

Clinical Trials Corner: Healthy Competition

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Dear Readers,

The Clinical Trials Corner of *Kidney Cancer* highlights planned or ongoing high-impact studies in renal cell carcinoma (RCC). In this issue, we highlight the COSMIC-313 trial, an important study evaluating the addition of cabozantinib to immune checkpoint inhibitor therapy in newly diagnosed metastatic RCC.

In the future, if you feel that you would like to draw attention to a specific trial, please feel free to email us at mbparikh@ucdavis.edu or kca@iospress.com.

Sincerely,

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A Randomized, Double-Blind, Controlled Phase 3 Study of Cabozantinib in Combination with Nivolumab and Ipilimumab versus Nivolumab and Ipilimumab in Subjects with Previously Untreated Advanced or Metastatic Renal Cell Carcinoma of Intermediate or Poor Risk.

Status: Recruiting

Clinicaltrials.gov identifier: NCT03937219

Sponsor: Exelixis

Enrollment: 676

Rationale: The combination of nivolumab and ipilimumab was demonstrated to be superior to sunitinib in the treatment of patients with intermediate or poor risk advanced RCC in the CheckMate-214 trial, and thus has become an established therapy for these patients. Recently, the CheckMate 9ER trial demonstrated that the combination of nivolumab with cabozantinib was tolerated and was superior in radiographic progression free survival (PFS) and objective response rate (ORR) to sunitinib.

Study Design: This Phase III randomized trial enrolls patients with advanced RCC with a clear-cell component, who must be intermediate- or poor-risk by International Metastatic RCC Database Consortium (IMDC) criteria. Patients may not have had previous systemic therapy in the locally advanced or metastatic setting, and will be excluded if they have underlying, recent autoimmune disorders requiring systemic treatment. Patients will be randomized to receive either cabozantinib + nivolumab + ipilimumab (with nivolumab + ipilimumab received for 4 doses) followed by cabozantinib + nivolumab (experimental arm) or placebo + nivolumab + ipilimumab (for 4 doses) followed by placebo + nivolumab (control arm). Patients will be treated until disease progression or unacceptable toxicity.

Endpoints: The primary endpoint of this trial is duration of PFS. The secondary outcome measure is duration of overall survival (OS).

Comments: While the COSMIC-313 study, sponsored by Exelixis, was initiated prior to the availability of results of CheckMate 9ER, it will inadvertently build on the findings recently reported by Dr. Choueiri at ESMO. While prior studies that combined sunitinib or pazopanib with checkpoint inhibitors have been plagued by toxicity that limited the evaluation of these combinations, the combination of cabozantinib and nivolumab has an acceptable toxicity profile. Prior Phase III studies, such as CheckMate 9ER, CheckMate 214, KEYNOTE 426, and JAVELIN Renal 100, have all utilized sunitinib as the comparator. In the current treatment landscape, however, for patients with intermediate or poor risk disease, sunitinib is not the optimal active comparator. The COSMIC-313 trial will provide meaningful results about the benefit of addition of cabozantinib to checkpoint inhibitors, particularly because the active comparator arm is nivolumab combined with ipilimumab, now a standard therapy for intermediate or poor risk advanced RCC. In addition, it will interrogate whether the combination of these three agents can be tolerated safely.

CONFLICT OF INTEREST

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