Prostate Cancer Foundation of Australia

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BLUE SKY NEWS

AUSTRALIAN FIRST

Global Phase 3 Clinical Trial into new treatment

FOCAL THERAPY

Improving outcomes for men with prostate cancer

CONTENTS

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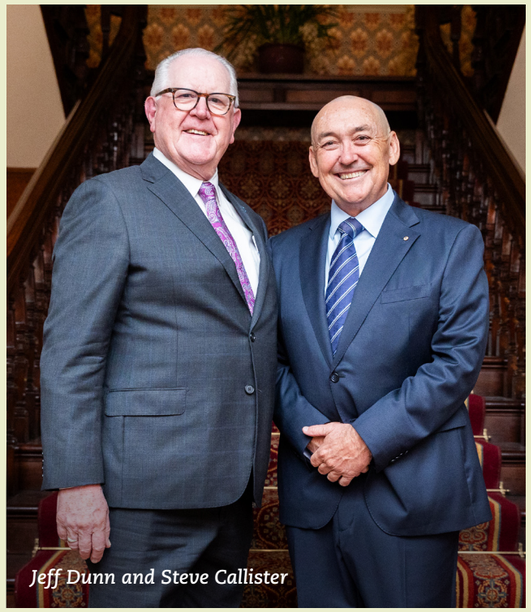

Jeff Dunn and Steve Callister

Your fighting fund

Welcome to the January 2024 edition of Blue Sky News. In this edition, we provide you with an in-depth look at new and emerging treatments that are saving the lives of men with prostate cancer.

We also provide more information on game-changing new medicines that are improving the lives of men with prostate cancer. Your donations are key to our success. Thank you for backing us.

With your Will, we can find a way. If your life has been impacted by prostate cancer, please consider leaving a gift in your Will to PCFA's Prostate Cancer Future Fund.

When you decide to leave a gift in your Will to PCFA, your legacy will help to create a world without prostate cancer for current and future generations.

Please call our team today on 1800 22 00 99 to find out more.

Adjunct A/Prof Steve Callister
National Board Chairman

Professor Jeff Dunn AO
Chief of Mission & Head of Research

For wording, go to **pcfau.org/Wills**

Research supports early use of LuPSMA in prostate cancer

Researchers have shown LuPSMA therapy can be safely used as a first-line treatment for men with newly diagnosed prostate cancer, potentially revolutionising treatment for aggressive forms of the disease.

The world-first research, recently published in the journal *European Urology*, studied the effects of men receiving the highly-targeted radioactive treatment known as LuPSMA before their cancerous prostate was surgically removed.

LuPSMA is an infusion containing radioactive Lutetium-177 which is attracted to PSMA (Prostate Specific Membrane Antigen) on prostate cancer cells wherever they are in the body, killing these cells.

Head of the Prostate Cancer Theranostics and Imaging Centre of Excellence at the Peter MacCallum Cancer Centre (Peter Mac), Professor Michael Hofman, said LuPSMA was generally used as a last-line treatment in cases where the cancer had spread beyond the prostate.

Landmark trials have shown LuPSMA can improve quality of life and survival for these men with late-stage, aggressive prostate cancers.

"In the LuTectomy study, men with newly diagnosed, localised prostate cancer received upfront radiation treatment with LuPSMA before surgical removal of their prostate," says Professor Hofman.

"Some types of radiotherapy can result in damage to surrounding tissue making surgery afterwards more complex, therefore treatments like LuPSMA are generally performed only after surgery has taken place."

The study showed LuPSMA therapy did not increase the technical difficulty of later surgery or add to risk of post-operative complications, and was therefore safe to give to men ahead of prostate removal.

"While we know that early-stage localised prostate cancer can be cured with surgery or external-beam radiotherapy, around half of the men with high-risk cancer will develop disease recurrence and metastases," Professor Hofman says.

"We hope that this new application of LuPSMA therapy, before surgery, will ultimately cure more patients."

