

Theranostics two years on | 2021

# A vision realised



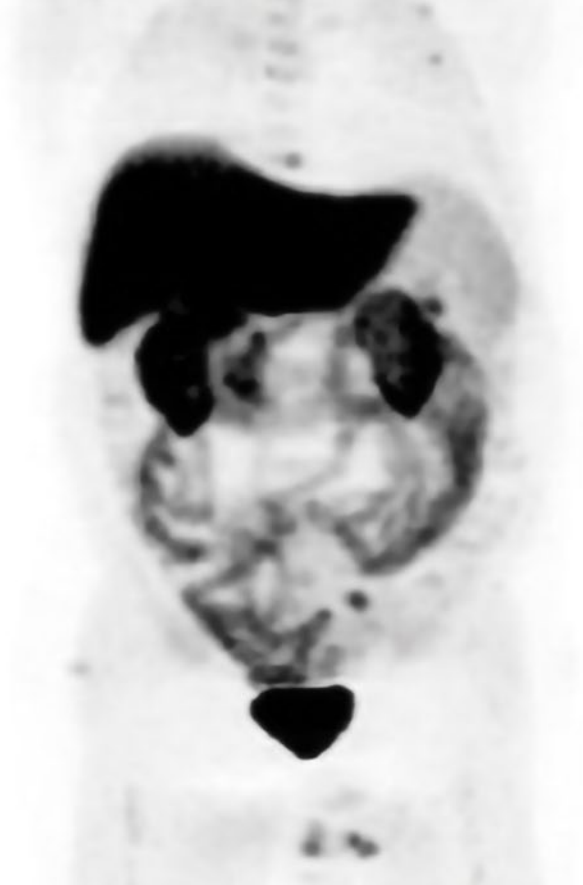
**"<sup>177</sup>Lutetium PSMA therapy.  
Two years with GenesisCare  
– more than 100 patients  
and powerful new evidence"**

Dr Yong Du

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## Theranostics – a vision realised

The treatment of metastatic castration-resistant prostate cancer (mCRPC) recorded another breakthrough in June 2021 as the important open-label phase 3 VISION trial, highlighted the importance of <sup>177</sup>Lutetium PSMA Therapy – a personalised cancer treatment that combines diagnostics and therapy (often referred to as Theranostics) - in prolonging survival in metastatic disease.<sup>1</sup> For GenesisCare, the result of this trial, which involved 821 patients, is validation of the success we have been experiencing since the start of our own UK Theranostics service in May 2019.

The service is led by Dr Yong Du, Clinical Director – Nuclear Medicine and Theranostics who was the first in the UK to hold an Administration of Radioactive Substances Advisory Committee (ARSAC) licence for <sup>177</sup>Lutetium PSMA therapy. He is supported by an experienced multidisciplinary team of nuclear medicine experts, including nuclear medicine physicians, physicists, imaging professionals and a radionuclide therapy nurse. The service was based on the success and learnings of our colleagues in Australia, with GenesisCare becoming the first independent healthcare provider in the UK to treat patients clinically with this revolutionary treatment. We have now treated more patients with <sup>177</sup>Lutetium PSMA therapy than any other healthcare provider in the UK both private or public, with more than 100 patients receiving more than 250 cycles to date and many new patients currently in referral. Dr Du was also involved in the Vision trial in the UK at The Royal Marsden. Here he shares his experience of the last two years and how the team's vision has become a reality, with so many patients benefiting.

**Dr Yong Du**  
Clinical Director –  
Nuclear Medicine  
and Theranostics  
GenesisCare UK



# Two years on – more than 100 patients and powerful new evidence

For patients with metastatic castration-resistant prostate cancer, the median survival is just over a year and the chance of surviving for five years is less than 1 in 6 and so the clinician's focus of care switches to overall survival and quality of life. Amongst the treatments being explored, one of the most promising is Theranostics, a molecular-based therapy which seeks out and destroys cancer cells using prostate-specific membrane antigen (PSMA)-targeting radioligands. This highly personalised approach, described as the therapeutic equivalent of a smart homing missile, exploits the fact that prostate-specific membrane antigen (PSMA) is highly expressed in prostate cancer and mCRPC lesions. By combining the PSMA specific ligand with <sup>177</sup>Lutetium,  $\beta$ -particle, radiation can be delivered to these PSMA-expressing cells and the surrounding microenvironment.

The goal is to slow tumour growth, reduce symptoms and improve quality of life.

**A 40% reduction in risk of death, compared with standard of care alone<sup>1</sup>**

Based on mounting evidence, over the last two years we have seen extremely favourable results in our patients treated with <sup>177</sup>Lutetium PSMA therapy in the UK. The outcome of this phase 3 trial far outweighs all previous evidence and is further validation of everything we've been seeing.

The open-label phase 3 VISION trial (NCT03511664) included 831 patients with progressive PSMA-positive mCRPC who received at least 1 novel androgen axis drug (e.g., enzalutamide [Xtandi] or abiraterone acetate [Zytiga]) and were previously treated with 1 to 2 taxane regimens. Men who received <sup>177</sup>Lu-PSMA-617 plus best standard of care had a 38% reduction in risk of death (median overall survival benefit of 4 months) and a 60% reduction in the risk of radiographic disease progression or death (median radiographic progression free survival benefit of 5 months) compared to best standard of care alone.

