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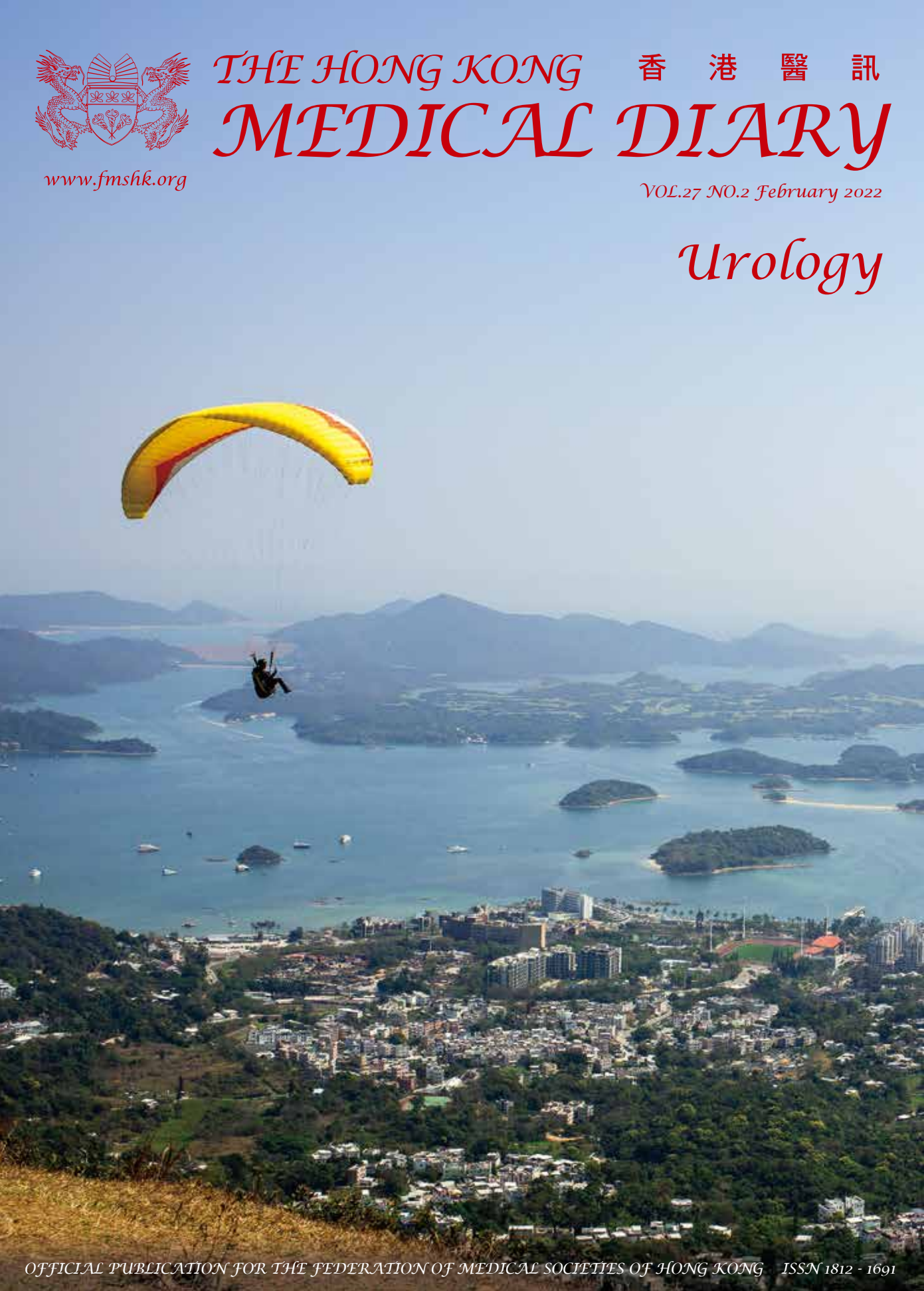

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Reference: 1. Schumacher HR Jr et al. Rheumatology. 2009;48(2):188-194.
2. Lee J-W et al. Int Urol Nephrol. 2019;51(3):467-473.

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The Cover Shot

In the pandemic era of COVID-19, Hong Kong people have refrained from overseas travel because of the tight tourist control in most countries. Nonetheless, Hong Kong herself offers so many scenic sites. This photo was taken in Ngong Ping Plateau of Ma On Shan, a location famous for offering a breathtaking view of Sai Kung. The location is also one of the hot spots for paragliding. Unfortunately, my acrophobia does not allow me to engage in this exciting sport. I hence shot some photos to keep the moment from running away.

Dr Kin-man LAM
Specialist in Urology

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A New Beginning in the Year of the Tiger

Prof Bernard MY CHEUNG

President
The Federation of Medical Societies of Hong Kong

Prof Bernard M Y CHEUNG

一年春作首 百獸虎為王

The tiger is the third sign in the Chinese Zodiac, coming after the ox. Legend has it that the tiger, despite being the king of animals, was beaten in the race by the rat for its cleverness and the ox for its diligence. How true it is of the world today as it was in ancient China two thousand years ago! A successful person must have brains and must work hard. After that, necessary ingredients are speed, strength and self-confidence, the hallmarks of a tiger. It seems we have much to learn from this fearsome animal.

In a new year, it is customary to wish each other prosperity and good health. In this third year of the COVID pandemic, health has never been more important, and perhaps even more important than wealth. Hong Kong has come off quite well in terms of the number of COVID infections and deaths in comparison with the United Kingdom or the United States, but has paid an enormous price in restricting travel. Let's hope that in the new year, borders will reopen again to connect us with the Mainland and other parts of the world.

The key to opening borders and staying healthy at the same time is a high vaccination and re-vaccination rate. The Federation is at the forefront in advocating and promoting vaccination, from the publicity videos our committee members made, to hosting talks on vaccination by experts and to publishing a series of guidelines on vaccination for patients with different chronic illnesses. We echo the appeals by Dr the Hon David Lam Tzit-yuen, Prof Yu-lung Lau and others in the profession for more elderly and children to be vaccinated, especially because of the threat posed by the Omicron variant.

Out of necessity, we switched from face-to-face conferences and certificate courses to online or hybrid meetings. After overcoming a steep learning curve, we have become adept at organising and running these meetings. They have proven to be very popular, and we have managed to garner the kind of attendances we could only dream of several years ago. Life would never be the same after the pandemic, and is definitely for the better when it comes to harnessing internet technology.

Although 2021 has been dominated by the pandemic, people still fall ill with other conditions. Non-communicable diseases such as hypertension, diabetes, vascular and kidney diseases still kill, a fact of which we are painfully reminded when folks receiving vaccination got protected from COVID-19 but subsequently died from one of these common conditions. The Federation has always been keen on health promotion. Although we cannot hold public talks yet, some of us appeared on the live radio programme, Healthpedia (精靈一點), to talk about common medical conditions.

The Federation is very glad that legislation has now been enacted to ban e-cigarettes and heat-not-burn tobacco. This has been a long

campaign lasting for years. It has not been an easy path and there were opponents and critics of the legislation. However, when it comes to protecting a new generation from being addicted to nicotine, we must be resolute and bite the bullet. I hope that other parts of the world would also follow our example and thereby prevent an epidemic of nicotine addiction in youngsters.

While our continuous professional education programmes have gone online, the Hong Kong Medical Diary has gone from strength to strength as a welcome source of update on medical treatments. The issue editors and authors contributing articles are to be thanked for the enormous amount of time and effort that have gone into producing these miniature and highly collectable masterpieces.

Founded in 1965, the Federation was way ahead of its time by welcoming to the fold not just doctors, but nurses, pharmacists and other health professionals. Our common goal is to serve the health needs of the community and so a multidisciplinary approach is the only logical and effective one. I hope the Federation will continue to promote interdisciplinary cooperation and collaboration.

May I wish all of our readers a very vigorous Year of the Tiger:

騎牛踏雪去 跨虎報春來

祝 龍精虎猛 如虎添翼

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- PATIENTS ARE ASSOCIATED WITH 48% LESS RISKS OF CARDIOVASCULAR EVENTS WHEN RECEIVING FIRMAGON® COMPARED TO LHRH AGONISTS[5††]
- EAU RECOMMENDS LHRH ANTAGONISTS FOR PROSTATE CANCER PATIENTS WITH AN IMPENDING SPINAL CORD COMPRESSION OR BLADDER OUTLET OBSTRUCTION[7]

EAU: European Association of Urology; LHRH: luteinising hormone-releasing hormone; MOA: mechanism of action; PSA: prostate-specific antigen; QoL: quality of life

† A phase III, randomized, open-label trial that evaluated the efficacy of FIRMAGON vs leuprolide in achieving testosterone suppression in patients with prostate cancer (N=610). The primary endpoint was suppression of testosterone to ≤0.5 ng/mL at all monthly measurements from day 28 to day 364 (treatment response).

‡ Pooled analysis of 5 phase III/IIIb trials (N=1925) comparing prostate cancer disease control outcomes in patients received FIRMAGON vs LHRH agonists. Efficacy and safety outcomes were assessed.

†† Meta-analysis of 8 randomized controlled trials (N=2632) on clinical safety and oncologic outcomes in metastatic prostate cancer, in patients receiving FIRMAGON vs LHRH agonist±anti-androgen.

‡‡ A randomized, open-label trial comparing 3-month neoadjuvant FIRMAGON vs goserelin + bicalutamide in men with intermediate- to high-risk prostate cancer (N=244). Primary endpoint was total prostate volume reduction. Secondary objectives included the effect on lower urinary tract symptom relief and changes of quality of life related to urinary symptoms.

FOR PATIENTS WITH ADVANCED HORMONE-DEPENDENT PROSTATE CANCER[1,2]

START STRONG.
STAY IN CONTROL.

REFERENCES: 1) Hong Kong Product Package Insert of FIRMAGON 80mg (Date of revision: May 2015); 2). Hong Kong Product Package Insert of FIRMAGON 120mg (Date of revision: May 2015); 3) Klotz L, *et al. BJU Int.* 2008;102:1531–8; 4) Klotz L, *et al. Eur Urol.* 2014;66:1101–8; 5) Abufaraj M, *et al. Eur Urol.* 2021 Jan;79(1):44-53; 6) Mason M *et al. Clin Oncol.* 2013 Mar;25(3):190-6; 7) EAU Guidelines, Edn. presented at the EAU Annual Congress Amsterdam 2020.

Abbreviated Prescribing Information of FIRMAGON

Active Ingredient: Degarelix. **Indications:** Treatment of advanced hormone-dependent prostate cancer in adult males. **Dosage and Administration:** Initially 240 mg administered as 2 SC inj of 120 mg each. Maintenance: 80 mg administered as 1 SC inj mthly. The first maintenance dose should be given one mth after the starting dose. Administered as SC inj in abdominal region. **Contraindications:** Hypersensitivity. **Special Warnings and Precautions:** The vials should not be shaken. Administration of other conc is not recommended. Long-term androgen deprivation therapy may prolong QT interval. Use w/ caution in patients with Hx of QTc interval >450 msec, Hx or risk factors of torsades de pointes or CVD, Hx of severe untreated asthma, anaphylactic reactions, severe urticaria or angioedema. May decrease bone density. May reduce glucose tolerance, diabetic patients may require more frequent monitoring of blood glucose. Use w/ caution in patients w/ severe renal & hepatic impairment. ADR of fatigue & dizziness might influence ability to drive or operate machinery. May inhibit male fertility as long as the testosterone is suppressed. No relevant indication for use in women, children and adolescents. Must not be mixed with other medicinal products. **Side Effects:** Hot flush, inj site reactions, anaemia, increased wt, insomnia, dizziness, headache, diarrhoea, nausea, increased liver transaminases, hyperhidrosis (incl. night sweats), rash, musculoskeletal pain & discomfort, gynaecomastia, testicular atrophy, erectile dysfunction, chills, pyrexia, fatigue, flu-like illness. **Interactions:** Medicinal products known to prolong the QTc interval or able to induce torsades de pointes such as Class IA (e.g. quinidine, disopyramide) or Class III (amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmics, methadone, cisapride, moxifloxacin, antipsychotics.

Reference:
Hong Kong Product Package Insert of FIRMAGON 80mg (Date of revision: MAY 2015)
Hong Kong Product Package Insert of FIRMAGON 120mg (Date of revision: MAY 2015)

Product registration conditions differ internationally, please refer to country-specific product information for more details.

For additional information, please consult the product package insert before prescribing.

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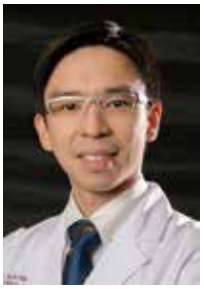

Dr Peter KF CHIU

Benign prostatic hyperplasia (BPH) is being diagnosed in a significant proportion of elderly men, leading to bothersome urinary symptoms and reduced quality of life. While transurethral resection of the prostate (TURP) has been the mainstay of surgical treatment for BPH, there are various novel surgical treatment options that can achieve similar symptom improvement with less morbidities.

According to the Hong Kong Cancer Registry, prostate cancer is the third most commonly diagnosed cancer among the male population in Hong Kong in 2019, and is the fourth most common cause of cancer death in men. Newer serum and urine biomarkers have been introduced to Hong Kong to aid urologists in selecting men at higher risk of prostate cancer for further investigation including imaging with MRI prostate and prostate biopsy. Transrectal ultrasound-guided prostate biopsy (TRUS biopsy) will soon become a historical term as it is gradually replaced by transperineal prostate biopsy with significantly less infective complications. Novel biomarkers, advanced imaging and accurate targeted biopsy facilitate screening and diagnosis of prostate cancer.

Minimally invasive surgery, particularly robotic radical prostatectomy, is currently the major modality of surgery in the public sector of Hong Kong for prostate cancer treatment.

For patients with metastatic prostate cancer, the newer novel hormonal agents help to prolong survival and improve the quality of life of these patients. A multidisciplinary team involving urologists, oncologists, and urology nurses will help to provide different choices and advice to the patient with the aim of providing individualised treatment for different patients and their family's needs.

The authors of the Hong Kong Medical Diary, February 2022 issue will bring to you state-of-the-art knowledge of the latest advances in BPH surgery, and investigation and treatment for prostate cancer.

New Advances in Surgery for Benign Prostatic Hyperplasia

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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 28 February 2022.

ABSTRACT

Benign prostatic hyperplasia causes prostatic enlargement and lower urinary tract symptoms in men. Transurethral resection of theprostate (TURP) has been considered the gold standard for surgical treatment of benign prostate hyperplasia (BPH) in the past decades. In recent years, new treatment options drastically changed how BPH is being treated.

INTRODUCTION

BPH is histopathologically characterised by an increase in epithelial and stromal cell numbers in the periurethral area of the prostate, and therefore BPH is benign prostatic hyperplasia and not hypertrophy. The exact molecular aetiology of this hyperplastic process is uncertain. The development of BPH may be due to embryonic reawakening of the inductive effect of prostatic stroma on epithelial cell proliferation[1], and impaired androgen-mediated programmed cell death leading to accumulation in the number of cells[2]. Benign prostate obstruction (BPO) is BPH with bladder outlet obstruction. Management of BPH can be divided into medical and surgical options. Surgery is reserved for patients with refractory retention of urine and obstructive uropathy due to BPO. Surgical treatment is also indicated in patients who experience BPE refractory to medical treatment and those with BPH complications, including hematuria, urinary tract infection, bladder stone and bladder diverticulum.

