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FASTRACK II TRIAL

Focal Ablative Stereotactic
Radiotherapy for Cancers of the Kidney

Professor Shankar Siva, Peter MacCallum Cancer Centre

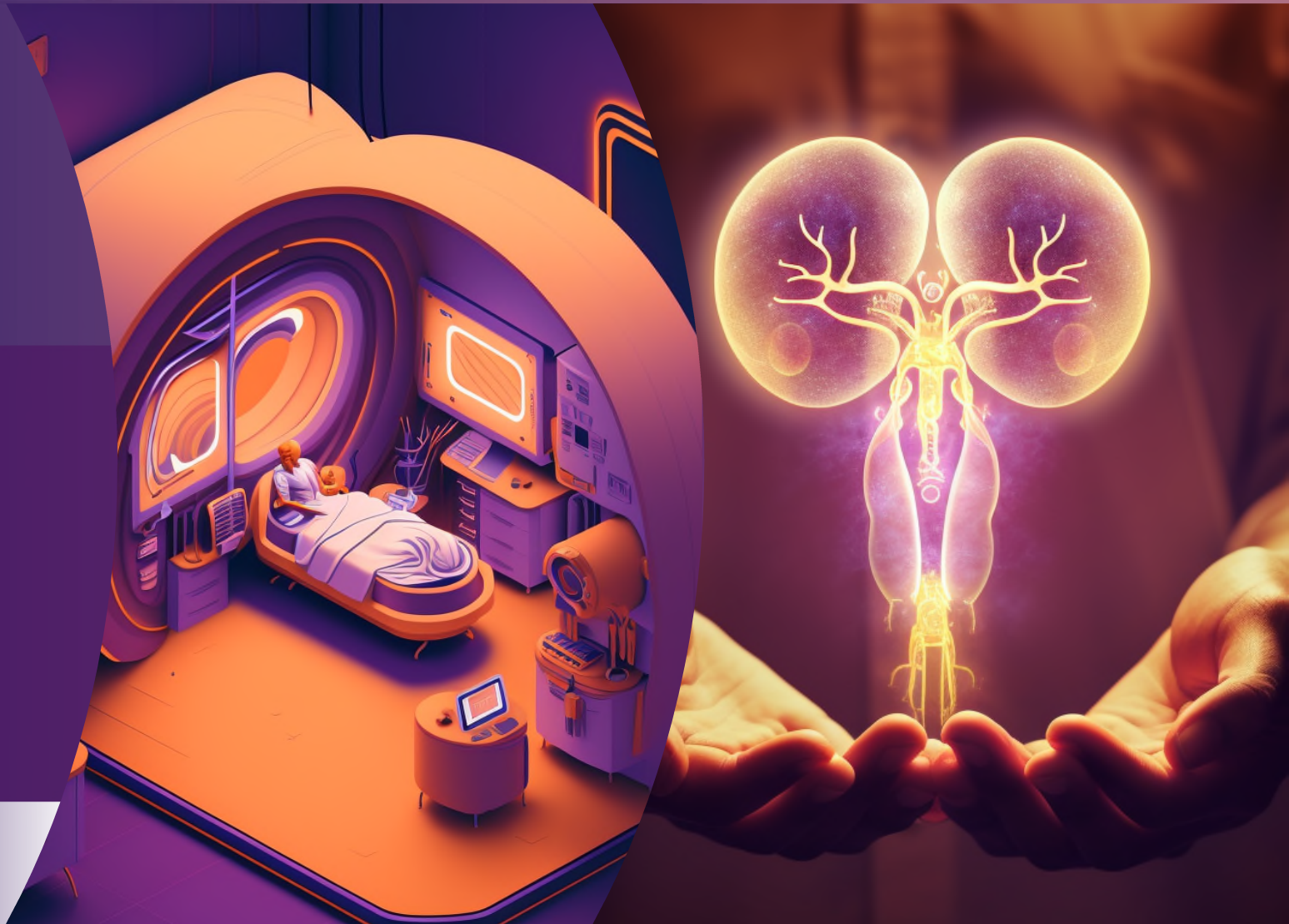


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DISCLOSURES

- Research Funding to Institution
 - Varian Industries
 - Merck-Sharp-Dohme
 - Bayer Pharmaceuticals
- Speaker Honoraria / Advisory Board
 - Astra Zeneca
 - Telix Pharmaceuticals
- AI images
 - Mid-Journey™