**What they found was that by adding the targeted radioligand therapy <sup>177</sup>Lu-PSMA-617 (LuPSMA) to standard of care led to a nearly 40% reduction in the risk of death versus standard of care alone in patients with progressive PSMA-positive mCRPC.<sup>1</sup>**

This is made even more impressive by the fact that the standard of care has improved overall in the two years since we've been offering Theranostics – and yet this study showed that still <sup>177</sup>Lutetium PSMA is outperforming this care and demonstrating positive outcomes. It is a very important prediction of the future – we know that we're getting even better at delivering this treatment, so clinical improvements will only continue.

1. ASCO 2021: Phase III Study of Lutetium-177-PSMA-617 in patients with Metastatic Castration-Resistant Prostate Cancer (VISION)

## Treatment overview

### How it works

PSMA is highly expressed in prostate cancer and mCRPC lesions. Theranostics uses PSMA ligands, which are specific to PSMA receptors on the surface of cancer cells, for diagnosis and treatment of mCRPC.

### Diagnosis

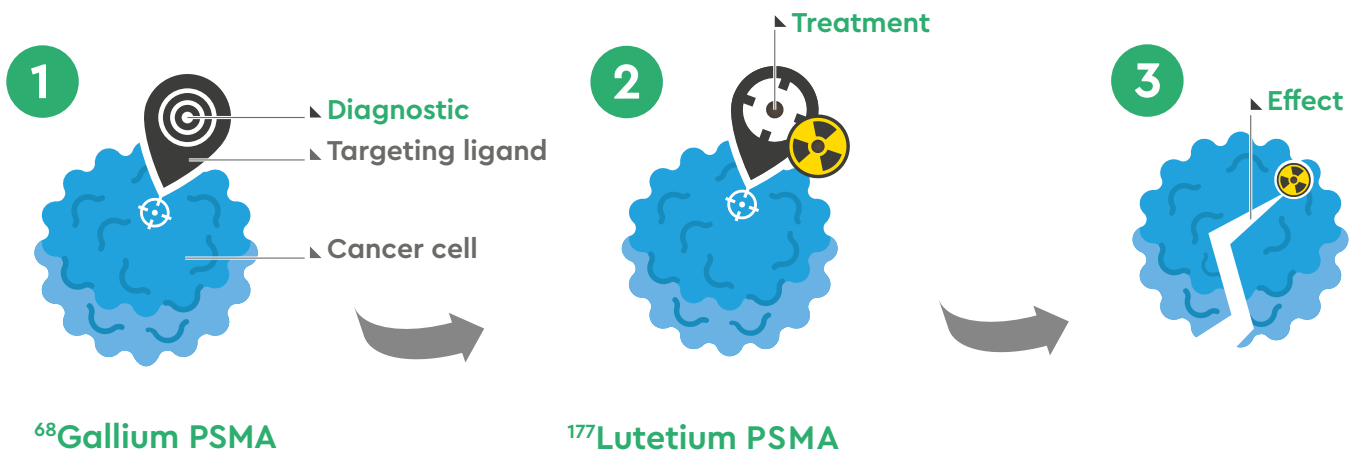
PET/CT is the modality used in Theranostics to prepare for PRRT therapy. We use the radiotracer <sup>68</sup>Gallium-PSMA due to its increased specificity with low PSA levels and sensitivity to tumour, lymph, and bone metastases.

### Treatment

The combination of PSMA-617 with the  $\beta$ -emitter lutetium allows for the targeted delivery of  $\beta$ -particle radiation to PSMA-expressing cells and the surrounding microenvironment. PSMA-targeting, or peptide receptor radionuclide therapy (PRRT), compared with external beam radiotherapy, can deliver 10–100 times the radiation dose direct to the target tumour.

**"The mechanism is fundamental to its effectiveness. It enables us to target the radiation very accurately and thus spare non-tumour critical organs from radiation. Due to its minimal toxicity, most patients can receive multiple cycles of treatment without developing significant adverse effects"**

Dr Yong Du



## Theranostics at GenesisCare

### We keep getting better

GenesisCare invested in a UK Theranostics service in 2019, and has so far treated more patients than any other healthcare provider in the UK. In that time, Dr Yong Du and his team have continued to refine their Theranostics service, gaining knowledge and experience that he readily shares with his colleagues around the UK in the NHS, and internationally. There are, he says, some key factors that have defined the success of the last two years.

**1. We are more experienced** – Theranostics underlines the essential role of clinical experience in delivering innovation. When we started there was limited experience of the criteria for patient selection, but over two years we have become much better at identifying which patients are more likely to benefit from the treatment and importantly, which patients are less likely to benefit. This is one of our strengths. We use a comprehensive assessment and understand that every patient's situation is different. With other treatment options available for metastatic disease, these decisions are critical.

