles was controlled by the wide population coverage of MMR. In 2016, the region of Americas was first declared free of endemic measles. However, the success in eradicating measles depends on the coverage, and vaccine hesitancy and inadequacy resulted in failure of eradication of disease AND come back of deadly infection when coverage drops. The community is required to maintain a minimum of 92 % vaccine coverage to sustain the herd immunity and maintain the measles elimination[15].

Since the COVID-19 pandemic has a devastating effect on the global healthcare system, the routine immunisation programmes have been hindered and resulted in the drop in measles vaccination in many resource sparse countries[16]. WHO and the United States Centers for Disease Control and Prevention (CDC) reported that there were worldwide around 40 million children who missed the measles vaccination (25 million of first dose and 14.7 million of second dose)[16, 17].

BCG AND MENINGOCOCCAL VACCINES - KILL TWO BIRDS WITH ONE STONE

To achieve two targets by doing one single action sounds amazing. One simple explanation is that many different pathogenic germs share the same or similar antigenic structured protein, and the successful development of one type of vaccine was found efficient in the prevention of another infection unintentionally. One example is BCG - the *Mycobacterium bovis* bacilli Calmette-Guerin vaccine, for which there are currently many different BCG vaccines in use, and all of them originated from M bovis strain. The BCG vaccine efficacy was widely varied, ranging from zero to 80 %[18]. BCG was proven highly protective against the most serious form of tuberculosis, namely tuberculous meningitis, military tuberculosis and pulmonary TB in young children[19]. Although no longer recommended in developed countries, including most European countries and United States, BCG is still included in the immunisation programme of Hong Kong[20]. This BCG vaccine decreased the risk of leprosy by 50 % to 80 % [21, 22].

A similar situation being repeated itself and discovered. After successfully launching the meningitis vaccination against the previously difficult developed group B meningococcal vaccine (4CMenB), it was found to be effective in preventing the infamous gonorrhoea infection. After two doses of 4CMenB vaccine, 33 % - 40 % vaccine efficacy was confirmed against infection with the gonorrhoea in adolescents in young adults[23]. The researchers are now working on the line on controlling both meningitis and gonorrhoea in one goal.

PNEUMOCOCCAL & HERPES ZOSTER INFECTION IN AGEING

Pneumococcal Vaccines

Contemporary medicine is facing the challenge of the effect of an ageing population. Hong Kong has 1.23 million people aged above 65 (16.4 % of the total population). For comparison, China has the largest population aged above 65 in the world, 166.37 million (11.9 % of the total population); India has 84.9 million (6.1 % of the total population); United States has 52.76 million (16 % of the total population); Japan has 35.58 million (28.2 % of the total population) [24].

The burden of infections related to ageing is particularly heavy in Hong Kong and these countries. In this particular group of patients, mortality and morbidity related to pneumococcus, influenza, herpes zoster infections can be modified by strategic use of available vaccines. To protect elderly from pneumococcal infection, there are two types available, the 23 valent pneumococcal polysaccharide vaccine (PPV23) (covering more pneumococcal serotypes) and the pneumococcal conjugate vaccine (currently widely used PCV13, next come to the market the PCV15 and PCV20) PCV13 and PPSV23 were advocated to be given in sequence to achieve the best immune protection, first by PCV13 followed by PPSV23 6 to 12 months later. For those already given PPSV23 in the past, PCV13 was recommended to be given one year later, or if more years have passed. Revaccination demonstrated minimal or mild adverse reaction. Therefore, whenever prior pneumococcal immunisation history is not certain, the pneumococcal vaccine is advised to be given.

The New Adjuvanted Recombinant Zoster Vaccine - Shingrix®

When getting older, our T-cell immunity drops and the incidence of herpes zoster increases drastically especially after the age of 50[25]. The first approved zoster vaccine was a live attenuated virus vaccine (approved in 2006). The initial efficacy was limited and the zoster risk reduction was 50 % and postherpetic neuralgia reduction was 60 % only. The nature of being a live attenuated virus has limited its use and cannot be recommended for immunocompromised patients. The new adjuvanted recombinant zoster vaccine (Shingrix®) is a breakthrough development. Shingrix® is an inactivated vaccine that comes with two vials, the lyophilised glycoprotein E (gE) antigen and the AS01B adjuvant suspension (stored at 2 - 8 °C). AS01B stimulates and induces a high gE specific cell mediated immune response. Two doses of intramuscular injections given two to six months apart will give a zoster prevention of 97.2 % for age 50 and older; 89.8 % for adults older than 70 years of age[26, 27, 28]. The immune response was not affected by previous herpes zoster nor the history of zoster live-virus vaccine injection. Co-administration of Shingrix with the quadrivalent seasonal influenza vaccine showed no reduction in immunogenicity. This adjuvanted recombinant zoster vaccine is recommended by the authority for any healthy adults older than 50 years of age AND any immunocompromised patient older than 19 years old. The most common side effects of this vaccine are local pain and reaction over the injection sites, and some may have a headache, malaise shivering and fever that is readily manageable[27, 28].

FUTURE

The journey of vaccine development and advances in technology is long and continuously changing. The novel vaccine technologies, including the mRNA have a significant impact on production of a safe and rapid development of vaccines within the shortest time to battle against pandemics. Furthermore, we have vaccines for the prevention of cancers, such as HPV vaccine to prevent cervical cancer and head & neck cancer; HBV vaccine to prevent liver cancer, respectively. We look forward to producing tailor-made vaccines to treat individuals with cancer in the future[29].

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "The Story of Vaccines" by Dr CHAN Kai-ming and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 September 2023. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary. (Address: Duke of Windsor Social Service Bldg., 4/Fl., 15 Hennessy Rd., Wan Chai. Enquiry: 2527 8898)

Questions 1-10: Please answer T (true) or F (false)

1. Nowadays, people believe that epidemics are caused by poisonous air called miasma.
2. Dr Edward Jenner is the father of vaccines who successfully vaccinated an 8-year-old boy with a cowpox sore materials to prevent smallpox infection.
3. Robert Koch postulated the germ theory in 1882, and he identified diphtheria bacillus & Mycobacterium tuberculosis as the causative agent of diphtheria & tuberculosis, respectively.
4. Diphtheria vaccine is a live attenuated vaccine.
5. The first varicella-chickenpox vaccine was approved in 2006 and was a live attenuated vaccine effective in the prevention of 60 % zoster infection.
6. Hong Kong was declared free of smallpox in 1979, and the smallpox vaccination programme was stopped afterwards.
7. In Hong Kong, BCG is not included in the Hong Kong Childhood Immunisation Programme because it cannot protect children from primary infection.
8. After injection of the group B meningococcal vaccine, young adults may be protected from acquiring the gonorrheal infection by 40 %.
9. Two doses of intramuscular injection of adjuvant recombinant zoster vaccine 2 - 6 months apart give a zoster protection of over 97 % for age 50 and older.
10. There are available selected vaccines against viral infection that can prevent head and neck cancers.

ANSWER SHEET FOR SEPTEMBER 2023

Please return the completed answer sheet to the Federation Secretariat on or before 30 September 2023 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

The Story of Vaccines

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Answers to August 2023 Issue

Non-invasive Prenatal Screening

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COVID-19 Vaccination in the Post Pandemic Era

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INTRODUCTION

The COVID-19 pandemic which commenced in December 2019 has resulted in more than 676 million confirmed cases and 6.8 million deaths worldwide (mortality rate 1%). The scale of this pandemic has far surpassed that of the SARS-2003 endemic which has resulted in 8,439 cases and 775 deaths (mortality rate 8.9 %). This pandemic of the century has once again reminded us the importance of infection control measures, research in the development of antiviral and vaccine against the emerging infectious diseases, but even more important, to respect the wildlife in the nature. Various institutes, governments and pharmaceuticals have worked together to develop effective COVID-19 antivirals and vaccines. The robust hybrid immunity by natural infection together with the high vaccination rate allows Hong Kong and the rest of the world to transit from a COVID-19 pandemic to endemic. While most infected individuals only experience mild symptoms with dry cough and fever like common upper respiratory tract infections, some patients might develop severe pneumonitis and multi-organ failure. Despite antivirals such as nirmatrelvir/ritonavir and monoclonal antibodies like tixagevimab/cilgavimab being proven to be effective in reducing the development of severe infection and mortality[1,2], vaccination remains to be the most effective in preventing the infection and hence spreading of the virus. The key concept of universal vaccination followed by mild natural infection is hybrid immunity, which allows the pandemic to pass to endemicity[3]. In this article, we are going to discuss the various platforms of vaccines that were developed against SARS-CoV-2, different vaccine booster regimens and how the vaccination process should be individualised according to recipient's age and comorbidity.

DIFFERENT VACCINE PLATFORMS

Different vaccine platform technologies were developed over the past two centuries since Edward Jenner pioneered the concept of vaccines in 1796 and created the world's first vaccine and smallpox vaccine.

Inactivated vaccines

One of the traditional approaches is giving recipients attenuated or inactivated pathogens, examples include MMR combined vaccine (Measles, Mumps, Rubella) and Varicella vaccine. This is like a controlled infection. Several COVID-19 vaccine candidates used this approach, including CoronaVac and BBIBP-CorV[4,5]. Adjuvant such as aluminium salt could be added, which produce local damage-associated molecular patterns (DAMPs) to boost the adaptive immune response. Inactivated virus vaccines were proven to be safe and protective against the initial strain of the SARS-CoV-2 virus. Nevertheless, with emergence of the variant strains, the protection is markedly reduced[6]. To enhance the protection of inactivated virus vaccine, the new generation of bivalent vaccine which includes the inactivated Omicron variant, and the wild-type virus is under development.

Messenger-RNA (mRNA) vaccines

Messenger-RNA (mRNA) vaccine is a novel vaccine platform used against COVID-19. The development of mRNA vaccine can be dated back to early 2000, when it was first designed to prime cellular immunity against tumours[7]. The advantages of mRNA vaccines include high potency, capacity for rapid development and low-cost manufacture[8]. mRNA COVID-19 vaccines have been extensively used, including the BNT162b2 and mRNA-1273[9,10]. mRNA vaccines are highly immunogenic with retained efficacy against the heterologous SARS-CoV-2 variants[11]. Bivalent mRNA vaccine consisting of both wild type and Omicron variant was proven to be safe and immunogenic[12]. Nevertheless, mRNA vaccination is associated with risk of myocarditis, particularly after the second dose in adolescent male individuals[13], and when the vaccine was accidentally given via the intravenous route[14].

Viral Vector Vaccine

Viral vector vaccine is an important platform used during the beginning of the pandemic, including the ChAdOx1 nCoV-19 which uses chimpanzee adenovirus[15], Ad5-nCoV which uses human adenovirus 5[16], and dNS1-RBD which uses influenza virus as the vector[17]. Viral vector vaccines can induce both potent antibody response as well as cellular immune response. Interestingly, if the vaccine recipients have pre-existing immunity against the viral vector, such as human adenoviruses, the immunogenicity of the vaccine maybe reduced[18]. Therefore, the ChAdOx1 nCoV-19 vaccine used chimpanzee adenovirus as the vector, which avoids the problem of pre-existing immunity in vaccine recipients. However, the ChAdOx1 nCoV-19 vaccine was reported to be associated with higher risk of venous thromboembolic events, resulting in a loss of favour to this vaccine[19]. An aerosolised Ad5-nCoV mucosal respiratory COVID-19 vaccine has also demonstrated

good safety profile and immunogenicity as heterologous boosting after three doses of inactivated COVID-19 vaccination in the healthy adults[20]. Nevertheless, the infection control measure needed during aerosolisation has to be further assessed. The intranasal dNS1-RBD vaccine has completed Phase 1 and 2 studies with proven safety and immunogenicity profile. Further trials will be needed to assess its effectiveness against the Omicron variants[21, 22].

Recombinant Nanoparticle Vaccine

Recombinant protein subunit vaccine against SARS-CoV-2, including the NVX-CoV2373, which was constructed from the full-length spike protein of SARS-CoV-2[23]. NVX-CoV2373 was proven to be safe and effective against the original strain of SARS-CoV-2. The vaccine effectiveness against the new Omicron variants has yet to be assessed.

BOOSTER-DOSE VACCINATION

The administration of booster dose was supported by reduction in vaccine-induced immunity over time. Studies have suggested that the serum level of neutralising antibody against SARS-CoV-2 significantly declined over six months after vaccination or COVID-19 infection[11, 24]. In addition, the emergence of the Omicron variants, causing immune escape in vaccinated individuals and patients who have recovered from COVID-19[25]. Studies have demonstrated that third dose booster vaccination can confer additional protection against Omicron variant[26]. Overall, the neutralising antibodies against SARS-CoV-2 variant is lower in individuals who received three doses of inactivated vaccine and patients who received inactivated vaccine after recovery from COVID-19, when compared to those who received vaccine of other platform[11]. In addition to humoral immunity, cellular immunity is also important for protection against severe COVID-19 infection. Cellular response can persist beyond 12 months post infection and is significantly longer than the serum antibodies[27, 28]. Besides, the T cell response against Omicron variant is preserved in most vaccine recipients and COVID-19 recovered patients, and a booster dose could further enhance protection against the Omicron variants[29, 30]. When choosing the boosting vaccine dose, a heterogenous prime-boost strategy, with two doses of inactivated followed by one dose of mRNA vaccination, has demonstrated a significantly better immunogenicity against the SARS-CoV-2 variants when compared to 3 doses of inactivated vaccine[31]. A heterozygous vaccine approach also resulted in higher binding affinity and increased breadth of reactivity against SARS-CoV-2 variants[32]. The latest clinical trial on the bivalent Omicron-containing booster mRNA-1273.214 vaccine has elicited a significantly higher neutralising antibody response against the Omicron when compared to the original monovalent mRNA-1273 vaccine with no safety concerns. Whether the higher neutralising antibody would translate into better clinical effectiveness need further study[12]. Regardless, a study has demonstrated three doses of the mRNA or inactivated COVID-19 vaccination resulted in a robust effectiveness in protection against severe infection, including the > 80 years old age group[33].

HIGH-RISK VACCINE RECIPIENTS

Patients who are immunodeficient, due to an inborn defective immune system, recipients of stem cells / organ transplant and on long term immunosuppressants, and HIV patients, should be receiving more frequent COVID-19 vaccination. These patients are at risk of developing severe COVID-19 infection because of impaired immune cell function. Their immune system may also fail to clear the virus, leading to a chronic SARS-CoV-2 carrier state[34]. Unfortunately, vaccination in post-transplant recipients might still be suboptimal after booster vaccination, who remain being seronegative with poor T cell responses[35]. These patients might benefit from receiving a dose of the monoclonal antibodies which have demonstrated to be effective in the prevention of COVID-19 infection[36].

Finally, vaccination for relatively immunodeficient or immunosenescent individuals, including patients on immunosuppressants, chemotherapy, immunotherapy or biologics, and elderly patients with or without past infections should be encouraged. These individuals are also at risk of developing severe infections and are mandated for a 6-monthly COVID-19 vaccination.

CONCLUSION

In conclusion, universal and regular COVID-19 vaccination should be made for selected high-risk groups, including those who are immunocompromised and elderly. Individualised COVID-19 vaccine schedule could better safeguard the safety and effectiveness of SARS-CoV-2 vaccination. Lastly, the long-term effect of novel vaccine platforms including the mRNA vaccine and nebulised COVID-19 vaccination on human health should be monitored.

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Indications: Delstrigo (doravirine 100 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300mg) is indicated for the treatment of adults infected with HIV-1 without past or present evidence of resistance to the NNRTI class, lamivudine, or tenofovir.

Contraindications: • Hypersensitivity to the active substances or to any of the excipients. Co-administration with medicinal products that are strong cytochrome P450 (CYP)3A enzyme inducers is contraindicated as significant decreases in doravirine plasma concentrations are expected to occur. For the list of contraindicated medicines, please consult the full prescribing information.

Precautions: • NNRTI substitutions and use of doravirine - Doravirine has not been evaluated in patients with previous virologic failure to any other antiretroviral therapy. There is not sufficient clinical evidence to support the use of doravirine in patients infected with HIV-1 with evidence of resistance to the NNRTI class. • Severe acute exacerbation of hepatitis B in patients co-infected with HIV-1 and HBV - All patients with HIV-1 should be tested for the presence of hepatitis B virus (HBV) before initiating antiretroviral therapy. Patients who are co-infected with HIV-1 and HBV should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment with Delstrigo. • New onset or worsening renal impairment - Delstrigo should be avoided with concurrent or recent use of nephrotoxic medicinal products (e.g., high-dose or multiple NSAIDs). Persistent or worsening bone pain, pain in extremities, fractures, and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function in at risk patients. • Bone loss and mineralisation defects - The effects of tenofovir disoproxil associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. Assessment of BMD should be considered for HIV-1 infected adult patients who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. • Co-administration with other antiviral products - Doravirine/lamivudine/tenofovir disoproxil must not be co-administered with other medicinal products containing lamivudine, or with medicinal products containing tenofovir disoproxil, or tenofovir alafenamide, or with adefovir dipivoxil. • Use with CYP3A inducers - Caution should be given to prescribing doravirine with medicinal products that may reduce the exposure of doravirine. • Immune reactivation syndrome - Immune reactivation syndrome has been reported in patients treated with combination antiretroviral therapy.

