



CÁNCER RENAL METASTÁSICO: ¿HAY HUECO PARA LA RADIOTERAPIA?

DR. IGNACIO NAVARRO RUIZ DE ADANA

MÉDICO RESIDENTE 3º AÑO

ONCOLOGÍA RADIOTERÁPICA

DÍAZ

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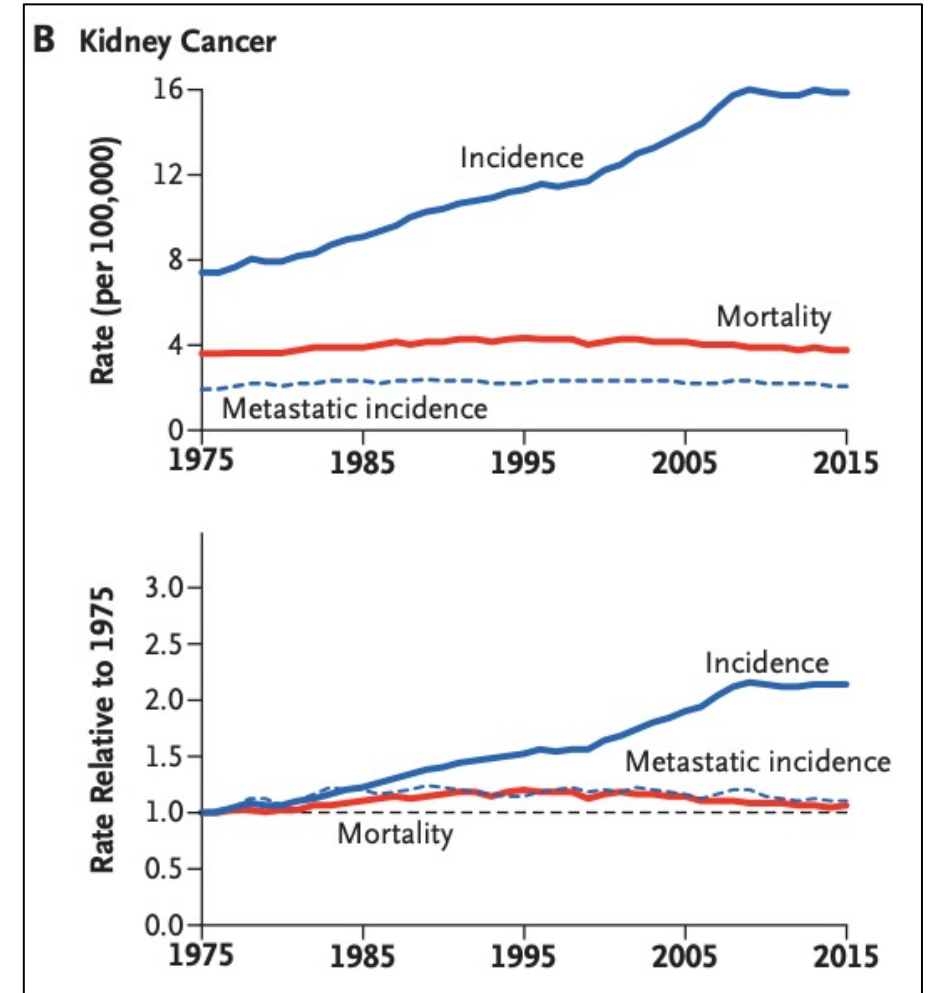




1. INTRODUCCIÓN Y EPIDEMIOLOGÍA

- 2-3% de todos los tumores malignos en el adulto
- Se suelen diagnosticar entre la 4ª y la 6ª década
- 2x más frecuente en hombres
- 50 % pacientes tratados con intención radical presentarán recaídas
- Raza: más frecuente en afroamericanos
- Factores de riesgo:
 - ❖ Tabaco
 - ❖ Exposición
 - ❖ Analgesia
- Histología:
 - ❖ Células claras (80%)
 - ❖ Papilar (15%)
 - ❖ Cromóforo y oncocitoma (5%).

Welch HG et al. N Engl J Med. 2019





2. RADIORRESISTENCIA. ¿EXISTE EN REALIDAD?

● *Oncology Intelligence*

A REVIEW OF HUMAN CELL RADIOSENSITIVITY *IN VITRO*

PATRICK J. DESCHAVANNE, PH.D.* AND BERNARD FERTIL, PH.D.†

*Laboratoire de mutagenèse, Institut J. Monod, CNRS, Université Paris VII, 2, place Jussieu, 75005 Paris, France,
†INSERM U.66, 91 bl de l'Hôpital, 75634, Paris, France

Deschavanne PJ et al. Int J Radiat Oncol Biol Phys. 1996

Sixth Conference on Radioimmunodetection and
Radioimmunotherapy of Cancer

Supplement to Cancer

Radiobiologic Studies of Radioimmunotherapy and External Beam Radiotherapy In Vitro and In Vivo in Human Renal Cell Carcinoma Xenografts

Ning S et al. Cancer. 1997

- Históricamente tumor radiorresistente
- Estudios *in vitro* e *in vivo*
- Normofraccionamiento NO es suficiente para eliminar tumores de células renales.



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**¿TRADUCCIÓN
CLÍNICA?**



2. RADIORRESISTENCIA. ¿EXISTE EN REALIDAD?

British Journal of Urology (1973), 45, 258–269

CARCINOMA OF THE KIDNEY

B. VAN DER WERF-MESSING, MD

van der Werf-Messing B. Cancer. 1973

Scand J Urol Nephrol 21: 285–289, 1987

A RANDOMIZED TRIAL OF POSTOPERATIVE RADIOTHERAPY VERSUS OBSERVATION IN STAGE II AND III RENAL ADENOCARCINOMA

A Study by the Copenhagen Renal Cancer Study Group

Mogens Kjaer,¹ Peter Iversen,² Valdemar Hvidt,³ Eywin Bruun,⁴ Poul Skaarup,⁵
Jørgen Bech Hansen⁶ and Peter L. Frederiksen⁷

From the Departments of ¹Oncology II, Finsen Institute, Copenhagen, ²Urology, Hvidovre Hospital, Copenhagen, ³Urological Surgery D, Bispebjerg Hospital, Copenhagen, ⁴Urology, Gentofte Hospital, University of Copenhagen, Copenhagen, ⁵Urological Surgery H, Copenhagen County Hospital, Herlev, ⁶Surgery K, Frederiksberg Hospital, Copenhagen and ⁷Oncology and Radiotherapy R, Copenhagen County Hospital, Herlev, Denmark

Kjaer M, et al. Scand J Urol Nephrol. 1987

The Value of Radiotherapy in the Treatment of Hypernephroma—a Clinical Trial

R. FINNEY

Regional Radiotherapy Centre, Newcastle-upon-Tyne University Hospitals

Finney R. Br J Urol. 1973

original article

*Annals of Oncology 21: 1839–1845, 2010
doi:10.1093/annonc/mdq028
Published online 5 February 2010*

Need for a new trial to evaluate postoperative radiotherapy in renal cell carcinoma: a meta-analysis of randomized controlled trials

M. A. Tunio^{1*}, A. Hashmi² & M. Rafi¹

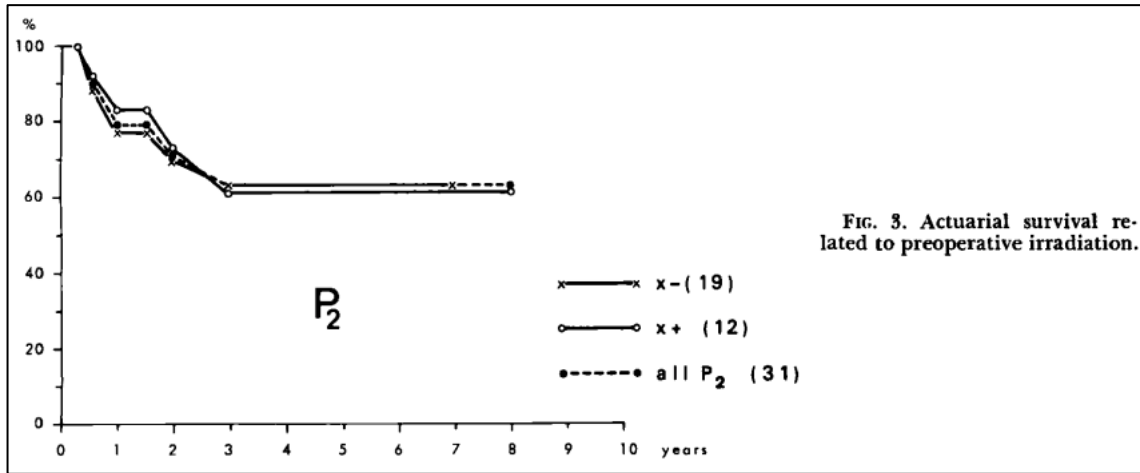
¹Departments of Radiation Oncology and ²Urology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan

