Research Letters

Influence of Prior Tyrosine Kinase Inhibitor on Survival for Patients with Metastatic Renal Cell Carcinoma Treated with Nivolumab or Cabozantinib: Data from a Literature-based Meta-analysis

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First-line treatment of metastatic renal cell carcinoma still involves small-molecule tyrosine kinase inhibitors (TKIs) such as sunitinib and pazopanib, which mainly target the vascular endothelial growth factor receptor (VEGFR) [1]. It has recently been shown that two agents improve survival in second-line treatment. In the METEOR trial [2], cabozantinib, a multikinase inhibitor targeting the VEGFR and other pathways including MET, RET and AXL, and in the CheckMate 025 study [3], nivolumab, an immunotherapeutic agent that inhibits the T-cell checkpoint regulator PD-1, were compared to everolimus and showed a survival advantage. However the most effective sequence after first-line TKI treatment is still unknown, so there is a need to identify factors that predict the response to nivolumab and cabozantinib. The aim of this letter is to focus on the survival of patients treated with nivolumab and cabozantinib according to prior first-line TKI. We used data from CheckMate 025 and METEOR for a subsequent subgroup analysis (Table 1) [4,5]. A pooled analysis according to prior TKI treatment revealed that survival was significantly improved to a greater extent after prior treatment with pazopanib (hazard ratio [HR] 0.62, 95% confidence interval [CI] 0.47–0.82; $p = 0.0009$) when comparison to sunitinib (HR 0.76, 95% CI 0.62–0.92; $p = 0.005$; Fig. 1).

Athough a limitation of this analysis is that literature data were used rather than a meta-analysis of data for individual patients, so that definitive conclusions need to be considered carefully, our data show that cabozantinib and

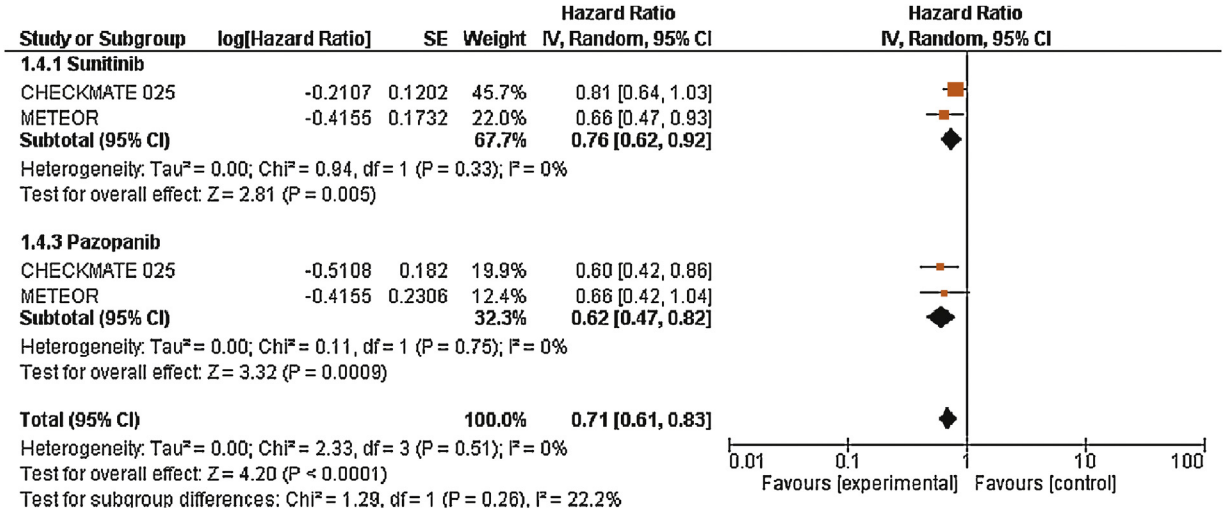

Fig. 1 – Subgroup analysis for overall survival among patients receiving nivolumab and cabozantinib according to prior sunitinib or pazopanib. CI = confidence interval.

Table 1 – Characteristics of the trials analyzed and data on survival according to prior treatment

Trial	Drug	Overall survival	
		Patients (*n*)	Median (mo)
Sunitinib			
CheckMate 025	Nivolumab vs everolimus	257 vs 261	23.6 vs 19.8
METEOR	Cabozantinib vs everolimus	135 vs 132	Not reported
Pazopanib			
CheckMate 025	Nivolumab vs everolimus	126 vs 136	Not reached vs 17.6
METEOR	Cabozantinib vs everolimus	88 vs 83	Not reported

nivolumab seem to reduce the risk of death in patients treated with prior pazopanib compared with sunitinib. These data will require further evaluation in prospective randomized clinical trials.

Conflicts of interest: The authors have nothing to disclose.

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Hyperpolarized 1-[^{13}C]-Pyruvate Magnetic Resonance Imaging Detects an Early Metabolic Response to Androgen Ablation Therapy in Prostate Cancer

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Hyperpolarized (HP) ^{13}C magnetic resonance spectroscopic imaging (MRSI) is a novel imaging technique that allows rapid and noninvasive monitoring of dynamic pathway-specific metabolic and physiologic processes [1] with unprecedented gain in sensitivity (10 000–200 000 fold increase) for imaging of ^{13}C-labeled biomolecules that are endogenous, nontoxic, and nonradioactive [2,3]. We previously reported the first-in-human phase 1 clinical study of HP [^{13}C]-pyruvate MRSI in patients with prostate cancer on active surveillance, and confirmed the feasibility of capturing regions of accelerated HP pyruvate-to-lactate flux in high-grade versus low-grade cancer versus benign tissue [4].

Here we describe the first results demonstrating the metabolic response to androgen deprivation therapy (ADT) using HP [^{13}C]-pyruvate MRSI. The patient presented with serum prostate-specific antigen (PSA) of 25.2 ng/ml and Gleason 4 + 5 prostate adenocarcinoma on biopsy. Cross-sectional imaging demonstrated metastases within the pelvic nodes and osseous structures. Baseline multiparametric (mp) ^{1}H MRI of the prostate (anatomic imaging, diffusion-weighted imaging [DWI], dynamic contrast-enhanced [DCE] imaging, and 3D ^{1}H MRSI) with HP [^{13}C]-pyruvate revealed a bulky tumor involving the left apex, mid gland, and base peripheral and transition zones, and right apex, mid gland, and base peripheral zone, measuring 4.5 × 1.5 × 5.1 cm^3. T2-weighted MRI showed a well-defined focus of low signal intensity (T2 score 5/5; Fig. 1A). The lesion also had marked restricted diffusion (DWI score 5/5; apparent diffusion coefficient [ADC] 930)