• Lactose - Delstrigo contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Adverse events: • The most frequently reported adverse reactions considered possibly or probably related to doravirine were nausea (4%) and headache (3%). Other common adverse events (≥1% to <10%) associated with doravirine/lamivudine/tenofovir disoproxil include abnormal dreams, insomnia, headache, dizziness, somnolence, cough, nasal symptoms, nausea, diarrhoea, abdominal pain, vomiting, flatulence, alopecia, rash, muscle disorders, fatigue, fever and alanine aminotransferase increased. For detailed side effects, please consult the full prescribing information.

Drug interactions: Delstrigo is a complete regimen for the treatment of HIV-1 infection; therefore, Delstrigo should not be administered with other antiretroviral medicinal products. *Effects of other medicinal products on doravirine, lamivudine, and tenofovir disoproxil* • Doravirine - Doravirine is primarily metabolised by CYP3A, and medicinal products that induce or inhibit CYP3A are expected to affect the clearance of doravirine. • Lamivudine - Because lamivudine is primarily eliminated by the kidneys through a combination of glomerular filtration and active tubular secretion, co-administration of doravirine/lamivudine/tenofovir disoproxil with medicinal products that reduce renal function or compete for active tubular secretion may increase serum concentrations of lamivudine. • Tenofovir disoproxil - Because tenofovir is primarily eliminated by the kidneys through a combination of glomerular filtration and active tubular secretion, co-administration of doravirine/lamivudine/tenofovir disoproxil with medicinal products that reduce renal function or compete for active tubular secretion via OAT1, OAT3 or MRP4 may increase serum concentrations of tenofovir. *Effects of doravirine, lamivudine, and tenofovir disoproxil on other medicinal products* • Doravirine - Doravirine at a dose of 100 mg once daily is not likely to have a clinically relevant effect on the plasma concentrations of medicinal products that are dependent on transport proteins for absorption and/or elimination or that are metabolised by CYP enzymes. • Lamivudine - Lamivudine does not inhibit or induce CYP enzymes. • Tenofovir - Based on the results of in vitro experiments and the known elimination pathway of tenofovir, the potential for CYP-mediated interactions involving tenofovir with other medicinal products is low. **Before prescribing, please consult the full prescribing information.**

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Favourable 28-day all-cause mortality for the subgroups of vHAP and previous failure of antibiotics for current nosocomial pneumonia episode

MICROBIOLOGICAL RESPONSE RATE
Higher microbiologic eradication rates in ME population with *P. aeruginosa*

Study Design: A randomized, controlled, double-blind, non-inferiority trial conducted between Jan 16, 2015 and April 27, 2018 at 263 hospitals in 34 countries. Patients were randomly assigned (1:1), and stratified by type of nosocomial pneumonia (either VAP or vHAP) and age (<65 years vs ≥65 years), to receive either 3 g ZERBAXA® or 1 g meropenem intravenously every 8 h for 8–14 days. The primary endpoint was 28-Day all-cause mortality (at a 10% non-inferiority margin). ME population: patients with key gram-negative lower respiratory tract pathogens at baseline

Reference: 1. ZERBAXA® Hong Kong Product Circular. **2.** Kollef N *et al.* Ceftolozane–tazobactam versus meropenem for treatment of nosocomial pneumonia (ASPECT-NP): a randomised, controlled, double-blind, phase 3, non-inferiority trial. *The Lancet, Infectious Diseases*, 2019;19(12):1299–1311.

ICU = Intensive Care Unit, ITT = Intent-to-treat, vHAP = ventilated Hospital-acquired Pneumonia, HAP = Hospital-acquired pneumonia, ME population = Microbiologically evaluable, VAP = ventilator-associated Pneumonia

Zerbaxa® Selected Safety Information

Indications:
Zerbaxa® is indicated for the treatment of the following infections in adults:
- Complicated intra-abdominal infections;
- Complicated urinary tract infections, including pyelonephritis;
- Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP)

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Contraindications:
ZERBAXA® is contraindicated in patients with known serious hypersensitivity to the components of ZERBAXA® (ceftolozane and tazobactam), piperacillin/tazobactam, or other members of the beta-lactam class.

Precautions:
- Decreased Efficacy in Patients with Baseline Creatinine Clearance of 30 to 50 mL/min

  In a subgroup analysis of a Phase 3 cIAI trial, clinical cure rates were lower in patients with baseline CrCl of 30 to 50 mL/min compared to those with CrCl greater than 50 mL/min (below Table). The reduction in clinical cure rates was more marked in the ZERBAXA® plus metronidazole arm compared to the meropenem arm. A similar trend was also seen in the cUTI trial. Monitor CrCl at least daily in patients with changing renal function and adjust the dosage of ZERBAXA® accordingly [see Dosage].

Clinical Cure Rates in a Phase 3 Trial of cIAI by Baseline Renal Function (MITT Population)

Baseline Renal Function	ZERBAXA® plus Metronidazole n/N (%)	Meropenem n/N (%)
CrCl greater than 50 mL/min	312/366 (85.2)	355/404 (87.9)
CrCl 30 to 50 mL/min	11/23 (47.8)	9/13 (69.2)

- Hypersensitivity reactions

  Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam antibacterial drugs.
  Before initiating therapy with ZERBAXA®, make careful inquiry about previous hypersensitivity reactions to other cephalosporins, penicillins, or other beta-lactams. If this product is to be given to a patient with a cephalosporin, penicillin, or other beta-lactam allergy, exercise caution because cross sensitivity has been established. If an anaphylactic reaction to ZERBAXA® occurs, discontinue the drug and institute appropriate therapy.
- *Clostridium difficile*-associated diarrhea

  Clostridium difficile-associated diarrhea (CDAD) has been reported for nearly all systemic antibacterial agents, including ZERBAXA®, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of *C. difficile*. *C. difficile* produces toxins A and B which contribute to the development of CDAD. CDAD must be considered in all patients who present with diarrhea following antibacterial use. Careful medical history is necessary because CDAD has been reported to occur more than 2 months after the administration of antibacterial agents.
  If CDAD is confirmed, discontinue antibacterials not directed against *C. difficile*, if possible. Manage fluid and electrolyte levels as appropriate, supplement protein intake monitor antibacterial treatment of *C. difficile*, and institute surgical evaluation as clinically indicated.
- Development of Drug-Resistant Bacteria

  Prescribing ZERBAXA® in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

Adverse Events:
- Complicated Intra-abdominal Infections and Complicated Urinary Tract Infections, Including Pyelonephritis

  The most common adverse reactions (5% or greater in either indication) occurring in patients receiving ZERBAXA® were nausea, diarrhea, headache, and pyrexia.
- Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP)

  The most common adverse reactions (2% or greater) occurring in patients receiving ZERBAXA® were hepatic transaminase increased[1], renal impairment/renal failure[2], diarrhea, intracranial hemorrhage[3], vomiting, clostridium difficile colitis[4].

[1] Includes alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, hypertransaminasaemia, liver function test abnormal.
[2] Includes acute renal failure, anuria, azotemia, oliguria, prerenal failure, renal failure, renal impairment.
[3] Includes cerebellar hemorrhage, cerebral hematoma, cerebral hemorrhage, hemorrhage intracranial, hemorrhagic stroke, hemorrhagic transformation stroke, intraventricular hemorrhage, subarachnoid hemorrhage, subdural hematoma.
[4] Includes Clostridium difficile colitis, Clostridium difficile infection, Clostridium test positive.

- Laboratory Values

  In clinical trials, there was no evidence of hemolysis in patients who developed a positive direct Coombs test in any treatment group.

Before prescribing, please consult the full prescribing information

MSD

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HK-ZER-00005 Dec2020

Demything Vaccine Allergies: Must-Know Precautions vs. Over-precaution

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INTRODUCTION

Vaccinations have been one of the most important medical achievements in the history of humankind. Vaccines have led to the complete eradication of smallpox and, more recently, eventual control of the global COVID-19 pandemic. All currently commercially available vaccines have been provensafe, effective and can confer long lasting protection against pathogens. Most vaccines work by "boosting" or "training" the immune system against specific pathogens among recipients, but even unvaccinated individuals may also benefit from herd immunity when a critical (large) proportion of the population becomes immunised.

Following decades of experience, vaccinations have proven extremely safe and allergic reactions are exceedingly rare[1]. Especially prior to 2019, vaccine allergy was an infrequently discussed topic as suspected or confirmed cases were so infrequent. However, especially since the rollout of the global COVID-19 vaccination campaign, the public and many frontline physicians have become excessively concerned about vaccine side effects. Both patients and physicians mistakenly label non-immune mediated reactions as "allergy" due to inappropriate concerns or incorrect diagnoses. Unnecessary avoidance or delay in vaccinations render patients vulnerable weakens herd immunity, which can lead to devastating consequences on a population level - as exemplified by the tragic loss of many vulnerable individuals during the fifth COVID-19 wave in Hong Kong.

This article aims to review the must-dos (essential precautions) and don't dos (over-precautions) when evaluating a patient planning for vaccination, from an allergy perspective. We hope to better equip readers with the basic knowledge and skills to handle cases of suspected, or feared, vaccine "allergy" cases.

WHAT IS "VACCINE ALLERGY"?

"Allergy" is defined as an inappropriate immunological response against a usually harmless substance (e.g. vaccines). Common "appropriate" reactions such as fever, myalgia, localised and self-limiting injection site tenderness/rashes are known as reactogenic reactions and, despite being immunological in nature, are generally not considered as "vaccine allergy". Patients should be reassured of the benign nature of such reactions and encouraged to proceed with future vaccinations.

Genuine vaccine allergy is clinically classified into two types - immediate and delayed (non-immediate). Immediate-type reactions can range from self-limiting cutaneous reactions to life-threatening anaphylaxis. They are caused by the presence of specific immunoglobulin E (to vaccine components) that bind to high-affinity FcεRI receptors on mast cells and basophils. Cross-linkage by specific allergens triggers a cascade of signals eventually leading to degranulation of mast cells with the release of histamine and other chemical mediators. Symptoms appear almost immediately, usually within minutes following vaccination. Typical mast cell-mediated manifestations include flushing, urticarial rash, angioedema, bronchoconstriction, or even anaphylactic shock. Hence, all vaccination centres should have access to resuscitation facilities and be prepared to treat possible anaphylaxis[2].

In contrast, delayed-type reactions often occur hours or days following vaccination and are T-cell mediated. The most common manifestations are delayed-onset exanthemas, although more severe reactions such as Stephen-Johnson syndrome/toxic-epidermal necrolysis have been occasionally reported[3]. It is important to note that non-severe, delayed-type hypersensitivity reactions to vaccines are usually self-limiting and do not contraindicate the administration of future doses of the same vaccine[4].

Although exceedingly rare, there are different substances or components in a vaccine that could potentially lead to allergic reactions. These include the vaccine antigens, preservatives, adjuvants, stabilisers, emulsifiers, leached packaging components, residual antibiotics, cell culture materials and inactivating ingredients[5]. The necessary precautions while approaching a case of vaccine allergy is covered in the next section.

MUST-KNOW PRECAUTIONS/ MUST DOS!

All patients who have a previous history of anaphylaxis or severe reaction to a vaccine must be referred to a Specialist in Immunology & Allergy for detailed assessment and work up prior to receiving any additional doses of the same vaccine.

However, there are only a few precautions regarding vaccine components for those who are vaccine naïve or have never experienced prior allergic reactions to the anticipated vaccine. In order to correctly counsel patients or identify the culprit of possible allergic reactions, a full allergy history and all components of the index vaccine must be known. Common vaccine components that may be relevant in patients with known pre-existing allergies are listed in Table 1.

Unfortunately, many patients with egg allergy are still frequently and inappropriately denied vaccinations despite Hong Kong having its own recommendations for egg allergic patients since 2018[6]. Measles-Mumps-Rubella (MMR) or MMR-Varicella (MMRV) vaccines are

no longer contraindicated in patients with egg allergy after abundant evidence proving its safety[7]. Similarly, only patients who have previously required admission to an intensive care unit for severe anaphylaxis to egg should be referred for further evaluation prior to influenza vaccination[6]. On the contrary, yellow fever vaccines are extracted from chicken embryos, where a large amount of residual ovalbumin (a major component of egg white) can be found. Therefore, egg allergic patients require further allergy assessment and testing prior to yellow fever vaccination due to potential risk of anaphylaxis.

In addition, certain brands of MMR vaccines may contain gelatine, which has been implicated as a potential culprit among patients with proven gelatine allergy. Therefore, patients who have a history of gelatine allergy should receive gelatine-free MMR/MMRV vaccinations or, if not available, refer to a Specialist in Immunology & Allergy for further assessment. The same principle should be applied to patients with a history of documented yeast allergy prior to receiving Hepatitis B virus, Human papillomavirus vaccination in view of rare cases of reported anaphylaxis[8]. Antibiotics, such as aminoglycosides or Polimixin B, are used in certain vaccines to prevent bacterial contamination during the manufacturing process. Patients with a history of anaphylaxis to the relevant antibiotics found in those vaccines (such as MMR, varicella, inactivated Polio, Diphtheria-Tetanus-Pertussis) should be referred for further allergy assessment and testing prior to vaccination in view of reports of anaphylaxis to vaccines and medications with either component[9,10].

Table 1: Common vaccine components that may cause allergic reactions among patients with pre-existing allergies (Summarised by author)

Vaccine component	Vaccine	Precaution
Egg	Yellow Fever	**If history of egg allergy:** Refer to Specialist in Immunology & Allergy for further assessment.
	Influenza	**If history of anaphylaxis or intensive care admission after egg ingestion:** Refer to Specialist in Immunology & Allergy for further assessment.
Gelatine	Measles-Mumps-Rubella (MMR) / MMR-Varicella (MMRV)	**If history of gelatine allergy:** Administer gelatine-free vaccine; or if unavailable, refer to Specialist in Immunology & Allergy for further assessment.
Yeast	Hepatitis B virus, Human papillomavirus	**If history of yeast allergy:** Administer yeast-free vaccine; or if unavailable, refer to Specialist in Immunology & Allergy for further assessment yeast-free vaccine.
Antibiotics (e.g. aminoglycosides, polimixin B)	MMR, Varicella, Inactivated Polio, Diphtheria-Tetanus-Pertussis	**If history of anaphylaxis to relevant antibiotic:** Refer to Specialist in Immunology & Allergy for further assessment.

OVER-PRECAUTIONS/DON'T DOS!

Non-allergic reactions are often mistaken for allergic reactions, which may sometimes mimic anaphylaxis as patients may present with low blood pressure or loss of consciousness. To differentiate one from another, it is important to check for any presence of objective symptoms suggestive of mast-cell mediated reactions (such as urticaria, angioedema, bronchoconstriction, gastrointestinal involvement) which may point more towards genuine immediate-type allergy. It is important to ascertain a detailed history and consider non-allergic reactions first, prior to ascertaining all symptoms to possible "allergy".

Furthermore, several groups of patients who may be incorrectly advised against vaccination. This includes patients with a history of food or non-related drug allergy, history of atopy or history of non-vaccine/drug related anaphylaxis. None of which are contraindications to vaccines alone, without prior history of inappropriate immunological responses to vaccines or its components. During the course of the COVID-19 pandemic, there was an overwhelming number of patients who were denied vaccination and referred to allergists to "assess fitness for COVID-19 vaccination". Among those who were referred, > 98% of these cases were recommended for vaccination and the majority of referrals deemed inappropriate and unnecessary[11].

However, if history is compatible with genuine vaccine allergy, physicians should also avoid simply labelling patients with suspected vaccine "allergy" and leave the case as it is. Instead, these patients should be referred for further assessment to ensure minimal disruption to their vaccination schedule[12].

CONCLUSION

Genuine vaccine allergies are exceedingly rare and most patients can be vaccinated in the primary care setting without the need for specialist assessment. It is also vital to correctly identify whether a patient is suffering from genuine vaccine allergy to avoid incorrect vaccine allergy labels which may hinder the patient's vaccination schedule. There are only a few genuine precautions needed prior to vaccination among patients with pre-existing allergies. We hope more physicians can work together with allergists to demyth these common misconceptions regarding vaccine "allergy". We also emphasise the importance of taking a comprehensive allergy history for every patient before overzealous labelling of "allergy" or inappropriate deferral of vaccinations.

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Dermatology Quiz

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Specialist in Dermatology and Venereology

Dr KWAN Chi-keung

Fig. 1: Multiple erythematous papules over right elbow

In recent few months, this 60-year-old man living in an overcrowded temporary house complained of sudden onset of itchy papules over his forearms and legs. Clinical examination reviewed multiple erythematous papules over his limbs. There was some excoriation and scratching marks on the forearm and limbs. (Fig. 1)

Questions

1. What are the differential diagnoses of his skin lesion?
2. What investigation are you going to order?
3. How do you treat this patient?