Received 1 October 2009; revised 26 November 2009; accepted 4 January 2010

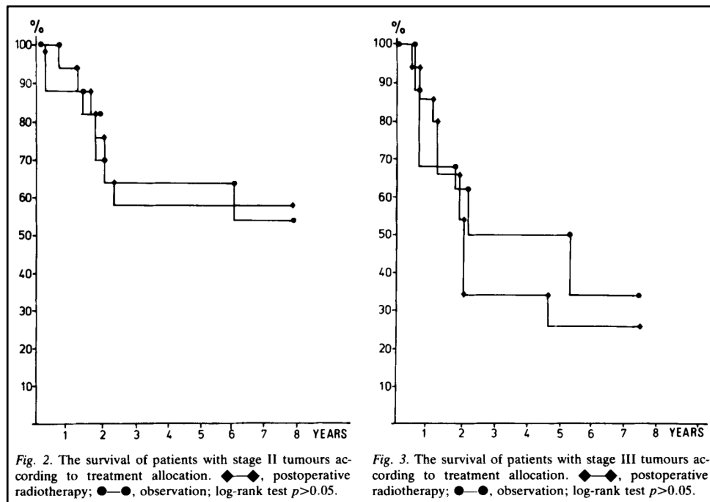
Tunio MA, et al. Ann Oncol. 2010



2. RADIORRESISTENCIA. ¿EXISTE EN REALIDAD?



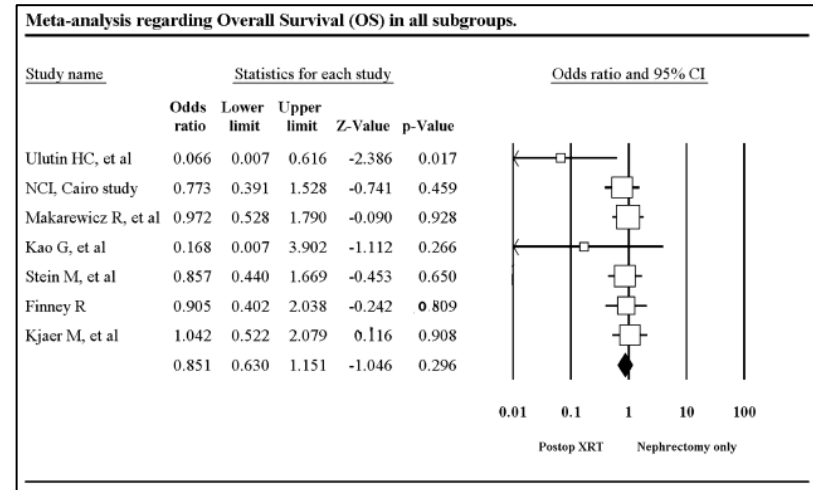
van der Werf-Messing B. Cancer. 1973



Kjaer M, et al. Scand J Urol Nephrol. 1987

Table VI With Radiotherapy—51 Cases				Table VII Without Radiotherapy—49 Cases			
Years at Risk	Numbers	Alive	Percentage Alive	Years at Risk	Numbers	Alive	Percentage Alive
1	51	37	72	1	49	41	83
3	41	25	61	3	38	25	66
5	30	11	36	5	27	12	44

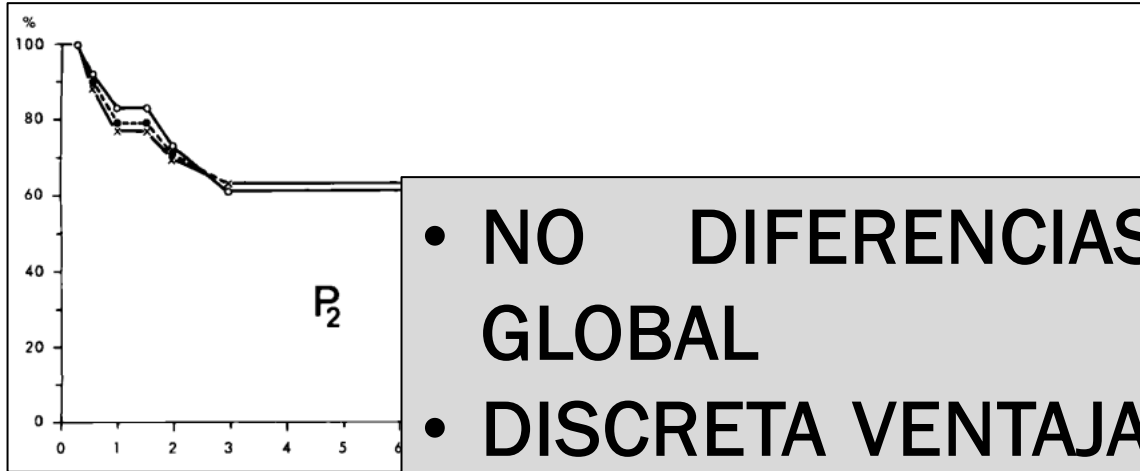
Finney R. Br J Urol. 1973



Tunio MA, et al. Ann Oncol. 2010



2. RADIORRESISTENCIA. ¿EXISTE EN REALIDAD?



van der We

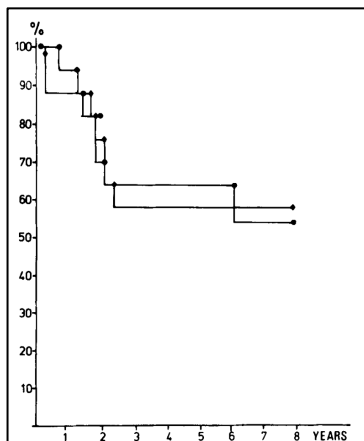


Fig. 2. The survival of patients with stage II tumours according to treatment allocation. ●—●, postoperative radiotherapy; ■—■, observation; log-rank test $p>0.05$.

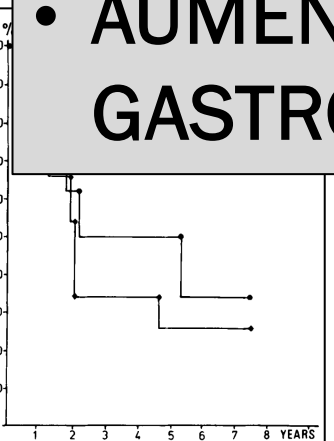


Fig. 3. The survival of patients with stage III tumours according to treatment allocation. ●—●, postoperative radiotherapy; ■—■, observation; log-rank test $p>0.05$.

- NO DIFERENCIAS EN SUPERVIVENCIA GLOBAL
- DISCRETA VENTAJA EN CUANTO A CONTROL LOCAL
- AUMENTO DE TOXICIDAD GASTROINTESTINAL

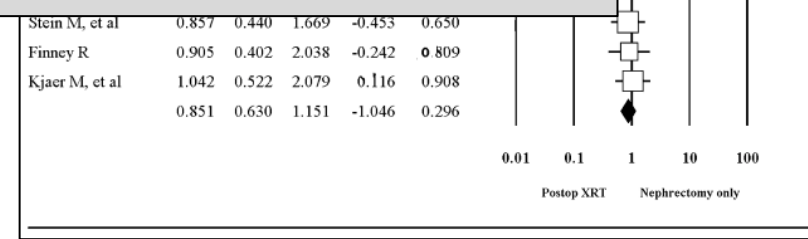
Table VI
With Radiotherapy—51 Cases

Years	Percentage
0	100
1	80
2	75
3	65
4	65
5	65
6	65

Table VII
Without Radiotherapy—49 Cases

Years	Numbers	Alive	Percentage Alive
0	49	41	83
1	38	25	66
2	27	12	44

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Tunio MA, et al. Ann Oncol. 2010



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- Estudios *in vitro* e *in vivo*
- Normofraccionamiento NO es suficiente para

¿RADIOTERAPIA?

Supplement to Cancer

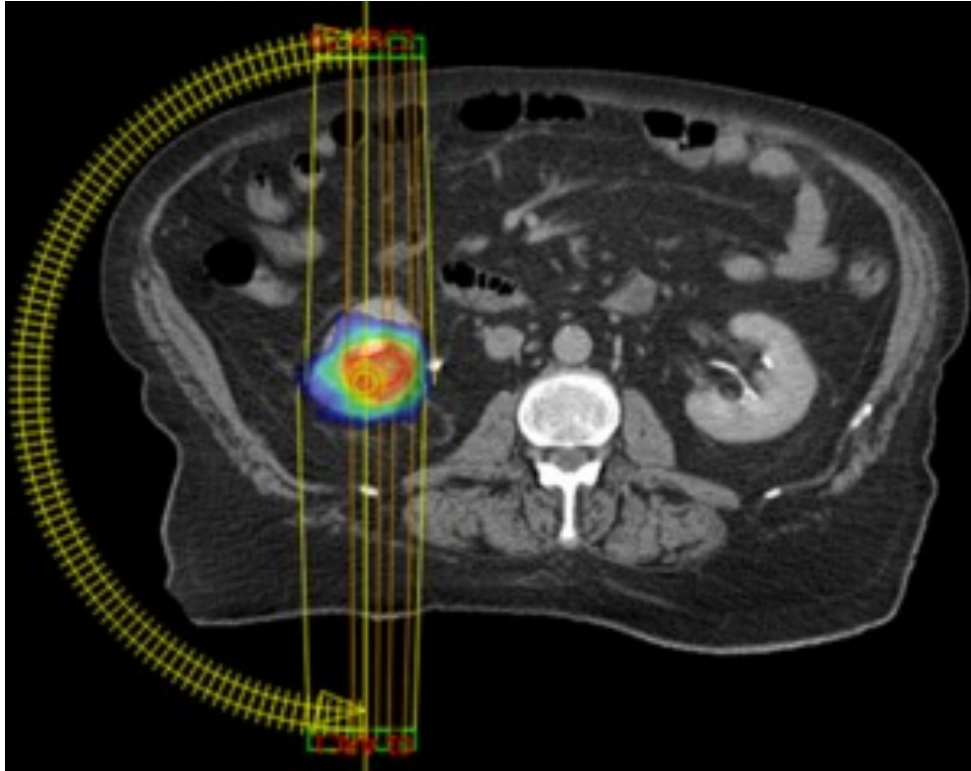
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Ning S et al. Cancer. 1997

¿TRADUCCIÓN CLÍNICA?