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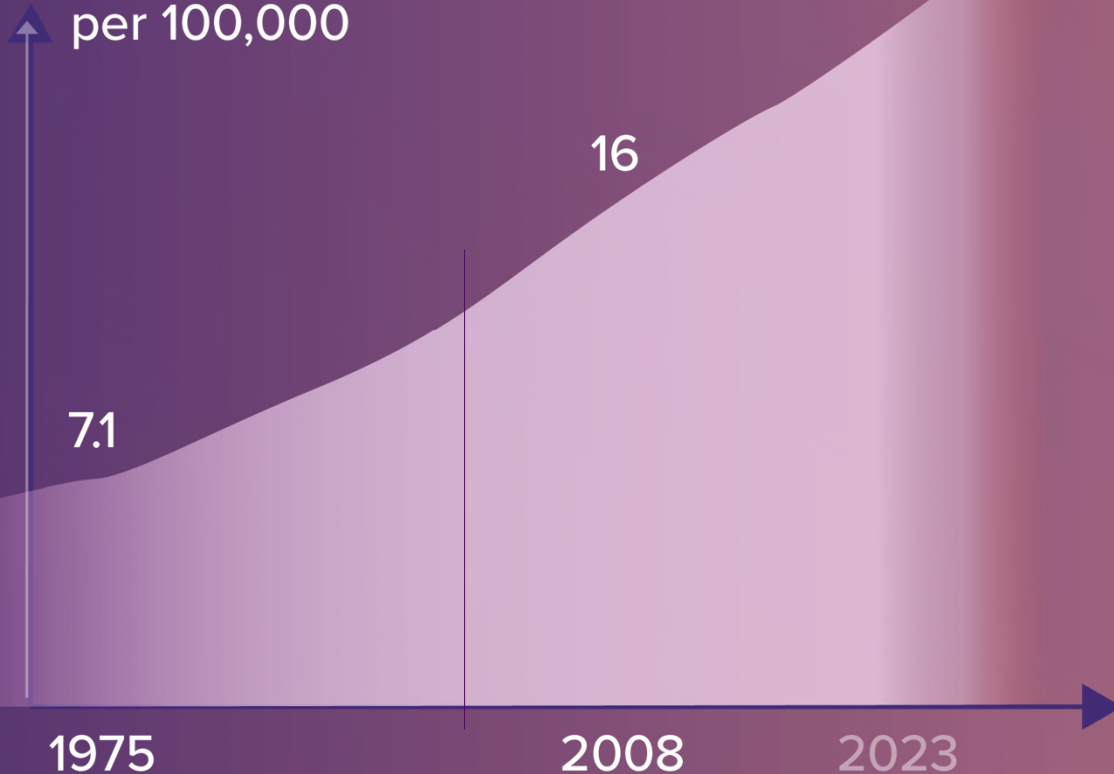
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BACKGROUND Worldwide increase of RCC



Incidence of kidney cancer per 100,000

Most rapidly increasing in >70s age group



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The Standard of Care



Partial Nephrectomy

Surgery is the standard of care.

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


















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SABR as an alternative ticks all the boxes

	Avoids general anaesthetic	Peri-hilar tumours	Large tumours	Non-invasive
 Surgery				
 Thermal ablation				
 SABR				

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Trial objective

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 $\leq 80\%$ considered not worthy of proceeding to a future randomized controlled trial.



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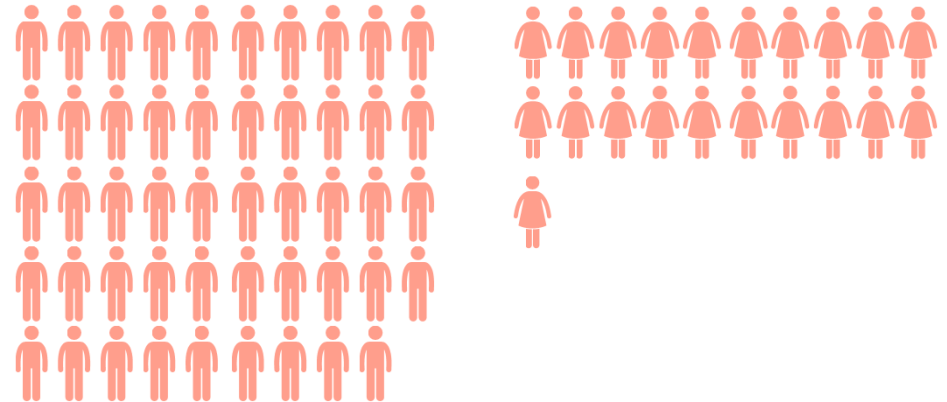
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TransTasman Radiation Oncology Group