CONVENTIONAL TURP

Maximillian Stern introduced the first resectoscope and transurethral resection of the prostate (TURP) in 1926. Since then, TURP has remained the gold standard for surgical treatment of benign prostatic obstruction, with excellent long-term efficacy. TURP is performed using an electrical wire-loop to remove excessive prostatic tissue while sparing the prostatic capsule. However, this procedure is associated with morbidities, including anaesthetic risk, bleeding, transurethral resection (TUR) syndrome, urinary incontinence, urethral stricture, erectile dysfunction, and retrograde ejaculation. In 10% of patients with TURP performed, surgical re-treatment was needed after eight years[3] Meta-analysis has demonstrated that bipolar TURP offers promising long-term efficacy compared to monopolar TURP, the former being associated with less bleeding, fewer transfusion and lower risk of TUR syndrome[4]. With the advancement of technology in the era of personalised medicine, new surgical techniques have been introduced and should be tailored to treat patients individually. Doctors and patients should consider these important factors before choosing between various modes of surgical treatments: anaesthetic risk, age, comorbidity, the presence of a pacemaker, bleeding tendency, and use of anti-coagulants. Surgeons should pay further attention to the following factors when choosing between different surgical treatments: the prostate size, the presence of a median lobe, the severity of lower urinary tract symptoms due to benign prostate obstruction (BPO), associated bladder stone and bladder diverticulum.

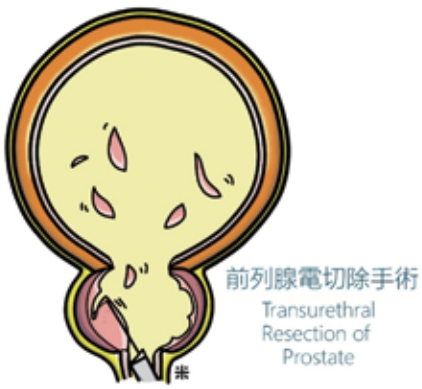

Fig 1. Transurethral resection of the prostate (TURP) using bipolar energy (Reproduced with permission from SH Ho Urology Centre website urologycentre.com.hk)

PHOTOSELECTIVE VAPORISATION OF THE PROSTATE (PVP)

PVP, aka Greenlight LASER, is the use of neodymium-doped in YAG crystal LASER. The beam passes via a lithium borate crystal, to emit green light with wavelength 532nm, which is absorbed by haemoglobin, to vaporise prostatic tissue and achieve effective coagulation. Current evidence indicates that

this procedure can be optimally used in BPH with prostate less than 80ml in volume and in patients on anti-platelets or anti-coagulants. Compared with conventional TURP, short- and mid-term results have demonstrated that PVP offers similar efficacy, but with less bleeding, fewer blood transfusions, shorter catheterisation time, shorter length of stay in hospital and absence of TUR syndrome[4,5]. However, PVP does not allow histological examination of prostatic tissue. PVP is also associated with a longer operative time than TURP.

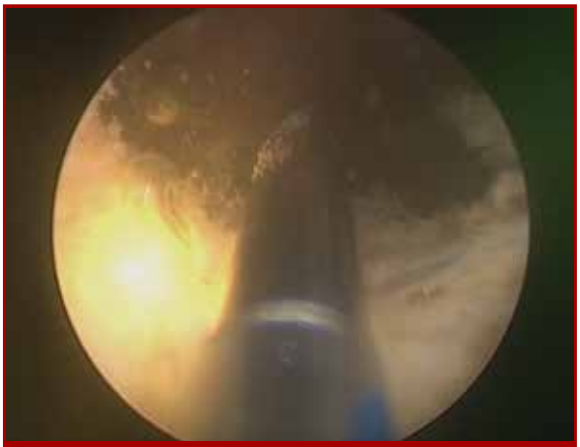

Fig 2. Photoselective vaporisation of the prostate (Greenlight laser) (Personal collection of Dr Peter KF Chiu)

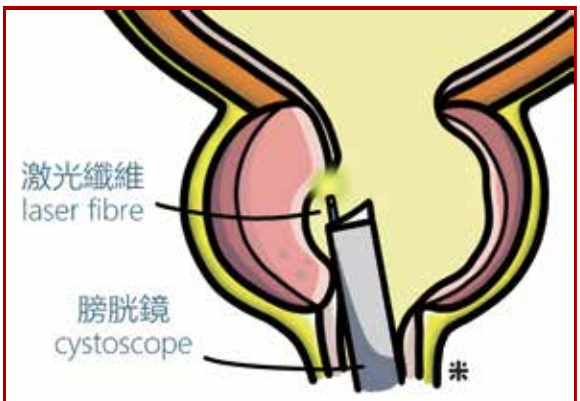

Fig 3. Greenlaser vaporisation of the prostate (Reproduced with permission from SH Ho Urology Centre website urologycentre.com.hk)

ENUCLEATION

Open prostatectomy is the enucleation of the prostate in an open manner. It was traditionally performed for a prostate larger than 80ml in volume and with coexisting large bladder stone or diverticulum. It is associated with lower re-treatment rate compared with conventional TURP. In contrast, enucleation is more invasive and is associated with higher incidence of haemorrhage, the need for blood transfusion, longer catheterisation time and increased incidence of urinary incontinence. Endoscopic enucleation is to replicate the technique of open prostatectomy endoscopically, by removing the prostatic adenoma while sparing the capsule. Common energy source include Holmium: YAG laser, Thulium: YAG laser and bipolar electrode. Meta-analysis has shown that laser and bipolar enucleation of the prostate carry similar efficacy and operative time compared with open prostatectomy. They also carry better complication profiles with regard to bleeding and transfusion, catheterisation time and re-treatment rate of around 4% in 8 years[4]. However, the incidence of urinary incontinence, urethral stricture, retrograde ejaculation and sexual dysfunction are similar[4]. Compared to conventional TURP, endoscopic enucleation is associated with longer operative time, a steeper learning curve, and increased risk of bladder injury; the procedure requires a morcellator[6].

Fig 4. Enucleation of prostate adenoma using Bipolar TURP loop (Personal collection of Dr Peter KF Chiu)

WATER JET ABLATION

The water jet ablation technique uses a thin jet of pressurised water to cut soft tissue. Aquablation using the AquaBeam system and high-velocity saline to perform hydrodissection under an ultrasound-guided robotic system. The procedure can be performed under general or regional anaesthesia. The user determines the area to be treated under ultrasound-guidance. The semi-automated ablation process takes 5-10 minutes to perform, irrespective of prostate size. Hemostasis is achieved by TURP loop electrocautery followed by balloon catheter traction. Compared with conventional TURP, an RCT has shown that Aquablation has similar therapeutic efficacy, but less anejaculation[7,8]. However, it also reported a higher incidence of haemorrhage, blood transfusion requirement and re-operation rate for hemostasis was observed in Aquablation compared with conventional TURP [7,8].

Fig 5. Aquablation device inserted to the prostatic urethra with the cystoscopic view (Personal collection of Dr Peter KF Chiu)

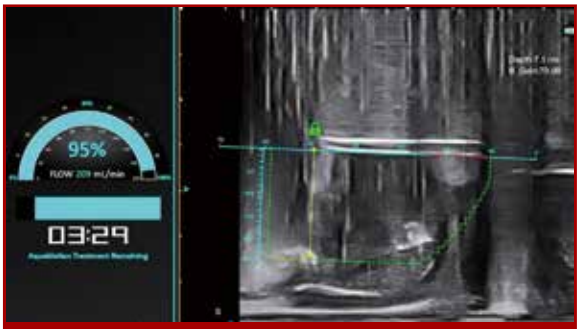

Fig 6. Real-time ultrasound showing hydrodissection of prostate in Aquablation (Personal collection of Dr Peter KF Chiu)

CONVECTIVE WATER VAPOUR TREATMENT

Rezūm is the currently available system that uses radiofrequency power to heat water, which converts into steam at 103°C. A needle is inserted into the prostate endoscopically and hot steam is delivered to cause necrosis. The needle is then repositioned several times to treat all desired areas. Rezūm can be performed as a day case procedure under local anaesthesia or sedation. Compared with conventional TURP, Rezūm carries an acceptable therapeutic efficacy. The procedure preserves ejaculatory and erectile function, and has a slightly higher though acceptable re-treatment rate of 4.4% in 5 years[9]. However, the procedure is not desirable for larger prostates > 80g. Treated patients need to be catheterised for an average duration of 4 days (usually 3-7 days depending on prostate size) post-surgery.

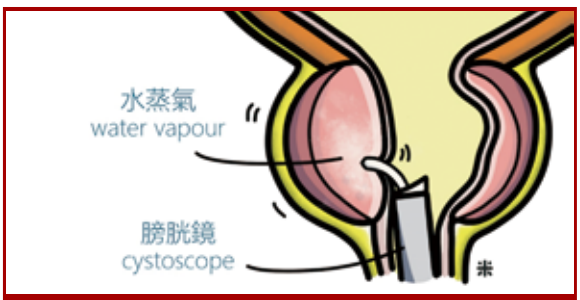

Fig 7. Steam injection (Rezūm) (Reproduced with permission from SH Ho Urology Centre website urologycentre.com.hk)

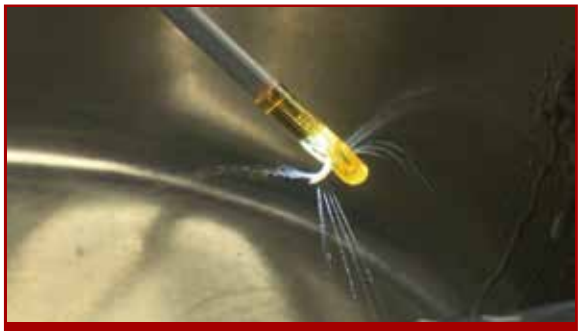

Fig 8. Demonstration of ex-vivo water jet testing at the tip of Rezūm device (Personal collection of Dr Peter KF Chiu)

Fig 9. Cystoscopic view of Rezūm needle inserted into prostate adenoma and steam being injected (Personal collection of Dr Peter KF Chiu)

PROSTATIC URETHRAL LIFT

Prostatic urethral lift is a technique where a permanent suture-based implant is inserted to retract the lateral lobes of the prostate for creating a continuous anterior channel. The implant is composed of nitinol, polyester suture and stainless steel. The prostatic urethral lift can be performed as a day procedure under local anaesthesia with or without sedation. Compared with conventional TURP, it preserves ejaculatory and erectile function and has a slightly higher but acceptable re-treatment rate. However, it is not desirable in large prostate. Compared with Rezūm, the prostatic urethral lift does not require catheterisation after the operation, but carries a higher re-treatment rate of 14% in 5 years[10].

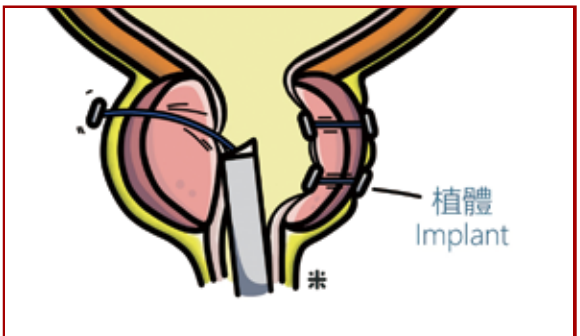

Fig 10. Prostatic urethral lift (Urolift) (Reproduced with permission from SH Ho Urology Centre website urologycentre.com.hk)

Fig 11. Urolift device (Excerpted from Urolift website www.Urolift.com)

PROSTATIC STENT

Memokath and Allium prostatic stents are commonly used in patients unfit for procedures involving general or regional anaesthesia. Memokath is a thermal-expandable non-epithelialising nitinol prostatic stent with a memory-shape effect. It expands when the temperature is above 55°C and shrinks when the temperature is below 10°C. Allium triangular prostate stent is a self-expandable, triangular urethral stent with a trans-sphincteric wire. It is composed of nitinol coated with co-polymer to prevent mucosal hyperplasia and encrustation. Nonetheless, there is currently no high-quality randomised long-term data comparing prostatic stents with other BPO surgical treatments.

Fig 12. Prostatic Memokath metallic stent (Excerpted from Memokath website https://pnnmedical.com/memokath/)

Fig 13. Allium covered prostatic stent (Excerpted from Allium Medical website https://www.allium-medical.com/)

TEMPORARY IMPLANTABLE NITINOL DEVICE

iTIND is a temporary implantable nitinol device, to compress obstructive prostate tissue, causing ischemic necrosis. It is placed in the prostatic urethra transurethrally and removed after five days. It is a quick minimally invasive procedure that has been shown to be safe and feasible with promising early results.

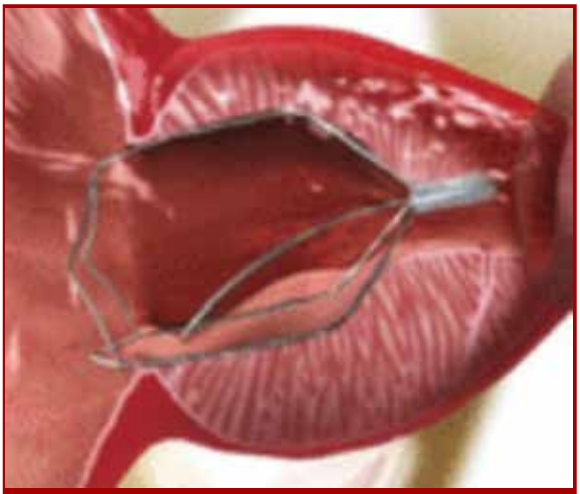

Fig 14. iTind temporary implantable nitinol device (Excerpted from itind website https://www.itind.com/)

PROSTATIC ARTERY EMBOLISATION

Prostatic artery embolisation (PAE) was first performed for benign prostate obstruction in 2000. Interventional radiologists perform super-selective cannulisation of the prostatic artery, followed by embolisation with microparticles, resulting in ischemic necrosis and shrinkage of the organ. CT-angiogram is required to be performed prior to the procedure, as up to 30% of patients may not be a suitable candidate and 40% have dual prostatic arteries[11,12]. PAE can be performed as day surgery under local anaesthesia with high technical success rate of embolisation. Embolisation may shrink the prostate volume by around 25% and it is associated with fewer risks of ejaculatory and erectile dysfunction[13,14]. It is usually reserved for patients with BPH with or without refractory urinary retention, with higher surgical risks and/or who wish to preserve their erectile and ejaculatory function. Compared with conventional TURP, PAE is associated with less prostate volume reduction, longer operative time, and higher re-treatment rate of 15% at one year[13,14]. Rare potential complications of PAE include post-embolisation syndrome, ischemia of penis and bladder, as well as radiation and contrast nephropathy. This procedure is contraindicated in patients with contrast allergy, renal impairment, and vascular disease involving the iliac artery and femoral artery, and in those with previous major pelvic surgery.