Surgeon and Director of Genitourinary Oncology at Peter Mac, Professor Declan Murphy, says the targeted nature of LuPSMA reduced the impact on healthy tissue around a tumour.

"Therapeutic radiation from LuPSMA therapy travels only 1mm resulting in highly targeted tumour killing, while sparing normal tissue.

"This study shows we can safely add LuPSMA therapy before surgery and, if this is also shown to improve cure rates, it will revolutionise how we manage men with high-risk prostate cancers," Professor Murphy says.

Prostate Cancer Foundation of Australia co-funded the ProPSMA and TheraP Clinical Trials. ◆

"This study shows we can safely add LuPSMA therapy before surgery and, if this is also shown to improve cure rates, it will revolutionise how we manage men with high-risk prostate cancers."

Professor Declan Murphy

To find out more about new clinical trials, call our **Telenursing Service** on **1800 22 00 99**

Aussie man first in the world to take part in global study

An Australian man with an aggressive form of prostate cancer has become the first patient in the world to start treatment in a Phase 3 clinical trial using a new form of nuclear medicine.

A global study has just begun to test the effectiveness of a new treatment that could extend the lives of thousands of Australian men each year, preventing avoidable deaths from prostate cancer.

Impressively, this trial is being driven by an Australian-headquartered company and led by Australian-based researchers, using therapeutic agents in a novel combination with real world standard of care.

Prostate Cancer Foundation of Australia Chief of Mission and Head of Research, Professor Jeff Dunn AO, says Australia is leading the world in prostate cancer research.

"We are on the verge of a complete transformation in prostate cancer treatment, giving men with the most aggressive and deadly forms of this disease a greater hope of survival.

"Australia is a world leader in this field and our hope is that more Australian men will survive their disease as a result."

At a broad level, the researchers are investigating an emerging field of nuclear medicine known as PSMA theranostics.

The trial, called ProstACT GLOBAL, is sponsored by Melbourne-headquartered Telix Pharmaceuticals and driven by Telix's global medical and clinical operations team.

"Theranostics combines therapy and diagnostics to improve our understanding of each man's prostate cancer, and how it can be most effectively treated," says Dr Shams Arifeen, Telix Medical Director for the APAC region.

"The therapeutic agent we are trialling here is attracted to Prostate Specific Membrane Antigen, a protein found on the surface of prostate cancer cells. After being injected into the blood stream, the drug can track down rogue prostate cancer cells in other parts of the body.

"This research uses a special nuclear medicine radiotracer known as lutetium therapy that attaches itself to the PSMA and deploys targeted radiation to destroy the killer cancer cells.

"Notably, this trial is the first Phase 3 study of a therapeutic agent using an antibody as a targeting molecule, known as a radio-antibody drug conjugate (or rADC for short).

"Until now, nuclear medicine therapies like this have relied on small molecules, which require higher doses compared to using an antibody as the targeting molecule.

"Previous studies have shown that this antibody attaches to the tumour for longer, lengthening the therapeutic duration, meaning greater potential effect on cancerous cells.

"The objective of the study is to investigate and confirm the risks and benefits associated with Telix's TLX591 candidate administered together with Standard of Care (SoC), as compared to SoC alone.

Principal Investigator, Professor Nat Lenzo, says the antibody approach has the potential to make a meaningful difference in cancer treatment.

"It is really exciting to see further development of this PSMA-targeting radiotherapeutic and we are pleased to have initiated this Phase 3 study here in Australia."

"An antibody approach helps reduce excretion of the agent in the patient's urine, as well as having reduced salivary gland toxicity, which can be a side effect of nuclear medicine therapies based on small molecule targeting agents.

"Previous studies have confirmed the suitability of the short, simple treatment duration with two doses administered two weeks apart.

"I have also been encouraged with the safety profile, tolerability and early efficacy observed to date, in particular for symptom control."

Prostate cancer is the leading cause of cancer-related hospitalisations in Australia, accounting for nearly 1 in 10 of all cancer-related hospitalisations for total costs of more than $1.35B every year.

