XLI Reunión MANCHEGO-EXTREMEÑA DE UROLOGÍA

4 y 5 de Mayo

Viernes 4

15:00 Bienvenida.

15:00-17:00 Coctel de Bienvenica.

17:00-17:30 Recepción y entrega de documentación.

17:30-18:00 **CONFERENCIA MAGISTRAL.**
Visión objetiva de la HBP basada en la urodinámica.
Manuel Esteban Fuertes
Presidente de la AEU

18:00-18:15 *Pausa Café.*

18:15-19:00 **SESIÓN UROLÓGICA FUNCIONAL.**
Tratamiento quirúrgico de STUI.
Rosana Barriga Guijo
(Hospital Universitario de Guadalajara).

STUI y DSE.
Juan Alonso Cabo González
(Hospital Infanta Cristina de Badajoz).

19:00-21:00 **Presentacion de trabajos.**
Moderadores:
Alejandro Puerto Puerto
(Hospital General Universitario de Ciudad Real).
Angel Urbina Lima
(Hospital Virgen del Puerto. Plasencia)

21:00 *Cena*

Abierto el plazo para envío de resúmenes hasta el día 2 de abril de 2018 en nuestra web:
http://cme2018.aeu.es/

Sábado 5

9:30-10:00 **Cáncer de Próstata Hormono Sensible.**
Manuela Pacheco Moreno
(Hospital de Mérida).
Mesa organizada por Janssen

10:00-10:30 **Cáncer de Próstata CPRC.**
Mónica De Cabo Ripoll
(Hospital Virgen de La Cruz. Cuenca).

10:30-10:45 Discusión

10:45-11:15 **Manejo del Carcinoma Renal Avanzado.**
Ricardo Collado Martín
(Servicio de Oncología del Hospital Universitario San Pedro de Alcántara. Cáceres).

11:15-11:30 *Pausa Café.*

11:30-12:30 **SESIÓN DE ENDOUROLOGÍA.**
Manejo no quirúrgico de las litiasis.
David López Sánchez
(Hospital General Universitario de Ciudad Real).
Manejo quirúrgico de las litiasis.
Miguel Rodríguez Romero
(Hospital Universitario San Pedro de Alcántara. Cáceres).

12:30-14:30 **Presentacion de trabajos.**
Moderadores:
Jesús Martínez Ruiz
(Complejo Universitario de Albacete)
Gabriel Machado Fernández
(Hospital Universitario San Pedro de Alcántara. Cáceres).

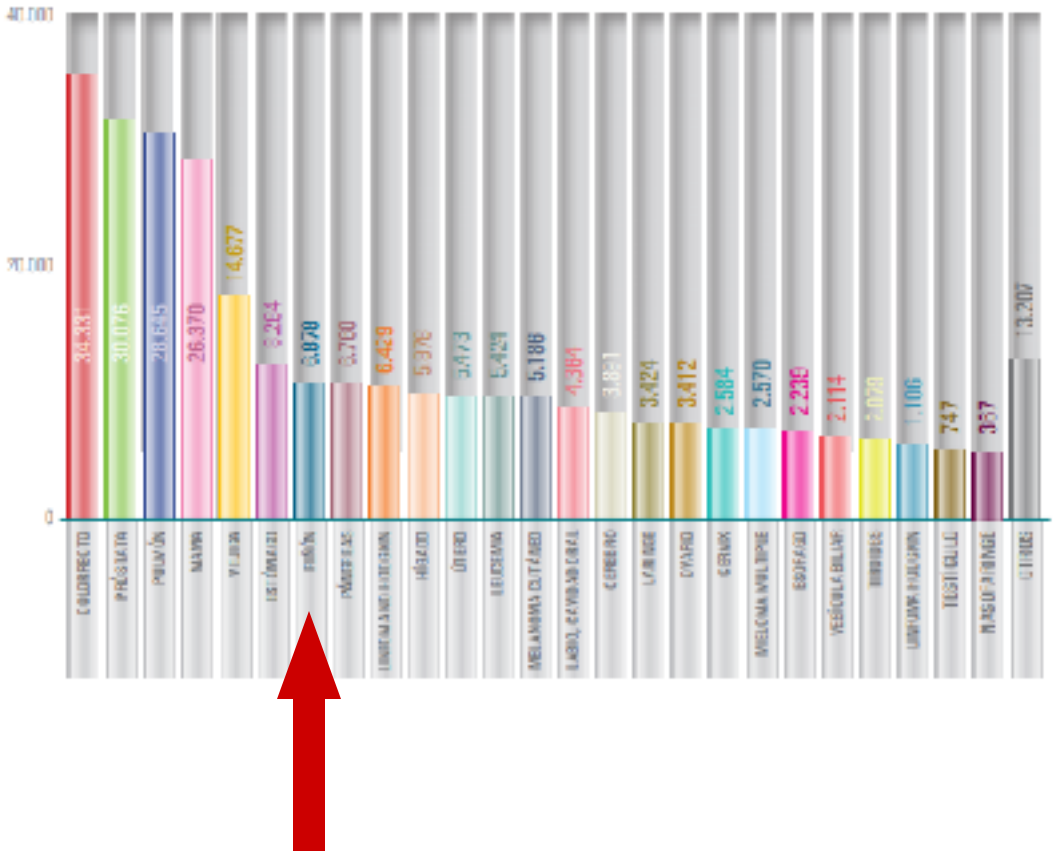
14:30 *Almuerzo de trabajo.*

17:00 **Asambleas.**

21:00 *Cena de Clausura*

Relevancia del cáncer de riñón

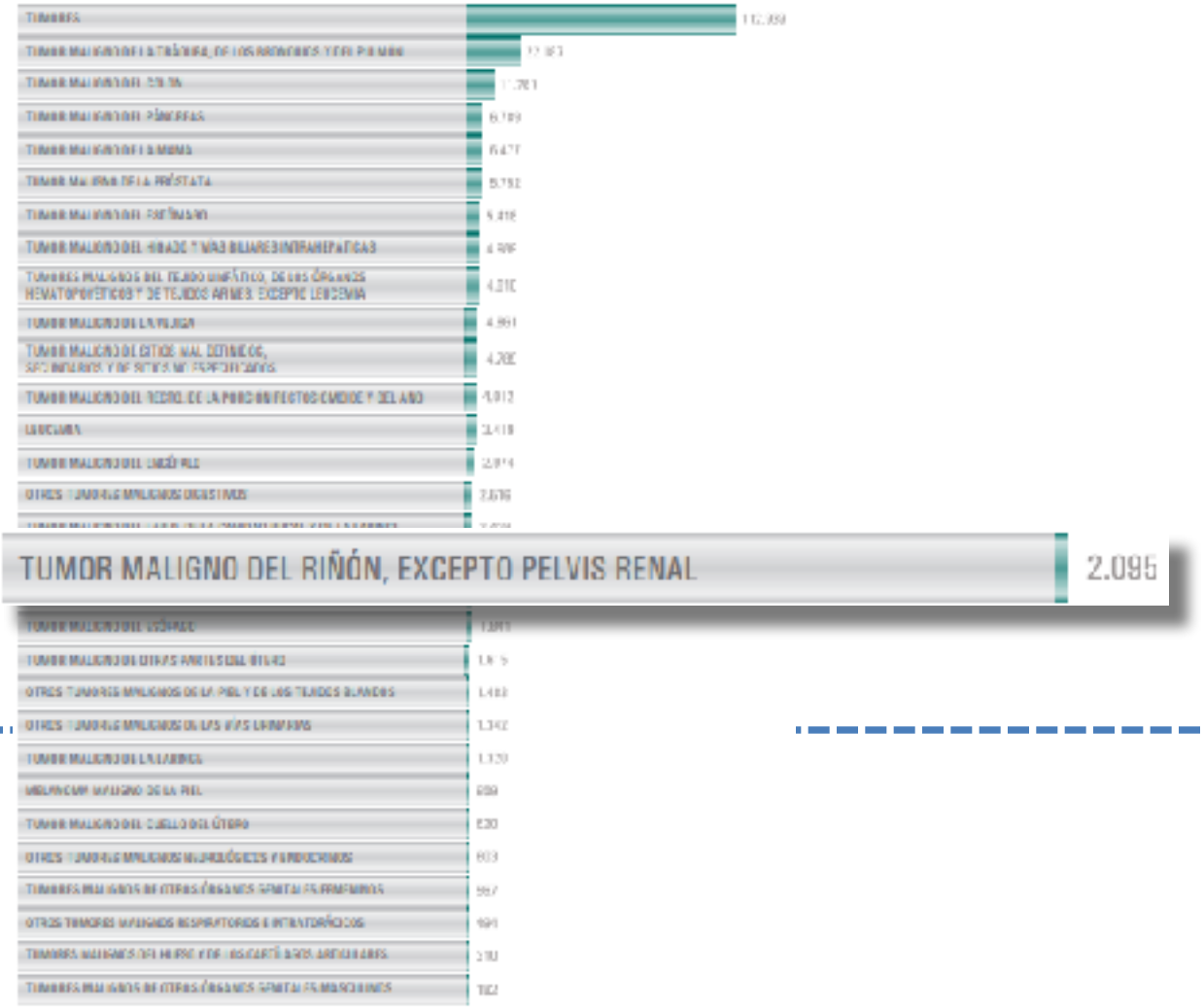
Incidencia



Las cifras del cáncer en España. 2018. En: www.seom.org

Relevancia del cáncer de riñón

Mortalidad



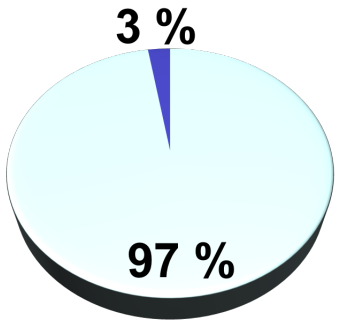
Las cifras del cáncer en España. 2018. En: www.seom.org

Relevancia del cáncer de riñón

Para los Interinos

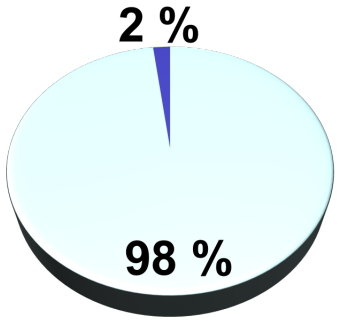
Relevancia del cáncer de riñón

Para los Interinos



Resto patologías
Cáncer renal

OPE Oncología Médica



Resto patologías
Cáncer renal

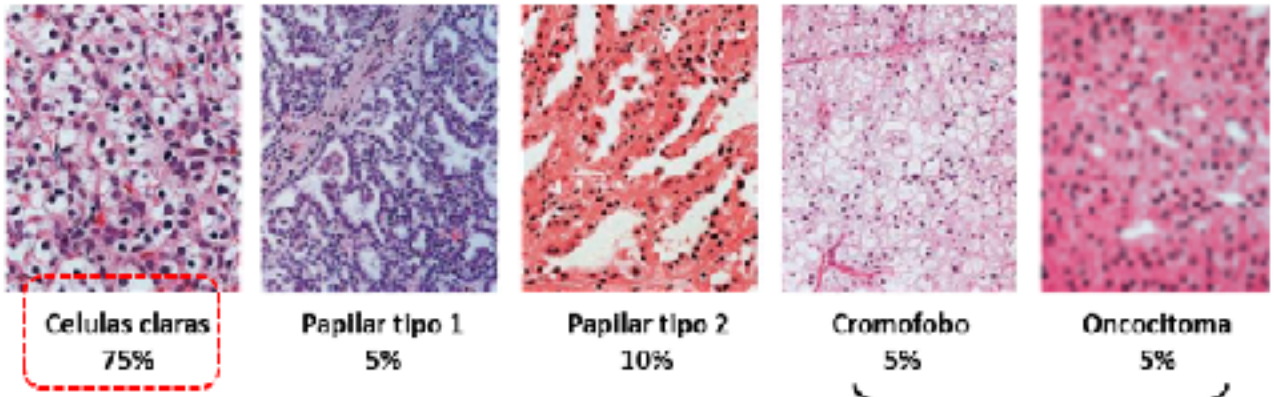
OPE Urología

Carcinoma renal

hay subtipos histológicos

y

no todos se comportan de la misma manera

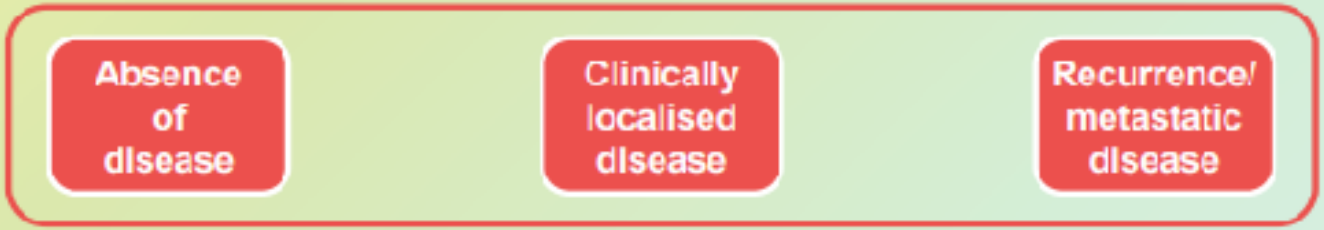


Además, existe heterogeneidad intra-tumoral y del tumor primario respecto a las metástasis

No se trata de una única enfermedad

Carcinoma renal

Presentación de la enfermedad



SEER Stat Facts: Kidney and Renal Pelvis Cancer available at: https://seer.cancer.gov/statfacts/html/kidrp.html (Accessed February 2018).

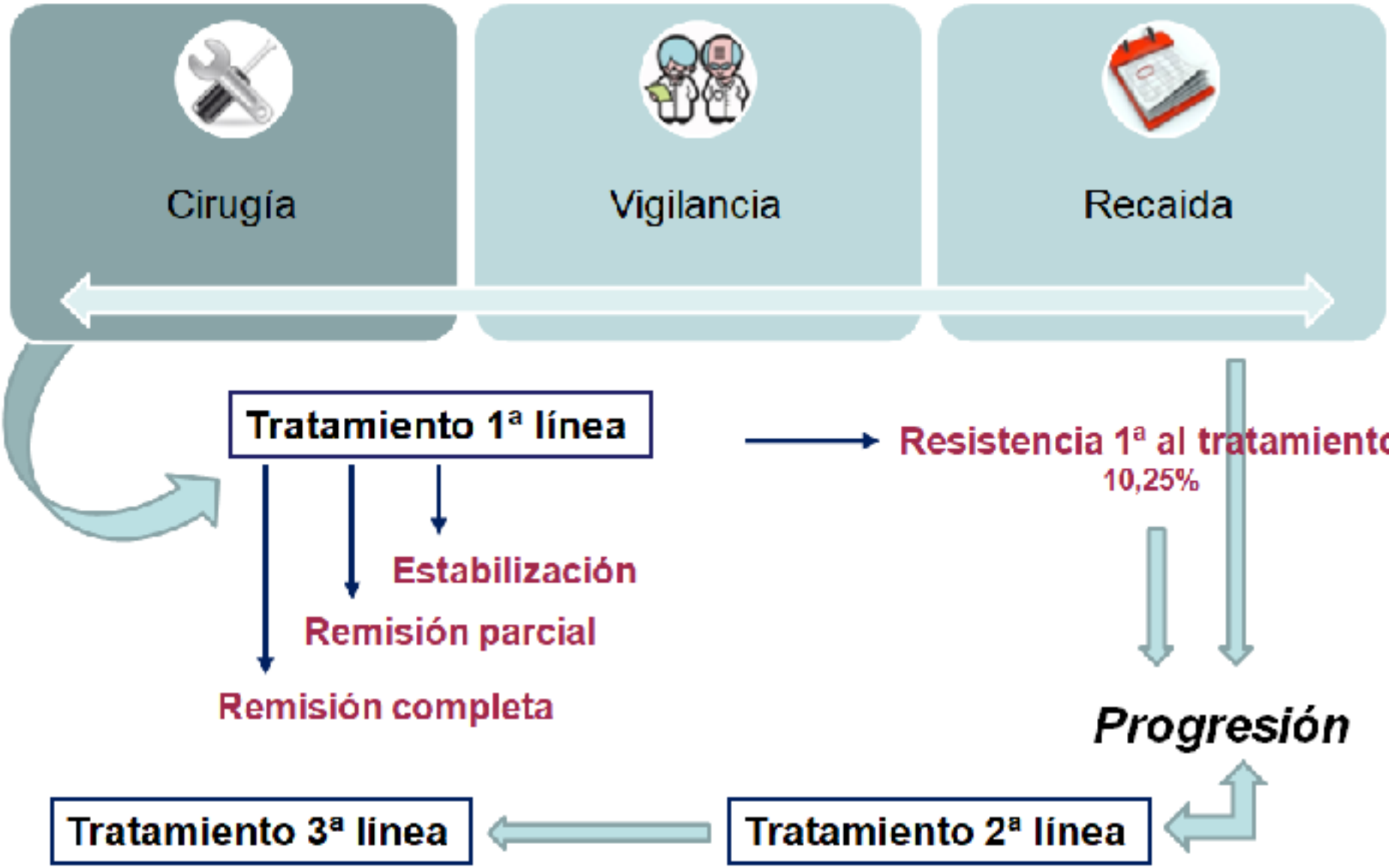
Carcinoma renal

Presentación de la enfermedad

SEER Stat Facts: Kidney and Renal Pelvis Cancer available at: https://seer.cancer.gov/statfacts/html/kidrp.html (Accessed February 2018).

Carcinoma renal

Algoritmo de enfermedad renal metastásica




CASO
CLÍNICO
1

Caso clínico

- Varón de 63 años con masa renal izquierda

- Se realizó nefrectomía radical izquierda, con AP:
  - Carcinoma renal de células claras G2, pT2pN1M0

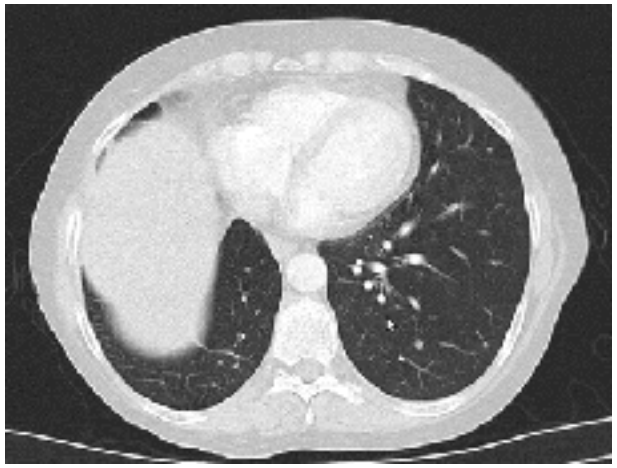
- Tras un ILE de 15 meses → progresión de enfermedad a nivel pulmonar

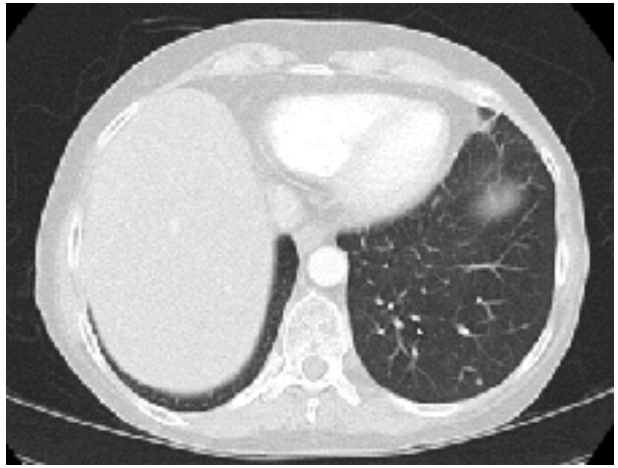
Caso clínico 1

- Varón de 63 años con masa renal izquierda

- Se realizó nefrectomía radical izquierda, con AP:
  - Carcinoma renal de células claras G2, pT2pN1M0

- Tras un ILE de 15 meses → progresión de enfermedad a nivel pulmonar





Caso clínico

Descripción	Valor	Unidad	Rango
Hematíes	1.32	mill/mm3	4.5-5.9
Hemoglobina	14.7	g/dl	11.5-17.5
Hematocrito	43.6	%	41-53
Volumen corpuscular medio	100.9	fl	78-102
Hemoglobina corpuscular media eritrocitaria	34	pg	26-34
Concentración de hemoglobina corpuscular media eritrocitaria	33.7	g/dl	31-37
Amplitud de distribución eritrocitaria	14.1		11-15
Leucocitos	6.8	mil/mm3	4.5-11
Neutrófilos %	50.5	%	45-70
Neutrófilos	3.4	mil/mm3	1.8-8
Linfocitos %	41.3	%	20-50
Linfocitos	2.8	mil/mm3	1-4.8
Monocitos %	5.3	%	4-12
Monocitos	0.4	mil/mm3	0.3-0.9
Eosinófilos %	2.5	%	0-5
Eosinófilos	0.2	mil/mm3	0-0.5
Basófilos %	0.4	%	0-1.5
Basófilos	0	mil/mm3	0-0.2
Plaquetas	229	mil/mm3	150-450
Volumen plaquetar medio	10.4	fl	6-12

Caso clínico

Descripción	Valor	Unidad	Rango
Hematies	4.32	mill/mm3	4.5-5.9
Hemoglobina	14.7	g/dl	13.5-17.5
Hematocrito	43.6	%	41-53
Volumen corpuscular medio	100.9	fl	78-102
Glucosa	98	mg/dL	70-110
Urea	45	mg/dL	10-50
Creatinina en sangre	1.59	mg/dL	0.70-1.20
Tasa estimada de filtración glomerular/1,73 metros cuadrados	48.7	ml/min	>60
Proteinas totales	6.8	g/dL	6.6-8.7
Albumina en sangre	4.2	g/dL	3.4-4.8
Bilirrubina total	0.37	mg/dL	0-1.0
Sodio	140	mmol/l	136-145
Potasio	4.39	mmol/L	3.3-5.1
Calcio	9.4	mg/dL	8.6-10.5
Fosfato	2.4	mg/dL	2.7-4.5
Triglicéridos	216	mg/dL	45-200
Colesterol	205	mg/dl	110-200
LDH	393	UI/L	240-480
Aspartato amino transferasa (GOT)	29	UI/L	5-37
Alanina aminotransferasa (GPT)	33	UI/L	7-41
Gamma glutamil transferasa (GGT)	33	UI/l	10-60
Fosfatasa alcalina total	39	UI/L	40-129
T4 libre	1.45	ng/dl	0.85-2.00
TSH	1.72	µU/ml	0.27-4.2

Caso clínico

1

		Rango
Hematies	mm3	4.5-5.9
Hemoglobina	dl	11.5-17.5
Hematocrito	%	41-53
Volumen corpuscul	fl	78-102
Glucosa	mg/dL	70-110
Urea	mg/dL	10-50
Creatinina en s	mg/dL	0.70-1.20
Tasa estimada f	ml/min	>60
Proteinas totale	g/dL	6.6-8.7
Albumina en sa	g/dL	3.4-4.8
Bilirrubina total	mg/dL	0-1.0
Sodio	mmol/l	136-145
Potasio	mmol/L	3.3-5.1
Calcio	mg/dL	8.6-10.5
Fosfato	mg/dL	2.7-4.5
Triglicéridos	mg/dL	45-200
Colesterol	mg/dl	110-200
LDH	UI/L	240-480
Aspartato amino	UI/L	5-37
Alanina aminotra	UI/L	7-41
Gamma glutami	UI/l	10-60
Fosfatasa alcali	UI/L	40-129
T4 libre	ng/dl	0.85-2.00
TSH	uU/ml	0.27-4.2

Estado funcional o de desempeño físico según Karnofsky

Categorías generales	Porcentaje	Característica del paciente, nivel de actividad
Capaz de realizar actividades normales, no requiere cuidados especiales	100	Actividad normal. Sin síntomas ni evidencia de enfermedad
	90	Actividad normal. Signos y síntomas leves de enfermedad
	80	Actividad normal con esfuerzo. Algunos signos o síntomas de enfermedad
Incapaz de trabajar, puede vivir en casa y autocuidarse con ayuda variable	70	Cuida de sí mismo pero es incapaz de llevar a cabo una actividad o trabajo normal
	60	Necesita ayuda ocasional de otros pero es capaz de cuidar de sí mismo para la mayor parte de sus necesidades
	50	Requiere ayuda considerable de otros y cuidados especiales frecuentes
	40	Incapacitado. Requiere cuidados especiales
Incapaz de su autocuidado. Requiere cuidados especiales, susceptible de hospitalización. Probable avance rápido de la enfermedad	30	Severamente incapacitado. Indicación de hospitalización aunque no hay indicios de muerte inminente
	20	Gravemente enfermo. Necesita asistencia activa de soporte
	10	Moribundo
	0	Fallecido

Caso clínico

Hemograma:

Hb:14.7 g/dl

Neutrófilos:3400 mil/mm3

plaquetas: 229.000 mil/mm3

Calcio corregido: 9.72 mg/dl

Tiempo desde el diagnóstico hasta tto sistémico > 1 año

KPS: 100%

IMDC risk: Bueno
(0 factores de riesgo)

Paciente de 63 años con RCC metástásico

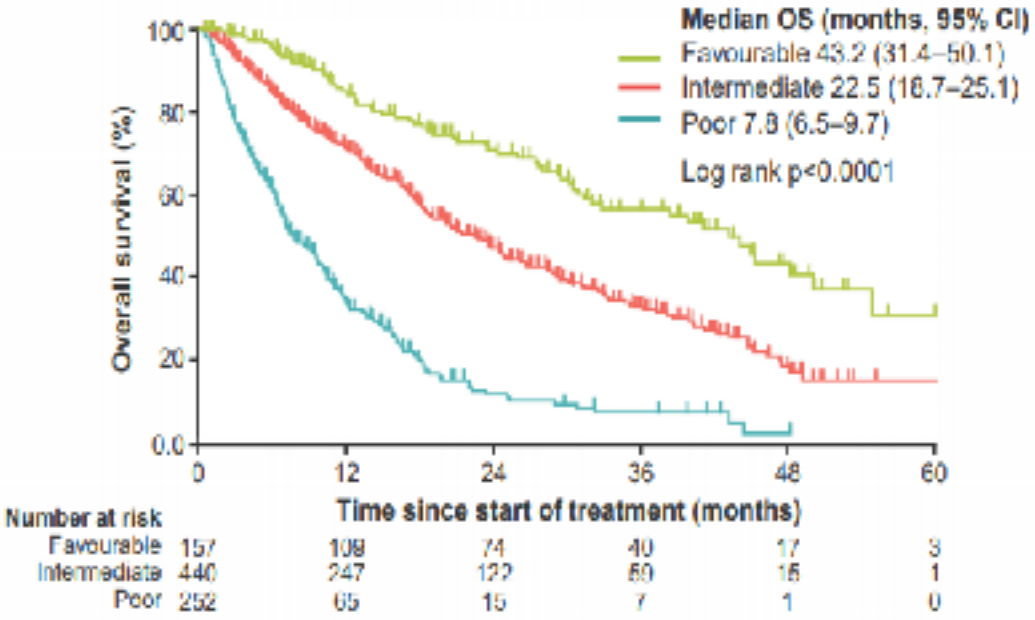
Tras 15 meses desde la cirugía presenta progresión pulmonar

Heng DY. J Clin Oncol. 2009;27:5794-5799

IMDC (International Metastatic Data Base Consosrtium) risk classification

IMDC risk classification	Number of risk factors
Favourable	0
Intermediate	1 or 2
Poor	≥3

IMDC risk factors
Karnofsky performance status <80%
Anaemia (haemoglobin concentration <lower limit of normal)
Hypercalcaemia (corrected calcium concentration >upper limit of normal)
Neutrophilia (neutrophil count >upper limit of normal)
<1 year since diagnosis
Thrombocytosis (platelet count >upper limit of normal)



Risk classification correlates with overall survival

Heng DY. J Clin Oncol. 2009;27:5794-5799

Caso clínico 1

¿Qué hay que tener en cuenta para el **tratamiento sistémico** del paciente con carcinoma renal?

Perfil de Efectos Adversos

Vía de administración

Circunstancias socio-familiares

Vías de administración

vía oral

- Todos los TKIs anti-angiogénicos:
  - Sunitinib
  - Sorafenib
  - Pazopanib
  - Cabozantinib
  - Lenvatinib
- Everolimus

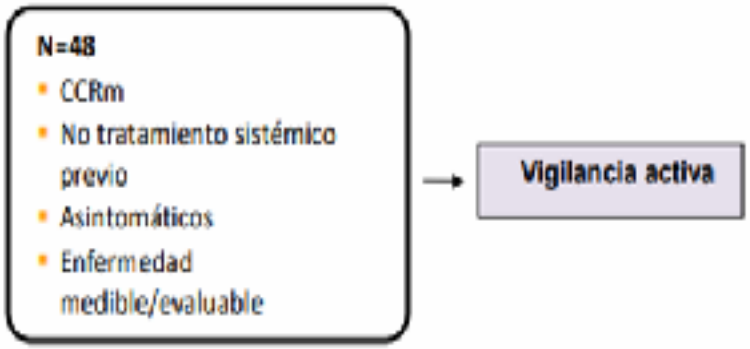
vía intravenosa

- Temsirolimus
- Todos los anticuerpos monoclonales, tanto los inhibidores de PD-1 (Nivolumab), Anti CTLA-4 (Ipilimumab), como el antiangiogénico Bevacizumab

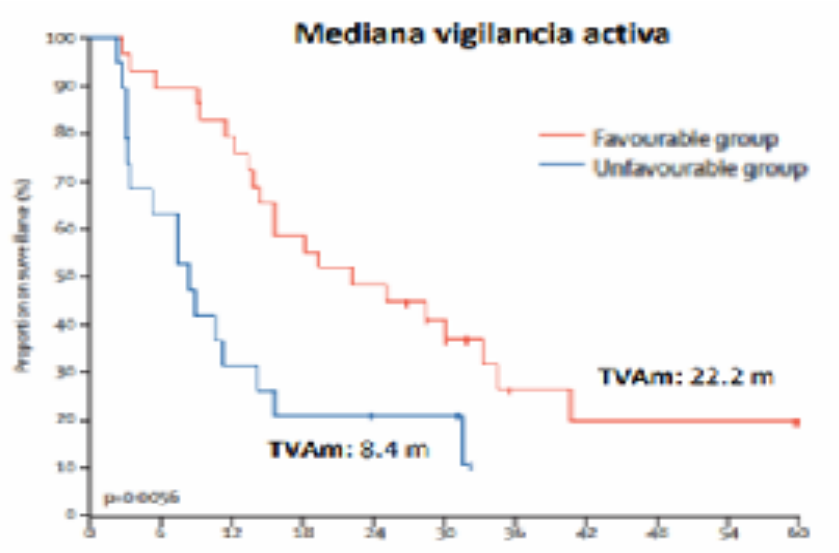
Caso clínico 1

Caso clínico 1

Vigilancia activa
Fase II Prospectivo



Objetivo 1º: tiempo desde vigilancia hasta tratamiento.



