Sydney Adventist Hospital

PARTICIPANT INFORMATION SHEET AND CONSENT FORM
for substitute consent make relevant throughout document

PILOT CASE SERIES

STUDY TITLE

Salvage ^{177}Lu PSMA for PSA Biochemical Failure After Radical Prostatectomy for High-Risk Prostate Cancer

Invitation
You are eligible to participate in this study looking at the effect of ^{177}Lutetium-PSMA-imaging and therapy (PSMA-I&T) on prostate specific antigen (PSA) after radical prostatectomy.

^{177}Lutetium-PSMA-I&T is a radioactive medication that targets cells making a protein called Prostate Specific Membrane Antigen (PSMA). This protein is mainly made by prostate cancer cells.

The study principal investigator is Professor Henry Woo and the associate investigators are Dr Edwin Szeto, Dr Lisa Tarlinton, Professor Gavin Marx, Mr Brian Sorensen, Dr Anika Jain and Dr Anthony-Joe Nassour.

Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. **'What is the purpose of this study?'**

Data shows that some men with high-risk prostate cancer will develop a rising PSA despite a successful and curative (i.e. potential to cure disease) radical prostatectomy. This is usually due to micrometastatic disease (i.e. The cancer cannot be seen on imaging, but your blood test suggests there is something there) and if left untreated, this rising PSA may eventually progress into advanced disease.

^{177}Lutetium is a new treatment that is proving to be effective and more tolerable compared to other existing radiation, chemical or hormone treatments.

The purpose of this pilot study is to understand the effect of a single dose of ^{177}Lutetium-PSMA-I&T on your rising PSA, determine if this treatment can clear any remaining micrometastatic disease, and delay the need for hormone or chemical therapy.

It is important to understand that the use of ^{177}Lutetium-PSMA-targeted therapy in this setting is considered off-label and not standard of care at our centre (meaning you are unable to obtain this treatment outside of a research setting).

2. 'Why have I been invited to participate in this study?'

You are eligible to participate in this pilot case series because you meet all the inclusion criteria and none of the exclusion criteria.

Inclusion Criteria

- Men who have undergone a radical prostatectomy for National Comprehensive Cancer Network (NCCN) definition of high or very high-risk prostate cancer.
- Negative surgical margins on radical prostatectomy histopathology.
- PSA initially undetectable following radical prostatectomy.
- PSA biochemical failure – defined as greater than or equal to 0.20ng/mL.
- PSMA expressing prostate cancer on pre-operative PSMA PET/CT
- PSMA PET/CT demonstrating no evidence of uptake to suggest. detectable residual or metastatic disease.
- No local recurrence on post-operative mpMRI.
- No artifact disrupting interpretation of initial prostate cancer imaging.
- Significant PSMA expressing tumour on initial staging.
- Ability to give written informed consent, participate in and comply with study.

Exclusion Criteria

- Previous treatment for prostate cancer.
- Positive surgical margin on radical prostatectomy specimen pathology.
- Non-PSMA expressing prostate cancer (e.g. ductal or neuroendocrine).
- Artifact disrupting interpretation of initial prostate cancer imaging (e.g. Total Hip Replacement).
- Presence of suspected metastatic disease on pre-operative and post-operative PSMA PET/CT scan or mpMRI.
- Undetectable serum testosterone.
- Contraindication to Gadolinium.
- Contraindication to ^{177}Lu-PSMA therapy.

3. 'What if I don't want to take part in this study, or if I want to withdraw later?'

Participation in this pilot case series is voluntary. It is completely up to you whether or not you participate. If you decide not to participate, it will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

4. 'What does this study involve?'

If you agree to participate in this case series, you will be asked to read and sign the Participant Consent Form.

Step 1 - You will then undergo a PSMA-PET/CT and a multi-parametric MRI (mpMRI) to exclude local disease recurrence at the prostate bed prior to arranging the administration of a single dose of ^{177}Lutetium-PSMA-targeted therapy.

Step 2 – Present to San Radiology and Nuclear Medicine to receive ^{177}Lutetium-PSMA-targeted therapy (This process will take approximately 60-minutes)

Step 3 – Present to San Radiology and Nuclear Medicine 24hrs following administration of the ^{177}Lutetium-PSMA-targeted therapy for a single-photon emission computerised tomography (SPECT) to confirm that the Lutetium has localised appropriately (This process will take approximately 30-minutes)

Step 4 – Present two more times to San Radiology and Nuclear Medicine over a 5-day period for two more SPECT scans to measure dosimetry (measurement of radiation used in the treatment and detection)

Step 5 – Present to the treating urologist with a repeat serum PSA 6-weeks following ^{177}Lutetium-PSMA-targeted therapy.