(See P.40 for answers)

Review on Invasive Pneumococcal Disease (IPD) and Use of Pneumococcal Vaccines in Hong Kong

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Dr Jacky MC CHAN

INTRODUCTION/BACKGROUND

Streptococcus pneumoniae is a leading bacterial cause of pneumonia worldwide. Invasive pneumococcal disease (IPD) caused by this bacterium, is a significant global health concern and is responsible for a wide range of illnesses such as pneumonia, meningitis, and sepsis. Every year, this pathogen causes millions of infections worldwide and a significant mortality, particularly among young children, the elderly and immunocompromised hosts[1]. In Hong Kong, the annual incidence of IPD ranged from 1.7 to 2.9 per 100,000 from 2007 to 2015. Since 9 January 2015, IPD has become a notifiable disease. Amid the COVID pandemic, the number of annual reported IPD cases in Hong Kong dropped during 2020 - 2022, partly attributed to strict personal hygiene adoption and mandating mask wearing policy (Fig. 1). At post COVID era, the number of reported cases has been on the rise during the first five months of 2023.

The development and widespread use of pneumococcal vaccines have been crucial in reducing the burden of IPD and protecting vulnerable populations.

In this article, we will explore the importance of pneumococcal vaccines, their types and formulations, as well as the recommended vaccination schedules for different age groups and risk categories. By understanding the role of pneumococcal vaccines in preventing severe illness and promoting public health, we can better appreciate the value of immunisation programmes and advocate for their continued implementation and improvement.

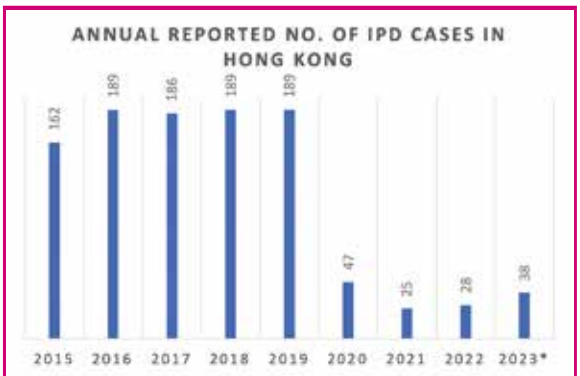

Fig. 1. Annual reported number of invasive pneumococcal diseases in Hong Kong (Excerpted from Centre for Health Protection Report)

*Data up to May 2023

HIGH RISK INDIVIDUALS OF INVASIVE PNEUMOCOCCAL DISEASE

Pneumococcal pneumonia with bacteremia, with or without lung empyema is the most common presentation of IPD, followed by pneumococcal bacteremia alone with an unidentified source. Meningitis, septic arthritis, osteomyelitis, soft tissue infection, endocarditis and peritonitis are other forms of IPD.

There are many risk factors for invasive pneumococcal disease. From 2015 - 2023, the majority (> 50 %) of IPD cases in Hong Kong were elderly aged 65 years or above[2]. The incidence of IPD is higher among individuals:

- Age <= 2 years or >= 65 years
- History of IPD
- Immunocompromised states: asplenia, HIV/AIDS, primary immunodeficiency, immunodeficiencies related to malignancy and transplantation, immunodeficiencies related to the use of immunosuppressive drugs or systemic steroid
- Chronic diseases: chronic cardiac, pulmonary, liver or renal disease, diabetes mellitus or cerebrospinal fluid leakage
- With cochlear implants

USE OF PNEUMOCOCCAL VACCINES IN HONG KONG

Pneumococcal vaccination is essential and effective key for preventing IPD, particularly in vulnerable populations. Currently, there are two types of pneumococcal vaccines available in Hong Kong, namely a 23-valent pneumococcal polysaccharide vaccine (23vPPV) and pneumococcal conjugate vaccine (PCV). Pneumococcal polysaccharide vaccines (PPV) contain polysaccharide antigens derived from the capsule of Streptococcus pneumoniae. Polysaccharide vaccine acts by interacting directly with B cells to simulate antibody production. However, polysaccharide vaccines are poorly immunogenic in children younger than two years of age.

Pneumococcal conjugate vaccines (PCV) contain polysaccharide antigens that have been covalently linked to a carrier protein. The most common carrier protein used was CRM197, a genetically altered variant of diphtheria toxin. PCV plays the role of mucosal

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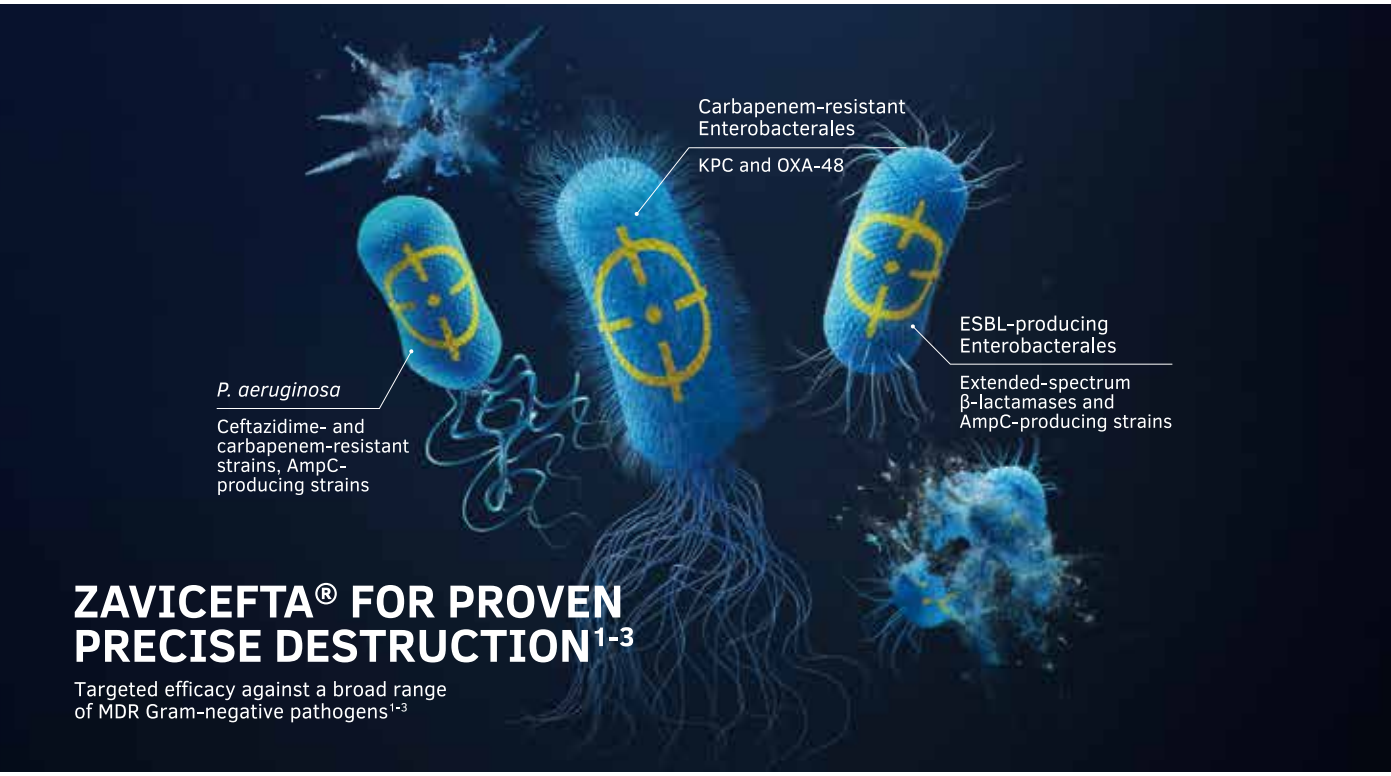
ceftazidime and avibactam



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Targeted efficacy against a broad range of MDR Gram-negative pathogens[1-3]

Indicated for[1]

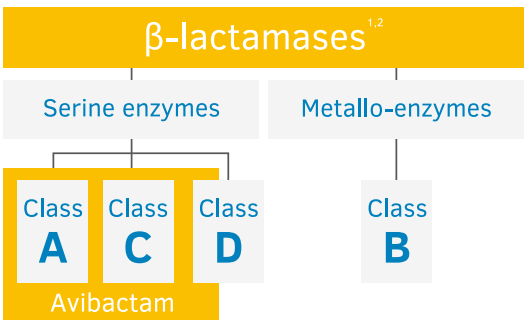
3 months and older

- *Complicated intra-abdominal infection (cIAI)*
- *Complicated urinary tract infection, including pyelonephritis (cUTI)*
- *Hospital-acquired pneumonia, including ventilator-associated pneumonia (HAP/VAP)*

Adults

ZAVICEFTA® is also indicated for the treatment of adult patients with bacteraemia that occurs in association with, or is suspected to be associated with, cUTI, cIAI or HAP/VAP

Novel β-Lactamases Inhibitor with Breakthrough Inhibition[1,2]



Avibactam inhibits both Ambler class A and class C β-lactamases and some class D enzymes, including :[1]*

• ESBLs • KPCs • OXA-48 carbapenemases • AmpC enzymes

* Avibactam does not inhibit class B enzymes (metallo-β-lactamases) and is not able to inhibit many class D enzymes.[1] ESBL, extended-spectrum β-lactamase; KPC, Klebsiella pneumoniae carbapenemase.

ZAVICEFTA ABBREVIATED PACKAGE INSERT

1. GENERIC NAME: ceftazidime pentahydrate/avibactam sodium **2. PRESENTATION:** Each vial contains ceftazidime pentahydrate equivalent to 2 g ceftazidime and avibactam sodium equivalent to 0.5 g avibactam. The medicinal product is supplied in packs of 10 vials. **3. INDICATIONS:** Zavicefta is indicated in adults and paediatric patients aged 3 months and older for the treatment of the following infections: (a) complicated intra-abdominal infection (cIAI); (b) complicated urinary tract infection (cUTI), including pyelonephritis; (c) hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP); treatment of adult patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above. Consideration should be given to official guidance on the appropriate use of antibacterial agents. **4. DOSAGE AND ADMINISTRATION: Adults:** 2.5g administered by intravenous infusion Q8H over 2 hours. The recommended treatment duration for cIAI is 5-14 days, for cUTI including pyelonephritis is 5-10 days, for HAP/CAP is 7-14 days, and for bacteremia associated with, or suspected to be associated with any of the above infections, the duration of treatment should be in accordance with the site of infection. **Age 6 months to <18 years:** 62.5mg/kg to a maximum of 2.5g administered by intravenous infusion Q8H over 2 hours. **Age 3 months to <6 months:** 50mg/kg administered by intravenous infusion Q8H over 2 hours. In paediatric patients aged 3 months to <18 years, the recommended treatment duration for cIAI is 5-14 days, for cUTI including pyelonephritis is 5-14 days, and for HAP/CAP is 7-14 days. No dosage adjustment is required in elderly patients and in hepatic impairment. The safety and efficacy of Zavicefta in paediatric patients <3 months old have not been established. Please refer to prescribing information for dosage adjustments in patients with renal impairment. **Pregnancy and Lactation:** Zavicefta should only be used during pregnancy only if the potential benefit outweighs the possible risk. Ceftazidime is excreted in human milk in small quantities and a decision must be made whether to discontinue breast feeding or to discontinue/abstain from ceftazidime/avibactam therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. **5. CONTRAINDICATIONS:** Hypersensitivity to active substances, to any of the excipients or to any cephalosporin antibacterial agent. Severe hypersensitivity (e.g., anaphylactic reaction, severe skin reaction) to any other type of β-lactam antibacterial agent (e.g., penicillins, monobactams or carbapenems). **6. WARNINGS & PRECAUTIONS:** Hypersensitivity reactions and caution should be used if given to patients with a history of nßon-severe hypersensitivity to penicillins, monobactams or carbapenems; *Clostridioides difficile*-associated diarrhea; in patients with renal impairment; nephrotoxicity where concurrent treatment with high doses of cephalosporins an nephrotoxic medicinal products such as aminoglycosides or potent diuretics may adversely affect renal function; direct antiglobulin test (DAGT or Coombs test) seroconversion and potential risk of haemolytic anaemia; in patients with controlled sodium diet; in paediatric patients aged from 3 to less than 12 months of age where care should be taken when calculating the volume of administration of the dose; little or no activity against the majority of Gram-positive organisms and anaerobes. Ceftazidime may interfere with copper reduction methods (Benedict's, Fehling's, Clinitest) for detection of glycosuria leading to false-positive results. Ceftazidime does not interfere with enzyme-based tests for glycosuria. **7. DRUG INTERACTIONS:** Probenecid and chloramphenicol. Concurrent treatment with high doses of cephalosporins and nephrotoxic medicinal products such as aminoglycosides or potent diuretics (e.g., furosemide) may adversely affect renal function. **8. OVERDOSE:** Overdose with ceftazidime/avibactam can lead to neurological sequelae including encephalopathy, convulsions, and coma, due to the ceftazidime component. Serum levels of ceftazidime can be reduced by haemodialysis or peritoneal dialysis. **9. ADVERSE REACTION: Very Common:** Coombs direct test positive. **Common:** Candidiasis (including vulvovaginal candidiasis and oral candidiasis), eosinophilia, thrombocytosis, thrombocytopenia, headache, dizziness, diarrhea, abdominal pain, nausea, vomiting, alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, gamma-glutamyltransferase increased, blood lactate dehydrogenase increased, rash maculopapular, urticaria, pruritus, infusion site thrombosis, infusion site phlebitis, pyrexia. **10. PHARMACEUTICAL PRECAUTIONS:** Each vial is for single use only. The powder must be reconstituted with 10 mL of sterile water for injections and the resulting concentrate must then be immediately diluted prior to use. The reconstituted solution is a pale yellow solution and is free of particles. Please refer to the full prescribing information for the appropriate ceftazidime dose, volume of reconstituted solution, and volume of diluent. The total time interval between starting reconstitution and completing preparation of the intravenous infusion should not exceed 30 minutes.

Reference: ZAVICEFTA HK PI (version: February 2021) **Date of preparation:** Jan 2022 **Identifier number:** ZAVI0122

FULL PRESCRIBING INFORMATION IS AVAILABLE UPON REQUEST.

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Pfizer

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PP-ZVA-HKG-0062 03/2022

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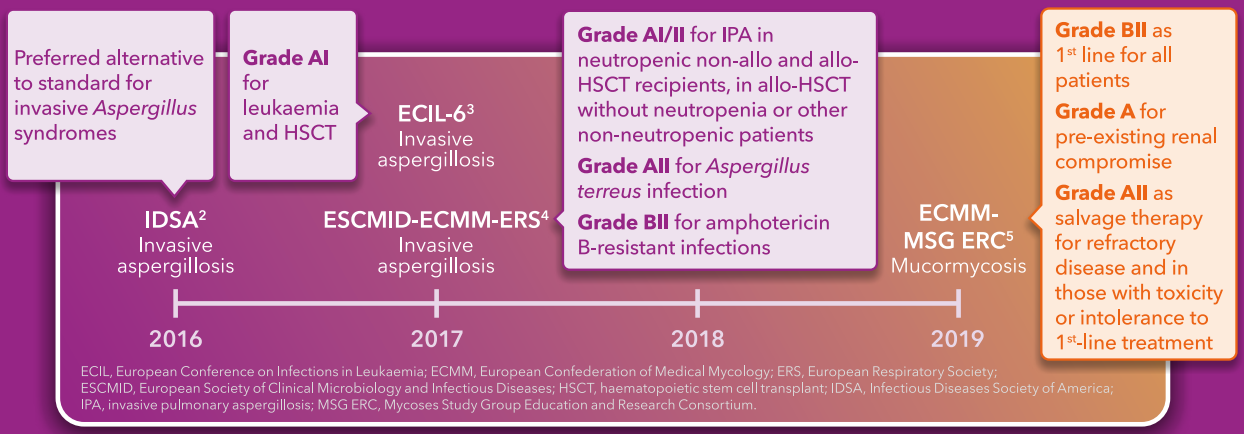
- Indicated for the treatment of invasive aspergillosis, and mucormycosis in patients for whom amphotericin B is inappropriate[1]
- Designed for more than just survival*; recommended by the latest international guidelines[2–5]



ECIL, European Conference on Infections in Leukaemia; ECMM, European Confederation of Medical Mycology; ERS, European Respiratory Society; ESCMID, European Society of Clinical Microbiology and Infectious Diseases; HSCT, haematopoietic stem cell transplant; IDSA, Infectious Diseases Society of America; IPA, invasive pulmonary aspergillosis; MSG ERC, Mycoses Study Group Education and Research Consortium.