- Mediana de seguimiento: 38.1 meses
- Tiempo a inicio de tratamiento: 14.9 meses
- SLP 12 m: 41%
- SG: 44.5 m
- Análisis multivariante:
  - Nº de órganos afectos: 1/2 vs >2
  - Nº de factores IDMC: 0/1 vs >2

Rini BI. Lancet Oncol 2016; 17:1317

Caso clínico

- Varón de 63 años con masa renal izquierda

- Se realizó nefrectomía radical izquierda, con AP:
  - Carcinoma renal de células claras G2, pT2pN1M0

- Tras un ILE de 15 meses → progresión de enfermedad a nivel pulmonar y adenopatías retroperitoneales

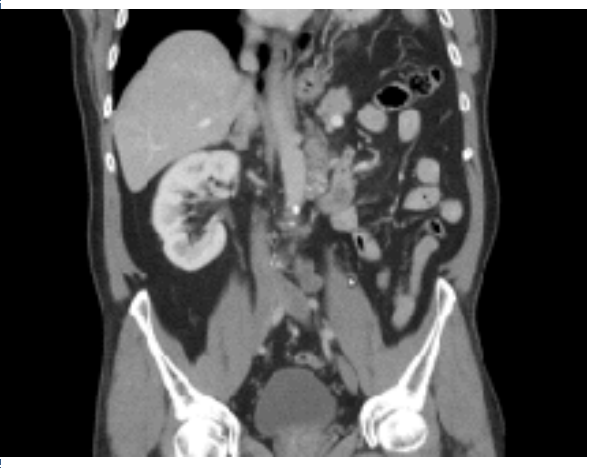
Caso clínico

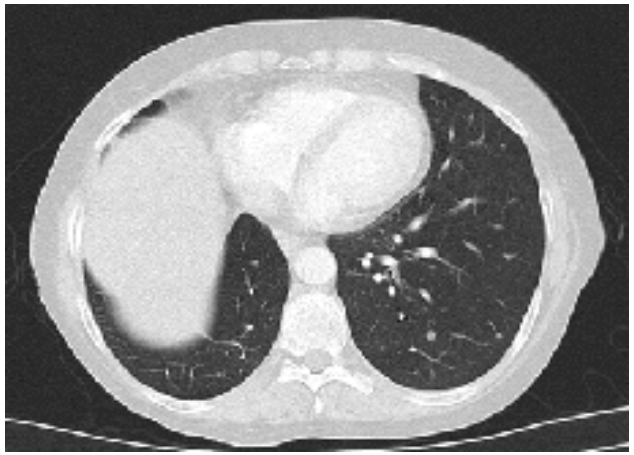
1

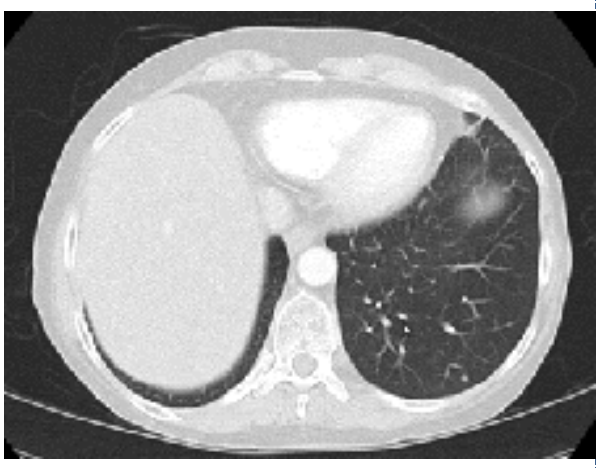
- Varón de 63 años con masa renal izquierda

- Se realizó nefrectomía radical izquierda, con AP:
  - Carcinoma renal de células claras G2, pT2pN1M0

- Tras un ILE de 15 meses → progresión de enfermedad a nivel pulmonar y adenopatías retroperitoneales





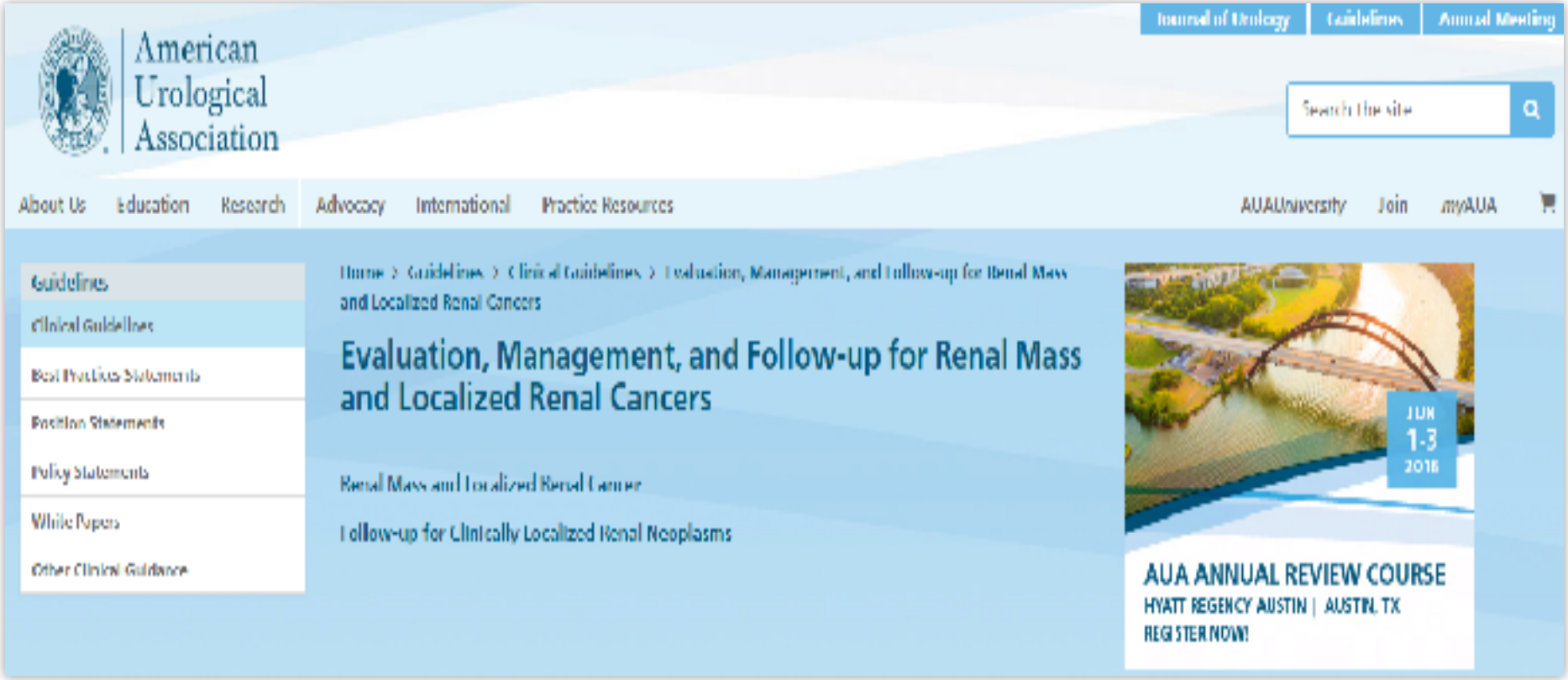


Caso clínico 1

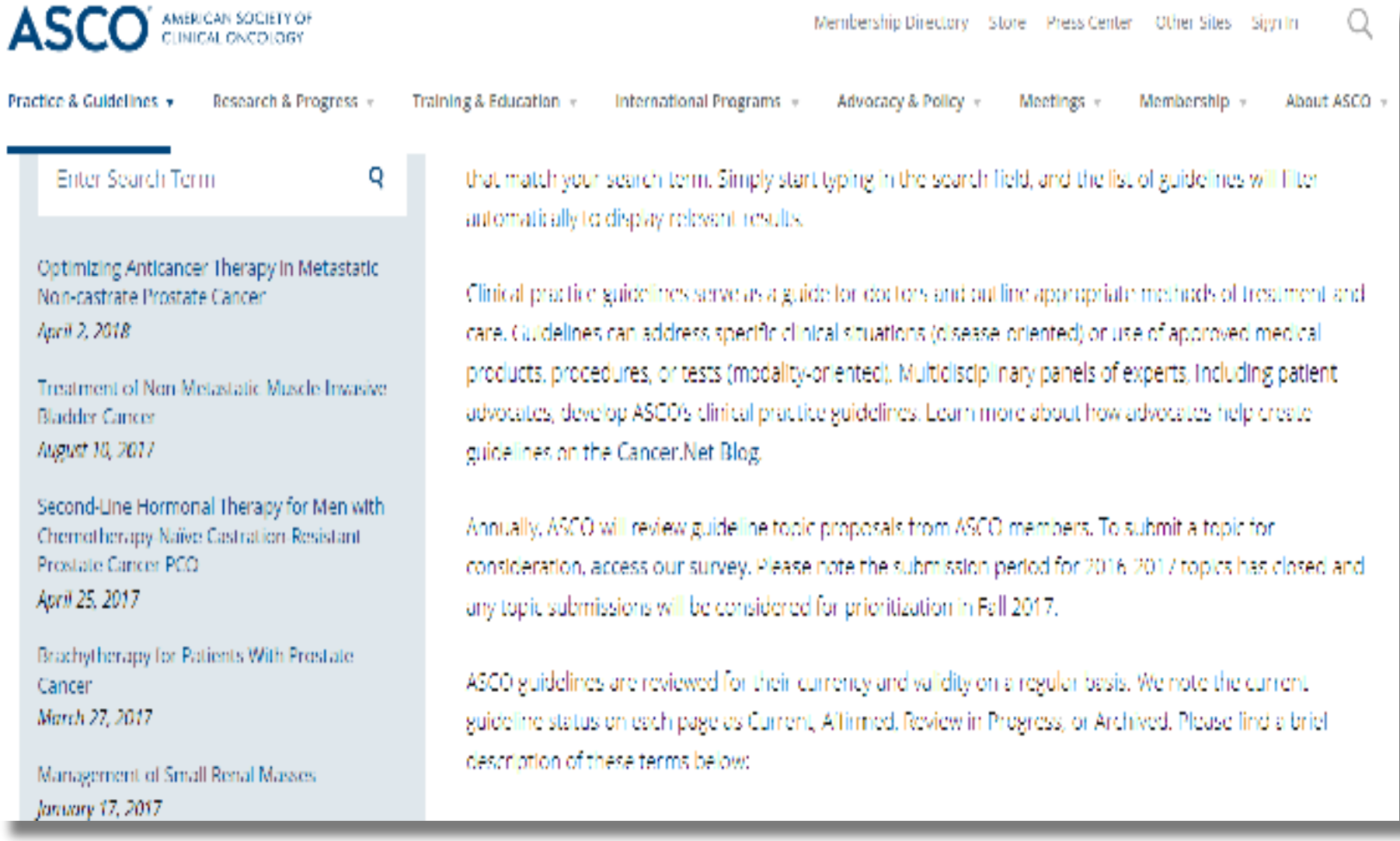

guidelines
Medical
development
supervision
electronic
health
knowledge
Design
Gap
case
ion
modelling
diagnosis
systems
methods
management
Model-based
Interactive
MHB
Bridging
Formal
study
Improving
representations
approach
solution
supporting
heart


WHO
WHAT
WHERE
WHEN
WHY
HOW
QUESTIONS
ANSWERS

American Urological Association



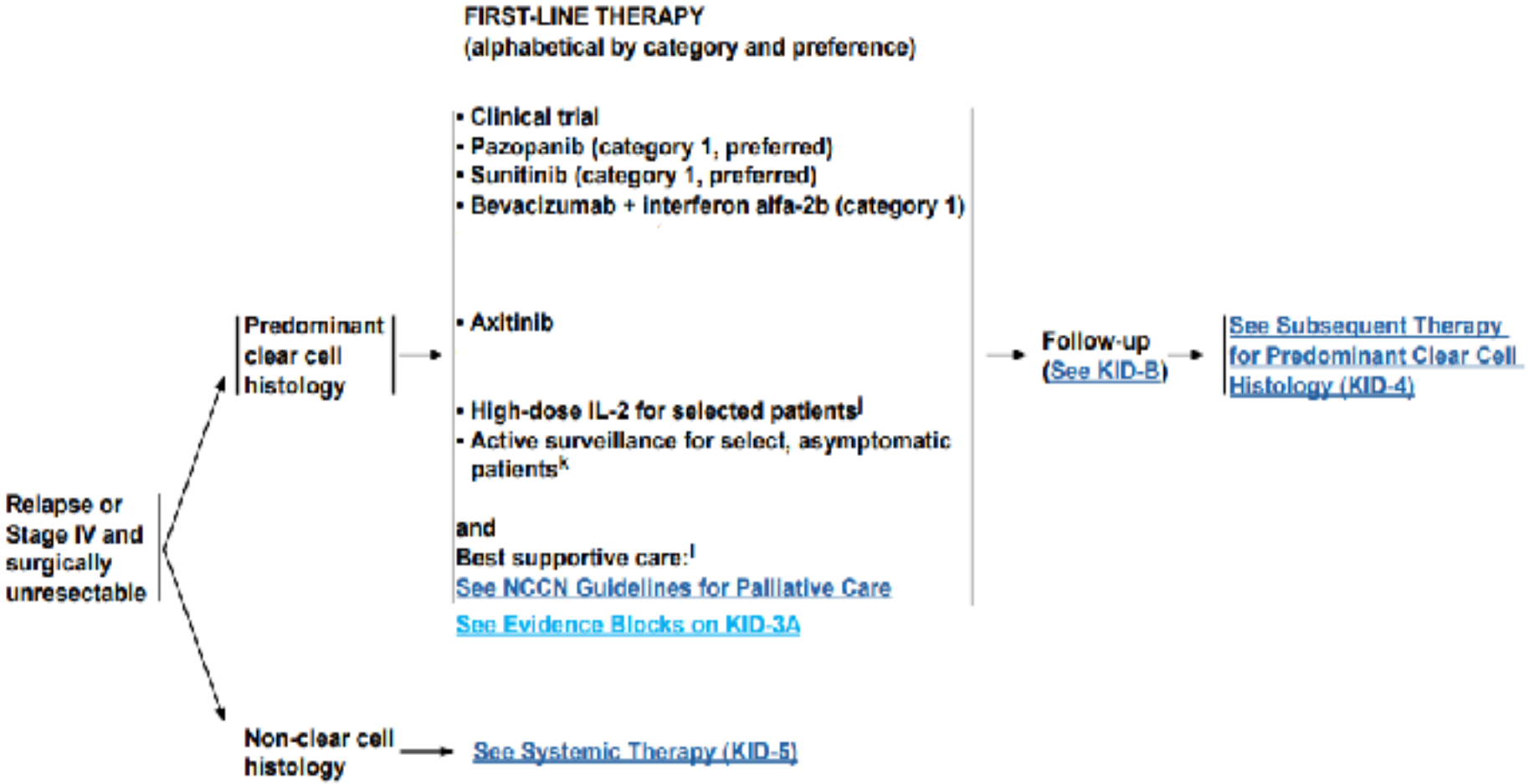
American Society of Clinical Oncology



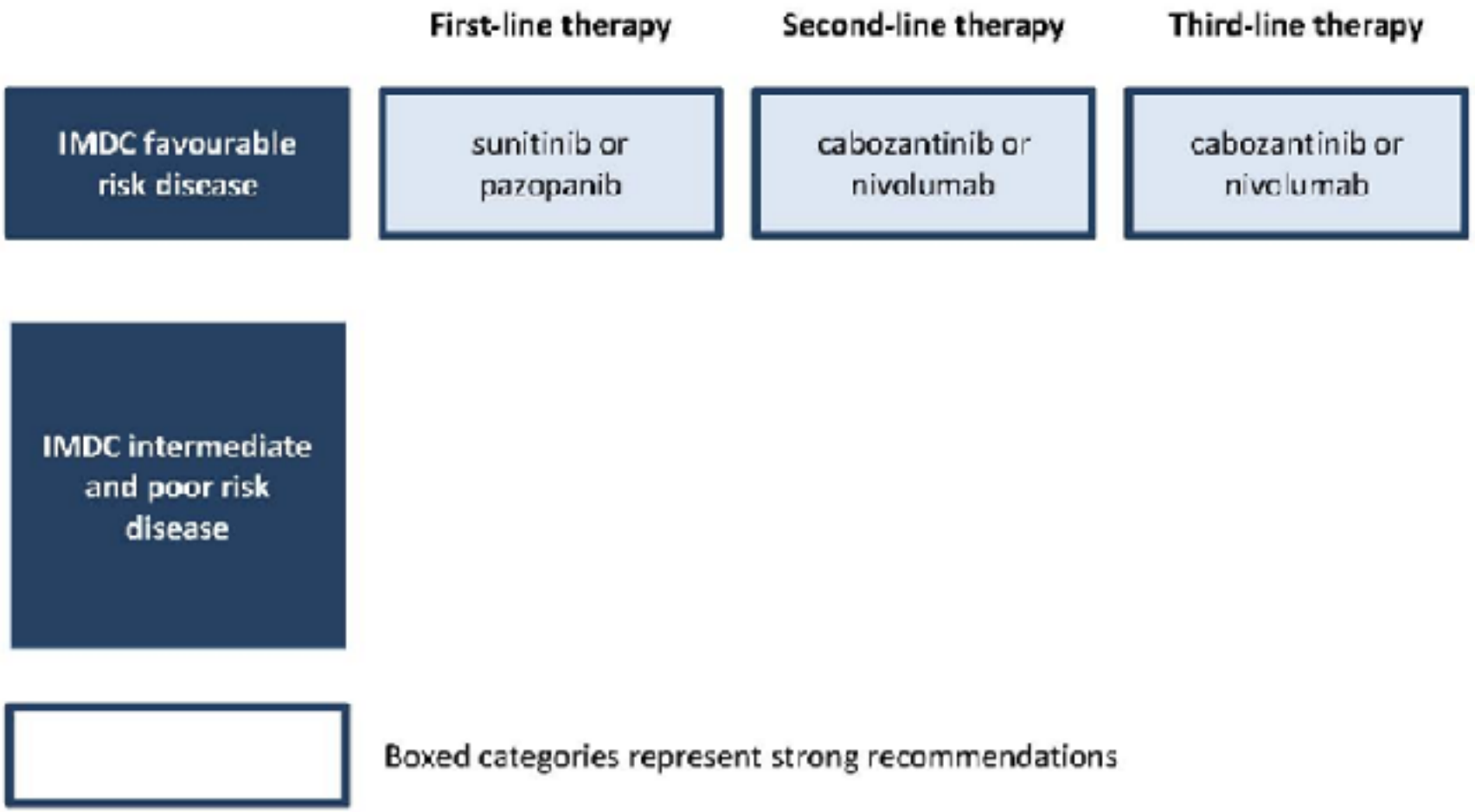
National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2018
Kidney Cancer
NCCN Evidence Blocks™

NCCN Guidelines Index
Table of Contents
Discussion

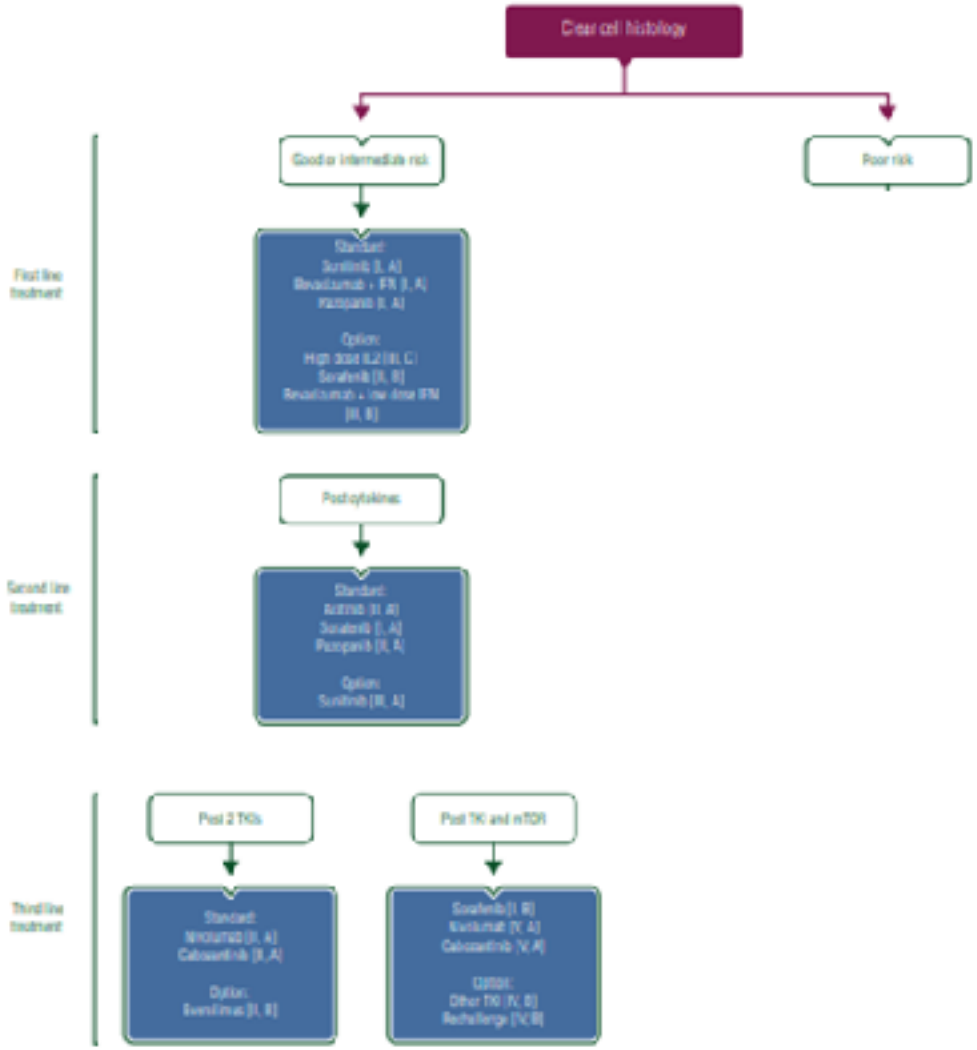


Updated European Association of Urology Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer



B. Ljungberg. EAU Clinical Guideline. 2017

Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up



Annals of Oncology 27 (Supplement 5): v58–v68, 2016

SEOM clinical guideline for treatment of kidney cancer (2017)

Recommendations

- In patients with good or intermediate prognosis, sunitinib and pazopanib are the most recommended options for the first-line treatment of mRCC with clear-cell histology. Level of evidence: I., Grade of recommendation: A.

Clin Transl Oncol (2018) 20:47–56

Fases III

N=750
- CCRm
- Histología de células claras
- Sin tratamiento sistémico previo
- ECOG PS 0 o 1

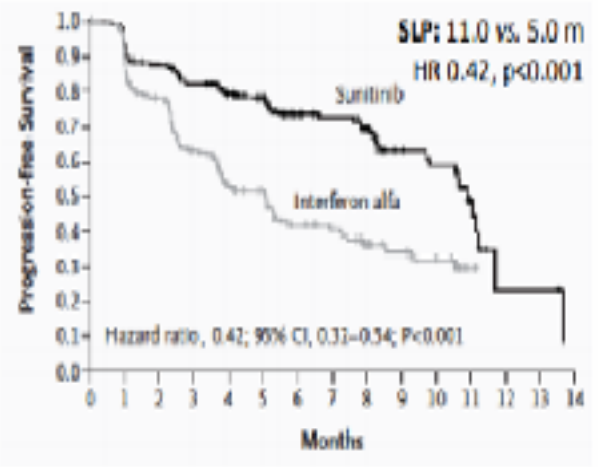
Objetivo 1º: SLP

RANDOMIZACION

SUNITINIB
50 mg diario (esquema 4/2)

IFNα
3 MU s.c. 3/s, primera semana
6 MU s.c. 3s, segunda semana
9 MU s.c. 3/s, posteriorm

Mediana de SLP



N=435
- CCRm
- Histología de células claras > 50%
- Sin tratamiento sistémico previo (Permitidas citoquinas)
- Pxco favorable/intermedio

Objetivo 1º: SLP

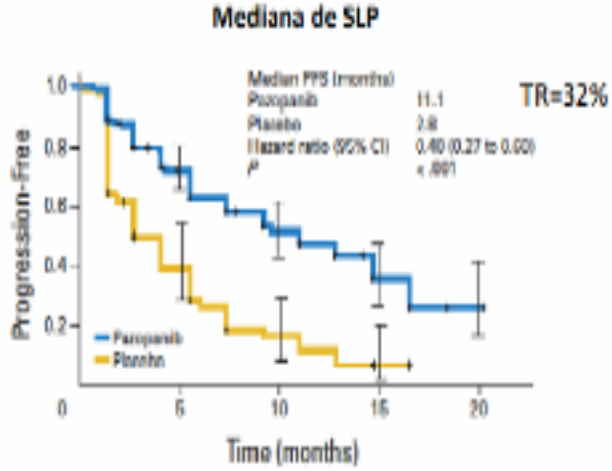
RANDOMIZACION

2:1

PAZOPANIB
800 mg diario

PLACEBO

Mediana de SLP



Motzer RJ. N Engl J Med 2007;356 (2):115
Motzer RJ. J Clin Oncol 2009; 27 (22):3584
Sternberg CN. J Clin Oncol 2010; 28 (6):1061
Sternberg CN. Eur J Cancer 2013; 49:1287

Fases III

AVOREN

N=649
- CCRm
- Componente céls claras > 50%
- No tratamiento sistémico previo
- Karnofsky ≥ 70
- Nefrectomía previa

Objetivo 1º: SG -> SLP

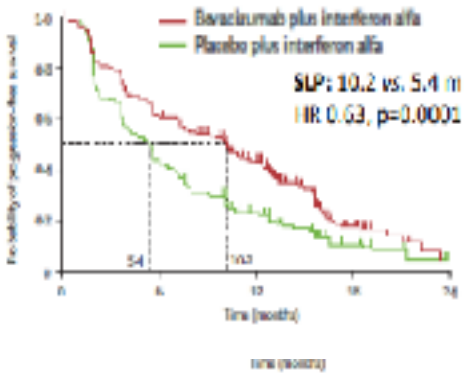
RANDOMIZACION

BEVACIZUMAB
10 mg/kg/2 semanas i.v.
IFNα
9 MU 3vc/sem s.c.

IFNα
9 MU s.c. 3vc/s s.c.
PLACEBO

AVOREN

Mediana de SLP



TR=31%

CALGB 90206

N=732
- CCRm
- Componente céls claras
- No tratamiento sistémico previo
- Karnofsky ≥ 70

Objetivo 1º: SG

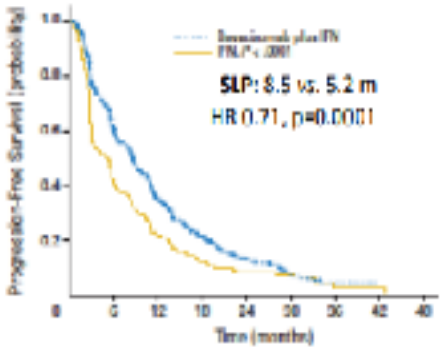
RANDOMIZACION

BEVACIZUMAB
10 mg/kg/2 semanas i.v.
IFNα
9 MU 3vc/sem s.c.

IFNα
9 MU s.c. 3vc/s s.c.

Esc
Rini BI.

