Lutetium-177-PSMA I&T for progressing metastatic castrate-resistant prostate cancer: A single NZ centre experience

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Organisation/s: Mercy Radiology and AUT University, Auckland

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Objectives

- To assess the efficacy of Lutetium-177-PSMA-I&T therapy to palliate end stage mCRPC

- To review tolerability and impact on QOL of Lutetium-177-PSMA-I&T therapy
Metastatic Castration resistant prostate cancer (mCRPC)

A proportion of prostate cancer patients will continue to progress following systemic treatment and cease to respond to hormonal manipulation or chemotherapy.

Features:
- No response to Androgen deprivation therapy (ADT)
- Continuous rise in the PSA value
- Metastatic spread to bone, lymph nodes and visceral organs
- Reduction in the overall survival rate of patients
- Life expectancy of the patients’ usually 14-16 months
Metastatic Castration resistant prostate cancer (mCRPC) and PSMA

- 90-95% metastatic prostate cancer cells expresses Prostate specific membrane antigen (PSMA) transmembrane protein

- PSMA can be a target for imaging and treatment of prostate cancer

- Lu-177 PSMA therapy currently only available privately
### Various PSMA ligands and radionuclides suitable for labelling

#### PSMA ligands in use currently

| J591       | PSMA-617 | PSMA-I&T |

<table>
<thead>
<tr>
<th>Radionuclides</th>
<th>Half-life</th>
<th>Gamma energy</th>
<th>Beta energy (max)</th>
<th>Mean penetration of Beta particle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodine-131</td>
<td>8.02 days</td>
<td>364.5 keV</td>
<td>0.6 MeV</td>
<td>2 mm</td>
</tr>
<tr>
<td>Yttrium-90</td>
<td>2.67 days</td>
<td>No gamma emission</td>
<td>2.28 MeV</td>
<td>12 mm</td>
</tr>
<tr>
<td>Copper-67</td>
<td>2.58 days</td>
<td>185 keV</td>
<td>0.54 MeV</td>
<td>1.8 mm</td>
</tr>
<tr>
<td>Rhenium-186</td>
<td>3.77 days</td>
<td>131 keV</td>
<td>1.08 MeV</td>
<td>5 mm</td>
</tr>
<tr>
<td>Lutetium-177</td>
<td>6.7 days</td>
<td>208 keV (10% abundance) and 113 keV (6% abundance)</td>
<td>0.497 MeV</td>
<td>1.5 mm</td>
</tr>
</tbody>
</table>
Lu177-PSMA and Mechanism of therapy

Lu-177-PSMA-I&G delivers DNA damaging radiation directly to the site of disease and kills the metastatic cells only.
Lu$^{177}$-PSMA
First reported outcome for Lu177-PSMA-617
Inclusion criteria

- Patients diagnosed with castrate-resistant, progressive metastatic prostate cancer following conventional systemic treatment.
- PSMA expressing tumour confirmed with baseline Ga68-PSMA PET/CT scan
- Life expectancy of at least 6 months
- White cell count (WBC) (Normal range 4.0-11.0X10^9/L)
- Haemoglobin (Hb) (Normal range 130-175 g/L)
- Platelets (Normal range 150-400X10^9/L)
- Creatinine (micro mol/L)
- eGFR (>90 mL/min/1.73m2)
- No renal outflow obstruction
- Eastern Cooperative Oncology Group (ECOG) performance status score <2
Exclusion criteria

• Low level or minimal PSMA expression in their tumour
• Diffuse marrow disease deemed to be at high risk of marrow failure with therapy or marrow failure
• Reduced renal function/renal obstructive outflow
Treatment protocol

Identified patient
End stage mCRPC
PSMA avid disease
PSA progression

Follow up Ga68 PSMA-11 PET-CT scan and PSA status

1st Tx 2nd Tx

Follow up Ga68 PSMA-11 PET-CT scan and PSA status

3rd Tx 4th Tx

Each Tx delivered with a gap of 6-8 weeks
Biochemical response: PSA response (>50% reduction from baseline)

Imaging response: Reduction in SUV of lesions on interim PSMA PET/CT
Treatment protocol