2. RADIORRESISTENCIA. ¿EXISTE EN REALIDAD?



SBRT





2. RADIORRESISTENCIA. ¿EXISTE EN REALIDAD?

- Radioterapia externa
- Altas dosis
- 1-5 fracciones
- Volúmenes extracraneales
- Tumores primarios y metastásicos (pulmón, próstata, renal, etc)
- Diferentes técnicas:
 - IMRT
 - VMAT
 - RM LINAC
 - CYBERKNIFE, GAMMAKNIFE





2. RADIORRESISTENCIA. ¿EXISTE EN REALIDAD?

Kidney Cancer

Efficacy of Ablative High-Dose-per-Fraction Radiation for Implanted Human Renal Cell Cancer in a Nude Mouse Model

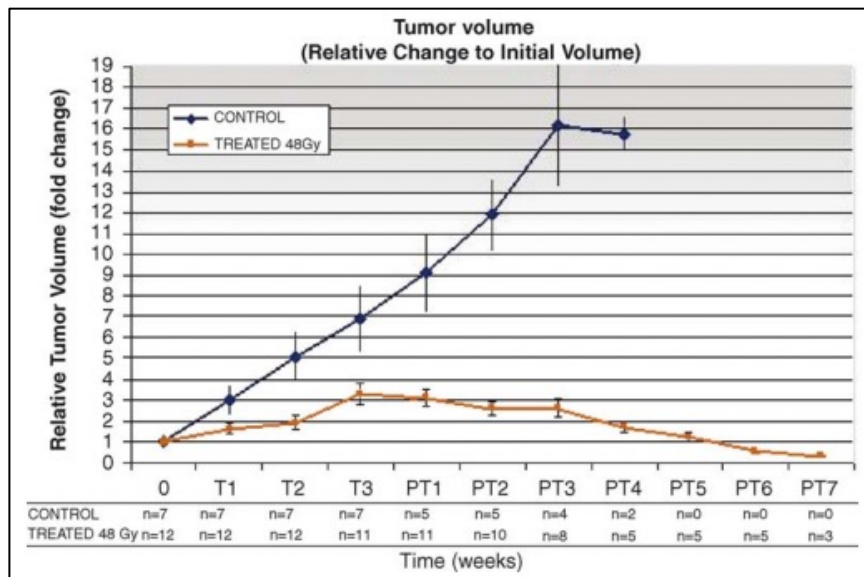
Lance Walsh^a, Jennifer L. Stanfield^a, L. Chinsoo Cho^b, Cheng-hui Chang^b, Kenneth Forster^b, Wareef Kabbani^c, Jeffrey A. Cadeddu^a, Jer-Tsong Hsieh^a, Hak Choy^b, Robert Timmerman^b, Yair Lotan^{a,*}

^a Department of Urology, The University of Texas Southwestern Medical Center, Dallas, Texas, USA

^b Department of Radiation Oncology, The University of Texas Southwestern Medical Center, Dallas, Texas, USA

^c Department of Pathology, The University of Texas Southwestern Medical Center, Dallas, Texas, USA

Walsh L, et al. Eur Urol. 2006

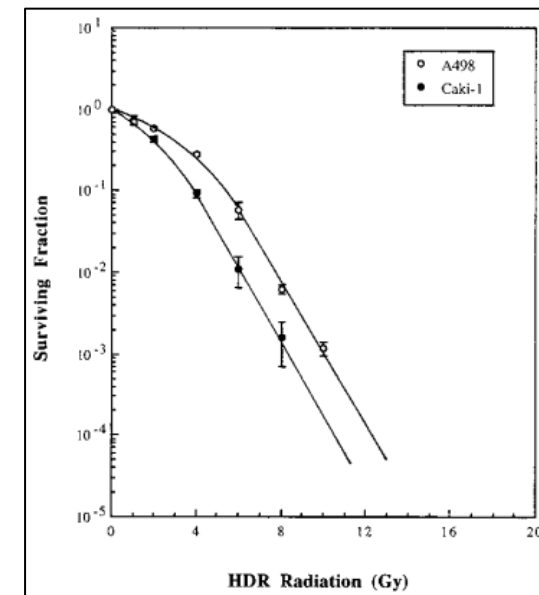


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^aDepartm

^bDepartm

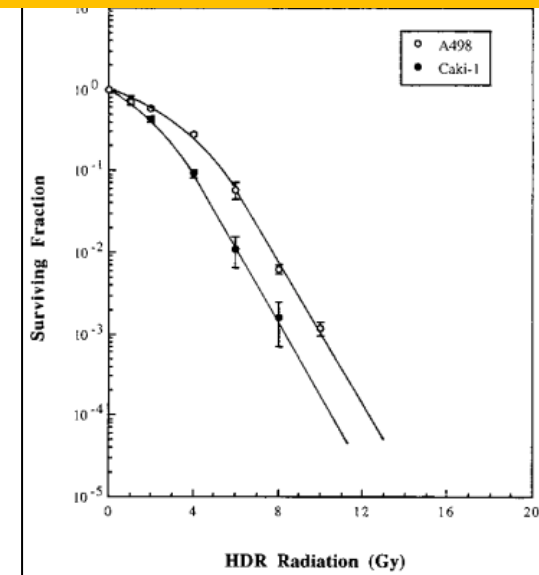
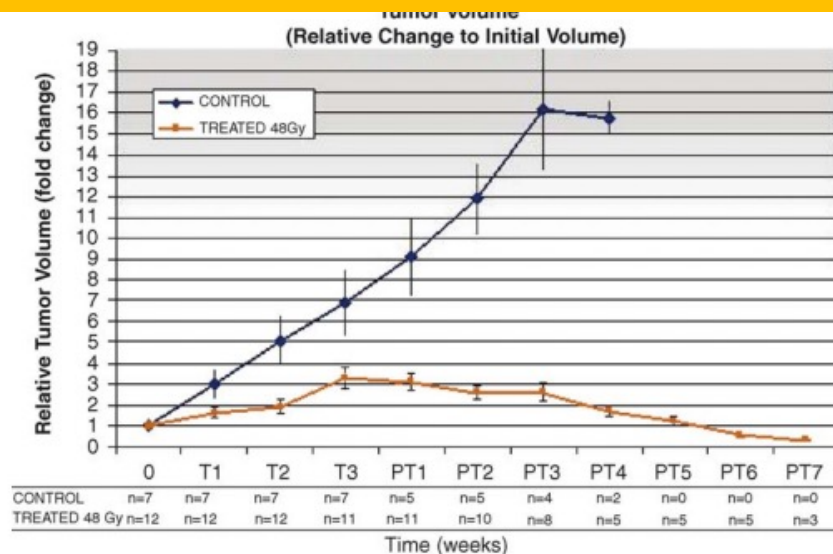
^cDepartm

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¿TRADUCCIÓN CLÍNICA?





3. OLIGOMETÁSTASIS/OLIGOPROGRESIÓN.

CONCEPTO

Consensus

Defining oligometastatic disease from a radiation oncology perspective:
An ESTRO-ASTRO consensus document



Yolande Lievens^{a,*}, Matthias Guckenberger^b, Daniel Gomez^c, Morten Hoyer^d, Puneeth Iyengar^e,
Isabelle Kindts^f, Alejandra Méndez Romero^g, Daan Nevens^h, David Palmaⁱ, Catherine Park^j,
Umberto Ricardi^k, Marta Scorsetti^l, James Yu^m, Wendy A. Woodward^c

Lievens Y, et al. Radiother Oncol. 2020

¿Nº metástasis?

¿Sincrónico vs Metacrónico?

¿Curabilidad?



