

III JORNADA DE ACTUALIZACIÓN EN
URO-ONCOLOGÍA:
UPDATE 2026

Madrid, 17 de febrero de 2026



Tratamiento de primera línea en carcinoma renal no célula clara: Cabozantinib

Javier Molina Cerrillo, MD, MSc, PhD
Medical Oncology Department
Genitourinary, Germ cell and Endocrine Tumors
Clinical Professor, School of Medicine, Alcalá de Henares University
Ramón y Cajal Health Research Institute (IRYCIS)
Madrid - Spain

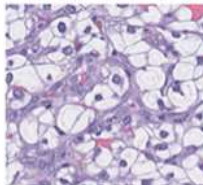
DISCLOSURES

Personal conflicts of interest: Scientific Consultancy Role (speaker and advisory role) and travel grant: *IPSEN, Pfizer, Roche, Bayer, Sanofi, Janssen, Astellas, Eisai, Adacap, Lilly, Novartis, BMS, MSD, Adium, Asofarma, Recordati Rare Diseases, Exelisis*

Participation in Clinical trials: *Roche, BMS, MSD, Pfizer, Novartis, IPSEN, Exelisis, AstraZeneca-Medimmune, Janssen, Lilly, Eisai, Astellas.*

Research support: *Roche, Pfizer, IPSEN, Janssen, Exelisis, MSD*

ARE ALL NON CLEAR CELL THE SAME?

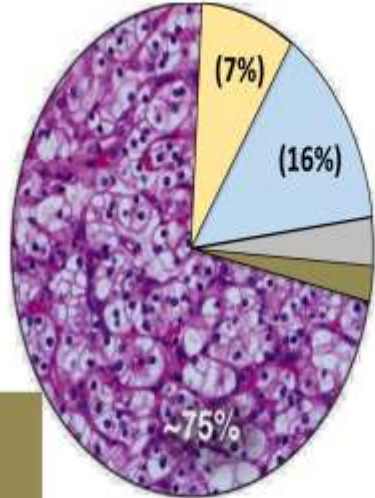
Clear Cell RCC	
	
Incidence:	75%
Median Age:	62
Prognosis:	Variable
Molecular Alterations:	3p loss, VHL
Therapeutic Targets:	HIF, VEGF, mTOR

Clear cell
VHL / Chr3p loss

PBRM1, SETD2,
BAP1, KDM5C
TSC1/2, MTOR

• Collecting duct →
NF2, CDKN2A, SETD2
• Other entities
• Not otherwise classified NOS

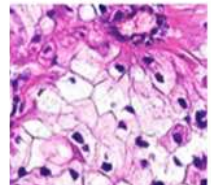
Chromophobe → TP53, PTEN, MT-ND
MTORC1



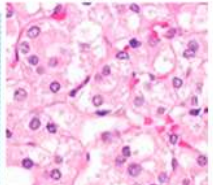
Papillary
Classic pattern of PRCC:
Old "type 1" → MET, Chr7 trisomy
Old "type 2" → CDKN2A, MYC, NRF2/ARE
Other morphological patterns:
Biphasic PRCC → NF2 loss
PRCC rev polarity → KRAS mut
And: Brisk inflammatory mimicking Whartin tumor, predominant solid growth or vacuolated
Add Grading

Molecularly defined entities

- FH-deficient/HLRCC → FH mutation
- SDH-deficient → SDH mutation
- ALK-rearranged → ALK fusions
- TFE3 rearranged → TFE3 fusion
- TFEB altered → TFEB fusion
- ELOC (TCEB1) mut → ELOC mutation
- SMARCB1 deficient → SMARCB1 loss

