

Single agent Samba? Doublet dance? Mambo combo? Mastering the Rhythm of Treatment Selection and Sequencing in RCC – Tweetorial #3

References

Tweet 6

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer (v2.2022). Updated September 8, 2021. Accessed September 29, 2021. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf

Ljungberg B, Albiges L, Bedke J, et al. *EAU Guidelines on Renal Cell Carcinoma*. EAU Annual Congress Milan; 2021. <https://uroweb.org/guideline/renal-cell-carcinoma/>

Powles T, Albiges L, Bex A, et al. ESMO Clinical Practice Guideline update on the use of immunotherapy in early stage and advanced renal cell carcinoma. *Ann Oncol*. 2021;doi:10.1016/j.annonc.2021.09.014

Tweet 7

Powles T, Plimack ER, Soulières D, et al. Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. *Lancet Oncol*. 2020;21(12):1563-1573. doi:10.1016/s1470-2045(20)30436-8

Rini BI, Plimack ER, Stus V, et al. Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Results from 42-month follow-up of KEYNOTE-426. *J Clin Oncol*. 2021;39(15_suppl):4500-4500. doi:10.1200/JCO.2021.39.15_suppl.4500

Choueiri TK, Motzer RJ, Rini BI, et al. Updated efficacy results from the JAVELIN Renal 101 trial: first-line avelumab plus axitinib versus sunitinib in patients with advanced renal cell carcinoma. *Ann Oncol*. 2020;31(8):1030-1039. doi:10.1016/j.annonc.2020.04.010

Choueiri TK, Powles T, Burotto M, et al. Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2021;384(9):829-841. doi:10.1056/NEJMoa2026982

Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med*. 2021;384(14):1289-1300. doi:10.1056/NEJMoa2035716

Choueiri TK, Powles T, Porta C, et al. A phase 3 trial of lenvatinib plus pembrolizumab versus sunitinib as a first-line treatment for patients with advanced renal cell carcinoma: overall survival follow-up analysis (the CLEAR study). Presented at: Kidney Cancer Research Summit; 2021; Philadelphia, PA, USA. Accessed October 19, 2021. <https://kcrs.kidneycan.org/wp-content/uploads/2021/10/Abstracts-Book-KCRS-2021-v2-10112021.pdf>

Albiges L, Tannir NM, Burotto M, et al. Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended 4-year follow-up of the phase III CheckMate 214 trial. *ESMO Open*. 2020;5(6):e001079. doi:10.1136/esmoopen-2020-001079

Tweet 8

Powles T, Plimack ER, Soulières D, et al. Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. *Lancet Oncol*. 2020;21(12):1563-1573. doi:10.1016/s1470-2045(20)30436-8

Rini BI, Plimack ER, Stus V, et al. Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Results from 42-month follow-up of KEYNOTE-426. *J Clin Oncol*. 2021;39(15_suppl):4500-4500. doi:10.1200/JCO.2021.39.15_suppl.4500

Choueiri TK, Motzer RJ, Rini BI, et al. Updated efficacy results from the JAVELIN Renal 101 trial: first-line avelumab plus axitinib versus sunitinib in patients with advanced renal cell carcinoma. *Ann Oncol*. 2020;31(8):1030-1039. doi:10.1016/j.annonc.2020.04.010

Choueiri TK, Powles T, Burotto M, et al. Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2021;384(9):829-841. doi:10.1056/NEJMoa2026982

Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med*. 2021;384(14):1289-1300. doi:10.1056/NEJMoa2035716

Choueiri TK, Powles T, Porta C, et al. A phase 3 trial of lenvatinib plus pembrolizumab versus sunitinib as a first-line treatment for patients with advanced renal cell carcinoma: overall survival follow-up analysis (the CLEAR study). Presented at: Kidney Cancer Research Summit; 2021; Philadelphia, PA, USA. Accessed October 19, 2021. <https://kcrs.kidneycan.org/wp-content/uploads/2021/10/Abstracts-Book-KCRS-2021-v2-10112021.pdf>

Albiges L, Tannir NM, Burotto M, et al. Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended 4-year follow-up of the phase III CheckMate 214 trial. *ESMO Open*. 2020;5(6):e001079. doi:10.1136/esmoopen-2020-001079