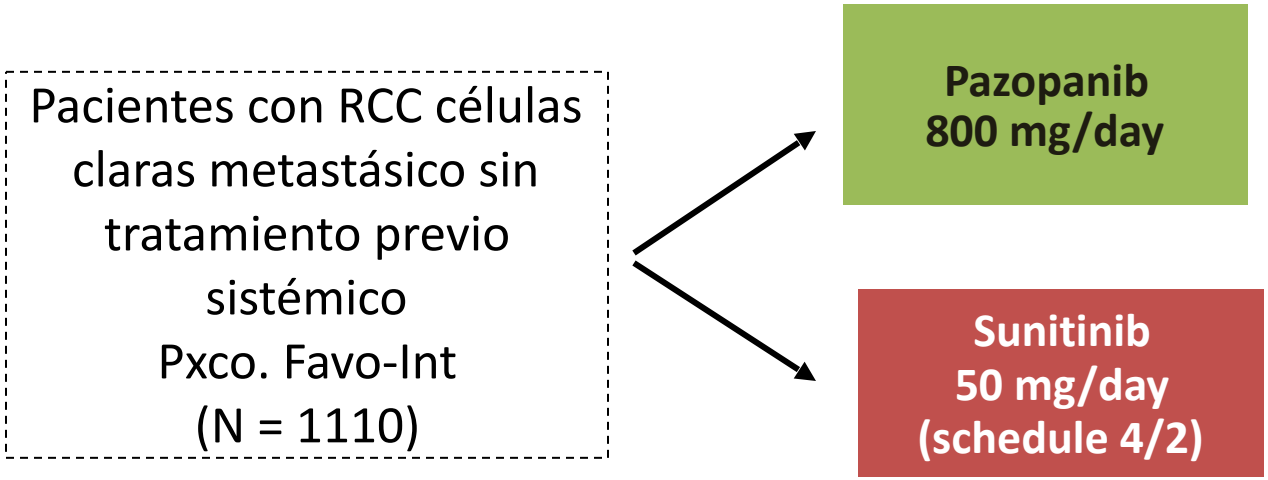
CALGB 90206



TR=25.5
%

Escudier B. Lancet 2007;370:2103
Rini BI. J Clin Oncol 2008;26(33):5422

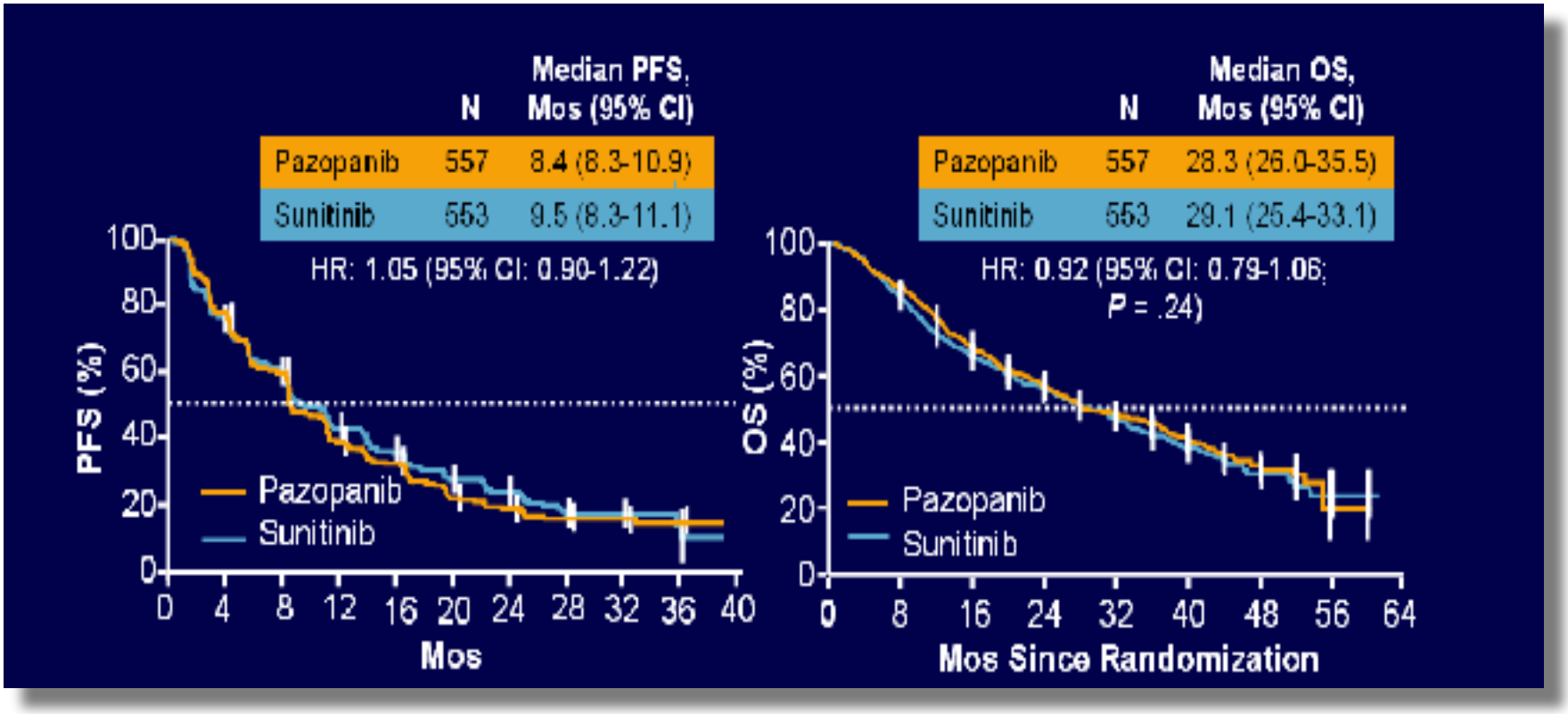
COMPARZ (Fase III)
Primera línea Pazopanib vs Sunitinib
como tratamiento de 1ª línea para RCC metastásico



- Objetivo primario: PFS
- Objetivos secundarios: OS, ORR, tiempo hasta la respuesta, seguridad, QoL, utilización de recursos sanitarios

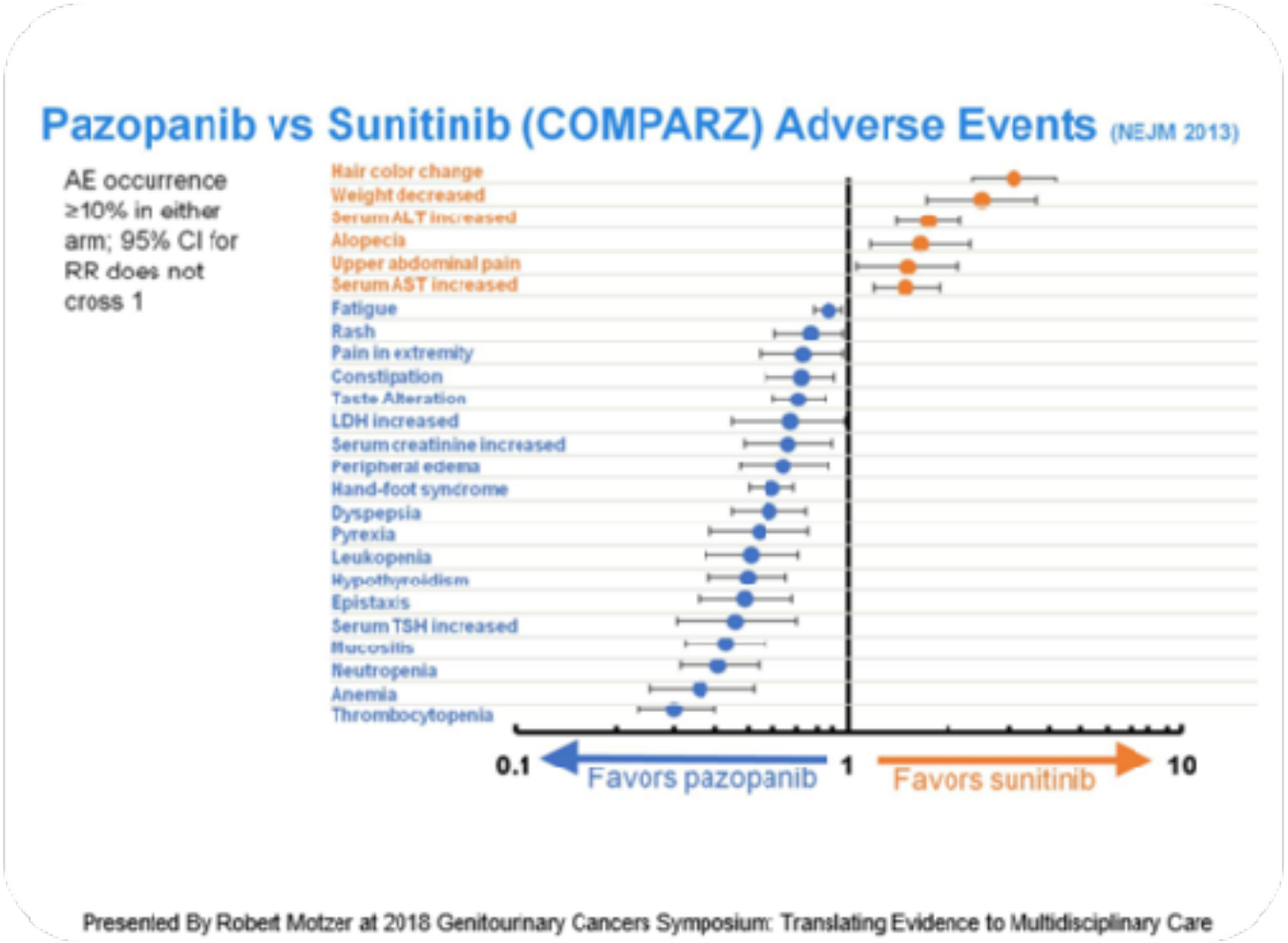
Motzer RJ, et al. N Engl J Med. 2013;369:722-731

COMPARZ (Fase III): EFICACIA



Motzer RJ, et al. N Engl J Med. 2013;369:722-731
Motzer RJ, et al. N Engl J Med. 2014;370:1769-1770

COMPARZ: AEs



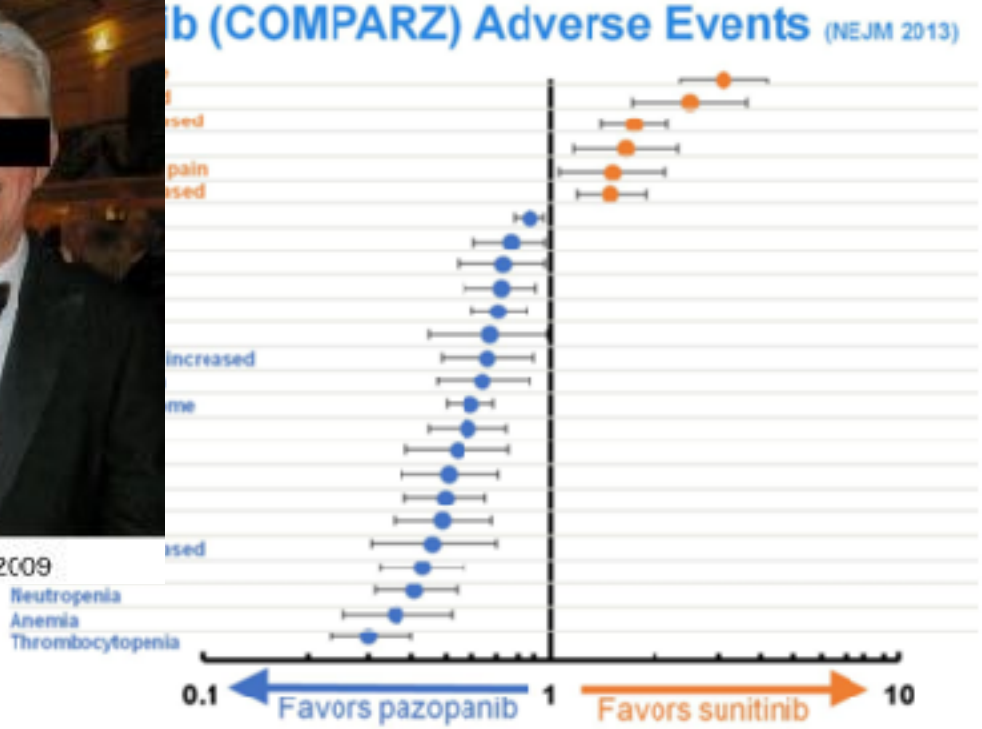
Presented By Robert Motzer at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

COMPARZ: AEs

With kind permission

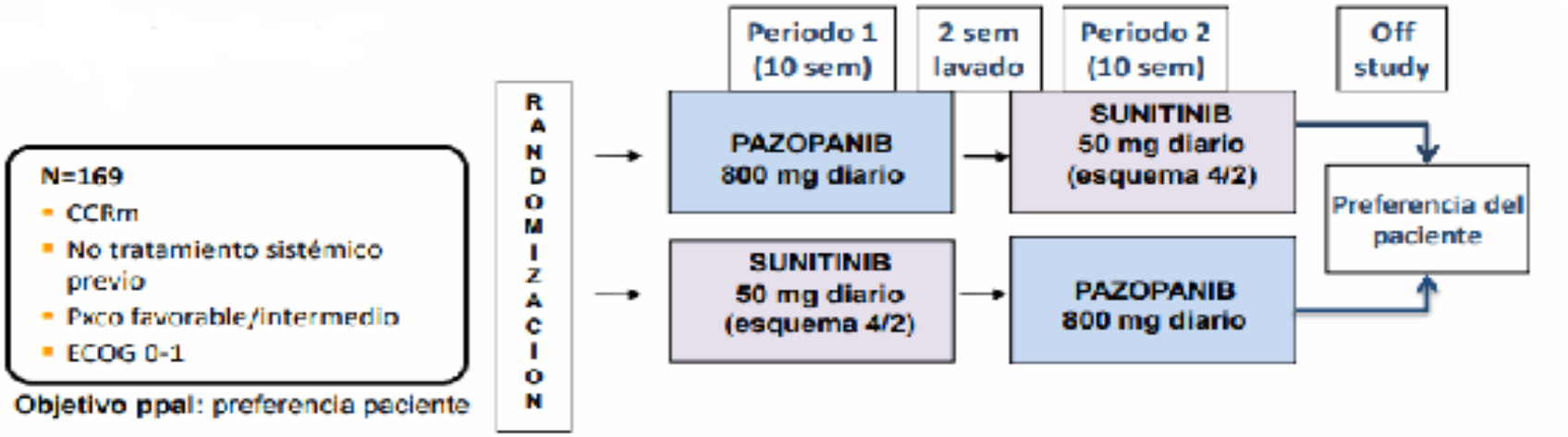
Oct 2007

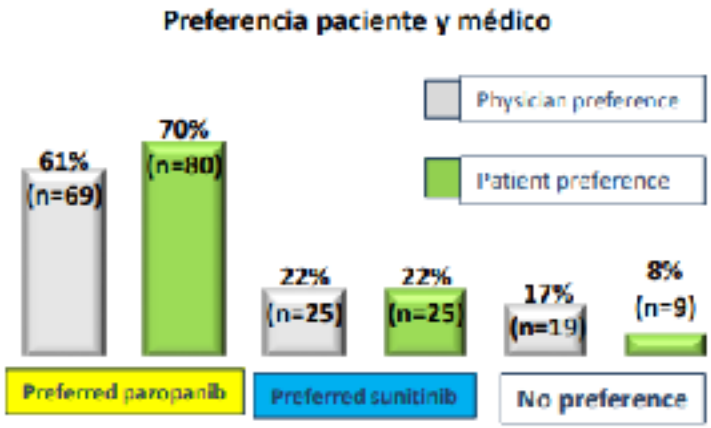
Oct 2009

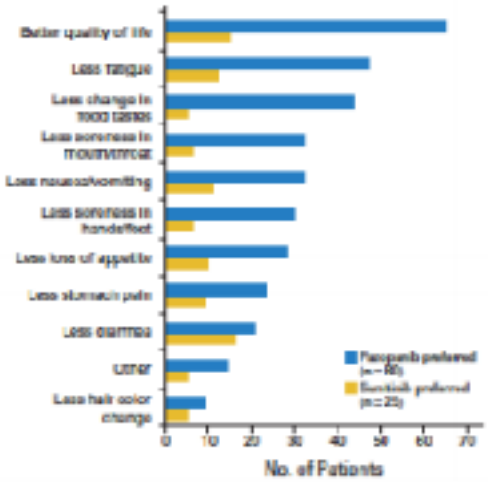


Presented By Robert Motzer at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

Fases III: Pisces







Escudier B. J Clin Oncol 2014;32(14):1412

Caso clínico

1

¿Y si el paciente es de mal pronóstico?

Hemograma:

Hb:10 g/dl

Calcio corregido: 9.72 mg/dl

Tiempo desde el diagnóstico hasta tto sistémico < 1 año

KPS: 70%

IMDC risk: Pobre
(≥3 factores de riesgo)

Paciente de 62 años con RCC.Tras 11 meses desde la cirugía, presenta progresión pulmonar y ganglionar

El paciente desea tratamiento

NCCN

FIRST-LINE THERAPY
(alphabetical by category and preference)

Predominant clear cell histology	• **Clinical trial** • **Pazopanib (category 1, preferred)** • **Sunitinib (category 1, preferred)** • **Bevacizumab + interferon alfa-2b (category 1)** • **Temsirolimus (category 1 for poor-prognosis patients,[h] category 2B for selected patients of other risk groups)** • **Axitinib** • **Cabozantinib (for poor- and intermediate-risk groups)[i]** • **High-dose IL-2 for selected patients[j]** • **Active surveillance for select, asymptomatic patients[k]**

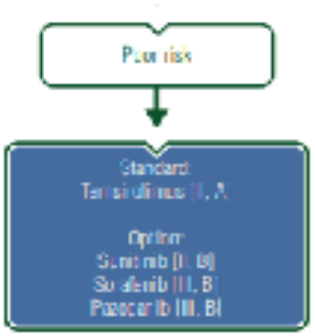
and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

SEOM

Recommendations

- In patients with good or intermediate prognosis, sunitinib and pazopanib are the most recommended options for the first-line treatment of mRCC with clear-cell histology. Level of evidence: I., Grade of recommendation: A.
- For patients with poor prognosis, temsirolimus is the only option supported by a phase III trial. Level of evidence: I. Grade of recommendation: A.
- Sunitinib and pazopanib have also shown benefit in the treatment of poor-prognosis patients. Level of evidence: III. Grade of recommendation: B.

ESMO



Hudges G. NenglJ. 2007
NCCN Guideline Kidney Cancer version 3.2018
Clin Transl Oncol (2018) 20:47–56
Annals of Oncology 27 (Supplement 5): v58–v68, 2016

NCCN

FIRST-LINE THERAPY
(alphabetical by category and preference)

Predominant clear cell histology →

- Clinical trial
- Pazopanib (category 1, preferred)
- Sunitinib (category 1, preferred)
- Bevacizumab + interferon alfa-2b (category 1)
- Temsirolimus (category 1 for poor-prognosis patients,[h] category 2B for selected patients of other risk groups)
- Axitinib
- Cabozantinib (for poor- and intermediate-risk groups)[i]
- High-dose IL-2 for selected patients[j]
- Active surveillance for select, asymptomatic patients[k]

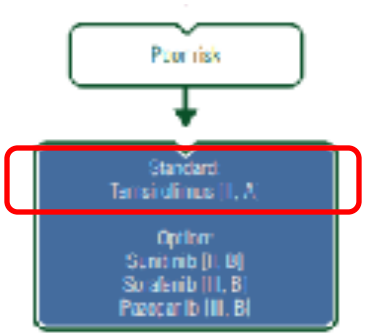
and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

SEOM

Recommendations

- In patients with good or intermediate prognosis, sunitinib and pazopanib are the most recommended options for the first-line treatment of mRCC with clear-cell histology. Level of evidence: I., Grade of recommendation: A.
- For patients with poor prognosis, temsirolimus is the only option supported by a phase III trial. Level of evidence: I. Grade of recommendation: A.
- Sunitinib and pazopanib have also shown benefit in the treatment of poor-prognosis patients. Level of evidence: III. Grade of recommendation: B.

ESMO

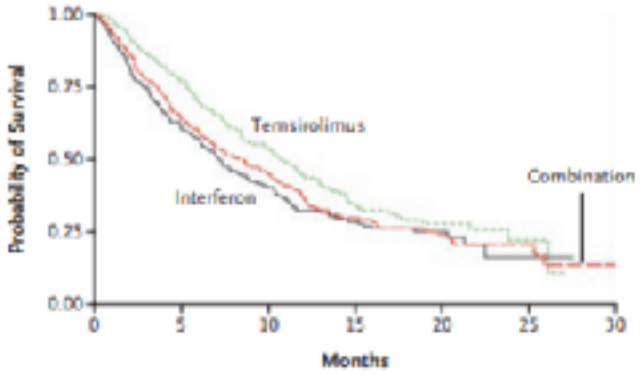


Hudges G. NenglJ. 2007
NCCN Guideline Kidney Cancer version 3.2018
Clin Transl Oncol (2018) 20:47–56
Annals of Oncology 27 (Supplement 5): v58–v68, 2016

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Temsirolimus, Interferon Alfa, or Both for Advanced Renal-Cell Carcinoma



No. at Risk							
Interferon	207	126	80	42	15	3	0
Temsirolimus	209	159	110	56	19	3	0
Combination	210	135	93	50	17	7	2

Hudes G. N Eng J Med 2007;356:2271-81

NCCN

FIRST-LINE THERAPY
(alphabetical by category and preference)

Predominant clear cell histology	• **Clinical trial** • **Pazopanib (category 1, preferred)** • **Sunitinib (category 1, preferred)** • **Bevacizumab + interferon alfa-2b (category 1)** • **Temsirolimus (category 1 for poor-prognosis patients,[h] category 2B for selected patients of other risk groups)** • **Axitinib** • **Cabozantinib (for poor- and intermediate-risk groups)[i]** • **High-dose IL-2 for selected patients[j]** • **Active surveillance for select, asymptomatic patients[k]**

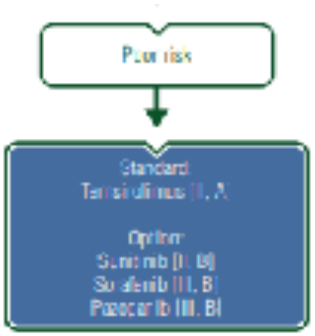
and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

SEOM

Recommendations

- In patients with good or intermediate prognosis, sunitinib and pazopanib are the most recommended options for the first-line treatment of mRCC with clear-cell histology. Level of evidence: I., Grade of recommendation: A.
- For patients with poor prognosis, temsirolimus is the only option supported by a phase III trial. Level of evidence: I. Grade of recommendation: A.
- Sunitinib and pazopanib have also shown benefit in the treatment of poor-prognosis patients. Level of evidence: III. Grade of recommendation: B.

ESMO



Hudges G. NenglJ. 2007
NCCN Guideline Kidney Cancer version 3.2018
Clin Transl Oncol (2018) 20:47–56
Annals of Oncology 27 (Supplement 5): v58–v68, 2016

NCCN

FIRST-LINE THERAPY
(alphabetical by category and preference)

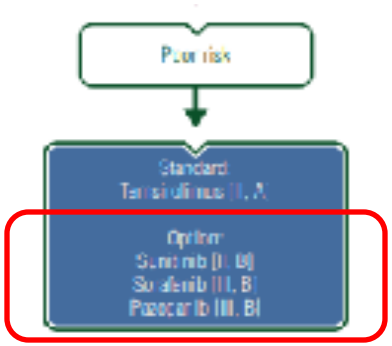
Predominant clear cell histology →	• **Clinical trial** • **Pazopanib (category 1, preferred)** • **Sunitinib (category 1, preferred)** • **Bevacizumab + interferon alfa-2b (category 1)** • **Temsirolimus (category 1 for poor-prognosis patients,[h] category 2B for selected patients of other risk groups)** • **Axitinib** • **Cabozantinib (for poor- and intermediate-risk groups)[i]** • **High-dose IL-2 for selected patients[j]** • **Active surveillance for select, asymptomatic patients[k]** **and** **Best supportive care:[l]** See NCCN Guidelines for Palliative Care

SEOM

Recommendations

- In patients with good or intermediate prognosis, sunitinib and pazopanib are the most recommended options for the first-line treatment of mRCC with clear-cell histology. Level of evidence: I., Grade of recommendation: A.
- For patients with poor prognosis, temsirolimus is the only option supported by a phase III trial. Level of evidence: I. Grade of recommendation: A.
- Sunitinib and pazopanib have also shown benefit in the treatment of poor-prognosis patients. Level of evidence: III. Grade of recommendation: B.

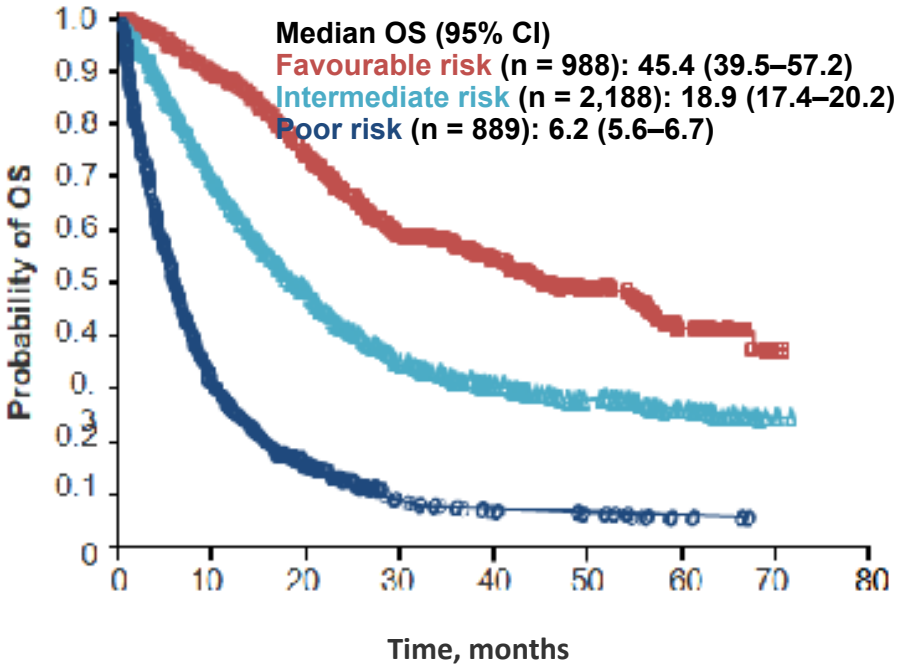
ESMO



Hudges G. NenglJ. 2007
NCCN Guideline Kidney Cancer version 3.2018
Clin Transl Oncol (2018) 20:47–56
Annals of Oncology 27 (Supplement 5): v58–v68, 2016

Global Expanded Access Programme: Real-world Experience of Sunitinib in aRCC

Global expanded access trial of 4,543 previously treated and treatment-naïve patients with aRCC who received ≥1 dose of sunitinib



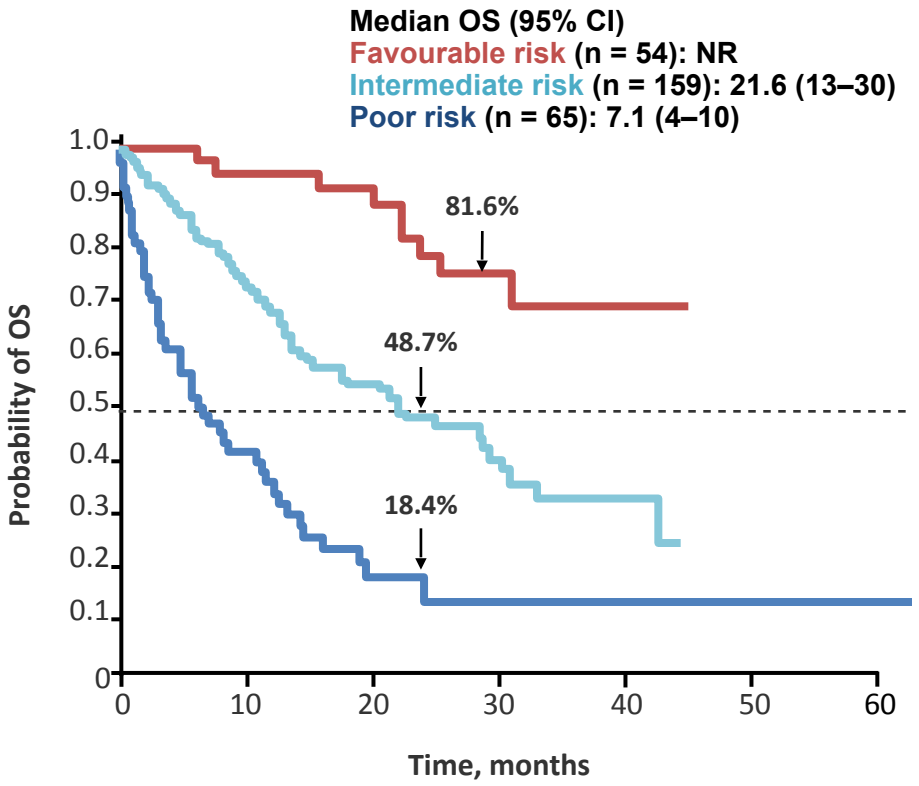
MSKCC risk	N	Median PFS, months (95% CI)	Median OS, months (95% CI)
Overall	4,219	9.4 (8.8–10.0)	18.7 (17.5–19.5)
Favourable	988	15.0 (13.8–16.3)	56.5 (41.6–NR)
Intermediate	2188	10.6 (9.4–11.1)	20.0 (18.4–21.3)
Poor	889	5.4 (5.1–5.7)	9.1 (8.4–9.7)

NR, not reached.

Gore ME et al. *Br J Cancer.* 2015;113:12–19

SOGUG SPAZO: First-line Pazopanib in Patients With aRCC

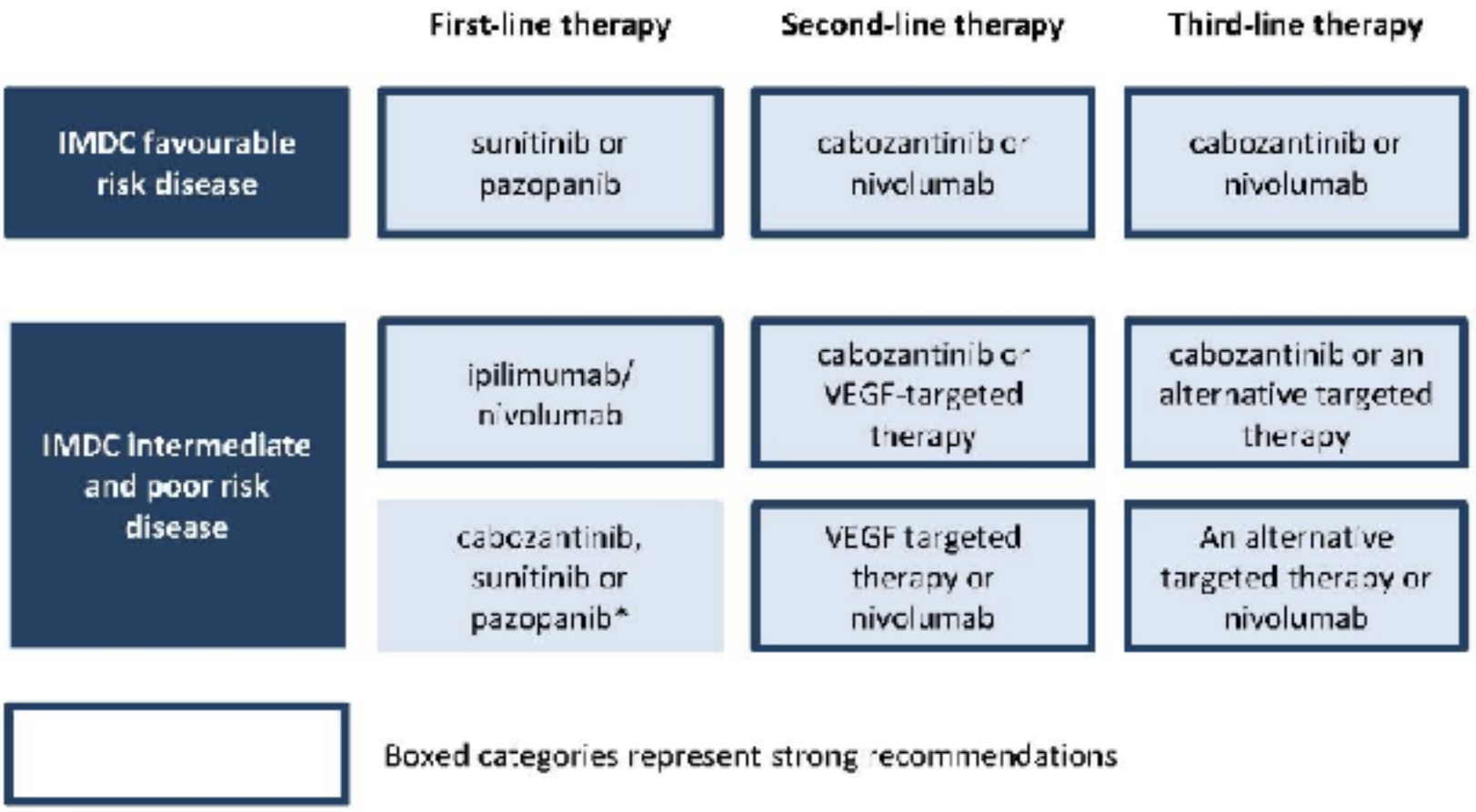
Retrospective review of 278 patients treated with first-line pazopanib (April 2011–June 2014) across 34 centres in Spain, and externally validated



IMDC risk	N	Median PFS, months (95% CI)	Median OS, months (95% CI)
Overall	278	11.1 (9–13)	22.2 (16–29)
Favourable	54	32.4 (14–50)	NR
Intermediate	159	11.1 (9–13)	21.6 (13–30)
Poor	65	4 (2–6)	7.1 (4–10)

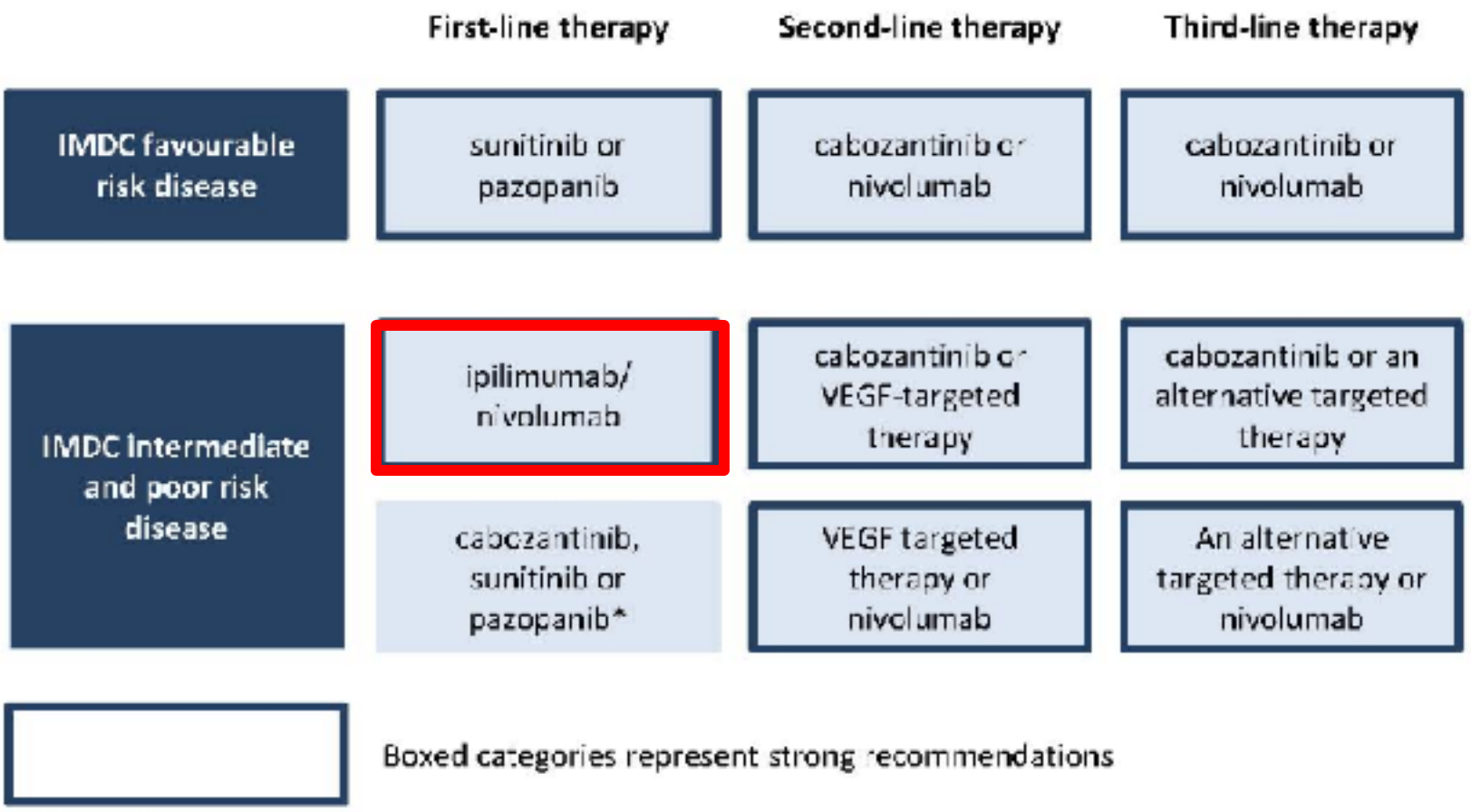
SOGUG, Spanish Oncologic Genitourinary Group.
Pérez-Valderrama B et al. *Ann Oncol.* 2016;27:706–711.

