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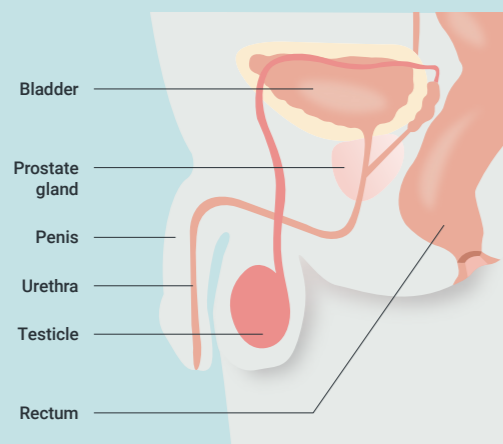
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MEN'S HEALTH: UNDERSTANDING PROSTATE HEALTH & CHANGES

It is important to take care of your prostate health as it is related to certain health issues, such as Benign Prostatic Hyperplasia (BPH) and prostate cancer. In Singapore, prostate cancer is the second most common cancer diagnosed in men¹. Meanwhile, BPH is one of the most common conditions affecting men over the age of 50².

Anatomy of the Male Pelvic Floor



What is the prostate?

The prostate is a walnut-sized gland present only in men. It is located below the bladder and just in front of the rectum. The prostate produces secretion, which nourishes the sperms in the semen.

As the prostate gland tends to grow larger with age, it may squeeze the urethra and cause problems in urination. An infection or a tumour could also enlarge the prostate. The 3 most common prostate problems are inflammation (prostatitis), BPH, and prostate cancer.

Inflammation (prostatitis)

Prostatitis is the inflammation of the prostate gland that may result from a bacterial infection.

Symptoms

- Trouble passing urine
- A burning feeling or pain when passing urine
- Strong, frequent urge to pass urine
- Chills and high fever
- Low back pain or body aches

- Pain in the groin area or behind the scrotum
- Rectal pressure or pain
- Genital and rectal throbbing

Having prostatitis does not increase your risk of any other prostate disease.

Tests and treatment

Several tests, such as Digital Rectal Exam (DRE) and a urine test, can be done to see if you have prostatitis. It is vital to get a correct diagnosis of the exact type of prostatitis so that you can get the right treatment for your condition.

Benign Prostatic Hyperplasia (BPH)

BPH, also known as enlarged prostate, is a common condition that affects the prostate gland in men as they age. "Benign" is a medical term used to describe a non-cancerous growth or condition, while "hyperplasia" refers to abnormal cell growth. As such, BPH is not linked to prostate cancer and does not increase the risk of getting prostate cancer, though the symptoms of both diseases can be similar.

Symptoms

- Trouble starting or having to push to release urine
- Weak or slow urine stream
- Stopping and starting again several times while urinating
- Feeling that the bladder is never fully empty
- Strong urge to pass urine often, especially at night
- A strong or sudden urge to urinate

Test and treatment

Depending on your symptoms, your doctor may conduct further tests to determine or confirm the diagnosis of BPH. Such tests include a urine flow study, DRE, and cystoscopy.

BPH cannot be cured, but there are several treatment options to relieve its symptoms. In cases where the symptoms are mild, BPH requires no treatment. However, when the symptoms are affecting your quality of life and overall health, consult your doctor for treatment options.

Prostate cancer

Prostate cancer is a tumour that grows in the prostate. Prostate cancers tend to be slow-growing and are typically confined to the prostate gland. However, there also exist aggressive types that can spread to other parts of the body, especially the bones and lymph nodes. Symptoms of prostate cancer are similar to those of BPH mentioned above; other symptoms of prostate cancer include:

- Blood in urine or semen
- Pelvic, back, or hip pain
- Bone pain that refuses to go away

It is important to note that in many cases, there are no symptoms as it can take years before a tumour gets big enough to cause symptoms.

Screening tests

Screening tests for prostate cancer include prostate-specific antigen (PSA) tests. PSA test is a blood test that measures the level of PSA – a protein produced by cells in the prostate gland. The higher the PSA level, the more likely that cancer cells are present. However, an elevated PSA level can also be caused by other factors.