1. Saline I/V infusion, lemon drink and anti nausea medicine prior to Therapy
2. Infusion of Lu-177-PSMA-I&T over 30 minutes
3. Immediate post Infusion injection of diuretic and additional IV Saline
4. Discharge patient after minimum of 3 hours and satisfactory radiation exposure reading
5. Post 24 hrs SPECT-CT scan
# Results: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristics (n=18)</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>69.36 (51-81)</td>
</tr>
<tr>
<td>PSA (ug/L)</td>
<td>139.72 (0.23-1310 ug/L)</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>119.89 (77-145 g/L)</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>76.38 (53-90 mL/min/1.73m²)</td>
</tr>
<tr>
<td>Creatinine (mol/L)</td>
<td>80.10 (43-118 mol/L)</td>
</tr>
<tr>
<td>Platelets count (/L)</td>
<td>258.23 (125-396 X10⁹/L)</td>
</tr>
<tr>
<td>WBC (/L)</td>
<td>6.81 (4.2-12.3X10⁹/L)</td>
</tr>
<tr>
<td>ECOG Performance status</td>
<td>1 (0-1)</td>
</tr>
<tr>
<td><strong>Total number of patient treated</strong></td>
<td>18</td>
</tr>
<tr>
<td>-----------------------------------</td>
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<tr>
<td><strong>Time period</strong></td>
<td>August 2018 to August 2019</td>
</tr>
<tr>
<td>Completed 4 cycles of treatment (responder)</td>
<td>(n=13)</td>
</tr>
<tr>
<td>Completed 2 cycles of treatment (non responder)</td>
<td>(n=4)</td>
</tr>
<tr>
<td>Completed 1 cycle of treatment (patient died after 1 x cycle)</td>
<td>(n=1)</td>
</tr>
<tr>
<td><strong>Nephrotoxicity</strong></td>
<td>No significant change in renal function observed</td>
</tr>
</tbody>
</table>
| **Haematoxicity**                | Thrombocytopenia: Grade 0 (n=16), Grade 1 (n=1), Grade 2 (n=1)  
|                                  | Anaemia: Grade 0 (n=13), Grade 1 (n=4), Grade 3 (n=1)  
|                                  | Leukocytopenia: Grade 0 (n=14), Grade 1 (n=3), Grade 2 (n=1) |
| **Side effects**                 | \(n=2\) reported Nausea  
|                                  | \(n=3\) Lethargic  
|                                  | \(n=13\) dry mouth post therapy |
| **Death during treatment**       | 1 patient died after a fall (1x infusion) |
PSA Response

>50% reduction of PSA 10/18 patients (58% response rate)

PSA response after 2 to 4 cycles of Treatment
Haematoxicity

**Thrombocytopenia**
- Grade 0: 84%
- Grade 1: 5%
- Grade 2: 5%
- Grade 3: 6%
- Grade 4: 0%

**Leukocytopenia**
- Grade 0: 78%
- Grade 1: 0%
- Grade 2: 5%
- Grade 3: 17%
- Grade 4: 0%

**Anaemia**
- Grade 0: 72%
- Grade 1: 6%
- Grade 2: 0%
- Grade 3: 0%
- Grade 4: 0%
**Quality of Life Outcomes**

**FACT-G changes**
- 70.58% Patients reported improvement in general health

**TOI changes**
- 70.58% Patients shows high treatment outcome index

**FACT-P Changes**
- 58.82% Patients reported improvement in prostate related general health
Quality of Life Outcomes

Physical well being (PWB)

82.35% Patients reported improvement in PWB

Social well being (SWB)

23.52% Patients reported improvement in SWB

Emotional well being (EWB)

64.70% Patients reported improvement in EWB

Functional well being (FWB)

47.05% Patients reported improvement in FWB
Quality of Life Outcomes

QoL of patients who received 2 cycles of Treatment
- Better: 80%
- No change: 20%
- Worse: 0%

QOL for patients who received 4 cycles of Treatment
- Improved: 62%
- Average: 23%
- Worse: 15%
Feedback from patients

“This treatment I found far better in comparison of the chemotherapy in terms of experiences.”

“I haven’t felt any change in my daily routine, this treatment is really comfortable and less worse in comparison of my other previous treatments...”

“It is pain less, stress less and a better experience every time in comparison of my previous treatment.”
Image evaluation for therapy responses

Pre therapy Ga68-PSMA scan

Post therapy Ga68-PSMA scan
Image evaluation for therapy responses

Pre therapy Ga68-PSMA scan

Post therapy Ga68-PSMA scan
Limitations

• Single arm study
• No follow up for delayed toxicity
• No long term follow up
Future plan

- Involve Control group
- More in depth evaluation of QoL using face to face interview of treated patients
- Longer term follow up of patients to evaluate for delayed toxicity and survival
Conclusion

• Lu177-PSMA-I&T is safe and effective in palliating patients with end-stage mCRPC patients

• Majority of patients experienced an improved quality of life whilst on treatment
References