3. OLIGOMETÁSTASIS/OLIGOPROGRESIÓN. CONCEPTO

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Lievens Y, et al. Radiother Oncol. 2020

- 3-5 metástasis. ¿Futuro?
- Pronóstico: Metacrónico > sincrónico.
- BED > 100 Gy
- Retraso/eliminación de terapia sistémica ± ¿curabilidad? → Investigación



3. OLIGOMETÁSTASIS/OLIGOPROGRESIÓN. CONCEPTO

Local Consolidative Therapy Vs. Maintenance Therapy or Observation for Patients With Oligometastatic Non-Small-Cell Lung Cancer: Long-Term Results of a Multi-Institutional, Phase II, Randomized Study

original report

Daniel R. Gomez, MD¹; Chad Tang, MD¹; Jianjun Zhang, MD, PhD¹; George R. Blumenschein Jr, MD¹; Mike Hernandez, MS¹; J. Jack Lee, PhD¹; Rong Ye, MS¹; David A. Palma, MD, PhD²; Alexander V. Louie, PhD, MSc²; D. Ross Camidge, MD, PhD³; Robert C. Doebele, MD, PhD³; Ferdinandos Skoulidis, MD, PhD¹; Laurie E. Gaspar, MD³; James W. Welsh, MD¹; Don L. Gibbons, MD¹; Jose A. Karam, MD¹; Brian D. Kavanagh, MD, MPH³; Anne S. Tsao, MD¹; Boris Sepesi, MD¹; Stephen G. Swisher, MD¹; and John V. Heymach, MD, PhD¹

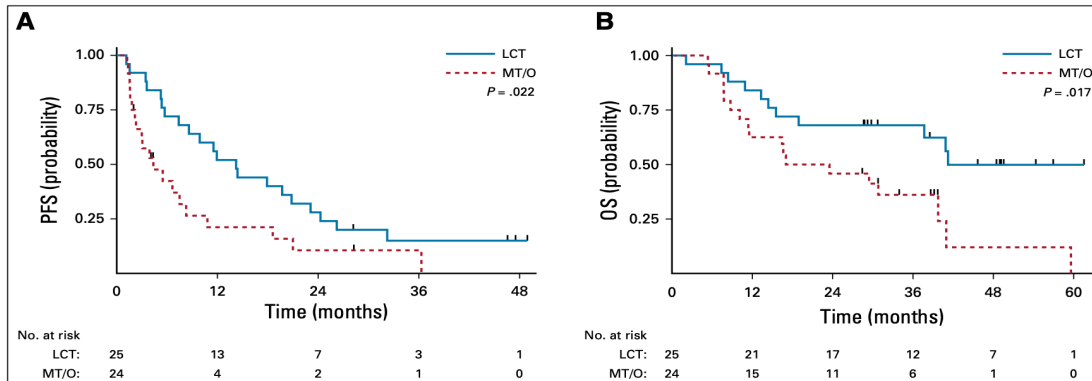


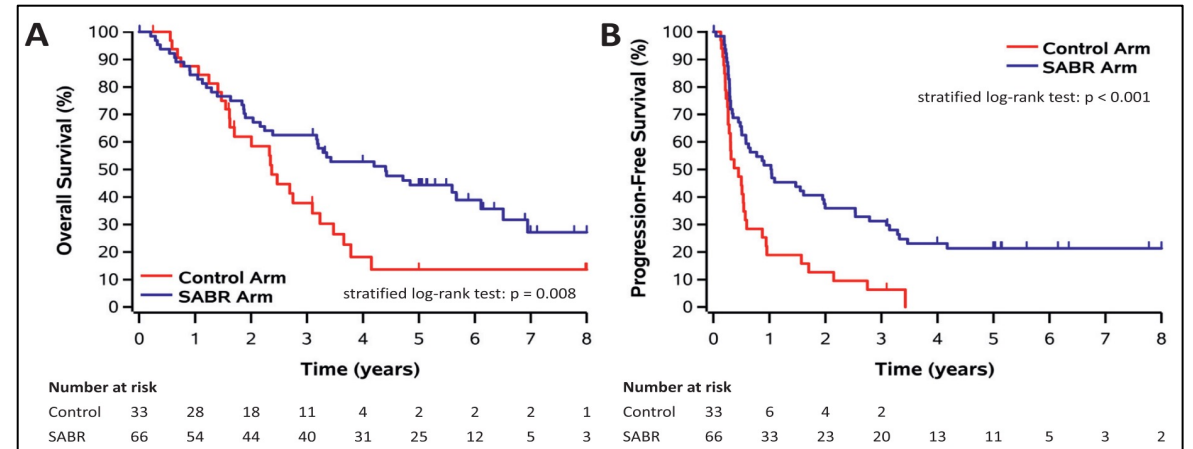
FIG 1. (A) Progression-free survival (PFS) and (B) overall survival (OS) in patients given local consolidative therapy (LCT) or maintenance therapy or observation (MT/O) for oligometastatic non-small-cell lung cancer.

Gomez DR, et al. J Clin Oncol. 2019

CLINICAL INVESTIGATION

Stereotactic Radiation for the Comprehensive Treatment of Oligometastases (SABR-COMET): Extended Long-Term Outcomes

Stephen Harrow, MBChB, PhD,* David A. Palma, MD, PhD,[†] Robert Olson, MD, MSc,[‡] Stewart Gaede, PhD,[†] Alexander V. Louie, MD, PhD,^{†,§} Cornelis Haasbeek, MD, PhD,^{||} Liam Mulroy, MD,[¶] Michael Lock, MD,[†] George B. Rodrigues, MD, PhD,[†] Brian P. Yaremko, MD, MSc, PEng,[†] Devin Schellenberg, MD,[#] Belal Ahmad, MD,[†] Sashendra Senthil, MD, PhD,** Anand Swaminath, MD,^{††} Neil Kopeck, MD,^{††} Mitchell Liu, MD,^{§§} Roel Schlijper, MD,[†] Glenn S. Bauman, MD,[†] Joanna Laba, MD,[†] X. Melody Qu, MD, MPH,[†] Andrew Warner, MSc,[†] and Suresh Senan, MBBS, PhD^{||}



Harrow S, Int J Radiat Oncol Biol Phys. 2022



4. SBRT EN CCR METASTÁSICO

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Efficacy of Ablative High-Dose-per-Fraction Radiation for Implanted Human Renal Cell Cancer in a Nude Mouse Model

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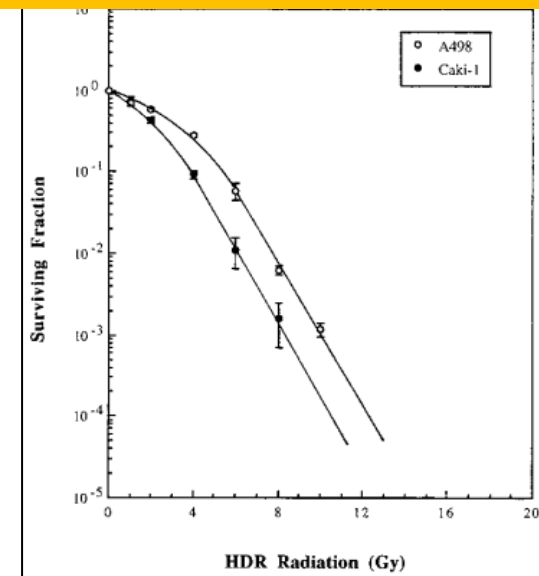
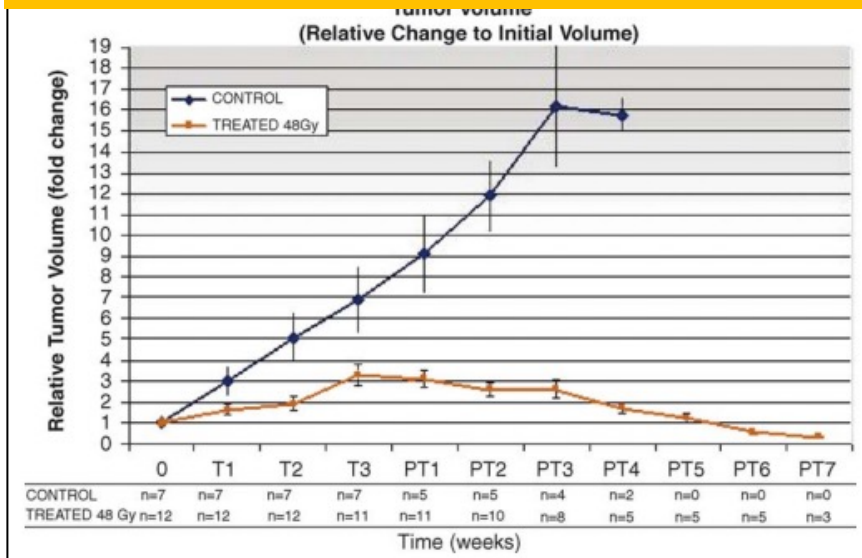
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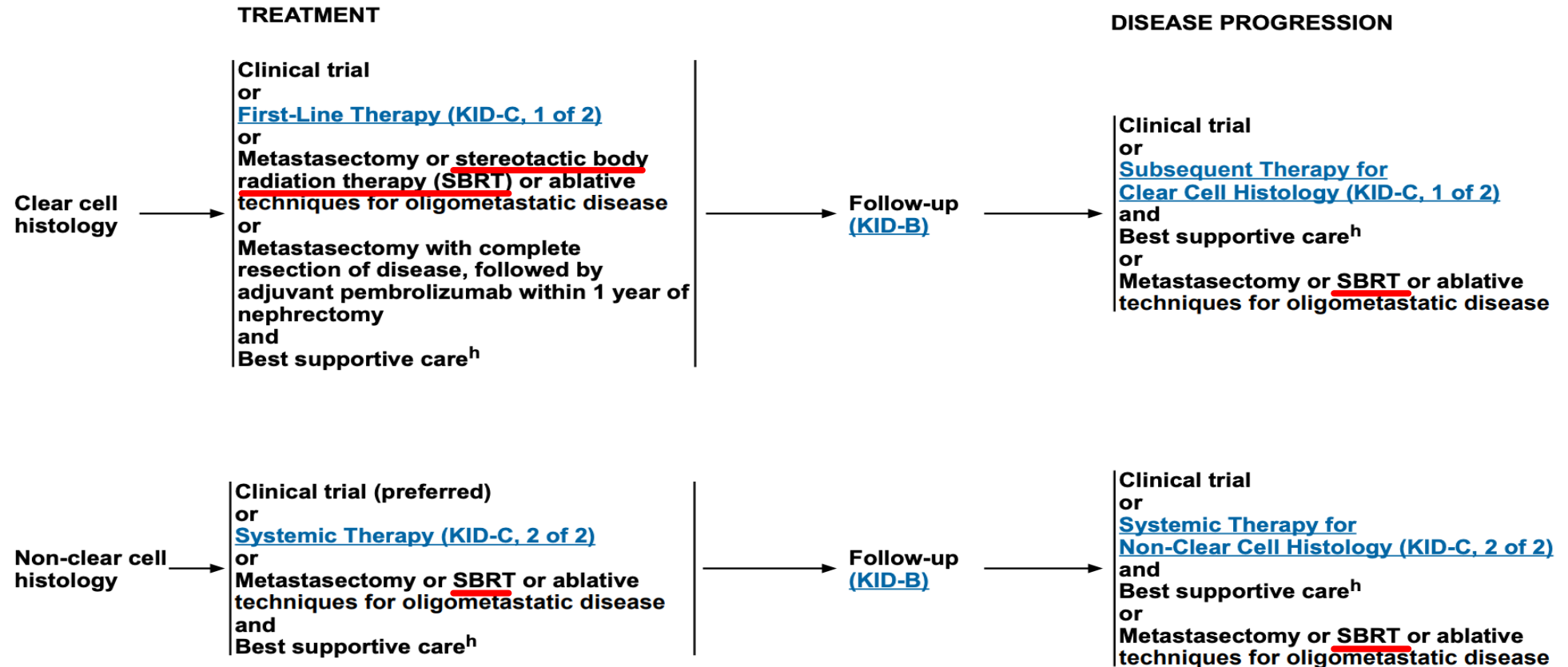