Worldwide, more than 1.4 million men are diagnosed with prostate cancer each year and more than 375,000 die from the disease. ◆

"We are on the verge of a complete transformation in prostate cancer treatment, giving men with the most aggressive and deadly forms of this disease a greater hope of survival."

Professor Jeff Dunn AO

To find out more about new clinical trials, call our **Telenursing Service** on **1800 22 00 99**

EMERGING TREATMENTS IN PROSTATE CANCER:

Focal therapy changes the game

Each year more than 21,000 Australian men will be newly diagnosed with prostate cancer that has not yet spread beyond the prostate. For many of these men, focal therapy is a game-changer, offering a treatment option that ablates the tumour without damaging surrounding nerves and tissues.

As many of our readers will know, the conventional treatments for localised prostate cancer treat the whole prostate gland, providing a highly effective way to eradicate the cancer.

However, because the prostate is surrounded by delicate erectile nerves and important parts of the anatomy, the side effects of surgery and conventional radiotherapy can have a significant impact on normal bodily functions and quality of life.

Urological surgeon and focal therapy pioneer, Associate Professor Jeremy Grummet, says evidence is mounting that focal therapy may be an ideal treatment option for men with intermediate-risk localised prostate cancer.

"Minimising risk of harm is a top priority. In patients with localised prostate cancer, this is attempted in several ways: by not treating low grade prostate cancers and instead keeping them under active surveillance; or in higher grade cancers, by performing erectile-nerve sparing techniques when performing prostatectomy; or by technologies that conform radiation dose more accurately to the shape of the prostate.

"Despite these advances, when standard

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"What's most important is that there are various registered studies actively recruiting in Australia now to help answer this question, as well as find out the long-term cancer outcomes."

Associate Professor Jeremy Grummet

→ treatment of localised prostate cancer is applied, erectile dysfunction, and urinary and rectal symptoms remain common. In their decision-making, patients are then faced with balancing the risk of cancer progressing by avoiding treatment versus the risk of loss of significant quality of life by going ahead.

"The proponents of focal therapy have long wondered whether we can find a middle path, whereby the cancer tumour can be destroyed while remaining healthy prostate tissue is preserved.

"It's the same oncological principle as the now long-accepted standard treatment of lumpectomy for early breast cancer – the rationale in prostate cancer being that if tissue destruction is kept to a minimum, injury to the all-important surrounding structures will also be minimised."

A/Professor Grummet says evidence from studies around the world has shown this to be true.

"Focal cancer ablation can be achieved using various different treatment modalities or energy sources, including radiation such as brachytherapy seed implantation, irreversible electroporation (also known as the NanoKnife), high-intensity focused ultrasound (or HIFU), cryotherapy, photodynamic therapy and laser. We don't yet know which of these modalities is most effective, as they are all still under investigation.

"What's most important is that there are various registered studies actively recruiting in Australia now to help answer this question, as well as find out the long-term cancer outcomes."

Interest in focal therapy has skyrocketed with the recent advent of imaging such as MRI and PSMA PET, which can finally reliably identify clinically significant forms of prostate cancer.

"Advances in imaging have led to far greater accuracy in diagnosis. The logical next step is to apply them to precise, targeted treatment," A/Professor Grummet says.

"It's important though to consider the opportunity as well as the risks. In theory, focal therapy sounds exactly what patients with localised prostate cancer have been desperate for – cancer cure with minimal side effects. But what might the risks be?

"The most obvious risk is that the cancer treated is not completely destroyed and can go on to progress locally or even spread. Another risk is that more cancer develops in the untreated parts of the prostate.

"And finally, it's possible that if focal therapy fails, it could impact the ability to perform salvage treatment, such as radical prostatectomy, if scar tissue forms at the treatment site."

