

Advancing Care in Non-Clear Cell RCC: Optimizing ICI and TKIs

Translating Data Into Practice for Optimal Management of nccRCC

Learning Objectives

- Improved ability to compare and contrast clinical trial data on current and emerging uses of ICIs, TKIs, and combination ICI/TKI therapy for nccRCC
- Increased knowledge and skills in understanding the clinical profiles of ICI- and TKI-based therapies for nccRCC

Treatment Recommendations Vary Across International Guidelines and nccRCC Subtype

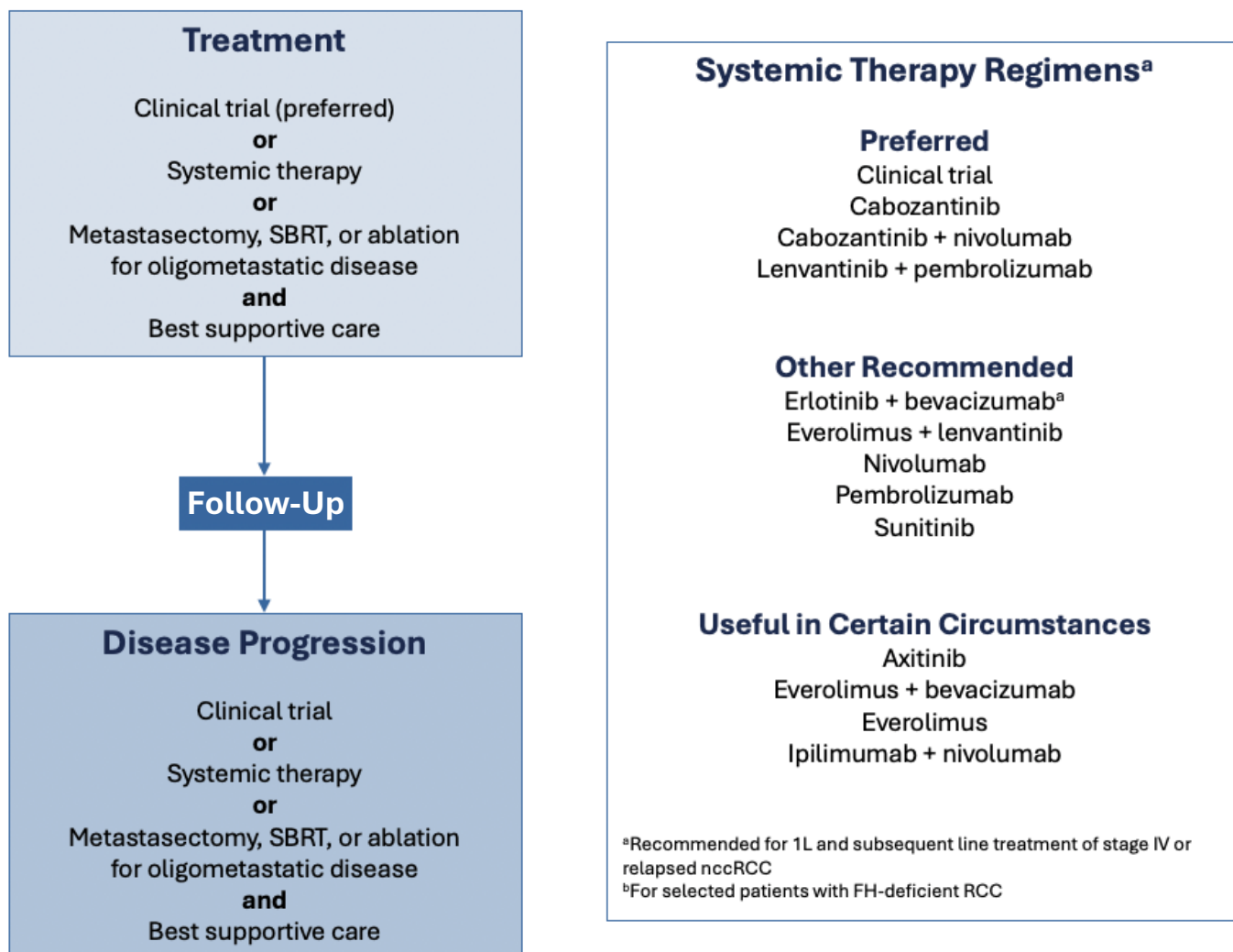
Guidelines	Metastatic papillary RCC ^a	Other nccRCC subtypes
ESMO ¹	Preferred: Cabozantinib	Recommendations vary
EAU ²	Alternatives include:	
NCCN ³	Lenvatinib + pembrolizumab Cabozantinib + nivolumab	