Diagnostic tests

If prostate cancer is suspected, a **prostate biopsy** will be carried out. This means that a sample tissue from the prostate will be removed to confirm the presence of cancer and the grade of cancer.

During a biopsy, **transrectal ultrasound** is often used to guide the needles into the part of the prostate gland where the tumour is suspected. MRI guidance may be used to target biopsy sites more accurately in challenging cases.

If prostate cancer is diagnosed, further tests may be conducted to determine the extent of cancer. For instance, MRI prostate, also known as prostate magnetic resonance imaging, can help to determine the local extent of cancer, including the spread of cancer to lymph nodes. MRI prostate is a medical imaging technique used to visualise the prostate gland.

To exclude distant metastases, prostate-specific membrane antigen positron emission tomography (PSMA PET) can be used in high-risk cases where the prostate-specific antigen (PSA) levels are high, or when the tumour is suspected to have a high T stage (indicating a more advanced and potentially aggressive cancer).

Towards a better prostate health

Understanding prostate health and being aware of changes that can occur is crucial for every man. While some changes are a natural part of ageing, others may indicate underlying issues that require attention. By being informed, you can identify the problems and seek professional help from your doctor when needed. ■



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¹Singapore Cancer Registry Annual Report 2020

²Lower Urinary Tract Symptoms. MOH & HPB, 2006



PARKWAY CANCER CENTRE 17TH ANNIVERSARY

In October, Parkway Cancer Centre (PCC) celebrated its 17th Anniversary with a floral-themed dinner and an exciting line-up of activities. Attendees showed up in a myriad of colours, perfectly encapsulating the theme for this year's memorable event.

The event, graced by special guest Dr Peter Chow, Acting Chief Executive Officer for IHH Healthcare Singapore, kicked off with an opening speech by PCC's Medical Director and Senior Consultant, Medical Oncology, Dr Ang Peng Tiam.

This was followed by a buffet-style dinner, where attendees were free to mingle around and connect with each other while indulging in delicious food of various cuisines. There was also a photobooth available where many took memorable photos together with the stunning backdrop.

Other than the exciting ice-breaking games, the organising team also put together a heartwarming photo montage of the various team bonding activities, namely the SCS TalkMed Relay for Life 2023 and team cooking, as well as birthday celebrations.

To award the attendees for taking the time and effort to dress up, several prizes were prepared for the Best Dressed Individual and Group. 12 lucky winners also walked away with exciting

prizes during the lucky draw! The evening was filled with joy and laughter, making it a memorable time for everyone.

Parkway Cancer Centre and CanHOPE

As we celebrate PCC's 17th anniversary, it is important to remember where we started from, be it our goals, our vision, or our mission.

Parkway Cancer Centre was established in 2006 with a goal of spreading hope in the face of this consequential disease. The centre is home to a multidisciplinary team of highly skilled medical doctors, nurses, counsellors, dietitians, and other paramedical professionals.

With 9 clinics across Singapore and more than 15 major cities around the region, PCC has grown into a substantial establishment that is fully equipped to join the battle against cancer and provide hope to all those affected.

Over the years, PCC has been utilising the latest advances in medical research and technology to provide optimal care to its patients. From immunotherapy to targeted therapy, PCC strives to offer the most appropriate solution to its patients, including optimal treatment outcomes and better cancer care.

PCC's non-profit cancer counselling and support arm, CanHOPE, offers patients psychosocial support wherever they are in the world. CanHOPE aims to support, empower, and inspire hope by providing access to resources and holistic care to those on their cancer journey.

From cancer rehabilitation to palliative care, CanHOPE ensures that its patients and their loved ones are fully supported with its comprehensive range of services. The non-profit organisation also has awareness and outreach programmes to help

spread awareness and advocate for early detection through educational opportunities.

Towards a hopeful future

As PCC goes into its 17th year, it will continue to provide a comprehensive and integrated premier cancer service with utmost care, comfort, and compassion, all while being patient-focused. Hope will continue to remain as PCC's guiding principle as it aspires to instil hope in its patients while giving them the optimal treatment they deserve.