For these reasons, there are three critically important points to make about focal therapy as it stands currently:

Associate Professor Jeremy Grummet and his daughters

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Associate Professor Jeremy Grummet

PHOTOGRAPHER: WILL SALTER. WWW.WILLSALTER.COM

1 PATIENT SELECTION IS CRUCIAL

Focal therapy is a treatment for relatively small, clinically significant prostate cancers that are visible on imaging. It's not necessary for patients with low-risk cancer, who can be safely managed on active surveillance. And it's insufficient treatment for large high-grade cancers. Its correct application is right in the middle of these two extremes.

2 CLOSE FOLLOW-UP IS ESSENTIAL

This consists of regular post-therapy PSA levels along with further imaging and biopsy to ensure significant cancer has been successfully destroyed. This also allows close observation of the remaining untreated prostate tissue.

3 MEASURING IMPACT THROUGH CLINICAL TRIAL OR REGISTRY IS IMPORTANT

Ideally focal therapy should be conducted within the setting of a clinical trial or registry, so evidence can be collected to inform all of us of the true long-term impact of this exciting new treatment option. ◆

For more information about focal therapy, call our **Telenursing Service** on **1800 22 00 99**

Australia's first living lab to beat deadly prostate cancers

Australian researchers are among the first scientists in the world to establish a living lab to help find new treatments and therapies for deadly forms of prostate cancer.

The ground-breaking project, funded by Prostate Cancer Foundation of Australia, aims to help end Australian deaths from the disease, expanding on the capabilities of the landmark Australian Prostate Cancer BioResource.

The existing BioResource will be enriched by seed funding to enable the inclusion of specimens and data from men with advanced metastatic disease, and will for the first time include unique collections of patient models of prostate cancer.

These precious resources will then be available for access by prostate cancer researchers around the country.

PCFA's Chief of Mission and Head of Research, Professor Jeff Dunn AO, hails the project a game-changer for men with advanced prostate cancer.

"The living lab will accelerate medical and scientific research and transform our ability to analyse deadly tumours and test new methods for preventing and eliminating prostate cancer."

The lab has been given the acronym ALLURe, short for the Australian Living Lab for Urological Repositories.

"This will be a world-leading biorepository of metastatic prostate cancer and will allow us to closely study and experiment with metastatic pros tate tumours to try and unlock new ways of defeating the disease," Professor Dunn says.

"Importantly, it will allow us to break down the barriers to survival, providing us with a platform to amass population-wide data to eliminate sampling bias that often arises due to inequities in care.

"The project is exciting for many reasons, including the fact that the platform will enable tissue samples and test results to be uploaded and shared across the research community, allowing scientists to work together nationally and globally to find solutions for one of the leading causes of cancer death among Australian men."

Around one in five Australian men will be diagnosed with prostate cancer in their lifetime, with 250,000 men alive today after a diagnosis of the disease.

Leading project proponent and world-leading prostate cancer researcher, Professor Lisa Butler, says the lab is expected to spark a revolution in research.

"We are confident the lab will accelerate research discoveries and result in new clinical trials that can be made available to patients more rapidly than ever before, extending and saving men's lives," Professor Butler says.

> **"Our hope is to unlock new precision medicines, allowing the development of therapies that are tailored to each patient, extending and saving lives."**
>
> *Professor Lisa Butler*

"The lab will give researchers access to high-quality living or preserved tissue and blood samples allowing researchers to access and compare hundreds of thousands of pieces of clinical information for the very first time.

"If we are successful in reaching our fundraising target to build the lab, Australia will stand at the forefront of worldwide research into prostate cancer, powering discoveries around the globe."

It is hoped the project will unlock discoveries that have the power to end deaths from prostate cancer within a decade.

"Until now, Australia has lacked a national repository for metastatic prostate cancer specimens, clinical data and lab-ready models," Professor Butler says.

"Thanks to the seed funding provided by PCFA, all that will change, putting us on a path to find the answers we need to solve the puzzle of prostate cancer.