**2. We have a highly specialised team** – Theranostics is complex to deliver, which is why so few centres can provide a service. At GenesisCare our multi-disciplinary team is comprehensive and includes a clinical nurse specialist (CNS) in radionuclide therapy, dedicated technologists, nuclear medicine physicist, diagnostics team, clinical co-ordinators, a resident medical officer (RMO) and two consultants. At our centre in Windsor we also have an on-site radiopharmacy and pharmacy team enabling us to produce our own <sup>68</sup>Gallium PSMA, ensuring patients have access to scans essential to their treatment without delay .



#### **Working together – the multi-disciplinary team at GenesisCare.**

Left to right: Matthew Patterson, Lead Nuclear Medicine Technologist; Anita Harte, Head of Theranostics and Imaging; Roberto Marvin Reyes, Senior PET/CT Radiographer; Carolyn Lory, Lead Nuclear Medicine Nurse; Annene Roodt, Senior PET/CT Radiographer; Nathaniel Scott, Medical Physicist – Nuclear Medicine; Dr Yong Du, Clinical Director Theranostics and Nuclear Medicine; Dr Rob Klobucar, RMO

**3. We have minimal reported side effects** – The beauty of this treatment is that side effects are minimal, and we also know how to manage each patient to further reduce the impact of treatment. Of the more than 100 patients we have treated here in the UK, treatment related toxicity was observed in a few patients and that is usually predictable. The average dose cycle is 4–6, but we have several patients who have received 10 with no adverse effects. We are collecting patient-reported outcomes (PROMs) data and hope to make these available in the near future.

**4. We receive excellent patient feedback** – For patients with advanced cancer, <sup>177</sup>Lutetium PSMA therapy has offered an opportunity to prolong survival with a better quality of life. For very many of our patients the lack of side effects and, often, symptom reduction has enabled them to continue with their day-to-day activities during treatment and so the feedback to this treatment has been overwhelmingly positive. The fact that their referring clinicians continue to send us patients for Theranostics is further evidence of an excellent patient experience.

### **In summary**

We put innovation at the heart of GenesisCare, because we want to provide our patients with the best diagnosis and treatment. Theranostics is one of these examples where diagnostic and treatment expertise come together to enhance patient outcomes. We plan to expand the availability of <sup>177</sup>Lutetium PSMA therapy to our other centres. We are also in the process of developing exciting clinical trials to test innovative Theranostics procedures in earlier stages of prostate cancer – followed by new Theranostics procedures for other tumour types – of which there are many in the pipeline. We plan to remain at the forefront.

Until two years ago, patients in the UK would have had to travel to Germany or Australia for this treatment. In this short time, we've come a long way and have been able to use our learnings to strengthen what we already knew about <sup>177</sup>Lutetium PSMA therapy. Now its efficacy has been confirmed in the VISION trial results, we couldn't be prouder and more positive about the future.

## **95% of our patients rated their experience of our Theranostics service as very good or excellent**

(6 or above on a scale of 1–7)

# Theranostics at GenesisCare

## Our service

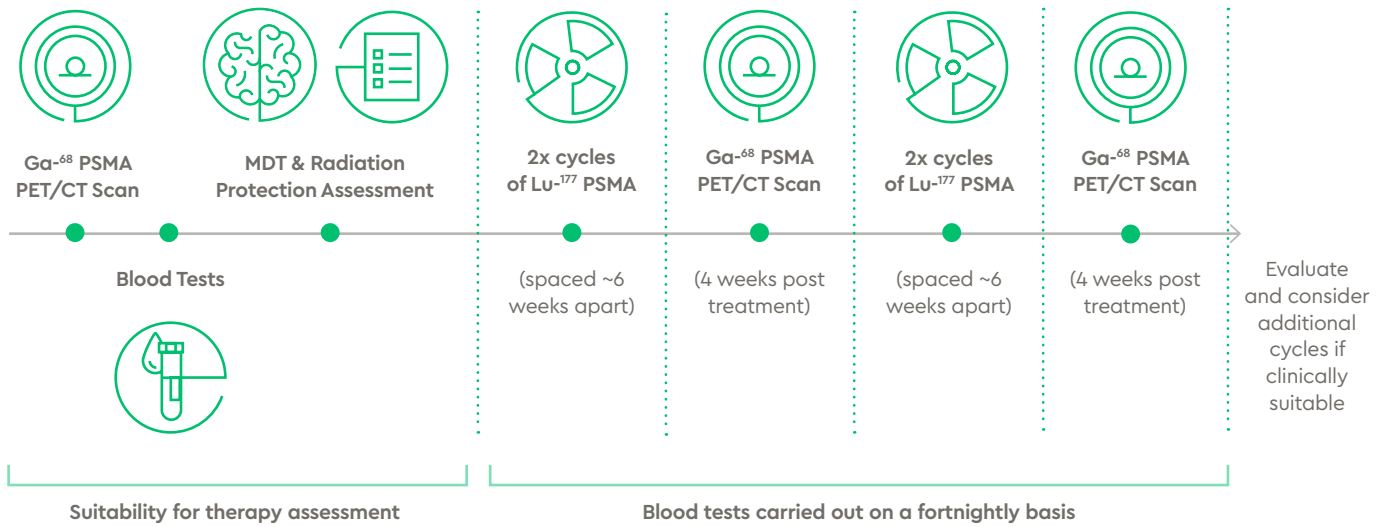


Fig 1: Current Protocol. Performed in an outpatient setting with a standard dosage of 7.4 GBq (reduction in activity considered for patients with poor renal function or other comorbidities)