By participating in this case series, you agree to grant the principal investigator access to your medical records to obtain information relevant to the study. The information collected will include:

- Demographic information
- Medical history
- Investigations
- Progress notes

Definitions

'Standard of care' refers to appropriate medical treatment that can be general or specific based on scientific evidence and collaboration between medical and allied health professionals involved in the treatment of a given condition.

'Pilot case series' A pilot study is a requisite initial step in exploring a novel intervention or an innovative application of an intervention. Pilot results can inform feasibility and identify modifications needed in the design of a larger, ensuing hypothesis testing study

5. **'How is this study being paid for?'**

This study is investigator initiated and not funded by any government or private entity. Participants are only expected to self-fund treatment that falls outside of routine standard of care. These include:

Item	Unit	Cost	Funding
^{177}Lutetium-PSMA-targeted therapy	1x	$5,500	Self-funded
SPECT scan	3x	$300	Self-funded

San radiology staff and consumables	1x	$5,000	Self-funded
mpMRI (post-radical prostatectomy)	1x	$450	Self-funded

Payments are made directly to San Nuclear Medicine and Radiology. No money is paid directly to the individual investigators as their time is dedicated entirely in kind. The total out of pocket expense will be approximately AUD $11,250.

6. 'What are the alternatives to participating in this study?'

If you decide not to participate in this study, and you wish to continue treatment, you will still receive the standard of care treatment available for your condition. It is important that you discuss the alternatives to participating in this study with your doctors.

7. 'Are there risks to me in taking part in this study?'

All medical procedures involve some risk of injury. In addition, there may be risks associated with this case series that are presently unknown or unforeseeable. Despite all reasonable precautions, you might develop medical complications from participating in this case series. The known risks of this study are primarily ^{177}Lutetium and radiation related.

Risk Profile ^{177}Lu-PSMA

- ^{177}Lutetium-PSMA has favourable characteristics as the emitted radiation penetration is less than 2mm. Thereby, minimising injury to neighbouring healthy tissue.
- Standard treatment protocols for advanced disease consists of 6-cycles over 6 weeks.
- Although high-grade toxicity remains low (less than 10%), this can be observed with as little as 2-3 cycles.
- A recent study of 1192 men who had the full 6 cycles of ^{177}Lu-PSMA reported severe (grade 3 or 4) adverse events to be less than 10%
    - Anaemia 8% - low blood iron level
    - Leukopaenia 4% - low immune blood cells
    - Thrombocytopaenia 4% - low clotting blood cells
    - Transaminitis 2% - Abnormal liver function test
    - Xerostomia 2% - Dry mouth
    - Anaphylaxis <0.01% - Severe allergic reaction
- We suspect the rate of adverse events in our study to be significantly lower given we will only be using a single cycle of ^{177}Lu-PSMA compared to the standard 2-6 cycles in the reported literature.
- Dry mouth remains the most common non-severe complication. Instructions on stimulating the salivary glands after the treatment will be provided to reduce the risk as much as possible. Permanent dry mouth is rare.

Risk Profile from radiation exposure

- Radiation exposure from the 3x SPECT over the 7-day period following administration of Lutetium is *negligible*.

- Should you undergo a complete CT scan the cumulative radiation dose of 2-5 mSv remains significantly below the 10 mSv and has no direct effects on human health in any 1-year (as per the Australian Radiation Protection and Nuclear Safety Agency)
- Overall, radiation exposure will not exceed what a will normally be received with standard of care alone.

Radiation exposure precautions

- Detailed factsheets will be provided.
    - The majority of Lutetium-177 is typically excreted in urine by 6-hours following administration.
    - For 5-days after treatment you must distance yourself from others (particularly women and children) by at least 2-meters.
    - By 30-days 99.9% of the Lutetium-177 emitted radiation would have dissipated

8. 'What happens if I suffer injury or complications as a result of the study?'

If you suffer any injuries or complications as a result of this study, you should contact the study doctor as soon as possible, who will assist you in arranging appropriate medical treatment.