National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Kidney Cancer

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[Discussion](#)

RELAPSE OR STAGE IV

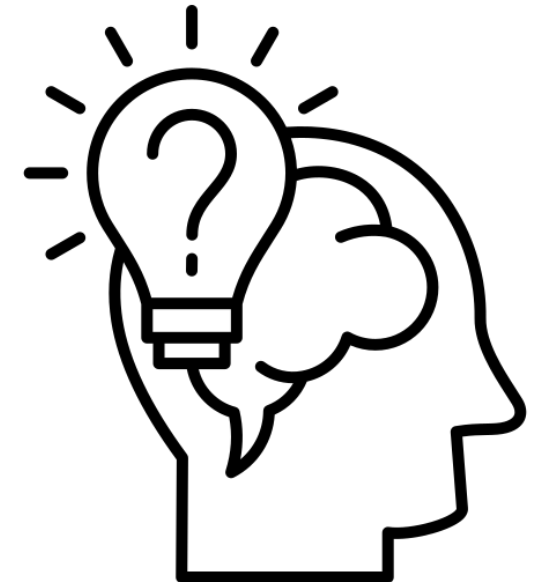




4. SBRT EN CCR METASTÁSICO

¿EVIDENCIA?

- Estudios retrospectivos y series de casos
- Heterogeneidad
- Buenos resultados:
 - CONTROL LOCAL
 - TOXICIDAD
- Coste - efectividad





4. SBRT EN CCR METASTÁSICO

Stereotactic ablative radiation therapy for oligometastatic renal cell carcinoma (SABR ORCA): a meta-analysis of 28 studies

Nicholas G. Zaorsky^{a,b,*}, Eric J. Lehrer^c, Gargi Kothari^d, Alexander V. Louie^e, Shankar Siva^d

^a Department of Radiation Oncology, Penn State Cancer Institute, Hershey, PA, USA; ^b Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA, USA; ^c Department of Radiation Oncology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; ^d Department of Radiation Oncology, Peter MacCallum Cancer Centre, University of Melbourne, Melbourne, Australia; ^e Department of Radiation Oncology, Odette Cancer Centre – Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Zaorsky NG, et al. Eur Urol Oncol. 2019

REVIEW ARTICLE

Outcomes of stereotactic radiotherapy for cranial and extracranial metastatic renal cell carcinoma: A systematic review

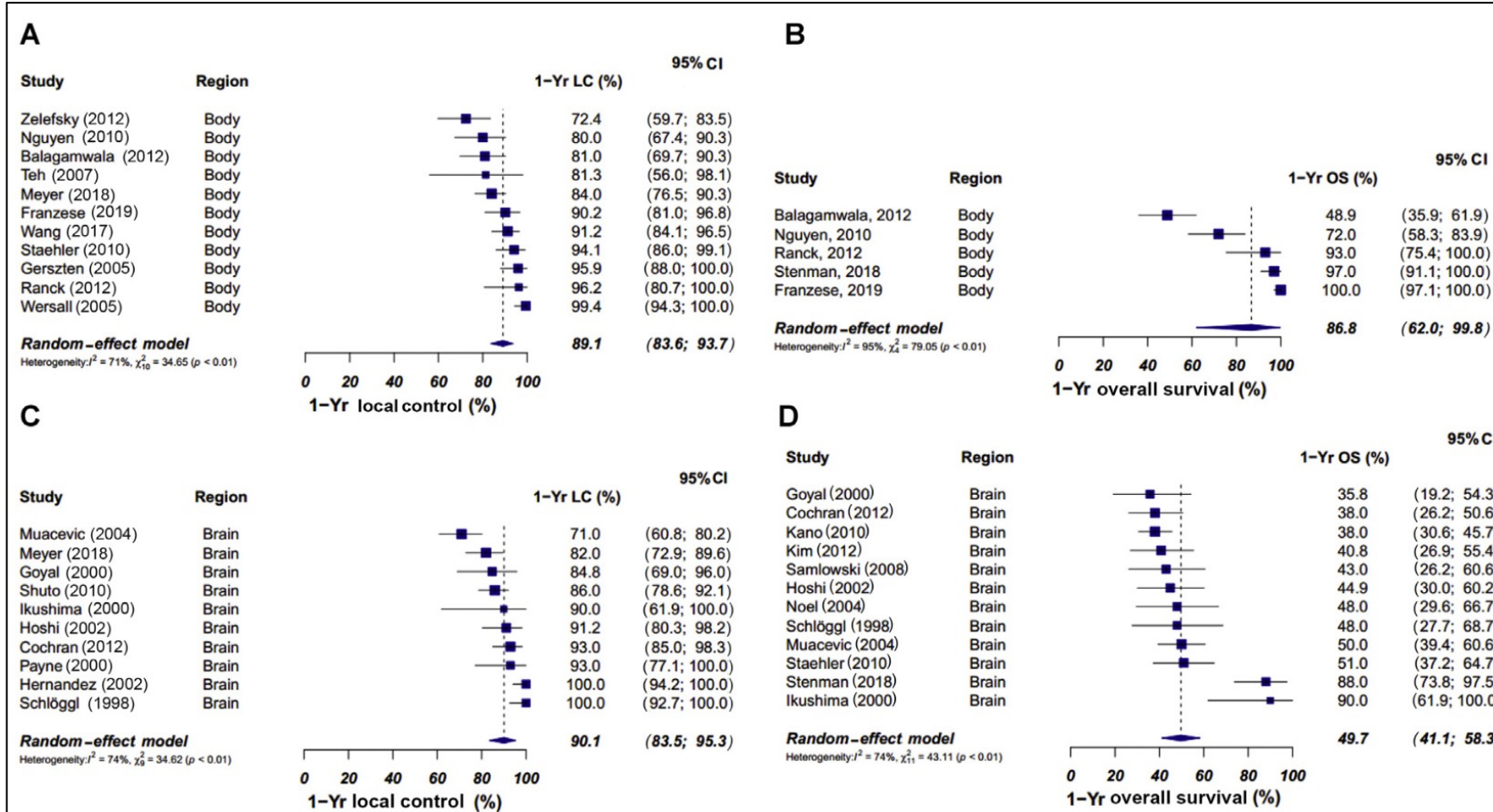
GARGI KOTHARI¹, FARSHAD FOROUDI^{1,2}, SUKI GILL¹, NIALL M. CORCORAN³ & SHANKAR SIVA^{1,2}