*CRESEMBA (isavuconazole) combines standard-of-care efficacy against invasive aspergillosis and mucormycosis with improved tolerability, fewer drug-drug interactions, a simple dosing regimen and predictable pharmacokinetics.[1–11]

CRESEMBA® provides[1,6–11]:

- **CONFIDENCE** with non-inferior efficacy
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CRESEMBA® ABBREVIATED PACKAGE INSERT
1. TRADE NAME: CRESEMBA® **2. PRESENTATION:** Each vial contains 200mg isavuconazole powder for concentrate for solution for infusion (as 372.6 mg isavuconazonium sulfate); Each capsule contains 100mg isavuconazole (as 186.3 mg isavuconazonium sulfate) **3. INDICATIONS:** In adults for the treatment of invasive aspergillosis and mucormycosis in patients for whom amphotericin B is inappropriate **4. DOSAGE & ADMINISTRATION:** Loading dose: 200mg of isavuconazole every 8 hours for the first 48 hours. Maintenance dose: 200mg of isavuconazole once daily, starting 12 to 24 hours after the last loading dose. **For infusions:** To be reconstituted and then further diluted to a concentration corresponding to approximately 0.8mg/mL isavuconazole prior to administration by intravenous infusion over a minimum of 1 hour. Must only be given as an intravenous infusion. **For capsules:** Can be taken with or without food and should be swallowed whole. Do not chew, crush, dissolve or open the capsules. **Switching between oral and intravenous isavuconazole:** On the basis of high oral bioavailability (98%), switching between intravenous and oral administration is appropriate when clinically indicated. **Renal/hepatic impairment:** No dose adjustment is needed. **Pediatric:** Safety and efficacy of Cresemba in children aged below 18 has not been established. **Elderly:** No dose adjustment needed. **5. CONTRAINDICATIONS:** Hypersensitivity to isavuconazole or its excipients. Co-administration with ketoconazole. Co-administration with high-dose ritonavir (>200 mg every 12 hours). Co-administration with strong or moderate CYP3A4/5 inducers. Patients with familial short QT syndrome. **6. WARNINGS & PRECAUTIONS:** Hypersensitivity to azoles; Infusion-related reactions (IV only); Severe cutaneous adverse reactions. Contraindicated in patients with familial short QT syndrome and caution in patients taking other medicinal products known to decrease the QT interval. Monitoring of hepatic enzymes or in patients with severe hepatic impairment. Caution in patients having co-administration with strong CYP3A4/5 inhibitors, or CYP2B6 substrates. Avoid co-administration with mild CYP3A4/5 inducers. Appropriate therapeutic drug monitoring and dose adjustment may be necessary in patients with concomitant use of Pgp substrates or CYP3A4/5 substrates including immunosuppressants. **7. INTERACTIONS:** CYP450 isoenzymes (CYP3A4/5 inhibitors or inducers, CYP2B6 substrates); P-glycoprotein substrates; BCRP substrates; Organic cation transporter 2 substrates; UGT substrates **(IMPORTANT: Please refer to detailed information on Interactions with other Medicinal Products) 8. PREGNANCY AND LACTATION:** Cresemba must not be used during pregnancy except in patients with severe or potentially life-threatening fungal infections. Breast-feeding should be discontinued during treatment with Cresemba. **9. SIDE EFFECTS:** Common treatment-related adverse reactions include elevated liver chemistry tests, nausea, vomiting, dyspnea, abdominal pain, diarrhea, injection site reaction, headache, hypokalemia and rash.
Reference: HK PI (Version Date Dec 2018) Date of preparation: Nov 2019 Identifier number: CRES1119 **FULL PRESCRIBING INFORMATION IS AVAILABLE UPON REQUEST.**

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and thus herd immunity. The Scientific Committee on Vaccine Preventable Diseases (SCVPD) in Hong Kong has recommended 23vPPV to high-risk individuals two years of age and older and elders 65 years of age and older since 2007[3] (Table 1). A 7-valent PCV (PCV7) was also incorporated into the Hong Kong Childhood Immunization Programme (HKCIP) for children under two years of age. In 2019, it was recommended that 13-valent PCV be received as primary doses at 2 and 4 months, followed by a booster dose of PCV13 at 12 months in children[4].

Table 1: Current recommendations on the use of 13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (23vPPV) for persons aged two years or above in Hong Kong (By SCVPD)
(Excerpted from Centre for Health Protection)

	Age 2 to 64 years	Age 65 years and above
Without high risk conditions	Not recommended	Either a single dose of PCV13 or a single dose of 23vPPV.
Individuals with high risk conditions who have not received any pneumococcal vaccines	One dose of PCV13 followed by one dose of 23vPPV one year after the previous PCV13 vaccination.	
Individuals with high risk conditions who have received 23vPPV	Single dose of PCV13 1 year after previous 23vPPV vaccination.	
Individuals with high risk conditions who have received PCV13	Single dose of 23vPPV one year after previous PCV13 vaccination.	

SEROTYPES COVERAGE OF CURRENT PNEUMOCOCCAL VACCINES USED IN HONG KONG

The most common serotype of Streptococcus pneumoniae identified in cases of IPD in Hong Kong was serotype 3. The serotypes and vaccine coverage of Streptococcus pneumoniae of reported IPD cases by year was summarised in table 2, including paediatric cases aged < 18 years[2]. From current pneumococcal vaccines suggested by SCVPD, the overall serotype coverage by either 23vPPv or PCV13 vaccines was greater than 80 %.

NEW PNEUMOCOCCAL VACCINES

In 2021 - 2022, two new pneumococcal PCV vaccines, namely 15-valent PCV (PCV15) and 20-valent PCV (PCV20) have been approved by US FDA for persons with indications for vaccination. The different serotypes covered by PCV13, PCV15, PCV20 and 23vPPV were shown in detail (Table 3). Pneumococcal 15-valent conjugate vaccine (PCV15) can be used as active immunisation for the prevention of invasive disease caused by Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F in individuals six weeks of age or older. PCV15 demonstrated acceptable safety and tolerability profiles and comparable responses to PCV13 in healthy infants[5].

Pneumococcal polysaccharide conjugate vaccine 20-valent (PCV20) is indicated for active immunisation for the prevention of invasive disease and pneumonia in individuals 18 years of age and older. It covers streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F. Studies have demonstrated vaccine safety and

Table 2. The Reported IPD cases by year and the percentage of coverage for serotypes of Streptococcus pneumoniae (for known cases) by pneumococcal vaccines in Hong Kong. (Excerpted from the report on Invasive Pneumococcal Disease, May 2023, Centre for Health Protection.)

Serotypes	2015	2016	2017	2018	2019	2020	2021	2022	2023 (up to 31/5)
Serotypes covered by either PCV13 or 23vPPV or both	139 (86%)	152 (83%)	149 (82%)	154 (85%)	148 (81%)	34 (79%)	11 (61%)	18 (82%)	29 (81%)
Non vaccine-covered serotypes	22	32	32	28	35	9	7	4	7
Unknown	1	5	5	7	6	4	7	6	2
Total	162	189	186	189	189	47	25	28	38

Table 3. Comparison of serotypes covered in different pneumococcal vaccines

Serotypes	1	2	3	4	5	6A	6B	7F	8	9N	9V	10A	11A	12F	14	15B	17F	18C	19A	19F	20	22F	23F	33F
PCV13	+		+	+	+	+	+	+			+				+			+	+	+			+	
PCV15	+		+	+	+	+	+	+			+				+			+	+	+		+	+	+
PCV20	+		+	+	+	+	+	+	+		+	+	+	+	+	+		+	+	+		+	+	+
23vPPV	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

immunologic non-inferiority to PCV13 in participants 18 years and older, regardless of pneumococcal vaccination history and high-risk underlying conditions[6,7,8,9].

Data on the 15-valent PCV (PCV15) and the 20-valent PCV (PCV20) immunogenicity were available yet limited. One month post vaccination, the antibody levels were similar for PCV15 or PCV20 compared with PCV13 for the serotypes commonly shared[10,11].

UPDATED RECOMMENDATIONS FROM US CDC ACIP

The US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization (ACIP) recommended the use of PCV15 as an option for pneumococcal conjugate vaccination of persons aged <= 18 years, according to currently recommended PCV13 dosing and schedules[12]. Findings from RCTs suggested that the immunogenicity and safety of PCV15 were comparable to PCV13.

For adults who aged >= 65 years or aged 19 - 64 with certain risk factors, the Committee recommended 15-valent PCV (PCV15) or 20-valent PCV (PCV20) for PCV-naïve persons. If PCV15 is used, it should be followed by a dose of 23vPPV, typically >= 1 year later[13]. A minimum interval of 8 weeks can be considered for adults with highest risk, including immunocompromised condition, cochlear implant, or cerebrospinal fluid leak to sminimise risk of IPD caused by serotypes unique to 23vPPV in these vulnerable groups[14].

For PCV20, the ACIP recommended a single shot for adults with indications for vaccination. For those recipients of prior pneumococcal vaccines, PCV15 or PCV20 can be an alternative for completing the simmunisation series. For adults who have received 23vPPV only, a dose of PCV20 or PCV15 at least a year after 23vPPV can be considered. For adults who have received PCV13 only, PCV20 can be an option for 23vPPV at least one year after PCV13.

SUMMARY

Invasive pneumococcal disease is an important global health issue, causing significant clinical presentation and mortality in high-risk individuals. With the background low burden of the disease and public awareness in Hong Kong, together with potential vaccination fatigue, the incidence of IPD may rise in the era of post COVID. For high-risk groups, this may lead to significant complications requiring prolonged hospitalisation or even death. Identification of at-risk individuals for pneumococcal vaccination is crucial. New pneumococcal conjugate vaccines are available including PCV15 and PCV20, which both demonstrated comparable safety and immunogenicity to PCV13. Hopefully, more public education on disease awareness and the importance of vaccination will be implemented. Further review of local pneumococcal vaccination policy may be needed for the effective prevention of invasive pneumococcal diseases.

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TRELEGY ELLIPTA

fluticasone furoate/umeclidinium/vilanterol

GSK

嶄新 乾粉吸入器

一開 一吸[1]

95%患者 都話易用易吸[2]

實話易吸

SAWADEE

TRELEGY ELLIPTA (fluticasone furoate/umeclidinium/vilanterol) Safety Information • Trelegy Ellipta should not be used in patients with asthma since it has not been studied in this population • Not for the treatment of acute episodes of bronchospasm, or to treat an acute COPD exacerbation (i.e. as a rescue therapy) • Use with caution in patients with unstable or life threatening cardiovascular disease • Do not stop therapy without physician supervision since symptoms may recur after discontinuation • Common adverse events: Pneumonia, sinusitis, headache, cough, arthralgia

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Human Papillomavirus Vaccine - a Journey from Individual to Community Health Protection

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Abbreviation:
ASR: age-standardised incidence rate
CBA: cost benefit analysis
CEA: cost effective analysis
CHP: Centre for Health Protection
DH: Department of Health
FDA: Food and Drug Administration
FOV: female only Vaccination
GNV: gender neutral vaccination
HGSIL: high grade squamous intraepithelial lesions
HK: Hong Kong
HNSCC: head and neck squamous cell carcinoma
HPV: human papillomavirus
hrHPV: high risk human papillomavirus
lrHPV: low risk human papillomavirus
2vHPVv: bivalent human papillomavirus vaccine
4vHPVv: quadrivalent human papillomavirus vaccine
9vHPVv: nonavalent human papillomavirus vaccine
LGSIL: low grade squamous intraepithelial lesions
OPSCC: oropharyngeal squamous cell carcinoma
VLP: virus-like particles
WHO: World Health Organization

The purpose of this article is to revisit the application of HPV vaccines in HPV diseases and cancers prevention from the past and forthcoming challenges in HK. HPV infection of the skin other than the mucosae is out of scope in this article.

BASIC VIROLOGY OF HPV

HPV is a small non-enveloped double stranded DNA virus. HPV is conventionally typed by the DNA sequence of the open reading frame of its major structural capsid protein L1. A unique genotype is defined by ≥ 10 % variation in the sequence compared to the known genotypes. There are now more than 200 genotypes of HPV identified, of which about 40 have cellular tropism, and so infecting human mucosal areas, including the anogenital and upper aerodigestive tract.

Conformation changes in the viral capsid L1 and L2 protein after complexing with the basement membrane proteoglycans are required to facilitate the virus entering and infecting the adjacent basal cell. The thin and fragile areas in the transformational zones of the endocervix, anorectum and around the tonsil are subjected to micro-abrasion, facilitating and initiating the infection process. The L1 capsid protein as both the major structural viral capsid protein and is involved in the infection process make it a strategic target for vaccine development.

Mucosal transmission is mainly through sexual contact (vaginal, anal and probably also oral sex) with an infected person. The transformation zone of the anogenital and upper aerodigestive tract is more susceptible to acquire the virus during these contacts. These 40 HPVs are divided into hrHPV and lrHPV according to their oncogenic potential (Table 1)[1]. Persistent infection of hrHPVs may cause cancer of the infected mucosae. Carcinogenesis involves the degradation of the infected cell's tumour suppressor p53 and retinoblastoma protein pRB by the hrHPV viral E6 and E7 proteins respectively. Though HPV infection is ubiquitous in the human population, only a small proportion of infected people will end up with cancer. The other factors and mechanisms in cancer formation are not yet fully clear.

Table 1: HPV genotypes according to the risk of causing anogenital cancer (genotypes included in the 9vHPV vaccine are highlighted red)[1]. HPV-26, 53, 66, 73, and 82 were subsequently identified as intermediate risk. There are a few other lrHPV not listed in this table. (Adapted from reference 1)

HPV group	HPV genotypes
High risk	HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, HPV59, HPV68
Low risk	HPV6, HPV11, HPV40, HPV42, HPV43, HPV44, HPV54, HPV61, HPV70, HPV72, HPV81

EPIDEMIOLOGY AND DISEASE BURDEN OF HPV INFECTIONS

According to the WHO estimation, the global HPV prevalence among adult females with normal cytology is estimated to be 12 % and 14 % in East Asia. It is estimated that 70 - 80 % of sexually active adults will be infected with HPV in their life. Up to 30% will be infected in the first year of sexual debut and reach about 50 % by three years. However, only a small proportion of those getting the infection will develop clinical disease. Moreover, based on observation of cervical infection, about 80 - 90% of LGSIL will be cleared of cytological features of HPV infection at two years. Those who have persistent hrHPV infection are, however at risk of cancer development.

CLINICAL HPV DISEASES

Benign And Premalignant Diseases

HPV infection may cause benign diseases and conditions with the potential for progression to cancer. These include anogenital warts, LGSIL and HGSIL involving the male and female anogenital regions, and respiratory papillomatosis. Globally and in HK HPV6 and 11 accounted for about 90 % of anogenital warts. The incidence of newly diagnosed genital warts among adult men in HK was estimated to be 292.2 per 100,000 person-years[2]. While both lrHPV and hrHPV can be identified in LGSIL, the hrHPV detection rate was found to increase as lesions progressed from LGSIL to premalignant HGSIL.

Cancers Attributable To HPV Infection

High risk HPV is estimated to contribute to 5 % of human cancers. Globally, the most prevalent hrHPV genotypes detected in human cancers are HPV16 (15.56 - 83.78 %) and HPV18 (3.4 - 41.1 %). Other hrHPV genotypes include HPV31 (1.37 - 8.89 %), HPV33 (0.74 - 9.1 %), HPV35 (0.5 - 3.2 %), HPV39 (0.7 - 13.33 %), HPV45 (0.8 - 9.1 %), HPV51 (0.3 - 18.8 %), HPV52 (1.08 - 40.74 %), HPV56 (0.2 - 9 %), HPV58 (1.9 - 15.6 %), HPV59 (0.6 - 4.4 %), and HPV68 (0.4 - 11.11 %)[3].

Based on data from 2018, de Martel et al. estimated that globally, 570,000 cases per year in women and 60,000 cases in men, respectively, are attributable to HPV and contributed to 8.6 % and 0.8 % of all cancers occurring worldwide. Cervical cancer alone accounted for about 83 % of HPV attributable cancers[4]. Other HPV attributable cancers include variable proportions of cancers other than cervical cancers in the anogenital regions and HNSCC. The number and corresponding attributable fraction of cancer cases are attributable to all HPV and 9vHPVv related types, and by cancer site are summarised in Table 2.

Table 2. The number and corresponding attributable fraction of cancer cases attributable to all HPV and 9vHPVv related types and by cancer site. (Adapted and modify from data from de Martel et al)[4].

HPV related cancer sites	Estimated number of cancers	Fraction attributed to HPV (%)	Fraction attributed to 9vHPVv[a] types out of all HPV types (%)	Estimated number of cancers caused by 9vHPVv HPV types	Number of cancers cases (%) and ASR recorded in HK in 2020[b]
Cervix	530,000	100	90	470,000	556 (3.7%[c]); ASR 7.6[c]
Anus	35,000	88	96	33,000	ASR 0.4[d]
Vulva	85,000	25	87	7,400	122 (0.7%[e]) ASR 1.2[e]
Vagina	12,000	78	85	9,900	
Penis	13,000	50	85	11,000	47 (0.28%[f]) ASR 0.6[f]
Oropharynx	29,000	31	90	34,000[g]	116[h] ASR 0.8
Total	~630,000	~54	~72	~570,000	

[a] 9vHPVv HPV types include HPV 16, 18, 31, 33, 45, 52, 58 (the 9vHPVv related type 6 and 11 are pertaining to lrHPV and so not relevant in cancer estimation)

[b] Source: Hong Kong Cancer Registry of the Hospital Authority

[c] percentage (%) of cervical cancers in all cancers in female and ASR in term of incidence per 100,000 female population

[d] Source: as there was no breakdown for anal cancer in Cancer Registry, the figure in the table is the number used in a local modelling study[5]

[e] percentage (%) of total number of vaginal, vulval and other female genital cancers in all cancers in female and ASR in term of incidence per 100,000 female population

[f] percentage (%) of total number of penile and other male genital cancers (not including testes and prostate) in all cancers in male and ASR in term of incidence per 100,000 male population

[g] figure includes ~2% of cancers each of the larynx and oral cavity. The attributable fraction for cancers at larynx and oral cavity are not shown in this table

[h] percentage (%) of total cancers at tonsil and oropharynx and ASR in term of incidence per 100,000 population (The breakdown of HNSCC are not detail enough in the local Cancer Registry to allow more accurate and detail analysis. Therefore, the data concerning "tonsil, oropharynx" is shown.) 92 of these 116 cases (79.3%) were male. Compared to 0.4 per 100 000 person in 2011, an increase of 2 fold is observed.