Updated European Association of Urology Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer



B. Ljungberg. EAU Clinical Guideline. 2017

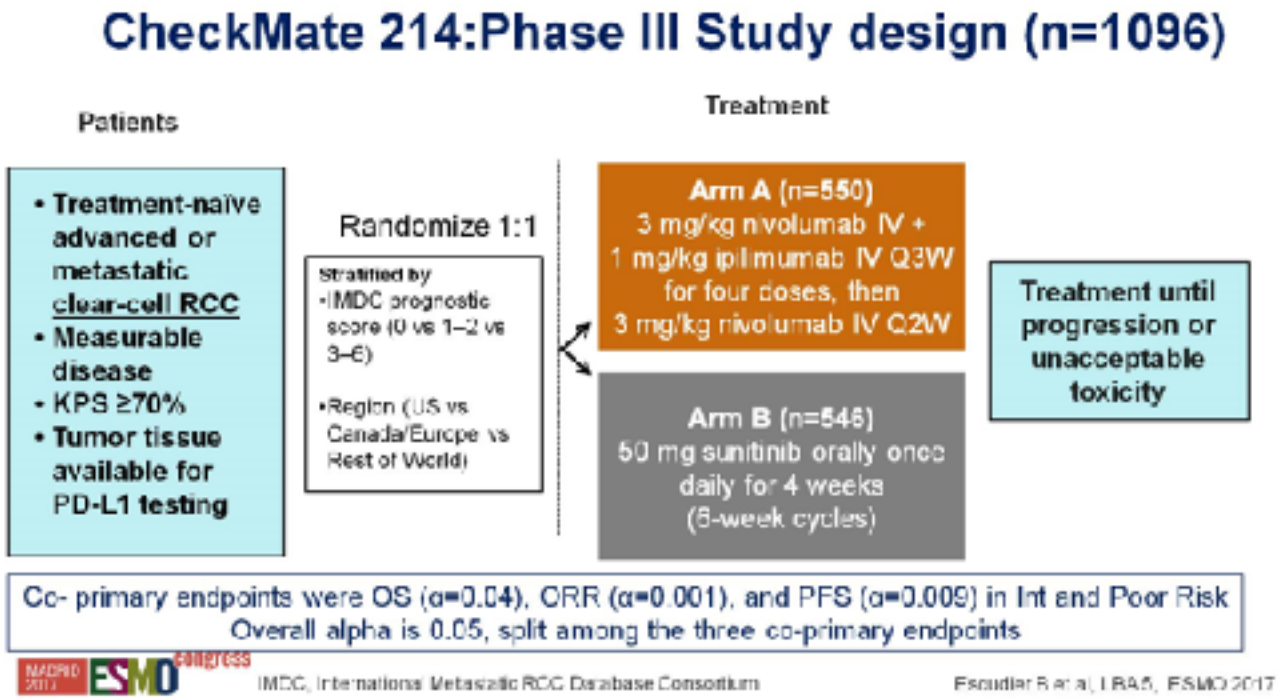
Updated European Association of Urology Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer.



B. Ljungberg. EAU Clinical Guideline. 2017

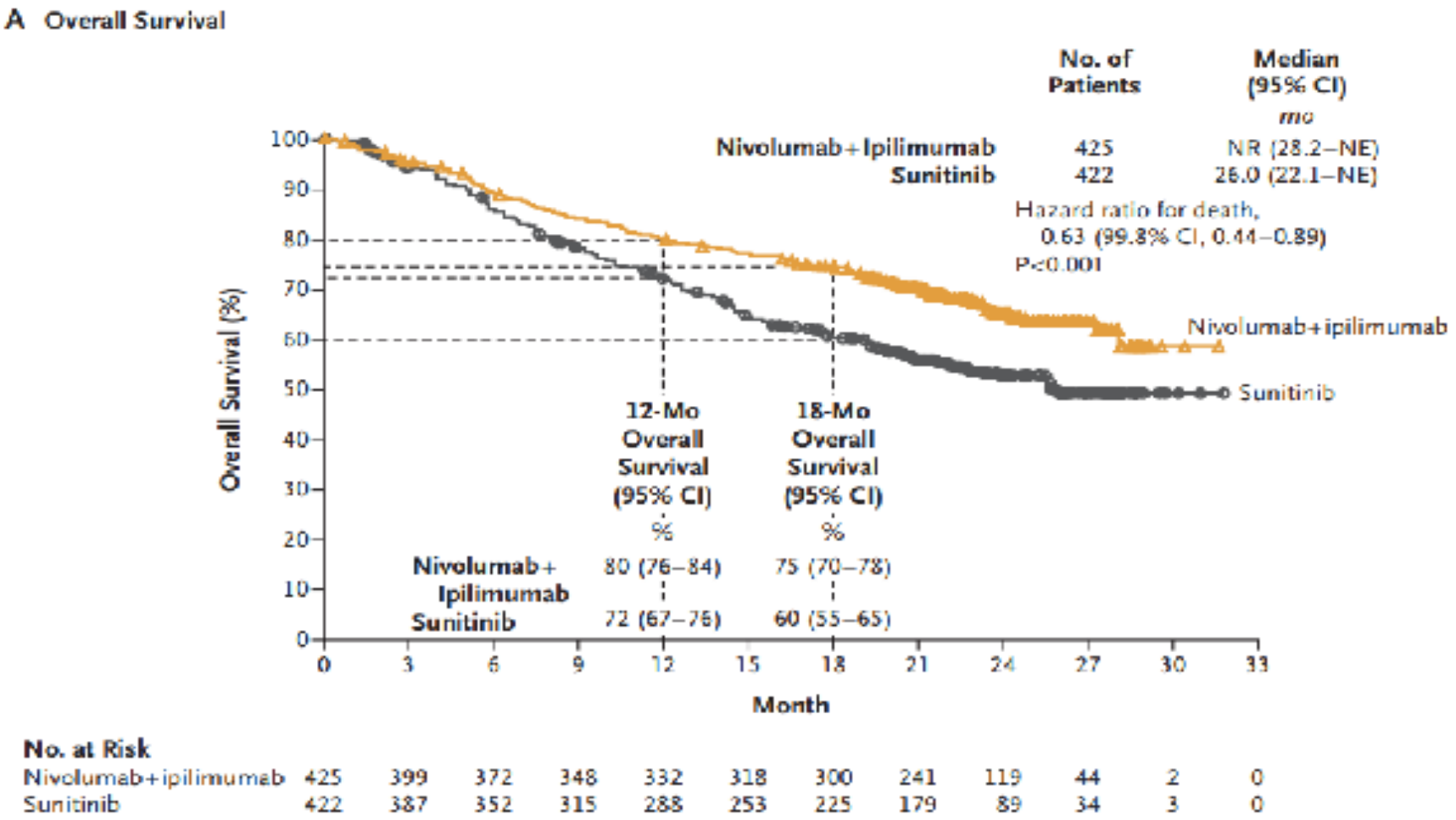
CheckMate 214: Ensayo fase III

Nivolumab + Ipilimumab vs Sunitinib en pacientes RCC avanzado o MTX sin tratamiento previo



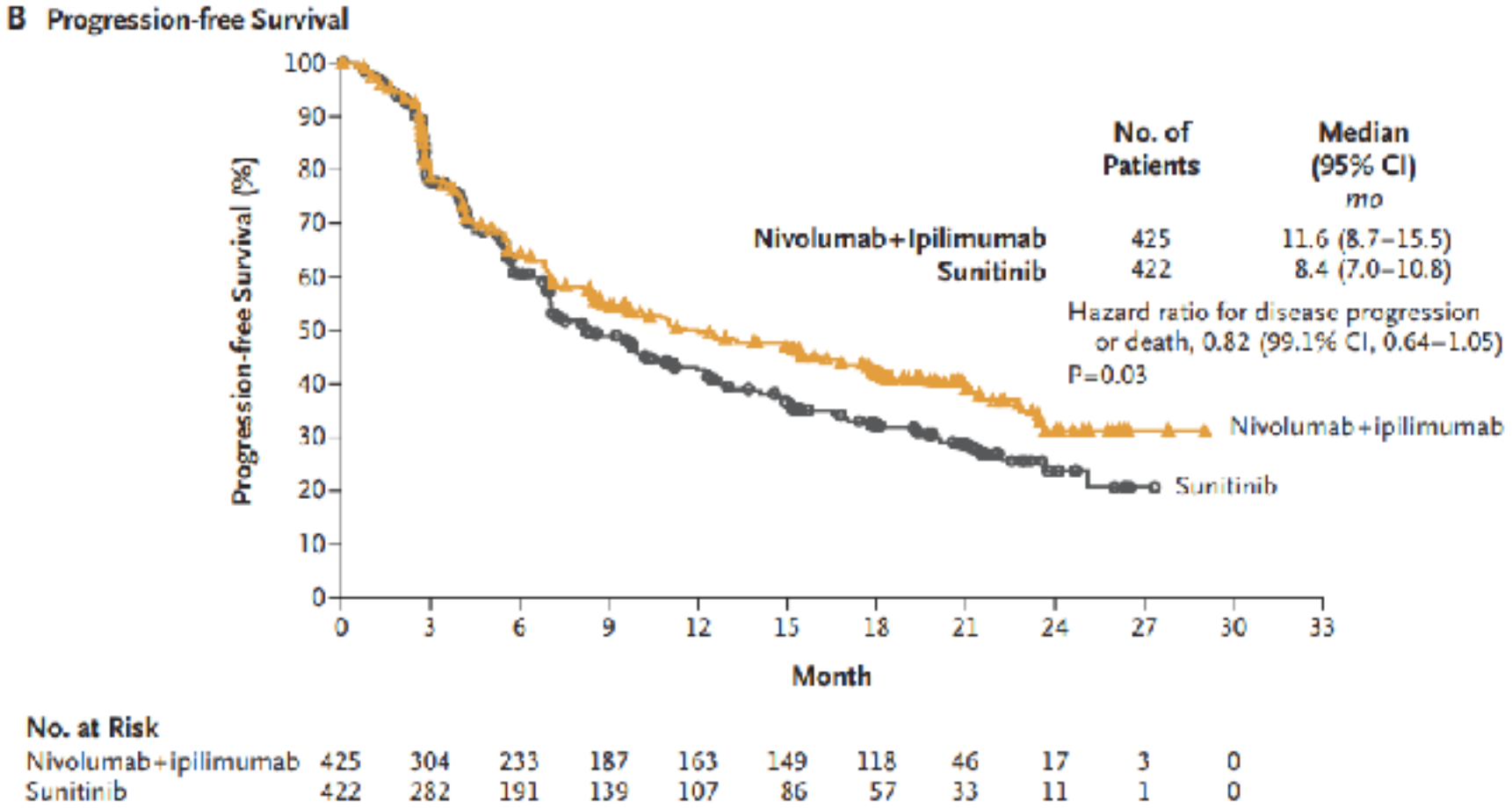
Presented By Cora Sternberg at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

CheckMate 214: OS (Objetivos Co-primarios) en IMDC riesgo pobre/intermedio



Motzer RJ. NEJM. 2018

CheckMate 214: PFS (Objetivos Co-primarios) en IMDC riesgo pobre/intermedio



Motzer RJ. NEJM. 2018

CheckMate 214: ORR en IMDC en pacientes con riesgo pobre/intermedio

Table 2. Antitumor Activity in IMDC Intermediate- and Poor-Risk Patients.*

Variable	Nivolumab plus Ipilimumab (N=425)	Sunitinib (N=422)
Confirmed objective response rate — % (95% CI)†	42 (37–47)‡	27 (22–31)‡
Confirmed best overall response — no. (%)†		
Complete response	40 (9)‡§	5 (1)‡§
Partial response	137 (32)	107 (25)
Stable disease	133 (31)	188 (45)
Progressive disease	83 (20)	72 (17)
Unable to determine or not reported	32 (8)	50 (12)
Median time to response (range) — mo	2.8 (0.9–11.3)	3.0 (0.6–15.0)
Median duration of response (95% CI) — mo	NR (21.8–NE)	18.2 (14.8–NE)
Patients with ongoing response — no./total no. (%)	128/177 (72)	71/112 (63)

Motzer RJ. NEJM. 2018

CheckMate 214: Seguridad en todos los pacientes tratados

Table 3. Treatment-Related Adverse Events Occurring in 15% or More of Treated Patients in Either Group.*

Event	Nivolumab plus Ipilimumab (N=547)		Sunitinib (N=535)	
	Any Grade†	Grade 3 or 4	Any Grade‡	Grade 3 or 4
	number of patients (percent)			
All events	509 (93)	250 (46)	521 (97)	335 (63)
Fatigue	202 (37)	23 (4)	264 (49)	49 (9)
Pruritus	154 (28)	3 (<1)	49 (9)	0
Diarrhea	145 (27)	21 (4)	278 (52)	28 (5)
Rash	118 (22)	8 (1)	67 (13)	0
Nausea	109 (20)	8 (1)	202 (38)	6 (1)
Increased lipase level	90 (16)	56 (10)	58 (11)	35 (7)
Hypothyroidism	85 (16)	2 (<1)	134 (25)	1 (<1)
Decreased appetite	75 (14)	7 (1)	133 (25)	5 (<1)
Asthenia	72 (13)	8 (1)	91 (17)	12 (2)
Vomiting	59 (11)	4 (<1)	110 (21)	10 (2)
Anemia	34 (6)	2 (<1)	83 (16)	24 (4)
Dysgeusia	31 (6)	0	179 (33)	1 (<1)
Stomatitis	23 (4)	0	149 (28)	14 (3)
Dyspepsia	15 (3)	0	96 (18)	0
Mucosal inflammation	13 (2)	0	152 (28)	14 (3)
Hypertension	12 (2)	4 (<1)	216 (40)	85 (16)
Palmar–plantar erythrodysesthesia	5 (<1)	0	231 (43)	49 (9)
Thrombocytopenia	2 (<1)	0	95 (18)	25 (5)

Motzer RJ. NEJM. 2018

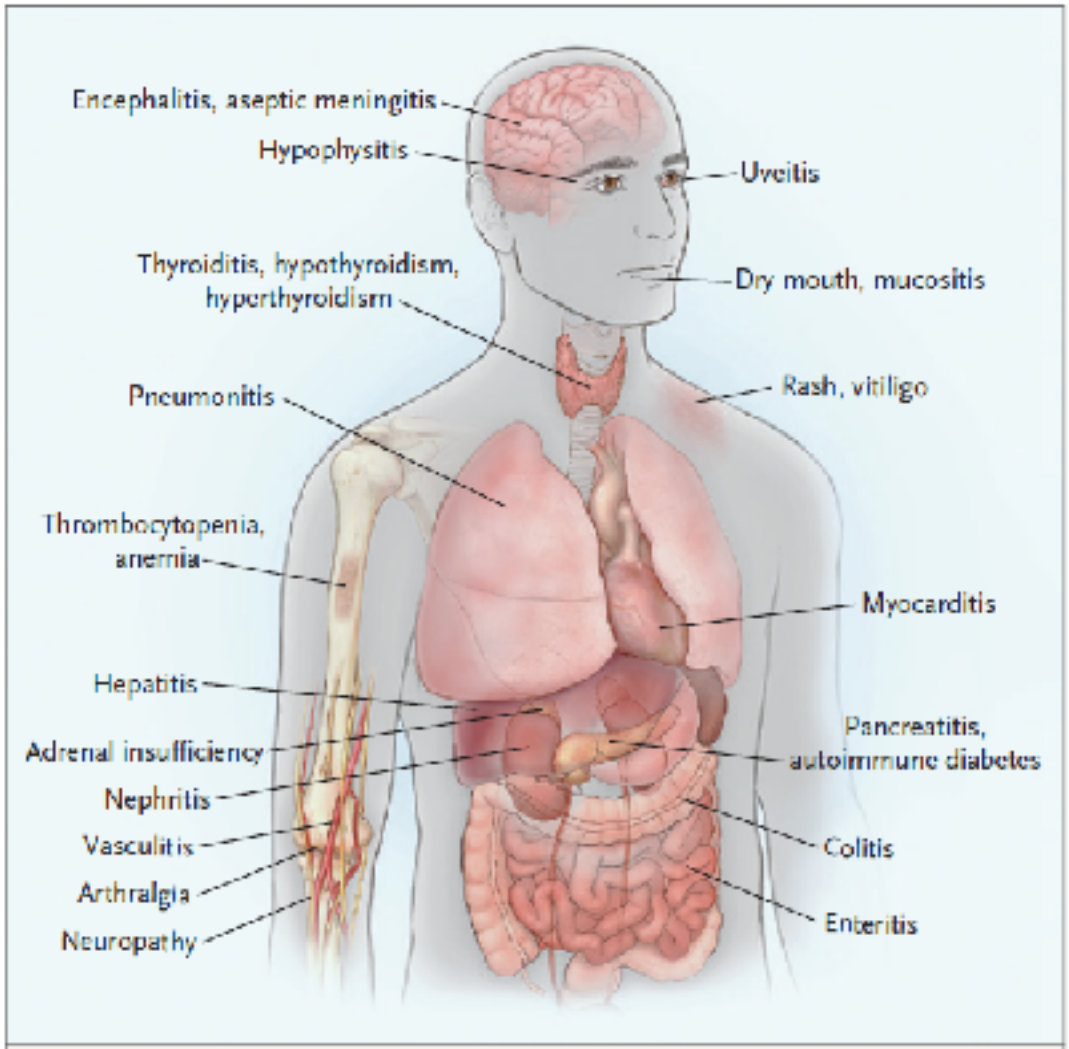


Figure 1. Organs Affected by Immune Checkpoint Blockade.

Immune checkpoint blockade can result in inflammation of any organ. Shown are the most common immune-related adverse events that clinicians encounter in patients treated with immune checkpoint blockade.

Toxicidades de los nuevos fármacos inhibidores de checkpoint, mecanismo de muerte programada celular.

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Immune-Related Adverse Events Associated with Immune Checkpoint Blockade

SORRY

THIS ITEM IS TEMPORARILY

OUT OF STOCK

Please check back soon for updates

EAU

First-line therapy

IMDC favourable risk disease	sunitinib or pazopanib
IMDC intermediate and poor risk disease	ipilimumab/ nivolumab
	cabozantinib, sunitinib or pazopanib*

Boxed categories represent strong recommendations

NCCN

FIRST-LINE THERAPY
(alphabetical by category and preference)

Predominant clear cell histology →

- **Clinical trial**
- **Pazopanib (category 1, preferred)**
- **Sunitinib (category 1, preferred)**
- **Bevacizumab + interferon alfa-2b (category 1)**
- **Temsirolimus (category 1 for poor-prognosis patients,[h] category 2B for selected patients of other risk groups)**
- **Axitinib**
- **Cabozantinib (for poor- and intermediate-risk groups)[i]**
- **High-dose IL-2 for selected patients[j]**
- **Active surveillance for select, asymptomatic patients[k]**

and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

B. Ljungberg. EAU Clinical Guideline. 2017
NCCN Guidelines Version 3.2018. Kidney cancer

EAU

First-line therapy

IMDC favourable risk disease	sunitinib or pazopanib
IMDC intermediate and poor risk disease	ipilimumab/ nivolumab
	cabozantinib, sunitinib or pazopanib*

Boxed categories represent strong recommendations

NCCN

FIRST-LINE THERAPY
(alphabetical by category and preference)

Predominant clear cell histology →

- Clinical trial
- **Pazopanib (category 1, preferred)**
- **Sunitinib (category 1, preferred)**
- **Bevacizumab + interferon alfa-2b (category 1)**
- **Temsirolimus (category 1 for poor-prognosis patients,[h] category 2B for selected patients of other risk groups)**
- ~~Axitinib~~
- **Cabozantinib (for poor- and intermediate-risk groups)[i]**
- ~~High-dose IL-2 for selected patients[j]~~
- **Active surveillance for select, asymptomatic patients[k]**

and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

B. Ljungberg. EAU Clinical Guideline. 2017
NCCN Guidelines Version 3.2018. Kidney cancer

VOLUME 35 · NUMBER 6 · FEBRUARY 20, 2017

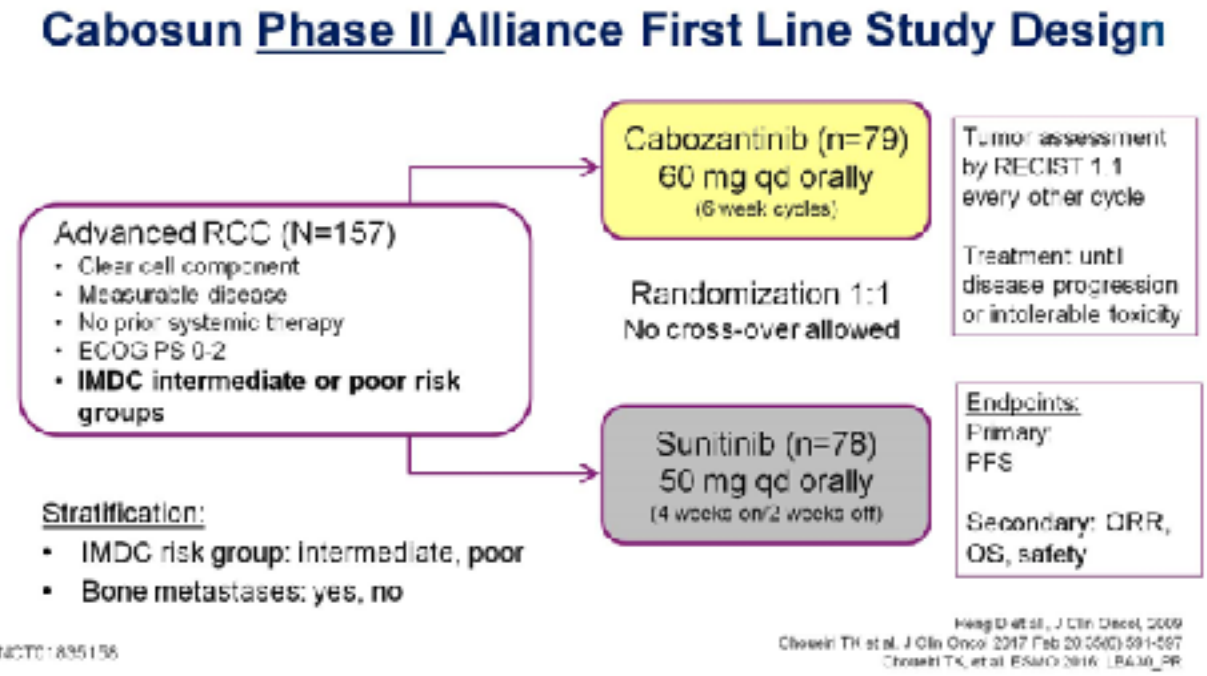
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Cabozantinib Versus Sunitinib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma of Poor or Intermediate Risk: The Alliance A031203 CABOSUN Trial

Toni K. Choueiri, Susan Halabi, Ben L. Sanford, Olwen Hahn, M. Dror Michaelson, Meghana K. Walsh, Darren R. Feldman, Thomas Olencki, Joel Picus, Eric J. Small, Shaker Dakhil, Daniel J. George, and Michael J. Morris

CABOSUN Ensayo fase II randomizado: Primera línea en RCC metastásico Cabozantinib vs Sunitinib



Presented By Dora Stambolic at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

CABOSUN Ensayo fase II randomizado: Primera línea en RCC metastásico
Cabozantinib vs Sunitinib

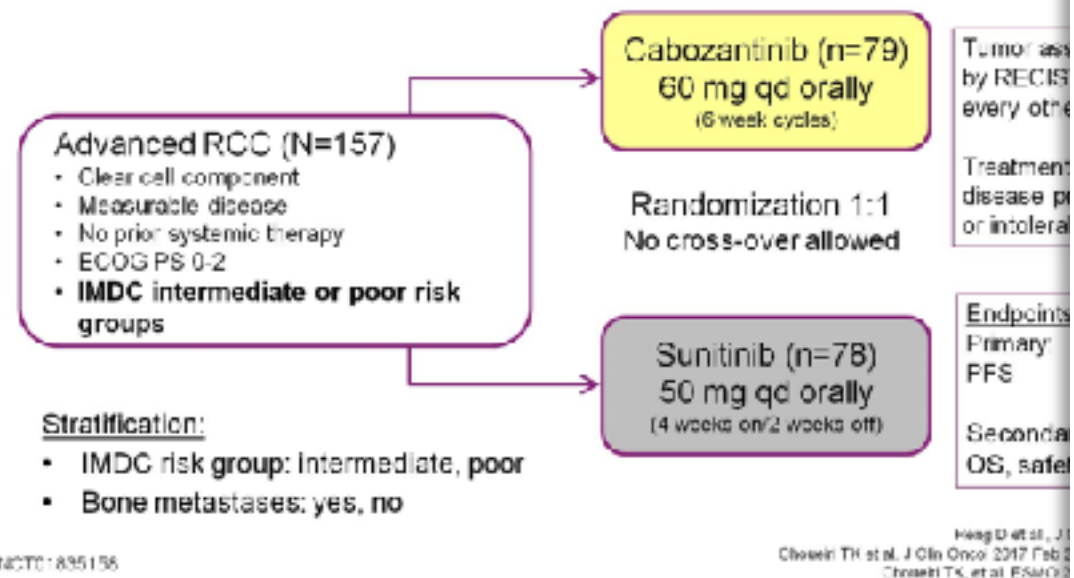


Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	No. (%) Cabozantinib (n = 79)	Sunitinib (n = 78)	Total (N = 157)
Age, years			
Median	63.0	64.0	63.0
Range	40.0-82.0	31.0-87.0	31.0-87.0
Sex			
Male	66 (83.5)	57 (73.1)	123 (78.3)
Female	13 (16.5)	21 (26.9)	34 (21.7)
Ethnic origin			
White	70 (88.6)	75 (96.2)	145 (92.4)
Black or African American	3 (3.8)	2 (2.6)	5 (3.2)
Native Hawaiian or Pacific Islander	1 (1.3)	0 (0.0)	1 (0.6)
Asian	1 (1.3)	0 (0.0)	1 (0.6)
American Indian or Alaska Native	1 (1.3)	0 (0.0)	1 (0.6)
Not reported	1 (1.3)	0 (0.0)	1 (0.6)
Unknown (patient unsure)	2 (2.5)	1 (1.3)	3 (1.9)
ECOG PS			
0	36 (45.6)	36 (46.2)	72 (45.9)
1	33 (41.8)	32 (41.0)	65 (41.4)
2	10 (12.7)	10 (12.8)	20 (12.7)
IMDC risk group			
Intermediate	64 (81.0)	63 (80.8)	127 (80.9)
Poor	15 (19.0)	15 (19.2)	30 (19.1)
Bone metastases			
Yes	29 (36.7)	28 (35.9)	57 (36.3)
No	50 (63.3)	50 (64.1)	100 (63.7)
Prior nephrectomy			
Yes	57 (72.2)	60 (76.9)	117 (74.5)
No	22 (27.8)	18 (23.1)	40 (25.5)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; IMDC, International Metastatic Renal Cell Carcinoma DataBase Consortium; PS, performance status.