^aIn NCCN guidelines, all regimens listed here are preferred generally for nccRCC (see next page)

Advancing Care in Non-Clear Cell RCC: Optimizing ICI and TKIs

Translating Data Into Practice for Optimal Management of nccRCC

NCCN Treatment Guidelines: Stage IV or Relapsed nccRCC



Advancing Care in Non-Clear Cell RCC

Optimizing ICI and TKIs

Translating Data Into Practice for Optimal Management of nccRCC

Treatment Efficacy Varies Across nccRCC Subtypes

Chromophobe RCC⁴⁻¹²

ORR
≤ 44%

Highest ORRs with...
mTOR inhibitor + TKI
mTOR inhibitor + VEGF inhibitor

Translocation-associated RCC^{4, 5, 7, 9-11, 13-15}

ORR
≤ 78%

Highest ORRs with...
ICI + VEGF inhibitor

SMARCB1-deficient medullary carcinoma^{12, 16, 17}

ORR
≤ 20%

Highest ORRs with...
TKI + VEGF inhibitor
Chemotherapy

Collecting duct carcinoma^{11, 18, 19}

ORR
≤ 35%

Highest ORRs with...
TKI

Key Takeaways

- Treatment recommendations vary across international guidelines and across nccRCC subtype
- nccRCC subtypes respond differently to different treatment regimens
 - For most subtypes, TKIs (monotherapy or combination therapy) have a key role in treatment

Advancing Care in Non-Clear Cell RCC: Optimizing ICI and TKIs

Translating Data Into Practice for Optimal Management of nccRCC

References

1. Powles T, Albiges L, Bex A, et al. Renal cell carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*. Aug 2024;35(8):692-706. doi:10.1016/j.annonc.2024.05.537. <https://pubmed.ncbi.nlm.nih.gov/38788900/>
2. Ljungberg B, Bex, A., Albiges, L., et al. EAU Guidelines on Renal Cell Carcinoma. 2024. <https://uroweb.org/guidelines/renal-cell-carcinoma>
3. National Comprehensive Cancer Network. NCCN Guidelines: Kidney Cancer. Version 2.2025. <https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1440>
4. Albiges L, Gurney H, Atduiev V, et al. Pembrolizumab plus lenvatinib as first-line therapy for advanced non-clear-cell renal cell carcinoma (KEYNOTE-B61): a single-arm, multicentre, phase 2 trial. *Lancet Oncol*. Aug 2023;24(8):881-891. doi:10.1016/S1470-2045(23)00276-0. <https://pubmed.ncbi.nlm.nih.gov/37451291/>
5. Armstrong AJ, Halabi S, Eisen T, et al. Everolimus versus sunitinib for patients with metastatic non-clear cell renal cell carcinoma (ASPEN): a multicentre, open-label, randomised phase 2 trial. *Lancet Oncol*. Mar 2016;17(3):378-388. doi:10.1016/S1470-2045(15)00515-X. <https://pubmed.ncbi.nlm.nih.gov/26794930/>
6. Hutson TE, Michaelson MD, Kuzel TM, et al. A single-arm, multicenter, phase 2 study of lenvatinib plus everolimus in patients with advanced non-clear cell renal cell carcinoma. *Eur Urol*. Aug 2021;80(2):162-170. doi:10.1016/j.eururo.2021.03.015. <https://pubmed.ncbi.nlm.nih.gov/33867192/>
7. Lee CH, Voss MH, Carlo MI, et al. Phase II trial of cabozantinib plus nivolumab in patients with non-clear-cell renal cell carcinoma and genomic correlates. *J Clin Oncol*. Jul 20 2022;40(21):2333-2341. doi:10.1200/JCO.21.01944. <https://pubmed.ncbi.nlm.nih.gov/35298296/>
8. McDermott DF, Lee JL, Ziobro M, et al. Open-label, single-arm, phase II study of pembrolizumab monotherapy as first-line therapy in patients with advanced non-clear cell renal cell carcinoma. *J Clin Oncol*. Mar 20 2021;39(9):1029-1039. doi:10.1200/JCO.20.02365. <https://pubmed.ncbi.nlm.nih.gov/33529058/>
9. McGregor BA, Huang J, Xie W, et al. Phase II study of cabozantinib (Cabo) with nivolumab (Nivo) and ipilimumab (Ipi) in advanced renal cell carcinoma with variant histologies (RCCvh). *J Clin Oncol*. 2023;41(16_suppl):4520-4520. doi:10.1200/JCO.2023.41.16_suppl.4520. https://ascopubs.org/toc/jco/41/16_suppl
10. Tannir NM, Jonasch E, Albiges L, et al. Everolimus versus sunitinib prospective evaluation in metastatic non-clear cell renal cell carcinoma (ESPN): a randomized multicenter phase 2 trial. *Eur Urol*. May 2016;69(5):866-74. doi:10.1016/j.eururo.2015.10.049. <https://pubmed.ncbi.nlm.nih.gov/26626617/>
11. Tykodi SS, Gordan LN, Alter RS, et al. Safety and efficacy of nivolumab plus ipilimumab in patients with advanced non-clear cell renal cell carcinoma: results from the phase 3b/4 CheckMate 920 trial. *J Immunother Cancer*. Feb 2022;10(2). doi:10.1136/jitc-2021-003844. <https://pubmed.ncbi.nlm.nih.gov/35210307/>

