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European Association of Urology

Letter to the Editor

Re: Ian D. Davis, Wanling Xie, Carmel Pezaro, et al. Efficacy of Second-line Targeted Therapy for Renal Cell Carcinoma According to Change from Baseline in International Metastatic Renal Cell Carcinoma Database Consortium Prognostic Category. Eur Urol 2017;71: 970–8

The Change in Baseline IMDC Prognostic Category: From the Past, Implications for the Future

We read with interest the paper by Davis and colleagues [1] about the different outcomes for second-line of therapy according to changes in prognostic class for patients with metastatic renal cell carcinoma (mRCC). This paper has at least three important points that need to be highlighted. First is the evidence that among mRCC patients, worsening of prognosis is more frequent than improvement. Second, as a consequence of the first point, is the evidence that prognosis is a dynamic parameter in mRCC and should be re-evaluated for each new line of therapy. Third, these findings may suggest a tailored approach when choosing a new line of therapy.

If this is true, is the evidence reported also useful in the new era of immunotherapy and MET/VEGFR tyrosine kinase inhibitors (TKIs)?

In this context, the prognostic class at the beginning of second-line therapy is a cornerstone in choosing the therapy sequence at present, when immunotherapy and the new generation of TKIs have both shown an increase in overall survival (OS) when used as second-line therapy [2,3]. The authors reported that patients with a prognostic improvement had a better outcome using a second TKI, while no difference was found for patients with no change or worsening of the prognostic class. Similarly, recent second-line phase 3 trials with cabozantinib and nivolumab reported that the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) classification retained its prognostic role. In clinical practice it is evident that patients with good prognosis at the beginning of second-line therapy experience longer survival and a higher probability of receiving further lines compared to other prognostic groups. Put simply, these patients have a strong probability of receiving both cabozantinib and nivolumab, but there are neither prospective nor retrospective studies on the sequence of these therapies to guide treatment choices. Considering that patients with a proven response and good tolerability to the first VEGFR TKI might be preferred for another line with a second VEGFR/MET TKI, the lack of a significant OS benefit in the good prognostic group for nivolumab in the Checkmate-025 trial, and the higher risk of progression as the best response for nivolumab (35%) compared to cabozantinib (14%) should be borne in mind [2,3]. Unfortunately, recent clinical trials have reported that only 40% of patients have good prognosis at the beginning of second-line therapy, and this group might be smaller in clinical practice, while no evidence is available for other prognostic groups.

Finally, although this study was performed in a population not representative of future second-line treatments, it remains interesting because of the prognostic role of IMDC classification, which is independent of the type of treatment used and has implications for an evolving scenario moving from TKI versus mTOR to TKI versus immunotherapy.

Conflicts of interest: Roberto Iacovelli has served as a consultant for Pfizer, Novartis, Ipsen, and Bayer. Walter Artibani and Giampaolo Tortora have nothing to disclose.

References

[1] Davis ID, Xie W, Pezaro C, et al. Efficacy of second-line targeted therapy for renal cell carcinoma according to change from baseline in International Metastatic Renal Cell Carcinoma Database Consortium prognostic category. Eur Urol 2017;71:970–8.

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