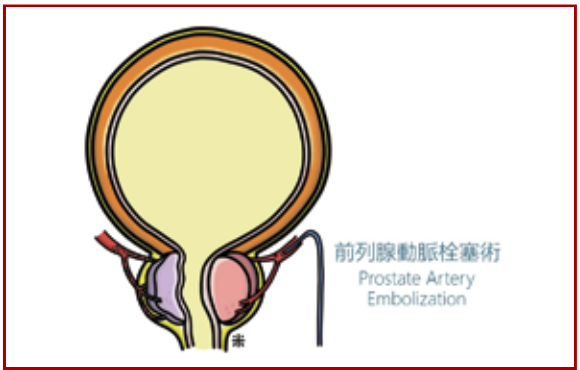

Fig 15. Prostate Artery Embolisation (PAE) (SH Ho Urology Centre website urologycentre.com.hk. Reproduced with permission from SH Ho Urology Centre)

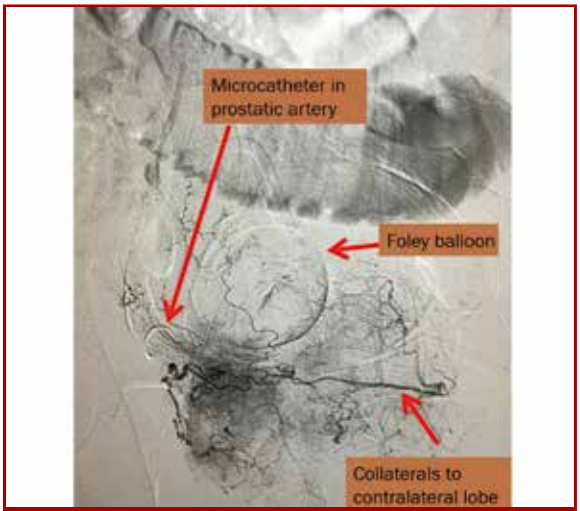

Fig 16. Fluoroscopic view of pelvic artery angiogram performed during PAE (Personal collection of Dr Peter KF Chiu)

CONCLUSION

Conventional TURP has been extensively studied and proven to have excellent long-term efficacy in the treatment of moderately enlarged prostate. However, it is a major procedure and not without significant risks. With recent advances in technology in an era of personalised medicine, a number of alternative surgical treatments are available, and we can tailor our surgical plan individually, taking into consideration the clinical need and patients' preferences.

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "New Advances in Surgery for Benign Prostatic Hyperplasia" by Dr Timothy CK NG and Dr Peter KF CHIU 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 28 February 2022. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

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

1. **Lower urinary tract symptoms in middle-aged men are all caused by benign prostate enlargement.**
2. **Surgery is indicated in patients with refractory retention of urine and obstructive uropathy due to benign prostate obstruction.**
3. **Prostate size is an important factor to consider when choosing between different surgical treatments.**
4. **Compared to conventional TURP, photoselective vaporisation of the prostate has a higher incidence of hemorrhage and TUR syndrome.**
5. **Endoscopic enucleation has a higher retreatment rate compared with conventional TURP.**
6. **Aquablation has a higher incidence of bleeding compared with conventional TURP.**
7. **Rezūm can be performed under local anaesthesia.**
8. **Prostatic urethral lift can be performed under local anaesthesia.**
9. **Memokath is a thermosensitive shape memory stent.**
10. **Prostatic artery embolisation is a therapeutic option for BPH patients who are not candidates for surgical treatment.**

ANSWER SHEET FOR FEBRUARY 2022

Please return the completed answer sheet to the Federation Secretariat on or before 28 February 2022 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

New Advances in Surgery for Benign Prostatic Hyperplasia

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Name (block letters):_____ HKMA No.: _____ CDSHK No.: _____

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Contact Tel No.:_____ MCHK No. / DCHK No.: _____(must fill in)

Answers to January 2022 Issue

Artificial Intelligence in Allergy Care

1. F 2. F 3. F 4. T 5. T 6. T 7. F 8. F 9. T 10. T

Detection of Prostate Cancer: Do We Have Anything Better than Prostate Specific Antigen (PSA)?

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INTODUCTION

Since the discovery of prostate specific antigen (PSA) in the 1970s[1] and its translation into clinical practice in prostate cancer screening by Catalona et al in 1991[2], there has been, over the course of the past 3 decades, a gradual increase in the incidence of prostate cancer. Prostate cancer was the third commonest male cancer in Hong Kong with 2,532 new cases diagnosed in the year 2019[3]. There was a double increase in the cancer incidence compared with early 2000s (Fig.1[4]). Although the incidence has been increasing, the mortality rate from the cancer has remained similar in the past 15 years, which could be attributed to a widespread usage of PSA.

PSA is a 34kD glycoprotein produced by prostate epithelial cells. It forms part of the semen coagulum, which is important in semen liquefaction and male fertility[5]. PSA is an organ-specific but not cancer-specific biomarker. It can be elevated when there is a change in the prostate architecture, such as benign prostate hyperplasia, prostatitis, recent prostatic procedure or prostate cancer. Traditionally, we are using 4.0 ng/mL as a cut-off for further investigation such as prostate biopsy. However, Catalona et al demonstrated its lack of specificity within 4.0 to 10.0 ng/mL in diagnosing prostate cancer. He found that only 25% of cases within this range were positive for malignancy[6]. Even if prostate cancer is found, some of these cancers belong to clinically insignificant prostate cancer which is indolent and does not cause harm during the patient's lifetime. Using PSA alone as a cancer detection tool may result in unnecessary investigation, over-diagnosing indolent cancer and thus creating superfluous patient anxiety.

Urologists have been using various PSA derivatives such as PSA velocity, PSA density and free to total PSA ratio (f/t PSA) in order to compensate for the low specificity of PSA. With rapid advancement in technology in recent years, different new tools including blood, urine and radiological tests have been introduced in the Urology field and have shown promising results.

PROSTATE HEALTH INDEX (PHI)

PHI is a novel blood test to predict overall and high-grade prostate cancer detection in biopsy. It is a mathematical formula (p2PSA/fPSA x √PSA) that combines three PSA isoforms (total PSA, free PSA and p2PSA) into a single score that can predict cancer risk. It is based on the theory that cancerous cells secreted more p2PSA and fewer fPSA; hence a higher PHI value would indicate a higher risk of prostate cancer.

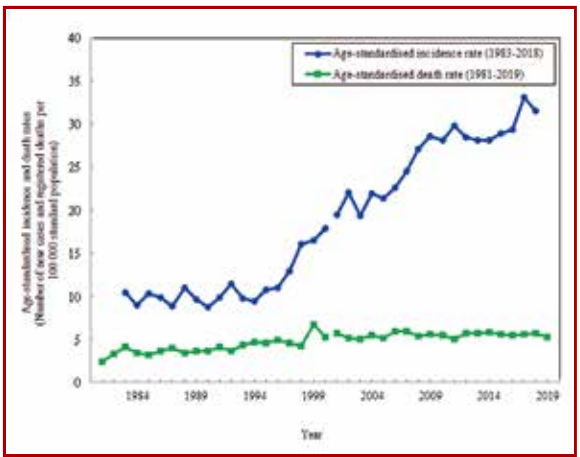

Fig 1. Age-standardised incidence and death rates of prostate cancer, 1981 – 2019 (Exerpted from Centre for Health Protection)

PHI was first applied by Catalona et al in USA in 2011. He demonstrated the superiority of PHI in the overall diagnosis of prostate cancer and high-risk prostate cancer than PSA alone and f/t PSA. A PHI reference guide with corresponding prostate cancer risk (Table 1) was developed, and applied mainly to Caucasian men with PSA 2-10 ng/mL and normal digital rectal examination (DRE) [7].

In the Asia-pacific region, the Chinese University of Hong Kong (CUHK) has conducted various PHI studies in the past decade. A new PHI reference range has been developed for Asian men with PSA 2-10 ng/dL and normal DRE (Table 1). Using PHI 40 in European men and 30 in Asian men, around 50% of biopsies and 30% of clinically insignificant prostate cancer diagnoses could be avoided[8].

The PHI test has been introduced in the Hospital Authority since 2016 and can be used in patients with PSA between 4 and 10 ng/mL. Another study done in CUHK showed that PHI could also be applied in Hong Kong Chinese men with PSA 10-20 ng/mL[9] and showed promising results. It is a useful triage test, enabling the clinician to counsel the patient whether a further biopsy is necessary.

Table 1. PHI reference table and risk of prostate cancer (Adapted from references 7 and 8)

Probability of prostate cancer by PHI in Caucasian patients with PSA 2-10 ng/mL (Catalona et al.)[7]				
PHI	0 – 24.9	25.0 – 34.9	35.0 – 54.9	> 55.0
Risk of prostate cancer (%)	11%	18%	33%	52%
Probability of prostate cancer by PHI in Chinese patients with PSA 2-10ng/mL (Chiu PK, Ng CF et al.)[8]				
PHI	0 – 24.9	25.0 – 34.9	35.0 – 54.9	> 55.0
Risk of prostate cancer (%)	5%	7.5%	26%	44%
Risk of high grade prostate cancer (%)	1%	1.9%	13%	30%

URINE PROSTATE CANCER ANTIGEN 3 (PCA3)

PCA3 is a segment of non-coding messenger RNA from chromosome[9], which is highly expressed in prostate cancer cells, around 100-fold greater than benign prostate tissue[10]. It can be found in urine and provides a PCA3 score (PCA3-mRNA/PSA-mRNA). Several studies have demonstrated the superiority of the PCA3 score over PSA alone in prostate cancer diagnosis. The test requires a collection of 30 ml voided urine after a 6-stroke attentive prostatic massage. Deras et al found that using a cut-off value of 35, the PCA3 score carried a sensitivity and specificity of 55% and 75% respectively in having positive findings in prostate biopsy[11]. The limited availability of the PCA3 test in Asia and the inconvenience of prostatic massage before urine collection have limited its use in Hong Kong.

URINE SPERMINE TEST

Spermine is involved in the secretory function of prostate epithelial cells and is highly concentrated in normal prostate tissue. It is found that urine spermine is lower in both prostate cancer tissue and the urine of prostate cancer patients. A recent study led by CUHK and the Baptist University of Hong Kong has shown the usefulness of urine spermine in elevating the risk of developing prostate cancer in patients with PSA between 4 to 20 ng/mL. Patients with normalised spermine less than 0.72 have a three-fold increase in prostate cancer risk and a 3.5-fold increase in high-risk prostate cancer. Their team has also proposed a four-factor Spermine Risk Score, which consists of spermine, prostate volume, PSA level and DRE findings. Using a cut-off score of 7, around 37% of biopsies and 24% of clinically insignificant prostate cancer diagnoses could be avoided[12]. Urine spermine test is a convenient and non-invasive test which avoids blood taking or DRE before urine collection. The test has been commercially available in Hong Kong since 2021.

MULTI-PARAMETRIC MRI (mpMRI) PROSTATE

mpMRI consists of four sequences: T1-weighted and T2-weighted images, diffusion-weighted images (DWI) and dynamic contrast-enhanced imaging (DCEI). Radiologists and urologists are currently using Prostate Imaging Reporting and Data System (PIRADS) version 2.1 in interpreting and reporting MRI images. The images and prostate lesions are categorised using a PIRADS scoring system, ranging from 1 to 5, in predicting the risk of prostate cancer. A recent meta-analysis showed that the higher the PIRADS score, the higher the chance of detecting a clinically significant prostate cancer (See Table 2)[13].

Table 2. Cancer detection rate at different PIRADS level (Adapted from Reference 13)

	PIRADS 1	PIRADS 2	PIRADS 3	PIRADS 4	PIRADS 5
CDR per lesion *	2%	4%	20%	52%	89%
CDR per patient #	6%	9%	16%	59%	85%

CDR: cancer detection rate
* Number of lesions with clinically significant prostate cancer divided by the overall number of lesions in a certain PI-RADSv2.1 assessment category
# Number of patients with clinically significant prostate cancer divided by the overall number of patients in a certain PI-RADSv2.1 assessment category

We are currently stepping into an era of "MRI first before biopsy" based on two landmark studies. PROMIS trial in 2017 showed that for men with PSA up to 15 ng/mL without prior biopsy, using MRI as a triage tool allowed 27% of patients to avoid a primary biopsy and 5% fewer clinically insignificant prostate cancer. MRI prostate has better sensitivity and higher negative predictive value than systematic biopsy[14]. PRECISION trial in 2018 recruited men with PSA up to 20 ng/mL without prior biopsy. It compared the diagnostic accuracy between traditional systematic biopsy versus MRI prostate then targeted biopsy if the lesion was greater or equal to PIRADS 3 (no biopsy if lower than PIRADS 3). It showed that MRI with targeted biopsy could achieve 12% higher CDR for clinically significant prostate cancer and 13% lower CDR for insignificant cancer[15]. Using an MRI-first protocol can avoid unnecessary biopsy and thus can reduce biopsy-related complications such as infection, bleeding and urinary retention.

WHOM SHOULD WE PICK FOR PROSTATE CANCER SCREENING?

The ERSPC trial updated in 2019 showed that prostate cancer screening with PSA (for asymptomatic men) could reduce the cancer-specific mortality by 20%, and the number needed to screen to reduce one cancer death was reduced to 570, which was comparable to breast cancer screening[16]. However, screening itself could lead to over-diagnosis of early stage prostate cancer and thus over-treatment. Healthcare providers (HCPs) should bear in mind that PSA screening is a shared decision making with the patient and HCPs should explain the potential advantages and disadvantages clearly.

The Hong Kong Urological Association (HKUA) has recommended PSA screening in the following conditions.

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Age group	Recommendation
Less than 40 years old	Not recommended
40 to 54 years old	Regular PSA screening if positive family history
55 to 77 years old	PSA screening after a shared decision making
More than 77 years old or life expectancy less than ten years	Not recommended

SUMMARY

PSA screening can reduce prostate cancer mortality, but PSA screening should be applied to the appropriate patient after shared-decision making between the doctor and the patient. In men with elevated PSA, the use of Prostate health index (PHI), Urine spermine test and/or MRI prostate in Hong Kong helps to triage patients to higher and lower risk groups. Such risk stratification could reduce unnecessary prostate biopsies, increase the diagnostic yield of clinically significant prostate cancer, and eventually improve the risk-benefit ratio of prostate cancer screening.

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"TREXIT": A Shift from Transrectal to Transperineal Prostate Biopsy

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INTRODUCTION

Despite the advancement in prostate imaging and biomarkers such as MRI and the prostate health index (PHI) test to aid prostate cancer diagnosis, a prostate biopsy is still necessary to diagnose prostate cancer based on histological proof. Transrectal ultrasound-guided prostate biopsy (TRUS biopsy) performed under local anaesthesia has been the gold standard in prostate biopsy since its introduction in the 1980s. In the recent decade, the transperineal route has been advocated for prostate biopsy because of its low sepsis risk. The term "TREXIT" has surfaced in recent years, a term representing "exit from transrectal prostate biopsy".