MIT family Translocation RCC


~ 1%
31-49
Often poor
TFE3/TFEB translocation
TFE3/PI3K/AKT/ mTOR

SDH-Deficient RCC


< 1%
38
Variable (often good)
SDHA, SDHB, SDHC, or SDHD
Metabolism

PATIENTS INCLUDED IN PHASE III TRIALS

ccRCC
75%

TOTAL DE PACIENTES

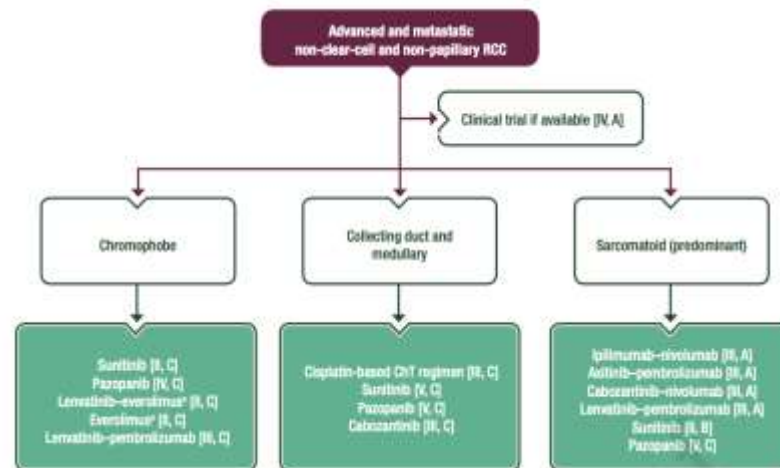
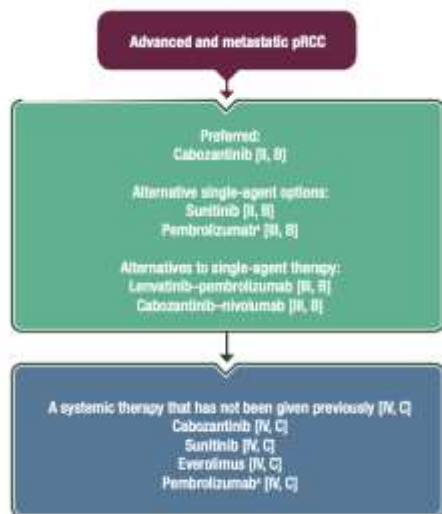
7,908

nccRCC
25%

CERO

0

GUIDELINES



Recommendations	Strength rating
Offer cabozantinib to patients with papillary RCC (pRCC) based on a positive randomised controlled trial.	Weak
Offer lenvatinib plus pembrolizumab or nivolumab plus cabozantinib to patients with pRCC based on small single-arm trials.	Weak

SYSTEMIC THERAPY FOR NON-CLEAR CELL HISTOLOGY ^h (IN ALPHABETICAL ORDER BY CATEGORY)		
Preferred	Other Recommended	Useful in Certain Circumstances
<ul style="list-style-type: none"> Clinical trial^f Cabozantinib Cabozantinib + Nivolumab^{b,c} Lenvatinib + Pembrolizumab^b 	<ul style="list-style-type: none"> Erlotinib + Bevacizumab^f for selected patients with advanced papillary RCC including hereditary leiomyomatosis and renal cell cancer (HLRCC)-associated RCC (HERED-RCC-D) Everolimus/Lenvatinib Nivolumab^{b,c} Pembrolizumab^b Sunitinib 	<ul style="list-style-type: none"> Axitinib Everolimus Everolimus + Bevacizumab^f Ipilimumab + Nivolumab^{b,d} (category 2B)

<p>CABOMETYX, en combinación con nivolumab, está indicado para el tratamiento de primera línea de pacientes adultos con carcinoma de células renales avanzado (ver sección 5.1).</p>	<p>Resuelto</p>	<p>No incluida</p>
<p>OPDIVO en combinación con cabozantinib está indicado para el tratamiento de primera línea de pacientes adultos con carcinoma de células renales avanzado (ver sección 5.1).</p>	<p>Resuelto</p>	<p>No incluida</p>
<p>Kisplyx esta indicado para el tratamiento de adultos con carcinoma de células renales (CCR) avanzado en combinación con pembrolizumab, como tratamiento de primera línea</p>	<p>Resuelto</p>	<p>No incluida</p>
<p>Kisplyx está indicado en combinación con everolimus para el tratamiento de pacientes adultos con carcinoma de células renales (CCR) avanzado tras un tratamiento previo dirigido al factor de crecimiento endotelial vascular.</p>	<p>Resuelto</p>	<p>No incluida</p>