70 patients
Recruited between
Jul. 2016 and Feb. 2020

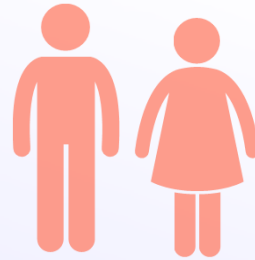


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Key Eligibility and Patient Characteristics

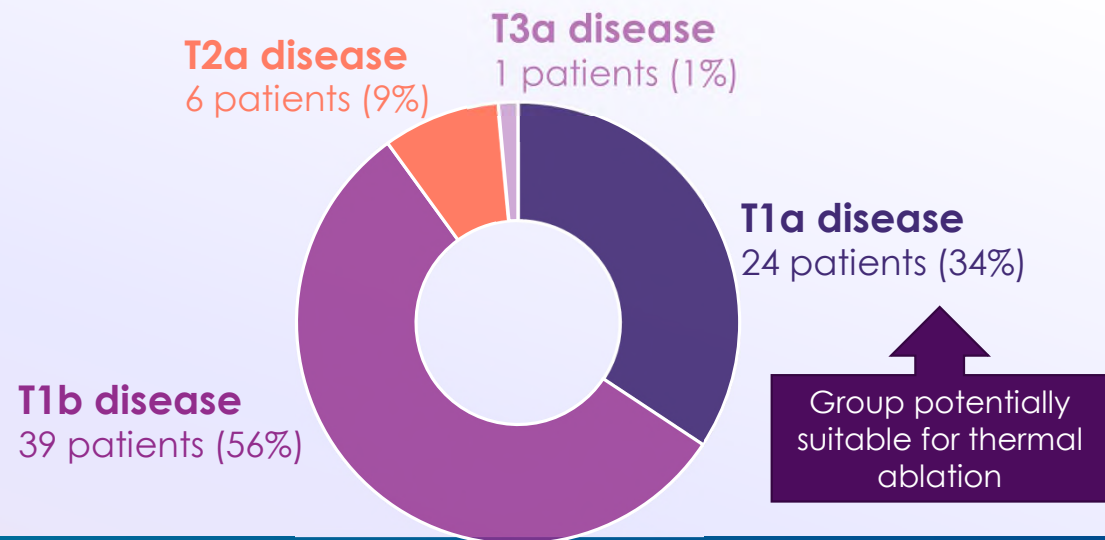
- Biopsy-confirmed diagnosis of primary RCC with a single lesion within a kidney
- Medically inoperable or high-risk for surgery
- Multidisciplinary decision has been made that active treatment is warranted
- Tumour not abutting bowel
- Tumour maximum dimension larger than 10cm