# "Theranostics is giving me hope and a new lease of life"

Hans, patient



Hans was diagnosed with metastatic prostate cancer in 2012. In May 2019 he became the first UK patient to receive <sup>177</sup>Lutetium PSMA therapy after being referred to Dr Yong Du at GenesisCare



Dr Yong Du invited Steve to discuss Theranostics treatment and <sup>177</sup>Lutetium PSMA therapy. Steve was impressed with the speed and ease of treatment and the lack of any after effects



When Steve and Hans met they discussed how their outlook on life had changed since having <sup>177</sup>Lutetium PSMA therapy. Both agreed they had been given hope

## Case study 1

# Theranostics led to significant local disease volume reduction, enabling consolidative radiotherapy

Dr Yong Du

### ■ Case presentation

A 57-year-old male, with progressive metastatic castration-resistant prostate cancer (mCRPC) unsuitable for localised treatment such as stereotactic ablative radiotherapy (SABR).

Diagnosed in 2015, the patient underwent several treatments, including a radical prostatectomy and lymph node sampling followed by adjuvant radiotherapy and androgen deprivation therapy. The patient had recurring cancer in his pelvic sidewall for which he received chemotherapy with docetaxel and hormonal therapy in 2017. Further disease progression meant the patient had a salvage left pelvic lymphadenectomy and treatment with abiraterone, followed by three cycles of chemotherapy with carboplatin and etoposide. The patient did not respond to the chemotherapy treatments and his PSA levels were rising, indicating the need for a different approach.

### ■ Challenges of presentation and choice of treatment

The patient had progressive metastatic prostate cancer with neuroendocrine differentiation, resistant to multiple lines of hormonal and chemotherapy treatments. A <sup>68</sup>Gallium PSMA PET/CT scan showed multiple left pelvic nodal metastases measuring up to 2cm in size, close to the rectum (figure 1). The size of the metastases meant the patient was not suitable for SABR and a different treatment approach would be needed. Alternative treatment options were limited in this case as the patient had exhausted all the conventional lines of treatment and he was anxious because his disease was progressing. After hearing about <sup>177</sup>Lutetium PSMA therapy, the patient was delighted this was made available in the UK at GenesisCare. <sup>177</sup>Lutetium PSMA therapy was considered a good choice because of the high response rates and minimal toxicity, supported by phase II trials of the treatment.

### ■ Theranostic treatment

From May 2019, the patient underwent five cycles of <sup>177</sup>Lutetium PSMA therapy intending to slow down cancer progression and promote tumour shrinkage. In our purpose-built Theranostics suite, the <sup>177</sup>Lutetium PSMA therapy was given as an outpatient procedure over two hours.

### ■ Results and follow-up

Following two cycles of treatment, the patient's PSA reduced from a baseline of 4.21 to 0.36ng/ml. A reassessment <sup>68</sup>Gallium PSMA PET/CT scan showed a very good partial response to treatment with a reduction in diameter of the biggest node from 2cm to 0.8cm (figure 2). After five cycles of treatment, the disease had stabilised, and the patient could proceed with consolidation radiotherapy. This is because the nodal metastases had reduced significantly in size, enabling a good separation between the lymph nodes from the rectum. The patient subsequently proceeded with consolidation SABR to the residual left mesorectal nodes.