Cervical Cancers and Other Anogenital Areas Cancers

Globally and in HK, HPV16 and 18 contribute to about 70 % of cervical cancer, but in HK HPV52 and 58 are more prevalent when compared with many other oversea countries and contribute to a higher proportion of cervical cancers and HGSIL[6]. A local study involving 236 Chinese women receiving cervical cancer treatment found that the most prevalent HPV types were HPV16 (60.2 %), HPV18 (21.6 %), HPV52 (11.9 %) and HPV58 (9.3 %). Together, HPV16, 18, 31, 33, 45, 52 and 58 accounts for about 90 % of cases of cervical cancer[7]. The incidence rate was quite stable over the preceding 10 years.

Head and Neck Cancers

An increasing incidence of HNSCC worldwide, particularly in the tongue and oropharynx of young adults was observed in many parts of the world. The incidence of HNSCC continues to rise and is anticipated to increase by 30% by 2030. In US, squamous cell carcinoma at areas around the Waldeyer's ring where transformation zones vulnerable to HPV infection are present, including the base of tongue where the lingual tonsil is located, pharyngeal tonsils, anterior and posterior tonsillar pillars, glossotonsillar sulci, soft palate and uvula, and lateral and posterior pharyngeal walls increased at about 2.1 % per annum from 2007 to 2016 comparing to an increase of 0.4 % per annum at the other part of the upper aerodigestive tract[8]. The discrepancy in the increase in incidence was ascribed to an increase in HPV infection in these sites in the oral and oropharyngeal areas. HPV infection was also proposed to contribute to > 70 % of cancers at these sites. The increase was also attributed to sexual behaviour conducive to HPV transmission[8].

In a local study, 20.8 % (43/207) of OPSCC and 29.0 % (36/124) of tonsillar squamous cell carcinoma was associated with HPV. HPV16 was identified in all except one case that was associated with HPV18[9]. In another local study, HPV was detected in 26 out of 166 (15.7 %) HNSCC. HPV16 and 18 were detected in 29 (88.5 %) and 1 (3.8 %) respectively in tumour tissues. Besides 10 out of 15 cases of OPSCC were HPV +ve, and all of these 10 cases were +ve for HPV16[10].

HPV VACCINES

Currently, there are three HPV vaccines registered in Hong Kong for the prevention of cervical cancer and/or other HPV-related diseases, namely the 2vHPVv Cervarix, 4vHPVv Gardasil and 9vHPVv Gardasil 9. The 4vHPVv, 2vHPVv and 9vHPVv were registered in 2006, 2008 and 2015 respectively. As the 2vHPVv and 4vHPVv have been phasing out in Hong Kong, only the 9vHPVv is discussed in this article. The vaccine attributes, regime and precautions are summarised in box 1.

Box 1: Nonavalent HPV vaccine attributes, regime, precaution and reproductive health concern (Adapted and modified from the internal reference of the pharmaceutical company)

COMPOSITION

L1 protein of HPV-6, 11, 16, 18, 31, 33, 45, 52, 58 in the form of virus-like particles (VLP) are produced in yeast cells by recombinant DNA technology and adsorbed on amorphous aluminium hydroxy phosphate sulphate adjuvant. The vaccine does not contain any genetic material of HPV.

INDICATIONS

The indication is for active immunisation against the vaccine types of HPVs so as to prevent HPV diseases caused by these types of HPV.

Individuals from the age of 9 years for prevention of the following HPV diseases:

- Premalignant lesions and cancers involving the cervix, vulva, vagina, and anus caused by the 9vHPVv related HPV types.
- Genital warts caused by specific HPV types.

Individuals from the age of 9 through 45 years for the prevention of the following HPV diseases:

- Cancers affecting the oropharynx and other head and neck sites caused by HPV types 16, 18, 31, 33, 45, 52, and 58.

The indication for prevention of OPSCC/HNSCC was approved by the US FDA under accelerated approval protocol based on the effectiveness and safety data in preventing the HPV anogenital disease caused by the 9vHPVv related HPV types. The indication was also approved earlier this year in HK.

VACCINATION REGIME

Vaccination by intramuscular injection

Individuals 9 to and including 14 years of age at time of first injection:
2-dose (0, 6 - 12 months) schedule. The 2nd dose should be administered between 5 and 13 months after the first dose.

Individuals 15 years of age and older at the time of the first injection:
3-dose (0, 2, 6 months) schedule. The 2nd dose have to be administered > 1 month after the 1st dose and the 3rd dose have to be administered > 3 months after the 2nd dose. All 3 doses are recommended to be given within a 12 months period.

As up to date, i.e., 16-17 years after the 4vHPVv was registered, there is no recommendation for a booster for those who completed the primary series.

PRECAUTION

Syncope*, sometimes associated with falling, can occur following, or even before vaccination. Vaccine recipient should be observed for approximately 15 minutes after vaccination. It is important that procedures are in place to avoid injury from fainting.

*This has attracted the attention of the public when HPV vaccination was first introduced, so it is highlighted in the internal reference of the pharmaceutical company and also agency like the WHO.

FERTILITY, PREGNANCY AND LACTATION

Pregnancy
A large amount of data on pregnant women (more than 1,000 pregnancy outcomes) indicates no malformative nor foeto/ neonatal toxicity of the 9vHPVv. Animal studies do not indicate reproductive toxicity. However, these data are considered insufficient to recommend the use of 9vHPVv during pregnancy. Vaccination should be postponed until completion of pregnancy.

Breastfeeding
Nonavalent HPV vaccine can be used during breastfeeding. There were no vaccine-related serious adverse experiences reported in infants who were breastfeeding during the vaccination period.

Fertility
Worry about adverse effects on fertility has once been aroused in the media. However, no human data on the effect of 9vHPVv on fertility are available. Animal studies do not indicate harmful effects on fertility. WHO stated that no association was found between HPV vaccination and fertility in its 2022 position paper[11].

Efficacy

Though the 9vHPVv is not as extensively studied as the two and 4vHPVv, the indication of 9vHPVv is based on:

- *Demonstration of efficacy of 4vHPVv to prevent persistent infection and disease related to HPV types 6, 11, 16 and 18 in females aged 16 to 45 years and males aged 16 to 26 years*[12,13,14,15].
- *Demonstration of non-inferior immunogenicity between 9vHPVv and the 4vHPVv for HPV Types 6, 11, 16 and 18 in girls aged 9 to 15 years, women and men aged 16 to 26 years; efficacy for 9vHPVv against persistent infection and disease related to HPV Types 6, 11, 16, or 18 can be inferred to be comparable to that of the 4vHPVv* [16,17,18,19].
- *Demonstration of efficacy against persistent infection and disease related to HPV Types 31, 33, 45, 52 and 58 in girls and women aged 16 to 26 years*[20], *and*
- *Demonstration of non-inferior immunogenicity against the 9vHPVv HPV types in boys and girls aged 9 to 15 years and men aged 16 to 26 years and women aged 27 to 45 years, compared to girls and women aged 16 to 26 years*[16.18,21].

Based on epidemiology studies, 9vHPVv is anticipated to protect against the HPV types that cause approximately: 90 % of cervical cancers, more than 95 % of adenocarcinoma in situ (AIS), 75 - 85 % of HPV related cervical HGSIL, 85 - 90 % of HPV related vulvar cancers, 90 - 95 % of HPV related vulvar HGSIL, 80 - 85 % of HPV related vaginal cancers, 75 - 85 % of HPV related vaginal HGSIL, 90 - 95 % of HPV related anal cancer, 85 - 90 % of HPV related anal HGSIL, and 90 % of genital warts (HGSIL is used herein to described CIN 2/3, VIN 2/3, VaIN 2/3, the pharmaceutical company's internal assessment).

The efficacy data for protection against HNSCC caused by HPV is not based on robust clinical trials as cervical cancer. However, because of the lack of a validated easily conducted test/protocol for squamous intraepithelial lesions as for cervical diseases and an understanding of the natural history of cancer

development as in cervical cancer, it is practically impossible to reproduce similar studies to support the efficacy of HPV vaccine for prevention of HPV related HNSCC. Therefore, data informing the impact of HPV vaccine on HPV diseases in the upper aerodigestive tract are limited to real World and observational studies demonstrating a reduction in HPV infection in the upper aerodigestive tract and the presence of relevant HPV antibodies in the oral fluid following vaccination with HPV vaccine[22,23].

Given these backgrounds, the US FDA granted approval for adding the indication for the prevention of head and neck cancer to the 9vHPVv vaccine in 2020. It is worth noting that the evidence for vaccination in male is largely derived from studies with male subjects up to 26 years old.

Undesirable Effects

HPV vaccines are generally well tolerated, and serious adverse effects are rare. The most common side effects include local injection site reactions, headache, syncope, nausea, vomiting, diarrhoea, abdominal pain, itchiness, rash, urticaria, myalgia, arthritis, fatigue and fever. However, they are transient and will resolve spontaneously without sequelae.

When the first 2 HPV vaccines were introduced in 2006 and 2008, there were concerns about serious adverse events, including anaphylaxis, syncope, Guillain-Barré syndrome (GBS), complex regional pain syndrome (CRPS), postural orthostatic tachycardia syndrome (POTS), premature ovarian insufficiency, primary ovarian failure (POF), venous thromboembolism, and deaths after administration of HPV vaccine. The regulatory authorities in North America and Europe, WHO as well as the Cochrane systemic review, have issued updated position statements or reports reassuring the safety of HPV vaccine on various occasions. There is not yet any additional safety signal of concern after 9vHPVv was introduced in HK.

JOURNEY FROM INDIVIDUAL TO COMMUNITY HEALTH PROTECTION

Local Journey From Indvidual To Community Health Protection

After the first HPV vaccine was licensed in HK, the Scientific Committees on AIDS and Sexually Transmitted Infection and Vaccine Preventable Diseases of CHP reviewed various relevant issues for its local application. After the first joint Committee meeting, the Committees identified issues including local disease epidemiological data, acceptability, cost-effectiveness, impact on population health, and programme operation that were required for further evaluation; HPV vaccination was in the first incident recommended for individual protection. Subsequently, CHP commissioned health economic studies, initially CEA and then CBA, to the School of Public Health of HKU[24].

As time lapsed, more data were published on the impact of a population based vaccination programme in the oversea countries, and the local acceptability showed that cost was a major factor deterring vaccination. In the meantime WHO published in May 2017 an updated position paper on HPV vaccine. It recognised the importance of cervical cancer and other HPV-related diseases as global public health problems and reiterated the recommendation that HPV vaccines should be included in national immunisation programmes[25].

Taking the results of the CBA study and recommendations of the two Scientific Committees, CHP recommended incorporating HPV vaccination into the local Childhood Immunisation Programme. Starting from the 2019/20 school year, eligible female primary school students are provided with HPV vaccine. School Immunisation Teams of the DH would visit schools to provide the first dose of 9vHPVv to primary five female students and the second dose to the girls when they reach primary six in the following school year free of charge[26]. As of July 2022, the coverage rate for the first and second doses of HPV vaccination for primary five and six female students in 2020/21 school year were 88 % and 86 % respectively[27].

In November 2021, the Scientific Committee on Vaccine Preventable Diseases under the CHP updated the use of HPV vaccine in HK and recommended the Government to provide mop-up HPV vaccination for secondary school female students or older girls (18 years or below). A one-off catch up programme is under planning, in which mop-up vaccination would be arranged for the girls in the aforementioned target group in 2023 to 2024. Details of the mop up exercise are still pending[27].

Gender Neutral Vaccination Programme

As of early 2023, more than 140 countries or territories have introduced HPV vaccination programme. Less than 50 of these adopt a GNV strategy[28]. Despite the efficacy of HPV vaccination programme in the prevention of HPV diseases, not too many countries, including the more affluent Western countries, achieve a high vaccine population coverage rate sufficient to eliminate HPV disease.

A modelling study showed that with a moderate 70 % vaccination coverage among both boys and girls, the GNV strategy has the best overall protective effectiveness attaining full control of HPV infections in the population. The same goal may only be achieved by 90% coverage in a FOV programme[29].

An industry funded local health economic modelling study taking into account other HPV diseases, including HNSCC, anogenital cancers, anogenital warts in addition to cervical cancer, concluded that comparing to FOV, routine GNV programme fell below the reference cost-effectiveness upper limit of HKD $382,046 per year (the 2019 per capita gross domestic product in HK), and so underscored the potential value of a routine GNV programme with the 9vHPVv among 12-year-olds (males and females) in HK to reduce the public health and economic burden of HPV diseases[5].

Given the relatively high coverage rate of our local FOV programme, factors that require to consider before embarking on a GNV programme may include supporting factors, including lower cost of the two dose regime for younger adolescents, shorter duration of years to achieve the target of elimination of HPV, the creeping rate of HNSCC in addition to the inherent deficiency of missing men who have sex with men and gender/health equity issue for a FOV programme, and non-supporting factors including higher overall cost with a diminished marginal benefit and so a less cost-effective programme, the relatively small actual additional number of HPV related cancer death averted per year.

SUMMARY

HPV infection is ubiquitous. Persistent hrHPV infection of the anogenital region and upper aerodigestive tract may cause cancer in the infected areas. HPV related cancers contributed to about 5 % of all cancers. Cervical cancer contributed to more than 80 % of all HPV related cancers. HPV16 and 18 accounted for about 70 % of cervical cancer and remain the most common hrHPV that causes cancer in other mucosal areas susceptible to HPV infection. HPV vaccine is highly efficacious in the prevention of HPV infection. The best time for having HPV vaccination is above 9 years old and before sex debut. HPV vaccination has been incorporated into the local childhood immunisation programme for schoolgirls. More than 140 countries have introduced HPV vaccination programme for the protection of community health, and no major safety signal has been observed. HPV vaccine is recommended for personal and community health protection. There are strengths and weaknesses for FOV and GNV vaccination programme.

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*The bioavailability and pharmacodynamics of different concentrations of omega-3 acid ethyl esters.Pronova Biocare, R&D, Vollsveien 6, N-1327 Lysaker, Norway 2006.

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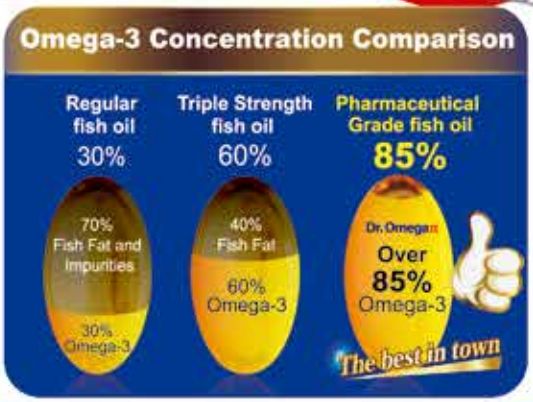

Kayaking - a Cool Sport

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For nature enthusiasts, adventurers, and water sports lovers, kayaking is an exhilarating way to navigate the tranquil waters, explore breathtaking landscapes and at the same time, engage in some heavy-duty sporting activity. For the athletic souls in Hong Kong, it is a wonderful and physically-challenging diversion from the sweltering summer heat and the hustle and bustle of city life.

A SPORT WITH A RICH HISTORY AND CULTURE

Kayaking dates back thousands of years with the indigenous Arctic cultures - the Inuit, Aleut, and Yupik peoples. These resourceful communities relied on kayaks for transportation, hunting, and fishing in the icy waters of the Arctic and sub-Arctic regions. Kayaks were ingeniously crafted using wooden frames, covered in animal skins, and sealed with whale fat or fish oil to make them watertight.

These traditional kayaks were remarkably efficient, allowing the people to navigate treacherous waters with agility and precision. The design of these kayaks evolved over centuries, with variations based on regional needs and available resources. The Inuit, for instance, developed narrower and faster kayaks for hunting sea mammals (Fig. 1), while the Aleut favoured wider and more stable designs for fishing in the rough waters of the Aleutian Islands.

Fig. 1. Inuits in their kayaks (Ref: https://www.thecanadianencyclopedia.ca/en/article/kayak)

FROM THE ARCTIC TO THE WORLD

As time passed, kayaking spread beyond the Arctic. In the 20th century, kayaking became a popular sport in Europe and North America and has since gained recognition as a recreational activity worldwide. Kayaks have evolved into various forms and designs, each tailored to specific purposes and environments. The development of new materials, such as evolution and later plastic, revolutionised kayak construction, making them more durable, lightweight, and accessible to a wider audience.