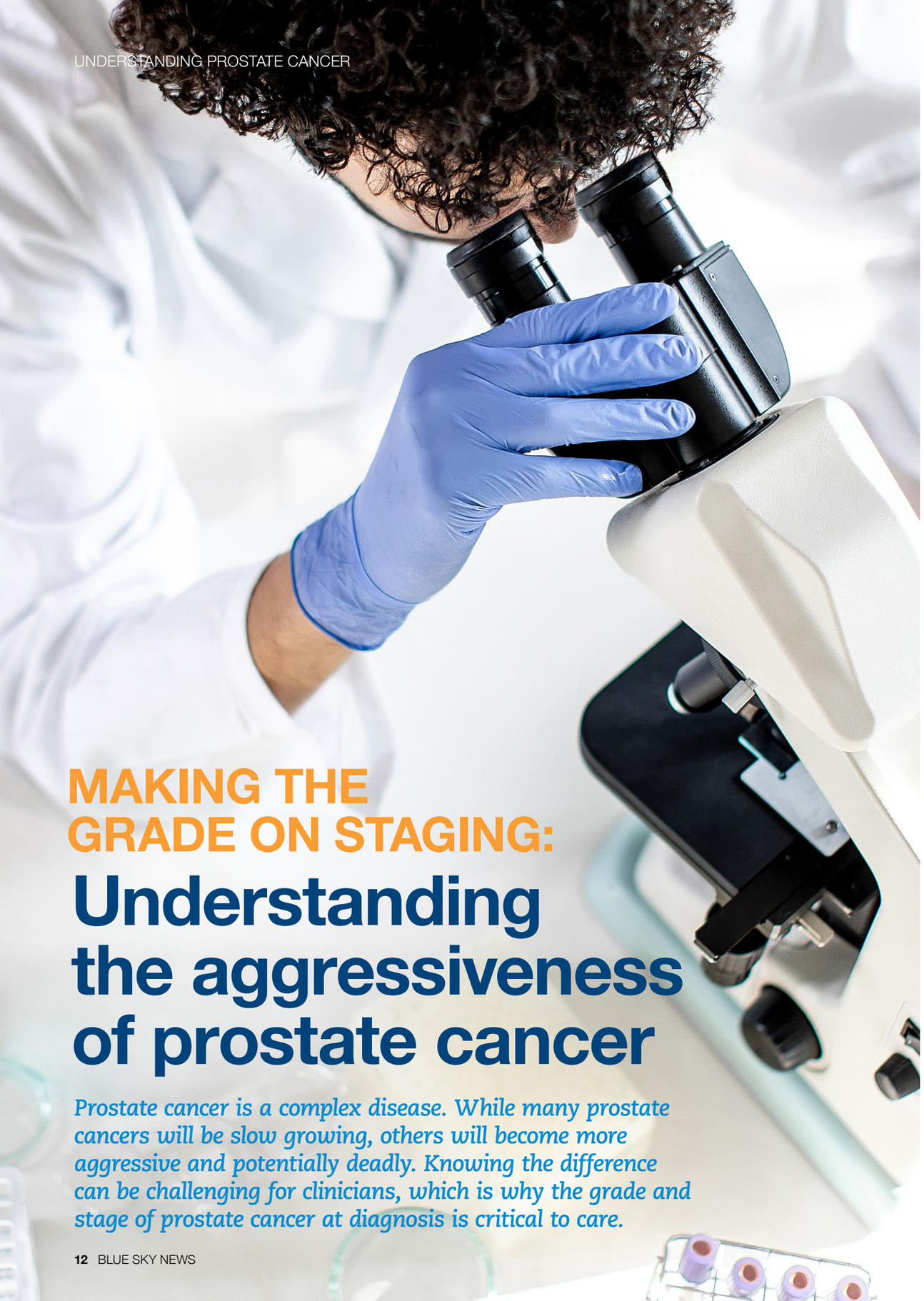
"Every researcher in Australia will have the opportunity to access the lab's data and specimens, strengthening our ability to synthesise medical and scientific investigations.

"Our hope is to unlock new precision medicines, allowing the development of therapies that are tailored to each patient, extending and saving lives.