Fig 1: <sup>68</sup>Gallium PSMA PET/CT scans before treatment

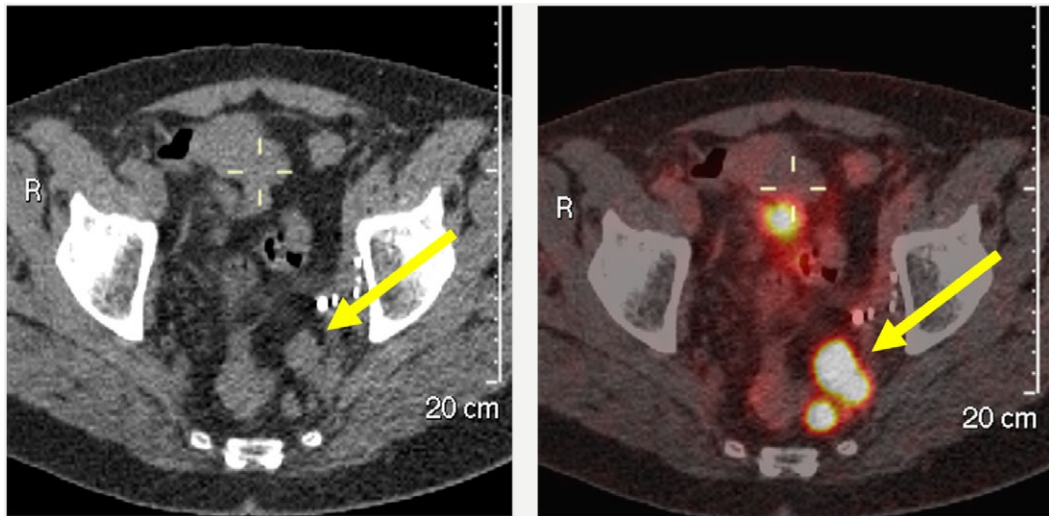
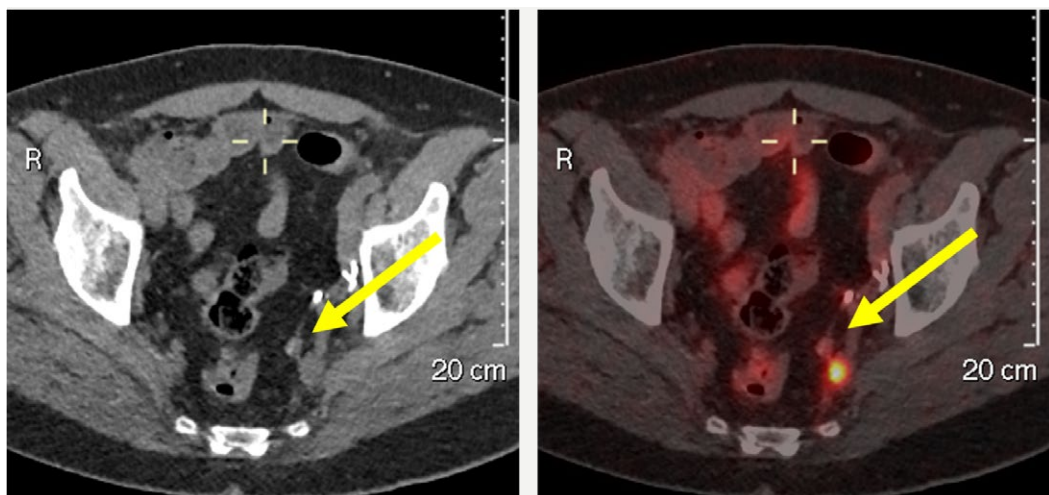


Fig 2: <sup>68</sup>Gallium PSMA PET/CT scans after two cycles of <sup>177</sup>Lutetium PSMA therapy



Being an active gentleman working full time as a physicist, the patient was very happy with the result because he experienced no treatment-induced toxicity or side effects throughout his treatment and could proceed with his normal life. The patient mentioned the innovative treatment had given him a more positive outlook on life and hope for the future.

## Discussion

With progressive mCRPC, the patient demonstrated disease progression over multiple lines of hormonal therapy and chemotherapy. Having multiple left pelvic nodal metastases meant the patient was not suitable for SABR treatment and a different approach was needed. <sup>177</sup>Lutetium PSMA therapy resulted in a good radiological response, reduced PSA levels, and significant tumour shrinkage, allowing the patient to undergo consolidative radiotherapy. The patient was pleased with the outcome of the treatment which resulted in no side effects and stabilisation of the disease.

## Case study 2

# Theranostics enables significant symptomatic relief and prolonged disease control

Dr Yong Du

### ■ Case presentation

A 76-year-old male with progressive metastatic castration-resistant prostate cancer (mCRPC) and multifocal bony pain.

The patient was first diagnosed with prostate cancer in 2005. Over 10 years, the patient had undergone androgen suppression treatment and had disease progression on multiple lines of hormonal therapy and chemotherapy, resulting in rising PSA levels and multifocal bony pain. As a retired businessman working part-time from home, the patient managed the pain using multiple painkillers.

### ■ Challenges of presentation and choice of treatment

The challenge here was that the patient had disease progression over multiple lines of hormone therapy, including abiraterone and enzalutamide, and two lines of chemotherapy, so alternative treatment options were limited. A <sup>68</sup>Gallium PSMA PET/CT scan showed multiple nodal metastases and widespread bony metastases (figure 1), and consequently, a highly targeted and personalised treatment was needed. The innovative treatment <sup>177</sup>Lutetium PSMA therapy was mentioned to the patient, and a subsequent scan revealed that he was a viable candidate. Phase II trials of <sup>177</sup>Lutetium PSMA therapy showed high response rates with minimal toxicity and a reduction in pain and therefore was considered a good choice for this patient.

### ■ Theranostic treatment

Two weeks after confirming his suitability for Theranostic treatment, the patient began his cycles in our purpose-built Theranostics suite. Over 15 months the patient received eight cycles of <sup>177</sup>Lutetium PSMA therapy intending to slow down cancer progression and promote tumour shrinkage.

### ■ Results and follow-up

The patient was very happy with the outcome of his treatment, finding it highly tolerable and reporting no side effects apart from mild fatigue and a dry mouth which would only last a couple of days. After six cycles of treatment, the patient's PSA levels significantly reduced from 327 to 16.6ng/ml. A reassessment <sup>68</sup>Gallium PSMA PET/CT scan showed a partial response to the PSMA treatment with a significant reduction of tumour volume. As shown in figure 2, there was a dramatic improvement from the baseline scan where the lymph node metastases are all resolved, and the bony metastases have significantly improved. Post-PSMA therapy, the patient's multifocal bony pain was resolved, and he was able to stop taking painkillers. This response was maintained for 14 months with no treatment-induced toxicity or side effects.