A KAYAK FOR EVERY PERSON AND EVERY NEED

Recreational Kayaks

Ideal for beginners and casual paddlers, recreational kayaks are designed for calm waters such as slow-moving rivers and calm coastal areas. They are typically wider and shorter, providing excellent stability and manoeuvrability.

Sit-on-top Kayak is a type of recreational Kayak that has gained huge popularity in recent years. They are usually available for daily rental in the coastal areas of Hong Kong, such as Sai Kung. Sit-on-top features an open cockpit design, where the paddler sits on the top deck of the Kayak rather than being enclosed within a cockpit like traditional kayaks (Fig. 2).

Fig. 2. Sit-on-top kayaks are very stable and are suitable for beginners and those with little paddling experience. (Personal Collection)

The design of sit-on-top kayaks is especially user-friendly to first-time paddlers and those with little experience. Unlike traditional kayaks that can

accumulate water in the cockpit, sit-on-top kayaks have scupper holes or drain plugs strategically placed throughout the hull. These openings allow any water that enters the Kayak to drain out, ensuring that the paddler remains relatively dry and water doesn't accumulate in the Kayak.

The open cockpit design also provides greater freedom of movement and ease of entry and exit. With their wider and flatter hull compared to traditional kayaks, sit-on-top kayaks are known for their stability. The downside of this stability is the added drag and relatively low speed when navigating in seawater, particularly where there is an opposing current or during choppy conditions.

Due to their open design, sit-on-top kayaks are less suitable for paddling in extremely rough waters or cold climates, as the lack of a cockpit offers less protection from the elements.

Touring Kayaks/Sea Kayaks

Sea kayaks, also known as touring kayaks, are specifically designed for paddling in open waters, including oceans and large lakes. Their features are designed so as to make them well-suited for navigating rough waters, long-distance touring, multi-day expeditions, and exploration of coastal areas.

Sea kayaks are typically longer and narrower which provide increased speed and efficiency while covering long distances. They are designed to improve tracking so that the Kayak can maintain a straight course despite windy or choppy conditions. The cockpit of a sea kayak is typically snug and well-fitted, which allows for a comfortable and efficient paddling position, and provides good support for the paddler's back and legs. There are adjustable foot braces in the cockpit to enable optimal power transfer during paddling strokes.

Sea kayaks are equipped with a skeg or rudder system to help counteract the effects of wind and currents, providing precise manoeuvring. They are often equipped with watertight hatches, typically located at the front and rear of the Kayak. These hatches provide storage space for essential gear and supplies needed for longer journeys. The hatches ensure that items remain dry and secure and allow paddlers to carry camping equipment, food, safety gear, and spare clothing (Fig. 3). For safety and additional storage, sea kayaks often have deck lines and bungee cords fitted along the 'Kayak's perimeter. They provide additional storage options for securing equipment, such as a paddle float, spare paddle, or deck bags, and also serve as safety features, allowing for easy re-entry into the Kayak in the event of a capsize or rescue situation.

Surfski

Surfski, short for "surf lifesaving ski," is a type of Kayak specifically designed for paddling in ocean surf conditions (Fig. 4). It combines elements of traditional kayaks and surfboards, resulting in a vessel that offers exceptional speed, stability, and manoeuvrability in rough waters.

Fig. 3. Typical gears of a kayaking day trip: paddles, life jacket, spray skirt, hydration, sun protection, hydration, food (in a waterproof dry bag) and emergency supply. (Personal Collection)

Fig. 4. A typical surfski can be up to 6 meters in length, but extremely light weight depending on the building material e.g. carbon fibre. Be aware that Hong Kong traffic law only permits a load that does not extend beyond 1.5 m in front of the vehicle and 1.4 m over the rear of the vehicle. (Personal Collection)

The design of a surfski features a long and narrow hull, resembling a sleek, elongated kayak with an open cockpit. The length of a surfski ranges from approximately 5 to 7 meters (16 to 23 feet), and the narrow width allows for efficient and swift paddling. The hull shape is designed to cut through waves and surf effortlessly, while the stern is often slightly raised to prevent burying the rear of the Kayak in larger waves.

Many surfskis have a secondary stability feature, such as a V-shaped hull or secondary keel, which enhances stability by preventing excessive rocking and rolling. This enhanced stability enables paddlers to maintain balance while riding waves or navigating challenging waters. One of the defining features of a surfski is the foot-controlled rudder system. The rudder helps with steering and maintaining control in varied conditions, enabling paddlers to manoeuvre quickly and efficiently.

The foot-controlled rudder is especially beneficial when surfing downwind, as it assists in catching and riding swells.

Surfskis are designed for experienced paddlers with high performance and responsiveness. Paddlers need to develop good balance, bracing skills, and the ability to handle dynamic water conditions. The sport of surfski has gained popularity worldwide, particularly in coastal regions with access to open water and consistent surf. It offers a thrilling experience for those seeking the challenge of riding ocean waves and maximising speed on the water. The waves and swells in Sai Kung and Hong Kong Island South are excellent for surfskiing.

Flat Water Racing Kayak

These specialised kayaks are built with a focus on speed and efficiency, allowing paddlers to achieve maximum performance on flat water (Fig. 5). Racing kayaks come in various classes, e.g. K1, K2, and K4, which indicate the number of paddlers in the Kayak. K1 refers to a solo racing kayak where a single paddler competes. K2 and K4 refer to a racing kayak for two and four paddlers. K2 and K4 require teamwork, coordination, and synchronicity between the athletes.

These racing kayaks are typically long and narrow, with a streamlined hull designed to minimise drag and maximise speed. The narrow width ensures optimal paddling efficiency and minimises resistance. Racing kayaks are commonly made from lightweight materials such as carbon fibre or fibreglass to further enhance speed. The cockpit of a racing kayak is designed to be snug and low-profile, allowing the paddler to have a more efficient and powerful paddle stroke. The seating position is often lower, helping to lower the Kayak's centre of gravity and improve stability.

Racing kayaks require a specific paddling technique to maximise speed and efficiency. Paddlers use a high-angle paddling style (also known as 'wing paddle'), placing the paddle blade in the water close to the Kayak's side and using an aggressive stroke to generate power. The paddling technique focuses on engaging the core muscles, torso rotation, and utilising the larger muscle groups to propel the Kayak forward. Due to their narrow width, racing kayaks are typically tippy which requires lots of dedicated practice to optimise power transfer while maintaining balance during the stroke cycle.

From the icy Arctic to subtropical Hong Kong, kayaks have come a long way. Whether you're seeking peaceful moments in serene lakes or embarking on adrenaline-fueled whitewater adventures, there is a kayak tailored to your needs.

So, gear up, paddle out, and immerse yourself in the wonders that await you on the water.

Happy kayaking!

Fig. 5. Riding a K1 in ocean water can be challenging but sometimes I see it as a form of active meditation or mindfulness practice. As I navigate the waterways, my focus shifts to the sensations of the body, the movement of the kayak, and the sights and sounds around me. Riding a racing kayak (K1) requires a special set of skills to maintain the balance while efficiently transfer your torso power to the water. The paddling stroke phases is divided into 1/entry, 2/catch, 3/pull, 4/exit and 5/recovery. (Personal Collection)

Fig. 6. My teammate and I winning a 20 km Tolo harbour race. Preparation, teamwork and mental toughness are all the ingredients to success! (Personal Collection)

Fig. 7. Kayaking offers a sense of adventure and exploration, enabling you to escape the confines of daily routines and immerse yourself in new experiences. Exploring unfamiliar waterways, discovering hidden coves can provide a sense of wonder and awe. Gliding through serene waters surrounded by picturesque landscapes can be incredibly calming and therapeutic. (Personal Collection)

Fig. 8. Kayaking provides the opportunity to immerse oneself in the beauty of the natural world and meet new friends. This was a paddling trip with friends from OBAA (Outward Bound Alumni Association). (Personal Collection)

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Lower serum bilirubin levels
20 μmol/L (BCAA) vs 30μmol/L (Control) at 6 months (P=0.026)

BCAA: branched chain amino acids; FACT-G: Functional Assessment of Cancer Therapy-General; HCC: hepatocellular carcinoma; TACE: transarterial chemoembolization

***Study design[1]: This was a randomized controlled trial in which patients undergoing chemoembolization for HCC were randomized to receive oral BCAA for up to four courses of chemoembolization (n=41) or did not receive any nutritional supplement (n=43). Morbidity, liver function, nutritional status, quality of life and long-term survival were compared between the two groups. The morbidity rate was the overall frequency of morbidity after only TACE session during the four TACE sessions.**

References: 1. Poon RT, et al. Aliment Pharmacol Ther. 2004;19:779-88.

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Causeway Bay, Hong Kong.
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Scan the QR code to our official website

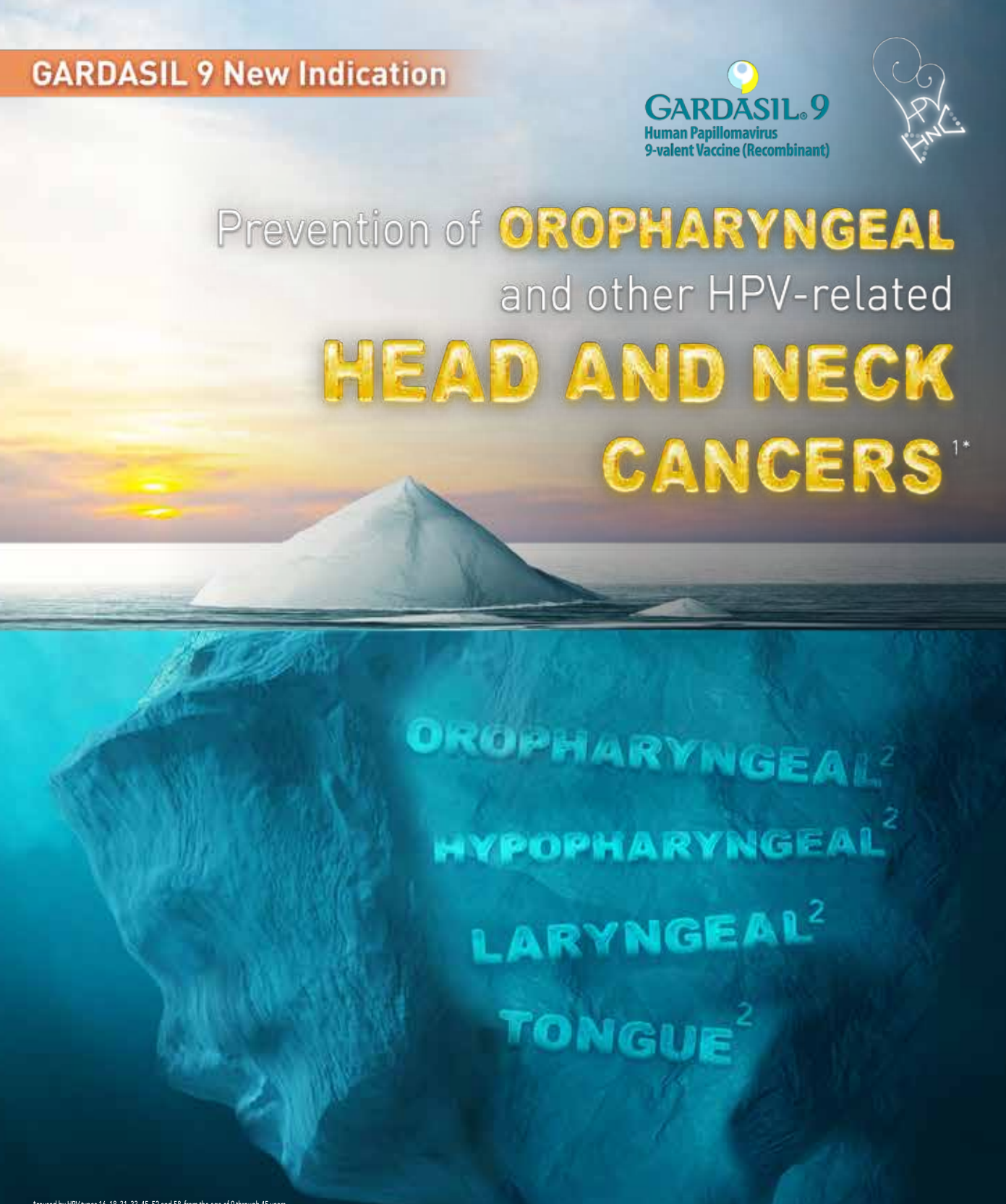
HKOP-AMN-EN-202205-001

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
					★Zoom Live Recent Advances in Deep Brain Stimulation for Parkinson's Diseases in Hong Kong **1**	**2**
3	★Zoom Live Personalized Management of Non-Neurogenic Male LUTS **4**	★In-person / Zoom Live HKMA-HKSH CME Programme 2022-2023 Topic: Cancer of Lung ★Certificate Course on Palliative Medicine for Health Care Workers 2023 (Video Lectures) **5**	★Zoom Live Latest Hypertension Management and Local Consensus Update **6**	★In-person Mental Health Challenges for Caregivers - What should be done as a health professional? ★Certificate Course on Cytogenomics 2023 (Video Lectures) **7**	**8**	**9**
10	★Zoom Live Influenza Management in High Risk Patient **11**	**12**	★The Hong Kong Neurosurgical Society Monthly Academic Meeting –To be confirmed ★In-person / Zoom Live HKMA-CUHK Medical Centre CME Programme 2023 Common health problems for the elderly - Topic: Managing Age-related Macular Degeneration ★Certificate Course on Respiratory Medicine 2023 (Video Lectures) **13**	★Certificate Course on Cytogenomics 2023 (Video Lectures) **14**	★23rd Regional Osteporosis Conference (ROC 2023) Organiser: The Osteoporosis Society of Hong Kong ★Zoom Live The Sweet Spot for HF Management - What's The Role of SGLT2 Inhibitor **15**	★23rd Regional Osteporosis Conference (ROC 2023) Organiser: The Osteoporosis Society of Hong Kong **16**
★23rd Regional Osteporosis Conference (ROC 2023) Organiser: The Osteoporosis Society of Hong Kong **17**	**18**	★Physical attendance in Central Premises or attend via ZOOM HKMA-GHK CME Programme 2023 - Strategies Of Tumor Clearance In Management Of Colorectal Diseases **19**	★Zoom Live Doctor, My Neck Hurts, Is It Related to My Smart Phone? ★Certificate Course on Respiratory Medicine 2023 (Video Lectures) **20**	★In-person Advancing Asthma Treatment with Triple Therapy: Right Therapy for Right Patients at Right Timing ★Certificate Course on Renal Medicine 2023 (Video Lectures) ★FMSHK Executive Committee Meeting **21**	★Zoom Live World Contraception Day: Patient Counselling on Family Planning **22**	★In-person The HKMA Medico legal Conference 2023 **23**
24	★Zoom Live Acute diarrhea Management in Pediatric Patients **25**	★Zoom Live Management of male LUTS: More Than Treating Symptoms? **26**	★Zoom Live HKMA Adult Immunization Campaign 2023 - Respiratory Syncytial Virus (RSV) in Older Adults ★Certificate Course on Respiratory Medicine 2023 (Video Lectures) **27**	★In-person / Zoom Live HKMA-HKSTP CME Lecture Topic: The Future of Non-Invasive Treatments for Ocular Diseases and beyond: Ultrasound Drug Delivery Platform ★Certificate Course on Renal Medicine 2023 (Video Lectures) **28**	★In-person COVID-19 Oral Antiviral Treatment Real World Evidence Update & Clinical Experience Sharing **29**	**30**

GARDASIL 9 New Indication

GARDASIL® 9
Human Papillomavirus
9-valent Vaccine (Recombinant)

Prevention of OROPHARYNGEAL and other HPV-related HEAD AND NECK CANCERS[1*]



*caused by HPV types 16, 18, 31, 33, 45, 52 and 58, from the age of 9 through 45 years

References: 1. Hong Kong Product Circular (GARDASIL® 9 MSD) **2.** Centers for Disease Control and Prevention. Head and Neck Cancers. https://www.cdc.gov/cancer/headneck/index.htm Accessed on: April 13, 2023.