Provided by



KidneyCancerAssociation™
Unstoppable Together.

Advancing Care in Non-Clear Cell RCC: Optimizing ICI and TKIs

Translating Data Into Practice for Optimal Management of nccRCC

References (continued)

12. Voss MH, Molina AM, Chen YB, et al. Phase II trial and correlative genomic analysis of everolimus plus bevacizumab in advanced non-clear cell renal cell carcinoma. *J Clin Oncol*. Nov 10 2016;34(32):3846-3853. doi:10.1200/JCO.2016.67.9084. <https://pubmed.ncbi.nlm.nih.gov/27601542/>
13. McGregor BA, Paul M, Xie W, et al. 1702P Updated results of phase II study of cabozantinib (Cabo) with nivolumab (Nivo) and ipilimumab (Ipi) in advanced renal cell carcinoma with divergent histologies (RCCdh). *Ann Oncol*. 2024;35. doi:10.1016/j.annonc.2024.08.1795. [https://www.annalsofoncology.org/issue/S0923-7534\(24\)X0007-1](https://www.annalsofoncology.org/issue/S0923-7534(24)X0007-1)
14. Alhalabi O, Thouvenin J, Negrier S, et al. Immune checkpoint therapy combinations in adult advanced MiT family translocation renal cell carcinomas. *Oncologist*. May 8 2023;28(5):433-439. doi:10.1093/oncolo/oyac262. <https://pubmed.ncbi.nlm.nih.gov/36640141/>
15. Bakouny Z, Sadagopan A, Ravi P, et al. Integrative clinical and molecular characterization of translocation renal cell carcinoma. *Cell Rep*. Jan 4 2022;38(1):110190. doi:10.1016/j.celrep.2021.110190. <https://pubmed.ncbi.nlm.nih.gov/34986355/>
16. Wiele AJ, Surasi DS, Rao P, et al. Efficacy and safety of bevacizumab plus erlotinib in patients with renal medullary carcinoma. *Cancers (Basel)*. Apr 30 2021;13(9). doi:10.3390/cancers13092170. <https://pubmed.ncbi.nlm.nih.gov/33946504/>
17. Wilson NR, Wiele AJ, Surasi DS, et al. Efficacy and safety of gemcitabine plus doxorubicin in patients with renal medullary carcinoma. *Clin Genitourin Cancer*. Dec 2021;19(6):e401-e408. doi:10.1016/j.clgc.2021.08.007. <https://pubmed.ncbi.nlm.nih.gov/34625389/>
18. Oudard S, Banu E, Vieillefond A, et al. Prospective multicenter phase II study of gemcitabine plus platinum salt for metastatic collecting duct carcinoma: results of a GETUG (Groupe d'Etudes des Tumeurs Uro-Genitales) study. *J Urol*. May 2007;177(5):1698-702. doi:10.1016/j.juro.2007.01.063. <https://pubmed.ncbi.nlm.nih.gov/17437788/>
19. Procopio G, Sepe P, Claps M, et al. Cabozantinib as first-line treatment in patients with metastatic collecting duct renal cell carcinoma: results of the BONSAI trial for the italian network for research in urologic-oncology (meet-URO 2 study). *JAMA Oncol*. Jun 1 2022;8(6):910-913. doi:10.1001/jamaoncol.2022.0238. <https://pubmed.ncbi.nlm.nih.gov/35420628/>

Provided by



The
France
Foundation



KidneyCancerAssociation™

Unstoppable Together.