NEFRECTOMIA CITORREDUCTORA EN CANCER RENAL METASTÁSICO VS QMT VS SBRT

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SUM

Sociedad Urológica Madrileña

Hospital Universitario Ramón y Cajal

INTRODUCCIÓN

- 15-30% de los pacientes presentan metástasis en el momento del diagnóstico.

- La supervivencia varia de un 15% a los 5 años hasta un 5% a los 10 años.

Microambiente Tumoral

Citoquinas proinflamatorias y quimiocinas ejercen una actividad promotora del tumor
Factores de crecimiento: VEGF; PDGF, FGF, TGF-β1
Células inmunitarias: Células mieloides supresoras (MDSC)
Expresión de moléculas específicas en la superficie de las células tumorales y las células T efectoras: CTLA-4, PD-L1, PD-1

La interrupción de esta estrecha interacción inmunosupresora entre citocinas, quimiocinas y células tumorales e inmunitarias proporciona una justificación biológica de por qué debe proponerse la NC

Reducción de volumen tumoral:

- Bloqueo del desarrollo potencial de clones agresivos capaces de inducir metástasis
- Eliminar el "sumidero" inmunológico en el que el tumor primario desvía las células inmunitarias circulantes impidiendo su actuación sobre las metástasis

Efecto inmunosupresor del tumor primario (microambiente tumoral)

- Secreción de citoquinas inmunosupresoras

FACTORES PRONÓSTICO

MSKCC

TABLE 63-1 Adverse Prognostic Factors and Risk Stratification Based on Adverse Prognostic Factors in 670 Patients Treated with Chemotherapy or Immunotherapy at the Memorial Sloan Kettering Cancer Center

ADVERSE PROGNOSTIC FACTORS

Karnofsky performance score <80%
Elevated lactate dehydrogenase (>1.5 times upper limit of normal)
Low hemoglobin (< lower limit of normal)
Elevated corrected calcium (>10 mg/dL)
Absence of prior nephrectomy

RISK STRATIFICATION BASED ON ADVERSE PROGNOSTIC FACTORS

RISK GROUP	NO. OF ADVERSE PROGNOSTIC FACTORS	MEDIAN OVERALL SURVIVAL
Good	0	20 months
Intermediate	1-2	10 months
Poor	3-5	4 months

Data from Motzer RJ, Mazumdar M, Bacik J, et al. Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. J Clin Oncol 1999;17:2530–40.

IMDC

TABLE 63-2 Adverse Prognostic Factors and Risk Stratification Based on Adverse Prognostic Factors in 849 Patients Treated with First-Line Vascular Endothelial Growth Factor (VEGF) Targeted Therapy

ADVERSE PROGNOSTIC FACTORS

Karnofsky performance score <80%
Neutrophilia (> upper limit of normal)
Low hemoglobin (< lower limit of normal)
Elevated corrected calcium (> upper limit of normal)
Thrombocytosis (> upper limit of normal)
<1 year from diagnosis to VEGF-targeted therapy

RISK STRATIFICATION BASED ON ADVERSE PROGNOSTIC FACTORS

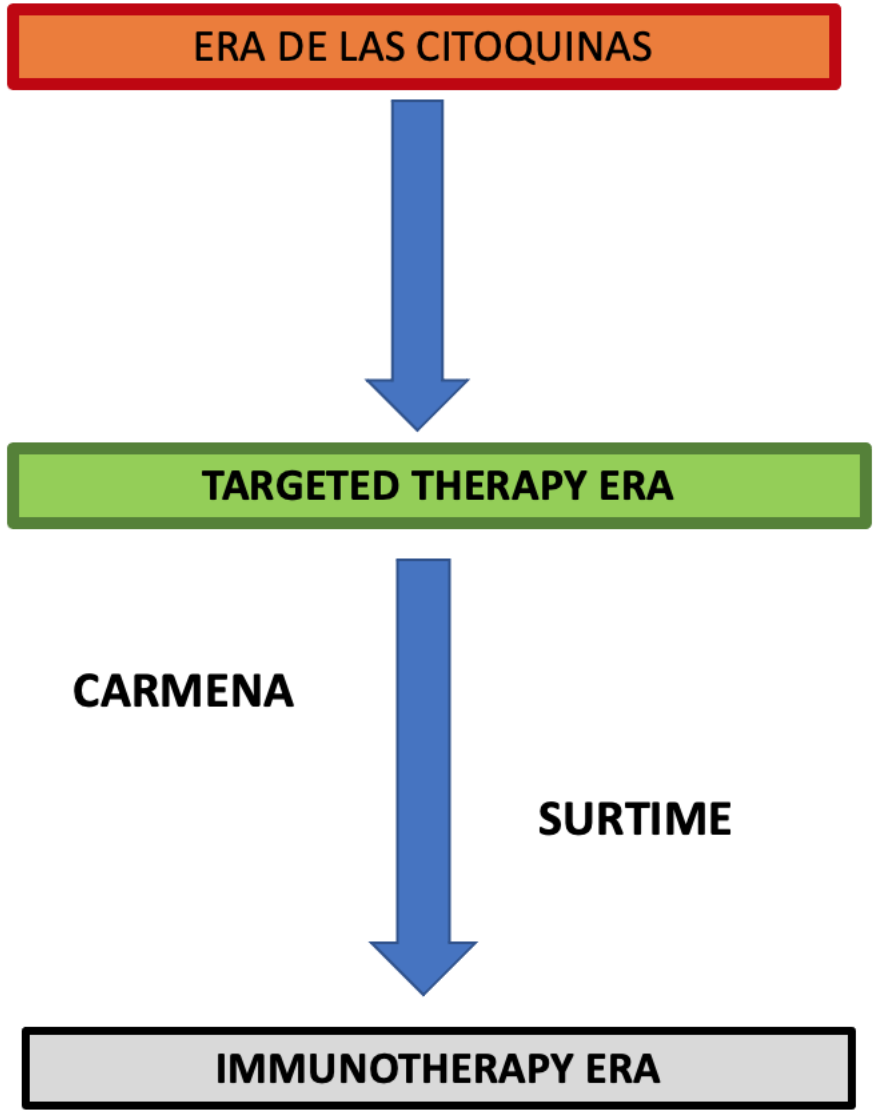
RISK GROUP	NO. OF ADVERSE PROGNOSTIC FACTORS	MEDIAN OVERALL SURVIVAL
Good	0	43.2 months
Intermediate	1-2	22.5 months
Poor	3-6	7.8 months

Data From Heng DY, Xie W, Regan MM, et al. External validation and comparison with other models of the International Metastatic Renal-Cell Carcinoma Database Consortium prognostic model: a population-based study. Lancet Oncol 2013;14:141–8.

MSKCC = Memorial Sloan Kettering Cancer Center IMDC = International Metastatic Renal Cancer Database Consortium

- La nefrectomía citorreductora (CN) ha tenido un papel importante siendo la terapia de elección durante más de 20 años.

- Su papel actual en la era de las terapias dirigidas y la inmunoterapia esta en duda.



ERA DE LAS CITOQUINAS

THE LANCET

ARTICLES

Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: a randomised trial

G H J Mickisch, A Garin, H van Poppel, L de Prijck, R Sylvester, and members of the European Organisation for Research and Treatment of Cancer (EORTC) Genitourinary Group

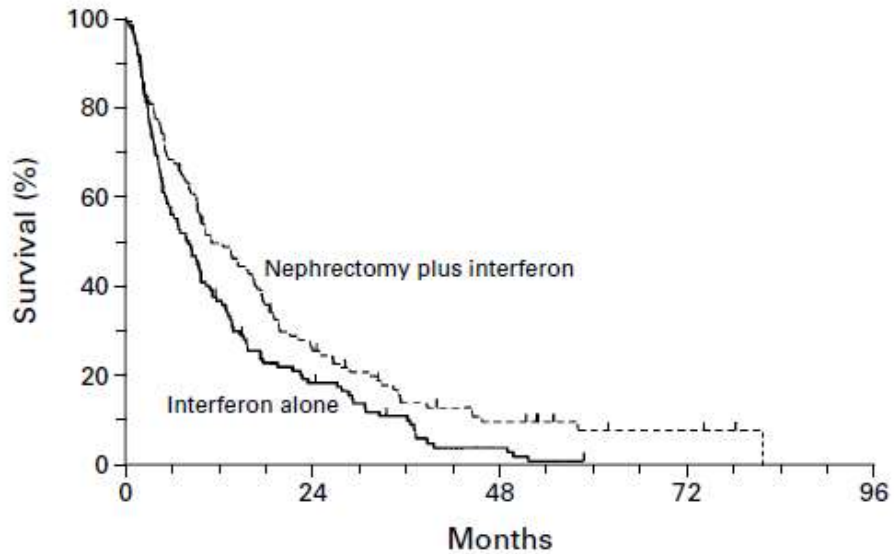
The New England
Journal of Medicine

VOLUME 345 DECEMBER 6, 2001 NUMBER 23

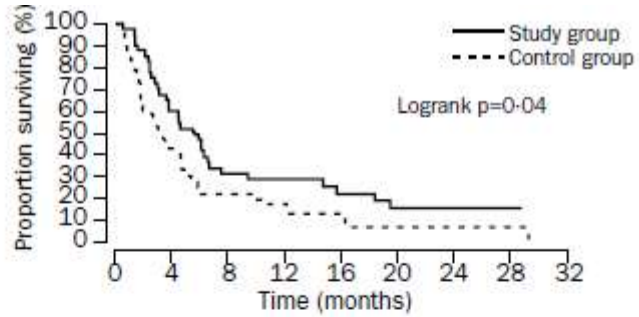
NEPHRECTOMY FOLLOWED BY INTERFERON ALFA-2b COMPARED WITH INTERFERON ALFA-2b ALONE FOR METASTATIC RENAL-CELL CANCER

ROBERT C. FLANIGAN, M.D., SYDNEY E. SALMON, M.D., BRENT A. BLUMENSTEIN, PH.D., SCOTT I. BEARMAN, M.D., VIVEK ROY, M.D., PATRICK C. MCGRATH, M.D., JOHN R. CATON, JR., M.D., NIKHIL MUNSHI, M.D., AND E. DAVID CRAWFORD, M.D.