Fig 1: Baseline <sup>68</sup>Gallium PSMA PET/CT scan in April 2020

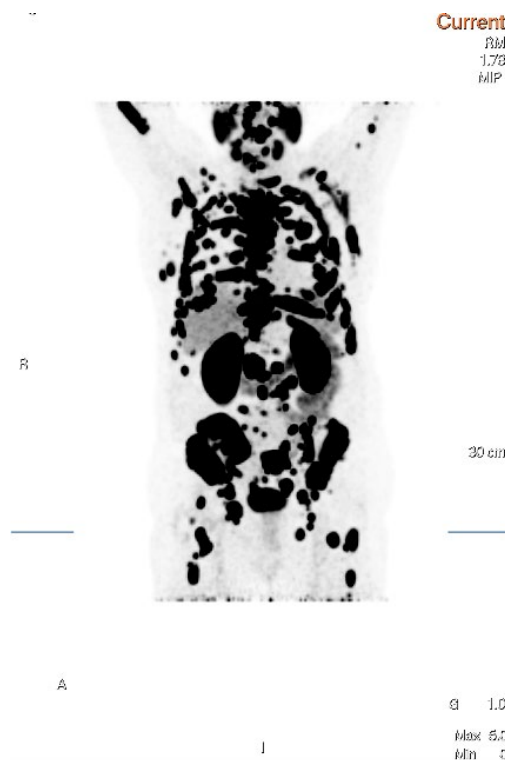
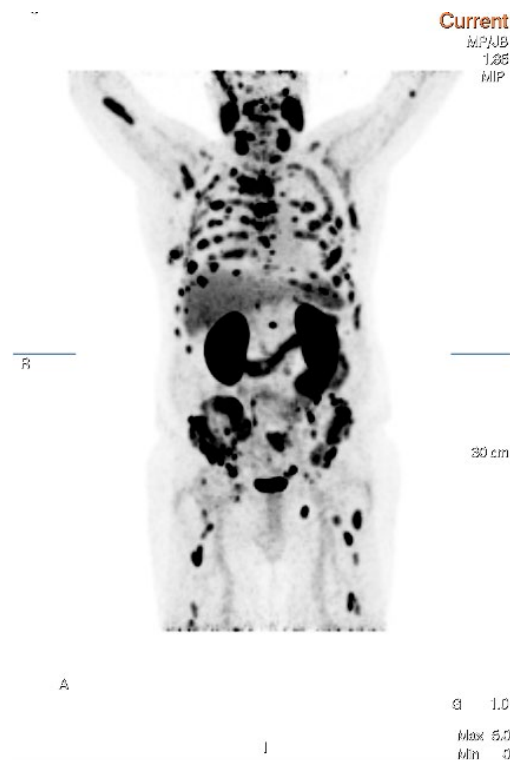


Fig 2: Follow-up <sup>68</sup>Gallium PSMA PET/CT scan after six cycles of <sup>177</sup>Lutetium PSMA therapy in March 2021



After eight cycles of the <sup>177</sup>Lutetium PSMA therapy, the patient's PSA levels rose slowly to 18.5ng/ml at the end of the treatment. A subsequent <sup>68</sup>Gallium PSMA PET/CT scan showed small scale disease progression and reactivation, indicating the development of resistance to treatment.

Theranostics treatment enabled significant relief of symptoms for this patient and a prolonged response with no toxicity or side effects. The patient was able to go back to his day-to-day tasks and was able to maintain a good quality of life.

## Discussion

This patient had limited treatment options as his mCRPC was resistant to multiple lines of hormonal therapy and chemotherapy. Theranostics significantly slowed his tumour growth and reduced his pain, enabling him to stop taking painkillers. Experiencing nearly no adverse side effects following the treatment, the patient was very pleased with the outcome and could have a prolonged and good quality of life as a result.

# Theranostics at GenesisCare

## Sharing our expertise



### ■ Dr Yong Du Clinical Director – Nuclear Medicine and Theranostics GenesisCare UK

Special interests: PET/CT, SPECT/CT, Radionuclide Target Therapy

Dr Yong Du graduated from Shandong Medical University and was awarded a PhD in Cancer Sciences at the University of Southampton for his work on lymphoma before completing full nuclear medicine specialist training at the Institute of Nuclear Medicine, University College Hospital in London. In June 2009, he became the first recipient of the national HEFCE Clinical Senior Lectureship Award in the Nuclear Medicine specialty. Prior to joining the Royal Marsden Hospital in February 2011, he had been a Consultant Physician in Nuclear Medicine at the UCLH and the Christie Hospital.