Presented By Dora Stambolic at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisci

CABOSUN Ensayo fase II randomizado: Primera línea en RCC metastásico
Cabozantinib vs Sunitinib

Cabosun Phase II Alliance First Line Study De

Advanced RCC (N=157)
- Clear cell component
- Measurable disease
- No prior systemic therapy
- ECOG PS 0-2
- **IMDC intermediate or poor risk groups**

Cabozantinib (n=79)
60 mg qd orally
(6 week cycles)

Randomization 1:1
No cross-over allowed

Sunitinib (n=78)
50 mg qd orally
(4 weeks on/2 weeks off)

Stratification:
- IMDC risk group: Intermediate, poor
- Bone metastases: yes, no

Tumor ass… by RECIST … every oth…

Treatment … disease p… or intolera…

Endpoints
Primary
PFS

Seconda…
OS, safet…

NCT0…835156

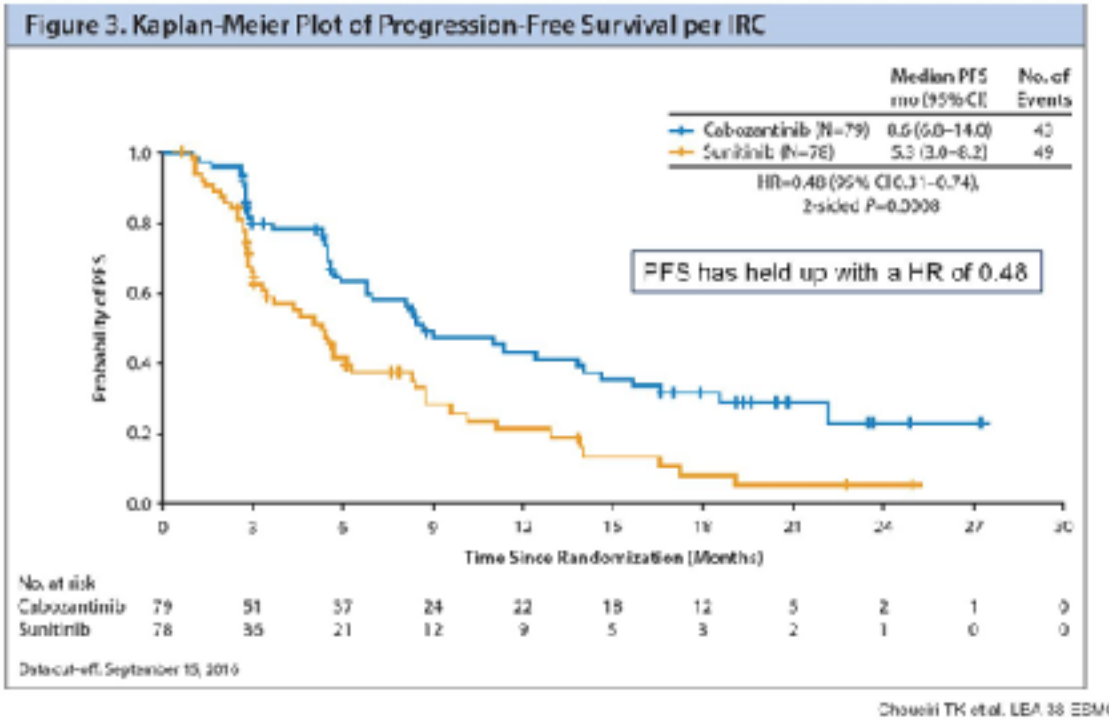
Presented By Dora Stambolic at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidiscipl…

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Cabozantinib (n = 79) No. (%)	Sunitinib (n = 78) No. (%)	Total (N = 157) No. (%)
Age, years			
Median	63.0	64.0	63.0
Range	40.0-82.0	31.0-87.0	31.0-87.0
Sex			
Male	66 (83.5)	57 (73.1)	123 (78.3)
Female	13 (16.5)	21 (26.9)	34 (21.7)
Ethnic origin			
White	70 (88.6)	75 (96.2)	145 (92.4)
Black or African American	3 (3.8)	2 (2.6)	5 (3.2)
Native Hawaiian or Pacific Islander	1 (1.3)	0 (0.0)	1 (0.6)
Asian	1 (1.3)	0 (0.0)	1 (0.6)
American Indian or Alaska Native	1 (1.3)	0 (0.0)	1 (0.6)
Not reported	1 (1.3)	0 (0.0)	1 (0.6)
Unknown (patient unsure)	2 (2.5)	1 (1.3)	3 (1.9)
ECOG PS			
0	36 (45.6)	36 (46.2)	72 (45.9)
1	33 (41.8)	32 (41.0)	65 (41.4)
2	10 (12.7)	10 (12.8)	20 (12.7)
IMDC risk group			
Intermediate	64 (81.0)	63 (80.8)	127 (80.9)
Poor	15 (19.0)	15 (19.2)	30 (19.1)
Bone metastases			
Yes	29 (36.7)	28 (35.9)	57 (36.3)
No	50 (63.3)	50 (64.1)	100 (63.7)
Prior nephrectomy			
Yes	57 (72.2)	60 (76.9)	117 (74.5)
No	22 (27.8)	18 (23.1)	40 (25.5)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; PS, performance status.

CABOSUN Ensayo fase II randomizado: PFS



Choueiri TK et al. LBA 38 ESMO 2017

Presented By Cora Sternberg at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

Phase 2 CABOSUN Study: Objective Response by Investigator Assessment

	Cabozantinib (n=79)	Sunitinib (n=78)
ORR, n (%)	36 (46)	14 (18)
95% CI, %	34–57	10–28
Best overall response, n		
Complete response	1	1
Partial response	35	13
Stable disease	26	28
Progressive disease	14	20
Not evaluable or missing	3	16

Choueiri TK et al. J Clin Oncol 2017 Feb 20;35(6):591-597.
Choueiri TK, et al. ESMO 2016: LBA36_PR

Presented By Cora Sternberg at 2018 Genitourinary Cancers Symposium: Translating Evidence to Multidisciplinary Care

CABOSUN Ensayo fase II randomizado: PFS

Adverse Event	Cabozantinib (n = 78)		Sunitinib (n = 72)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Any adverse event	77 (98.7)	52 (66.7)	71 (98.6)	49 (68.1)
Fatigue	67 (85.9)	5 (6.4)	59 (81.9)	11 (15.3)
Hypertension	63 (80.8)	22 (28.2)	49 (68.1)	16 (22.2)
Diarrhea	56 (71.8)	8 (10.3)	38 (52.8)	8 (11.1)
AST increased	48 (61.5)	2 (2.6)	23 (31.9)	2 (2.8)
ALT increased	43 (55.1)	4 (5.1)	20 (27.8)	0 (0)
Anorexia	37 (47.4)	4 (5.1)	23 (31.9)	0 (0)
PPES	33 (42.3)	6 (7.7)	24 (33.3)	3 (4.2)
Dysgeusia	32 (41.0)	0 (0)	21 (29.2)	0 (0)
Thrombocytopenia	31 (39.7)	1 (1.3)	45 (62.5)	8 (11.1)
Oral mucositis	28 (35.9)	4 (5.1)	21 (29.2)	4 (5.6)
Anemia	26 (33.3)	1 (1.3)	33 (45.8)	1 (1.4)
Nausea	25 (32.1)	2 (2.6)	28 (38.9)	3 (4.2)
Weight loss	25 (32.1)	3 (3.8)	12 (16.7)	0 (0)
Neutropenia	12 (15.4)	0 (0)	25 (34.7)	3 (4.2)
Leukopenia	9 (11.5)	0 (0)	25 (34.7)	2 (2.8)

Choueiri TK, et al. J Clin Oncol. 2017;35:591-597

FDA grants regular approval to Cabometyx for first-line treatment of advanced renal cell carcinoma

On December 19, 2017, the Food and Drug Administration granted regular approval to cabozantinib (Cabometyx, Exelixis, Inc.) for treatment of patients with advanced renal cell carcinoma (RCC).

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CABOMETYX safely and effectively. See full prescribing information for CABOMETYX.
CABOMETYX® (cabozantinib) tablets, for oral use
Initial U.S. Approval: 2012

RECENT MAJOR CHANGES

Indications and Usage (1)	12/2017
Warnings and Precautions (5)	12/2017

INDICATIONS AND USAGE

CABOMETYX is a kinase inhibitor indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

- Hypertension and Hypertensive Crisis: Monitor blood pressure regularly. Discontinue CABOMETYX for hypertensive crisis or severe hypertension that cannot be controlled with anti hypertensive therapy. (5.4)
- Diarrhea: May be severe. Interrupt CABOMETYX treatment immediately until diarrhea resolves or decreases to Grade 1. Recommend standard antidiarrheal treatments. (5.5)
- Palmar-plantar erythrodysesthesia (PPE): Interrupt CABOMETYX treatment until PPE resolves or decreases to Grade 1. (5.6)
- Reversible posterior leukoencephalopathy syndrome (RPLS): Discontinue CABOMETYX. (5.7)
- Fetal-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.8, 8.1, 8.3)

FDA grants regular approval to Cabometyx for first-line treatment of advanced renal cell carcinoma

On December 19, 2017, the Food and Drug Administration granted regular approval to cabozantinib (Cabometyx, Exelixis, Inc.) for treatment of patients with advanced renal cell carcinoma (RCC).

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CABOMETYX safely and effectively. See full prescribing information for CABOMETYX.
CABOMETYX® (cabozantinib) tablets, for oral use
Initial U.S. Approval: 2012

RECENT MAJOR CHANGES

Indications and Usage (1)	12/2017
Warnings and Precautions (5)	12/2017

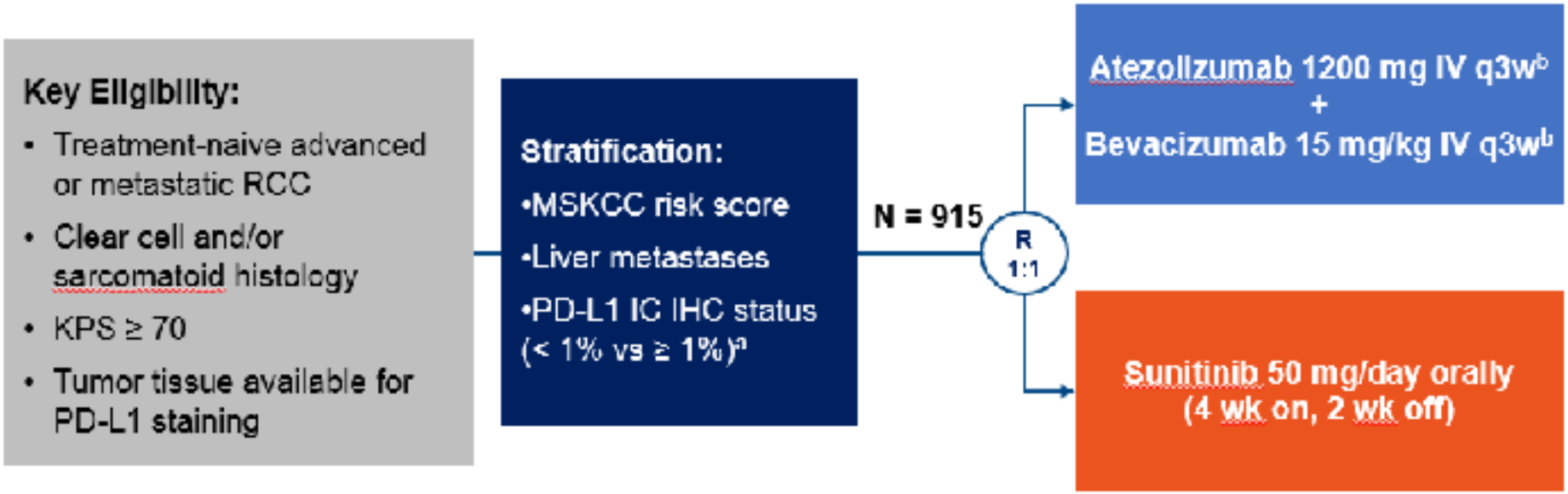
INDICATIONS AND USAGE

CABOMETYX is a kinase inhibitor indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

- Hypertension and Hypertensive Crisis: Monitor blood pressure regularly. Discontinue CABOMETYX for hypertensive crisis or severe hypertension that cannot be controlled with anti hypertensive therapy. (5.4)
- Diarrhea: May be severe. Interrupt CABOMETYX treatment immediately until diarrhea resolves or decreases to Grade 1. Recommend standard antidiarrheal treatments. (5.5)
- Palmar-plantar erythrodysesthesia (PPE): Interrupt CABOMETYX treatment until PPE resolves or decreases to Grade 1. (5.6)
- Reversible posterior leukoencephalopathy syndrome (RPLS): Discontinue CABOMETYX. (5.7)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.8, 8.1, 8.3)

Phase III IMmotion151 Trial: First-line Atezolizumab/Bevacizumab Combination Therapy vs Sunitinib in Metastatic RCC

Study Design

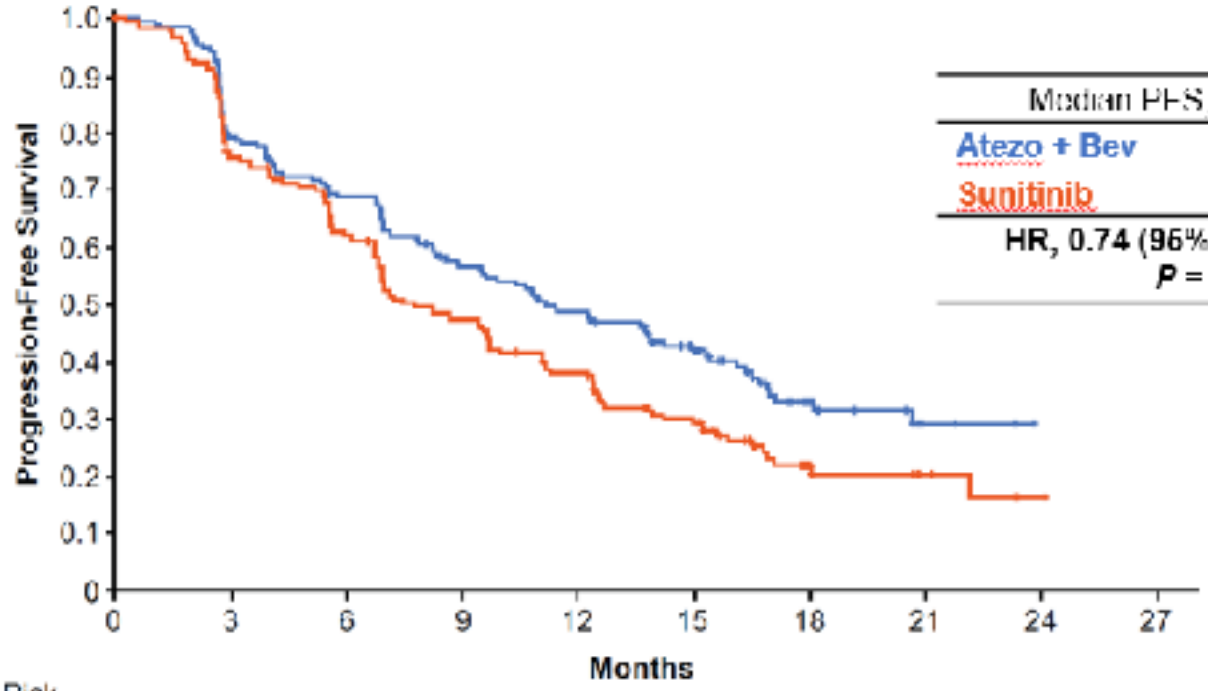


[a] ≥ 1% IC: 10% prevalence using SP142 IHC assay; [b] No dose reduction for atezolizumab or bevacizumab

IMmotion151: PFS PD-L1+

Co-Primary Endpoint

Progression-Free Survival in PD-L1+



Median PFS, mo (95% CI)	
Atezo + Bev	11.2 (8.9, 15.0)
Sunitinib	7.7 (6.8, 9.7)
HR, 0.74 (96% CI: 0.57, 0.96) *P* = 0.02	

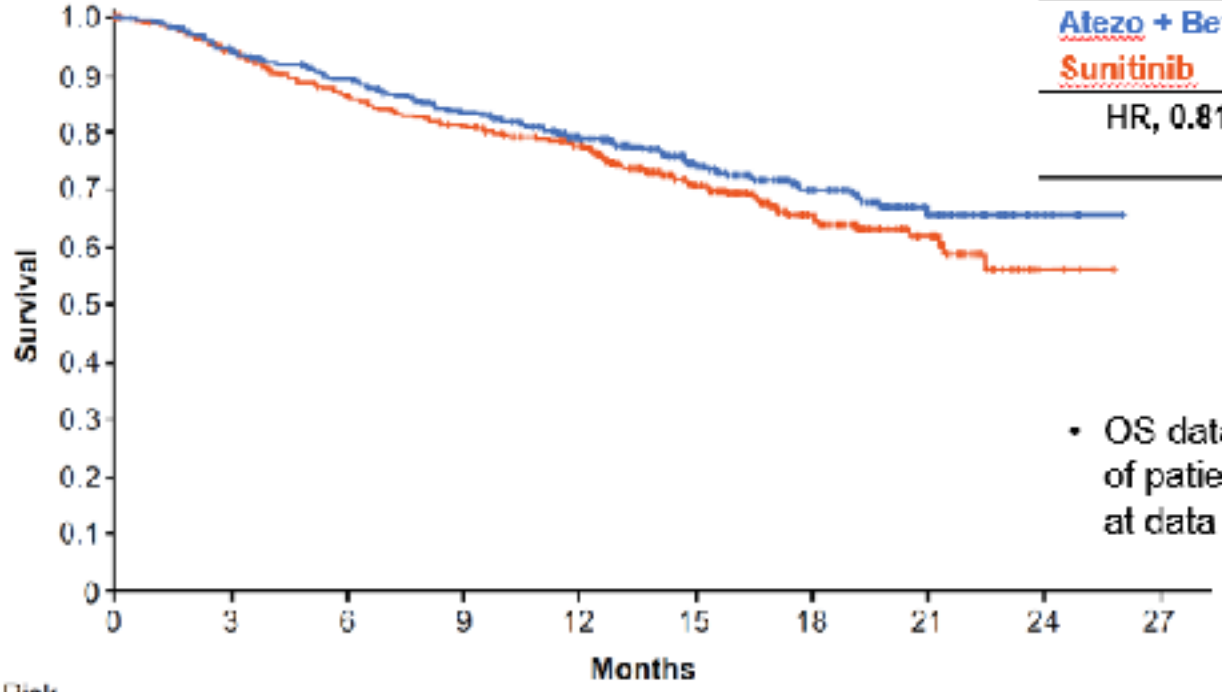
No. at Risk								
Atezo + Bev	178	137	117	94	79	55	22	5
Sunitinib	184	135	110	83	64	44	15	7	1

PFS assessed by investigators. Minimum follow-up, 12 mo. Median follow-up, 15 mo.
The PFS analysis passed the pre-specified *P* value boundary of alpha = 0.01.

IMmotion151: OS ITT

Co-Primary Endpoint

Overall Survival in ITT



Median OS, mo (95% CI)	
Atezo + Bev	Not reached
Sunitinib	Not reached

HR, 0.81 (95% CI: 0.63, 1.03)
***P* = 0.09**

- OS data are immature; 29% of patients had an OS event at data cutoff

No. at Risk									
Atezo + Bev	454	428	398	371	341	246	141	69	18
Sunitinib	461	422	384	357	331	227	126	65	15

Minimum follow up, 12 mo. Median of follow up, 15 mo. Event/patient ratio: 27% for atezo + bev, 31% for sunitinib.
The OS analysis did not pass the *P* value boundary of alpha = 0.0009 at the first interim analysis.

IMmotion151: AEs

Secondary Endpoint

Safety Summary in All-Treated Patients

Treatment-related AEs

All treated	Atezo + Bev n = 451	Sunitinib n = 446
Median treatment duration (range), mo	12.0 (0-26.2)	9.2 (0-26.6)
AEs, % Grade 3-4, %	91% 40%	96% 54%
AEs leading to discontinuation of treatment regimen, %	5%	8%
AEs leading to discontinuation of any treatment component, %[a]	12%	8%
Deaths, n	5[b]	1[c]

- Safety results were similar in all-treated patients and in those with PD-L1+ disease

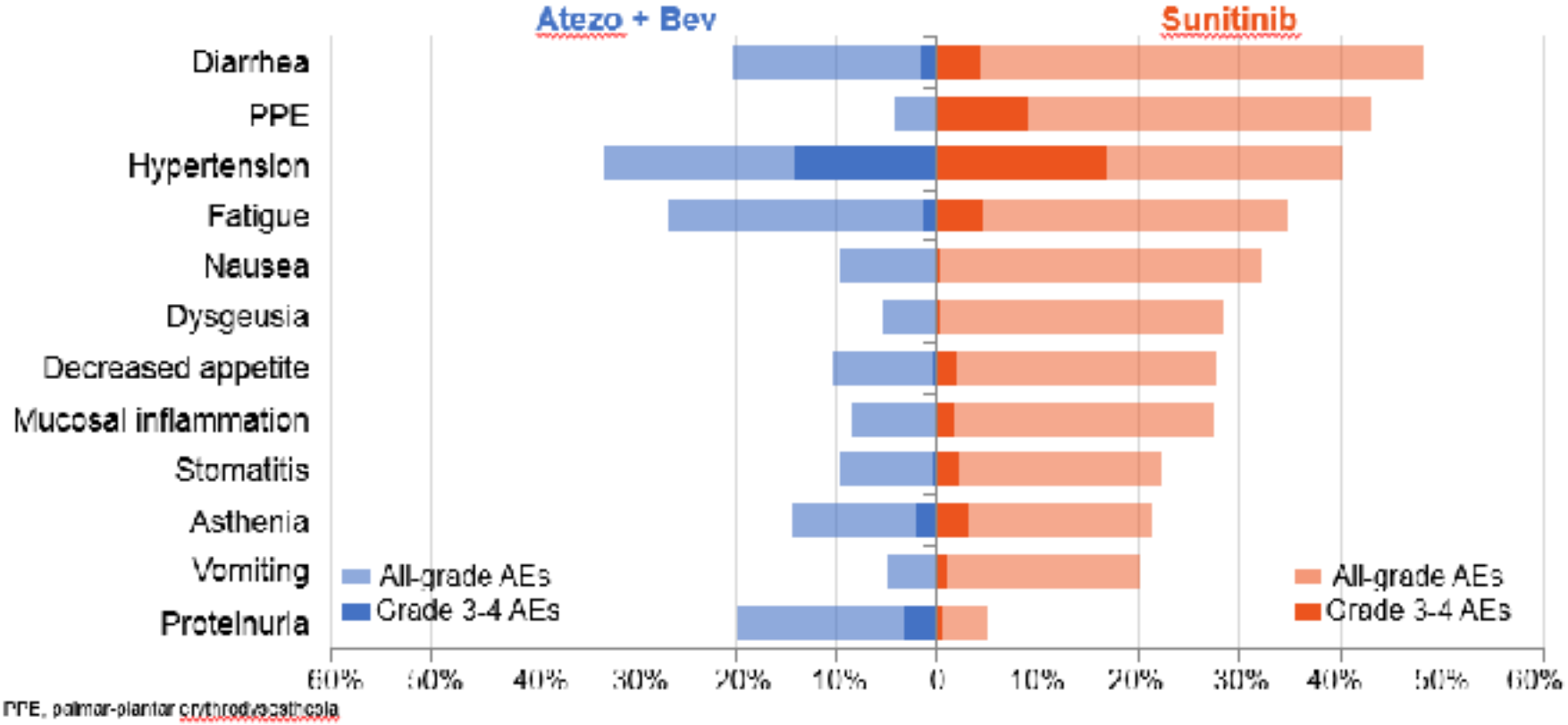
AEs, adverse events.
[a] Atezo + bev, 5%; atezo only, 2%; bev only, 5%.
[b] Cerebral infarction, intracranial haemorrhage, adrenal insufficiency, multiple organ dysfunction syndrome, sepsis. [c] Cardiac arrest.

IMmotion151: AEs

Secondary Endpoint

Treatment-related AEs

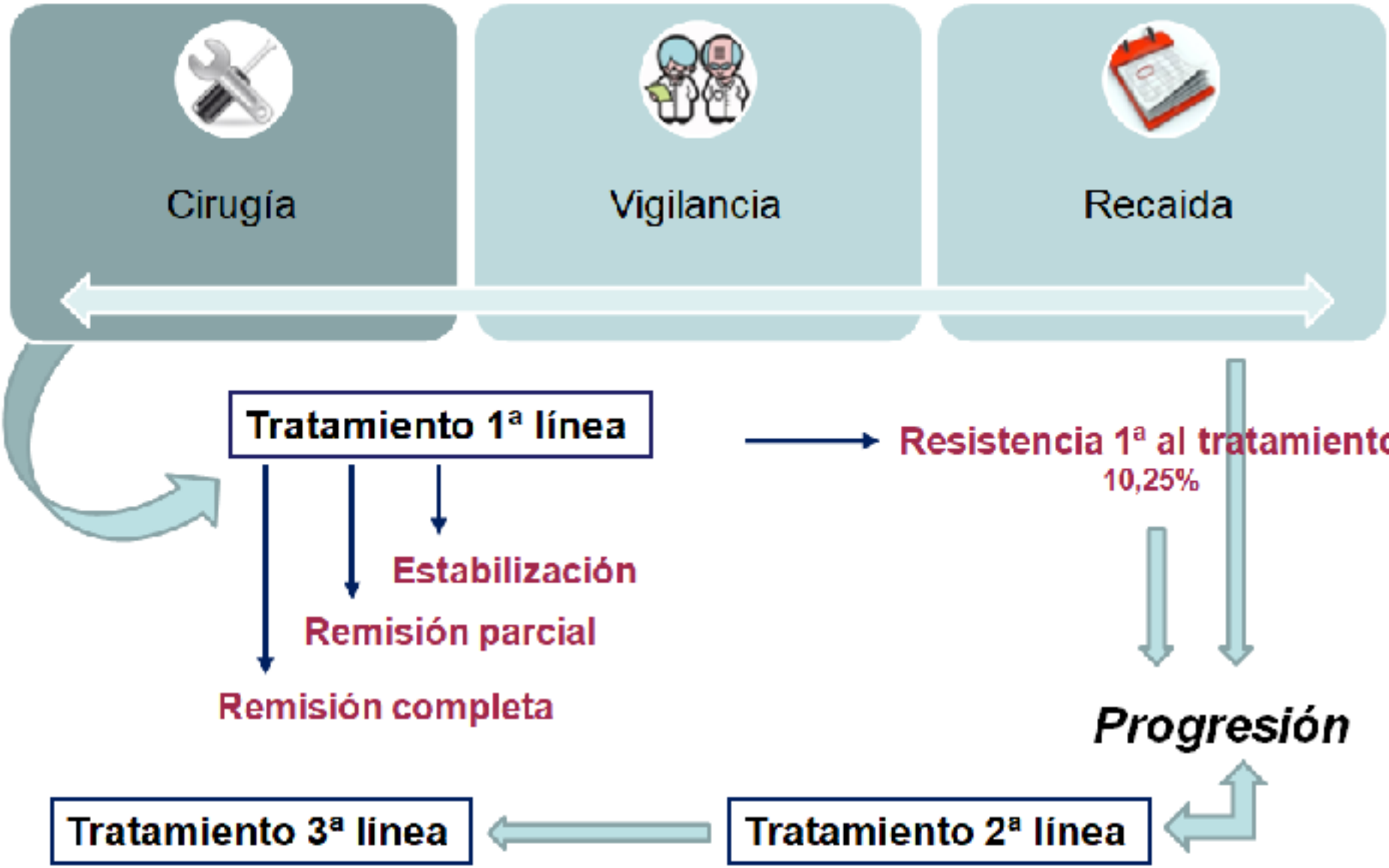
≥ 20% frequency in either arm and > 5% difference between arms



PPE, palmar-plantar erythrodysesthesia

Carcinoma renal

Algoritmo de enfermedad renal metastásica



Opciones de tratamiento después de la progresión


CASO
CLÍNICO
2

Caso clínico

Progresión tras TKI en primera línea

- Paciente de 64 años con Ca renal de células claras con MTX pulmonares en tratamiento con **pazopanib**

- Tras un ILP de 9 meses, se objetiva progresión de enfermedad a nivel pulmonar y mediastínico

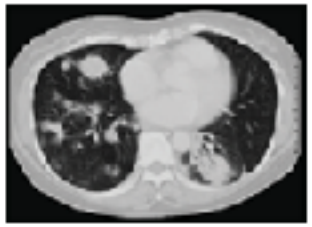
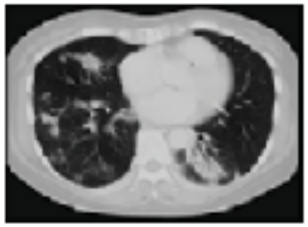
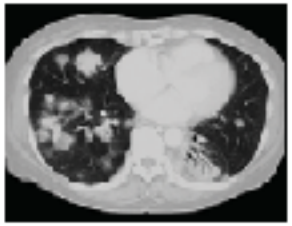
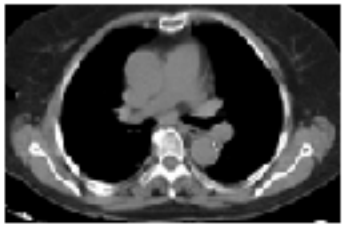
Caso clínico

2

Progresión tras TKI en primera línea

- Paciente de 64 años con Ca renal de células claras con MTX pulmonares en tratamiento con **pazopanib**

- Tras un ILP de 9 meses, se objetiva progresión de enfermedad a nivel pulmonar y mediastínico

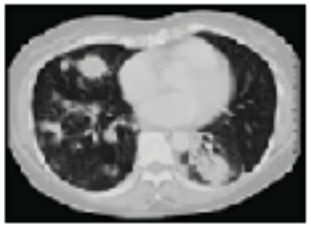
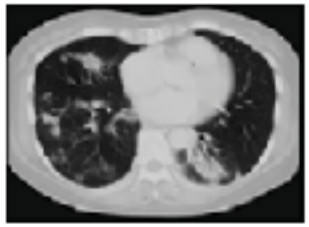
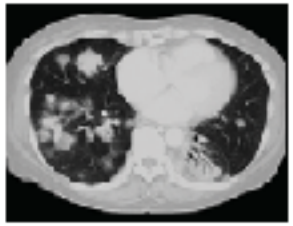
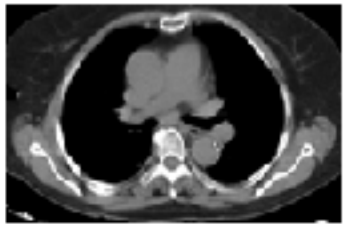
Caso clínico

2

Progresión tras TKI en primera línea

- Paciente de 64 años con Ca renal de células claras con MTX pulmonares en tratamiento con **pazopanib**
- Tras un ILP de 9 meses, se objetiva progresión de enfermedad a nivel pulmonar y mediastínico

- En ese momento el paciente:
  - IK: 100%
  - HTA bien controlada con lisinopril

EAU

	First-line therapy	Second-line therapy
IMDC favourable risk disease	sunitinib or pazopanib	cabozantinib or nivolumab
IMDC Intermediate and poor risk disease	ipilimumab/ nivolumab	cabozantinib or VEGF-targeted therapy
	cabozantinib, sunitinib or pazopanib[t]	VEGF targeted therapy or nivolumab