With a team of highly-skilled professionals and state-of-the-art facilities, PCC will continue to make significant strides in the ongoing fight against cancer. ■





STATE-OF-THE-ART TREATMENT OF METASTATIC MELANOMA IN 2023

At the recently concluded 25th World Congress of Dermatology 2023, Parkway Cancer Centre's Dr Richard Quek, Senior Consultant, Medical Oncology, was invited to speak on the state-of-the-art treatment for metastatic melanoma with emphasis on the growing body of literature on the neoadjuvant approaches in melanoma.

Over the last decade, advances in melanoma treatment have substantially improved patient survival. These treatments include immune checkpoint inhibitors and targeted therapy.

Within the field of immunotherapy, checkpoint inhibitors – such as anti-CTLA4 (ipilimumab), anti-PD-1 (pembrolizumab, nivolumab) and anti-PDL-1 (atezolizumab) – have all been approved for standard use. While in the field of *BRAF*-targeted therapy, doublet therapies such as dabrafenib/trametinib, encorafenib/binimetinib and vemurafenib/cobimetinib were added to the armamentarium in *BRAF*-mutated melanomas.

For years, the big questions faced by clinicians and patients alike were firstly, what is the optimal front-line option in patients with *BRAF*-mutated melanomas; is it immunotherapy or targeted therapy? The second big question was, should we use single agent immunotherapy (anti-PD-1 or PDL-1) or dual immunotherapy (anti-CTLA-4 plus anti-PD-1) in patients we opt to treat with immunotherapy?

Patients with *BRAF* mutation positive advanced melanoma

For patients with advanced melanoma, oncologists will firstly assess the tumour *BRAF* mutation status and stratify patients into *BRAF* mutations positive vs negative disease. If the tumour is *BRAF* mutation positive, both immunotherapy or targeted therapy are approved standard options. The treating oncologists will have to decide on whether to proceed with either an upfront immunotherapy or targeted therapy approach.

The recently published DREAMseq study¹ – a phase III randomised study conducted to determine which initial treatment or treatment sequence produced the best results in patients with advanced *BRAF* mutation positive melanoma, helped answer the first question.

In the trial, the patients had *BRAF*-mutated melanoma and were randomised into two groups:

The first group of patients started treatment with dual immunotherapy, consisting of both Nivolumab (NIVO) and Ipilimumab (IPI), monoclonal antibodies that work to activate the immune system by targeting both the PD-1 and CTLA-4 protein receptors respectively. At the time of cancer worsening, patients will then switch over to *BRAF*-MEK inhibitor combinations – in this case, dabrafenib and trametinib.

The other group of patients started treatment in the reverse order. They started with a *BRAF*-targeting strategy using dabrafenib and trametinib. At the time of cancer worsening, they switched over to immunotherapy using the same 2 immunotherapy drugs of NIVO and IPI.



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Dr Quek is a Senior Consultant Medical Oncologist. He is well versed in general medical oncology cases and his subspecialty interests include bone and soft tissue sarcomas, gastrointestinal stromal tumours (GIST), melanomas and lymphomas. Prior to joining PCC, he was the Deputy Head, Division of Medical Oncology at the National Cancer Centre Singapore from 2013–2018 as well as the Programme Director for the medical oncology senior residency programme.

¹Atkins M.B., et al. *Journal of Clinical Oncology*, 2023.



At the study's conclusion, the 2-year overall survival data strongly favoured the strategy with starting patients on treatment with immunotherapy (IPI and NIVO) before switching over to *BRAF*-targeting therapy at time of cancer progression. Additionally, the overall response rate (proportion of patients whose cancer shrink in size) was significantly higher at the time of switch over in the first group of patients.

As such, Dr Quek emphasised that for patients with advanced *BRAF*-mutation positive melanoma, in absence of contraindications, the optimal treatment approach would be dual immunotherapy with NIVO and IPI first, keeping *BRAF*-targeting agents in reserve.

Patients with *BRAF* mutation negative advanced melanoma

As for patients whose tumours are *BRAF* mutation negative, *BRAF*-targeting therapy is not an option.

The recurring clinical question oncologists faced was whether to start with single agent immunotherapy or dual agent immunotherapy. In other words, oncologists needed to decide whether to use one or two immunotherapy drugs upfront. From the information we had to date then, two drugs gave a better chance of shrinking the tumour but came at the expense of more frequent and more serious side effects. Additionally, we were uncertain if using 2 immunotherapy agents at the same time prolonged survival of patients to justify the expense of greater side effects.