"We call it a living lab, and for good reason – its role is to keep men alive," Professor Butler says. ◆

Donate to **ALLURe** via **pcfa.org.au/allure**

Professor Lisa Butler



MAKING THE GRADE ON STAGING:

Understanding the aggressiveness of prostate cancer

Prostate cancer is a complex disease. While many prostate cancers will be slow growing, others will become more aggressive and potentially deadly. Knowing the difference can be challenging for clinicians, which is why the grade and stage of prostate cancer at diagnosis is critical to care.

"Most of us have heard of the Gleason system for grading prostate cancer," says urologist and author of *Your Guide to Prostate Cancer*, Associate Professor Prem Rashid.

"A man's Gleason Score is determined after biopsy, based on the patterns of cancer evident in the biopsy sample.

"To decide how best to treat prostate cancer, doctors determine the aggressiveness of the cancer based on the biopsy and whether there is any sign the cancer has spread outside the prostate.

"Grade is determined by a pathologist and refers to the aggressiveness of the cancer cells and how quickly they are expected to grow."

Low grade cancers usually grow slowly and are less likely to spread, whereas higher grade cancers are more likely to grow quickly and spread to other parts of the body.

"Stage describes the cancer's size and whether it has spread beyond the prostate, based on diagnostic tests and results of imaging scans, commonly MRI and PSMA-PET scans," Associate Professor Rashid says.

"Normal tissue has an ordered pattern of growth but in cancer tissue, the pattern is disordered because of the unpredictable way cancer cells grow. The Gleason scoring system shows how abnormal or different the cancer tissue is compared to the normal tissue."

The prostate cancer Gleason grade scale was pattern 1 – 5 but now is simpler at 3 – 5. Grades 4 and 5 are aggressive.

"There is often more than one pattern of cancer present in the biopsy," says A/Professor Rashid.

"The two most common patterns of growth seen in the biopsy sample are each given a number from 3 to 5, and then these two numbers are added together to give the Gleason Score, for example, 4 + 3 = 7.

"If the first and second most common patterns in a biopsy are both pattern 3, then the Gleason Score would be 3 + 3 = 6. This is a low-grade cancer usually managed with surveillance initially.

"If both first and second most common patterns are grade 5, the Gleason Score will be 5 + 5 = 10. These cancers are very high grade.

A newer grading system, called the Grade Group (or ISUP Grade), is now also being used to decide the level of risk for each cancer grade. The Grade Group system helps in predicting how quickly the cancer will spread and the chance of death.

"The Grade Group system uses 5 grades. Grade Group 1 is low risk and Grade Group 5 is the highest risk and most aggressive cancer.

"Understanding a patient's Gleason Score, Grade Group and Stage are all very important in determining the right treatment pathway," Associate Professor Rashid says. ◆

GRADE GROUP	GLEASON SCORE	RISK
1	3 + 3 = 6	**Low risk:** The cancer is usually slow growing and less likely to spread
2	3 + 4 + 7	**Intermediate favourable risk:** The cancer is moderately likely to spread
3	4 + 3 = 7	**Intermediate unfavourable risk:** The cancer is moderately likely to spread
4	4 + 4 = 8	**High risk:** The cancer is likely to be fast growing and more likely to spread
5	9 or 10	**The highest risk:** The cancer is likely to be fast growing and most likely to spread

For more information and advice, call us on **1800 22 00 99**

New PBS drug listing for men with prostate cancer

The life-changing drug NUBEQA is now listed on the Pharmaceutical Benefits Scheme (PBS) for men with aggressive forms of prostate cancer, saving each patient $42,000 per year in prescription costs.

The listing is just the latest advancement in response to ongoing advocacy by Prostate Cancer Foundation of Australia, giving men access to triple therapy in the fight against prostate cancer.

NUBEQA, also known by the generic name Darolutamide, is now available for men with metastatic hormone-sensitive prostate cancer, a type of aggressive prostate cancer that has spread beyond the prostate to other parts of the body.

It will form part of a three-pronged treatment, used alongside chemotherapy and hormone therapy (androgen deprivation therapy or ADT).