HISTORY OF PROSTATE BIOPSY

The first reported prostate biopsy was performed in 1926 with an open transperineal method under general anaesthesia[1]. The technique later evolved into transperineal needle aspiration as suggested by Ferguson and transperineal punch biopsy as suggested by Barringer. Another school of thought supported transrectal biopsy, which was initially performed with a finger-guided method in 1937. Along with the development of ultrasound technology and transrectal ultrasound probe, transrectal ultrasound-guided prostate biopsy started to gain popularity since 1980s[2].

TRANSRECTAL PROSTATE BIOPSY

Having been a gold standard for prostate biopsy for more than 30 years, TRUS biopsy is commonly performed in Urology centres. TRUS biosy is done under local anaesthesia with a peri-prostatic nerve block. Biopsy cores should be taken from the prostate apex to base bilaterally, covering both peripheral zone and any suspicious lesion in ultrasound or digital rectal examination. One should aim more laterally in the peripheral zone[3]. (Fig. 1)

There is no standard protocol with regard to the number of prostate biopsy cores taken. Conventionally, 10-12 cores of systematic (i.e. location by location) biopsy are taken in each prostate biopsy session. Systematic review by Eichler et al. in 2006 suggested that 12-core biopsy is superior to 6-core biopsy with an improvement of 30% in cancer detection rate from the former[4]. The benefit of increasing systematic biopsy cores to 18-24 in improving cancer detection is limited, and it is associated with more adverse events[4]. Some even suggested saturation biopsy (> 20 cores) and various nomograms to improve the cancer detection rate, such as Vienna nomogram, which guides the adjustment of the number of cores based on prostate size and the age of patient.

Fig 1. Setting for transrectal prostate biopsy. The patient will be in a left lateral position. (Personal collection)

DRAWBACKS OF TRANSRECTAL PROSTATE BIOPSY

Post-TRUS biopsy sepsis is always the most fearful complication even with antibiotic prophylaxis. Post-TRUS biopsy sepsis can be a life-threatening event with significant morbidity and mortality. Patients usually require a prolonged hospital stay and a full course of intravenous antibiotics. According to Loeb et al., infection-related complications, namely high fever > 38.5°C, prostatitis, and epididymitis, happened in 2% of patients who underwent TRUS biopsy[5]. Other TRUS biopsy complications include haematuria (14.5%), haematospermia (37.5%), rectal bleeding (3%) and urinary retention (0.2%). Furthermore, it is difficult to sample anterior and apical prostate due to the direction of the biopsy needle, resulting in inadequate sampling and under-diagnosis or under-staging of the cancer.

We are facing more drug-resistant micro-organisms worldwide, especially in the gastrointestinal tract. One local review suggested the prevalence of rectal quinolone-resistant micro-organisms was around 40%[6]. Therefore, regimens involving combination of antibiotics are common in Hong Kong. Ways have been suggested to reduce the sepsis complication, including rectal swab culture with targeted antibiotics, and rectal preparation with betadine. However, there is no strong evidence to prove effectiveness of these measures in reducing sepsis.[10]

TRANSPERINEAL PROSTATE BIOPSY

With the aforementioned drawbacks of the transrectal route, there is a re-emergence of transperineal prostate biopsy. Early studies reported their experience on transperineal route biopsy under general anaesthesia as a day procedure. The patient was in a lithotomy position. Transrectal ultrasound was used to visualise the prostate (Fig. 2). A grid was applied at the perineum and 12-24 biopsy cores were taken at different spots in the grid[7]. There are also different types of transperineal biopsy guides, such as PrecisionPoint™ Transperineal Access System (Fig. 3), SureFire Transperineal Needle Guide (Fig. 4), etc. The technique of free-hand transperineal prostate biopsy (Fig. 5) without grid is becoming popular[13]. Local anaesthesia is also found to be feasible with the periprostatic injection of local anaesthesia[7].

Without breaching the rectal mucosa, transperineal prostate biopsy in fact can be considered a clean procedure[8]. Quinolone may not be necessary as skin flora becomes the main pathogen. Papdjonovic et al. reported his experience of zero sepsis after performing 577 transperineal prostate biopsy with a single dose of intravenous 2gram cephazolin prophylaxis on induction of general anaesthesia. Chiu et al. reported 0.3% sepsis rate after one dose of pre-biopsy oral Co-amoxiclav in Hong Kong[13]. Other reported complications include acute retention of urine (1.2%) and prostatitis (0.2%) [9].

Fig 2. Setting for transperineal prostate biopsy. The patient will be in lithotomy position. (Personal collection)

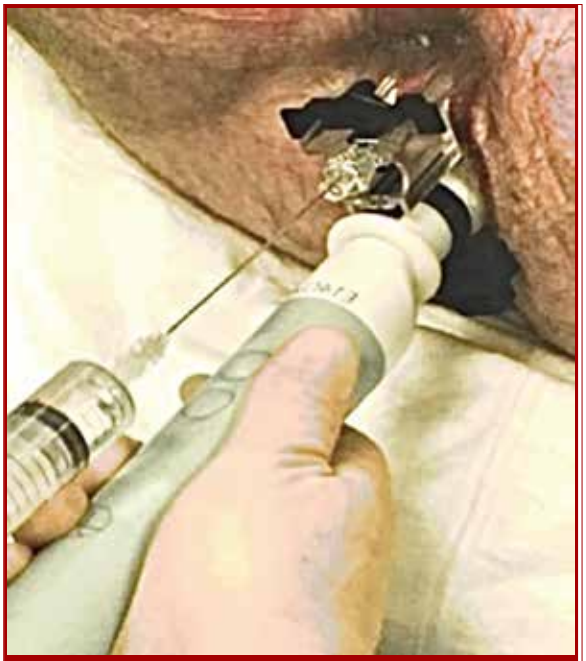

Fig 3. PrecisionPoint™ Transperineal Access System. (Personal collection)

Fig 4. SureFire Transperineal Needle Guide. (Personal collection)

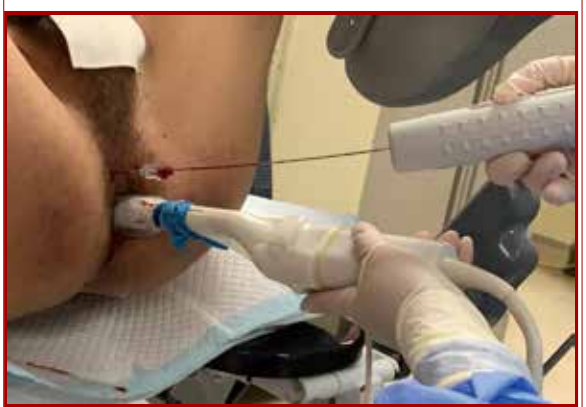

Fig 5. Free hand transperineal prostate biopsy with a needle trocar. (Personal collection)

COMPARING TRANSRECTAL AND TRANSPERINEAL PROSTATE BIOPSY

A recently published longitudinal cohort study[10] compared the sepsis rate of conventional transrectal biopsy, transrectal biopsy with rectal swab culture-guided antimicrobials, and free-hand transperineal biopsy. For the conventional transrectal group, 12-core systematic biopsy was taken under ultrasound guidance. Pre-biopsy ciprofloxacin and a single dose of intravenous gentamicin and metronidazole were administered. The second group had a prior rectal swab. Oral Fosfomycin would be given if there is no drug-resistant bacteria. Otherwise, intravenous amikacin and metronidazole would be administered. For the transperineal group, Ginsburg protocol was followed for the number of biopsy cores. Generally 18-24 cores were taken. A single dose of oral co-amoxiclav was given before the procedure if the biopsy was done under local anaesthesia. Otherwise intravenous co-amoxiclav will be given on induction of general anaesthesia.

Despite more biopsy cores taken in the transperineal group, the post-biopsy sepsis rate was higher in the transrectal group than the transperineal group. The sepsis rate was 2% in the conventional transrectal group compared to 2.2% in the prior rectal swab group. It was only 0.4% in the transperineal group. Even with rectal swab-guided antimicrobials, the sepsis risk was higher in those who had drug-resistant bacteria than those who did not (9.1% vs 1.1%). Interestingly, recent travelling to other countries was associated with increased incidence of ciprofloxacin-resistant rectal flora.

In 2021, for the first time, the European Association of Urology (EAU) guideline recommended transperineal route as the preferred route for prostate biopsy[3]. Besides the benefits mentioned above, transperineal prostate biopsy can better sample the anterior and apical parts of the prostate than transrectal biopsy, although one meta-analysis showed comparable cancer detection rates[11]. Performing transperineal prostate biopsy can also save medical costs as there is no need for rectal swab culture and minimal admission for infection; only a single antibiotic agent is needed. In a cost-analysis study in the U.K.[12], the cost per patient for non-elective readmission was less in the post-transperineal biopsy group. (GBP £2,225 versus GBP £1,758)

In Hong Kong, the majority of Urology Centres has switched to transperineal prostate biopsy in recent 1-2 years. Hopefully we can eliminate post-prostate biopsy sepsis altogether.

CONCLUSION

With the emergence of drug-resistant bacteria, switching from transrectal to transperineal prostate biopsy would benefit our patients by reducing post-biopsy sepsis risk. Furthermore, there are benefits of lower readmission rate and of reduction of hospital stay costs. Additionally, there is potential benefit of better anterior and apical prostate sampling. TREXIT is a global trend to improve our quality of care.

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References: 1. ERLEADA™ Hong Kong prescribing information. **2.** Chi KN, et al. N Engl J Med. 2019;381(1):13-24. **3.** Chi KN, et al. N Engl J Med. 2019;381(1):13-24. Supplementary information.

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Androgen Deprivation Therapy: Types, Differences and How to Choose

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INTRODUCTION

Since the initial discovery in 1941 that castration reduces acid phosphatase serum levels in men with metastatic prostate cancer[1], androgen deprivation therapy (ADT) has been foundational in the management of advanced prostate cancer. To achieve androgen deprivation, one can decrease the production of androgen or inhibit the action of androgen at the receptor level. The objective of this article is to review the types of standard ADT that primarily decrease testosterone secretion, which include bilateral orchidectomy, and luteinising hormone releasing hormone (LHRH) agonists and antagonists.

BACKGROUND

In recent years, newer androgen pathway inhibitors that further decrease androgen activity in combination with standard ADT have been shown to improve prostate cancer survival. While newer agents can augment the efficacy, standard ADT remains essential. Furthermore, ADT is indicated not only for patients with metastatic prostate cancer, but also for patients with locally advanced prostate cancer who are unfit for local radical treatments and for those with intermediate or high-risk localised prostate cancer who require ADT as an adjuvant treatment to radiotherapy.[2,3] Starting ADT for locally advanced or metastatic prostate cancer improves cancer-specific survival and delays disease progression. ADT has been shown to reduce the incidence of serious and morbid complications in carefully selected patients such as cord compression, pathological fractures, ureteric obstruction and retention of urine.[4]

TYPES, ADMINISTRATION and FEATURES

So far, there is no high-level evidence in favour of a specific type of ADT, with the exception of impending spinal cord compression, where either surgical castration by bilateral orchidectomy or the use of LHRH antagonists, is recommended.

1. Bilateral orchidectomy

Although the original form of castration by bilateral orchidectomy is still considered a primary treatment, surgical castration has gradually fallen out of favour since the less invasive options of LHRH agonist and antagonist became subsidised and readily available in public hospitals in Hong Kong.

Both bilateral orchidectomy and subcapsular pulpectomy have been reported as viable options with similar efficacy.[5] Both procedures are quick with few complications and can be done under local or general anaesthesia. The production of testosterone at the testes is directly removed. As the biological half-life of serum testosterone is only between 30 to 60 minutes,[6] castrate levels of testosterone can be quickly achieved within 3 to 12 hours following surgery.

Bilateral orchidectomy offers unique advantages: it is the most effective way to achieve castrate levels to relieve metastasis-related symptoms. It is a quick, relatively low-cost option that can spare patients from repeated administration of LHRH agonist or antagonist. It is particularly suitable for patients with impending spinal cord compression, with metastatic prostate cancer requiring long-term ADT, and/or with poor drug compliance. The disadvantages of orchidectomy include its irreversible nature and the psychological impact of losing both testes.

2. LHRH agonist

Two types of medical castration are currently available - LHRH agonist and LHRH antagonist. The principle mechanism of LHRH agonist is chronic stimulation and down-regulation of LHRH receptors, which subsequently suppresses the secretion of luteinising hormone (LH) and follicle-stimulating hormone (FSH) leading to a decrease in the production of testosterone in the testes.

As such, the LHRH agonist takes two to four weeks to reach castrate levels. The initial increase in LH and FSH following the first injection has historically raised concern over a flare-up phenomenon anticipated to last for approximately 1 to 2 weeks. During the flare-up phenomenon, potential local effects such as worsening of lower urinary tract symptoms, retention of urine, ureteric obstruction and systemic progression leading to cord compression by vertebral metastases, pathological fracture and thrombogenic events have been described.[7] However, a recent review of evidence did not support concerns of such detrimental effects of testosterone flare-up such as significantly increased PSA, disease progression or adverse events.[8] Nonetheless, anti-androgens, such as bicalutamide or flutamide, are routinely prescribed concurrently with the LHRH agonist to avoid such potential flare-up phenomenon, especially in men with extensive vertebral metastases.

Examples of LHRH agonists include leuprorelin, goserelin and triptorelin. Preparations available include implants, powder and microspheres. Leuprorelin and goserelin implants are ready to use, whereas leuprorelin microspheres, leuprorelin powder and triptorelin powder require reconstitution. In particular, leuprorelin powder (Eligard®) needs to be prepared cautiously while the patient is in the treatment room as it needs to be administered shortly after reconstitution (Table 1)[9].