Selected Safety Information Indications: GARDASIL® 9 is indicated for active immunisation of individuals from the age of 9 years against the following HPV diseases: Premalignant lesions and cancers affecting the cervix, vulva, vagina and anus caused by vaccine HPV types. Genital warts (Condyloma acuminata) caused by specific HPV types. GARDASIL® 9 is indicated for active immunisation of individuals from the age of 9 through 45 years against the following HPV diseases: Cancers affecting the oropharynx and other head and neck sites caused by HPV types 16, 18, 31, 33, 45, 52, and 58. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients. Individuals with hypersensitivity after previous administration of GARDASIL® 9 or Gardasil should not receive GARDASIL® 9. **Precautions:** The decision to vaccinate an individual should take into account the risk for previous HPV exposure and potential benefit from vaccination. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine. Vaccinees should be observed for approximately 15 minutes after vaccination. It is important that procedures are in place to avoid injury from fainting. Vaccination should be postponed in individuals suffering from an acute severe febrile illness. However, the presence of a minor infection, such as a mild upper respiratory tract infection or low-grade fever, is not a contraindication for immunisation. As with any vaccine, vaccination with GARDASIL® 9 may not result in protection in all vaccine recipients. The vaccine will only protect against diseases that are caused by HPV types targeted by the vaccine. Therefore, appropriate precautions against sexually transmitted diseases should continue to be used. The vaccine is for prophylactic use only and has no effect on active HPV infections or established clinical disease. The vaccine has not been shown to have a therapeutic effect. The vaccine is therefore not indicated for treatment of cervical, vulvar, vaginal, anal, oropharyngeal and other head and neck cancers, high-grade cervical, vulvar, vaginal and anal dysplastic lesions or genital warts. It is also not intended to prevent progression of other established HPV-related lesions. GARDASIL® 9 does not prevent lesions due to a vaccine HPV type in individuals infected with that HPV type at the time of vaccination. Vaccination is not a substitute for routine cervical screening. Routine cervical screening remains critically important and should follow local recommendations. There are no data on the use of GARDASIL® 9 in individuals with impaired immune responsiveness. Safety and immunogenicity of a qHPV vaccine have been assessed in individuals aged from 7 to 12 years who are known to be infected with human immunodeficiency virus (HIV). Individuals with impaired immune responsiveness, due to either the use of potent immunosuppressive therapy, a genetic defect, Human Immunodeficiency Virus (HIV) infection, or other causes, may not respond to the vaccine. This vaccine should be given with caution to individuals with thrombocytopaenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these individuals. There are no safety, immunogenicity or efficacy data to support interchangeability of GARDASIL® 9 with bivalent or quadrivalent HPV vaccines. **Adverse events:** The most common adverse reactions observed with GARDASIL® 9 were injection-site adverse reactions and headache. These adverse reactions usually were mild or moderate in intensity. Very common (≥1/10) or common (≥1/100 to <1/10) side effects include headache, injection site pain, swelling or erythema, dizziness, nausea, pyrexia, fatigue, injection site pruritus or bruising, etc. For detailed adverse events, please consult the full prescribing information. **Before prescribing, please consult the full prescribing information.**

MSD

MERCK SHARP & DOHME (ASIA) LTD.
27/F Lee Garden Two, 28 Yun Ping Road, Causeway Bay, Hong Kong.
TEL: (852) 3971 2800 FAX: (852) 2834 0756

Date / Time	Function	Enquiry / Remarks
1 FRI 2:00 PM	**Zoom Live** **Recent Advances in Deep Brain Stimulation for Parkinson's Diseases in Hong Kong** Organiser: The Hong Kong Medical Association Speaker: Dr Benedict Beng-teck TAW	HKMA CME Dept. Tel: 3108 2507 1 CME Point
4 MON 2:00 PM	**Zoom Live** **Personalized Management of Non-Neurogenic Male LUTS** Organiser: The Hong Kong Medical Association Speaker: Dr James Hok-leung TSU	HKMA CME Dept. Tel: 2527 8452 1 CME Point
5 TUE 1:00 PM	**In-person / Zoom Live** **HKMA-HKSH CME Programme 2022-2023** **Topic: Cancer of Lung** Organiser: The Hong Kong Medical Association & the Hong Kong Sanatorium & Hospital Speaker: Dr YAU Chun-chung Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 3108 2507 1 CME Point
7:00 PM	**Certificate Course on Palliative Medicine for Health Care Workers 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Benjamin Hon-wai CHENG	Ms Vienna LAM Tel: 2527 8898
6 WED 2:00 PM	**Zoom Live** **Latest Hypertension Management and Local Consensus Update** Organiser: The Hong Kong Medical Association Speaker: Dr AU Shek-yin	HKMA CME Dept. Tel: 3108 2507 1 CME Point
7 THU 1:00 PM	**In-person** **Mental Health Challenges for Caregivers - What should be done as a health professional?** Organiser: The HKMA District Health Network Speaker: Dr Calvin Pak-wing CHENG Venue: Atrium Function Room, Hong Kong Gold Coast Hotel, 1 Castle Peak Road, Hong Kong	Mr Peter HO Tel: 3108 2514 1 CME Point
7:00 PM	**Certificate Course on Cytogenomics 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Edmond Shiu-kwan MA	Ms Vienna LAM Tel: 2527 8898
11 MON 2:00 PM	**Zoom Live** **Influenza Management in High Risk Patient** Organiser: The Hong Kong Medical Association Speaker: Dr CHAN Tak-yan	HKMA CME Dept. Tel: 2527 8452 1 CME Point
13 WED 7:30 AM	**The Hong Kong Neurosurgical Society Monthly Academic Meeting –To be confirmed** Organiser: Hong Kong Neurosurgical Society Speaker: Dr Benjamin Hiu-ming LEUNG Chairman: Dr CHEUNG Fung-ching Venue: Conference Room, F2, Department of Neurosurgery, Queen Elizabeth Hospital; or via Zoom meeting	CME Accreditation College: 1.5 points College of Surgeons of Hong Kong Enquiry: Dr Calvin MAK Tel: 2595 6456 Fax. No.: 2965 4061
1:00 PM	**In-person / Zoom Live** **HKMA-CUHK Medical Centre CME Programme 2023** **Common health problems for the elderly - Topic: Managing Age-related Macular Degeneration** Organiser: The Hong Kong Medical Association & the CUHK-Medical Centre Speaker: Dr Theresa Shiu-ting MAK Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 3108 2507 1 CME Point
7:00 PM	**Certificate Course on Respiratory Medicine 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr TSUI Sui-na	Ms Vienna LAM Tel: 2527 8898
14 THU 7:00 PM	**Certificate Course on Cytogenomics 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr LUK Ho-ming	Ms Vienna LAM Tel: 2527 8898
15 FRI *(16,17)*	**23rd Regional Osteporosis Conference (ROC 2023)** Organiser: The Osteoporosis Society of Hong Kong Speaker: Please refer to www.oshk.org.HK	ROC 2023 Conference Secretariat Tel: 2559 9973
2:00 PM	**Zoom Live** **The Sweet Spot for HF Management - What's The Role of SGLT2 Inhibitor** Organiser: The Hong Kong Medical Association Speaker: Dr Sunny Chun-fung TSANG	HKMA CME Dept. Tel: 2527 8452 1 CME Point
19 TUE 2:00 PM	**Physical attendance in Central Premises or attend via ZOOM** **HKMA-GHK CME Programme 2023 - Strategies Of Tumor Clearance In Management Of Colorectal Diseases** Organiser: The Hong Kong Medical Association & the Gleneagles Hong Kong Hospital Speaker: Dr Alex Lik-hang LEUNG Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 3108 2507 1 CME Point
20 WED 2:00 PM	**Zoom Live** **Doctor, My Neck Hurts, Is It Related to My Smart Phone?** Organiser: The HKMA District Health Network Speaker: Dr KWOK Hau-yan	Mr Peter HO Tel: 3108 2514 1 CME Point
7:00 PM	**Certificate Course on Respiratory Medicine 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Stephanie CHU	Ms Vienna LAM Tel: 2527 8898

Certificate Course for Nurses and Allied Health Professionals • Course No. C399 • CME/CNE Course

Certificate Course on Respiratory Medicine 2023 (Video Lectures)

Jointly organised by

The Federation of Medical Societies of Hong Kong 香港醫學組織聯會

Hong Kong Thoracic Society Limited 香港胸肺學會

CHEST Delegation Hong Kong and Macau Limited

Date	Topics	Speakers
13 September 2023	Airway Diseases: Asthma & COPD	Dr. TSUI Sui Na Associate Consultant United Christian Hospital
20 September 2023	Lung Cancer	Dr. Stephanie CHU Associate Consultant Queen Elizabeth Hospital
27 September 2023	1. Interpretation of Chest X-Ray	Dr. WONG Wei Yin Consultant Haven of Hope Hospital
	2. Pulmonary Function Test & Arterial Blood Gas	Dr. KWOK Chin Tong Resident Specialist Princess Margaret Hospital
4 October 2023	High Flow Nasal Cannula, Noninvasive Ventilation & Mechanical Ventilation	Dr. LUN Chung Tat Associate Consultant Alice Ho Miu Ling Nethersole Hospital
11 October 2023	Tracheostomy & CPAP Therapy	Mr. NG Shu Wah Nurse Consultant United Christian Hospital Ms. Maggie LIT Nurse Consultant Queen Elizabeth Hospital

Date : 13, 20, 27 September and 4, 11 October 2023 (Wednesday)
Time : 7:00 p.m. – 9:00 p.m. (2 hours per session , total 5 sessions,)
Course Feature : Video lectures (with Q&A platform for participants to post the questions)
Language Media : Cantonese (Supplemented with English)
Course Fee : HK$1,200
Certificate : Awarded to participants with a minimum attendance of 70% (4 out of 5 sessions)
Deadline : 6 September 2023
Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax : 2865 0345 Email : vienna.lam@fmshk.org

Online Application from website: http://www.fmshk.org

Certificate Course for Nephrology Medical and Healthcare Professionals • Course No. C400 • CME/CNE Course

Certificate Course on Renal Medicine 2023 (Video Lectures)

Jointly organised by

The Federation of Medical Societies of Hong Kong

Hong Kong Society of Nephrology

Date	Topics	Speakers
21 September 2023	Common investigation tests for renal disease including approach to proteinuria and haematuria	Dr. Ronald LIN
	Update and management of acute kidney injury	Dr. Chun-Hay TAM
28 September 2023	Update and management of glomerular disease	Dr. Jason IP
	ABC of hemodialysis therapy	Dr. Connie Ping-kwan CHAN
5 October 2023	Nutritional management in kidney diseases	Ms. Cherry Pui-yee LAW
	Kidney involvement in multi-system disorders	Dr. Benjamin SO
12 October 2023	Drug prescribing in renal failure	Dr. Andrew LUK
	ABC of peritoneal dialysis therapy	Dr. Joseph Ho-Sing WONG
19 October 2023	Update on diabetic kidney disease	Dr. Sam LAU
	Update and management of chronic kidney disease	Dr. Lorraine KWAN 朱丹中醫師
26 October 2023	Update and management of hypertension	Dr. Lo-yi HO
	ABC of renal transplantation	Dr. Ivy Lok-yan WONG

Date : 21,28 September & 5, 12, 19, 26 October, 2023 (Thursday)
Time : 7:00 pm – 8:30 pm
Course Feature : Video lectures (with Q&A platform for participants to post the questions)
Language Media : Cantonese (Supplemented with English)
Course Fee : HK$1,000
Certificate : Awarded to participants with a minimum attendance of 70%
Deadline : 14 September 2023
Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax : 2865 0345 Email : vienna.lam@fmshk.org

Online Application from website: http://www.fmshk.org

Date / Time	Function	Enquiry / Remarks
21 THU 1:00 PM	**In-person** **Advancing Asthma Treatment with Triple Therapy: Right Therapy for Right Patients at Right Timing** Organiser: The HKMA District Health Network Speaker: Dr KWOK Yuk-lung Venue:5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wan Chai, Hong Kong	Mr Peter HO Tel: 3108 2514 1 CME Point
7:00 PM	**Certificate Course on Renal Medicine 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Ronald LIN, Dr TAM Chun-hay	Ms Vienna LAM Tel: 2527 8898
8:00 PM	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms Nancy CHAN Tel: 2527 8898
22 FRI 2:00 PM	**Zoom Live** **World Contraception Day: Patient Counselling on Family Planning** Organiser: The Hong Kong Medical Association Speaker: Dr CHAN Sum-yee	HKMA CME Dept. Tel: 2527 8452 1 CME Point
23 SAT 1:30 PM	**In-person** **The HKMA Medico legal Conference 2023** Organiser: The Hong Kong Medical Association Speaker: Various Venue: Sung Room, 4/F, Sheraton Hong Kong Hotel & Towers, 20 Nathan Road, Kowloon, Hong Kong	HKMA CME Dept. Tel: 2527 8452 3 CME Point
25 MON 2:00 PM	**Zoom Live** **Acute diarrhea Management in Pediatric Patients** Organiser: The Hong Kong Medical Association Speaker: Dr LAM Jenks Albinus	HKMA CME Dept. Tel: 3108 2507 1 CME Point
26 TUE 2:00 PM	**Zoom Live** **Management of male LUTS: More Than Treating Symptoms?** Organiser: The Hong Kong Medical Association Speaker: Dr Simon See-ming HOU	HKMA CME Dept. Tel: 3108 2507 1 CME Point
27 WED 2:00 PM	**Zoom Live** **HKMA Adult Immunization Campaign 2023 - Respiratory Syncytial Virus (RSV) in Older Adults** Organiser: The Hong Kong Medical Association Speaker: Dr Raymond TSO	HKMA CME Dept. Tel: 3108 2507 1 CME Point
7:00 PM	**Certificate Course on Respiratory Medicine 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr WONG Wei-yin, Dr KWOK Chin-tong	Ms Vienna LAM Tel: 2527 8898
28 THU 1:00 PM	**In-person / Zoom Live** **HKMA-HKSTP CME Lecture** **Topic: The Future of Non-Invasive Treatments for Ocular Diseases and beyond: Ultrasound Drug Delivery Platform** Organiser: The Hong Kong Medical Association & the Hong Kong Science Park Speaker: Dr Langston Wai-leung SUEN Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 3108 2507 1 CME Point
7:00 PM	**Certificate Course on Renal Medicine 2023 (Video Lectures)** Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Jason IP, Dr Connie Ping-kwan CHAN	Ms Vienna LAM Tel: 2527 8898
29 FRI 1:00 PM	**In-person** **COVID-19 Oral Antiviral Treatment Real World Evidence Update & Clinical Experience Sharing** Organiser: The HKMA District Health Network Speaker: Dr WONG King-ying Veune: Rich Garden Restaurant, C2/F, 114 Broadway Street, Mei Foo Sun Chuen Stage 8, Mei Foo	Mr Peter HO Tel: 3108 2514 1 CME Point

Answers to Dermatology Quiz

Answers:

1. The differential diagnoses of this gentleman include scabies, urticaria, papular eczema, drug eruptions and insect/arthropod bites. The most likely diagnosis is insect/arthropod bites and is probably due to bedbugs because of the poor and overcrowded living environment. The bedbugs often bite at night during the patient sleeping and lesions were in cluster with 3 - 5 bites together in a zigzag pattern. It is a parasitic arthropod less than 1 cm in length and reddish brown in colour. They are in furniture, floorboards or commonly in areas of clutter.

2. The typical history, such as overcrowded environment and full of clutter together with the classical clinical presentation reaches the diagnosis without any investigation needed. The classical bedbug bite presentation is erythematous papules, sometimes with urticarial components in a group of 3 - called "breakfast, lunch and dinner" (Fig. 1). The lesions of bedbugs bite may sometimes be confused with scabies, especially both share similar risk factors. Sometimes skin scraping for scabies may be necessary, especially skin burrows are suspected.

3. Treatment of bedbugs bite is mainly symptomatic. Topical steroid cream or oral antihistamines can be used for symptom relief. Topical antibiotic or antiseptic lotion is used for secondary bacterial infections. Besides treating the patient, cleansing the living environment and tidying up the clutter are equally important. Last but not the least, seeking advice from insect control and elimination experts may be needed to reduce and finally eliminate the bedbugs in the living environment.

Dr KWAN Chi-keung
MBBS(HK), MRCP (UK), FRCP(Lond, Glasg, Edin), Dip Derm(Glasg), PDipID(HK), FHKCP, FHKAM(Medicine)
Specialist in Dermatology and Venereology

SHINGRIX
(ZOSTER VACCINE RECOMBINANT, ADJUVANTED)

GSK

A NEW GENERATION OF HERPES ZOSTER VACCINE

PREVENT SHINGLES
DON'T GIVE A CHANCE[1]

ELIGIBLE GROUPS[1]

18+ YEARS OLD AT INCREASED HZ RISK

50+ YEARS OLD

THE ONLY HZV* WITH OVER 90% VACCINE EFFICACY[1-2]

* In adults aged 50 years or older

References: 1. GlaxoSimithKline. Shingrix Hong Kong Prescribing Information. GDS04. 2. MSD. Live attenuated Zoster Vaccine Prescribing Information.

For Shingrix Full Prescribing Information, please scan the below QR code

Important Safety Information: • SHINGRIX is contraindicated in anyone with hypersensitivity to the active substances or to any of the excipients • As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine • SHINGRIX should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following intramuscular administration to these subjects • Syncope (fainting) can be associated with the administration of injectable vaccines, including SHINGRIX. Procedures should be in place to avoid falling injury • In a post-marketing observational study in individuals aged 65 years or older, an increased risk of Guillain-Barré syndrome (estimated 3 excess cases per million doses administered) was observed during the 42 days following vaccination with SHINGRIX. Available information is insufficient to determine a causal relationship with SHINGRIX • In adults aged 50 years and above, the most frequently reported adverse reactions were pain at the injection site, myalgia, fatigue, and headache. Most of these reactions were not long-lasting (median duration of 2 to 3 days). Reactions reported as severe lasted 1 to 2 days • In adults ≥18 years of age who are immunodeficient or immunosuppressed due to disease or therapy (referred to as immunocompromised (IC)), the safety profile was consistent with that observed in adults ≥50 years of age. There are limited data in adults aged 18–49 years at increased risk of HZ who are not IC • Overall, there was a higher incidence of some adverse reactions in younger age groups:[1,2] • studies in IC adults ≥18 years of age (pooled analysis): the incidence of pain at the injection site, fatigue, myalgia, headache, shivering, and fever was higher in adults aged 18–49 years compared to those aged 50 years and above • studies in adults ≥50 years of age (pooled analysis): the incidence of myalgia, fatigue, headache, shivering, fever, and gastrointestinal symptoms was higher in adults aged 50–69 years compared to those aged 70 years and above • There are no data from the use of SHINGRIX in pregnant women. As a precautionary measure, it is preferable to avoid the use of SHINGRIX during pregnancy. It is unknown whether SHINGRIX is excreted in human milk • As with any vaccine, a protective immune response may not be elicited in all vaccinees.