Median age: **77 years**

BMI: **32 kg/m**

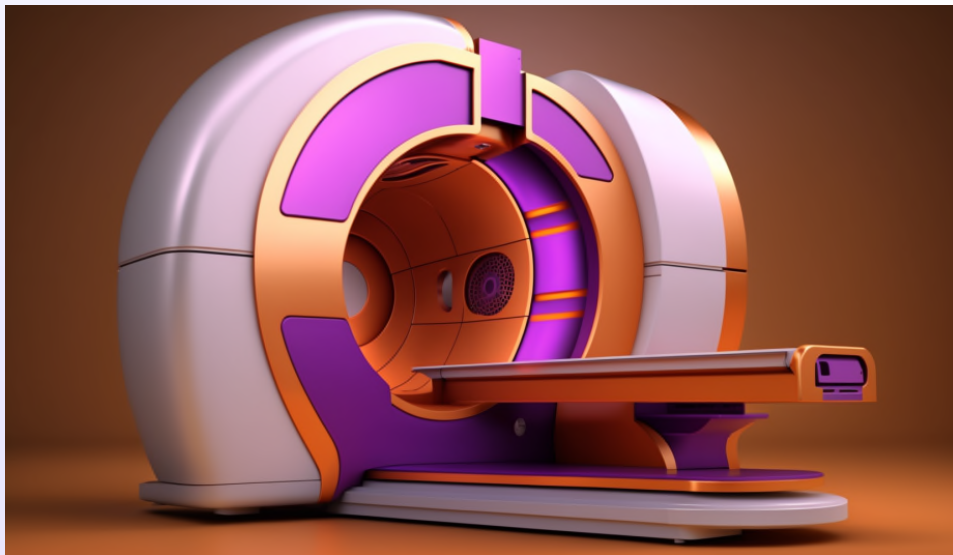
Charlson comorbidity index: **7**



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Planned SABR Treatment



**Single fraction
(26Gy)**
for tumours ≤ 4 cm



**3 fractions
(42Gy)**
for tumours > 4 cm

		
Tumour maximal dimension, mm		
Median [range]	33 [15 - 39]	53 [40 - 89]
R.E.N.A.L. complexity score		
Median [range]	7 [4 - 10]	9 [5 - 11]

← Too large and complex for Thermal Ablation



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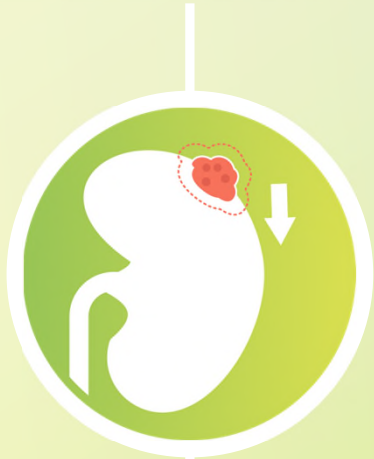
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Clinical outcomes

at a median follow-up of 43 months



Local control rate
100%



Freedom from distant failure

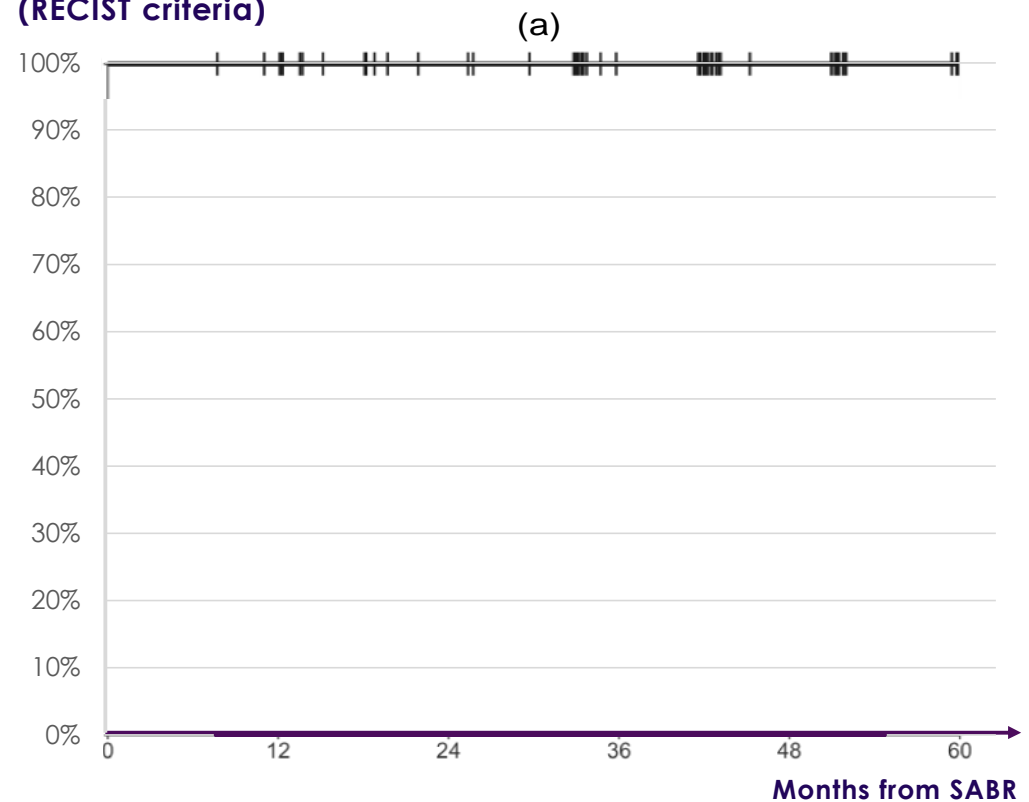


Cancer specific survival



Kidney function loss

Local Control rate (RECIST criteria)