In May 2020, the European Medicine Agency's safety committee issued recommendations for Eligard®, following reports of inadequate mixing during reconstitution and incorrect injection, both resulting in underdosing and lack of efficacy.[10]

A wide range of dosing frequency is available, and it has been reported that prostate cancer patients prefer 3- or 6-monthly dosing. This aligns with the monitoring frequency recommended in the European Association of Urology and has been shown to result in reduced annual costs.[9]

Table 1: Practical differences among the LHRH agonists for prostate cancer

	Leuprorelin -		Goserelin-	Triptorelin
Trade name	Eligard	Enantone	Zoladex	Diphereline
Preparation	Reconstitution	Reconstitution	Ready to use	Reconstitution
	Two syringes to mix	Prefilled syringe	Prefilled syringe for implants	Glass vial for powder & ampoule for solvent
Adminstration	Subcutaneous: < 30 mins of reconstitution	Subcutaneous: Immediately after reconstitution	Subcutaneous: any time	Subcutaneous/ Intramuscular
Dosing freqeuncy	3-,6-monthly	1-,3-,6-monthly	1-,3-monthly	1-,3-,6-monthly
Storage	Refrigerate, in original package	< 25°C, in original package; do not refrigerate	< 25oC	< 25oC

3. LHRH antagonist

LHRH antagonists directly block the LHRH receptors in the pituitary gland. It typically takes three days for testosterone to reach castrate levels. The injection form of the LHRH antagonist, degarelix, requires an induction dose of 240 mg followed by monthly 80 mg maintenance injections subcutaneously. The requirement of monthly degarelix administration means that the overall cost is comparatively more costly. Studies have shown a higher rate (40%) of painful injection-site reaction and chills (4%) following administration compared to intramuscular leuprorelin.[11] Reactions commonly occur at the first induction dose. Expert opinion suggested that injection-site reaction may be lowered to 10% by injecting degarelix as a deeper subcutaneous injection by trained administers, educating patients on avoiding irritation of the injection site, hygiene, ice therapy and pain medication.[12]

A new oral LHRH antagonist alternative, relugolix, was recently featured in a large phase 3 randomised controlled trial (RCT), the HERO trial. The trial randomised men with advanced prostate cancer to relugolix or 3-monthly intramuscular leuprorelin in a 2:1 ratio for 48 weeks. It demonstrated that relugolix produced sustained testosterone suppression to castrate levels throughout the trial period in 97.6% of patients, superior to 88.8% of patients on intramuscular leuprorelin.[13] The advantage of replacing painful regular injections with oral medication would provide patients with an alternative option in long-term medical castration. Relugolix also resulted in very low nadir testosterone levels and this may be associated with improved clinical outcomes and has prognostic value for time to castration-resistant progression.[14] One potential disadvantage in some patients is drug compliance, when treatment is given orally rather than administered by injection at clinics. Further studies are required to determine whether the properties of LHRH antagonists can translate to such clinical advantages.

4. Monitoring and side effects

Monitoring

Monitoring serum testosterone levels after initiating LHRH agonist or antagonist should be done to confirm if castration is adequate. Those who fail to achieve castrate level of testosterone with injections may need to be converted to orchidectomy or maximal androgen blockade using additional anti-androgens.

General side effects

While being the cornerstone of advanced prostate cancer treatment, ADT is well known to be associated with multiple side effects. Common side effects include hot flashes, loss of libido, erectile dysfunction, fatigue, mood changes and osteoporosis but there are also potential risks of metabolic syndrome, cardiovascular morbidity and cognitive decline.[15]

Cardiovascular risk

Cardiovascular mortality is the leading non-cancer cause of death for patients with prostate cancer.[16] In a large cross-sectional study, the prevalence of a metabolic-like syndrome was shown to be higher in men on ADT compared with men not receiving ADT.[17] Effects projected from observational studies include an increase in blood cholesterol, impaired fasting blood glucose, diabetes[18], higher body mass index and increased abdominal obesity. These factors may increase the risk of cardiovascular (CV) morbidity and mortality. There has been conflicting evidence on the causal relationship between ADT and CV mortality. Several meta-analyses based on RCTs showed no association with CV mortality.[19] However, when baseline cardiac comorbidity was considered in a recent meta-analysis of observational data, a consistent link between ADT and fatal and non-fatal CV disease was found.[20] Understandably some of these effects are from a combination of ageing and ADT especially when prostate cancer is diagnosed more commonly in the elderly. When adjusted for age at diagnosis and comorbidities, ADT exposure increases the risks of cardiovascular disease (CVD) and diabetes most notably in men older than 75 years and especially in

those with other comorbidities.[21] Large observational studies also suggest CVD risk was increased the most during the first six months of ADT in men who had pre-existing CVD, and the increase was higher in men on LHRH agonist compared with those who underwent orchidectomy.[22]

These concerns have led to the FDA warning and consensus paper from the American Heart Association, cancer societies and urological associations[23] mandating product safety information addressing the potential increased risk of adverse CVD.

LHRH antagonists have been suggested to be associated with less CV morbidity compared to LHRH agonists.[24] In a pooled analysis based on six RCTs, subgroup analysis of men with pre-existing CV disease had twice the incidence of CV events after one year of ADT when treated with an agonist rather than an antagonist. More recently in the HERO trial, as a secondary end-point, the risk of major adverse CV events (MACE) was 54% lower with relugolix than leuprorelin (2.9% vs 6.2%).[13] However, none of these trials were designed to compare CV events as a primary endpoint.

The PRONOUNCE trial was the first multicentre trial designed primarily to compare cardiovascular safety of degarelix versus leuprorelin in patients with advanced prostate cancer and concomitant cardiovascular disease. Men were randomised and the primary outcome was the time to first MACE in one year, which was a composite outcome, centrally adjudicated by cardiologists, including death from myocardial infarction and stroke. No difference was observed in the rate of MACE with degarelix compared to leuprolide. However, the study was terminated prematurely due to slow accrual and a smaller than planned number of MACE. Furthermore, all patients had compulsory cardiologists' assessment with optimisation of cardiovascular risk factors before the start of ADT, and more than 80% in both arms were prescribed statins. Therefore, the relative cardiovascular safety of LHRH antagonists compared with agonists remains inconclusive.[16] The 2018 National Comprehensive Cancer Network guidelines recommended a multidisciplinary approach involving primary care physicians and cardiologists to actively assess and manage traditional risk factors using the ABCDE approach (Table 2).[25]

Table 2: ABCDE approach for prostate cancer survivors

ABCDE approach for prostate cancer survivors		
A	Awareness	of cardiovascular signs and symptoms
	Aspirin	for prevention of cardiovascular events
B	Blood pressure	Aim < 140/90 mmHg
C	Cholesterol	Consider statin
	Cessation of smoking	
D	Diabetes	Monitoring yearly and considering metformin
	Diet	A healthy diet with adequate vitamin D (600 IU), calcium (1200 mg/d), but avoiding excessive alcohol
E	Exercise	150 min/ week of moderate intensity or 75 min/ week of vigorous intensity

BONE FRACTURE

There is an increased risk of non-metastatic bone fractures in men undergoing ADT in a dose-dependent relationship,[26] related to the increase in bone turnover and decrease in bone mineral density. The five-year risk of fractures was reported as 19.4% in men receiving ADT[27] and fractures in the elderly are highly associated with mortality. Methods to mitigate the risk includes general advice on weight bearing exercise, calcium and vitamin D supplements. The use of fracture risk algorithms, such as the FRAX® score to risk-stratify patients undergoing ADT is fundamental. This helps to identify patients who would benefit from the use of bone-modulating agents such as Denusomab or Zoledronic acid, reducing ADT-related bone morbidities.[27,28] Denosumab and Zoledronic acid have also been shown to prevent skeletal-related events in men with castration-resistant prostate cancer and bone metastasis.[28]

HOW TO CHOOSE

The choice of bilateral orchidectomy, LHRH agonist or antagonist depends on both disease and patient factors. In patients with extensive or symptomatic metastatic prostate cancer, rapid absolute castration is needed and as such bilateral orchidectomy or LHRH agonists are preferred. Non-steroidal anti-androgens are contraindicated in patients with severe liver impairment, hence, without coverage for testosterone flare-up, LHRH agonist should not be recommended. Patients with pre-existing or recent cardiovascular events and multiple risk factors who need ADT may consider LHRH antagonist. They may also require cardiology consultation and optimisation of risk factors before starting LHRH antagonist. Finally, the route, frequency and mode of administration of ADT can impact the quality of life of men with advanced prostate cancer significantly and should be taken into consideration.

CONCLUSION

ADT has consistently been shown to improve prostate cancer outcomes and remains the backbone in treatment for advanced prostate cancer. So far, neither surgical nor medical castration has shown superior efficacy. Each option has different advantages, as well as side effect profiles. Appropriate treatment needs to be personalised to the patient's condition such as the extent of prostate cancer, contraindications, cardiovascular risk factors and tolerance of cost and side effects, which should be assessed and managed in a multidisciplinary approach involving the urologist, oncologist, primary care physician and cardiologist. Oral LHRH antagonist is an emerging ADT option of but further research is required to confirm whether there are practice changing advantages. Transition from injections to oral ADT would also require careful consideration.

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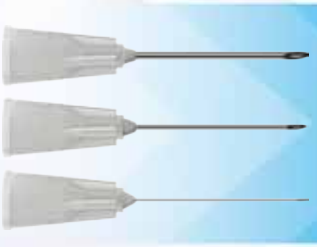

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Enantone 1-Month DPS 3.75 mg (ENTDPS1M0715PIHK2) **Enantone 3-Month DPS 11.25 mg** (ENTDPS3M0717PIHK) **Enantone 6-Month DPS 30 mg** (ENT6MDPS0613PIHK)

Active Ingredient: Leuprorelin acetate **Indication: Enantone 1-Month DPS 3.75 mg** Endometriosis; decrease of myoma volume and/or amelioration of symptoms in uterine myoma with hypermenorrhea, hypogastralgia, low back pain, anemia, etc; Premenopausal breast cancer (positive hormone receptor expression); Prostate cancer; Central precocious puberty. **Enantone 3-Month DPS 11.25 mg** In male: Prostate cancer and its secondarisms; In female: Endometriosis with genital and extra-genital localization (Phase I-IV); Breast cancer in pre and peri-menopausal women, where a hormone treatment is indicated; Uterine fibroids. In children: Precocious puberty (before 8 years in females and before 10 years in males). **Enantone 6-Month DPS 30 mg** Male adults for palliative treatment of advanced hormone-dependent prostate carcinoma. **Dosage/Administration: Enantone 1-Month DPS 3.75 mg** Endometriosis: Usually, for adults, 3.75 mg SC once every 4 weeks. Patient's weight <50 kg 1.88 mg may be used. Initiate administration on 1st-5th day after the start of the menstrual period. Uterine myoma: Usually, for adults, 1.88 mg SC once every 4 weeks. Patients with heavy weight or those with markedly enlarged uterus, 3.75mg is administered. Initiate administration on 1st-5th day after the start of menstrual period. Prostate cancer & premenopausal breast cancer: Usually, for adults, 3.75 mg SC once every 4 weeks. Central precocious puberty: Usually, a dose of 30 μg/kg SC once every 4 weeks. Depending upon the patient's condition, the dosage may be increased up to 180 μg/kg. **Enantone 3-Month DPS 11.25 mg** Male & female 11.25mg once every 3 months. Endometriosis & uterine fibroids 6 months treatment duration. Children <20 kg 5.63 mg once every 3 months; ≥20 kg 11.25 mg once every 3 months. **Enantone 6-Month DPS 30 mg** SC once every 6 months with interval of 168 days to maximum 182 days. **Contraindication: Enantone 1-Month DPS 3.75 mg** Patients with a history of hypersensitivity to any of the ingredients of this drug or synthetic LH-RH or LH-RH derivatives. Abnormal genital bleeding of indeterminable nature. Pregnant women or women having possibilities of being pregnant. or nursing mothers **Enantone 3-Month DPS 11.25mg** Hypersensitivity. Contraindicated in case of not diagnosed vaginal bleeding. Pregnancy & breast-feeding. **Enantone 6-Month DPS 30 mg** Hypersensitivity to leuprorelin or other GnRH analogues, polylactic acid. Pregnancy, lactation. 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Use non-hormonal contraceptive methods during treatment. Fertile women. Verify periodically the values of bone densitometry in case of prolonged treatment. Temporary worsening of clinical status. Increased risk of incidental depression (which may be serious) Girls: In girls affected with precocious puberty the gonadic stimulation can cause the outcome of little genital hemorrhages after the first injection which requires the additional of an adequate treatment only if this symptom goes on beyond the 1st month of treatment. Childhood: Gonadotropin-pituitary inhibition. Check regularly that the estradiol/testosterone levels are low in case the weight is near 20 kilos. **Enantone 6-Month DPS 30 mg** Patients with hypertension should be monitored closely. Initial short-term increase in the serum level of testosterone, potentially resulting in a transient exacerbation of certain disease symptoms. Patients with potential neurological complications, spinal metastases, or urinary tract obstruction should be monitored closely during the first few weeks of treatment. May be associated with increased risk of diabetes and certain cardiovascular diseases in men receiving these medications for the treatment of prostate cancer. **Adverse Reaction: Enantone 1-Month DPS 3.75 mg** Hot flushes, feeling of warmth, feeling of hot flushes, shoulder stiffness, headache, insomnia, dizziness or diaphoresis. Pains e.g. arthralgia & bone pain. **Enantone 3-Month DPS 11.25mg** Temperature, hypersensitive reactions including skin rash, itching and rarely a whistling sound, sleep disorders (drowsiness or insomnia), mood disorders (long-term use), depression (long-term use), headaches (occasionally severe), hot flushes, dyspnoea, constipation, vaginitis, vaginal dryness. **Enantone 6-Month DPS 30 mg** depression, mood changes, headache, hot flushes, nausea/vomiting, bone pain, joint or back pain, muscle weakness, decrease in or loss of libido and potency, reduction in testicle, gynaecomastia, nocturia, dysuria, pollakiuria, reactions at the injection site, increasing sweating, tiredness, peripheral edema, paraesthesia, sleep disturbances, weight gain, elevations of LDH, transaminases, gamma-GT and alkaline phosphatase which, however, can be a symptom of the underlying disease. **Drug interaction: Enantone 1-Month DPS 3.75 mg** Reduced effect with sex hormone preparation e.g. estradiol derivatives, estriol derivatives, conjugated estrogen preparations, combined preparation of estrogen & progesteron, mixed sex hormones, etc. **Enantone 3-Month DPS 11.25 mg** Since androgenic deprivation treatment may prolong the QT interval, it is necessary to carefully assess the use of Enantone 11.25mg with drugs known to extend the QT invertal or with drug capable of inducing Torsades de pointes like Class IA antiarrhythmic agents (e.g. quinidine, disopyramide) or class III ones (e.g. amiodarone, sotalol, dofetilide, ibutilide), metadone, moxifloxacin, antipsychotics, etc. **Enantone 6-Month DPS 30 mg** No drug interactions have been reported. **Presentation/Packing: Enantone 1-Month DPS 3.75 mg** pre-filled syringe. **Enantone 3-Month DPS 11.25 mg** pre-filled syringe. **Enantone 6-Month DPS 30 mg** pre-filled syringe.

Full prescribing information is available upon request.

To Report Suspected Side Effects for Takeda Products
AE.HongKong@takeda.com

Medical Information and other Inquiries for Takeda Products
medinfohk@takeda.com

References: 1. Data on file, Takeda **2.** Enantone 1 month DPS 3.75mg HK Prescribing information, ENTDPS1M0715PIHK2 **3.** Enantone 3 month DPS 11.25mg HK Prescribing information, ENTDPS3M0717PIHK **4.** Enantone 6 month DPS 30mg HK Prescribing information, ENT6MDPS0613PIHK

Disclaimer: Above product promotional material apply to HK and Macau only. Please refer the prescribing information from your home country / location as this may very depending on local approvals in each country / location.

Takeda ONCOLOGY

Further information is available upon request. Before prescribing, please consult local prescribing information.