NUBEQA helps to starve cancer cells of the hormones they need to grow and divide, and under this listing will be delivered in combination with conventional hormone deprivation therapy and chemotherapy. Conventional hormone therapy blocks the production of cancer-stimulating hormones, while chemotherapy works to destroy cancer cells.

"Sadly, prostate cancer remains the second greatest cancer killer of Australian men. New treatment options are desperately needed," says Medical Oncologist Dr Laurence Krieger.

Through the PBS, around 2,800 eligible men will pay just $7.30 (on concession) or $30.00 (general patients) each month for NUBEQA. Without the PBS subsidy, the tablets could cost more than $42,000 each year in addition to the cost of other anti-cancer medicines.

"Every year nearly 4,000 Australian men will be diagnosed with incurable Stage 3 or 4 prostate cancers," says PCFA CEO Anne Savage.

"The listing of medicines such as NUBEQA for more men is an important development for thousands of Australian fathers and sons," she said.

"However, we need to continue raising awareness so that all Australian men get a fair chance of detecting prostate cancer early, so that we can beat it."

The new listing expands access to the life-extending drug, which is also listed for men with non-metastatic hormone sensitive prostate cancer.

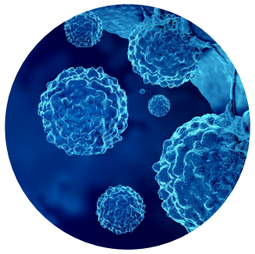
Prostate Cancer Foundation of Australia will be calling for a number of new listings this year, making submissions to Australia's Medical Services Advisory Committee and Pharmaceutical Benefits Advisory Committee. ◆

For more information and advice call **1800 22 00 99** or email **Telenurse@pcfa.org.au**

LATEST NEWS:
Progress in prostate cancer from around the world

We are proud to be part of a worldwide community working to combat prostate cancer. Every day, our work helps to inform new developments in the diagnosis and treatment of prostate cancer at home and abroad. Read more about what's in the news right now.

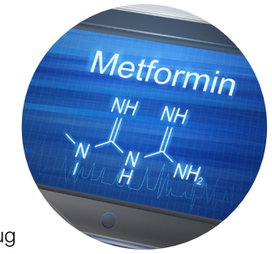
Research reveals new insights into treatment resistance



Two new studies led by researchers from the UCLA Jonsson Comprehensive Cancer Center give insight into how cells use energy to influence the way prostate tumours survive and grow — advancements that can help explain why some prostate cancers become resistant to hormone therapy, the most commonly used treatment for men with advanced stages of the disease.

Read more bit.ly/46OzU8y

New findings provide clarity on diabetes drug for prostate cancer



A new study from Columbia University researchers suggest that the diabetes drug metformin could be a promising drug to help prevent the progression of prostate cancer, but only for tumours with low levels of NKX3.1, which are more likely to develop into aggressive cancers. Until now, studies exploring metformin's power to prevent prostate cancer progression have been inconclusive.

Learn more bit.ly/416NhQe

ChatGPT performs poorly when classifying patients with prostate cancer

ChatGPT produces mixed results when evaluating patients with prostate cancer, according to research presented at the international 2023 Society of Urologic Oncology Annual Meeting. Researchers evaluated whether ChatGPT could review clinical information and provide accurate risk assessments and treatment recommendations. ChatGPT failed to accurately risk stratify 35% of patients studied, although the artificial intelligence chatbot did provide accurate treatment recommendations.

Read more bit.ly/47HB1rY

Erlyand drives ultra-low PSA levels in mCSPC

The groundbreaking TITAN study has found more patients with metastatic castration-sensitive prostate cancer achieved ultra-low prostate-specific antigen values when given Eryland vs placebo. Regardless of disease volume, these rapid and deep ultra-low PSA values correlated with significantly improved survival outcomes among patients. Erlyand is listed on the PBS for men with metastatic castration-sensitive prostate cancer.

Learn more bit.ly/46P9nrz

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