Tweet 9

Powles T, Plimack ER, Soulières D, et al. Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. *Lancet Oncol*. 2020;21(12):1563-1573. doi:10.1016/s1470-2045(20)30436-8

Choueiri TK, Motzer RJ, Rini BI, et al. Updated efficacy results from the JAVELIN Renal 101 trial: first-line avelumab plus axitinib versus sunitinib in patients with advanced renal cell carcinoma. *Ann Oncol*. 2020;31(8):1030-1039. doi:10.1016/j.annonc.2020.04.010

Choueiri TK, Powles T, Burotto M, et al. Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2021;384(9):829-841. doi:10.1056/NEJMoa2026982

Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med*. 2021;384(14):1289-1300. doi:10.1056/NEJMoa2035716

Choueiri TK, Powles T, Porta C, et al. A phase 3 trial of lenvatinib plus pembrolizumab versus sunitinib as a first-line treatment for patients with advanced renal cell carcinoma: overall survival follow-up analysis (the CLEAR study). Presented at: Kidney Cancer Research Summit; 2021; Philadelphia, PA, USA. Accessed October 19, 2021. <https://kcrs.kidneycan.org/wp-content/uploads/2021/10/Abstracts-Book-KCRS-2021-v2-10112021.pdf>

Albiges L, Tannir NM, Burotto M, et al. Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended 4-year follow-up of the phase III CheckMate 214 trial. *ESMO Open*. 2020;5(6):e001079. doi:10.1136/esmoopen-2020-001079

Tweet 10

Powles T, Plimack ER, Soulières D, et al. Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. *Lancet Oncol*. 2020;21(12):1563-1573. doi:10.1016/s1470-2045(20)30436-8

Choueiri TK, Powles T, Burotto M, et al. Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2021;384(9):829-841. doi:10.1056/NEJMoa2026982

Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med*. 2021;384(14):1289-1300. doi:10.1056/NEJMoa2035716

Motzer RJ, Penkov K, Haanen J, et al. Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2019;380(12):1103-1115. doi:10.1056/NEJMoa1816047

Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2018;378(14):1277-1290. doi:10.1056/NEJMoa1712126

Tweet 11

Powles T, Plimack ER, Soulières D, et al. Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial. *Lancet Oncol*. 2020;21(12):1563-1573. doi:10.1016/s1470-2045(20)30436-8

Choueiri TK, Powles T, Burotto M, et al. Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2021;384(9):829-841. doi:10.1056/NEJMoa2026982

Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med*. 2021;384(14):1289-1300. doi:10.1056/NEJMoa2035716

Motzer RJ, Penkov K, Haanen J, et al. Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2019;380(12):1103-1115. doi:10.1056/NEJMoa1816047

Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2018;378(14):1277-1290. doi:10.1056/NEJMoa1712126

Gadd M, Pranavan G, Malik L. Association between tyrosine-kinase inhibitor induced hypertension and treatment outcomes in metastatic renal cancer. *Cancer Rep (Hoboken)*. 2020;3(5):e1275. doi:10.1002/cnr2.1275

Ptinopoulou AG, Sprangers B. Tyrosine kinase inhibitor-induced hypertension-marker of anti-tumour treatment efficacy or cardiovascular risk factor? *Clin Kidney J*. 2021;14(1):14-17. doi:10.1093/ckj/sfaa174

Tweet 13

LENVIMA® (lenvatinib) [prescribing information]. Eisai Inc. Approved 2015. Revised August 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/206947s019lbl.pdf

Maitland ML, Bakris GL, Black HR, et al. Initial assessment, surveillance, and management of blood pressure in patients receiving vascular endothelial growth factor signaling pathway inhibitors. *J Natl Cancer Inst*. 2010;102(9):596-604. doi:10.1093/jnci/djq091

Tweet 14

Ljungberg B, Albiges L, Bedke J, et al. *EAU Guidelines on Renal Cell Carcinoma*. EAU Annual Congress Milan; 2021. <https://uroweb.org/guideline/renal-cell-carcinoma/>