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C-APROM/HK/ENT/0011 (11/2021)

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Qinlock: the FIRST switch-control kinase inhibitor
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Category 1

GIST=gastrointestinal stromal tumor
*Advanced GIST can be locally advanced or metastatic[3]

Reference: 1. QINLOCK Abbreviated Prescribing information. Jun 2020 **2.** NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastrointestinal Stromal Tumors (GISTs) V.1.2021. ©National Comprehensive Cancer Network, Inc. 2020. Accessed October 30, 2020. **3.** Understanding Advanced and Metastatic Cancer. American Cancer Society. https://www.cancer.org/treatment/understanding-your-diagnosis/advanced-cancer/what-is.html. Accessed on May 5, 2021.

Abbreviated Prescribing Information

INDICATIONS
Qinlock is indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with imatinib, sunitinib, and regorafenib.

DOSAGE AND ADMINISTRATION
150mg (three 50mg tablets) taken orally once daily. Dosage reduction for adverse reaction is 100mg orally once daily. Permanently discontinue QINLOCK in patients who are unable to tolerate 100 mg orally once daily. Please refer to the full prescribing information for recommended dosage modifications for adverse reactions and missed dose.
Qinlock is not indicated in pediatrics (<18 years old). No dose adjustment is required for geriatrics (≥65 years old).
Renal impairment - No dose adjustment is recommended for patients with mild and moderate renal impairment [creatinine clearance (CrCl) 30 to 89 mL/min estimated by Cockcroft-Gault]. The pharmacokinetics and safety of Qinlock in patients with end-stage renal disease (CrCl <15mL/min estimated by Cockcroft-Gault or requiring dialysis) or severe renal impairment (CrCl 15 to 29 mL/min) have not been studied.
Hepatic impairment - No dose adjustment is recommended in patients with mild hepatic impairment (total bilirubin ≤1 x ULN and AST >1 x ULN, or total bilirubin 1.0 to 1.5 x ULN). The pharmacokinetics and safety of Qinlock in patients with moderate or severe hepatic impairment have not been studied.

CONTRAINDICATIONS
Hypersensitivity to ripretinib or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

WARNINGS AND PRECAUTIONS
The following are clinically significant adverse events: 1) Cardiac dysfunction. Cardiac failure and Grade 3 decreased ejection fraction has occurred in clinical study. Cardiac dysfunction has led to dose discontinuation. An assessment of the ejection fraction by echocardiogram or MUGA scan is recommended prior to initiation and during treatment, as clinically indicated. Permanently discontinue Qinlock for Grade 3 or 4 left ventricular systolic dysfunction; 2) Hypertension. Higher incidence of hypertension in patients treated with Qinlock than in placebo-treated patients in clinical study. Do not initiate Qinlock in patients with uncontrolled hypertension. Adequately control blood pressure prior to initiating Qinlock; 3) New primary cutaneous malignancies. Squamous cell carcinoma (SCC) of the skin and melanoma, actinic keratosis, keratoacanthoma and melanoma were reported in patients who received Qinlock in clinical study. Dermatological assessment should be performed when initiating Qinlock and patients should receive dermatological examinations routinely.
Other warnings and precautions include cardiac ischaemic events, hypersensitivity, wound healing, reproduction, fertility, palmar-plantar erythrodysesthesia syndrome [PPES] and photosensitivity.

PREGNANCY AND BREAST-FEEDING
Pregnancy - Qinlock should not be administered to pregnant women. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception to commence 2 weeks prior to treatment, during treatment and for at least one complete uterine cycle after the final dose of Qinlock.
Breast-feeding - Advise women not to breastfeed during treatment and for at least 2 weeks after the final dose.

ADVERSE REACTIONS
The most common adverse events (≥20%) observed in clinical study were alopecia, fatigue, nausea, abdominal pain, constipation, myalgia, diarrhea, decreased appetite, palmar-plantar erythrodysesthesia syndrome, and vomiting. Serious adverse events occurred in 31% of patients who received Qinlock. Serious adverse reactions that occurred in >2% of patients were abdominal pain (4.7%), anemia (3.5%), nausea (2.4%), vomiting (2.4%).
Dosage interruptions due to an adverse event occurred in 23.5% of patients who received Qinlock. Adverse events requiring dosage interruption in >2% of patients included nausea (3.5%), increased blood bilirubin (2.4%), and PPES (2.4%).
Dose reductions due to an adverse event occurred in 7.1% of patients who received Qinlock. Adverse events resulting in a dose reduction in ≥1.2% of patients were abdominal pain, agitation, alopecia, arthritis, dermatosis, gastrointestinal disorder, hyperesthesia, myalgia, PPES, and decreased weight.
Permanent discontinuation due to an adverse event occurred in 8.2% of patients who received Qinlock. Adverse events resulting in permanent discontinuation in ≥1% of patients included general physical health deterioration (2.4%), anemia (1.2%), cardiac failure (1.2%), PPES (1.2%), and vomiting (1.2%).

DRUG INTERACTIONS
In vitro data suggested that CYP3A4/5 is the major metabolizer of ripretinib. Potential interactions may occur with drugs/foods/herbs that are inhibitors or inducers of this enzyme system. Monitor patients more frequently for adverse reactions if Qinlock is given concurrently with a strong CYP3A inhibitor. Avoid concomitant use of Qinlock with strong CYP3A inducers. Monitor patients who ingest grapefruit juiced while taking Qinlock. Avoid concomitant use with St. John's wort.
Please refer to the full prescribing information before prescribing.
Ref. HKPI Nov 2020 (Canadian PM 19 Jun 2020)

HK-QIN-202104-03

zai lab

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North Point, Hong Kong, P.R. China
T: +852-3844 8100

Radiology Quiz

Dr Hoi-to LAU
MBBS,FRCR

Dr Hoi-to LAU

Photo 1

History

28-year-old female patient presented to the emergency department with facial trauma. The facial radiograph was taken.

Questions

1. What is the abnormality in this radiograph (photo 1)?
2. What is the next investigation required?

(See P.40 for answers)

LEGO Creation for Fun

Dr Lysander Hin CHAU

MBBS, FRCS(Ed)(Urology), FCSHK, FHKAM(Surgery)
Consultant
Division of Urology, Department of Surgery, Tuen Mun Hospital

Dr Lysander Hin CHAU

LEGO has enjoyed a long history of more than 80 years and is much older than the majority of you and me. Regardless of age, LEGO is a lot of fun to play with. LEGO has become a regular item on the shelves of any toy shop you walk into nowadays. The LEGO sets are often unique with great designs and are fun to build and play with. There are multifarious themes, ideas, topics and other genres, such as Starwars and Marvel, to ensure that one should find something he or she likes. The set can be a tiny box or pack with just a few parts. On the other hand, it can be a huge set with thousands of parts and an instruction manual which reads like a dictionary. At first, you may think this is just a kid's toy, but in reality, numerous adults worldwide are crazy fans of LEGO, including myself.

I first encountered a LEGO set in 1987 when I was in primary school. The set was a classic space set which had already retired for a long time. If you still have one maintained in a sealed box (MISB), the market price must be beyond your imagination! At first I just followed the steps and built the work with satisfaction. Then I broke it down into pieces and tried to create similar things but in a random way. Like other kids when growing up, I developed other interests with my friends, such as playing sports or TV games. This phenomenon is common in the LEGO community, and we commonly call this "Dark Age".

Years later while at my first job as a medical officer in a hospital, I encountered another "space" set in a toy shop. It was a Starwars theme and I bought the famous X-wing set. The design was just so great that it had an immense impact on me. Since then, I have become a collector to get all these great sets at my home and later on I have even needed a warehouse to store them. However, it is well known that not every topic or theme is covered by the LEGO company; people may not be satisfied with the current design resulting in the fans taking their own initiative to modify or create on their own in order to render their LEGO work/collection perfect or unique. I so happened to be one of such fans, starting My Own Creations (MOCs) life afterwards.

Nowadays for me, there is no limitation to my creation: from my favourite topics such as a "cool" spaceship from a movie, a building complex just completed in my locality, a historical architecture in the world, a luxury cruiser where I just finished my staycation, a cat which I do not need to feed in my home, etc MOCs are usually created by fans who combine LEGO with their other hobbies or interests (such as characters & scenes from a movie). Because of license issues, you will never come across some anime topics crossing over with LEGO toys, such as the Gundam series. However, you can create your own based on the LEGO parts you have. The question is how to accomplish this?

There are different ways to go about creating MOCs. The first step is usually started by modification of an existing product, i.e. simply adding parts or changing some parts while leaving the major structure intact in order to make the structure look much "cooler" or even functional. One example is to make a car's bonnet open to expose the engine details inside, such details being non-existent in the original product. In this way, one can save the time for figuring out how to start building from zero and the outlook will not deviate too much from one's expectation. Subsequently, if you are still not satisfied with this level of creative re- building, you may choose to build purely from actual bricks and experiment with the pieces you have in your hands. The more the reference photos from different angles of view, the better the outlook will be. Once you are familiar with the parts, choosing the right part to match the needed part of your work will be less time-consuming.

In the modern-day hi-tech era, I strongly recommend that you make good use of various free-building software so that you can design your MOCs digitally first and use the vast unlimited supply of parts that the software offers without compromising one's imagination. Once you finish the digital design, you can start physical building by collecting parts systematically and following your own instruction.Digital building is a more sound way of creation as you can design or amend or modify till perfection so that you can avoid squandering acquired pieces which turn out not to be useful in the later phase of building. For digital design, an average laptop or desktop PC where famous software such as Stud.io or LDD can be installed. I strongly recommend using Stud.io, which is free to download from Bricklink.com (an official LEGO certified website for LEGO parts/sets online market).

Proudly, I recently built a school campus model in the image of the actual building based on the Stud.io software and donated my completed work to my alma mater to celebrate her 170th anniversary. Most of the parts used had also been purchased from the website via an online system. Because of the part-time nature of this creative work after a whole day of busy clinical duty, I spent almost a year to finish the model. Rewardingly, my creative work is on display at the school campus. More importantly, I hope my work on displaly can inspire young minds to create things based on building toys and to have more creative thinking. I do believe such creative thinking is being applied in my medical

practice, such that I invented the usage of a navigation system during percutaneous nephrolithotomy procedure; this system was granted a prize in an international Urology conference a few years ago.

Along with the advancement of computer technology, digital building has become a more powerful phenomenon than simply creative play. One can make the work look extremely real such that one cannot differentiate whether it is an actual building or not. This is the beauty of software rendering and photo-editing processes. Once you input your works' digital files into rendering software, the results will be excellent photos after processing (even better than using the advanced camera to shoot my actual works, in my opinion). This is particularly good if you just want to share in various social media such as Facebook, Instagram, Twitter, YouTube, etc. It is particularly suitable in Hong Kong as we have space limitation and it is really difficult to display all the works at home. Physical building is undertaken only when I have a special reason for this. Do you believe that most of the published MOC photos in this article are all computer rendering works? Because of this unlimited building potential of the software, I can try to create different things. Currently, I have various public social media platforms where I share my updated works with the whole community. I also promote and teach people to master the building software for free.

If you are interested in my work, look me up in social media (Lysander's Stud Studio). I am glad to have nearly 2,500 followers from the world at present. See you all there and happy building!

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- To reduce misunderstanding between healthcare workers and patients
- To improve the interpersonal skills through systematic learning
- To understand the concept of mediation, win-win and interest-based resolution
- To communicate better with patients and their family

Date	Topics	Speakers
16 Feb 2022	Mediation & Healthcare	Dr. CHOO Kah-lin 俞佳琳醫生 Consultant (Medicine) Accredited Mediator
23 Feb 2022	DOs and DON'Ts in Healthcare Mediation	Dr. TSOI Chun-hing Ludwig 蔡振興醫生 Consultant (Emergency Medicine) Accredited Mediator
2 Mar 2022	Listening Skills & Use of Body Language	Dr. TSOI Chun-hing Ludwig 蔡振興醫生 Consultant (Emergency Medicine) Accredited Mediator
9 Mar 2022	Perception Check, Paraphrasing & Summarizing Skills	Dr. TSOI Chun-hing Ludwig 蔡振興醫生 Consultant (Emergency Medicine) Accredited Mediator
16 Mar 2022	Reframing & Facilitative Skills	Dr. ONG Kim-lian 王金蓮醫生 Consultant (Emergency Medicine) Accredited Mediator
23 Mar 2022	Negotiation Skills & Empowerment	Dr. CHAN Kit-ying Sandy 陳潔瑩博士 Registered Nurse Accredited Mediator

Date : 16, 23 February & 2, 9, 16, 23 March 2022 (Every Wednesday)
Duration of session: 1.5 hours
Time : 7:00 pm – 8:30 pm
Course Feature: Video lectures (with Q&A platform for participants to post the questions)
Quiz for doctors: DOCTORS are required to complete a quiz after the completion of each lecture
Language Media : Cantonese (Supplemented with English)
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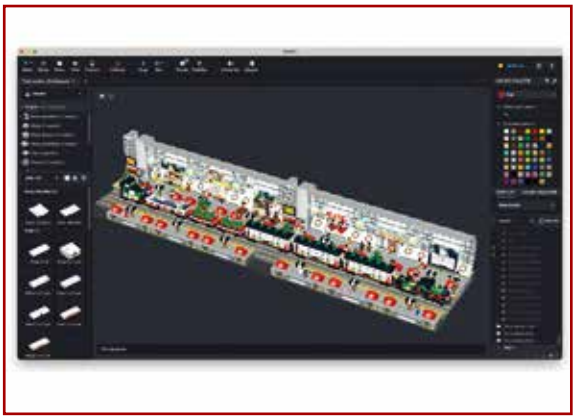

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Spedra® avanafil

Please refer to full prescribing information for further information.

* A 52 week, open-label extension study of 712 adult males with erectile dysfunction (ED) who had previously completed either of the phase 3, 12 week, randomised, double blind, placebo-controlled studies. Patients were initially treated with avanafil 100 mg but the dose could be increased to 200 mg for increased efficacy or decreased to 50 mg for improved tolerability. 173/535 men in the 100 mg and 200 mg group attempted to have intercourse within 15 minutes of dosage. Of these, 143/173 (83%) of men experienced successful intercourse. Belkoff LH *et al. Int J Clin Pract.* 2013;67(4):333-341.

References: **1.** SPEDRA® Approved Product Information, 2016. **2.** Goldstein I *et al. J Sex Med.* 2012; 9 (4): 1122-1133. **3.** Belkoff LH *et al. Int J Clin Pract.* 2013;67(4):333-341.

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HK/SPE/042021/102 (Oct 2021)

MENARINI

Hong Kong College of Cardiology Statement on Aspirin Use to Prevent Cardiovascular Disease (December 2021)

Dr Godwin TC LEUNG
Chairman, Public Health Education Committee, Hong Kong College of Cardiology

Dr Andy WK CHAN
President, Hong Kong College of Cardiology

Dr Godwin TC LEUNG Dr Andy WK CHAN

BACKGROUND

On October 12, 2021, the US Preventive Services Task Force (USPSTF) released a draft recommendation statement on Aspirin Use to Prevent Cardiovascular Disease (CVD). The USPSTF recommends that the decision to initiate low-dose aspirin use for the primary prevention of CVD in adults ages 40 to 59 years who have a 10% or greater 10-year CVD risk should be an individual one, and recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults age 60 years or older.

