Focal Ablative STereotactic RAdiotherapy for Cancers of the Kidney

Professor Shankar Siva, Peter MacCallum Cancer Centre
DISCLOSURES

- Research Funding to Institution
  - Varian Industries
  - Merck-Sharp-Dohme
  - Bayer Pharmaceuticals

- Speaker Honoraria / Advisory Board
  - Astra Zeneca
  - Telix Pharmaceuticals

- AI images
  - Mid-Journey™
BACKGROUND Worldwide increase of RCC

Incidence of kidney cancer per 100,000

- 1975: 7.1
- 2008: 16
- 2023: (increasing)

Most rapidly increasing in >70s age group
The Standard of Care

Surgery is the standard of care.

But there are limited curative treatment options for medically inoperable patients.

Partial Nephrectomy
SABR as an alternative ticks all the boxes

<table>
<thead>
<tr>
<th></th>
<th>Avoids general anaesthetic</th>
<th>Peri-hilar tumours</th>
<th>Large tumours</th>
<th>Non-invasive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Thermal ablation</td>
<td>✓</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>SABR</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
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</table>
To Investigate the efficacy of SABR in the first multicentre phase II trial of non-surgical therapy for primary RCC.

Primary outcome/hypothesis:
Evaluate local control after SABR; Local control ≤80% considered not worthy of proceeding to a future randomized controlled trial.
TransTasman Radiation Oncology Group

70 patients
Recruited between
Jul. 2016 and Feb. 2020

1 centre in the Netherlands
7 centres in Australia
Key Eligibility and Patient Characteristics

- Biopsy-confirmed diagnosis of primary RCC with a single lesion within a kidney
- Medically inoperable or high-risk for surgery
- Multidisciplinary decision has been made that active treatment is warranted
- Tumour not abutting bowel
- Tumour maximum dimension larger than 10cm

Median age: **77 years**
BMI: **32 kg/m²**
Charlson comorbidity index: **7**

- **T1a disease**: 24 patients (34%)
  - Biopsy-confirmed diagnosis of primary RCC with a single lesion within a kidney
  - Medically inoperable or high-risk for surgery
  - Multidisciplinary decision has been made that active treatment is warranted
  - Tumour not abutting bowel
  - Tumour maximum dimension larger than 10cm

- **T1b disease**: 39 patients (56%)

- **T2a disease**: 6 patients (9%)
- **T3a disease**: 1 patient (1%)
- **T1a disease**: 24 patients (34%)

Group potentially suitable for thermal ablation
Planned SABR Treatment

**Tumour maximal dimension, mm**

<table>
<thead>
<tr>
<th></th>
<th>Median [range]</th>
</tr>
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<tbody>
<tr>
<td><strong>Tumour maximal dimension, mm</strong></td>
<td><strong>R.E.N.A.L. complexity score</strong></td>
</tr>
<tr>
<td>7 [4 - 10]</td>
<td>9 [5 - 11]</td>
</tr>
</tbody>
</table>

Too large and complex for Thermal Ablation

**Single fraction**

(26Gy)

*for tumours ≤4 cm*

**3 fractions**

(42Gy)

*for tumours >4 cm*
Clinical outcomes at a median follow-up of 43 months

Local control rate

100%
Clinical outcomes at a median follow-up of 43 months

**Freedom from distant failure**
- 3 yrs 99%
- 5 yrs 92%

**Local control rate**

**Cancer specific survival**

**Kidney function loss**

<table>
<thead>
<tr>
<th>Months from SABR</th>
<th>No. at risk</th>
<th>No. events</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>All 70 (0)</td>
<td>68 (0)</td>
</tr>
<tr>
<td>12</td>
<td>55 (0)</td>
<td>40 (0)</td>
</tr>
<tr>
<td>24</td>
<td>40 (0)</td>
<td>23 (0)</td>
</tr>
<tr>
<td>36</td>
<td>23 (0)</td>
<td>11 (0)</td>
</tr>
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Clinical outcomes at a median follow-up of 43 months

<table>
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<th>Local control rate</th>
<th>Freedom from distant failure</th>
<th>Cancer specific survival</th>
<th>Kidney function loss</th>
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<tr>
<td>70 (0)</td>
<td>68 (0)</td>
<td>100%</td>
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Clinical outcomes at a median follow-up of 43 months

Kidney function loss
-14.6 mls/min

One patient underwent dialysis; 59mm central tumour and baseline eGFR of 34 mls/min.
Clinical outcomes at a median follow-up of 43 months

- Local control rate: 100%
- Freedom from distant failure: 99%
- Cancer specific survival: 100%
- Kidney function loss (1 patient underwent dialysis): -14.6 mls/min
Conclusions

SABR is effective in primary RCC.

- Exceptional cancer control rates
- No cancer-related deaths
- Modest renal function decline after treatment
SABR is now an established therapy for primary kidney cancer not suited to surgery.

These outcomes support the design of a future randomised clinical trial of SABR versus surgery for primary RCC.
Thank you

Trial Management Committee
David Pryor, Jeremy Ruben, Farshad Foroudi, Braden Higgs, Nathan Lawrentschuk, Mathias Bressel, Alex Car, Swetha Sridharan, Mark Sidhom, Ben Vanneste (MAASTRO)

Physics: Tomas Kron, Nick Hardcastle

Radiotherapy: Daniel Pham, Brent Chesson, Andrew Lim

Nuclear Medicine: Michael Hofman, Jason Callahan, Price Jackson

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