ERA DE LAS CITOQUINAS

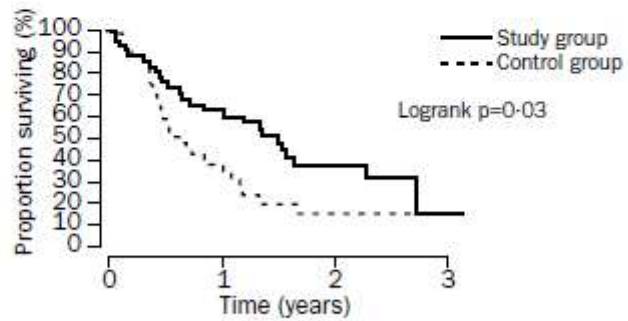


No. at Risk					
Interferon alone	121	21	4	0	
Nephrectomy plus interferon	120	29	9	3	0



	Observed number of events	Number of patients at risk							
Study group	32	42	23	12	10	7	4	2	1
Controls	37	42	17	8	5	2	1	1	1

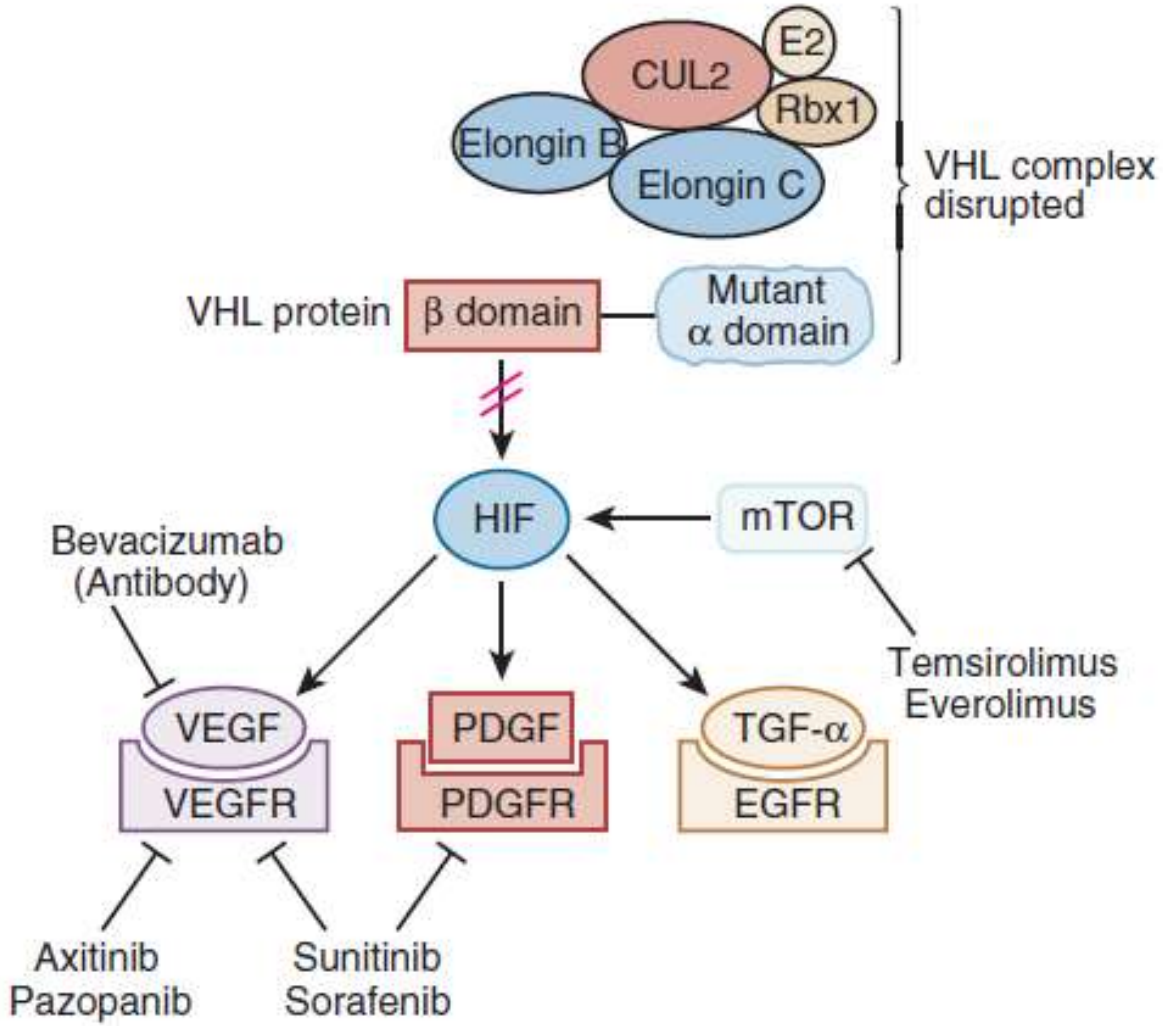
Figure 2: **Kaplan-Meier curves showing time to progression**
O=Observed number of events.



	Observed number of events	Number of patients at risk			
Study group	25	42	22	7	1
Controls	30	42	12	2	0

Figure 3: **Kaplan-Meier curves showing overall survival**
O=Observed number of events.

TARGETED THERAPY ERA



TARGETED THERAPY ERA

TABLE 63-10 Summary of Selected Studies of Selective VEGFR Antagonists in Metastatic Renal Cell Carcinoma

STUDY	AGENT(S)	PHASE	STUDY POPULATION	NO. OF PATIENTS	OVERALL RESPONSE RATE (RECIST)*	MEDIAN PFS (mo)*	MEDIAN OS (mo)*
Sternberg et al, 2010, 2013	Pazopanib vs. placebo	Randomized phase III	Metastatic clear cell patients with 0-1 prior cytokine therapy	435	**30% vs. 3%**	**9.2 vs. 4.2**	22.9 vs. 20.5
Motzer et al, 2013d	Tivozanib vs. sorafenib	Randomized phase III	Metastatic clear cell; 0-1 prior therapies	517	**33% vs. 23%**	**11.9 vs. 9.1**	28.8 vs. 29.3
Rini et al, 2011;	Axitinib vs. sorafenib	Randomized phase III	Second-line clear cell	723	**19% vs. 9%**	6.7 vs. 4.7	20.1 vs. 19.2
Motzer et al, 2013b							
Motzer et al, 2013c	Pazopanib vs. sunitinib	Randomized phase III	Previously untreated clear cell	1110	**31% vs. 25%**	10.5 vs. 10.2	28.4 vs. 29.3

NA, not available; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; VEGFR, vascular endothelial growth factor receptor.
*Statistically significant differences indicated in bold.