Boxed categories represent strong recommendations

NCCN

SUBSEQUENT THERAPY[m]
(alphabetical by category and preference)

- **Clinical trial**
- **Cabozantinib (category 1, preferred)[n]**
- **Nivolumab (category 1, preferred)[n]**
- **Axitinib (category 1)**
- **Lenvatinib + everolimus (category 1)**
- **Everolimus**
- **Pazopanib**
- **Sorafenib**
- **Sunitinib**
- **Bevacizumab (category 2B)**
- **High-dose IL-2 for selected patients[j] (category 2B)**
- **Temsirolimus (category 2B)**

and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

See Evidence Blocks on KID-4A

SEOM

Second-line treatment in advanced disease

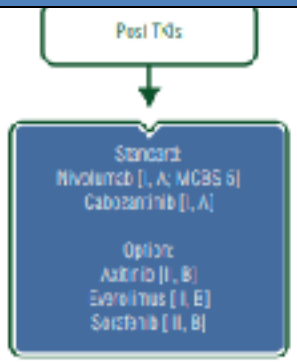
Nivolumab and cabozantinib have shown increased OS in patients with advanced ccRCC previously treated with antiangiogenics, and the recommended treatments for these patients. Level of evidence: I. Grade of recommendation: A

Decisions to use either agent may be based on the expected toxicity and on contraindications for each drug, as randomized data is lack Level of evidence: IV. Grade of recommendation: D

Lenvatinib in combination with everolimus has shown increased OS in patients with advanced ccRCC in a randomized phase II trial, a another valid alternative for these patients. Level of evidence: II. Grade of recommendation: B

Axitinib and everolimus have not shown increased OS after prior antiangiogenic therapy and should not be used before the previous ag Nevertheless they may remain acceptable options following such agents, although they have not been tested in randomized trials in setting. Level of evidence: II. Grade of recommendation: B

ESMO



EAU

	First-line therapy	Second-line therapy
IMDC favourable risk disease	sunitinib or pazopanib	cabozantinib or nivolumab
IMDC Intermediate and poor risk disease	ipilimumab/ nivolumab	cabozantinib or VEGF-targeted therapy
	cabozantinib, sunitinib or pazopanib[†]	VEGF targeted therapy or nivolumab

Boxed categories represent strong recommendations

NCCN

SUBSEQUENT THERAPY[m]
(alphabetical by category and preference)

- **Clinical trial**
- **Cabozantinib (category 1, preferred)[n]**
- **Nivolumab (category 1, preferred)[n]**
- **Axitinib (category 1)**
- **Lenvatinib + everolimus (category 1)**
- **Everolimus**
- **Pazopanib**
- **Sorafenib**
- **Sunitinib**
- **Bevacizumab (category 2B)**
- **High-dose IL-2 for selected patients[i] (category 2B)**
- **Temsirolimus (category 2B)**

and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

See Evidence Blocks on KID-4A

SEOM

Second-line treatment in advanced disease

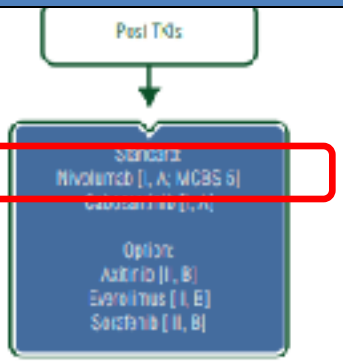
Nivolumab and cabozantinib have shown increased OS in patients with advanced ccRCC previously treated with antiangiogenics, and the recommended treatments for these patients. Level of evidence: I. Grade of recommendation: A

Decisions to use either agent may be based on the expected toxicity and on contraindications for each drug, as randomized data is lack Level of evidence: IV. Grade of recommendation: D

Lenvatinib in combination with everolimus has shown increased OS in patients with advanced ccRCC in a randomized phase II trial, a another valid alternative for these patients. Level of evidence: II. Grade of recommendation: B

Axitinib and everolimus have not shown increased OS after prior antiangiogenic therapy and should not be used before the previous ag Nevertheless they may remain acceptable options following such agents, although they have not been tested in randomized trials in setting. Level of evidence: II. Grade of recommendation: B

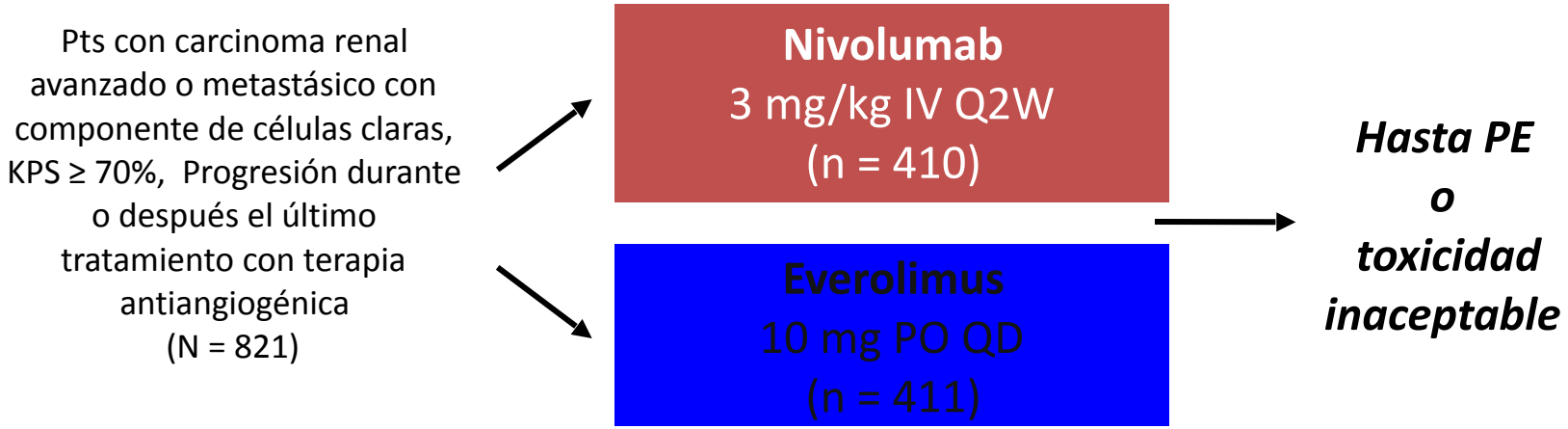
ESMO



CheckMate 025:

Ensayo Fase III de Nivolumab vs Everolimus en RCC ya tratados

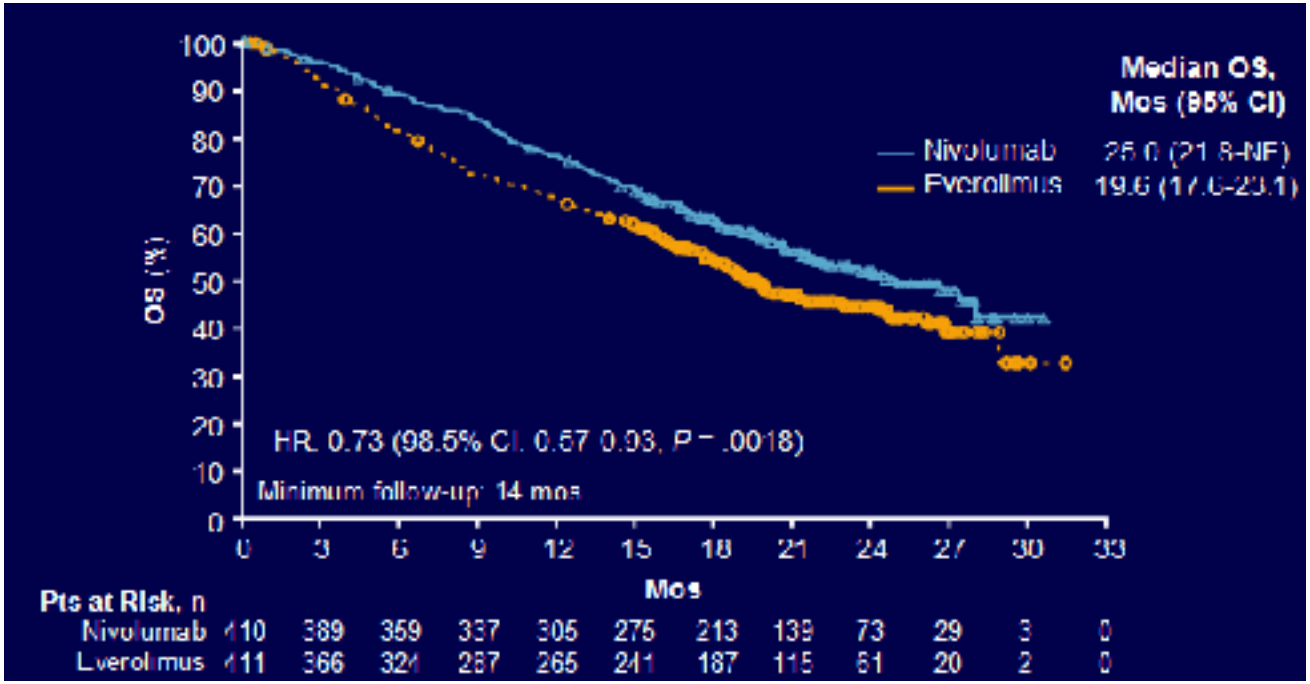
- Estudio Fase III randomizado



- Objetivo primario: OS
- Objetivos secundarios: PFS, ORR, Duración de respuesta, seguridad

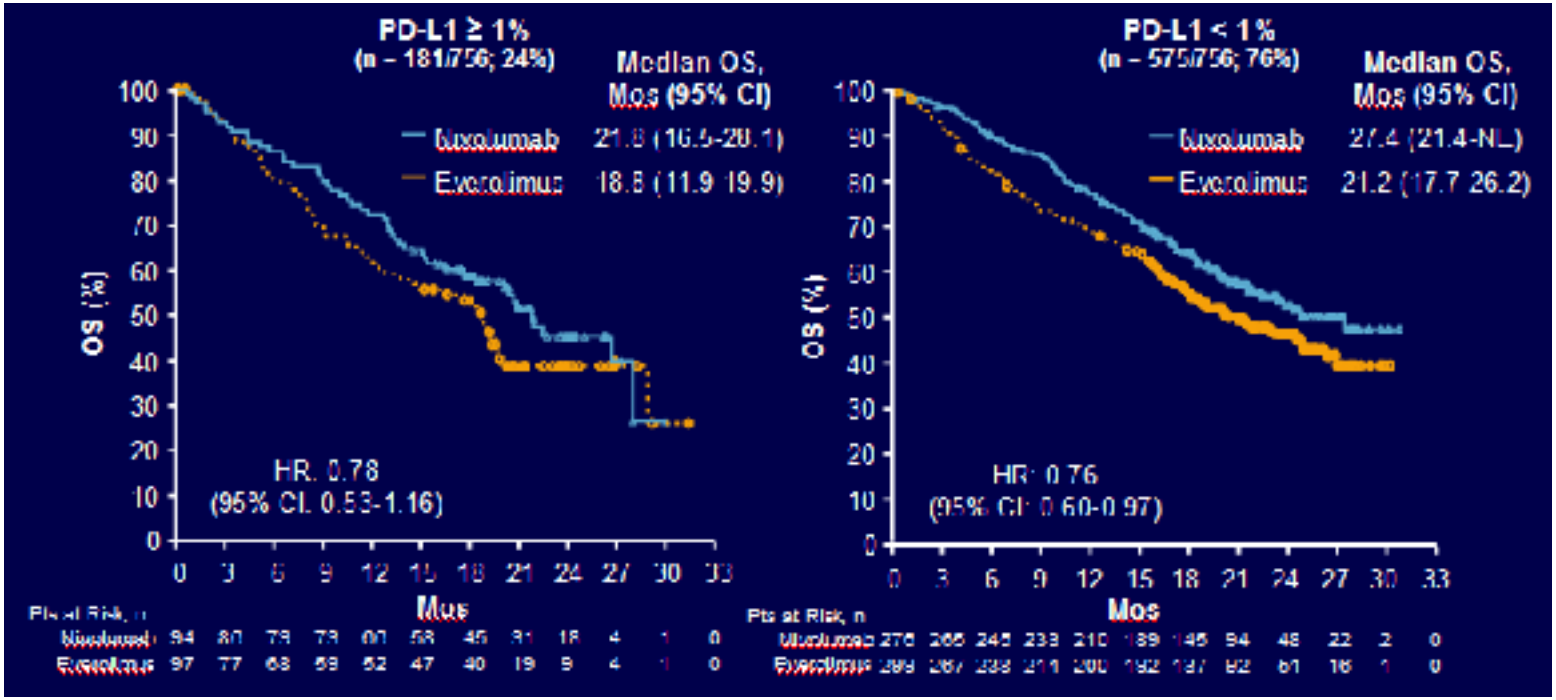
Motzer RJ, et al. N Engl J Med. 2015;373:1803-1813

Checkmate 025: os



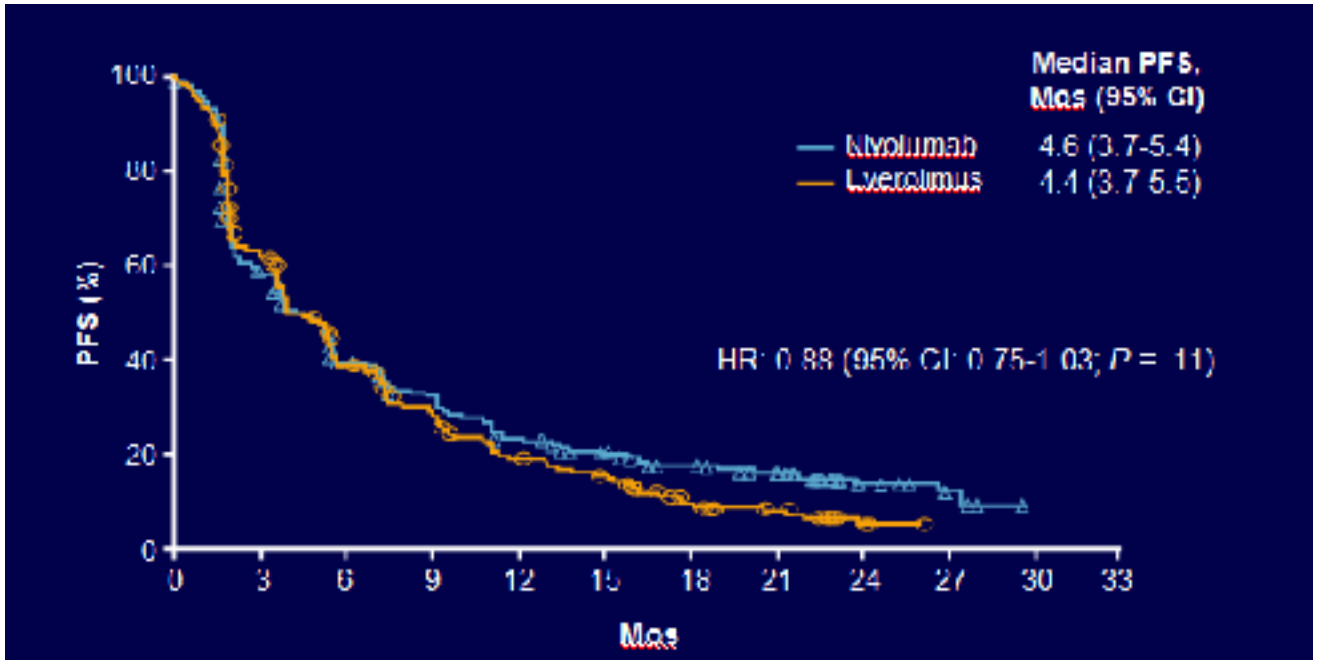
Motzer RJ, et al. N Engl J Med. 2015;373:1803-1813

Checkmate 025: OS estratificada por PD-L1



Motzer RJ, et al. N Engl J Med. 2015;373:1803-1813

Checkmate 025: PFS



Motzer RJ, et al. N Engl J Med. 2015;373:1803-1813

Checkmate 025: Tasa de respuesta

Response	Nivolumab (n = 410)	Everolimus (n = 411)
ORR*	25	5
• Odds ratio (95% CI)	5.98 (3.58-9.72)	
Best overall response, %		
• CR/PR	21.5	3.9
• SD	34	55
• PD	35	28
• Not evaluated	6	12
Median time to response, mos (range)	3.5 (1.4-24.8)	3.7 (1.5-11.2)
Median duration of response, mos (range)	12.0 (0-27.6)	12.0 (0-22.2)

Motzer RJ, et al. N Engl J Med. 2015;373:1803-1813

Checkmate 025: Seguridad

Adverse Events	Nivolumab (n = 406)		Everolimus (n = 397)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Treatment-related AEs, %	79	19	88	37
Treatment-related AEs leading to discontinuation, %	6	--	13	--
Treatment-related deaths, n	0		2*	

TRAE in ≥ 10% of Pts, %	Nivolumab (n = 406)		Everolimus (n = 397)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Dyspnea	7	1	13	1
Peripheral edema	4	0	14	1
Pneumonitis	4	1	15	3
Mucosal inflammation	3	0	19	3
Dysgeusia	3	0	13	0
Hyperglycemia	2	1	12	4
Stomatitis	2	0	29	4
Hypertriglyceridemia	1	0	16	5
Epistaxis	1	0	10	0

TRAE in ≥ 10% of Pts, %	Nivolumab (n = 406)		Everolimus (n = 397)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
All events	79	19	88	37
Fatigue	33	2	34	3
Nausea	14	< 1	17	1
Pruritus	14	0	10	0
Diarrhea	12	1	21	1
Decreased appetite	12	< 1	21	1
Rash	10	< 1	20	1
Cough	9	0	19	0
Anemia	8	2	24	8

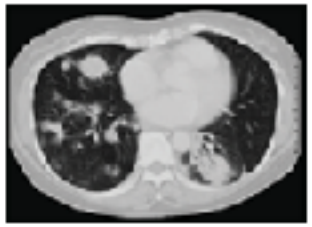
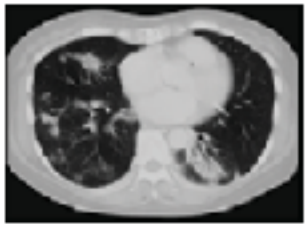
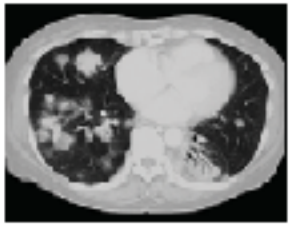
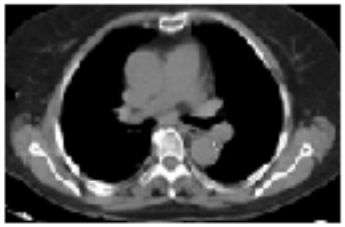
Motzer RJ, et al. N Engl J Med. 2015;373:1803-1813

Caso clínico

2

Progresión tras TKI en primera línea

- Paciente de 64 años con Ca renal de células claras con MTX pulmonares en tratamiento con **pazopanib**.
- Tras un ILP de 9 meses, se objetiva progresión de enfermedad a nivel pulmonar y mediastínico y **óseas a nivel de fémur derecho**

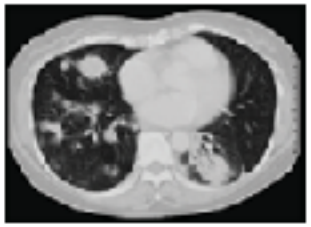
Caso clínico

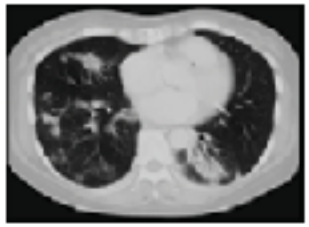
2

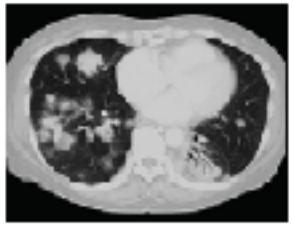
Progresión tras TKI en primera línea

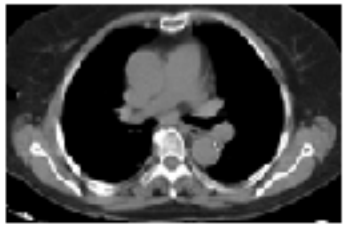
- Paciente de 64 años con Ca renal de células claras con MTX pulmonares en tratamiento con pazopanib

- Tras un ILP de 9 meses, se objetiva progresión de enfermedad a nivel pulmonar y mediastínico y **óseas a nivel de fémur derecho**









EAU

	First-line therapy	Second-line therapy
IMDC favourable risk disease	sunitinib or pazopanib	cabozantinib or nivolumab
IMDC Intermediate and poor risk disease	ipilimumab/ nivolumab	cabozantinib or VEGF-targeted therapy
	cabozantinib, sunitinib or pazopanib[t]	VEGF targeted therapy or nivolumab

Boxed categories represent strong recommendations

NCCN

SUBSEQUENT THERAPY[m]
(alphabetical by category and preference)

- **Clinical trial**
- **Cabozantinib (category 1, preferred)[n]**
- **Nivolumab (category 1, preferred)[n]**
- **Axitinib (category 1)**
- **Lenvatinib + everolimus (category 1)**
- **Everolimus**
- **Pazopanib**
- **Sorafenib**
- **Sunitinib**
- **Bevacizumab (category 2B)**
- **High-dose IL-2 for selected patients[j] (category 2B)**
- **Temsirolimus (category 2B)**

and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

See Evidence Blocks on KID-4A

SEOM

Second-line treatment in advanced disease

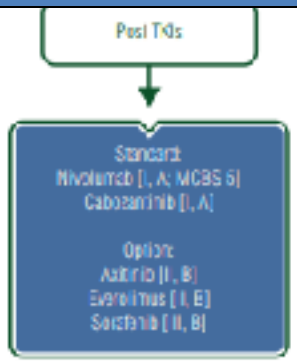
Nivolumab and cabozantinib have shown increased OS in patients with advanced ccRCC previously treated with antiangiogenics, and the recommended treatments for these patients. Level of evidence: I. Grade of recommendation: A

Decisions to use either agent may be based on the expected toxicity and on contraindications for each drug, as randomized data is lack Level of evidence: IV. Grade of recommendation: D

Lenvatinib in combination with everolimus has shown increased OS in patients with advanced ccRCC in a randomized phase II trial, a another valid alternative for these patients. Level of evidence: II. Grade of recommendation: B

Axitinib and everolimus have not shown increased OS after prior antiangiogenic therapy and should not be used before the previous ag Nevertheless they may remain acceptable options following such agents, although they have not been tested in randomized trials in setting. Level of evidence: II. Grade of recommendation: B

ESMO



EAU

	First-line therapy	Second-line therapy
IMDC favourable risk disease	sunitinib or pazopanib	cabozantinib or nivolumab
IMDC Intermediate and poor risk disease	ipilimumab/ nivolumab	cabozantinib or VEGF-targeted therapy
	cabozantinib, sunitinib or pazopanib[k]	VEGF targeted therapy or nivolumab

Boxed categories represent strong recommendations

NCCN

SUBSEQUENT THERAPY[m]
(alphabetical by category and preference)

- ~~Clinical trial~~
- **Cabozantinib (category 1, preferred)[n]**
- ~~Nivolumab (category 1, preferred)[n]~~
- **Axitinib (category 1)**
- **Lenvatinib + everolimus (category 1)**
- **Everolimus**
- **Pazopanib**
- **Sorafenib**
- **Sunitinib**
- **Bevacizumab (category 2B)**
- **High-dose IL-2 for selected patients[i] (category 2B)**
- **Temsirolimus (category 2B)**

and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

See Evidence Blocks on KID-4A

SEOM

Second-line treatment in advanced disease

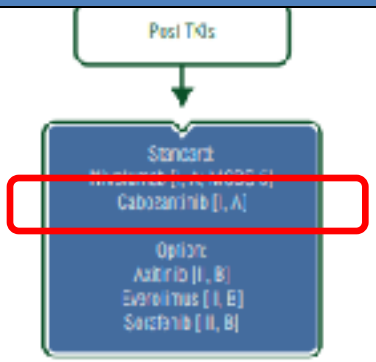
Nivolumab and cabozantinib have shown increased OS in patients with advanced ccRCC previously treated with antiangiogenics, and the recommended treatments for these patients. Level of evidence: I. Grade of recommendation: A

Decisions to use either agent may be based on the expected toxicity and on contraindications for each drug, as randomized data is lack Level of evidence: IV. Grade of recommendation: D

Lenvatinib in combination with everolimus has shown increased OS in patients with advanced ccRCC in a randomized phase II trial, a another valid alternative for these patients. Level of evidence: II. Grade of recommendation: B

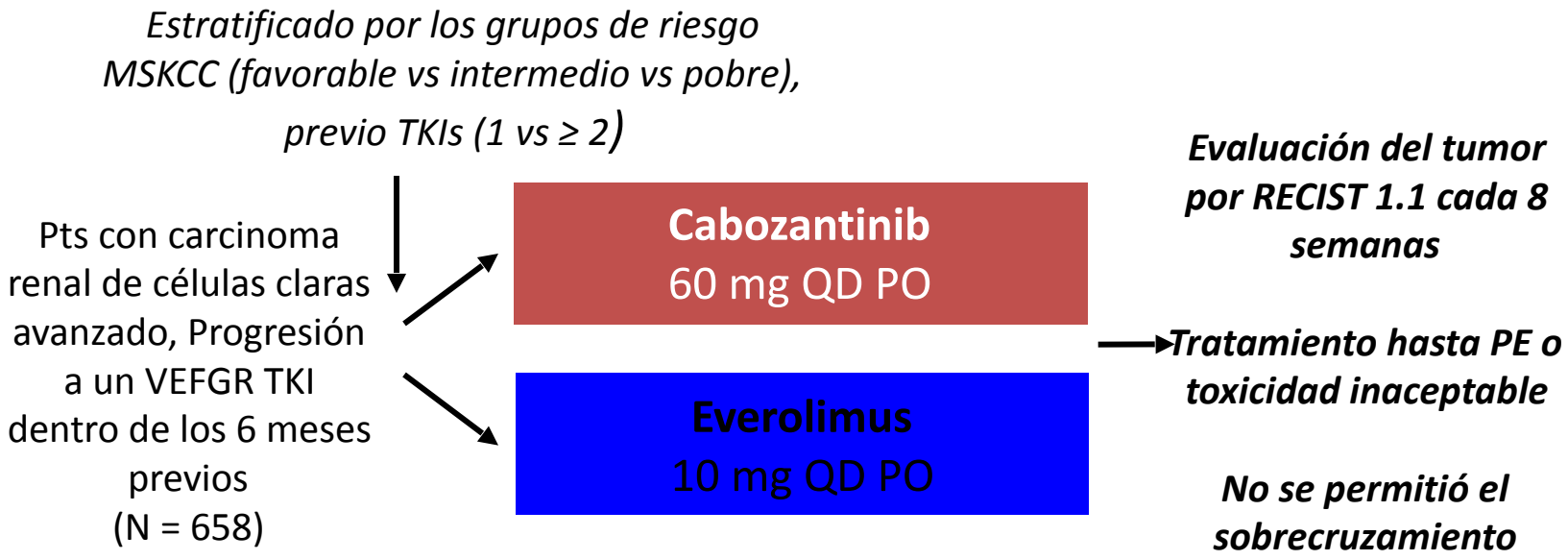
Axitinib and everolimus have not shown increased OS after prior antiangiogenic therapy and should not be used before the previous ag Nevertheless they may remain acceptable options following such agents, although they have not been tested in randomized trials in setting. Level of evidence: II. Grade of recommendation: B

ESMO



METEOR:

Cabozantinib vs Everolimus en RCC avanzado

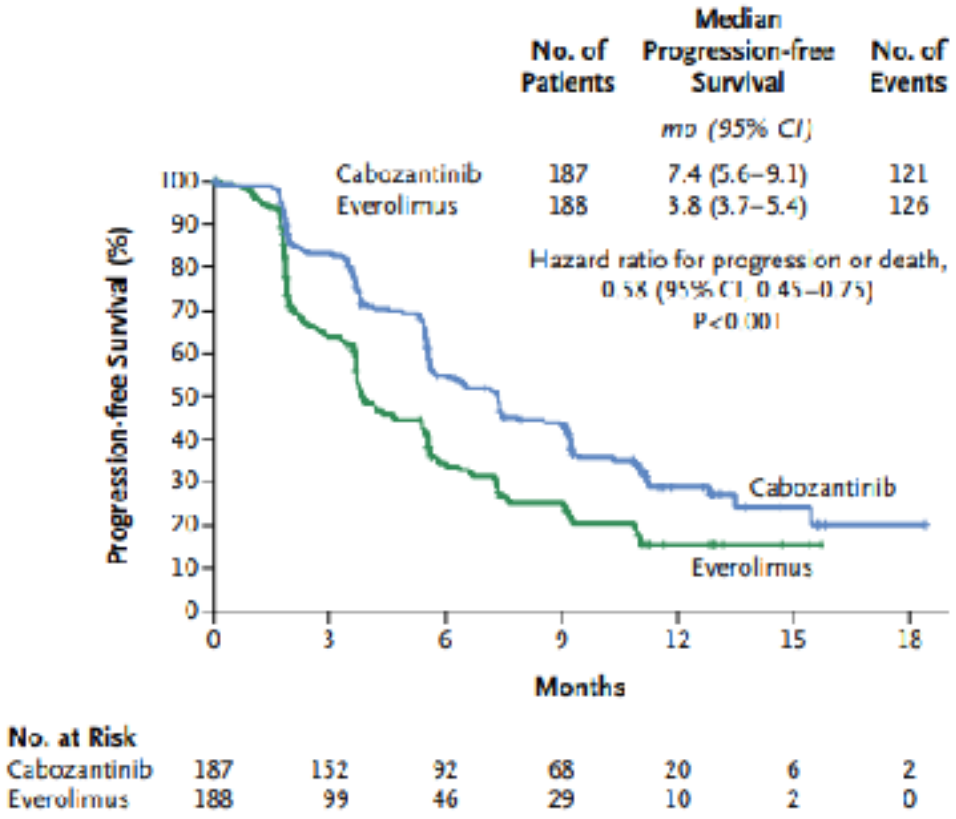


- Objetivo primario: PFS
- Objetivos secundarios: OS, ORR, seguridad

Choueiri TK, et al. Lancet Oncol. 2016;17:917-927

METEOR:

