

# Managing the treatment of patients with advanced renal cell carcinoma



# Online activity details



This resource has been downloaded from a touchEXPERT BRIEFING, hosted on touchONCOLOGY. The full activity, which includes video resources, can be accessed at:

[www.touchoncologytmc.com/renal-cancer/learning-zone/managing-treatment-of-patients-with-advanced-renal-cell-carcinoma](http://www.touchoncologytmc.com/renal-cancer/learning-zone/managing-treatment-of-patients-with-advanced-renal-cell-carcinoma)

This content is for healthcare professionals in Europe (excluding UK) only.

# Learning objectives



After watching the touchEXPERT BRIEFING activity, you should be able to:

- ✓ Provide an overview of the development of advanced RCC, treatment options and disease outcomes.
- ✓ Describe the standard of care treatment options for advanced RCC and associated disease outcomes.
- ✓ Discuss common AEs with standard of care treatment and management strategies to facilitate good treatment outcomes.



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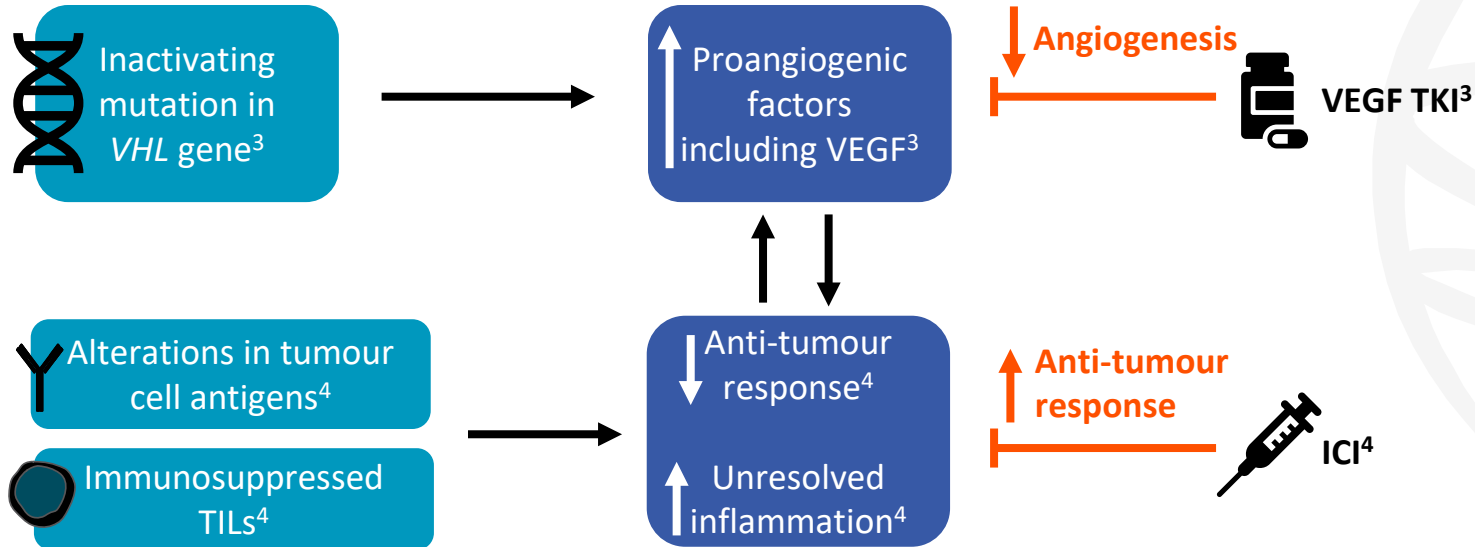