¹Division of Radiation Oncology and Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia, ²Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, Victoria, Australia and ³Departments of Urology and Surgery, Royal Melbourne Hospital and the University of Melbourne, Parkville, Victoria, Australia

Kothari G, et al. Acta Oncol. 2015



4. SBRT EN CCR METASTÁSICO



- LC a 1 año:
 - ❖ Cerebral > 90,1 %
 - ❖ Corporal > 89,1 %
- OS a 1 año:
 - ❖ Cerebral > 49,7 %
 - ❖ Corporal > 86,8 %



4. SBRT EN CCR METASTÁSICO

Stereotactic Radiotherapy for Oligoprogression in Metastatic Renal Cell Cancer Patients Receiving Tyrosine Kinase Inhibitor Therapy: A Phase 2 Prospective Multicenter Study

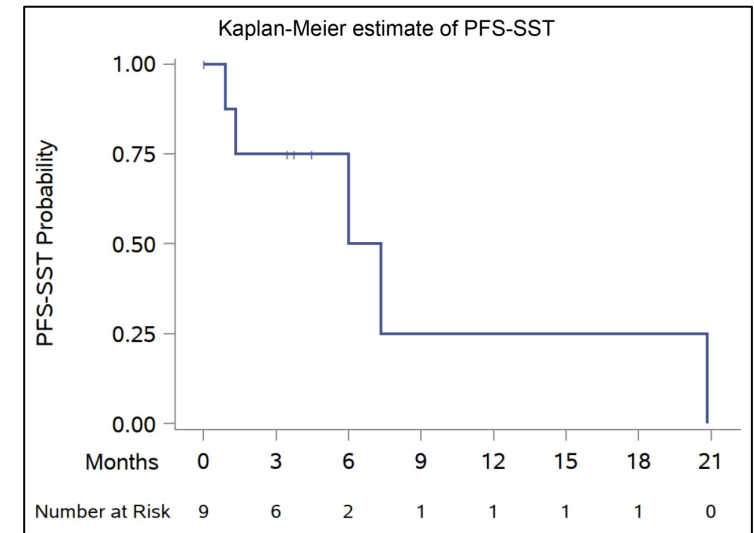
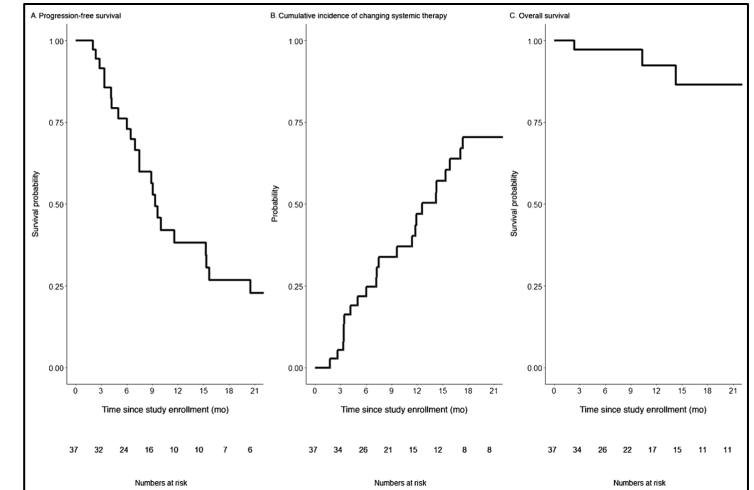
Patrick Cheung^a, Samir Patel^b, Scott A. North^c, Arjun Sahgal^a, William Chu^a, Hany Soliman^a, Belal Ahmad^d, Eric Winquist^e, Tamim Niazi^f, Francois Patenaude^g, Gerald Lim^h, Daniel Yick Chin Hengⁱ, Arbind Dubey^j, Piotr Czaykowski^k, Rebecca K.S. Wong^l, Anand Swaminath^m, Scott C. Morganⁿ, Rupi Mangat^o, Sareh Keshavarzi^p, Georg A. Bjarnason^{q,*}

Cheung P, et al. Eur Urol. 2021

Phase II Trial of Stereotactic Ablative Radiation for Oligoprogressive Metastatic Kidney Cancer

Raquibul Hannan^{a,b,*}, Michael Christensen^a, Hans Hammers^{b,c}, Alana Christie^b, Brendan Paulman^a, Dandan Lin^a, Aurelie Garant^{a,b}, Waddah Arafat^{b,c}, Kevin Courtney^{b,c}, Isaac Bowman^{b,c}, Suzanne Cole^{b,c}, David Sher^a, Chul Ahn^c, Hak Choy^a, Robert Timmerman^{a,b,*}, James Brugarolas^{b,c,*}

Hannan R, et al. Eur Urol Oncol. 2022





4. SBRT EN CCR METASTÁSICO



Definitive radiotherapy in lieu of systemic therapy for oligometastatic renal cell carcinoma: a single-arm, single-centre, feasibility, phase 2 trial

Chad Tang, Pavlos Msaouel*, Kieko Hara, Haesun Choi, Venus Le, Amishi Y Shah, Jennifer Wang, Eric Jonasch, Seungtaek Choi, Quynh-nhu Nguyen, Prajnan Das, Surendra Prajapati, Zhiqian Yu, Khaja Khan, Steven Powell, Ravi Murthy, Kanishka Sircar, Nizar M Tannir*

Tang C, et al. Lancet Oncol. 2021

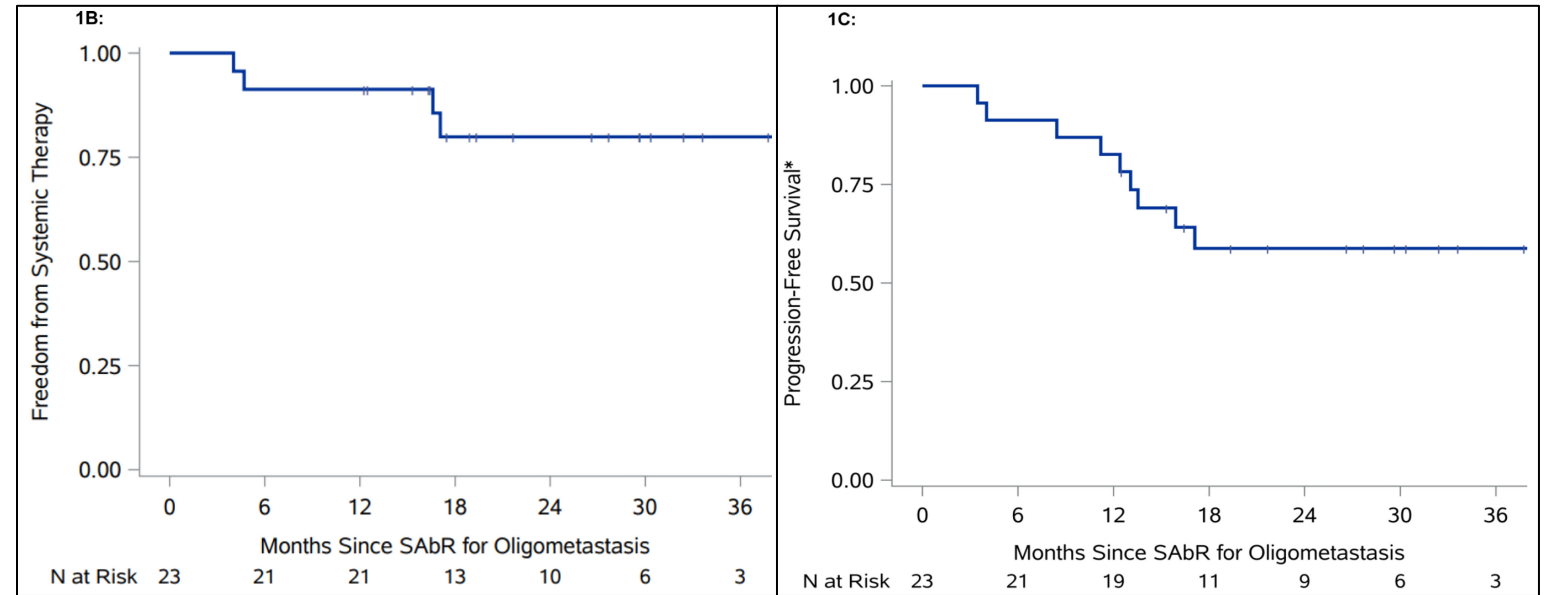
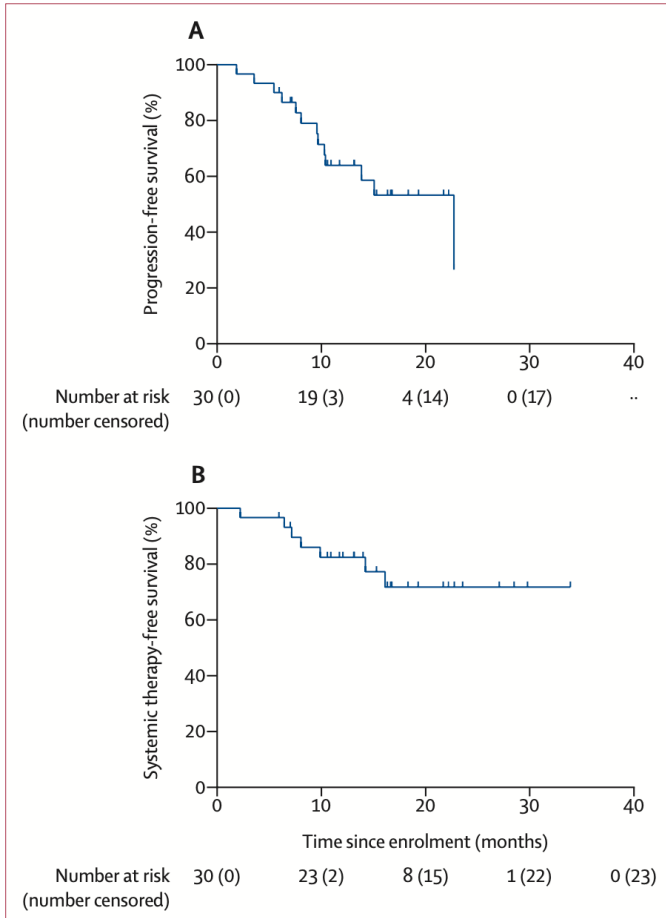
Stereotactic Ablative Radiation for Systemic Therapy Naïve Oligometastatic Kidney Cancer

