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INVITED EDITORIAL

Health-Related Quality of Life and Cost-Effectiveness of Treatment: Components to Be Included in Clinical Decision Making

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The treatment landscape for renal cell carcinoma (RCC) has evolved over the past 20 years.¹ Clinical trials have led to the FDA approval of several novel agents, expanding the array of options for first-line therapies. Largely similar efficacy outcomes across first-line clinical trials have generated greater focus on health-related quality of life (HR-QOL) and economic issues of treatment as differentiators. Each of these factors constitute important elements of broader clinical decision making.² Two recent studies published in *European Urology Oncology* may be able to help guide these such discussions. The first of these compared the efficacy and HR-QOL outcomes of two important trials that led to the approval of pembrolizumab plus axitinib (KEYNOTE-426) in 2019, and the approval of nivolumab plus cabozantinib (CheckMate 9ER) in 2021.³⁻⁵ The second study compared the cost-effectiveness of the current National Comprehensive Cancer Network-recommended first-line and second-line regimens for metastatic RCC (mRCC) in the USA.⁶ Both studies add to the existing literature base and inform future research towards robust data for clinical decision making.

McGregor and colleagues performed a matching-adjusted indirect comparison of clinical outcomes and HR-QOL between pembrolizumab plus axitinib and nivolumab plus cabozantinib based on the KEYNOTE-426 and CheckMate 9ER trials in which sunitinib had been used as control arm.² Using patient level data from CheckMate 9ER and study level data from KEYNOTE-426, the authors conclude that nivolumab plus cabozantinib had a more favorable efficacy profile, with a progression-free survival hazard ratio (HR) of 0.70 (95%CI 0.53-0.93; P=0.01) and an 8.4% improvement in response rate (95%CI -1.7 to 18.4; P=0.10) as compared to pembrolizumab plus axitinib.³ With regard to HR-QOL, assessed with the Functional Assessment of Cancer Therapy—Kidney Cancer Symptom Index (FKSI-DRS) and the EQ-5D-3L VAS, the indirect comparison suggested that nivolumab plus cabozantinib had better HR-QOL results compared with pembrolizumab plus axitinib. Notably, patients treated with nivolumab and cabozantinib presented with lower risk of first deterioration in EQ-5D-3L VAS and confirmed deterioration in FKSI-DRS.³

Mason and colleagues provide further context for clinical decision making utilizing a comprehensive Markov model to analyze cost-effectiveness of various treatment sequences of first and second-line regimens from a US payer perspective.⁶ This modeling simulated patient cohorts using the patient characteristics from 8 clinical trials. Endpoint included total costs, life years, quality adjusted life years (QALYs) and incremental cost-effectiveness ratios over a 5-year time horizon.⁶ Broadly speaking, findings suggests that pembrolizumab plus axitinib (or pembrolizumab plus lenvatinib), followed by cabozantinib, were reasonable cost-effective treatment options. Among those with favorable risk, pembrolizumab plus axitinib followed by cabozantinib dominated nivolumab plus cabozantinib followed by lenvatinib plus everolimus, whereas for patients with intermediate or poor IMDC risk, nivolumab plus ipilimumab followed by cabozantinib was the most cost-effective treatment sequence.⁶ These findings align with previous studies in this domain.⁷

It is interesting that these two studies, addressing HR-QOL and cost-effectiveness, respectively, point to distinct options as preferred for first-line treatment. Both studies have numerous caveats – in the study by McGregor and colleagues, patient-level data is incorporated from CheckMate 9ER but not from KEYNOTE-426, creating an obvious imbalance. HR-QOL was an exploratory endpoint and the sample size was limited for its analysis. The study by Mason and colleagues, in contrast, is predicated entirely on trial level data with complex modelling strategies used to arrive at their conclusions. Indirect comparisons and Markov simulations provide weaker evidence than randomized clinical trials. Furthermore, this study is a simulation exercise making several assumptions about patients transition from a hypothetical first-line regimen to a hypothetical second-line regimen. A large degree of imperfection likely exists in estimating the efficacy of sequential therapies, as there is substantial attrition across lines of therapy in mRCC.⁸

Despite the fact that previous studies have shown that immunotherapy (alone or in combination with targeted therapy) is a cost-effective option for patients with RCC, with long-

term survival benefits and fewer side effects, this can vary from patient to patient ^{7,9} Indeed, costs can vary based on the specificity of histology, disease stage and overall health of the patient. For instance, patients with papillary mRCC appear to have more modest gains with immunotherapy as compared to those with clear cell histology – studies of cabozantinib with immunotherapy appear to show lower response rates here as compared to clear cell histology.¹⁰ Also, with immunotherapy now representing a standard measure in the adjuvant setting, cost-effectiveness must be considered. In the adjuvant setting, the duration of therapy is finite and clinical benefit is measured in terms of disease-free survival (as compared to progression-free survival), as well as HR-QOL and QALYs for economic evaluation.

Measuring both HR-QOL and cost-effectiveness in prospective randomized clinical trials is an important strategy to improve patients' outcomes, to guide treatment decisions (patient and physician can make more informed decision that take into account the cost and value of a particular treatment), reimbursement decisions to optimize the allocation of resources (best outcome at the lowest cost), improving the patient experience by reducing the negative impact of treatments on patient's overall well-being. Thus, with the multiple treatment options that have led to improved clinical outcomes, and questions surrounding the cost-effectiveness of immunotherapy-based combination therapies, future studies should continue to seek clarity with regard to what is truly meaningful to patients and health authorities.

References

1. Gulati S, Philip E, Salgia S, Pal SK. Evolving treatment paradigm in metastatic non clear cell renal cell carcinoma. *Cancer Treat Res Commun.* 2020;23:100172.
2. Kucnerowicz K, Pietrzak A, Cholewiński W, et al. The quality-adjusted life-years in the oncological patients' health-related quality of life. *Sci Rep.* 2022;12(1):13562
3. McGregor B, Geynisman DM, Burotto M, et al. A matching-adjusted indirect comparison of nivolumab plus cabozantinib versus pembrolizumab plus axitinib in patients with advanced renal cell carcinoma. *Eur Urol Oncol.* 2023
4. 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. *Lancet Oncol.* 2020;21(12):1563-1573
5. Choueiri TK, Powles T, Burotto M, et al. CheckMate 9ER Investigators. Nivolumab plus cabozantinib versus sunitinib for advanced renal-cell carcinoma. *N Engl J Med.* 2021;384(9):829-884
6. Mason NT, Joshi VB, Adashek JJ, et al. Cost effectiveness of treatment sequences in advanced renal cell carcinoma. *Eur Urol Oncol.* 2023
7. Watson TR, Gao X, Reynolds KL, Kong CY. Cost-effectiveness of Pembrolizumab Plus Axitinib Vs Nivolumab Plus Ipilimumab as First-Line Treatment of Advanced Renal Cell Carcinoma in the US. *JAMA Netw Open.* 2020;3(10):e2016144
8. Bosma NA, Warkentin MT, Gan CL, et al. Efficacy and Safety of First-line Systemic Therapy for Metastatic Renal Cell Carcinoma: A Systematic Review and Network Meta-analysis. *Eur Urol Open Sci.* 2022;37:14-26
9. Wu B, Zhang Q, Sun J. Cost-effectiveness of nivolumab plus ipilimumab as first-line therapy in advanced renal-cell carcinoma. *J Immunother Cancer.* 2018;6(1):124

10. 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*. 2022;40(21):2333-2341.