# **Pathological features of advanced RCC and treatment options**

# Pathology of advanced RCC

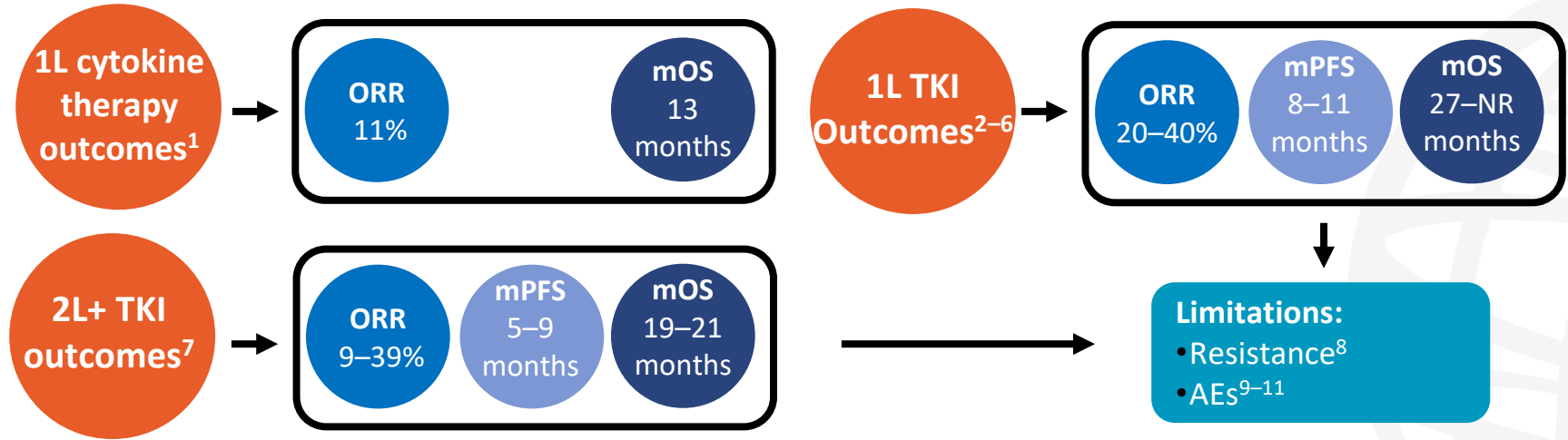
Clear cell RCC is the most common (70%) RCC subtype<sup>1</sup> and is frequently associated with mutations in the *VHL* gene.<sup>2</sup>



1. American Cancer Society. What Is Kidney Cancer. Available at: <https://www.cancer.org/cancer/kidney-cancer/about/what-is-kidney-cancer.html> (accessed July 2022); 2. Cancer Genome Atlas Research Network. *Nature*. 2013;499(7456):43-9; 3 Tannir NM, et al. *Oncologist*. 2018;23(5):540-555; 4. Díaz-Montero CM, et al. *Nat Rev Nephrol*. 2020;16(12):721-735.

ICI, immune checkpoint inhibitor; RCC, renal cell carcinoma; TIL, tumor infiltrating lymphocytes; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor; VHL, von Hippel-Lindau.

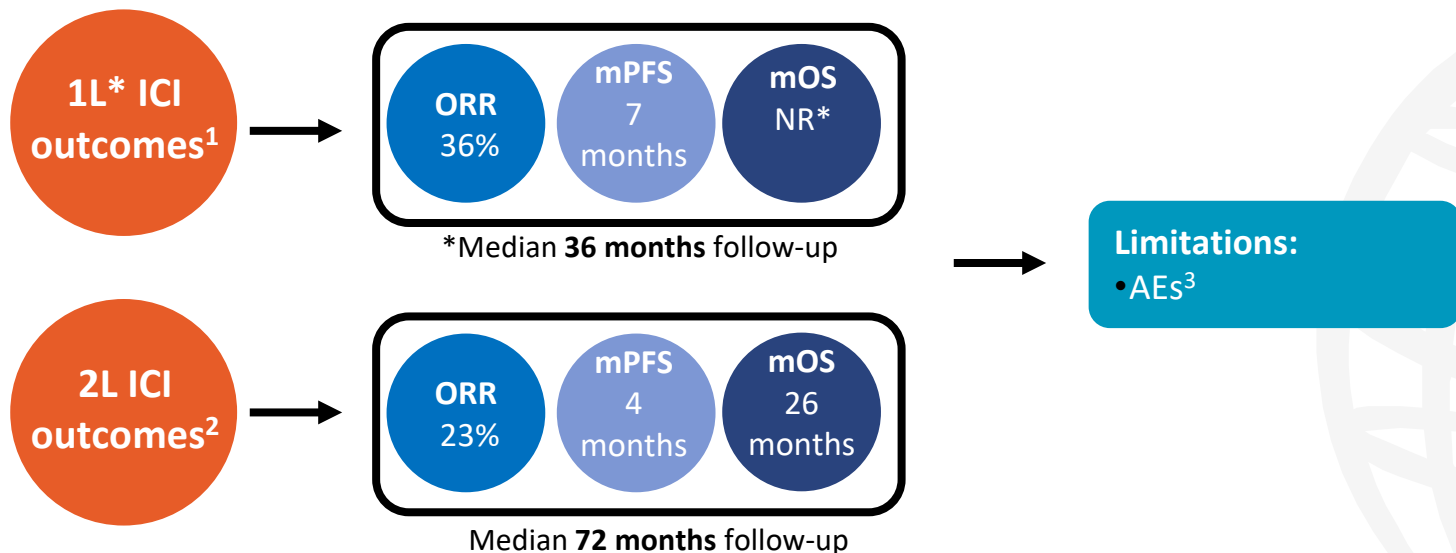
# Advanced RCC outcomes: impact of VEGF receptor TKI