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Clinical outcomes

at a median follow-up of 43 months



Local control rate



Freedom from distant failure

3 yrs **99%**

5 yrs **92%**

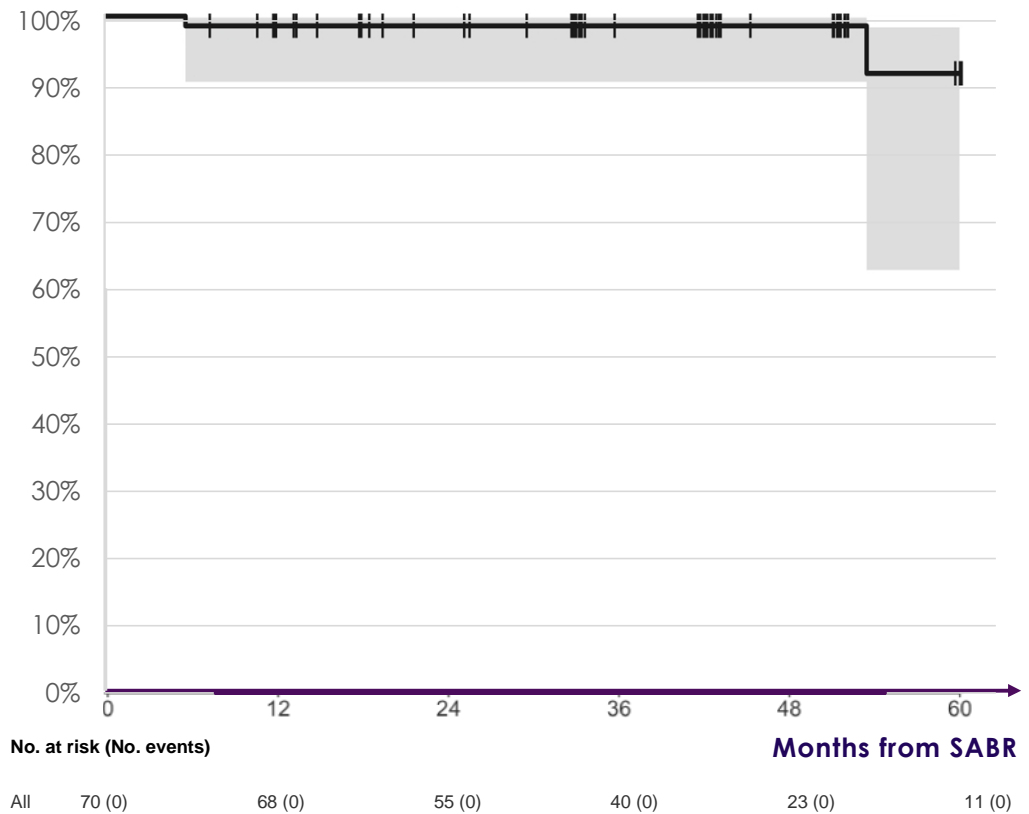


Cancer specific survival



Kidney function loss

Freedom from distant failure



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Clinical outcomes

at a median follow-up of 43 months



Local control rate



Freedom from distant failure