The doctor responsible and licenced to administer your treatment is Nuclear Medicine Physician Dr Edwin Szeto. Dr Edwin Szeto has extensive experience using Lutetium and would be best to address *injuries, complications or concerns* that arise **within** 30-days following the administration of ^{177}Lutetium-PSMA-I&T. Contacting Dr Szeto can be done by:

1- Contacting San Radiology and Nuclear Medicine on (02)9480 9850 (between 8am-4pm)
2- Contacting Sydney Adventist Hospital Switch on (02)9480 9111 and requesting Dr Szeto (8am-4pm)
3- Contacting associate investigator Dr Anthony-Joe Nassour on 0405959444 (all other times)

Injuries, complications, or concerns that arise 30-days **after** treatment can be relayed to Dr Anthony-Joe Nassour who will triage, address, and refer on appropriately. He can be contacted by:

1- Mobile or via email (0405959444 or anthony-joe.nassour@sah.org.au).

We take all complications very seriously and these are discussed anonymously at our multi-disciplinary meetings which take place every fortnight. Our multi-disciplinary meetings are well attended by a diverse range of medical, surgical, and allied health specialists to provide the most holistic and effective treatment plan for you.

We encourage participants to provide feedback (positive or negative). Complaints can be relayed to Dr Anthony-Joe Nassour or to the Clinical Governance Team at Sydney Adventist Hospital. The Clinical Governance Team can be contacted on:

- (02) 9480 9426 – Monday, Wednesday, Thursday, Friday

- (02) 94809741 – Tuesday

If you feel that your complaint has not been adequately addressed, remain unhappy with the outcome, or believe there was negligence in your care, you have the right to seek independent legal advice and assistance. If you are not eligible for compensation for your injury or complication under the law, but are eligible for Medicare, then you can receive any medical treatment required for your injury or complication free of charge as a public patient in any Australian public hospital. This study is investigator initiated and independent of Sydney Adventist Hospital.

9. 'Will I benefit from the study?'

This study aims to further medical knowledge and may improve future treatment algorithm for undetectable biochemical failure following prostatectomy. However, it may not directly benefit you.

10. 'Will taking part in this study cost me anything, and will I be paid?

Participants are only expected to self-fund treatment that falls outside of routine standard of care. Payments are made directly to San Nuclear Medicine and Radiology. No money is paid directly to the individual investigators as their time is dedicated entirely in kind. The total out of pocket expense will be approximately AUD 11,250$.

These include:

Item	Unit	Cost	Funding
^{177}Lutetium-PSMA-targeted therapy	1x	$5,500	Self-funded
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mpMRI (post-radical prostatectomy)	1x	$450	Self-funded

11. 'How will my confidentiality be protected?'

Only the principal, associate investigators and allied health staff members involved in your treatment will have access to your medical records. Any identifiable information that is collected about you in connection with this case series will remain confidential and will be disclosed only with your permission, or except as required by law. Only the researchers named above and the Human Research Ethics Committee (HREC) if required for monitoring purposes, those persons monitoring the conduct of the study on behalf of the sponsor and, regulatory bodies (such as Therapeutic Goods Administration) will have access to your details and results that will be held securely at institution where the participant is consented, and study visits conducted. If applicable Only non-identifiable information will be sent off site. This will only occur when necessary and the provisions of Australian privacy law will be complied with.

12. 'What happens with the results?'

If you give us your permission by signing the consent document, we plan to discuss/publish the results in urology and oncology peer-reviewed journal as part of a publication. The results of this project may also be presented at international conferences and pave the way for future clinical trials.

In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you, if you wish.

However, it is important to recognize and understand that due to the nature of case series being limited to only 10-participants re-identification by those involved in your care might be possible.

13. 'What happens to my treatment when the study is finished?'

After the case series is concluded off-label treatment will cease but continuity of care will not.

14. 'What should I do if I want to discuss this study further before I decide?'

When you have read this information, the researcher Dr Anthony-Joe Nassour will discuss it with you and any queries you may have. If you would like to know more at any stage, please do not hesitate to contact him on 0405959444.

15. 'Who should I contact if I have concerns about the conduct of this study?'

This study has been approved by the Adventist Healthcare Limited Human Research Ethics Committee (HREC). Any person with concerns or complaints about the conduct of this study should contact the Research Office who is nominated to receive complaints from research participants. You should contact them on +61 2 9480 9604 and quote HREC reference number (XXX).

16. The conduct of this study at the Sydney Adventist Hospital has been ethically reviewed by the AHCL Human Research Ethics Committee and authorised by Adventist Healthcare Limited Research Governance Office. Any person with concerns or complaints about the conduct of this study may also contact:

Name	Research Governance **Officer**
Email	research@sah.org.au
Phone Number	+61 2 9480 9604
AHCL Reference ID	2022-036

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

Sydney Adventist Hospital

PARTICIPANT INFORMATION SHEET AND CONSENT FORM
for substitute consent make relevant throughout document

PILOT CASE SERIES

STUDY TITLE

Salvage ^{177}Lu PSMA for PSA Biochemical Failure After Radical Prostatectomy for High-Risk Prostate Cancer

1. I,.....
   of.....
   agree to participate as a subject in the study described in the Participant Information Sheet set out above **(or: attached to this form).**

2. I acknowledge that I have read the Participant Information Sheet, which explains why I have been selected, the aims of the study and the nature and the possible risks of the investigation, and the statement has been explained to me to my satisfaction.