VEGF receptor TKI monotherapy improves clinical outcomes in patients with advanced RCC,<sup>2-7</sup> but is associated with several limitations.<sup>9-11</sup>

1. Coppin C, et al. *Cochrane Database Syst Rev.* 2005;(1):CD001425. 2. Motzer RJ, et al. *N Engl J Med.* 2013;369(8):722-31; 3. Choueiri TK, et al. *Eur J Cancer.* 2018;94:115-125; 4. Powles T, et al. *Lancet Oncol.* 2020;21(12):1563-1573; 5. Choueiri TK, et al. *N Engl J Med.* 2021;384(9):829-841; 6. Motzer R, et al. *N Engl J Med.* 2021;384(14):1289-1300; 7. Tannir NM, et al. *Oncologist.* 2018;23(5):540-555; 8. Choueiri TK, Kaelin WG Jr. *Nat Med.* 2020;26(10):1519-1530; 9. Inlyta (axitinib) tablets. Available at: [https://www.ema.europa.eu/en/documents/product-information/inlyta-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/inlyta-epar-product-information_en.pdf) (accessed July 2022); 10. Cabometyx (cabozantinib) tablets. Available at: [https://www.ema.europa.eu/en/documents/product-information/cabometyx-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/cabometyx-epar-product-information_en.pdf) (accessed July 2022); 11. Kisplyx (lenvatinib) capsules. Available at: [https://www.ema.europa.eu/en/documents/product-information/kisplyx-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/kisplyx-epar-product-information_en.pdf) (accessed July 2022).  
AEs, adverse events; mPFS, median progression-free survival; mOS, median overall survival; ORR, overall response rate; RCC, renal cell carcinoma; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor.

# Advanced RCC outcomes: impact of ICI monotherapy



Compared with everolimus, 2L ICI monotherapy is associated with improved ORR and OS in patients with advanced RCC,<sup>1,2</sup> but is associated with toxicity limitations.<sup>3</sup>

\*ICI monotherapy is not indicated for 1L RCC therapy

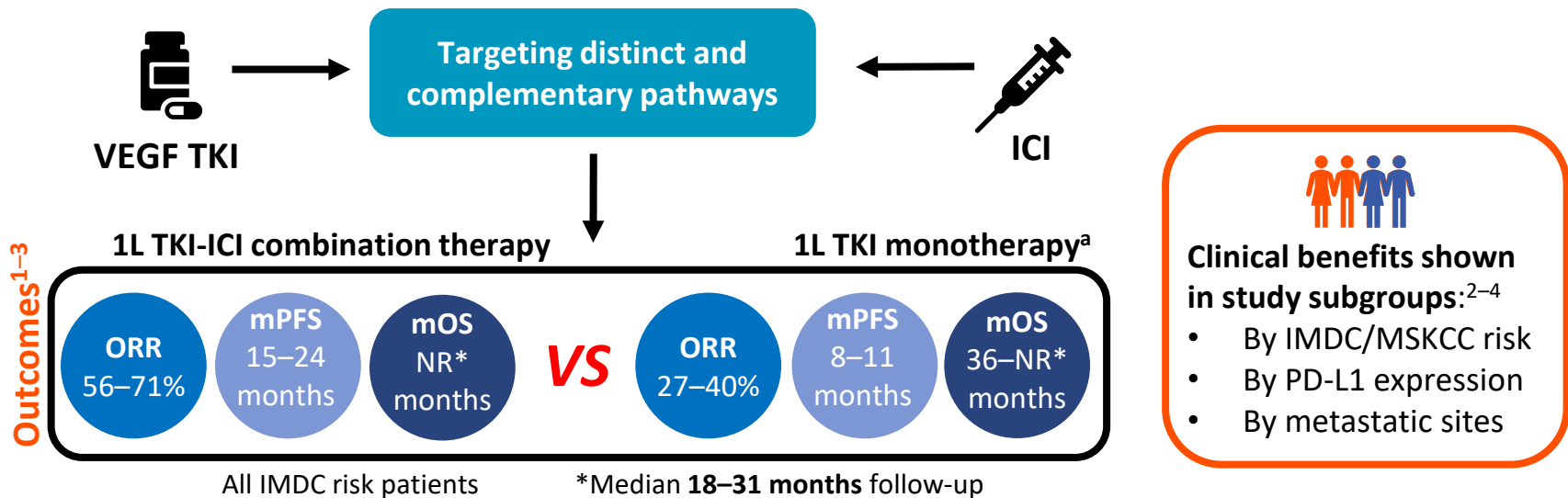
1. McDermott DF, et al. *J Clin Oncol.* 2021;39(9):1020-1028; 2. Motzer RJ, et al. *Cancer.* 2020;126(18):4156-4167; 3. Spain L, et al. *J. Cancer Treat Rev.* 2016;44:51-60; AE, adverse event; ICI, immune checkpoint inhibitor; mOS, median overall survival; mPFS, median progression-free survival; NR, not reached; ORR, overall response rate; RCC, renal cell carcinoma; TKI, tyrosine receptor kinase.