TARGETED THERAPY ERA

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 2, 2018 VOL. 379 NO. 5

Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma

A. Méjean, A. Ravaud, S. Thezenas, S. Colas, J.-B. Beauval, K. Bensalah, L. Geoffrois, A. Thiery-Vuillemin, L. Cormier, H. Lang, L. Guy, G. Gravis, F. Rolland, C. Linassier, E. Lechevallier, C. Beisland, M. Aitchison, S. Oudard, J.-J. Patard, C. Theodore, C. Chevreau, B. Laguerre, J. Hubert, M. Gross-Goupil, J.-C. Bernhard, L. Albiges, M.-O. Timsit, T. Lebret, and B. Escudier

Cancer du Rein Metastatique Nephrectomie et Antiangiogeniques (CARMENA) trial

CARMENA: Prospective, multicenter, open-label, randomized, phase 3 non-inferiority study

EMUC18
8-11 November 2018
Amsterdam, The Netherlands

- Confirmed metastatic clear cell RCC / Biopsy
- ECOG-PS 0-1
- Amenable to nephrectomy
- Eligible for sunitinib
- Brain metastases absent/controlled by treatment
- No prior systemic therapy for RCC

R 1:1

Stratification
- MSKCC risk group
- Center location

Arm A

Nephrectomy → 3-6 weeks → Sunitinib 50 mg QD 4 wks on / 2 wks off

Arm B

Sunitinib 50 mg QD 4 wks on / 2 wks off

Primary endpoint: Overall survival

Secondary endpoints: Progression-free survival, objective response rate, clinical benefit, safety

LPI, last patient included; MSKCC, Memorial Sloan Kettering Cancer Center; QD, once daily; R, randomization; RCC, renal cell carcinoma

ESMO ESTRO RADIOTHERAPY & ONCOLOGY eau European Association of Urology

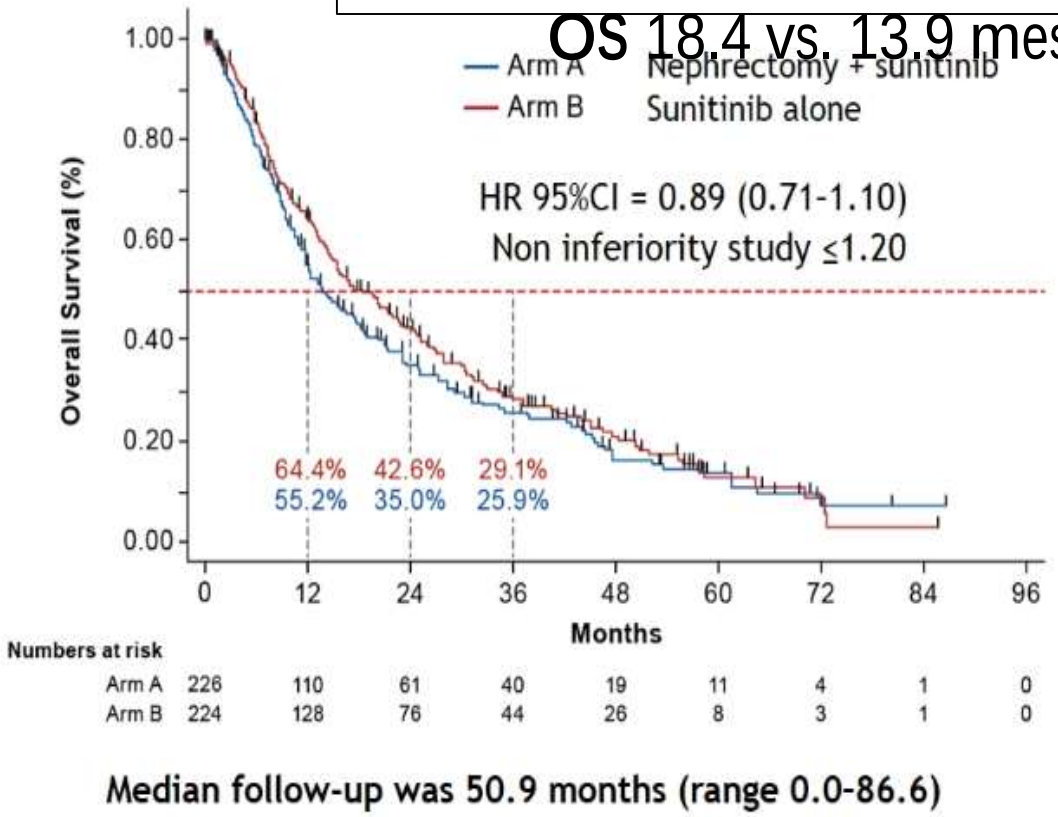
www.emuc18.org

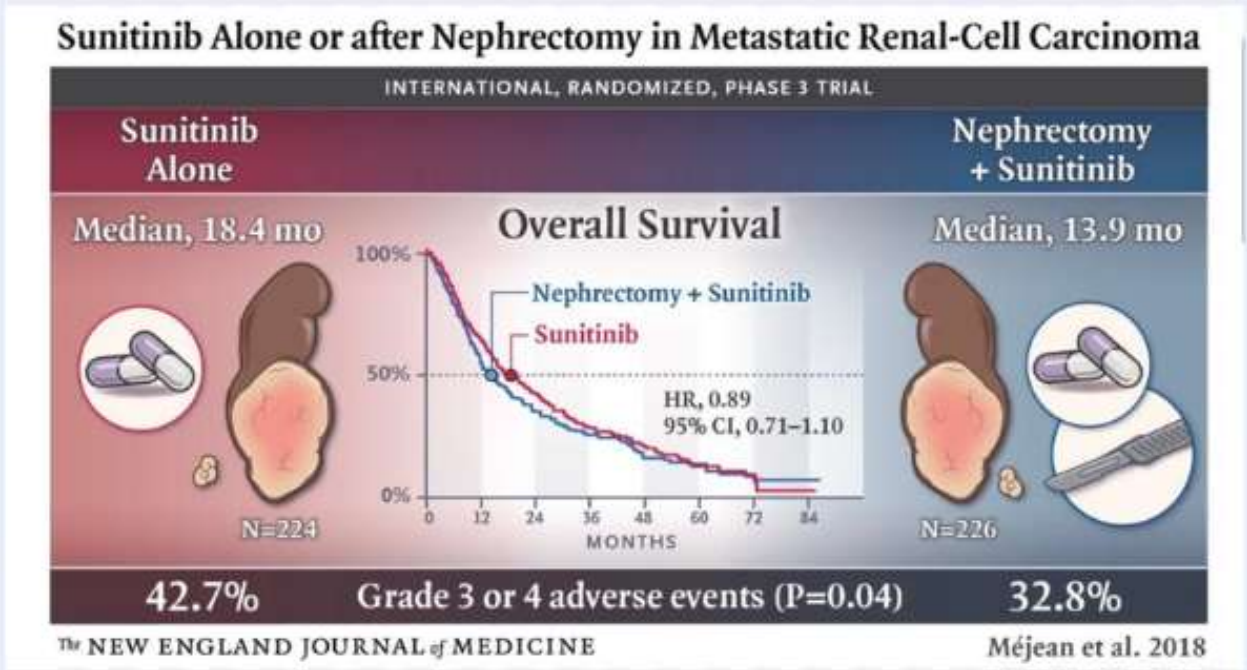
Estudio de NO INFERIORIDAD (margen superior 1.2)
Clasificación pronóstica: MSKCC
Riesgo intermedio (57%) y pobre (43%)

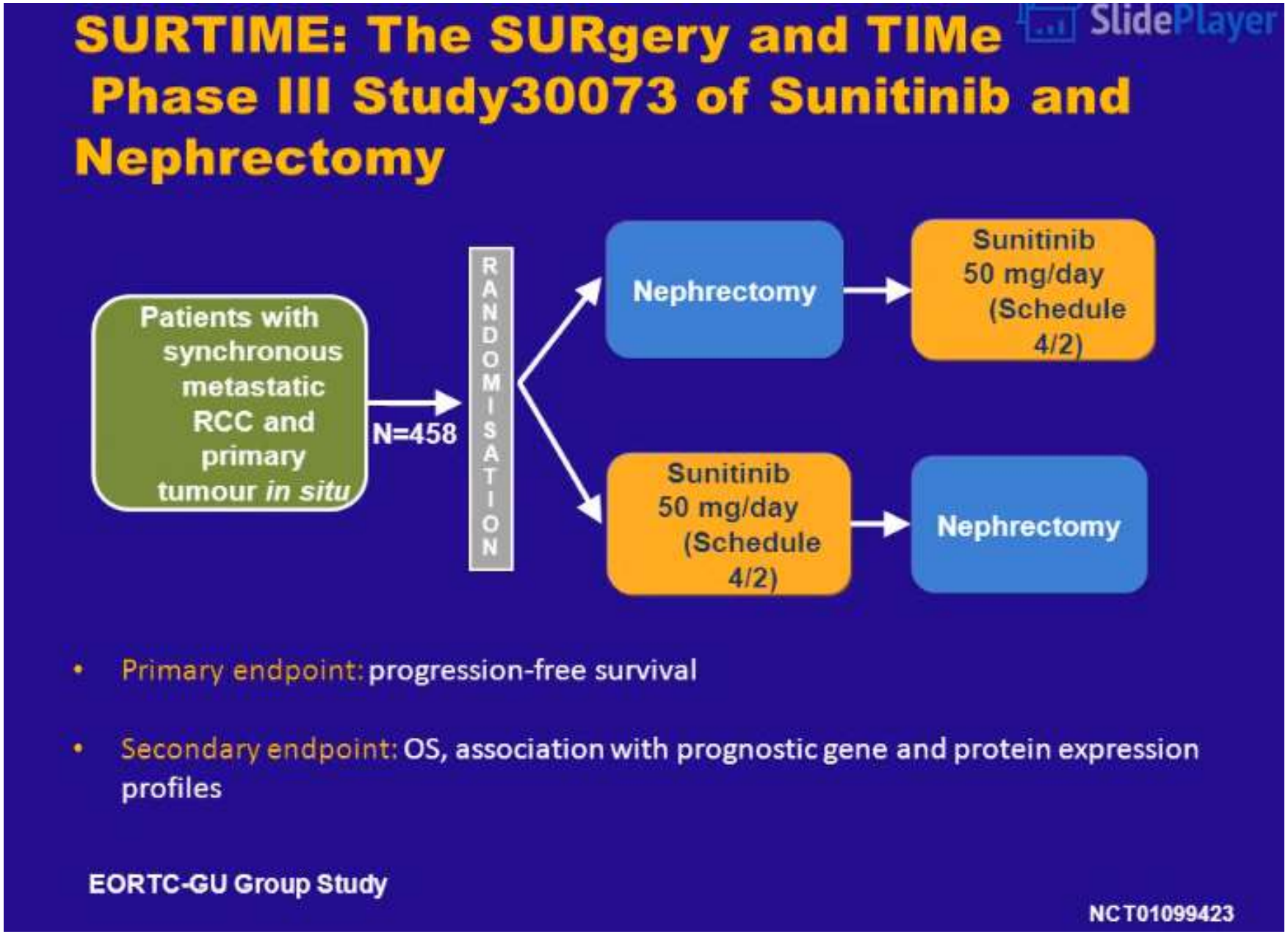
TARGETED THERAPY ERA

Sunitinib en monoterapia fue NO inferior a NC seguido de sunitinib

OS 18.4 vs. 13.9 meses; HR 0.89; 95% CI (0.71–1.1)