Barata P JCO 2024
 Albigeres J Lancet Oncol 2024
 Fitzgerald et al Eur Urol 2024
 Bergmann L et al Ann Oncol 2025

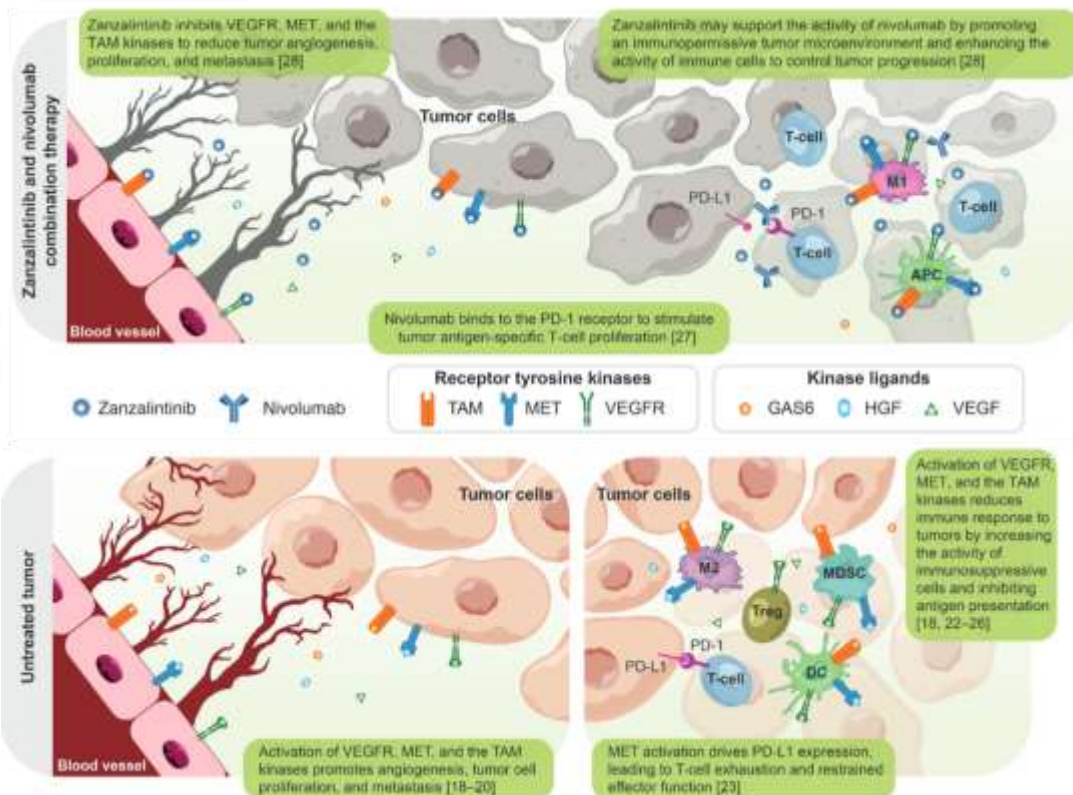
FUTURE

CLINICAL TRIAL PROTOCOL

OPEN ACCESS [Check for updates](#)

STELLAR-304: a phase III study of zanzalitinib (XL092) plus nivolumab in advanced non-clear cell renal cell carcinoma

Sumanta K. Pal , Thomas Powles², Ravindran Kaneswaran , Javier Molina-Cerrillo , Darren R. Feldman , Pedro Barata , Mohan Liu , Aarohi Bhatt³, Zhong Wang³, Prachi Nandoskar³ and Cristina Suarez 



CONCLUSIONES

- Non clear cell tumors are heterogeneous association of completely different tumors
- Cabozantinib seems the best option in pRCC attending to phase II randomized trial
- New immunotherapies and combinations are promising but today we have no solid randomized data
- We urgently need randomized phase III trials in nccRCC
- Biomarkers are conspicuous by their absence in kidney cancer

THANK YOU FOR YOUR ATTENTION