Powles T, Albiges L, Bex A, et al. ESMO Clinical Practice Guideline update on the use of immunotherapy in early stage and advanced renal cell carcinoma. *Ann Oncol*. 2021;doi:10.1016/j.annonc.2021.09.014

Johnson DB, Sullivan RJ, Menzies AM. Immune checkpoint inhibitors in challenging populations. *Cancer*. 2017;123(11):1904-1911. doi:10.1002/cncr.30642

Choueiri TK, Hessel C, Halabi S, et al. Cabozantinib versus sunitinib as initial therapy for metastatic renal cell carcinoma of intermediate or poor risk (Alliance A031203 CABOSUN randomised trial): Progression-free survival by independent review and overall survival update. *Eur J Cancer*. 2018;94:115-125. doi:10.1016/j.ejca.2018.02.012

Motzer RJ, Hutson TE, Cella D, et al. Pazopanib versus sunitinib in metastatic renal-cell carcinoma. *N Engl J Med*. 2013;369(8):722-31. doi:10.1056/NEJMoa1303989

Motzer RJ, Hutson TE, Tomczak P, et al. Overall survival and updated results for sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. *J Clin Oncol*. 2009;27(22):3584-90. doi:10.1200/JCO.2008.20.1293

Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med*. 2007;356(2):115-24. doi:10.1056/NEJMoa065044

Motzer RJ, Nosov D, Eisen T, et al. Tivozanib versus sorafenib as initial targeted therapy for patients with metastatic renal cell carcinoma: results from a phase III trial. *J Clin Oncol*. 2013;31(30):3791-9. doi:10.1200/JCO.2012.47.4940

Tweet 15

Choueiri TK, Hessel C, Halabi S, et al. Cabozantinib versus sunitinib as initial therapy for metastatic renal cell carcinoma of intermediate or poor risk (Alliance A031203 CABOSUN randomised trial): Progression-free survival by independent review and overall survival update. *Eur J Cancer*. 2018;94:115-125. doi:10.1016/j.ejca.2018.02.012

Motzer RJ, Hutson TE, Cella D, et al. Pazopanib versus sunitinib in metastatic renal-cell carcinoma. *N Engl J Med*. 2013;369(8):722-31. doi:10.1056/NEJMoa1303989

Motzer RJ, Hutson TE, Tomczak P, et al. Overall survival and updated results for sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. *J Clin Oncol*. 2009;27(22):3584-90. doi:10.1200/JCO.2008.20.1293

Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med*. 2007;356(2):115-24. doi:10.1056/NEJMoa065044

Motzer RJ, Nosov D, Eisen T, et al. Tivozanib versus sorafenib as initial targeted therapy for patients with metastatic renal cell carcinoma: results from a phase III trial. *J Clin Oncol*. 2013;31(30):3791-9. doi:10.1200/JCO.2012.47.4940

Wong MK, Mohamed AF, Hauber AB, et al. Patients rank toxicity against progression free survival in second-line treatment of advanced renal cell carcinoma. *J Med Econ*. 2012;15(6):1139-48. doi:10.3111/13696998.2012.708689

Glossary

AE, adverse event
ALT, alanine transaminase
aRCC, advanced renal cell carcinoma
AST, aspartate transaminase
Axi, axitinib
BP, blood pressure
CR, complete response
EAU, European Association of Urology
ESMO, European Society for Medical Oncology
HBV, hepatitis B virus
HCV, hepatitis C virus
HIV, human immunodeficiency virus
HR, hazard ratio
I/O, immunotherapy
I/P, intermediate/poor
IMDC, International Metastatic RCC Database Consortium
INF, interferon
Ipi, ipilimumab
ITT, intent to treat
Len, Lenvatinib
NCCN, National Comprehensive Cancer Network
NA, not applicable
NE, not evaluable
Nivo, nivolumab
NR, not reported
ORR, objective response rate
OS, overall survival
Pembro, pembrolizumab
PFS, progression-free survival
PPES, palmar–plantar erythrodysesthesia syndrome
RCC, renal cell carcinoma

SOC, standard of care

TKI, tyrosine kinase inhibitor

VEGF, vascular endothelial growth factor

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