Cabozantinib vs Everolimus en RCC avanzado PFS

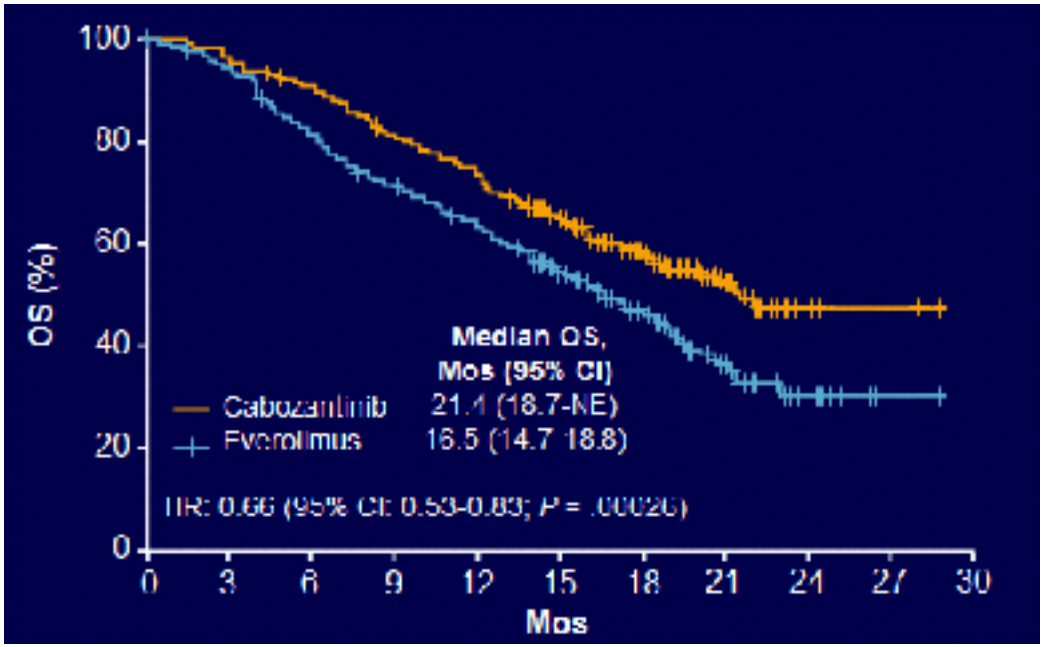


Choueiri TK, et al. N Engl J Med. 2015;373:1814-1823

METEOR:

Cabozantinib vs Everolimus en RCC avanzado

OS

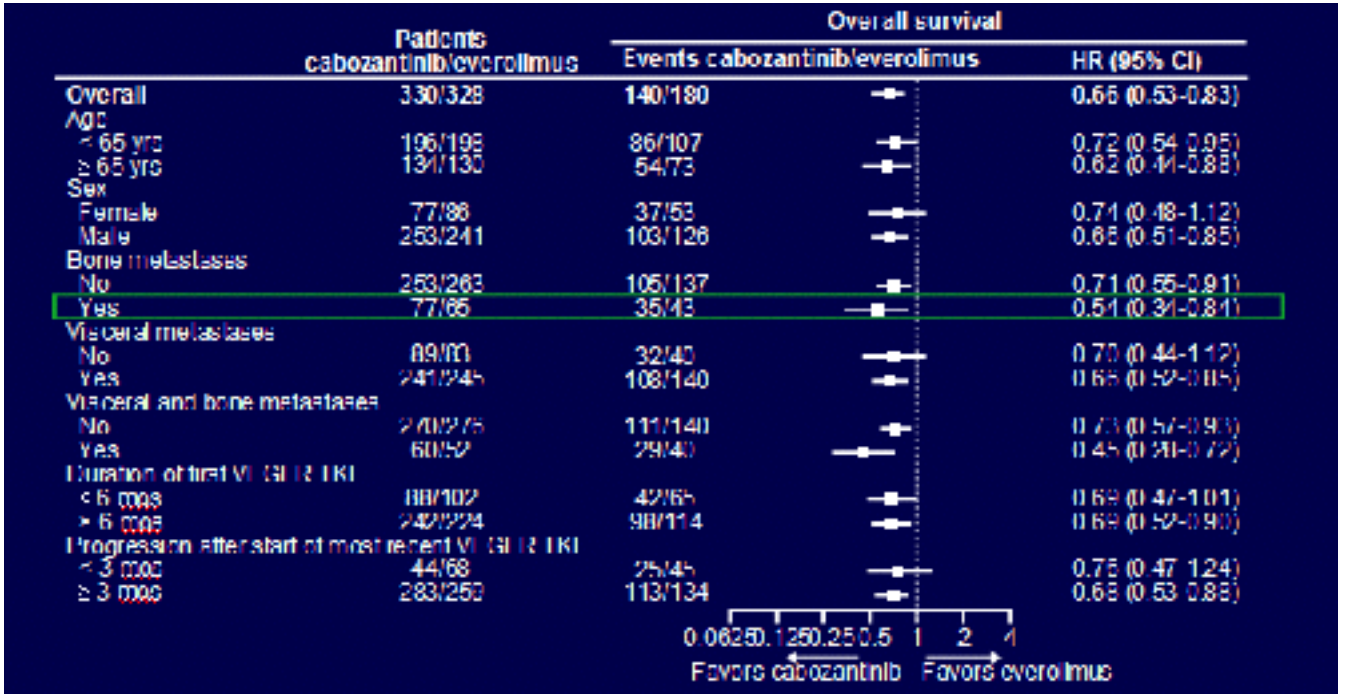


Choueiri TK, et al. Lancet Oncol. 2016;17:917-927

METEOR:

Cabozantinib vs Everolimus en RCC avanzado

OS por subgrupos



Choueiri TK, et al. Lancet Oncol. 2016;17:917-927

METEOR:
Cabozantinib vs Everolimus en RCC avanzado
ORR

Tabla 4: Resumen de los resultados de la TRO según la revisión del comité de radiología independiente (CRI) y la revisión del investigador

	Análisis TRO principal según CRI - Población con intención de tratar		TRO según la revisión del investigador - Población con intención de tratar	
Variable	**CABOMETYX**	**Everolimus**	**CABOMETYX**	**Everolimus**
	N = 330	N = 328	N = 330	N = 328
TRO (solo respuestas parciales) (IC 95 %)	17 % (13 %, 22 %)	3 % (2 %, 6 %)	24 % (19 %, 29 %)	4 % (2 %, 7 %)
valor de p[1]	p<0,0001		p< 0,0001	
Respuesta parcial	17 %	3 %	24 %	4 %
Mediana de tiempo hasta la Primera respuesta, meses (IC 95 %)	1,91 (1,6, 11,0)	2,14 (1,9, 9,2)	1,91 (1,3, 9,8)	3,50 (1,8, 5,6)
Enfermedad estable como Mejor respuesta	65 %	62%	63%	63%
Enfermedad progresiva como Mejor respuesta	12 %	27 %	9 %	27 %

[1] prueba de chi-cuadrado

METEOR:

Cabozantinib vs Everolimus en RCC avanzado Seguridad

Grade 3/4 AEs in ≥ 5% of Pts in Either Arm, %	Cabo (n = 331)	Eve (n = 322)
Any AE	71	60
Hypertension	15	4
Diarrhea	13	2
Fatigue	11	7
HFS	8	1
Decreased appetite	6	1
Anemia	6	16
Hypomagnesemia	5	0
Asthenia	5	2
Nausea	5	0
Hyperglycemia	1	5

Choueiri TK, et al. Lancet Oncol. 2016;17:917-927

EAU

	First-line therapy	Second-line therapy
IMDC favourable risk disease	sunitinib or pazopanib	cabozantinib or nivolumab
IMDC Intermediate and poor risk disease	ipilimumab/ nivolumab	cabozantinib or VEGF-targeted therapy
	cabozantinib, sunitinib or pazopanib[t]	VEGF targeted therapy or nivolumab

Boxed categories represent strong recommendations

NCCN

SUBSEQUENT THERAPY[m]
(alphabetical by category and preference)

- **Clinical trial**
- **Cabozantinib (category 1, preferred)[n]**
- **Nivolumab (category 1, preferred)[n]**
- **Axitinib (category 1)**
- **Lenvatinib + everolimus (category 1)**
- **Everolimus**
- **Pazopanib**
- **Sorafenib**
- **Sunitinib**
- **Bevacizumab (category 2B)**
- **High-dose IL-2 for selected patients[j] (category 2B)**
- **Temsirolimus (category 2B)**

and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

See Evidence Blocks on KID-4A

SEOM

Second-line treatment in advanced disease

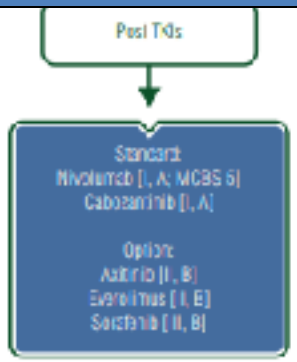
Nivolumab and cabozantinib have shown increased OS in patients with advanced ccRCC previously treated with antiangiogenics, and the recommended treatments for these patients. Level of evidence: I. Grade of recommendation: A

Decisions to use either agent may be based on the expected toxicity and on contraindications for each drug, as randomized data is lack Level of evidence: IV. Grade of recommendation: D

Lenvatinib in combination with everolimus has shown increased OS in patients with advanced ccRCC in a randomized phase II trial, a another valid alternative for these patients. Level of evidence: II. Grade of recommendation: B

Axitinib and everolimus have not shown increased OS after prior antiangiogenic therapy and should not be used before the previous ag Nevertheless they may remain acceptable options following such agents, although they have not been tested in randomized trials in setting. Level of evidence: II. Grade of recommendation: B

ESMO



EAU

	First-line therapy	Second-line therapy
IMDC favourable risk disease	sunitinib or pazopanib	cabozantinib or nivolumab
IMDC Intermediate and poor risk disease	ipilimumab/ nivolumab	cabozantinib or VEGF-targeted therapy
	cabozantinib, sunitinib or pazopanib[t]	VEGF targeted therapy or nivolumab

Boxed categories represent strong recommendations

NCCN

SUBSEQUENT THERAPY[m]
(alphabetical by category and preference)

- **Clinical trial**
- **Cabozantinib (category 1, preferred)[n]**
- **Nivolumab (category 1, preferred)[n]**
- **Axitinib (category 1)**
- **Lenvatinib + everolimus (category 1)**
- **Everolimus**
- **Pazopanib**
- **Sorafenib**
- **Sunitinib**
- **Bevacizumab (category 2B)**
- **High-dose IL-2 for selected patients[i] (category 2B)**
- **Temsirolimus (category 2B)**

and
Best supportive care:[l]
See NCCN Guidelines for Palliative Care

See Evidence Blocks on KID-4A

SEOM

Second-line treatment in advanced disease

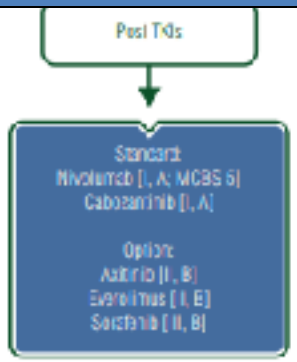
Nivolumab and cabozantinib have shown increased OS in patients with advanced ccRCC previously treated with antiangiogenics, and the recommended treatments for these patients. Level of evidence: I. Grade of recommendation: A

Level of evidence: IV. Grade of recommendation: D

Lenvatinib in combination with everolimus has shown increased OS in patients with advanced ccRCC in a randomized phase II trial, and another valid alternative for these patients. Level of evidence: II. Grade of recommendation: B

Axitinib and everolimus have not shown increased OS after prior antiangiogenic therapy and should not be used before the previous ag Nevertheless they may remain acceptable options following such agents, although they have not been tested in randomized trials in setting. Level of evidence: II. Grade of recommendation: B

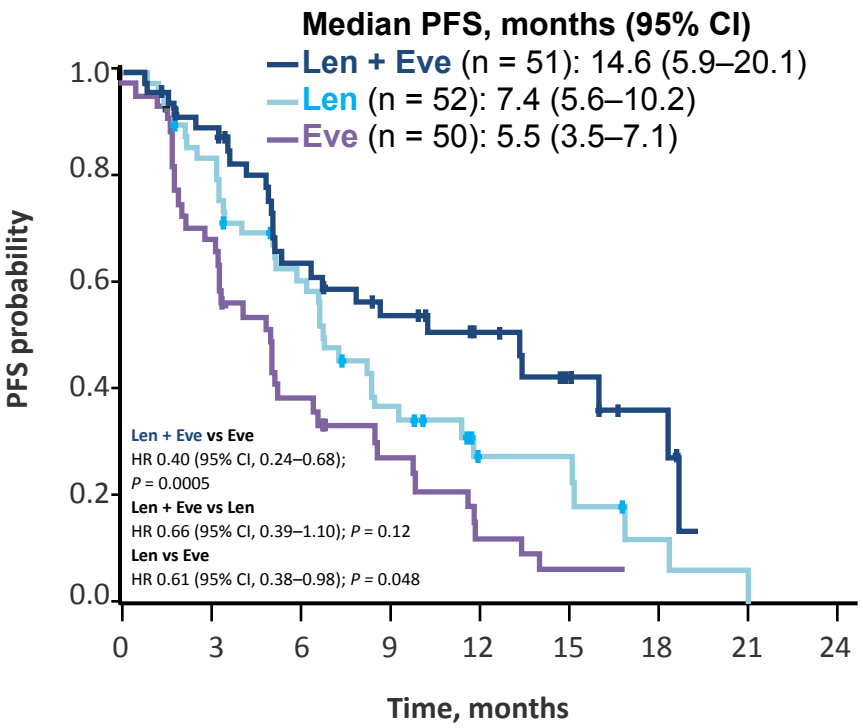
ESMO



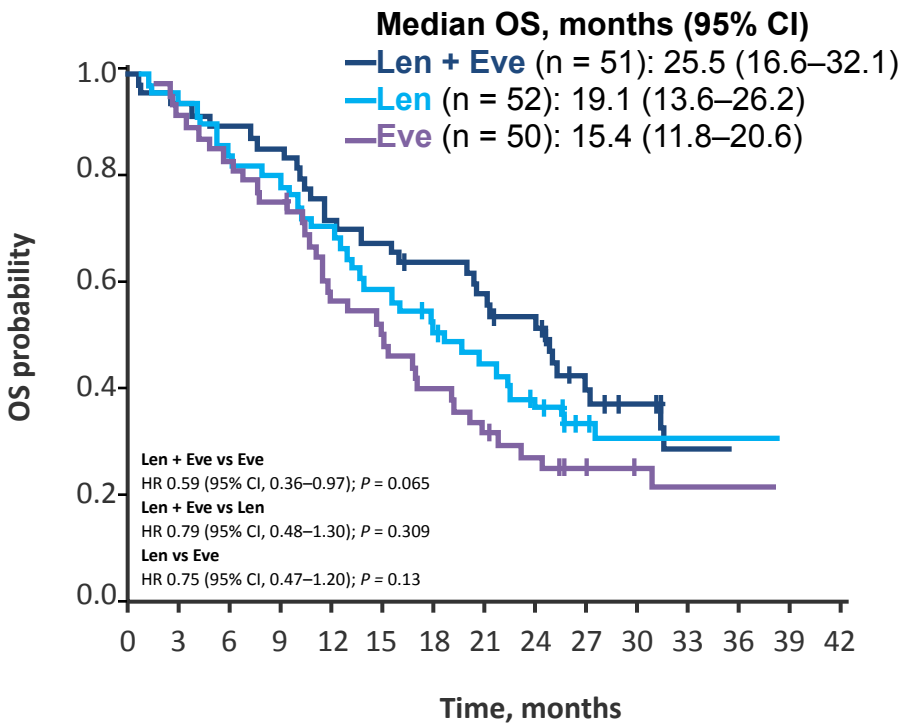
Phase 2 Study:

Efficacy of Second-line Lenvatinib + Everolimus

Progression-free survival



Overall survival



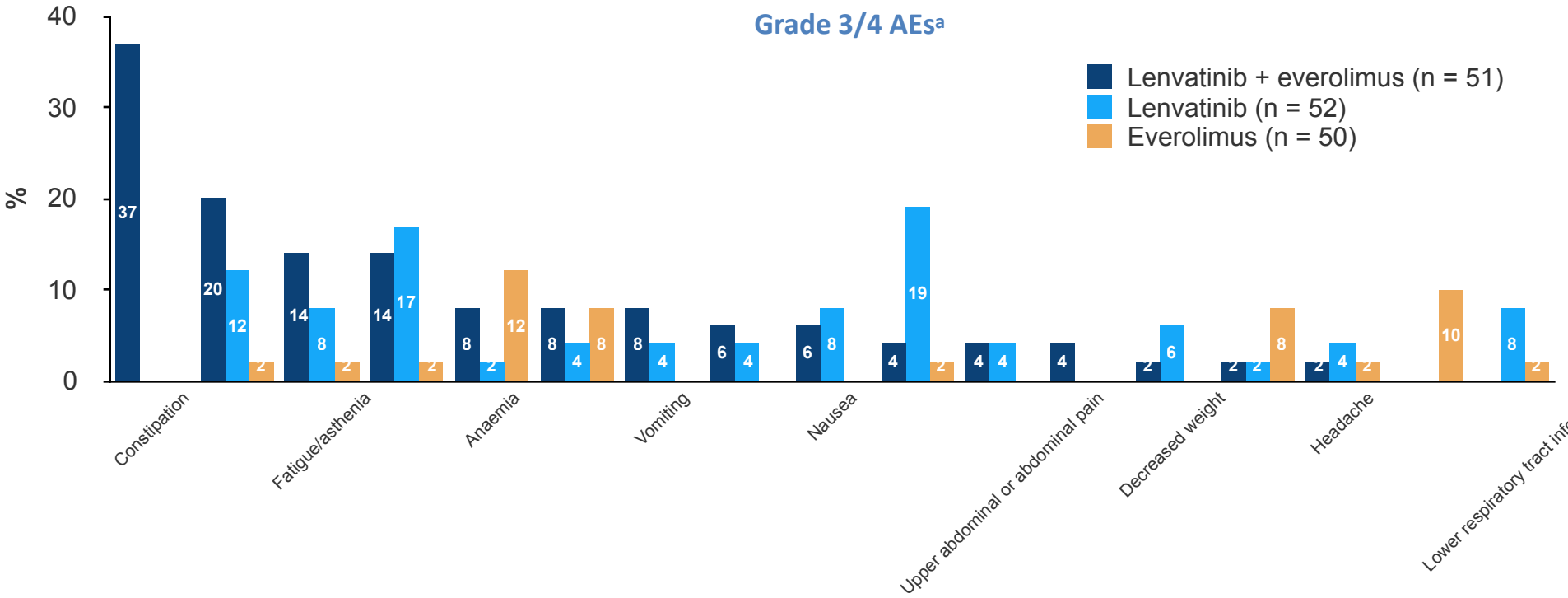
Eve, everolimus; Len, lenvantinib

Motzer RJ et al. *Lancet Oncol.* 2015;16:1473–1482

Hutson TE et al. Presented at: ASCO 2016 Annual Meeting; June 3–7; Chicago. Abstract 4553

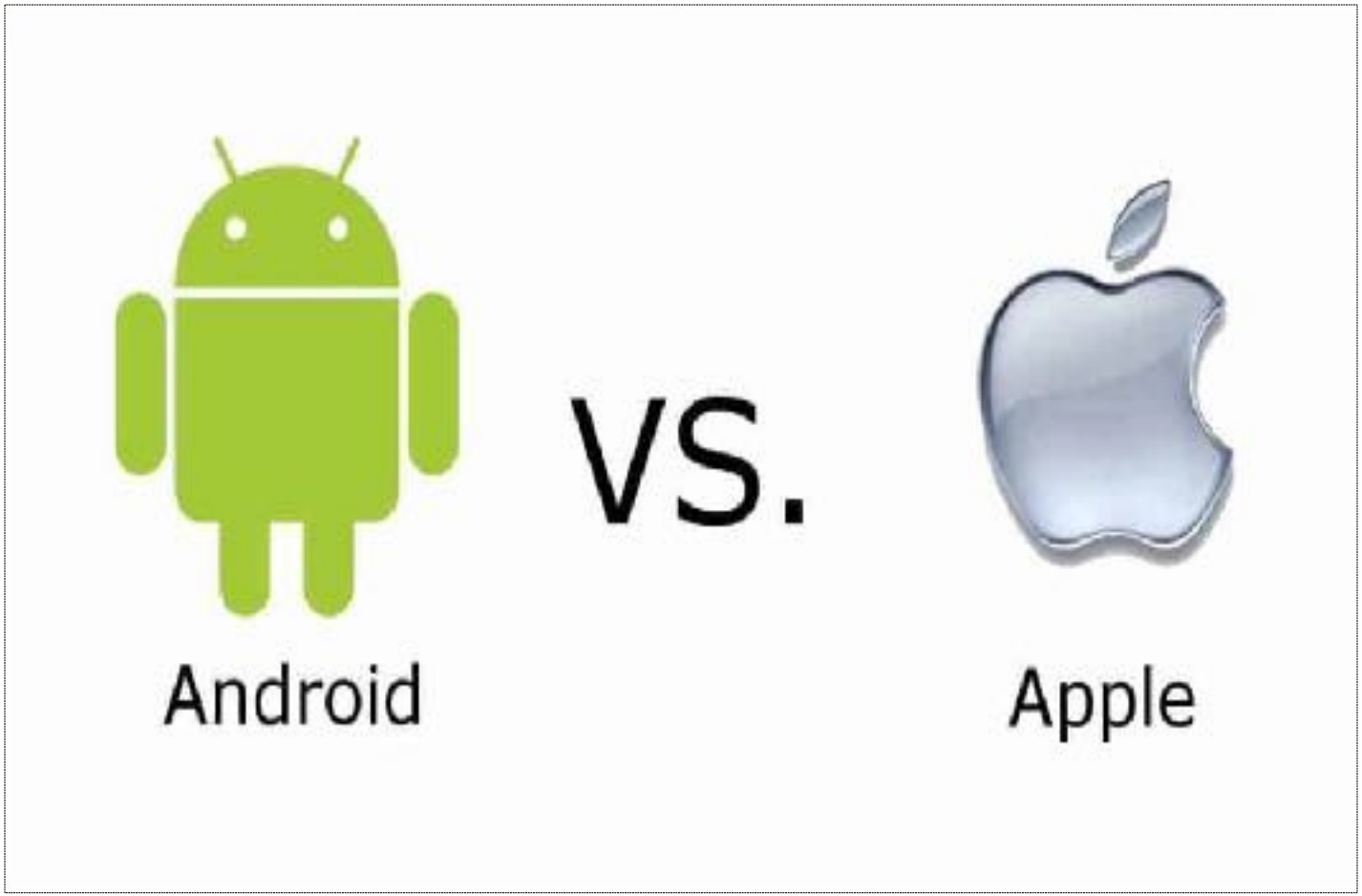
Phase 2 Study:

Grade 3/4 Treatment-Related AEs With Second-Line Lenvatinib + Everolimus



[a]Occurring in >1 patient (>2%) in any arm

Motzer RJ et al. *Lancet Oncol.* 2015;16:1473–1482


VS.
Android
Apple


Cabometyx 20 mg
Filmtabletten
Cabozantinib
Zum Einnehmen
30
Cabometyx 40 mg
Filmtabletten
Cabozantinib
Zum Einnehmen
30
Cabometyx 60 mg

VS.

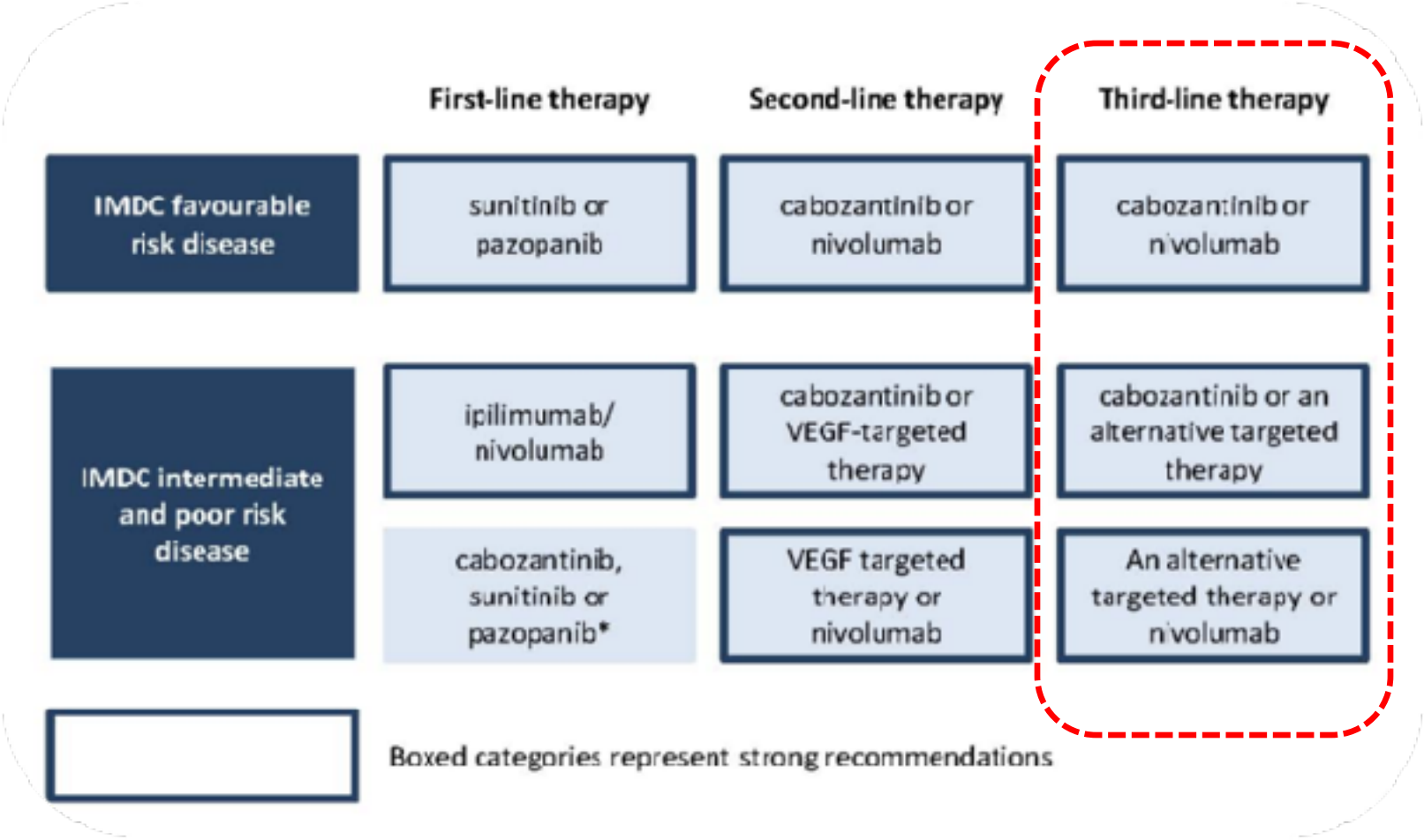

Opdivo


CASO
CLÍNICO
3

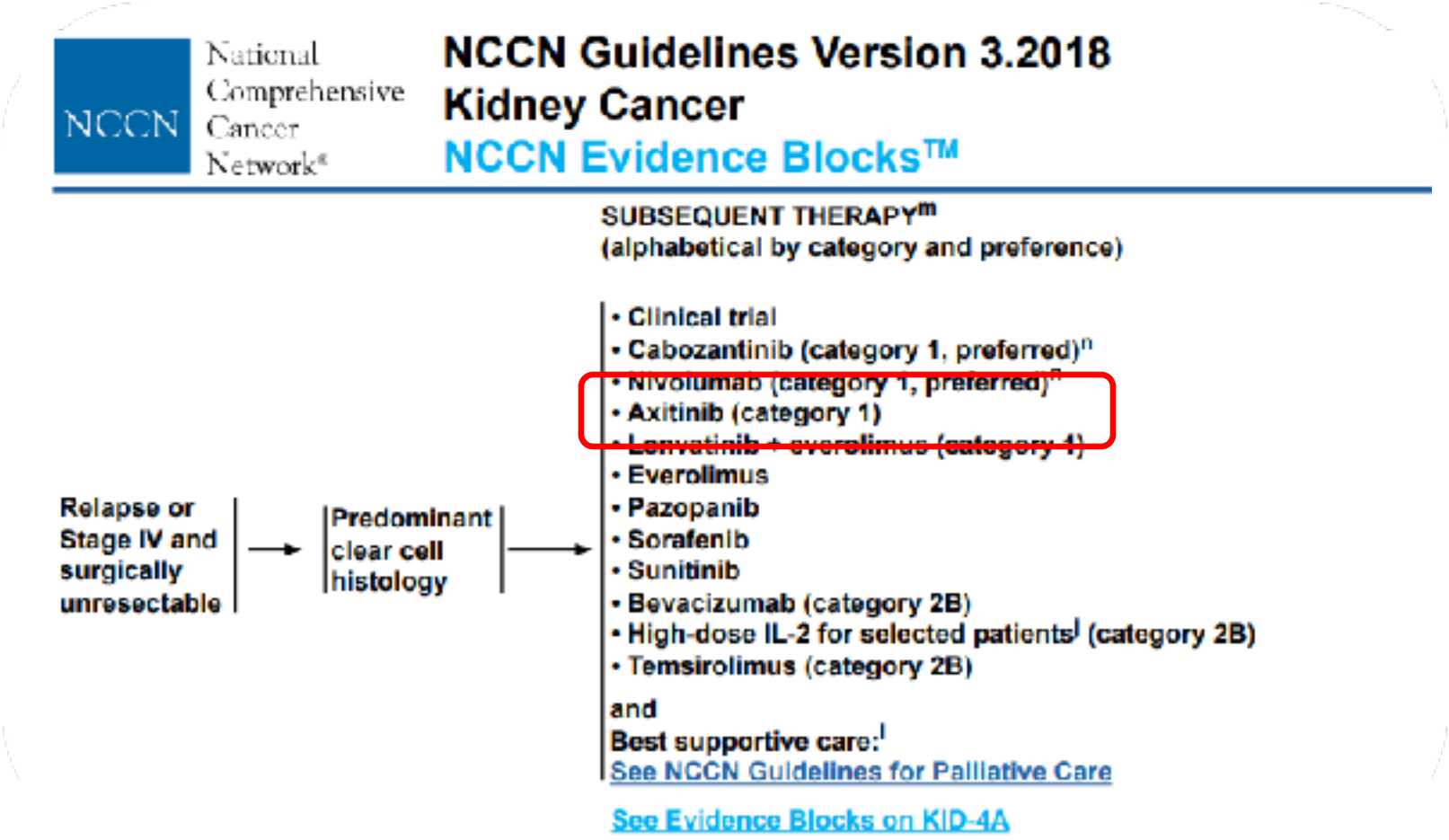
Caso 3: Selección del tratamiento en función de las comorbilidades del paciente

- Paciente de 59 años con tumor renal de células claras intervenido con MTX pulmonares, mediastínicas y pancreática
- Otros AP: artriritis reumatoide y está en tratamiento con adalimumab
- Progresión a pazopanib y cabozantinib. No hay disponibilidad de utilizar lenvatinib+ everolimus

Updated European Association of Urology Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer



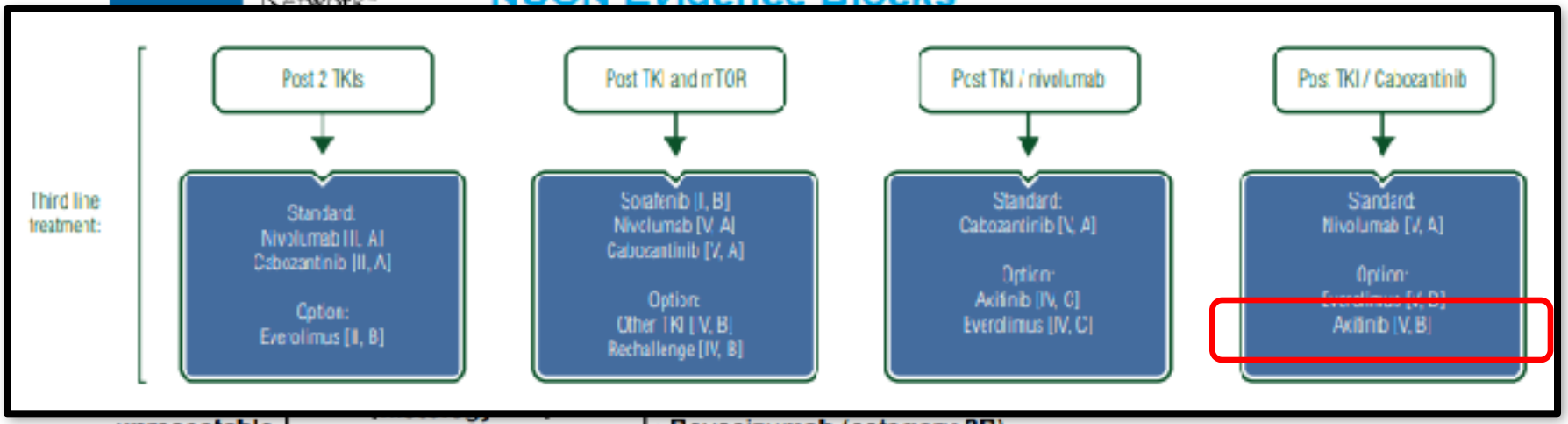
Updated European Association of Urology Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer



Updated European Association of Urology Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2018
Kidney Cancer
NCCN Evidence Blocks™



unresectable [l]

- **Bevacizumab (category 2B)**
- **High-dose IL-2 for selected patients[j] (category 2B)**
- **Temsirolimus (category 2B)**

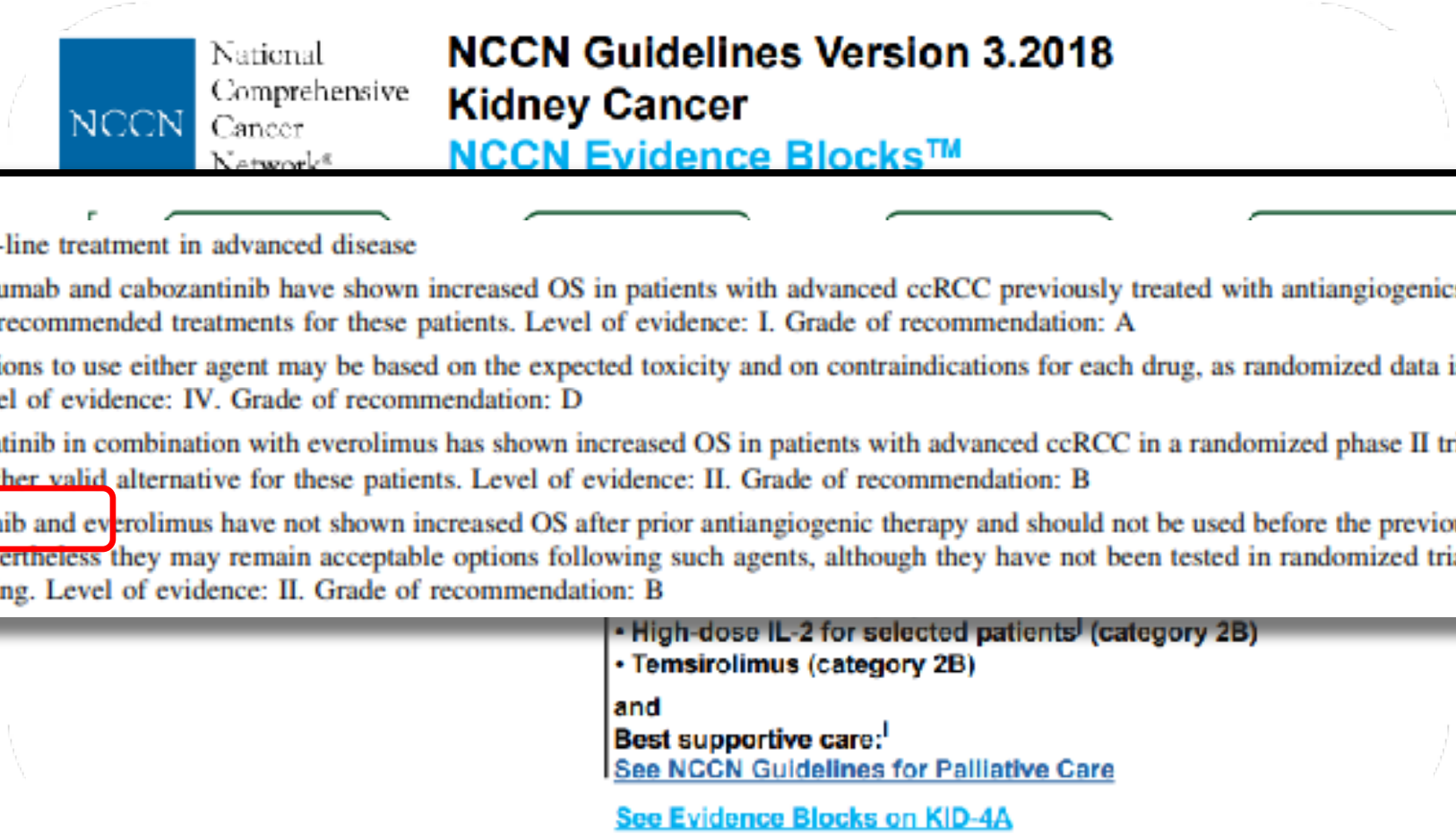
and

Best supportive care:[l]

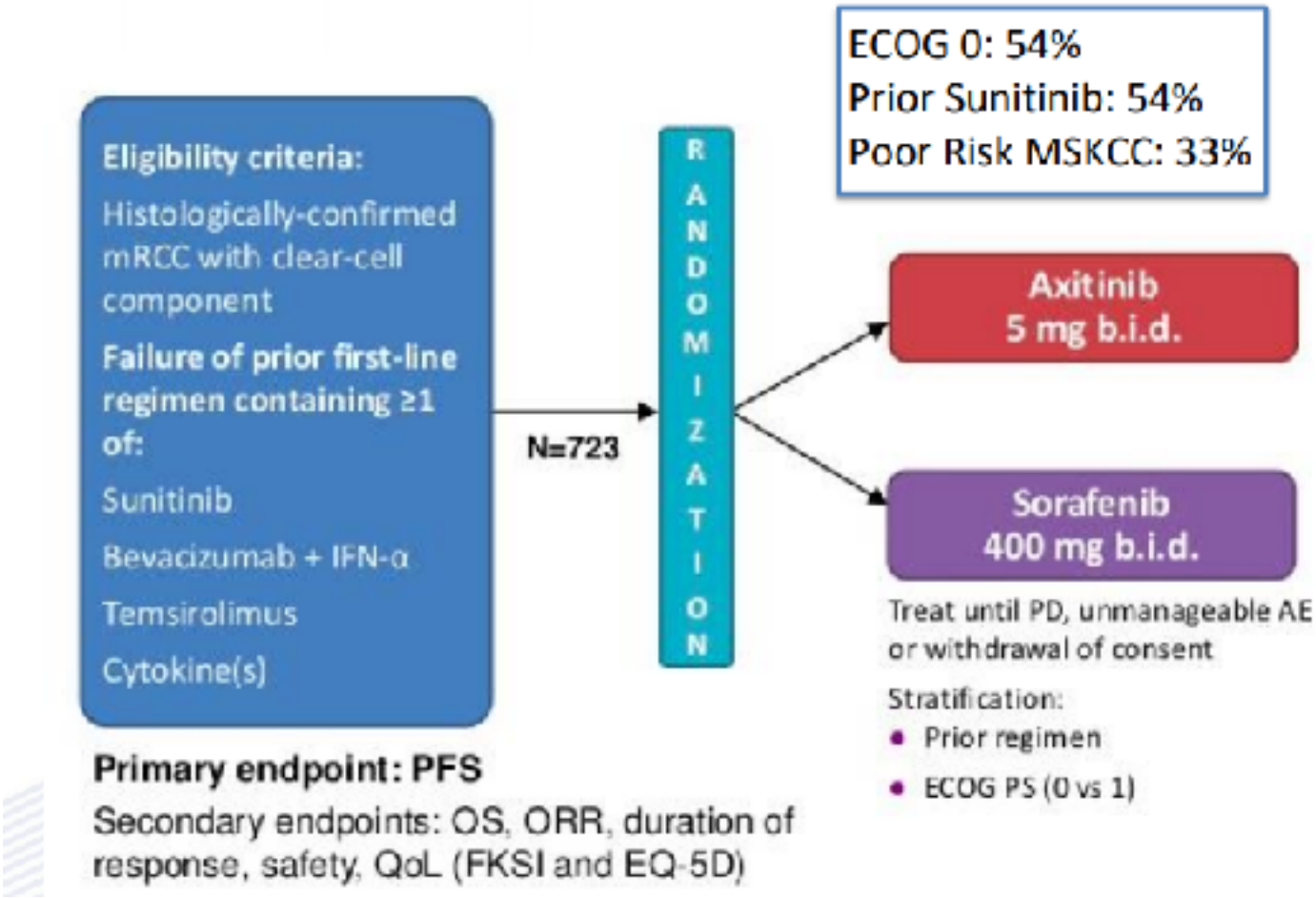
See NCCN Guidelines for Palliative Care

See Evidence Blocks on KID-4A

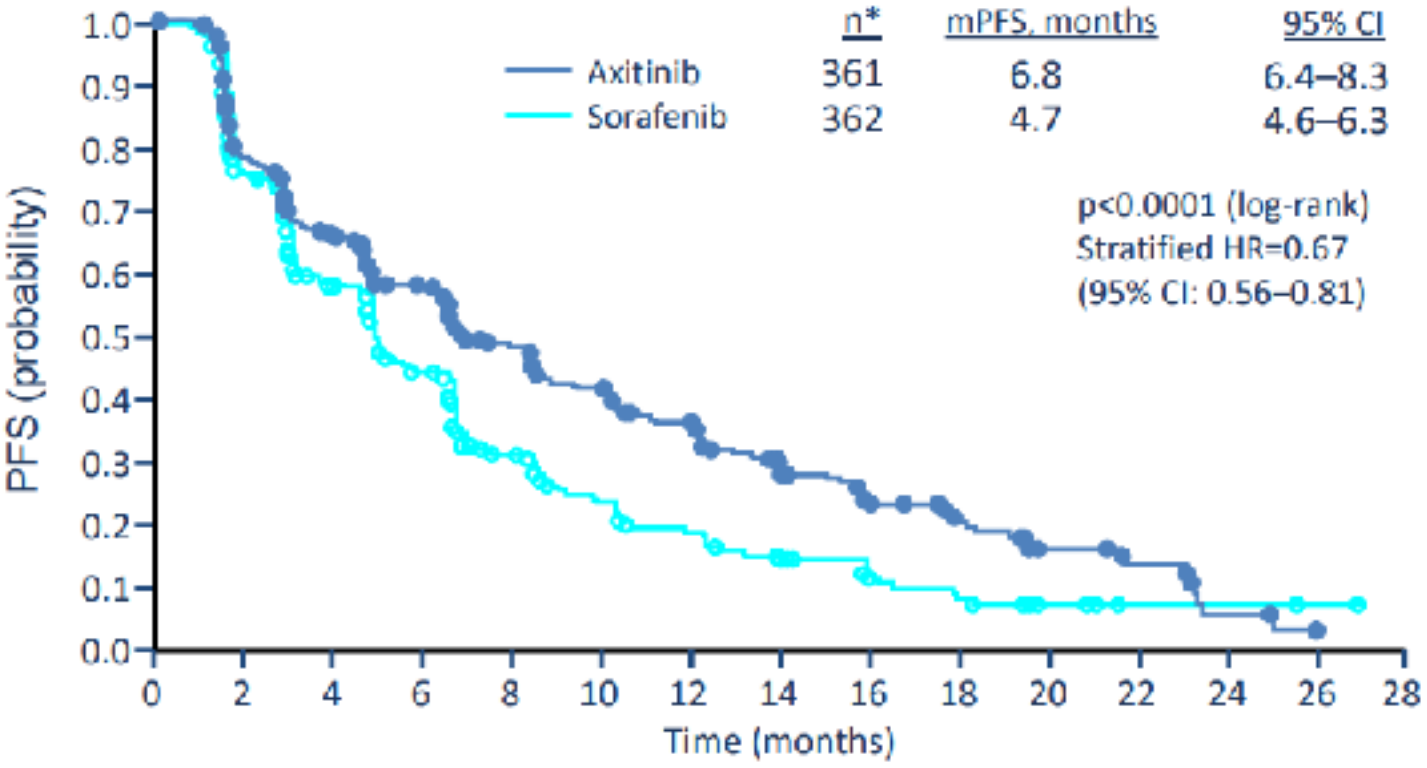
Updated European Association of Urology Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer

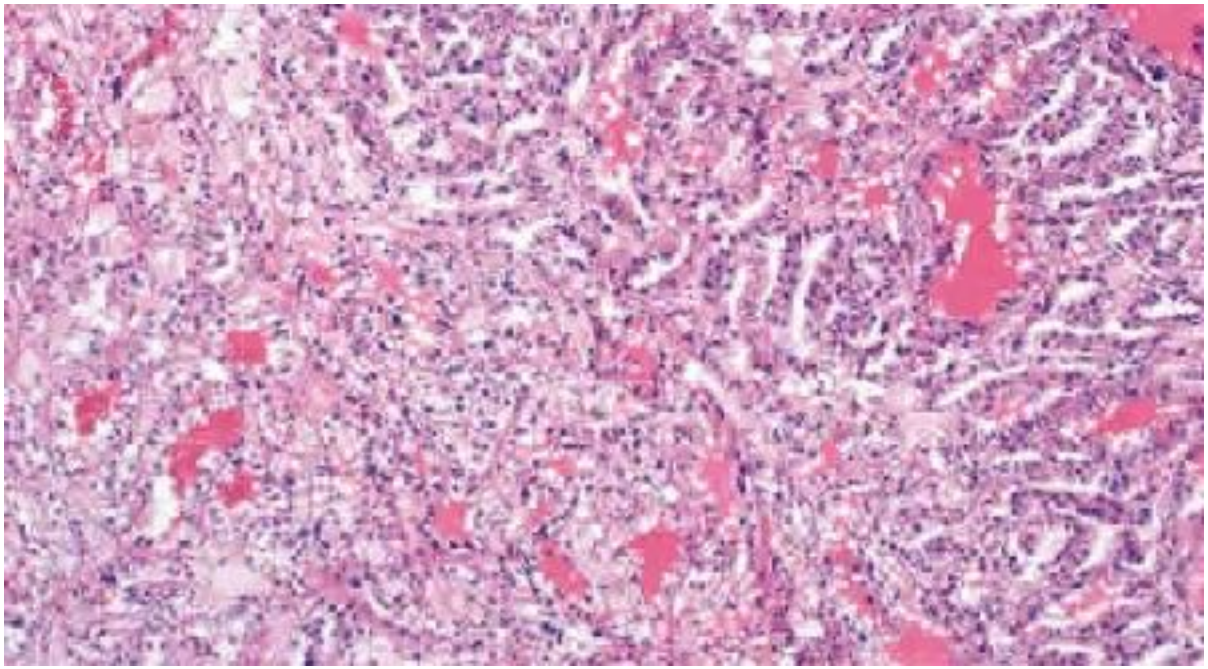


Axis


ECOG 0: 54%
Prior Sunitinib: 54%
Poor Risk MSKCC: 33%
Eligibility criteria:
Histologically-confirmed mRCC with clear-cell component
Failure of prior first-line regimen containing ≥1 of:
Sunitinib
Bevacizumab + IFN-α
Temsirolimus
Cytokine(s)
N=723
RANDOMIZATION
Axitinib 5 mg b.i.d.
Sorafenib 400 mg b.i.d.
Treat until PD, unmanageable AE or withdrawal of consent
Stratification:
Prior regimen
ECOG PS (0 vs 1)
Primary endpoint: PFS
Secondary endpoints: OS, ORR, duration of response, safety, QoL (FKSI and EQ-5D)

Axis: PFS


n*
mPFS, months
95% CI
Axitinib
361
6.8
6.4–8.3
Sorafenib
362
4.7
4.6–6.3
p<0.0001 (log-rank)
Stratified HR=0.67
(95% CI: 0.56–0.81)
PFS (probability)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Time (months)

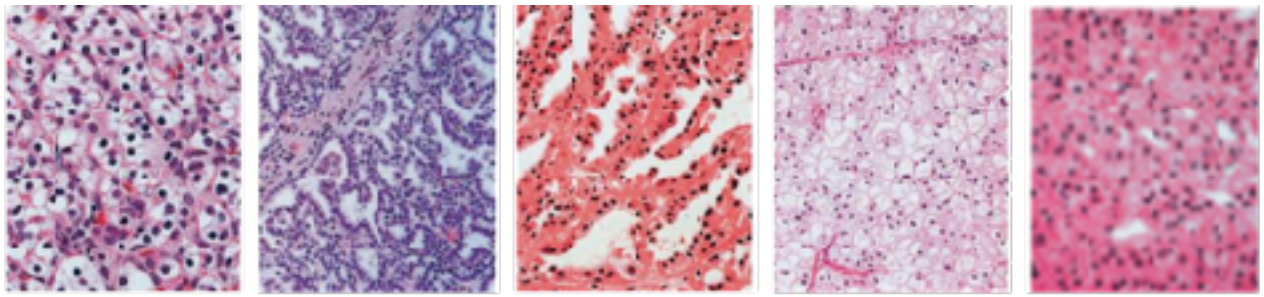


Carcinoma renal

hay subtipos histológicos

y

no todos se comportan de la misma manera



Tipo	Celulas claras	Papilar tipo 1	Papilar tipo 2	Cromofobo	Oncocitoma
	75%	5%	10%	5%	5%
Gen	VHL	Met	FH	BHD	

Además, existe heterogeneidad intra-tumoral y del tumor primario respecto a las metástasis

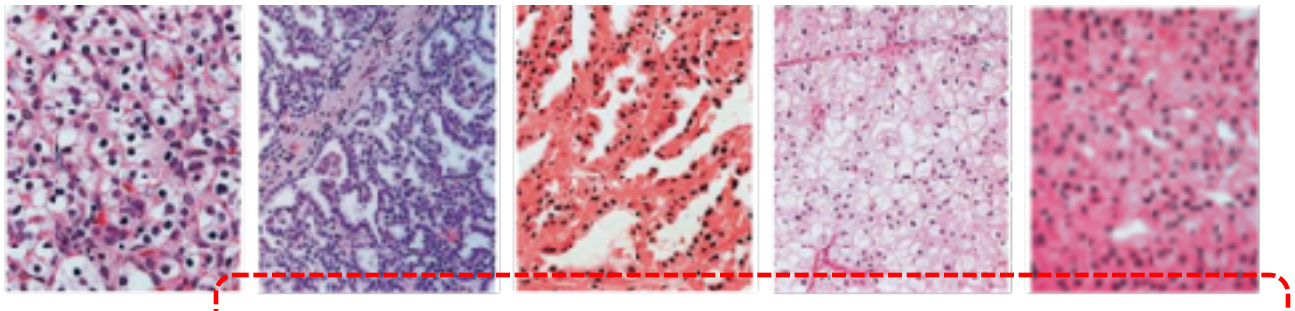
No se trata de una única enfermedad

Carcinoma renal

hay subtipos histológicos

y

no todos se comportan de la misma manera



Tipo	Celulas claras	Papilar tipo 1	Papilar tipo 2	Cromofobo	Oncocitoma
	75%	5%	10%	5%	5%
Gen	VHL	Met	FH	BHD	

Además, existe heterogeneidad intra-tumoral y del tumor primario respecto a las metástasis

No se trata de una única enfermedad

Cáncer renal Células no claras

Table 2 – Summary of main outcomes and harms of the included studies: overall survival (OS), progression free survival (PFS), Response Evaluation Criteria in Solid Tumors (RECIST), and toxicity

RCT	Comparator	Age (range)	Sex, male/female	Patients non-clear RCC [n]	Non-clear RCC [%]	OS [mo]	OS HR	PFS [mo]	PFS HR	Response RECIST [n]	Toxicity Grades 3–4	Toxicity Grade 3–4 types
ESPN first line	Everolimus	58 (23–73)	24/11	35	100	14.3 95% CI (8–23.4)		4.1 95% CI (2.7–10.5)	1.16 95% CI (0.67–2.01)	CR: 0 PR: 1 SD: 24 PD: 8	54%	Anemia: 5/35 Fatigue: 2/35
	Sunitinib	60 (28–75)	19/14	33		10.2 95% CI (14.2–NA)		5.1 95% CI (4.2–9.4)		CR: 0 PR: 3 SD: 21 PD: 9	88%	Fatigue 13/33 Hypertension 9/33 Diarrhea 8/33 Neutropenia 4/33
ASPEN	Everolimus	58 (29–90)	44/13	57	100	19.2 95% CI (9.7–37.9)	1.12 95% CI (0.7–2.)	5.6 95% CI (3.5–8.0)	1.41 80% CI (1.08–1.92) 1.41 95% CI (0.88–2.27)	CR: 1 PR: 4 SD: 33 PD: 13	67%	Anemia 8/57 Stomatitis 5/57
	Sunitinib	64 (24–100)	37/14	51		31.5 95% CI (14.8–NA)		8.3 95% CI (5.8–11.4)		CR: 0 PR: 9 SD: 30 PD: 10	78%	Hypertension 13/51 Infection 5/51 Diarrhea 5/51 Thrombocytopenia 4/51
RECORD3 first line	Everolimus	62 (20–83)[b]	165/72[b]	31	13	[a]		5.1 Range (2.6–7.9)	1.5 95% CI (0.9–2.8)	[a]	[a]	[a]
	Sunitinib	62 (25–84)[b]	170/57[b]	35	15	–[a]		7.2 Range (5.4–10.8)		–[a]	–[a]	–[a]
ARCC	Interferon-α	61	25/11	36	17	4.3 95% CI (2.2–7.5)	0.48 95% CI (0.29–0.85)	1.8 95% CI (1.5–2.1)	0.38 95% CI (0.25–0.62)	CR+PR: 3 CR+PR+SD: 5	–[a]	–[a]
	Temsirolimus	63	24/13	37	18	11.8 95% CI (8.9–13)		3 95% CI (3.9–5.9)		CR+PR: 2 CR+PR+SD: 15	–[a]	–[a]
SWOG 1177	Tivozanib	64	34/16	29	100	10.5	–	2	–	RR: 0	32%	Anemia 2/29 Nausea 1/29 Neutropenia 1/25
	Tivozanib + Erlotinib			25	100	11.3		5.4		RR: 0	56%	Rash 2/25 Transaminases 2/25 Anemia 1/25 Myocardial infarction 1/25

Eur Urology 71 (2017) 426–436

NCCN

SYSTEMIC THERAPY[m,o]
(alphabetical by category and preference)

- **Clinical trial (preferred)**
- **Sunitinib (preferred)**
- **Axitinib**
- **Bevacizumab**
- **Bevacizumab + erlotinib for selected patients with advanced papillary RCC including HLRCC**
- **Bevacizumab + everolimus for selected patients with advanced papillary RCC including HLRCC**
- **Cabozantinib**
- **Erlotinib**
- **Everolimus**
- **Lenvatinib + everolimus**
- **Nivolumab**
- **Pazopanib**
- **Sorafenib**
- **Temsirolimus (category 1 for poor-prognosis patients;[h] category 2A for other risk groups)**

and
Best supportive care:[l] See NCCN Guidelines for Palliative Care

SEOM

Recommendation

- VEGFR inhibitors, such as sunitinib, are the preferred option for papillary RCC. Level of evidence: II. Grade of recommendation: B.

ESMO

EAU

Both mTOR inhibitors (everolimus and temsirolimus) and VEGF-targeted therapies (sunitinib or sorafenib) have limited oncological efficacy in non-clear cell RCC. There is a non-significant trend for improved oncological outcomes for sunitinib, over everolimus.	2a
Offer sunitinib as first-line therapy for non-clear cell metastatic RCC.	Weak

KEEP
CALM
ITS
THE
CONCLUSION

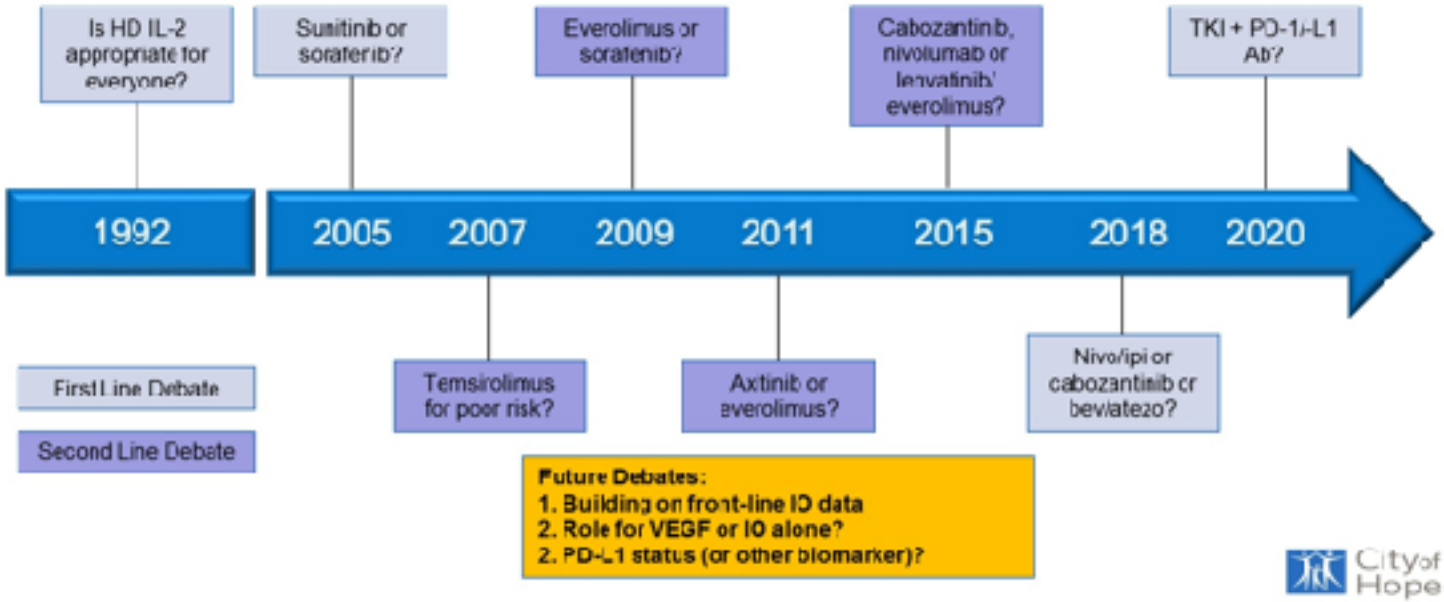
Algorithm incorporating emerging first-line options

Treatment	First-Line	Second-Line
Good risk	Bevacizumab/Atezolizumab	Cabozantinib
	Cabozantinib*	Nivolumab
Intermediate/Poor-risk	Bevacizumab/Atezolizumab Nivolumab/Ipilimumab	Cabozantinib
	Cabozantinib*	Nivolumab

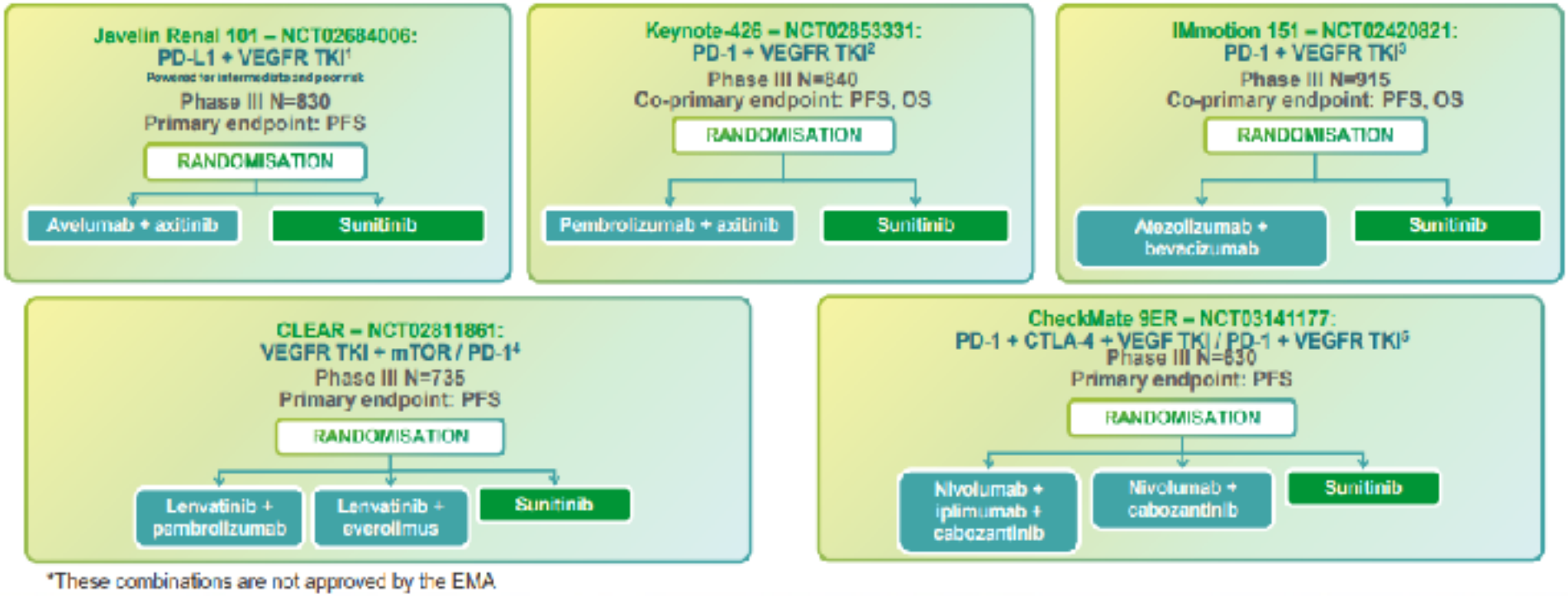
* For special populations (e.g., bony metastatic disease)

City of Hope

Beyond the current debate …



VEGFR + PD-1 / PD-L1



*These combinations are not approved by the EMA

Gracias

ricardo.collado@salud-juntaex.es