Raquibul Hannan, MD, PhD^{a,c,*}, Michael Christensen, MD^a, Alana Christie, MS^c, Aurelie Garant, MD^{a,c}, Liliana Robles, BA^a, Samantha Mannala, BA^a, Chiachien Wang, MD, PhD^a, Hans Hammers, MD^{b,c}, Waddah Arafat, MD^{b,c}, Kevin Courtney, MD, PhD^{b,c}, Isaac A. Bowman, MD^{b,c}, David Sher, MD^a, Chul Ahn, PhD^c, Suzanne Cole, MD^{b,c}, Hak Choy, MD^a, Robert Timmerman, MD^{a,c,*}, James Brugarolas, MD, PhD^{b,c,*}

Hannan R, Eur Urol Oncol. 2022



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Hannan R, Eur Urol Oncol. 2022

Tang C, et al. Lancet Oncol. 2021



4. SBRT EN CCR METASTÁSICO

Stereotactic Radiotherapy and Short-course Pembrolizumab for Oligometastatic Renal Cell Carcinoma—The RAPPOR Trial

Shankar Siva^{a,b,}, Mathias Bressel^a, Simon T. Wood^{c,d}, Mark G. Shaw^a, Sherene Loi^{a,b}, Shahneen K. Sandhu^{a,b}, Ben Tran^{a,b}, Arun A. Azad^{a,b}, Jeremy H. Lewin^a, Katharine E. Cuff^{c,d}, Howard Y. Liu^{c,d}, Daniel Moon^{a,e}, Jeremy Goad^a, Lih-Ming Wong^e, Michael LimJoon^a, Jennifer Mooi^a, Sarat Chander^a, Declan G. Murphy^{a,b}, Nathan Lawrentschuk^{a,e}, David Pryor^{c,f}*

Siva S, et al. Eur Urol. 2022

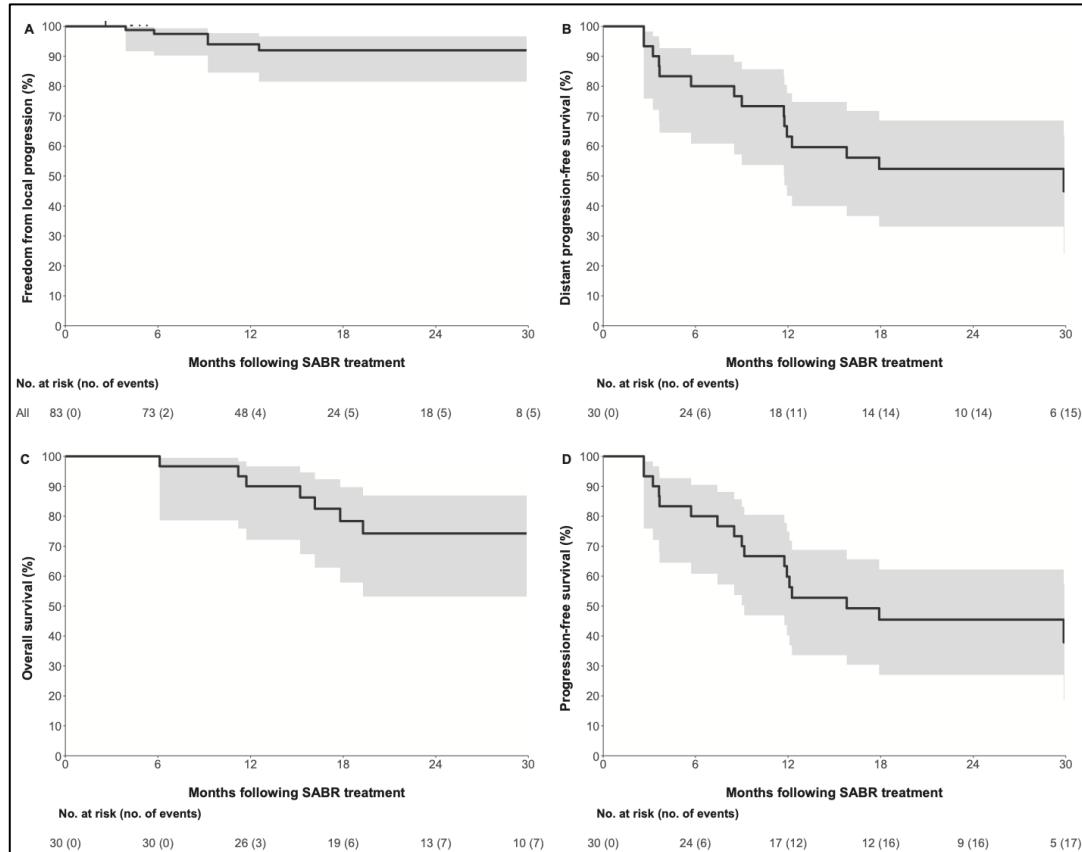
Nivolumab in Combination with Stereotactic Body Radiotherapy in Pretreated Patients with Metastatic Renal Cell Carcinoma. Results of the Phase II NIVES Study

Cristina Masini^{a,}, Cinzia Iotti^b, Ugo De Giorgi^c, Roberto Salvatore Bellia^d, Sebastiano Buti^e, Francesco Salaroli^f, Ilaria Zampiva^g, Renzo Mazzarotto^h, Claudia Mucciariniⁱ, Maria Giuseppa Vitale^j, Alessio Bruni^k, Frank Lohr^k, Giuseppe Procopio^l, Orazio Caffo^m, Franco Noleⁿ, Franco Morelli^o, Susanne Baier^p, Consuelo Buttigliero^q, Patrizia Ciammella^b, Giorgia Timon^b, Emanuela Fantinel^a, Gabriele Carlinfante^r, Annalisa Berselli^a, Carmine Pinto^a*