SURTIME: The SURgery and TIMe Phase III Study30073 of Sunitinib and Nephrectomy
SlidePlayer
Patients with synchronous metastatic RCC and primary tumour in situ
N=458
RANDOMISATION
Nephrectomy
Sunitinib 50 mg/day (Schedule 4/2)
Sunitinib 50 mg/day (Schedule 4/2)
Nephrectomy
• Primary endpoint: progression-free survival
• Secondary endpoint: OS, association with prognostic gene and protein expression profiles
EORTC-GU Group Study
NCT01099423

The **I**mmediate **S**urgery or **S**urgery after **S**unitinib Malate in **T**reating **P**atients with **M**etastatic **K**idney **C**ancer (SURTIME)

Objetivo: Evaluar si el tratamiento (antes de la cirugía) con terapia sistémica mejoraría los los resultados identificando a los pacientes que probablemente no se beneficiarían de la CN

Los pacientes se asignaron aleatoriamente a:

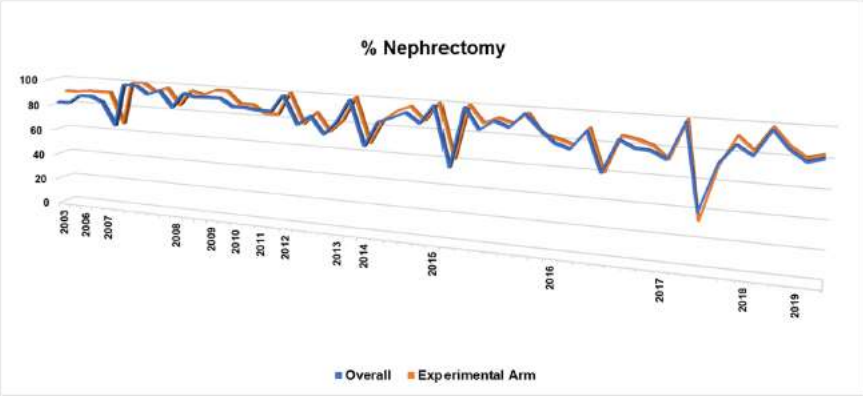
- **NC inmediata**: NC seguida de sunitinib 50 mg/día durante 4 semanas **ON** seguidas de 2 semanas **OFF**
- **NC diferida**: sunitinib durante 3 ciclos seguidos de NC

Problemas: Reclutamiento: 99 pacientes

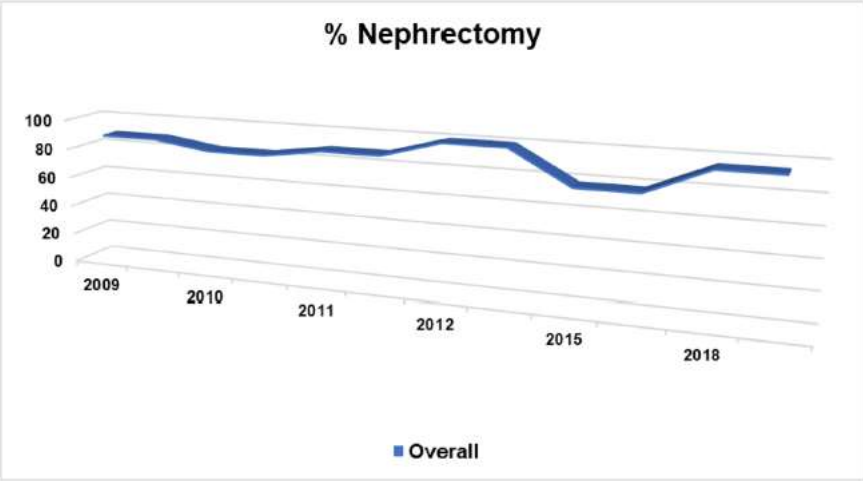
NO RESULTADOS CONCLUYENTES

Evolución de la Nefrectomía Citorreductora

RCTs



EAP



¿Y después de 2019-CARMENA-SURTIME?

LIMITACIONES (CARMENA / SURTIME)

- Reclutamiento lento (8 años) e incompleto (450 / 576)
- Elevada tasa de pacientes de alto riesgo del MSKCC (44%)
- Metástasis a distancia de gran volumen
- Alto porcentaje de pacientes con nefrectomía diferida en el grupo de sunitinib solo (17%)
- Número de pacientes que no recibieron sunitinib después de la NC (17,7%)

En el análisis de subgrupos estratificado por grupos de riesgo del MSKCC, la **no inferioridad** se observó en el grupo de **riesgo pobre**

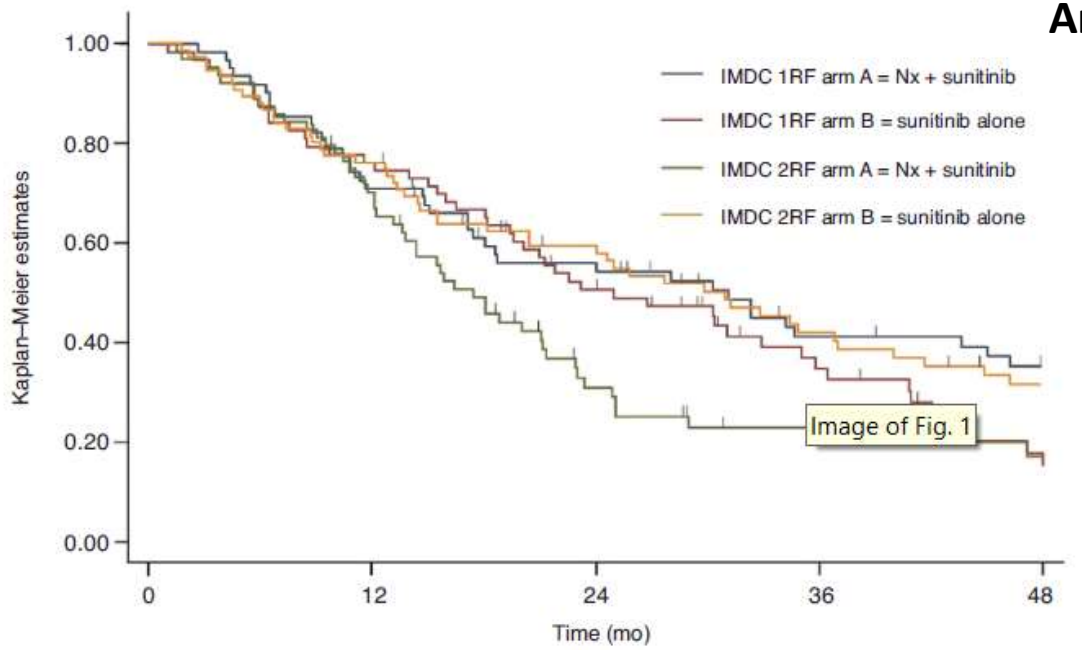
- Riesgo pobre **(HR 0,86; IC 95%: 0,62-1,17)**
- Riesgo intermedio (HR 0,92; IC del 95%: 0,6-1,24).

TARGETED THERAPY ERA

Sunitinib Alone or After Nephrectomy for Patients with Metastatic Renal Cell Carcinoma: Is There Still a Role for Cytoreductive Nephrectomy?