3. Before signing this consent form, I have been given the opportunity of asking any questions relating to any possible physical and mental harm I might suffer as a result of my participation and I have received satisfactory answers.

4. I understand that I can withdraw from the study at any time without prejudice to my relationship to the investigators.

5. I agree that research data gathered from the results of the study may be published, provided that I cannot be identified.

6. I understand that if I have any questions relating to my participation in this research, I may contact Dr Anthony-Joe Nassour via on 0405959444 who will be happy to answer them.

7. I acknowledge receipt of a copy of this Consent Form and the Participant Information Sheet.

Any queries relating to the study please contact:
Dr. Anthony-Joe Nassour
anthony-joe.nassour@sah.org.au
0405959444
Clinical Research Fellow, Sydney Adventist Hospital

Signature of participant	Please PRINT name	Date
_____		
Signature of witness	**Please PRINT name**	**Date**
_____		
Signature of investigator	**Please PRINT name**	**Date**

CONSENT TO RECEIVE ^{177}Lutetium-PSMA-I&T

I ……
(name of patient or parent / guardian)

consent to receive ^{177}Lutetium-PSMA-I&T for the purposes of undetectable biochemical failure in this pilot case series titled 'Salvage Lutetium PSMA for PSA Biochemical Failure After Radical Prostatectomy for High-Risk Prostate Cancer - SLAP study'.

- I understand that this product is not approved for use first line treatment in undetectable biochemical failure, but that use of the product has been approved under the provisions of section 19(5) or section 41HC of the Therapeutic Goods Act 1989 as last line therapy in resistant metastatic prostate cancer.

- I understand that Dr Edwin Szeto has Authorised Prescriber status from the Therapeutic Goods Administration to prescribe this product.

- I understand that I cannot seek ^{177}Lutetium-PSMA-I&T treatment outside the setting of this case series or another clinical trial unless it is for the treatment of metastatic prostate cancer that is unresponsive to other systematic therapy.

- I understand that the reported side effects / reactions to ^{177}Lutetium-PSMA-I&T are generally mild and of short duration with a single cycle and may include:

Common Possible Side Effects (>10%)	**Less Common Possible Side Effects (1-10%)**
Reduction in white blood cells which could increase the likelihood of bleeding	Increased creatinine indicating a possible effect on your kidneys
Reduction in white blood cells making it more difficult to fight infection	Fever associated with reduced white cells
Reaction at the site of infusion	Anxiety
Feeling tired	Depression
Weight loss	Confusion
Nausea	Reduction in the number of red blood cells
Localised pain	Headaches
Joint pain	Memory loss
Shortness of breath	Abdominal pain
Loss of appetite	Weakness
Swelling in your limbs	Irregular heartbeat
Constipation	Chest pain
Diarrhea	Dry mouth
INS0mnia	Flu-like symptoms
Increased urination	Indigestion
Cough	Blood in urine
Increased levels of liver enzymes	Nose bleeds

	Hypertension
	Numbness
	Rash
	Discolouration of the skin or mucous membranes
	Blood clots

- I confirm that the above statements have been explained to me and with this knowledge I agree to administration of the product to me.

Patients' name ……...

Signature of patient …… **Date** …….
(or parent / guardian)

Signature of witness …… **Date** …….

I have explained the above statements to the patient or the patient/s parent / guardian.

Treating physician ……

Signature …… **Date** ……..

This form should be kept on the patient's file

Sydney Adventist Hospital

Case Series / Pilot study

STUDY TITLE

Salvage ^{177}Lu PSMA for PSA Biochemical Failure After Radical Prostatectomy for High-Risk Prostate Cancer

REVOCATION OF CONSENT

I hereby wish to **WITHDRAW** my consent to participate in the study described above and understand that such withdrawal **WILL NOT** jeopardise any treatment or my relationship with the Sydney Adventist Hospital or my medical attendants

Signature Date

Please PRINT Name

The section for Revocation of Consent should be forwarded to:

Dr Anthony-Joe Nassour
E: *anthony-joe.nassour@sah.gov.au*
T: 0405959444