The USPSTF draft recommendation has been reported in the media and has aroused public attention. It is important to note that this recommendation only applies to individuals who have no history of CVD, and are not already taking daily aspirin. Hong Kong College of Cardiology (HKCC) is concerned that some people who are taking aspirin may stop taking it without seeking medical advice. For this reason, HKCC would like to issue the following statements on the use of aspirin:

1. Aspirin can help to reduce heart attack and stroke, but this must be balanced against the risk of bleeding.

2. Aspirin is recommended in the secondary prevention of cardiovascular disease. For people already diagnosed with cardiovascular diseases, such as coronary artery disease or stroke, and who have not previously suffered from major internal bleeding, the reduced level of risk for further heart attack or stroke usually outweighs the increased risk of bleeding. For these people, aspirin is recommended unless they are known to be unable to take aspirin.

3. Aspirin should not be routinely initiated for primary prevention of cardiovascular disease. For people without a previous diagnosis of cardiovascular disease, the balance of benefits against harms from aspirin is small. For these people, daily aspirin is not generally advised. Aspirin may be considered beneficial if an individual's future risk of stroke or heart attack is high. Aspirin should only be considered after an assessment of that individual's risk by his or her doctor.

4. People who are currently taking aspirin should not stop taking the drug themselves without seeking medical advice. They should discuss the benefits and harms of taking aspirin with their doctors.

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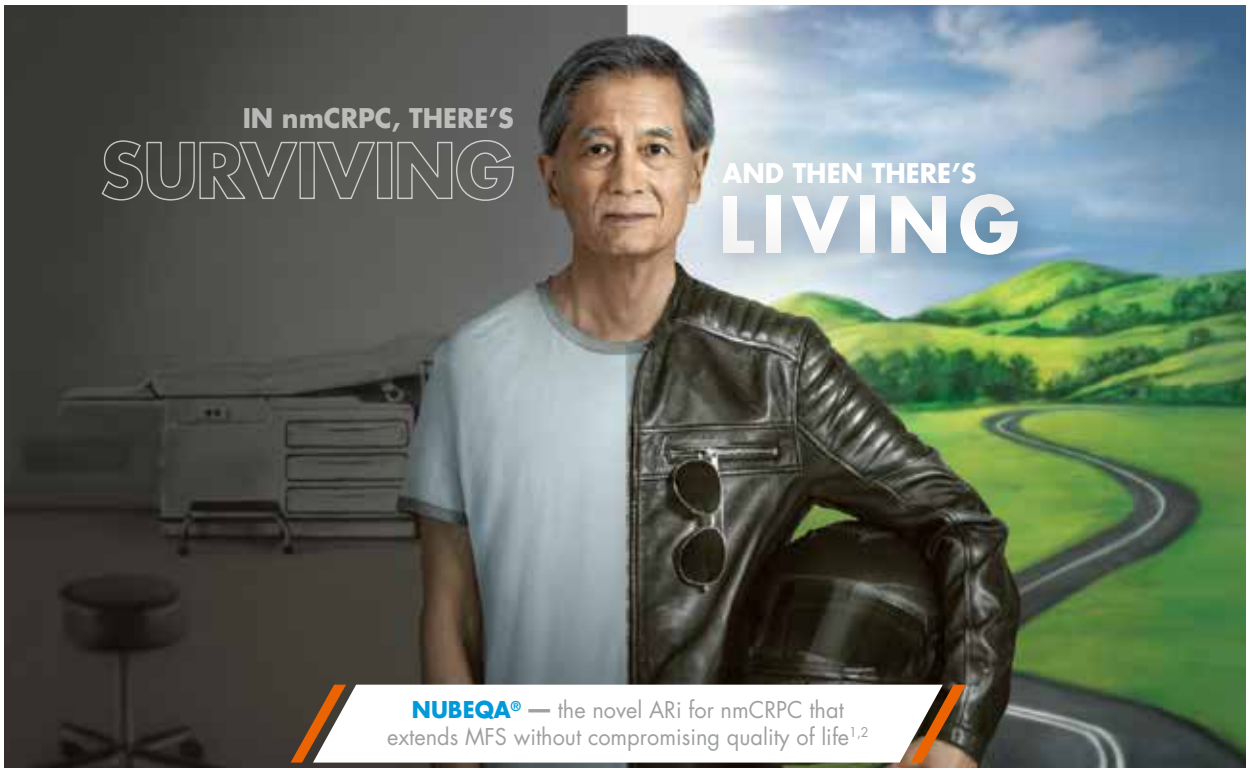
VIATRIS
暉致

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		1	2	3	4	5
6	7	★Zoom Live HKMA-HKSH CME Programme 2021-2022 Topic: Management of Triple Negative Breast Cancer - (Online) 8	9	★Zoom Live Personalized Management in Heart Failure and the Importance of Heart Rate Control 10	★Zoom Live Heavy Menstrual Bleeding – Optimizing Treatment and Patient Counselling 11	12
13	14	★Zoom Live Update on the Management of Osteoarthritis - Online 15	★Zoom Live Pancreatic Exocrine Insufficiency (PEI) in Patients with Diabetic Mellitus - Online 16	17	★Zoom Live Updates on Insomnia Management 18	19
20	★Zoom Live Diabetes: More Than Just A Thromboembolic Risk Factor in AF Patients - Online 21	★Zoom Live HKMA-GHK CME Programme 2021 - 2022 - Updated In Musculoskeletal Tumor (Online) 22	23	★Zoom Live Personalized Approach in Angina Treatment, How Close Are We? (Online) ★Professorial Webinar One Hundred (and 10) Years of Solitude: Evolution of Esophageal Surgery (or How I Grew to Love the Esophagus) 24	25	26
27	★Zoom Live Latest Insights into Allergic Rhinitis (Online) 28					

NUBEQA®
(darolutamide) 300 mg tablets

BAYER



SURVIVING

40 MONTHS median MFS[1]

31% LOWER RISK of death[1]

QUALITY OF LIVING

FREQUENCY OF AEs COMPARABLE to ADT alone[1]

NO INCREASE IN DISCONTINUATION due to AE[1]

Men treated with NUBEQA + ADT vs ADT alone

Indication of NUBEQA:

NUBEQA is indicated for the treatment of adult men with non-metastatic castration-resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease[2]

Abbreviation: ADT=androgen deprivation therapy; AE=adverse event; ARi= Androgen Receptor inhibitor; MFS= metastatic-free survival; nmCRPC= non-metastatic Castration-Resistant Prostate Cancer

References: 1. Fizazi K, Shore N, Tammela TL, et al. Nonmetastatic, Castration-Resistant Prostate Cancer and Survival with Darolutamide. N Engl J Med 2020;383:1040-9. **2.** NUBEQA (darolutamide) HK full prescribing information (June 2020).

Abbreviated Package Insert for Nubeqa

Nubeqa 300 mg film-coated tablets. Approved name of the active ingredient Darolutamide. **Indication** Nubeqa is indicated for the treatment of adult men with non-metastatic castration-resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease. **Dosage and method of administration** Recommended dose is 600 mg darolutamide (two tablets of 300 mg) taken orally twice daily, equivalent to a total daily dose of 1200 mg. If a patient experiences ≥ grade 3 toxicity or intolerable adverse reaction, withhold dose or reduce dose to 300 mg twice daily until symptoms improve; may resume to 600 mg twice daily afterwards. **Contraindications** Hypersensitivity to the active substance or to any of the excipients, or women who are or may become pregnant. **Special warnings and precautions for use** Renal impairment: Limited data in patients with severe renal impairment; Closely monitored for adverse reaction as exposure might be increased in these patients. Recommended starting dose for severe renal impairment not receiving haemodialysis (eGFR: 15-29mL/min/1.73m²) is 300 mg twice daily. Hepatic impairment: No dose adjustment necessary for mild hepatic impairment (Child-Pugh A). Recommended starting dose for patients with moderate and severe hepatic impairment (Child-Pugh B and C respectively) is 300 mg twice daily. Recent Cardiovascular disease: The safety of darolutamide has not been characterised in patients with recent (within 6 months) cardiovascular events, including uncontrolled hypertension, stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, and NYHA Class III or IV congestive heart failure, as these patients were excluded from the pivotal study. If prescribing Nubeqa, treat these conditions according to established guideline. Concomitant use with other medicinal products: Not recommended to use strong CYP3A4 and P-gp inducers (eg carbamazepine, phenobarbital, St John's Wart) with darolutamide unless no alternative; consider alterative medicinal product with lower induction potential. Monitor for adverse reactions of BCRP, OATP1B1 and OATP1B3 substrates (eg methotrexate, sulfasalazine, fluvastatin, atorvastatin, pitavastatin) when using concomitantly with darolutamide. Avoid concomitant use with rosuvastatin unless no alternative. **Fertility, pregnancy and lactation** Not indicated in women of childbearing potential and not to be used in women who are, or may be, pregnant or breast-feeding. Advise men who are sexually active to use condoms and their female partners of reproductive potential to use a highly effective contraceptive method during and for 1 week after last dose of Nubeqa. Fertility: No human data. Darolutamide may impair fertility in males of reproductive potential based on animal study. **Undesirable effects** Very common adverse reactions (≥10%): fatigue (15.8% for darolutamide vs 11.4% for placebo), neutrophil count decreased (19.6% vs 9.4%), bilirubin increased (16.4% vs 6.9%), AST increased (22.5% vs 13.6%). Common adverse reactions (≥1%, <10%): rash, pain in extremity, musculoskeletal pain, fractures (4.2 vs 3.6%), ischaemic heart disease (3.2 vs 2.5%), heart failure (1.9% vs 0.9%). Date of revision of text November 2020.

Please refer to full prescribing information dated June 2020 for more information. For healthcare professionals only.

PP-M_DAR-HK-0002-1

Bayer HealthCare Limited
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Date / Time	Function	Enquiry / Remarks
8 TUE 2:00 PM	**Zoom Live** **HKMA-HKSH CME Programme 2021-2022** **Topic: Management of Triple Negative Breast Cancer - (Online)** Organiser: Hong Kong Medical Association & Hong Kong Sanatorium & Hospital Speaker: Dr. KAM Koon Ming, Michael	HKMA CME Dept. Tel: 3108 2507 1 CME Point
10 THU 2:00 PM	**Zoom Live** **Personalized Management in Heart Failure and the Importance of Heart Rate Control** Organiser: HKMA-Kowloon East Community Network Speaker: Dr MUI Chun Yue, Nestor	Mr. Jeffrey Cheung Tel: 2861 1979 1 CME Point
11 FRI 2:00 PM	**Zoom Live** **Heavy Menstrual Bleeding – Optimizing Treatment and Patient Counselling** Organiser: HKMA-Yau Tsim Mong Community Network Speaker: Dr. CHAN Ming Chung	Ms. Candice Tong Tel: 3108 2513 1 CME Point
15 TUE 2:00 PM	**Zoom Live** **Update on the Management of Osteoarthritis - Online** Organiser: HKMA-KLN West Community Network Speaker: Dr. YUEN Shiu Him, Jonathan	Mr. Jeffrey Cheung Tel: 2861 1979 1 CME Point
16 WED 2:00 PM	**Zoom Live** **Pancreatic Exocrine Insufficiency (PEI) in Patients with Diabetic Mellitus - Online** Organiser: Hong Kong Medical Association Speaker: Dr. CHOK Siu Ho, Kenneth	HKMA CME Dept. Tel: 3108 2507 1 CME Point
18 FRI 2:00 PM	**Zoom Live** **Updates on Insomnia Management** Organiser: HKMA-Shatin Community Network Speaker: Dr. LUI Wing Cheong, Victor	Ms. Candice Tong Tel: 3108 2513 1 CME Point
21 MON 2:00 PM	**Zoom Live** **Diabetes: More Than Just A Thromboembolic Risk Factor in AF Patients - Online** Organiser: Hong Kong Medical Association Speaker: Dr. CHUNG Yat Kiu, Edward	HKMA CME Dept. Tel: 3108 2507 1 CME Point
22 TUE 2:00 PM	**Zoom Live** **HKMA-GHK CME Programme 2021 - 2022 - Updated In Musculoskeletal Tumor (Online)** Organiser: Hong Kong Medical Association & Gleneagles Hong Kong Hospital Speaker: Dr. SO Yat Cheong, Timothy	HKMA CME Dept Tel: 3108 2507 1 CME Point
24 THU 2:00 PM	**Zoom Live** **Personalized Approach in Angina Treatment, How Close Are We? (Online)** Organiser: HKMA-HK East Community Network Speaker: Dr. TANG King Fun	Ms. Candice Tong Tel: 3108 2513 1 CME Point
7:30 PM	**Professorial Webinar** **One Hundred (and 10) Years of Solitude: Evolution of Esophageal Surgery (or How I Grew to Love the Esophagus)** Organiser: Hong Kong Chinese Medical Association Ltd Speaker: Prof. Simon YK LAW	Ms. Cordelia Wu / Ms. Iris Hau Tel: 2527 8898 1 CME Point
28 MON 2:00 PM	**Zoom Live** **Latest Insights into Allergic Rhinitis (Online)** Organiser: Hong Kong Medical Association Speaker: Dr. LI Hok Nam	HKMA CME Dept Tel: 3108 2507 1 CME Point

Certificate Course for Medical Practitioner, Nurse, Health Care Providers & Allied Health Workers who interested in wilderness medicine. • CME/CNE Course • Course No. C376

Certificate Course on

Wilderness Medicine 2022

(Video Lectures)

Jointly organised by

The Federation of Medical Societies of Hong Kong

Hong Kong Society for Emergency Medicine and Surgery

Objectives:

Wilderness activities have rapidly grained an increase in popularity in recent years. However the exotic environment possesses totally different and unpredictable threats and dangers to the participants who are involved in wilderness activities. Wilderness Medicine is practiced by those who have specially interest in wilderness emergency medical management. In this course, we use six file series to illustrate practical information and management in six medical problems commonly encountered in wilderness.