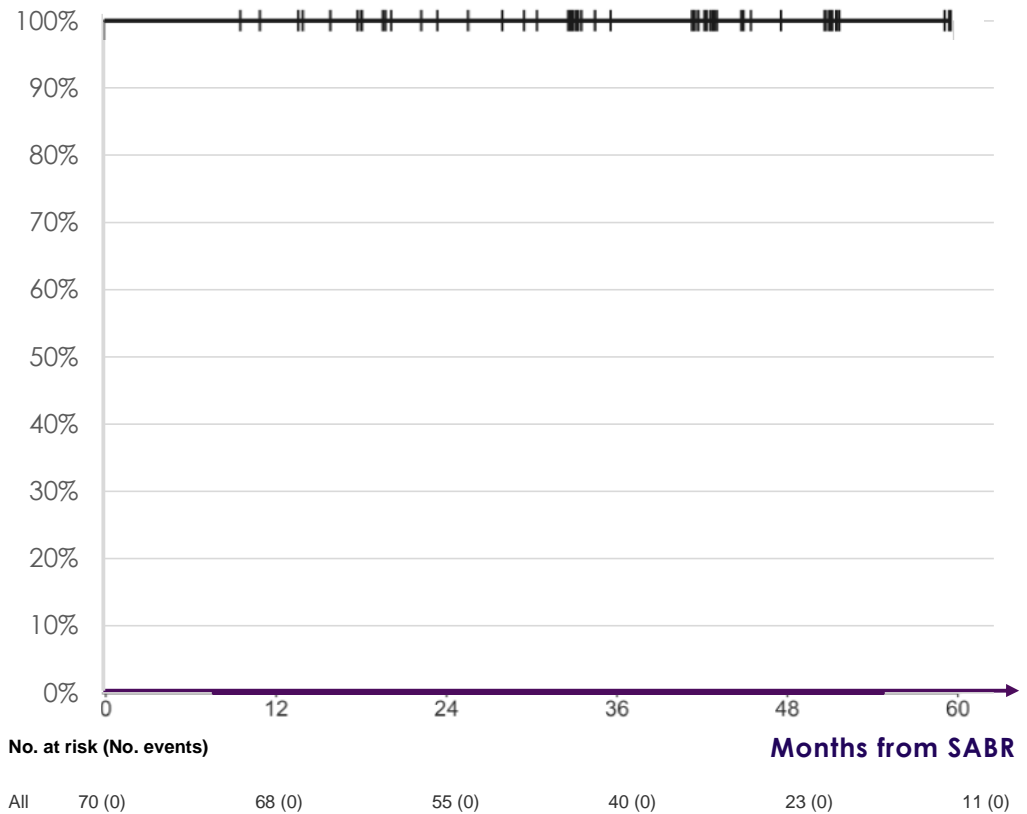
Cancer specific survival

100%



Kidney function loss

Cancer specific survival



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Clinical outcomes

at a median follow-up of 43 months



Local control rate



Freedom from distant failure



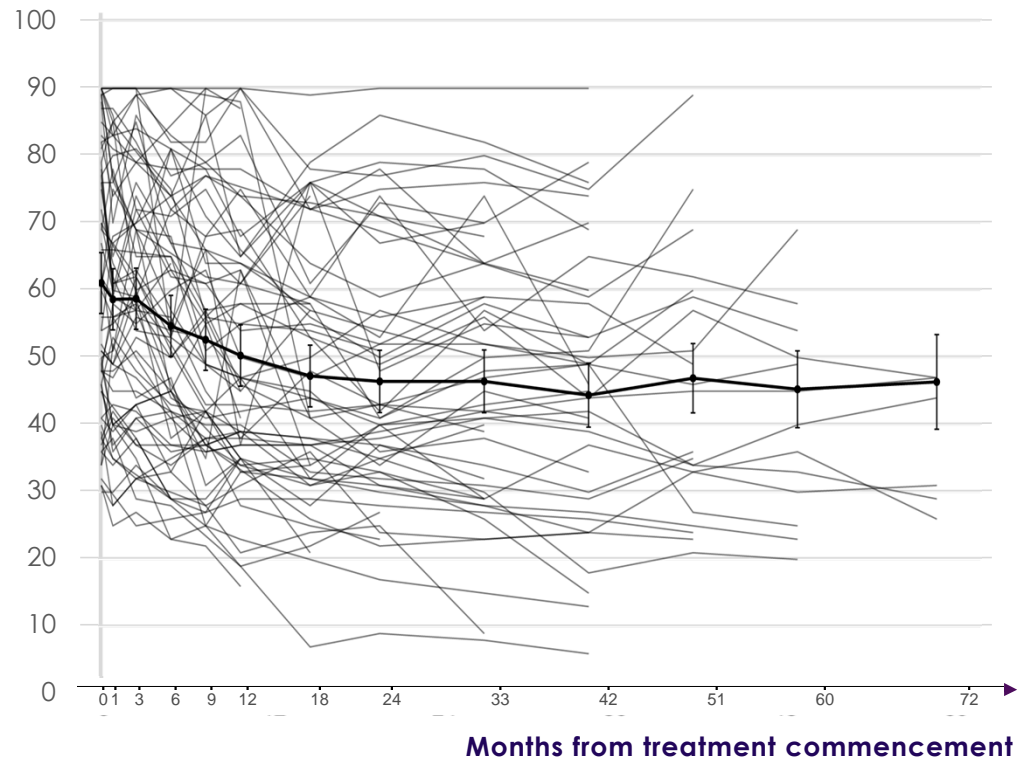
Cancer specific survival



Kidney function loss
-14.6_{mls/min}

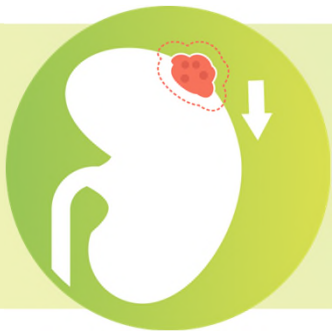
One patient underwent dialysis; 59mm central tumour and baseline eGFR of 34mls/min.