For adverse event reporting, please call GlaxoSmithKline Limited at (852) 3189 8989 (Hong Kong) [or (853) 2871 5569 (Macau)], or send an email to us at HKAdverseEvent@gsk.com. Please read the full prescribing information prior to administration. Full Prescribing Information is available upon request at GSK, 23/F, Tower 6, The Gateway, 9 Canton Road, Tsim Sha Tsui, HK.

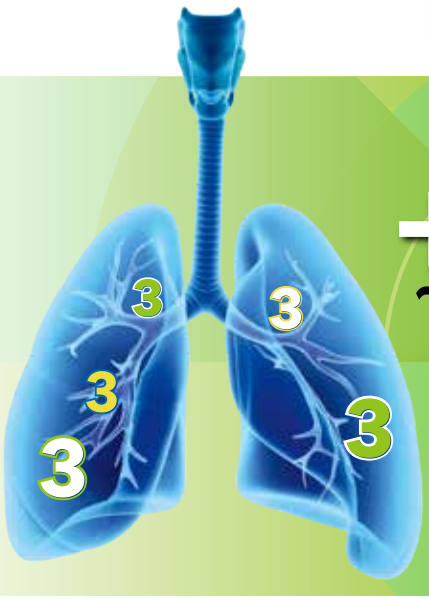
PM-HK-SGX-PSTR-220001 (10/2024) Date of preparation: 16 Nov 2022

MSD

Vaxneuvance®
Pneumococcal 15-valent
Conjugate Vaccine

TARGET OUR BURDEN

Paediatric indication
Approved in HK



±~60%

According to a Phase 3 trial, Vaxneuvance® (PCV15) is

~60% higher immunogenicity[a]

to PCV13 for shared Serotype 3[1]

(GMT Ratio 1.60, 95% CI 1.38, 1.85)

NEW Pneumococcal Conjugate Vaccine since 2011[2]

SEROTYPE 3 is the **NO.1 Burden** of IPD[b] in Hong Kong[3]

Vaxneuvance® (PCV15) was **SUPERIOR**[a] to PCV13 for shared Serotype 3[1] (≥50 years old)

ALL

Vaxneuvance® (PCV15) was noninferior[a] to PCV13 for all 13 shared serotype[1]

Vaxneuvance® (PCV15) was **SUPERIOR**[a] to PCV13 for **unique serotypes 22F and 33F**[1]

in adults ≥ 50 years old

[a]in terms of OPA GMTs (according to a Phase 3 trial) [b]IPD: invasive pneumococcal disease

Safety Result: The majority of participants experienced at least 1 adverse event (67.9% after V114 and 58.2% after PCV13). The most frequently reported AEs (>5% of participants in either group) were the solicited events of injection-site pain, injection-site erythema, injection-site swelling, arthralgia, fatigue, headache, and myalgia.[1]

CI: confidence interval; GMT: geometric mean titers; IPD: invasive pneumococcal disease; OPA: opsonophagocytic activity; PCV13: 13-valent pneumococcal conjugate vaccine; PCV15: 15-valent pneumococcal conjugate vaccine

Study design: This was a phase 3, randomized, double-blind, active comparator- controlled study to evaluate the safety, tolerability, and immunogenicity of VAXNEUVANCE compared to PCV13 in healthy pneumococcal-vaccine naïve adults 50 years of age or older (Protocol V114-019). The study was conducted from June 2019 through March 2020 at 30 sites. The study enrolled 1,202 participants randomized in a 1:1 ratio to receive a single dose of Vaxneuvance (n=602) or PCV13 (n=600). Randomization was stratified by participant age at enrollment. The primary immunogenicity objectives were to compare Vaxneuvance to PCV13 for noninferiority of immune responses at 30 days postvaccination for shared serotypes (noninferiority met when lower bound of the 2 sided 95% CI of the OPA GMT ratio >0.5) and superiority of immune response at 30 days postvaccination for serotypes unique to Vaxneuvance (superiority met when lower bound of the 2-sided 95% CI of the OPA GMT ratio >2, and the lower bound of the 2-sided 95% CI of the difference between the proportions of participants with a ≥ 4-fold rise >0.1). The secondary immunogenicity objective was to assess superiority of immune response for serotype 3 at 30 days postvaccination (superiority met when lower bound of the 2-sided 95% CI of the OPA GMT ratio >1.2, and the lower bound of the 2-sided 95% CI of the difference between the proportions of participants with a ≥4-fold rise >0)[1].

References: 1. Platt HL *et al; Vaccine* 2022; 40(1):162-172. doi: 10.1016/j.vaccine.2021.08.049 2. Centre for Health Protection. Scientific Committee on Vaccine Preventable Diseases. Updated Recommendations on the Use of 13-valent Pneumococcal Conjugate Vaccine in Childhood Immunisation Programme; 2019. Adopted from: https://www.chp.gov.hk/files/pdf/updated_recommendation_on_the_use_of_ pcv3_in_ hkcip_march2019_accessibility.pdf. Accessed on Nov 17, 2022. 3. Centre for Health Protection. Communicable Diseases Watch. *IPD* (2015-2021).

Vaxneuvance Selected Safety Information

Indications: • Vaxneuvance is indicated for active immunisation for the prevention of invasive disease, pneumonia and acute otitis media caused by *Streptococcus pneumoniae* in infants, children and adolescents from 6 weeks to less than 18 years of age • Vaxneuvance is indicated for active immunisation for the prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* in individuals 18 years of age and older. • The use of Vaxneuvance should be in accordance with official recommendations.

Dosing: Vaccination with Vaxneuvance is recommended for selected individuals as follows: Individuals 18 years of age and older • 1 dose (0.5 mL). • The need for revaccination with a subsequent dose of Vaxneuvance has not been established. Paediatric population • The safety and efficacy of Vaxneuvance in children and adolescents less than 18 years of age please consult the full prescribing information. Special populations • One dose of Vaxneuvance may be given to individuals who have one or more underlying conditions predisposing them to an increased risk of pneumococcal disease (e.g., adults living with human immunodeficiency virus (HIV) or immunocompetent adults 18 to 49 years of age with risk factors for pneumococcal disease).

Contraindications: Hypersensitivity to the active substances, to any of the excipients, or to any diphtheria toxoid-containing vaccine.

Precautions: • In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. • Vaxneuvance must not be administered intravascularly. • As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine. • Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination. • As with other intramuscular injections, the vaccine should be given with caution to individuals receiving anticoagulant therapy, or to those with thrombocytopenia or any coagulation disorder such as haemophilia. Bleeding or bruising may occur following an intramuscular administration in these individuals. • The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination generally should not be withheld or delayed. • Immunocompromised individuals, whether due to the use of immuno-suppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation. • Safety and immunogenicity data for Vaxneuvance are available for individuals living with HIV infection. Safety and immunogenicity data for Vaxneuvance are not available for individuals in other specific immunocompromised groups (e.g., haematopoietic stem cell transplant) and vaccination should be considered on an individual basis. • As with any vaccine, vaccination with Vaxneuvance may not protect all vaccine recipients. Vaxneuvance will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine. • This medicinal product contains less than 1 mmol sodium (23 milligrams) per dose, i.e. essentially 'sodium-free'.

Adverse events: The most frequently reported adverse reactions following vaccination with Vaxneuvance were solicited. The most frequent adverse reactions were pyrexia, injection-site pain, fatigue, myalgia, headache, injection-site swelling, injection-site erythema and arthralgia. The majority of solicited adverse reactions were mild (based on intensity or size) and of short duration (≤ 3 days); severe reactions (defined as being extremely distressed or unable to do usual activities or size > 7.6 cm) occurred in ≤ 4.5% of children and adolescents; severe reactions (defined as an event that prevents normal daily activity or size > 10 cm) occurred in ≤ 1.5% of adults across the clinical program. • Older adults reported fewer adverse reactions than younger adults. • For detailed side effects, please consult the full prescribing information.

Drug interactions: • Different injectable vaccines should always be administered at different injection sites. • Immunosuppressive therapies may reduce the immune responses to vaccines.

Infants and children aged 6 weeks to less than 2 years • Vaxneuvance can be given concomitantly with any of the following vaccine antigens, either as monovalent or combination vaccines: diphtheria, tetanus, pertussis, poliomyelitis (serotypes 1, 2 and 3), hepatitis A, hepatitis B, Haemophilus influenzae type b, measles, mumps, rubella, varicella and rotavirus vaccine. Children and adolescents 2 to less than 18 years of age: • There are no data on the concomitant administration of Vaxneuvance with other vaccines. Data from a post-marketing clinical study evaluating the impact of prophylactic use of antipyretics (ibuprofen and paracetamol) on the immune response to other pneumococcal vaccines suggest that administration of antipyretics concomitantly or within the same day of vaccination may reduce the immune response after the infant series. Responses to the booster dose administered at 12 months were unaffected. The clinical significance of this observation is unknown. Adults: • Vaxneuvance can be administered concomitantly with seasonal quadrivalent influenza vaccine (split virion, inactivated). There are no data on the concomitant administration of Vaxneuvance with other vaccines.

Pregnancy: • There is limited experience with the use of Vaxneuvance in pregnant women. • Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. • Administration of Vaxneuvance in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and the foetus.

Breast-feeding: It is unknown whether Vaxneuvance is excreted in human milk.

Fertility: • No human data on the effect of Vaxneuvance on fertility are available. Animal studies in female rats do not indicate harmful effects.

Before prescribing, please consult the full prescribing information.

MSD

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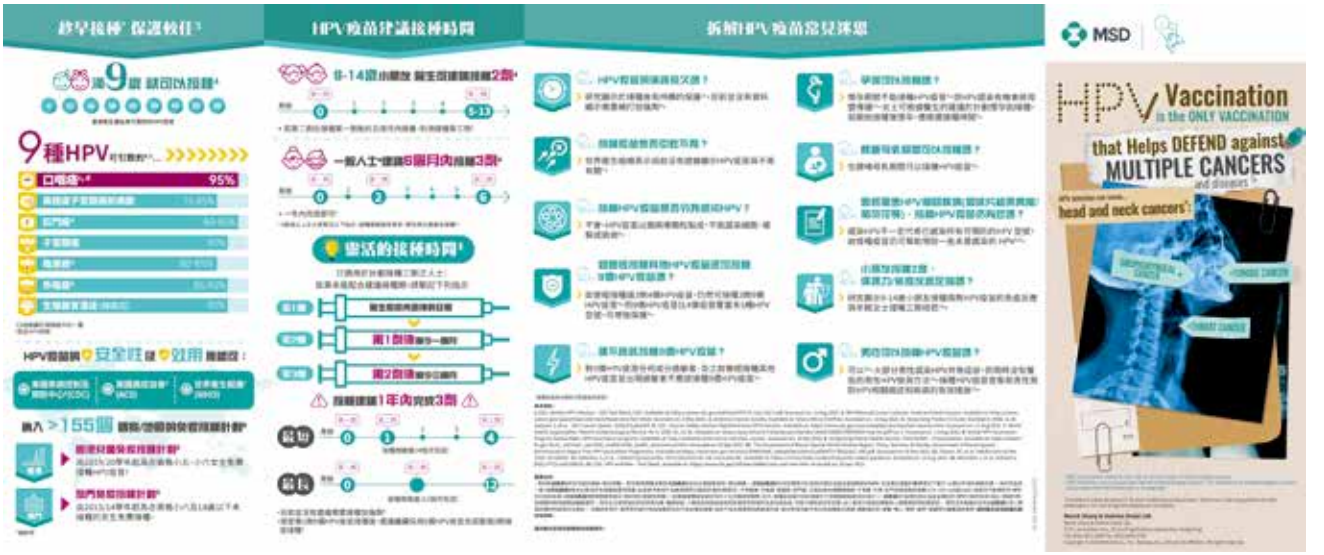
越早接種 保護越佳!
HPV疫苗建議接種時間
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MSD
HPV Vaccination
is the ONLY VACCINATION
that Helps DEFEND against
MULTIPLE CANCERS
head and neck cancers

INSERT

SHINGRIX
(ZOSTER VACCINE RECOMBINANT, ADJUVANTED)

GSK

Vaccination as a public health strategy[1]

for HERPES ZOSTER prevention in Hong Kong

Herpes zoster (shingles) in Hong Kong

Shingles is a painful, blistering rash usually lasting for 2-4 weeks. The risk of shingles increases with age, especially from 50 years of age, owing to declining immunity. In Hong Kong, ***the burden of shingles is increasing*** due to an ***aging population with increasing life expectancy.***

Shingles can cause complications, ***affecting patients' health and quality of life***, and result in hospitalizations and productivity loss for individuals and society.

Vaccination can prevent shingles and reduce disease burden

Since 2021, two shingles vaccines are available in Hong Kong:

Zoster Vaccine Live (ZVL) AND **Recombinant Zoster Vaccine (RZV)**

Using **mathematical modeling**, this study compared the public health impact of different shingles vaccination strategies:*

No vaccination

VS

ZVL

RZV

Vaccination

Herpes Zoster cases and its complications contribute to direct medical costs on individual patients

- per out-patient case
  ~USD 309
  (~HKD 2,422)^
- per inpatient case
  ~USD 2,887-4,883
  (~HKD 22,628 - 38,273)^

^This is based on current exchange rate,as of 16 May 2023

*Information presented below are modeled from 3.13 million Hong Kong adults ≥50 years of age in their remaining lifetime

Reference:
1.Chan PKS, Wong MCS, Chan M, Ching K, Giannelos N. Ng C Public health impact of herpes zoster vaccination on older adults in Hong Kong. Hum Vaccin Immunother. 2023;19(1)

Access Full Publication:

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With shingles vaccination, **public health burden** of shingles would be **reduced**

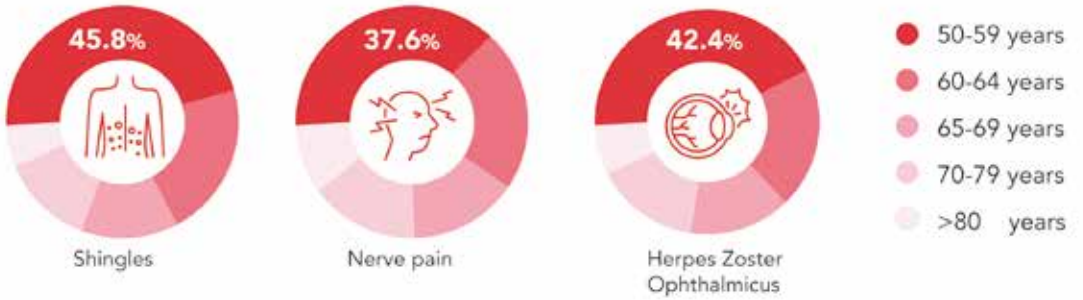
Vaccination with ZVL or RZV (versus no vaccination) was estimated to ***reduce the number of cases of shingles and complications.***

	ZVL (40% vaccination rate)	RZV (40% vaccination rate)
Shingles	▼ 47,477	▼ 204,875
Nerve pain	▼ 7,701	▼ 31,949
Herpes Zoster Ophthalmicus	▼ 1,769	▼ 8,471
Death	▼ 1	▼ 20

Comparing the two vaccines, RZV avoided ***4-5 times*** the number of cases compared with ZVL

***Earlier RZV vaccination**, it would have a **greater public health impact** than vaccination at a later age*

The percentage of cases ***avoided with RZV*** (versus no vaccination) was the ***highest 50-59 years of age*** compared with other age groups.



> **These results may support value assessment and decision-making on public health vaccination strategies for shingles prevention in Hong Kong.**

Shingrix Succinct Safety Statement

Contraindications: Hypersensitivity to the active substances or to any of the excipients.

Special warnings and precautions for use: As with all injectable vaccines,appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine. As with other vaccines, vaccination with Shingrix should be postponed in subjects suffering from an acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination. Do not administer the vaccine intravascularly or intradermally. Subcutaneous administration is not recommended. Maladministration via the subcutaneous route may lead to an increase in transient local reactions. Shingrix should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following intramuscular administration to these subjects. Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints. There are no safety, immunogenicity or efficacy data to support replacing a dose of Shingrix with a dose of another HZ vaccine. There are limited data to support the use of Shingrix in individuals with a history of HZ and in frail individuals including those with multiple comorbidities. Healthcare professionals therefore need to weigh the benefits and risks of HZ vaccination on an individual basis.

Material Code: PM-HK-SGX-CRD-230002 (04/2025)
Date of Preparation: 7 May 2023

For Shingrix Full Prescribing Information, please scan the QR code

GSK