The background features a light gray globe with a grid of latitude and longitude lines on the right side. On the left side, there is a white curved line and several blue dots of varying sizes arranged in a semi-circular pattern. The text is centered in a dark blue, bold font.

**Standard of care  
treatment options  
and outcomes for  
advanced RCC**

# VEGF receptor TKI and ICI combinations in advanced RCC

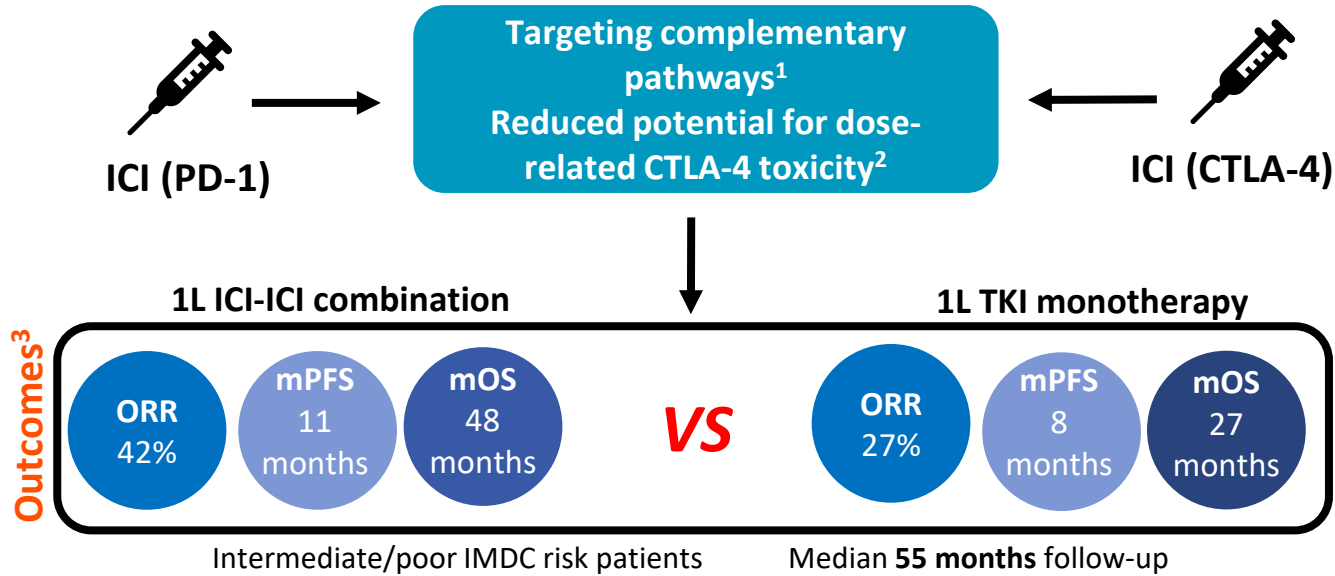


VEGF TKI-ICI combination therapy is recommended as a standard of care 1L treatment for advanced RCC.<sup>5,6</sup>

<sup>a</sup>Only results for direct comparisons within a trial are included.