eGFR, mls/min (CDK-EPI)



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



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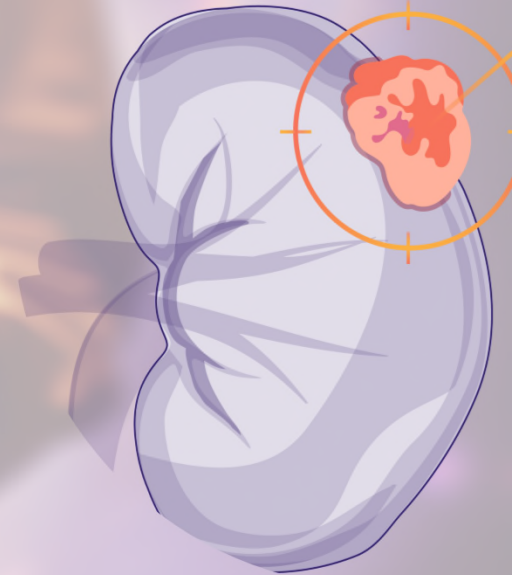
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Conclusions



SABR is effective in primary RCC.

- Exceptional cancer control rates
- No cancer-related deaths
- Modest renal function decline after treatment



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Interpretation



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.



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 An international prospective phase 3 study of Focal Ablative Stereotactic Radiotherapy for Cancers of the Kidney

Background
 The incidence of Renal Cell Carcinoma (RCC) has been steadily increasing worldwide, particularly in the age group over 70.

Surgery
 has been the standard treatment. However, for patients, morbidity is significant due to advanced age or comorbidities. There are limited curative treatment options.

Thermal ablation
 is an alternative intervention for small tumours typically <3cm, but it has limited efficacy and increased complications for larger masses.

Stereotactic Ablative Body Radiotherapy (SABR)
 is an emerging non-invasive treatment option for patients who are unsuitable for surgery.

The trial
 70 patients of median age 77 years were enrolled between Jul 2016 and Oct 2020 (30 years / 27 weeks).

Inclusion criteria:
 - Primary renal malignancy of primary RCC with a single lesion without metastases
 - ECOG performance 0-2
 - Medically inoperable or high risk for surgery

Median tumour size (cm): 4.6cm (37/5)

3 fractions (21Gy)
 for tumours <4cm
 5 fractions (27Gy) & boost (30Gy) for >4cm (27 patients)

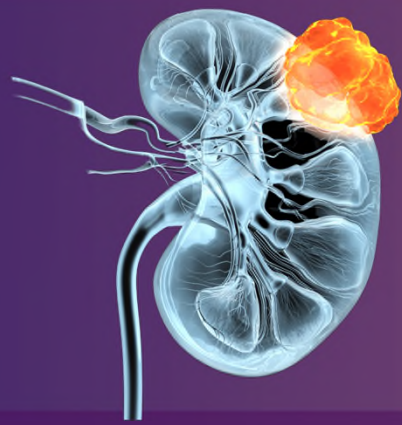
Assessment

Assessment	CT (Phase Assessment)	uHb (PSA APG)	SpR renal function test & subsequent GFR	Whole body bone scan
Baseline	✓	✓	✓	✓
Year 1	A, E, S, G, D	3 months	✓	✓
Year 2	6 months	6 months	✓	✓
Year 3	9 months	9 months	✓	✓
Year 4	Annually	Annually	✓	✓

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 (a single patient underwent dialysis): **-14.6**

Interpretation
 SABR is a new standard of care for primary kidney cancer not suited to surgery. These outcomes support the design of a future randomized clinical trial of SABR versus surgery for primary RCC.



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Thank you

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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

Imaging: Arian Lasocki, Eddie Lau, Bimal Kumar, James Korte

TROG: Bec Montgomery, Alisha Moore, Olivia Cook, Ryan Davey



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