To shed more light on this clinical dilemma, Dr Quek cited the updated Checkmate 067 study², which demonstrated the impressive overall survival rate of using combined IPI and NIVO together, as compared to using either IPI or NIVO alone. The median survival duration of patients with advanced metastatic melanoma treated with 2 immunotherapy agents (IPI and NIVO) was approximately 6 years as compared to 3 years when treated with NIVO alone. These survival figures were hugely impressive in a patient population with very poor prognosis. Just a decade ago, these same patients had no effective treatment and whose survival was less than a year. This data validates the strength of using dual agent immuno-oncology.

However, serious treatment-related toxicities of using both IPI and NIVO are significant, at the rate of 59% as compared to 21%, when only NIVO is used. Thankfully, these days, treating oncologists are more aware of such immune-related side effects, able to recognise them earlier, and better equipped to manage them appropriately.

New drugs in Melanoma: Combined RELATLIMAB (RELA) AND NIVOLUMAB (NIVO)

Relatlimab (RELA) – an anti-LAG-3 checkpoint inhibitor – has recently been approved by the United States Food and Drug Administration (U.S. FDA) and Health Science Authority (HSA)

Singapore for use in combination with Nivolumab (NIVO) in patients with advanced melanoma.

LAG3 and PD-1 are distinct immune checkpoints, often expressed on tumour-infiltrating lymphocytes (TILs) – a form of immune cell therapy. The two checkpoints contribute to tumour-mediated T-cell exhaustion, which prevents optimal control of infection and tumours.

In preclinical models, LAG-3 and PD-1 inhibitors demonstrated synergistic anti-tumour activity³, including durable, objective responses in patients with relapsed or refractory melanoma.

In a large international phase 3 study, Relativity-047⁴, the use of combined RELA and NIVO demonstrated superior progression-free survival (PFS) – time from random assignment in a clinical trial to disease progression or death from any cause – to NIVO alone. The two inhibitors also demonstrated a manageable safety profile on top of showing a numerically improved overall survival and tumour objective response rate – an important assessment of the tumour burden which demonstrates the efficacy of a treatment. Notably, serious side effects occurred in less than 20% of patients treated with RELA and NIVO. This compares favourably to the approximately 60% seen in the current standard of IPI and NIVO.

While data is not available to guide the choice between the front line options of IPI and NIVO versus RELA and NIVO, Dr Quek posits that if the patient is relatively young and has a good performance status, IPI and NIVO – the current standard with good long-term survival data – is a preferred option. While older patients, with a poorer performance status or do not have easy access to a medical facility (should complications occur), may be more suited for RELA and NIVO instead.

As of now, treatment-related toxicities play a significant part in choosing the appropriate treatment. However, we hope that in time to come, more matured data becomes available to allow a proper comparison between the two front-line immunotherapy treatment strategies.

What's next for patients with advanced melanoma?

Over the past decade, there have been several significant advances made in the systemic treatment for advanced melanoma, including *BRAF*-targeted therapy, dual agent immune-oncology with IPI and NIVO.

Now, with the novel addition of RELA, we have another potent treatment strategy in melanoma. The low toxicities of RELA and NIVO propel both patients and oncologists alike onto a more hopeful path as we await future possibilities in the treatment of advanced melanoma. ■

²Wolchok J.D., et al. ASCO 2021.

³Woo S-R, et al. Cancer Res 2012.

⁴Tawbi, et al. N Engl J Med 2022.



COPING WITH LONELINESS DURING THE FESTIVE SEASON

'Tis the season to be jolly, but even the merriest of holidays has its blues. Holiday loneliness happens even to the best of us, so it is important to understand that you're not alone. Here are some tips on how to manage loneliness during the most festive time of the year.

Loneliness is a complex personal state that is characterised by a sense of isolation, disconnection, and a lack of meaningful social interaction and companionship. Although much of the research surrounding loneliness focuses on older adults, loneliness can affect individuals of any age. Normalise it: Most of us would have gone through seasons of loneliness in our lives.

Loneliness is different from aloneness; the former is subjective. One could be surrounded by friends and family but still feel lonely. Alternatively, you could be alone and feel completely at ease. What, then, exactly contributes to this complex emotion?