Arnaud Méjean [a,], Alain Ravaud [b], Simon Thezenas [c], Christine Chevreau [d], Karim Bensalah [e], Lionnel Geoffrois [f], Antoine Thiery-Vuillemin [g], Luc Cormier [h], Hervé Lang [i], Laurent Guy [j,k], Gwenaelle Gravis [l], Frederic Rolland [m], Claude Linassier [n], Eric Lechevallier [o], Stephane Oudard [a], Brigitte Laguerre [p], Marine Gross-Goupil [b], Jean Christophe Bernhard [b], Sandra Colas [q], Laurence Albiges [r], Thierry Lebret [s], Jean-Marc Treluyer [a], Marc-Olivier Timsit [a], Bernard Escudier [r]*

EUROPEAN UROLOGY 80 (2021) 417–424



Number at risk

IMDC 1RF arm A = Nx + sunitinib	63	44	33	22	18
IMDC 1RF arm B = sunitinib alone	63	48	31	17	7
IMDC 2RF arm A = Nx + sunitinib	64	44	16	9	6
IMDC 2RF arm B = sunitinib alone	76	57	39	25	17

Fig. 1 – Overall survival in patients with intermediate IMDC risk score (ITT population), stratified by one versus two risk factors. The x-axis was truncated at the final timepoint where all treatment groups had at least five patients at risk. IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; ITT = intention to treat; Nx = nephrectomy; RF = risk factor.

Análisis en función del NUMERO DE FACTORES DE RIESGO

RIESGO INTERMEDIO 1 FACTOR DE RIESGO: SG 31,4 frente a 25,2 meses; HR 1,29; IC 95%: 0,85-1,98
p = 0.23

CN + Sunitinib → 31,4 meses
Sunitinib → 25,2 meses

1 FR

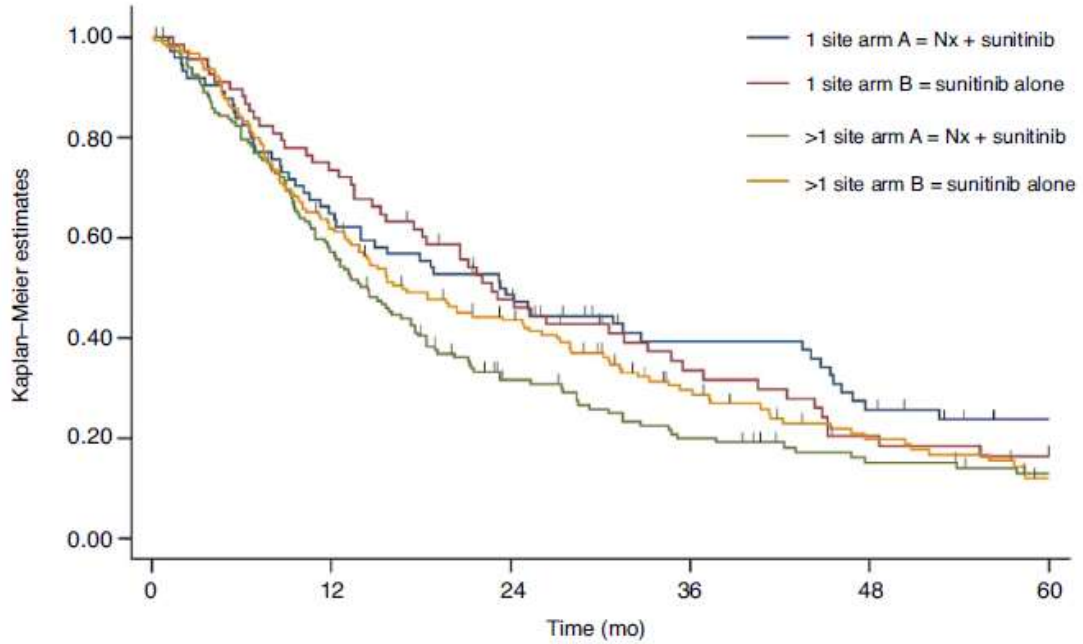
CN + Sunitinib → 17,6 meses
Sunitinib --> 31,2 meses

2 FR

TARGETED THERAPY ERA

Análisis en función del NUMERO DE SITIOS METASTÁSICOS

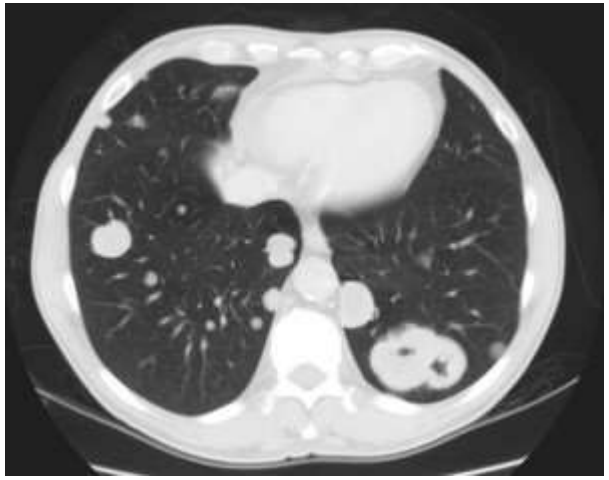
La SG fue superior para aquéllos pacientes con una única localización metastásica



Number at risk

1 site arm A = Nx + sunitinib	75	48	35	23	15	8
1 site arm B = sunitinib alone	68	50	29	18	10	7
>1 site arm A = Nx + sunitinib	148	83	39	24	15	10
>1 site arm B = sunitinib alone	155	94	61	33	19	9

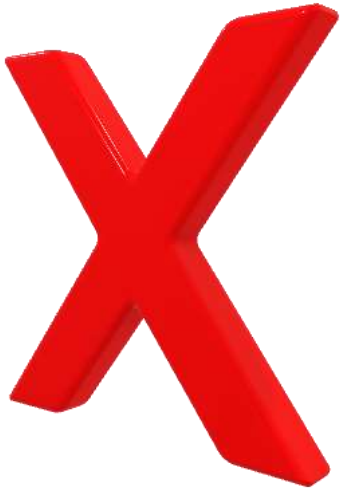
Fig. 2 – Overall survival in patients (ITT population), stratified by one metastatic site versus two or more metastatic sites. The x-axis was truncated at the final timepoint where all treatment groups had at least five patients at risk. ITT = intention to treat; Nx = nephrectomy.



Metástasis pulmonares
Nefrectomía-Sunitinib vs Sunitinib
44 m vs 31,5 m (HR 1,24)

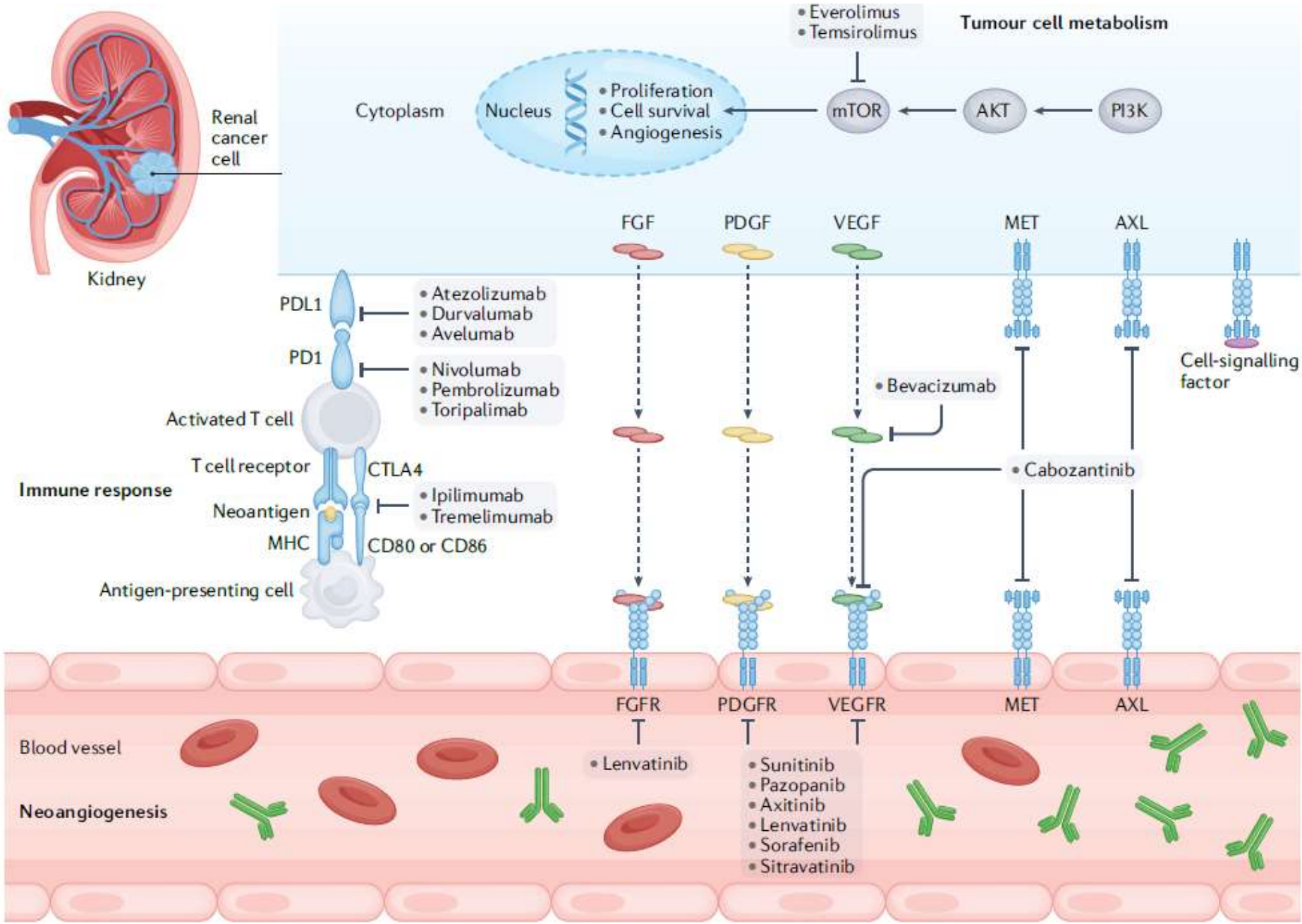
TARGETED THERAPY ERA

- Buen estado funcional
- IMDC de buen pronóstico o riesgo intermedio con un solo factor de riesgo
- Carga tumoral metastásica limitada (metástasis pulmonares)
- Síntomas del tumor primario (dolor y/o hematuria).