Alongside his clinical practice, Dr Yong Du would research the role, efficacy and limitations of PET/CT in various cancers, to optimise its use and inform tailored treatments for individual patients. Dr Yong Du led the Radionuclide Therapy Services at the Royal Marsden for over 10 years and has in depth expertise in radionuclide targeted therapy. Some of his other accomplishments include treating over 150 patients with neuroendocrine tumour with PRRT, chairing multiple national training courses for the clinical application of Radium-223, and pioneering the <sup>177</sup>Lutetium PSMA therapy for advanced prostate cancer patients in the UK. He is interested in improving radionuclide targeted therapy for cancer patients by combining innovative therapeutic approaches with fast advancing functional imaging technology. In collaboration with researchers across the country, Dr Yong Du has led and contributed to international and national studies and subsequently published first-authored research papers in high-impact oncology journals including Journal of Clinical Oncology, Blood and Cancer Research.

As a Trustee of the British Nuclear Medicine Society, Dr Yong Du regularly teaches at national and international conferences. He serves at several other international and national medical committees including the NCRI PET Research Network, the NCRI Clinical Translational Radiotherapy (CTRad) Research Working Group and NCRI Advisory Panel for Clinical Trials.

### ■ Dr Du has recently presented at:

British Institute of Radiology – Invited talk at the “BIR Theranostics update 2021” Meeting in January 2021  
“PSMA Theranostics in Prostate Cancer: A Gamer Changer?”

European Association of Nuclear Medicine – Invited talk at the 2020 EANM Annual Meeting in October 2020  
“<sup>68</sup>Ga-PSMA-11: the PET/CT imaging Tracer that has changed the management of Prostate Cancer”

British Nuclear Medicine Society – Invited talk at the 2019 BNMS Autumn Annual Meeting in September 2019  
“Seeing is Believing: The Fast Advancement of Theranostics”

**Get in touch**

## Refer for <sup>177</sup>Lutetium PSMA therapy

We consider referrals for <sup>177</sup>Lutetium PSMA therapy for patients with metastatic castration-resistant prostate cancer (mCRPC) who have exhausted or are ineligible for approved alternative options. They must demonstrate adequate uptake of PSMA ligands based on a pre-therapy imaging study to be considered for treatment.

<sup>177</sup>Lutetium PSMA therapy is delivered as an outpatient appointment at our GenesisCare centre in Windsor.