Reasons for holiday loneliness

Loneliness is biologically motivated; we are genetically coded to meet this basic need for connection. However, this complex emotion could peak during the holidays for a few reasons.

1. Unrealistic expectations

During the festive season, you may compare your life with those around you and set several unrealistic expectations for your holiday life. Social media can often contribute to these unrealistic expectations. When these expectations

are not met, you may feel a myriad of negative emotions which can contribute to loneliness.

2. Grief or depression

Loneliness can be compounded by existing feelings of grief or depression, often caused by the loss of a loved one or the loss of a relationship. The festive mood can be a painful reminder of the ones we lost as their absence can intensify feelings of loneliness and grief.

3. Missing loved ones

If your loved ones live far away, the distance can make it difficult to be together during the holiday season. Many often celebrate the joyous festivities with their loved ones, so not being able to do so could result in loneliness.



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How to cope with holiday loneliness

Feeling lonely is a natural occurrence, but there are ways to help yourself through it and alleviate the feeling. Here are some strategies you can adopt to mitigate your feelings of loneliness.



1. Lending a helping hand

Volunteering is an effective way to lower the risk of loneliness¹ as isolation tends to draw people's attention inwards, while giving back turns it outwards. When your attention is drawn inwards, you tend to internalise and compound whatever negative emotions you have. On the other hand, by volunteering, your negative feelings are allowed to dissipate and transform into positive emotions as you help others.

Additionally, in a 2013 study² that investigated the association between support provision and mortality rates, it was found that helping behaviour reduces mortality because it buffers the association between stress and mortality. This means that helping others will in turn help to alleviate your stress levels, leading to better overall health and reduced mortality.

During the festive season, you can look to give back to those in need and celebrate the festivities by helping others.



2. Engage in creative activities

There is growing research³ that links creative expression to reduced loneliness as being creative can act as an outlet for the negative emotions that accompany loneliness. Creative expression can also help individuals to connect with themselves on a deeper level and foster a sense of self-awareness and introspection, both of which are vital in times of loneliness.

There are various ways to unleash your creativity; you can engage in arts and craft, write a poem, play an instrument, or learn a dance routine. Since Christmas is coming, you can even create Christmas cards, craft a Christmas-themed poem, or write a short Christmas jingle for your loved ones.

If creativity does not come naturally to you, you can start by spending time around others who engage in creative activities. For instance, you can attend a friend's concert or performance. This has the added benefit of social interaction, which can definitely mitigate feelings of loneliness.



3. Practise gratitude

Practising gratitude is a powerful tool for improving your mental health and overall well-being as it helps you to focus on and appreciate the positive aspects of your life, even amidst difficulties.

During the festive season, our expectations are often high and it is easy to be disappointed when things do not go exactly as planned. As such, practising gratitude will be vital in directing your attention towards what you have instead of what you do not have. It will help you understand how lucky you are and draw your focus away from all the negativity and disappointment you may have during the festive celebrations.

You can practise gratitude by noting down all the things you are grateful for, especially during the holidays. Perhaps you would like to use this season of gifting to express your love and appreciation to family or friends. It is important to reflect and be grateful for even the little things in your life, as this will help you to have a more positive outlook on your life.

Ultimately, it is important to understand that you are not alone, as experiencing loneliness during the festive season is a common occurrence. If you have such feelings, do not deny or feel ashamed about it. Instead, be kind to yourself and try to make peace with your loneliness. It is only when we allow ourselves to feel lonely that we can even start to relieve it.

Reach out for support

If these feelings of loneliness persist or remain overwhelming enough to affect your daily functioning, you may speak to a counsellor or a mental health professional to help tide you through this season. Counselling can be a safe place for you to voice your feelings and process your thoughts without fear of judgement. ■

¹Cho J, Xiang X. *The Relationship Between Volunteering and the Occurrence of Loneliness Among Older Adults: A Longitudinal Study with 12 Years of Follow-Up.* 2023.

²Poulin et al. *Giving to Others and the Association Between Stress and Mortality.* 2013.

³Pauly T et al. *COVID-19, Time to Oneself, and Loneliness: Creativity as a Resource.* 2022.



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