野外活動在過去幾年迅速普及。但野外環境對於野外活動的參與者，會造成完全不同類型及不可預料的威脅和危險。野外醫學是對於野外緊急醫療治理有特殊興趣練的實踐。在這課程中，我們透過六個檔案以說明六種在野外環境中最常可能出現的醫療問題及其相關實用之處理技巧。

Date	Topics	Speakers
10 Mar 2022	A hiker facing thunderstorm in wilderness (Wilderness survival and lightening related injuries) 徒步旅行者在荒野面對雷雨 (野外生存及雷擊相關的傷害)	Dr. Chee Pay Yun, Peter 池丕恩醫生 香港急症科醫學院院士
17 Mar 2022	A hiking trip to Everest Basecamp (High altitude related wilderness problems) 前往珠峰大本營的徒步行程 (野外高海拔的相關問題)	Dr. Ho Man Kam 何文錦醫生 香港急症科醫學院院士
24 Mar 2022	A hiker bitten by deathful venomous creature (Poisonous stings and bites in wilderness) 一個被致命毒物咬傷的徒步旅行者 (野外被毒物螫咬)	Dr. Ng Wah Shan 伍華山醫生 香港急症科醫學院院士
31 Mar 2022	A hiking trip to extreme climate zone (Heat and cold related problem in wilderness) 一個前往極端氣候區的徒步行程 (野外高溫及低溫所引致的問題)	Dr. Law Kam Leung 羅金亮醫生 香港急症科醫學院院士
7 Apr 2022	A hiker fall from cliff with multiple injuries (Trauma and wound management in wilderness) 從懸崖讓下而多處受傷的徒步旅行者 (野外意外創傷及傷口的處理)	Dr. Siu Yuet Chung, Axel 蕭粵中醫生 香港急症科醫學院院士
14 Apr 2022	A hiker fall into a stream in Sai Kung (Mountain Rescue and Helicopter Search And Rescue in HK) 一個在西貢讓落山溝的徒步旅行者 (香港的山地救援及直升機搜尋)	Mr. Kwok Shing Lam 郭成霖先生 政府飛行服務隊 航空醫療護士/急症室護士長

Date : 10, 17, 24, 31 Mar & 7, 14 Apr, 2022 (Every Thursday)
Duration of session: 1.5 hours (6 sessions)
Time : 7:00 pm – 8:30 pm
Course Feature: Video lectures (with Q&A platform for participants to post the questions)
Quiz for doctors: DOCTORS are required to complete a quiz after the completion of each lecture
Language Media : Cantonese (Supplemented with English)
Course Fee : HK$1,000
Certificate : Awarded to participants with a minimum attendance of 70% (4 out of 6 sessions)
Deadline : 2 March 2022
Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax : 2865 0345 Email : vienna.lam@fmshk.org

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Answers to Radiology Quiz

Answers:

1. There is "teardrop sign" on the right side (photo 2, with 2 green arrows). This represents that intraorbital fat +- inferior rectus muscle has protruded through an inferior orbital wall fracture, signifying orbital floor blow-out fracture.

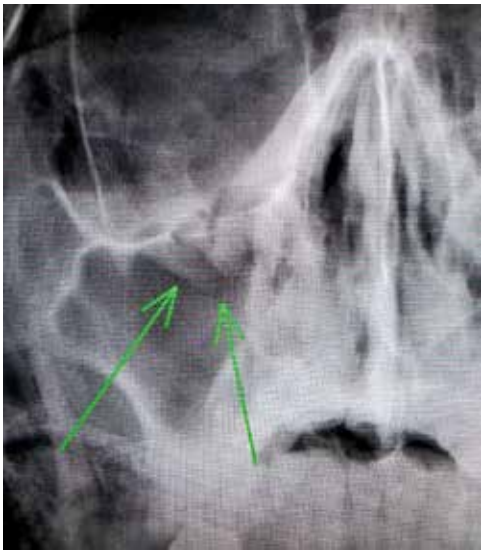

Photo 2

2. CT orbit would be required for confirmation.
Subsequent CT orbit of this patient confirmed the findings of right orbital floor blow-out fracture (photo 3, with green arrow)

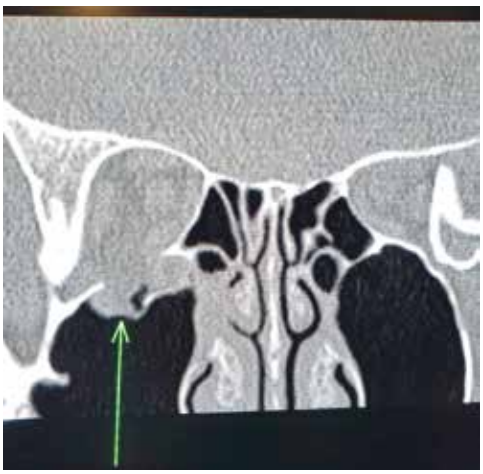

Photo 3

Dr Hoi-to LAU
MBBS,FRCR

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black for PERIPHERAL ADMINISTRATION

ω-3 enriched PN – proven to improve clinical outcomes with excellent safety profile[1]:

- Significantly reduced length of hospital stay overall by **3 days**.
- Significantly reduced infection rate by **39%**

- Available in different bag sizes (Central: 493/986/1477/1970 ml, Peripheral: 1206/1448/1904 ml)
- Extensive compatibility data with micronutrients

Complete parenteral nutrition therapy with micronutrients

- All PN prescriptions should include a daily dose of multi-vitamins and trace elements[2-3]
- After surgery, in those patients who are unable to be fed via the enteral route, and in whom total or near total parenteral nutrition is required, a full range of vitamins and trace elements should be supplemented on a daily basis[3]

Approved for children ≥ 2 years

References :
1. L. Pradelli et al. Clinical Nutrition 33 (2014) 785-792
2. Singer et al. (2009) ESPEN Guidelines on parenteral nutrition: Intensive Care. Clinical Nutrition 28: 387-400
3. Braga et al. (2009) ESPEN Guidelines on Parenteral Nutrition: Surgery. Clinical Nutrition, 28: 378-386
4. Biesalski HK. Gastroenterology 2009;137(5):92-104 http://www.espen.org/espenguidelines.html

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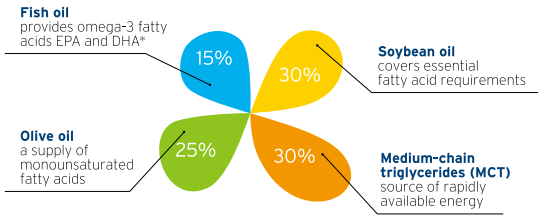
SMOFlipid® – A 4-oil mix with a well-balanced fatty acid pattern containing purified natural fish oil



*EPA: eicosapentaenoic acid, DHA: docosahexaenoic acid

+ additional vitamin E
(approx. 200 mg α-tocopherol/liter) to counteract lipid peroxidation and oxidative stress[4]

Dipeptiven® 5 Glutamine

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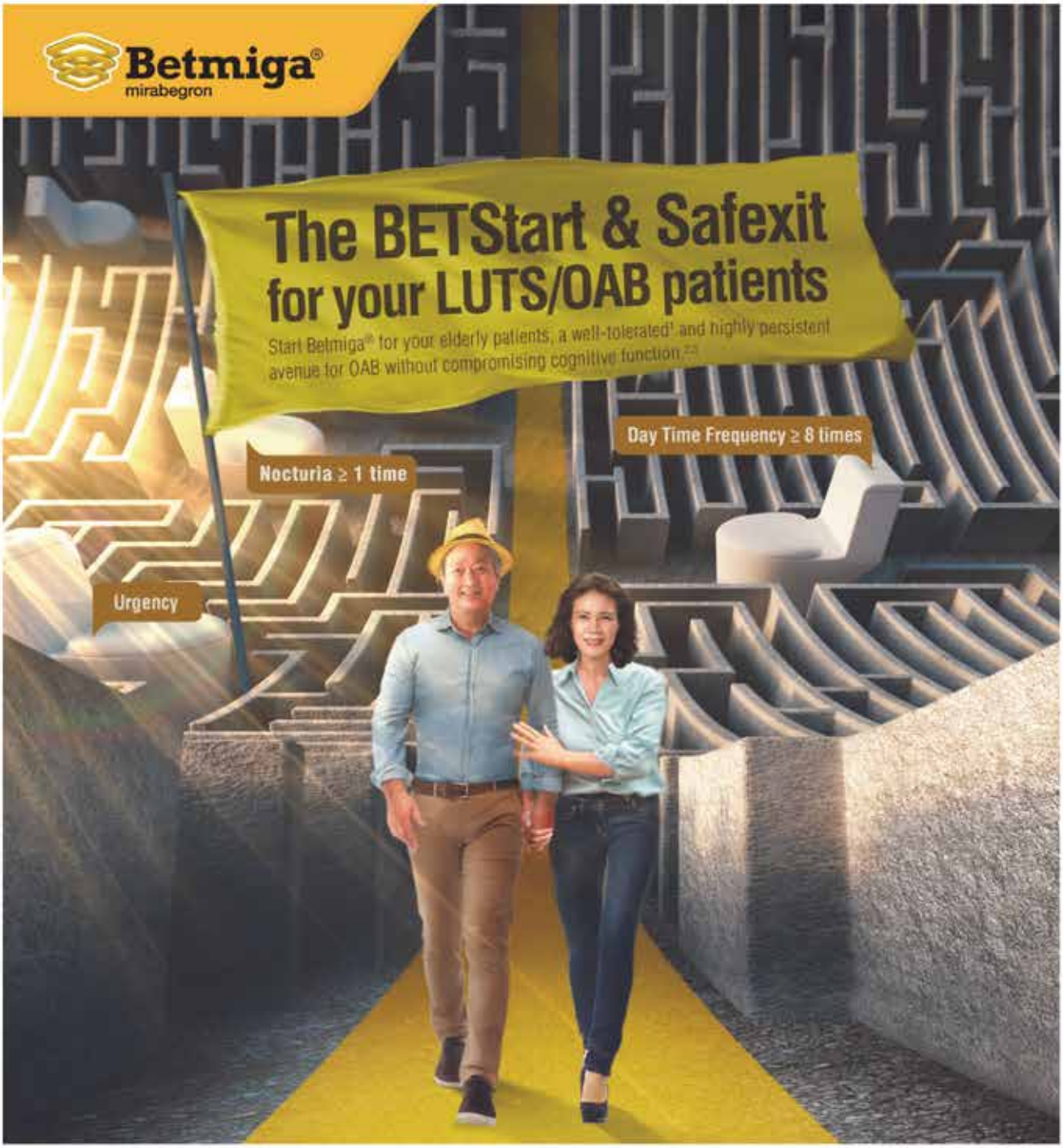

Abbreviations: LUTS, lower urinary tract symptoms; **OAB**, overactive bladder

References: 1. Wagg A, et al. Efficacy, safety and tolerability of mirabegron in patients aged≥ 65 yr with overactive bladder well, a phase IV, double-blind, randomised, placebo-controlled study (FILLAR). Eur Urol. 2020;77(2):211-20. 2. Grebling TL, et al. Effect of mirabegron on cognitive function in elderly patients with overactive bladder: MoCA results from a phase 4 randomized, placebo-controlled study (FILLAR). BMC Geriatr. 2020;20(1):1-13. 3. Chapple CR, et al. Persistence and adherence with mirabegron versus antimuscarinic agents in patients with overactive bladder: a retrospective observational study in UK clinical practice. Eur Urol. 2017;72(3):399-06.

Abbreviated prescribing information of Betmiga® prolonged-release tablets

Version: 003 **Composition:** Mirabegron **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Dosage:** Adult including elderly: 50 mg once daily with or without food. **Administration:** Swallow whole with liquids. Do not chew/divide/crush. **Contraindications:** Mirabegron is contraindicated in patients with: • Hypersensitivity to the active substance or to any of the excipients. • Severe uncontrolled hypertension defined as systolic blood pressure ≥ 180 mm Hg and/or diastolic blood pressure ≥ 110 mm Hg. **Special warnings and precautions for use:** Renal impairment Betmiga has not been studied in patients with end stage renal disease (GFR = 15 mL/min/1.73 m² or patients requiring haemodialysis) and, therefore, it is not recommended for use in this patient population. Data are limited in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73 m²) based on a pharmacokinetic study a dose reduction to 25 mg is recommended in this population. Betmiga is not recommended for use in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73 m²) concomitantly receiving strong CYP3A inhibitors. Hepatic impairment Betmiga has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and, therefore, it is not recommended for use in this patient population. Betmiga is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B) concomitantly receiving strong CYP3A inhibitors. Hypertension Mirabegron can increase blood pressure. Blood pressure should be measured at baseline and periodically during treatment with Betmiga, especially in hypertensive patients. Data are limited in patients with stage 2 hypertension (systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 100 mm Hg). Patients with congenital or acquired QT prolongation Betmiga, at therapeutic doses, has not demonstrated clinically relevant QT prolongation in clinical studies. However, since patients with a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval were not included in these studies, the effects of mirabegron in these patients is unknown. Caution should be exercised when administering mirabegron in these patients. Patients with bladder outlet obstruction and patients taking antimuscarinic medications for OAB Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in patients treated with Betmiga; however, Betmiga should be administered with caution to patients with clinically significant BOO. Betmiga should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB. **Undesirable effects:** Summary of the safety profile The safety of Betmiga was evaluated in 8,428 patients with OAB, of which 5,646 received at least one dose of mirabegron in the phase 2/3 clinical programs, and 622 patients received Betmiga for at least 1 year (365 days). In the three 12-week phase 3 double blind, placebo controlled studies, 88% of the patients completed treatment with Betmiga, and 4% of the patients discontinued due to adverse events. Most adverse reactions were mild to moderate in severity. The most common adverse reactions reported for patients treated with Betmiga 50 mg during the three 12-week phase 3 double blind placebo controlled studies are tachycardia and urinary tract infections. The frequency of tachycardia was 0.2% in patients receiving Betmiga 50 mg. Tachycardia led to discontinuation in 0.1% patients receiving Betmiga 50 mg. The frequency of urinary tract infections was 2.9% in patients receiving Betmiga 50 mg. Urinary tract infections led to discontinuations in none of the patients receiving Betmiga 50 mg. Serious adverse reactions included atrial fibrillation (0.2%). Adverse reactions observed during the 1-year (long term) active controlled (muscarinic antagonist) study were similar in type and severity to those observed in the three 12-week phase 3 double blind, placebo controlled studies. List of adverse reactions The table below reflects the adverse reactions observed with mirabegron in the three 12-week phase 3 double blind, placebo controlled studies. The frequency of adverse reactions is defined as follows: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing serious reaction. **Infections and infestations: Common:** Urinary tract infection, **Uncommon:** Vaginal infection, Cystitis **Psychiatric disorders: Not known (cannot be estimated from the available data):** Insomnia[*] **Eye disorders: Rare:** Eyelid oedema **Cardiac disorders: Common:** Tachycardia **Uncommon:** Palpitation, Atrial fibrillation **Vascular disorders: Very rare:** Hypertensive crisis[*] **Gastrointestinal disorders: Common:** Nausea[*], Constipation[*], Diarrhoea[*] **Uncommon:** Dyspepsia, Gastritis **Rare:** Lip oedema **Skin and subcutaneous tissue disorders: Uncommon:** Urticaria, Rash, Rash macular, Rash papular, Pruritus, **Rare:** Leukocytoclastic vasculitis, Purpura, Angioedema[*] **Musculoskeletal and connective tissue disorders: Uncommon:** Joint swelling **Reproductive system and breast disorders: Uncommon:** Vulvovaginal pruritus **Investigations: Uncommon:** Blood pressure increased, GGT increased, AST increased, ALT increased **Renal and urinary disorders: Rare:** Urinary retention[*] **Nervous system disorders: Common:** Headache[*], Dizziness[*] [*]observed during post-marketing experience **Full prescribing information is available upon request.**

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