- MSKCC/IMDC de riesgo pobre
- Pacientes con estado funcional deficiente
- Elevada carga de enfermedad metastásica
- Metástasis hepáticas / cerebrales

IMMUNOTHERPY ERA



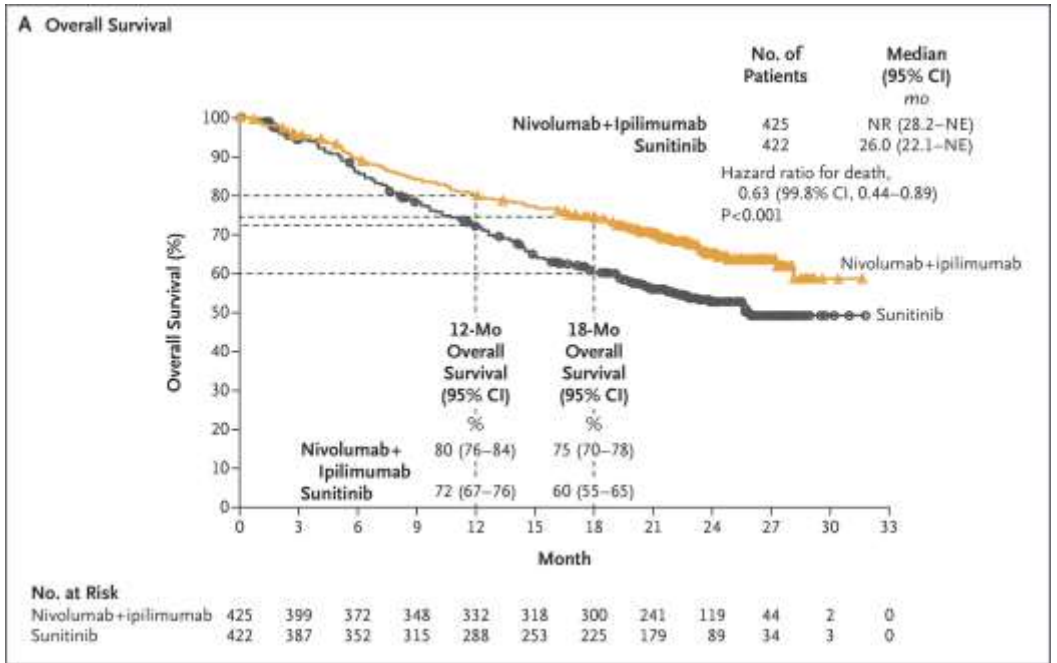
IMMUNOTHERPY ERA

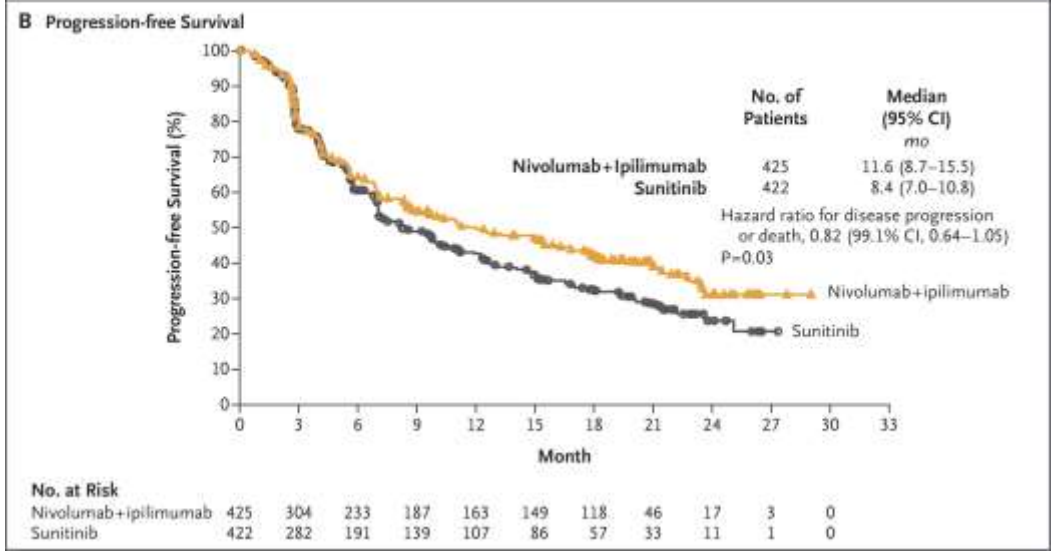
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 5, 2018 VOL. 378 NO. 14

Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma

R.J. Motzer, N.M. Tannir, D.F. McDermott, O. Arén Frontera, B. Melichar, T.K. Choueiri, E.R. Plimack, P. Barthélémy, C. Porta, S. George, T. Powles, F. Donskov, V. Neiman, C.K. Kollmannsberger, P. Salman, H. Gurney, R. Hawkins, A. Ravaud, M.-O. Grimm, S. Bracarda, C.H. Barrios, Y. Tomita, D. Castellano, B.I. Rini, A.C. Chen, S. Mekan, M.B. McHenry, M. Wind-Rotolo, J. Doan, P. Sharma, H.J. Hammers, and B. Escudier, for the CheckMate 214 Investigators*





Las conclusiones obtenidas en la era de las Terapias Dirigidas pueden no ser aplicables en la era de la Inmunoterapia dado que los mecanismos de acción son completamente diferentes

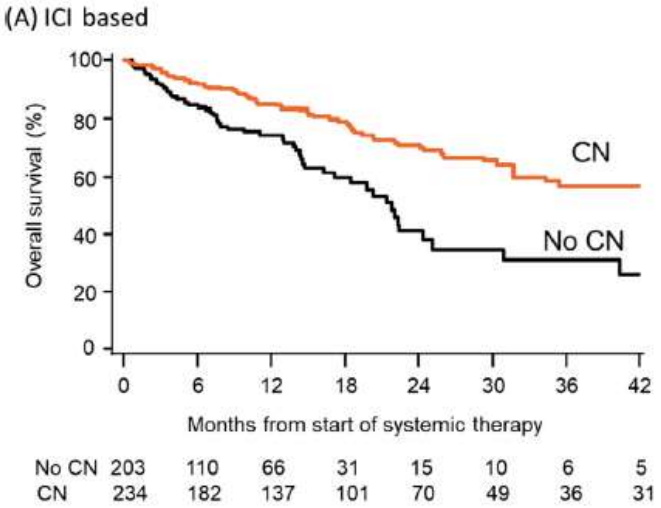
Upfront Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma Treated with Immune Checkpoint Inhibitors or Targeted Therapy: An Observational Study from the International Metastatic Renal Cell Carcinoma Database Consortium

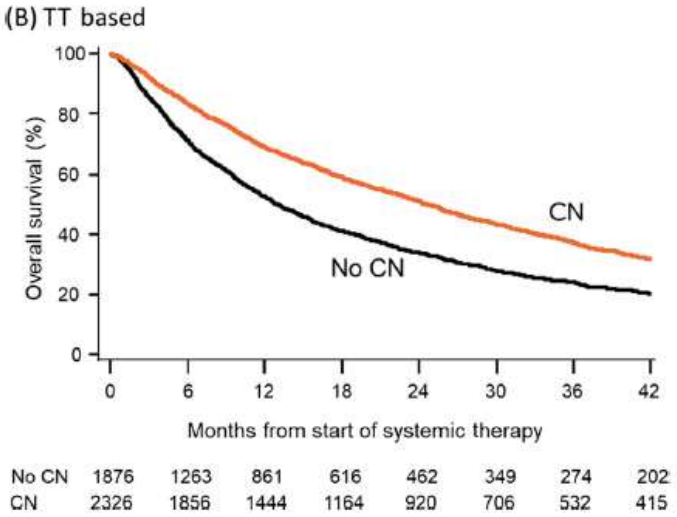
EUROPEAN UROLOGY 83 (2023) 145–151

Los pacientes

- más jóvenes
- con menos factores de riesgo de IMDC
- sin metástasis en localizaciones adversas (óseas, cerebrales o hepáticas)
- mejor estado funcional

Tenían más probabilidades de ser tratados con CN inicial





IMMUNOTHERPY ERA

The effect of immune checkpoint inhibitor combination therapies in metastatic renal cell carcinoma patients with and without previous cytoreductive nephrectomy: A systematic review and *meta*-analysis

Keiichiro Mori [a,b,*], Fahad Quhal [a,c], Takafumi Yanagisawa [a,b], Satoshi Katayama [a,d], Benjamin Pradere [a], Ekaterina Laukhtina [a,e], Pawel Rajwa [a,f], Hadi Mostafaei [a,g], Reza Sari Motlagh [a,h], Takahiro Kimura [b], Shin Egawa [b], Karim Bensalah [i], Pierre I. Karakiewicz [j], Manuela Schmidinger [a], Shahrokh F. Shariat [a,f,k,l,m,n,o]

International Immunopharmacology 108 (2022)

4.346 pacientes
Terapia combinada con ICI (n = 2.155; 49,6%)
Sunitinib (n= 2,191; 50.4%)

9-21% Riesgo pobre
69 – 84% NC

Table 1
Study demographics.