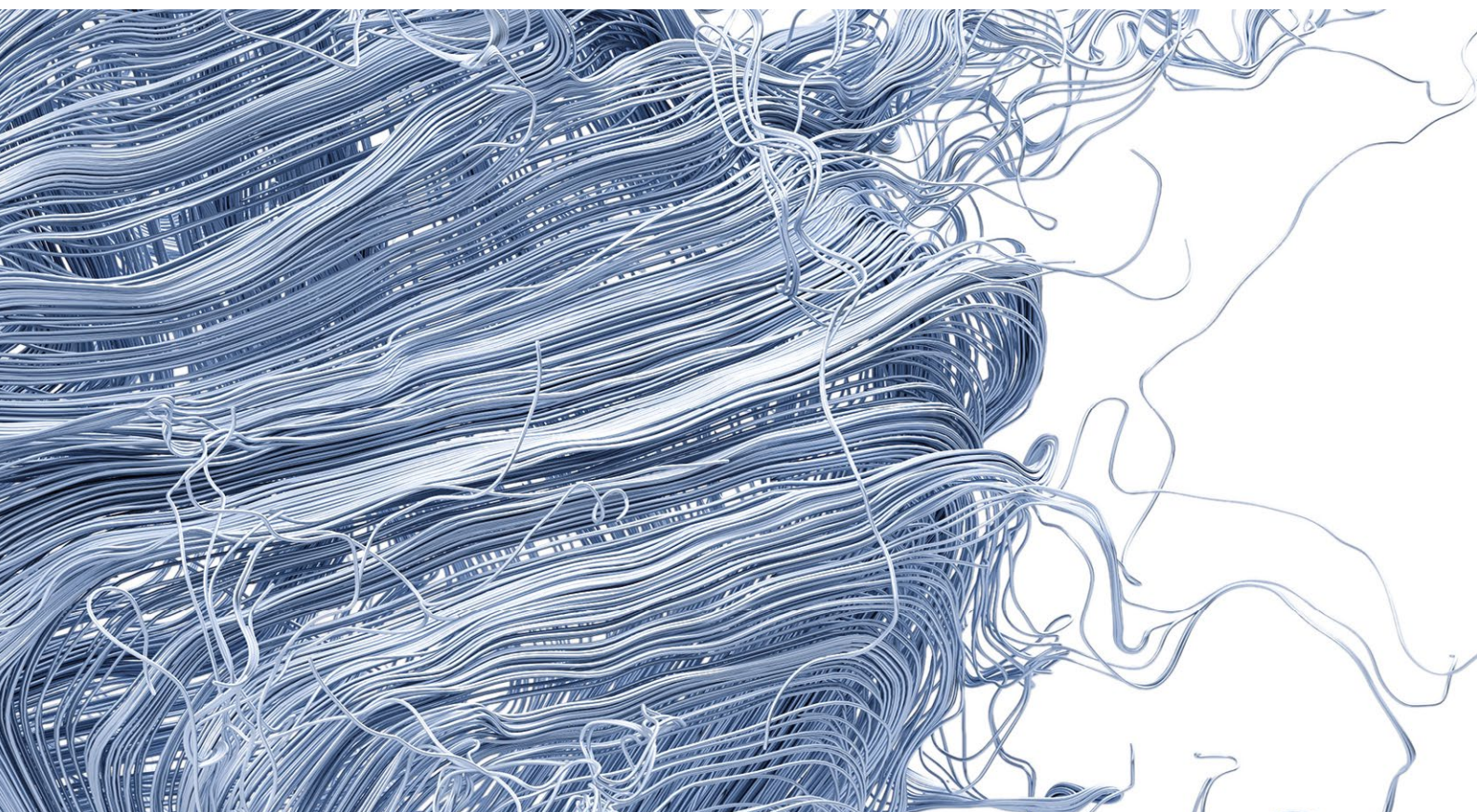


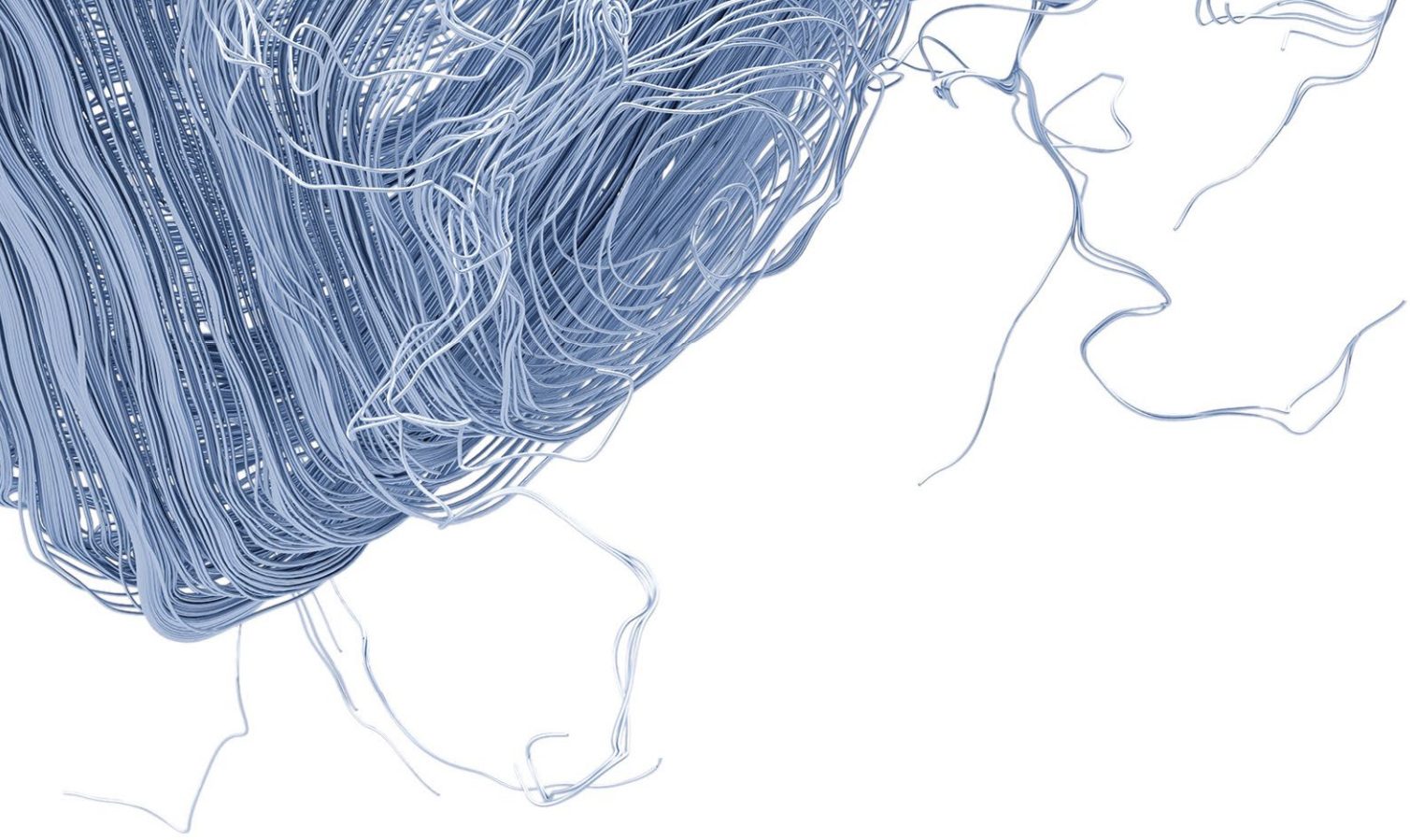
**Please enquire:**

**0808 301 9752**

**[enquiries@genesiscare.co.uk](mailto:enquiries@genesiscare.co.uk)**

**GenesisCare is in the top 1% of healthcare providers worldwide and we consistently achieve a net promoter (patient satisfaction) score over 95%**





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091\_V1\_08.2024