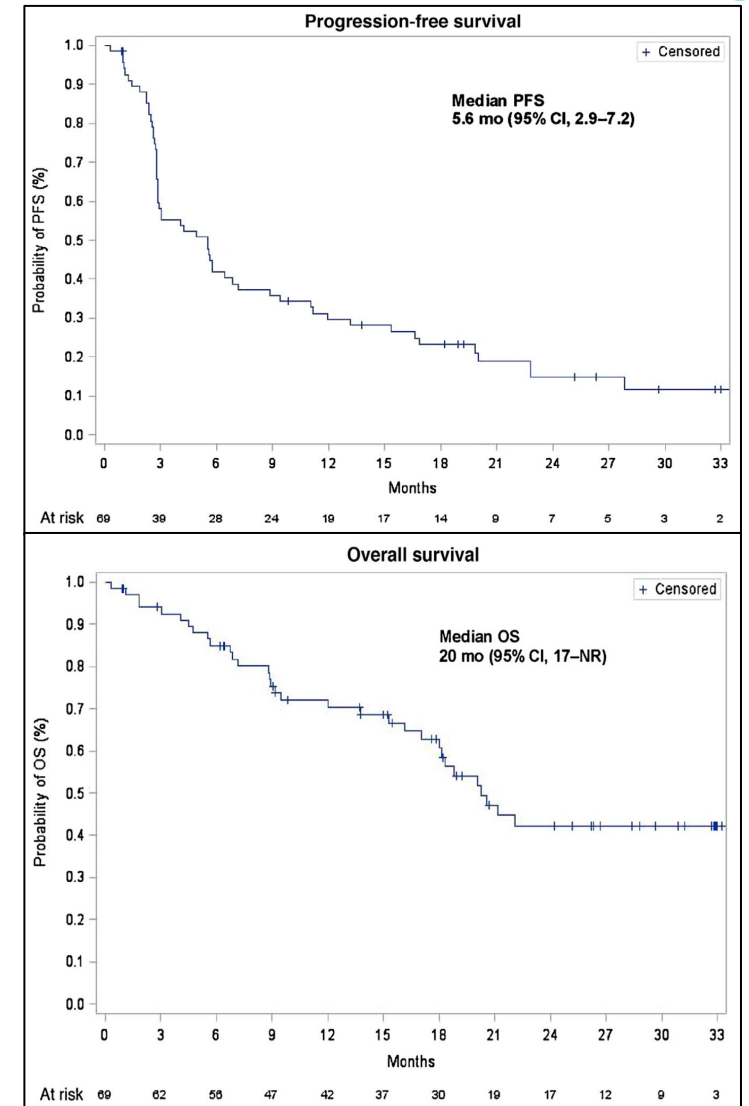
Masini C, et al. Eur Urol. 2022



4. SBRT EN CCR METASTÁSICO



Siva S, et al. Eur Urol. 2022



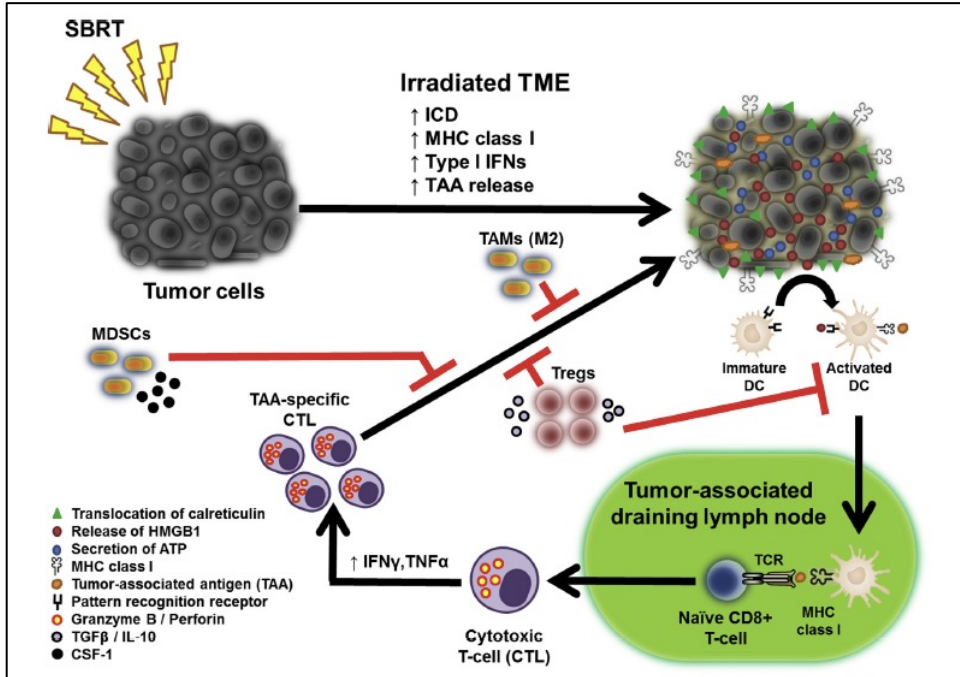
Masini C, et al. Eur Urol. 2022

4. SBRT EN CCR METASTÁSICO

¿EFECTO
ABSCOPAL?

RENAL CELL CANCER

Phase II trial of cytoreductive stereotactic hypofractionated radiotherapy with combination ipilimumab/nivolumab for metastatic kidney cancer (CYTOSHRINK).



RECRUITING ⓘ

Testing the Addition of Stereotactic Radiation Therapy With Immune Therapy for the Treatment of Patients With Unresectable or Metastatic Renal Cell Cancer, SAMURAI Study (SAMURAI)

ClinicalTrials.gov ID ⓘ NCT05327686

Sponsor ⓘ NRG Oncology


Information provided by ⓘ NRG Oncology (Responsible Party)

Last Update Posted ⓘ 2023-08-02



5. CONCLUSIONES

- Altas tasas de control local
- Perfiles de toxicidad bajos ($G3-5 \leq 5\%$)
- ¿Curación? ¿Retraso de inicio/cambio de terapia sistémica?
- ¿Impacto en la supervivencia global?
- Selección de pacientes → **COMITÉS**
- Inmunoterapia. Efecto abscopal
- Investigación



Nothing in life is to be feared,
it is only to be understood.
Now is the time to understand
more, so that **we may fear less.**

– Marie Curie

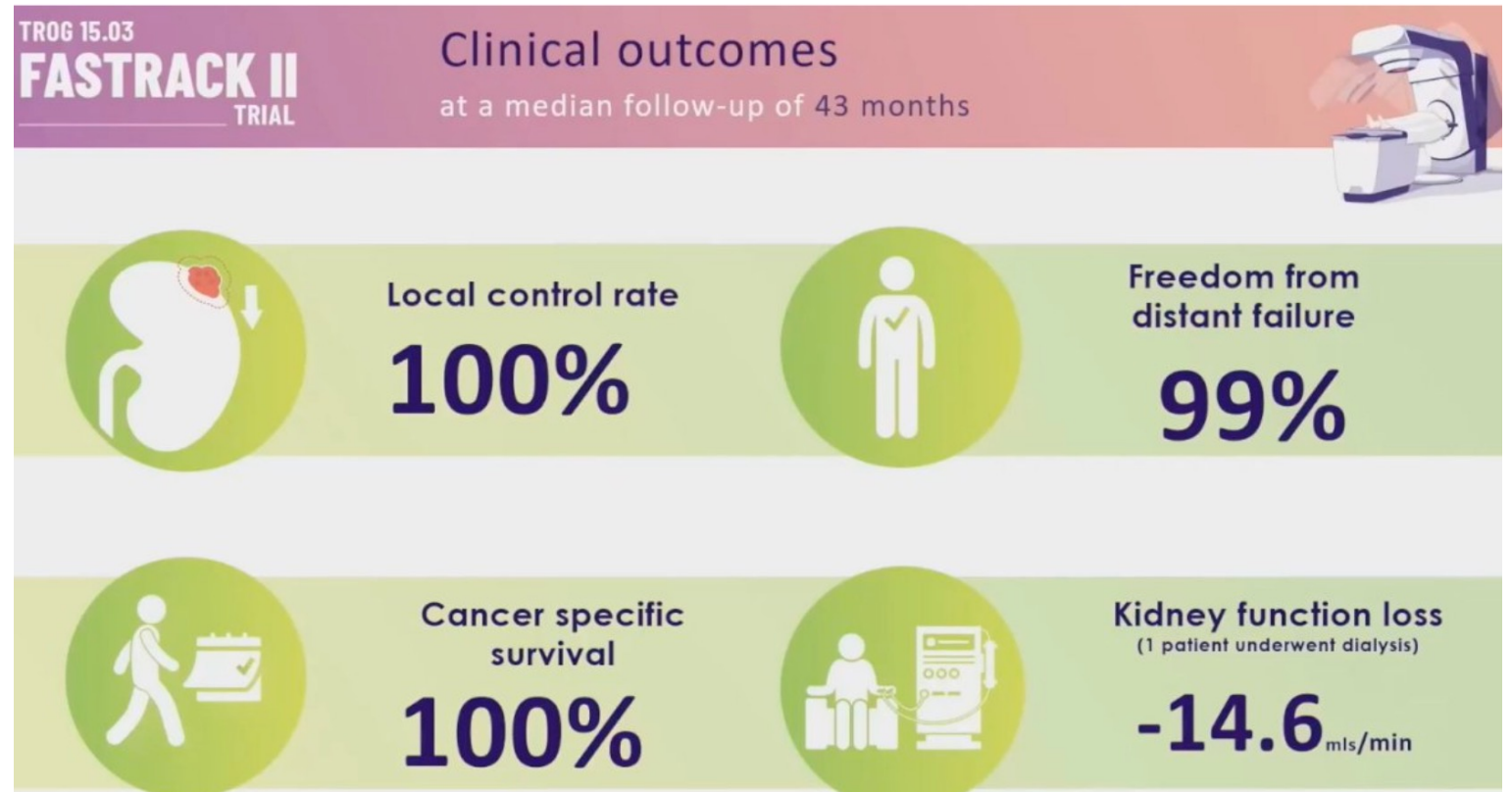


5 | VOLUME 117, ISSUE 2, SUPPLEMENT , S3, OCTOBER 01, 2023

TROG 15.03/ANZUP International Multicenter Phase II Trial of Focal Ablative STereotactic RAdiotherapy for Cancers of the Kidney (FASTRACK II)

S. Siva • M. Bressel • M. Sidhom • ... T. Kron • J.M. Martin • D.I. Pryor • [Show all authors](#)

S. Siva, et al. International Journal of Radiation Oncology Biology Physics, 2023,





Primary RCC: Nephron Sparing Options

	Partial Nephrectomy	Thermal Ablation		SABR
		Cryo	RFA	
Avoids general anaesthetic?	✗	✓	✓	✓
Peri-hilar tumors?	✓	✗	✗	✓
Large tumors?	✓	✗	✗	✓
Non-invasive?	✗	✗	✗	✓

 **100%**  **-14.6_{mls/min}**

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