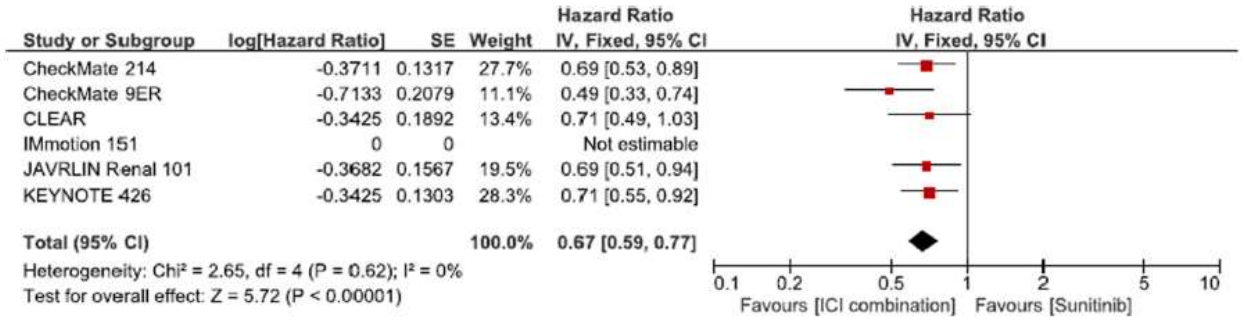
Study	IMmotion151	JAVELIN Renal 101	CheckMate 214	KEYNOTE 426	CheckMate 9ER	CLEAR
Year	2019	2019	2018	2019	2021	2021
Compound	Atezolizumab plus bevacizumab	Avelumab plus axitinib	Nivolumab plus ipilimumab	Pembrolizumab plus axitinib	Nivolumab plus cabozantinib	Pembrolizumab plus lenvatinib
Control	Sunitinib	Sunitinib	Sunitinib	Sunitinib	Sunitinib	Sunitinib
Number (treatment/ control)	178/184	442/444	425/422	432/429	323/355	355/357
Age (treatment/control)	62/59	62/61	62/61	62/61	62/61	64/61
Male (treatment/ control)	67%/79%	72%/78%	74%/71%	71%/75%	77%/71%	72%/77%
Poor risk (treatment/ control)	11%/11%19vs20	12%/10% 72vs71	21%/21% 91vs89	13%/12% 56vs52	19%/21% 61vs68	9%/10% 32vs32
Nephrectomy (treatment/control)	84%/83%	80%/80%	80%/76%	83%/83%	69%/71%	74%/77%
PD-L1 positivity	100%/100%	61%/65%	26%/29%	59%/62%	26%/25%	30%/33%
Median OS (treatment/ control)	34.0/32.7	NRE/NRE	NRE/26.0	NRE/35.7	NRE/NRE	NRE/NRE
Median PFS (treatment/ control)	11.2/7.7	13.3/8.4	11.6/8.4	15.4/11.1	16.6/8.3	23.9/9.2
Median ORR (treatment/ control)	43%/35%	51%/26%	42%/27%	60%/40%	56%/27%	71%/36%
Subsequent treatment	44%/55%	21%/39%	39%/54%	54%/69%	19%/33%	33%/58%
Median follow up	15 months	10.8/8.6 months	25.2 months	30.6 months	18.1 months	26.6 months

Abbreviation: NR (not reported), NRE (not reached), ORR (objective response rate), OS (overall survival), PD-L1 (programmed death ligand 1), PFS (progression free survival)

IMMUNOTHERPY ERA

SUPERVIVENCIA GLOBAL

A) With cytoreductive nephrectomy



B) Without cytoreductive nephrectomy

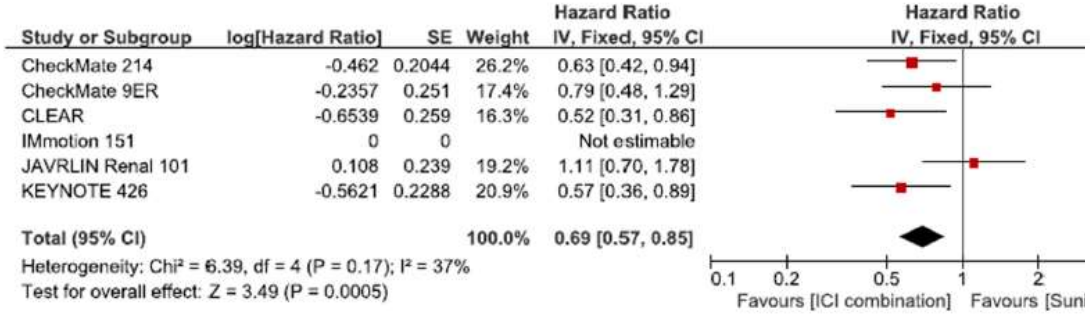
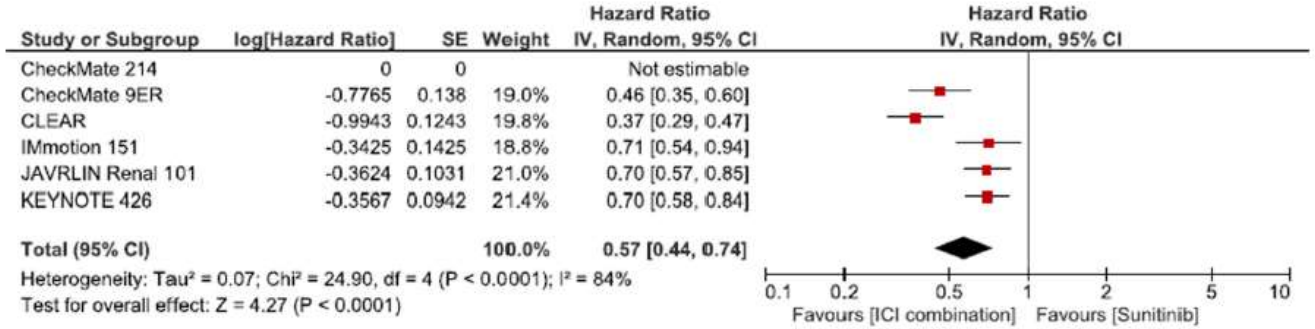


Fig. 1. Forest plots showing the association between treatment and overall survival in metastatic renal cell carcinoma (immune checkpoint therapy versus sunitinib). With cytoreductive nephrectomy. (B) Without cytoreductive nephrectomy.