1. Powles T, et al. *Lancet Oncol.* 2020;21(12):1563-1573; 2. Choueiri TK, et al. *N Engl J Med.* 2021;384(9):829-841; 3. Motzer R, et al. *N Engl J Med.* 2021;384(14):1289-1300; 4. Rini BI, et al. *N Engl J Med.* 2019;380(12):1116-1127; 5. Ljungberg B, et al. *Eur Urol.* 2022:S0302-2838(22)01676-1; 6. Powles T, et al. *Ann Oncol.* 2021;32(12):1511-1519. AE, adverse event; ICI, immune checkpoint inhibitor; MSKCC, Memorial Sloan Kettering Cancer Center; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; mOS, median overall survival; mPFS, median progression-free survival; NR, not reached; ORR, overall response rate; PD-L1, programmed death ligand 1; RCC, renal cell carcinoma; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor.

# ICI combinations in advanced RCC



ICI combination therapy is recommended as standard of care  
1L treatment for advanced RCC in patients with IMDC intermediate/poor risk.<sup>4,5</sup>

1. Curran MA, et al. *Proc Natl Acad Sci U S A*. 2010;107(9):4275–80; 2. Motzer RJ, et al. *N Engl J Med*. 2018;378(14):1277–1290; 3. Albiges L, et al. *ESMO Open*. 2020;5(6):e001079; 4. Ljungberg B, et al. *Eur Urol*. 2022;S0302–2838(22)01676–1; 5. Powles T, et al. *Ann Oncol*. 2021;32(12):1511–1519.  
CTLA-4, cytotoxic T-lymphocyte-associated antigen 4; ICI, immune checkpoint inhibitor; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; PD-L1, programmed death ligand 1; RCC, renal cell carcinoma; TKI, tyrosine kinase inhibitor.

# Impact of combination treatment on HRQoL



HRQoL  
score



HRQoL  
deterioration



VEGF TKI + ICI  
combination<sup>1,2</sup>



Similar or improved  
HRQoL  
vs TKI monotherapy

Reduced risk of first or  
definitive deterioration  
vs TKI monotherapy



ICI + ICI  
combination<sup>3</sup>



Increased HRQoL  
vs TKI monotherapy

Reduced risk of first  
deterioration vs TKI  
monotherapy



# Managing AEs in advanced RCC

# Common AEs with combination treatment

VEGF TKI + ICI <sup>1-3</sup>		
AE	Any grade	Grade ≥3
Diarrhoea	54–64%	7–11%
Fatigue	32–40%	3–4%
Appetite decrease	23–40%	2–4%
Hypertension	35–55%	13–28%
Hand-foot skin reactions	29–40%	4–8%
Stomatitis	15–35%	1–3%

ICI + ICI <sup>4</sup>		
AE	Any grade	Grade ≥3
Fatigue	37%	4%
Pruritus	28%	<1%
Diarrhoea	27%	4%
Rash	22%	1%
Nausea	20%	1%
Lipase level increase	16%	10%

1. Powles T, et al. *Lancet Oncol.* 2020;21(12):1563–1573; 2. Choueiri TK, et al. *N Engl J Med.* 2021;384(9):829–841; 3. Motzer R, et al. *N Engl J Med.* 2021;384(14):1289–1300;

4. Motzer RJ, et al. *N Engl J Med.* 2018;378(14):1277–1290.

AE, adverse event; ICI, immune checkpoint inhibitor; TKI, tyrosine receptor kinase; VEGF, vascular endothelial growth factor.

# Common AEs management strategies

AE management is critical for ensuring patients can continue to receive treatment combinations for as long as possible to maximise efficacy.<sup>1,2</sup>

## Proactive management

- **Specific strategies** can be used to manage AEs, even if mild at initiation to avoid them becoming more serious.<sup>1</sup>
- **E.g. for diarrhoea**, changing the patient's diet, addressing dehydration, providing anti-diarrhoea agents and adjusting targeted therapy dose can relieve symptoms.<sup>2</sup>

## Patient-physician collaboration

- **Patients:** education can manage expectations and facilitate self-monitoring.<sup>3</sup>
- **Physicians:** a MDT approach is recommended due to the broad multisystem nature of AEs.<sup>2</sup>
  - e.g. hypertension can be managed on an individual patient basis with coloration from oncologists and cardiologists.<sup>4</sup>

1. Eisen T, et al. *J Natl Cancer Inst.* 2012;104(2):93-113; 2. McGregor B, et al. *Cancer Treat Rev.* 2022;103:102333; 3. Ravaud A. *Oncologist.* 2011;16(Suppl 2):32-44;

4. Schmidinger M, Bergler-Klein J. *Int J Urol.* 2012;19(9):796-804.

AE, adverse event; MDT, multidisciplinary team.



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