SUPERVIVENCIA LIBRE DE PROGRESIÓN

A) With cytoreductive nephrectomy



B) Without cytoreductive nephrectomy

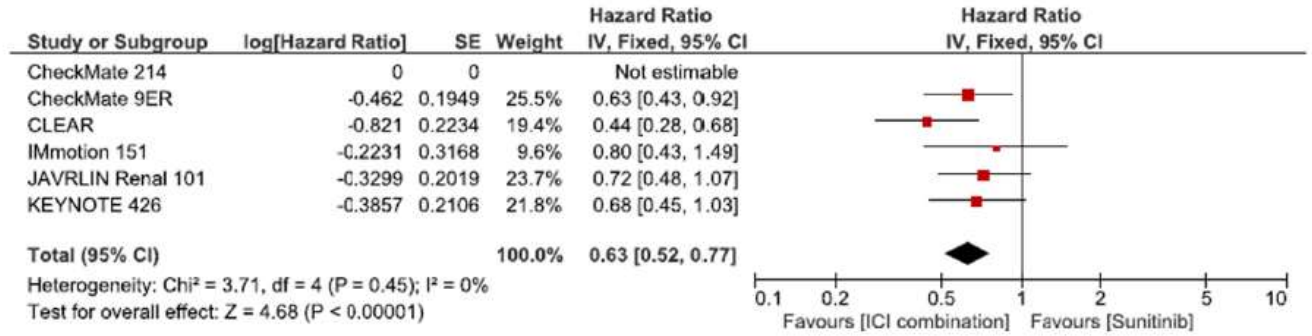


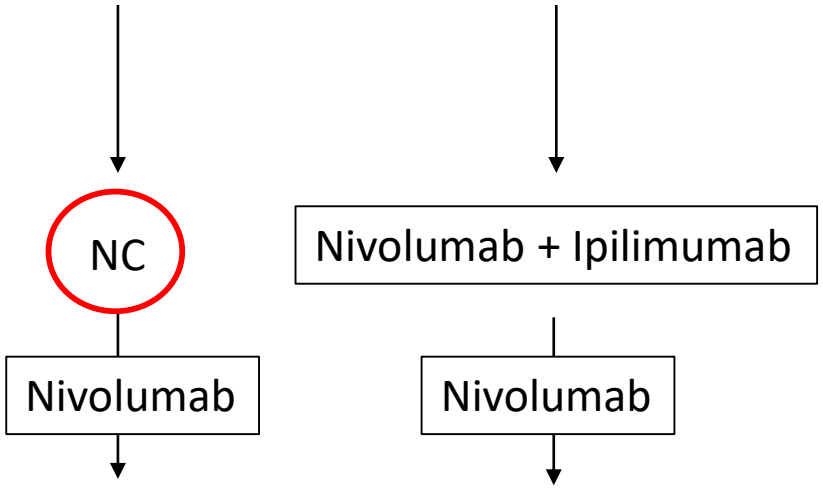
Fig. 2. Forest plots showing the association between treatment and progression free survival in metastatic renal cell carcinoma (immune checkpoint inhibitor combination therapy versus sunitinib). (A) With cytoreductive nephrectomy. (B) Without cytoreductive nephrectomy.

ENSAYOS CLÍNICOS EN CURSO

IMMUNOTHERPY ERA

NORDIC-SUN trial (NCT03977571)

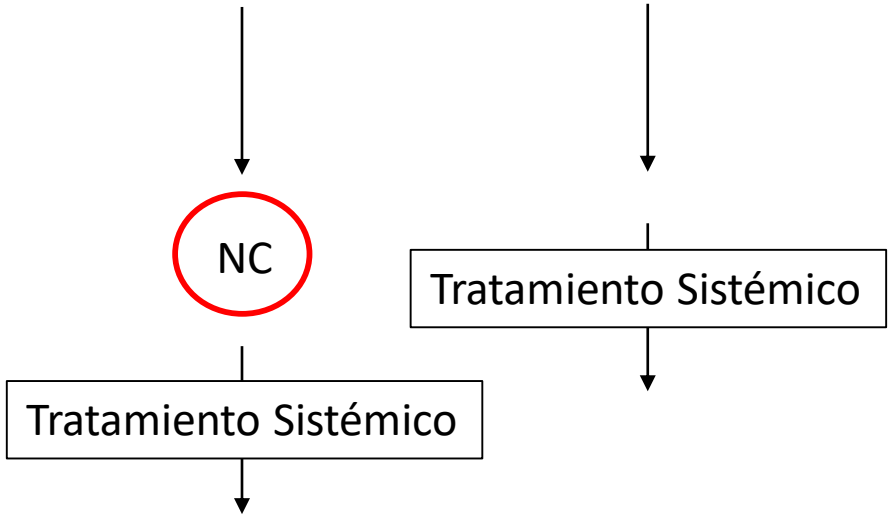
400 pacientes



PROBE (NCT04510597)

CCRm en tratamiento
con régimen basado en inmunoterapia

- Respuesta parcial
- Enfermedad estable
- Beneficio clínico



No hay información suficiente del papel de la cirugía citorreductora en el contexto del **tratamiento inmunoterápico**

Nefrectomía Citorreductora: Morbi-mortalidad

La morbilidad postoperatoria podría impedir o retrasar el uso de terapias sistémicas posteriores y, por tanto, afectar la evolución de la enfermedad

Rates and Predictors of Perioperative Complications in Cytoreductive Nephrectomy: Analysis of the Registry for Metastatic Renal Cell Carcinoma

Eduard Roussel[a], *Riccardo Campi*[b,c], *Alessandro Larcher*[d], *Annelies Verbiest*[e], *Alessandro Antonelli*[f], *Carlotta Palumbo*[f], *Ithaar Derweesh*[g], *Fady Ghali*[g], *Aaron Bradshaw*[g], *Margaret F. Meagher*[g], *Matthias Heck*[h], *Thomas Amiel*[h], *Maximilian C. Kriegmair*[i], *Jose Rubio*[j], *Mireia Musquera*[k], *Maurizio D'Anna*[k], *Riccardo Autorino*[l], *Georgi Guruli*[l], *Alessandro Veccia*[l], *Estefania Linares-Espinos*[m], *Siska Van Bruwaene*[n], *Vital Hevia*[o], *Francesco Porpiglia*[p], *Enrico Checcucci*[p], *Andrea Minervini*[b,c], *Andrea Mari*[b,c], *Nicola Pavan*[q], *Francesco Claps*[p], *Michele Marchioni*[r,s], *Umberto Capitanio*[d], *Benoit Beuselinck*[e], *Maria C. Mir*[j,†,*], *Maarten Albersen*[a,†],

EUROPEANUROLOGYONCOLOGY3(2020)523–529

N= 637

29,5% de complicaciones postoperatorias

6,1% Alto Grado
1,4% Mortalidad

Seroma: 5,7%
Sangrado postoperatorio: 5,3%
Ileo paralitico: 4,5%
Fracaso renal agudo: 2,2%
Otras 1% (linfocele, hematoma, TVP, fiebre)

Se observaron **complicaciones intraoperatorias** en 69 pacientes (11%)

- Hemorragia (25 casos, 36%)
- Laceración del bazo (13 casos, 19%)
- Lesiones vasculares (11 casos, 16%)

Días de ingreso medio: 8 (6-11)

Table 3 – Details of postoperative complications per location.

Site		Percentage of total	% High grade
Cardiopulmonary	35	4.8	2.9
Acute myocardial infarction	1	0.1	
Arrhythmia	10	1.4	
Pulmonary embolus	9	1.2	
Respiratory failure	6	0.8	
Pneumothorax	9	1.2	
Vascular/lymphatic	67	9.1	1.1
Lymphocele	10	1.4	
Postoperative bleeding	39	5.3	
Low hemoglobin	5	0.7	
Intra-abdominal hematoma	5	0.7	
Deep vein thrombosis	8	1.1	
Neurological	7	1.0	0
Nerve injury	3	0.4	
Cerebrovascular accident	2	0.3	
Severe mental confusion	2	0.3	
Gastrointestinal	33	4.5	0.5
Prolonged ileus	18	2.5	
Bowel obstruction	4	0.5	
Nausea/vomiting	3	0.4	
Enteric fistula	3	0.4	
Pancreatic injury	5	0.7	
Urological	23	3.1	0.8
Acute renal insufficiency	16	2.2	
Acute urinary retention	5	0.7	
Scrotal swelling/hematoma	2	0.3	
Wound/skin	13	1.8	0.1
Wound infection	5	0.7	
Dehiscence	3	0.4	
Hematoma	2	0.3	
Pressure skin ulcer	2	0.3	
Seroma	1	0.1	
Infection/metabolic	42	5.7	0.7
Malignant hyperthermia	2	0.3	
Sepsis	5	0.7	
Abscess	1	0.1	
Urinary tract infection	4	0.5	
Pneumonia	24	3.3	
Other infections	2	0.3	
Addisonian crisis	1	0.1	
Total	217	29.5	6.1

GUIAS CLINICAS EUROPEAS 2023

Figure 7.1: Updated EAU Guidelines recommendations for the first-line treatment of cc-mRCC

	Standard of Care	Alternative in patients who can not receive or tolerate immune checkpoint inhibitors
IMDC favourable risk	nivolumab/cabozantinib [1b] pembrolizumab/axitinib [1b] pembrolizumab/lenvatinib [1b]	sunitinib* [1b] pazopanib* [1b]
IMDC intermediate and poor risk	nivolumab/cabozantinib [1b] pembrolizumab/axitinib [1b] pembrolizumab/lenvatinib [1b] nivolumab/ipilimumab [1b]	cabozantinib* [2a] sunitinib*[1b] pazopanib* [1b]

Recommendations	**Strength rating**
Do not perform cytoreductive nephrectomy (CN) in MSKCC poor-risk patients.	Strong
Do not perform immediate CN in intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy.	Weak
Start systemic therapy without CN in intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy.	Weak
Discuss delayed CN with patients who derive clinical benefit from systemic therapy.	Weak
Perform immediate CN in patients with a good performance status who do not require systemic therapy.	Weak
Perform immediate CN in patients with oligometastases when complete local treatment of the metastases can be achieved.	Weak

RIESGO FAVORABLE: Cirugía citorreductora +/- tratamiento de la metástasis

RIESGO INTERMEDIO:

1 Factor de riesgo: Cirugía citorreductora + Tratamiento sistémico

2 Factores de riesgo: Tratamiento sistémico + CN diferida

RIESGO POBRE: Tratamiento sistémico

La **NEFRECTOMÍA DIFERIDA** puede ser siempre una opción en función de la respuesta al tratamiento y el estado clínico del paciente