

# Clinical Trials Corner: Contact After the First Round

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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 CONTACT-03 trial, a study evaluating the role of further checkpoint inhibitor therapy after initial treatment for mRCC.

In the future, if you feel that you would like to draw attention to a specific trial, please feel free to email us at E-mail: [mbparikh@ucdavis.edu](mailto:mbparikh@ucdavis.edu). or E-mail: [kca@iospress.com](mailto:kca@iospress.com).

Sincerely,

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**A Phase III, Multicenter, Randomized, Open-Label Study to Evaluate the Efficacy and Safety of Atezolizumab Given in Combination With Cabozantinib Versus Cabozantinib Alone in Patients With Inoperable, Locally Advanced, or Metastatic Renal Cell Carcinoma Who Experienced Radiographic Tumor Progression During or After Immune Checkpoint Inhibitor Treatment.**

Status: Recruiting

Clinicaltrials.gov identifier: NCT04338269

Sponsor: Hoffmann-La Roche

Enrollment: 500

Rationale: In recent years, combination immune checkpoint inhibitor (ICI) therapy has become standard first-line treatment of mRCC. Pembrolizumab plus axitinib, pembrolizumab plus lenvatinib and nivolumab plus cabozantinib are all combinations that have been approved for use based on randomized trials in which these combinations demonstrated an overall survival benefit compared to sunitinib, regardless of risk stratification. Nivolumab plus ipilimumab has also demonstrated overall survival benefit in patients with intermediate- or poor-risk disease as compared to sunitinib, and thus is also an option for first-line treatment in select patients.

Clinical data on sequencing further treatment after progression on initial immune checkpoint-based therapy is limited, and in particular whether there is further benefit to combining immune checkpoint inhibitor therapy with VEGF-directed therapies remains unclear. This trial seeks to interrogate that question..

**Study Design:** This Phase III randomized trial enrolls patients with histologically proven clear cell or non-clear cell metastatic RCC, though those with chromophobe subtype must have sarcomatoid differentiation. Patients must have radiographic evidence of disease progression during or following treatment with an anti-PD-L1 or anti-PD1 antibody (including atezolizumab, avelumab, pembrolizumab, or nivolumab). Patients may not have received prior cabozantinib, or more than one anti-PD-L1 or anti-PD-1 therapy prior to enrollment. They also may not have received more than two prior lines of therapy in the locally advanced or metastatic setting. While brain metastases are not an exclusion, patients with symptomatic, untreated or actively progressing CNS metastases or leptomeningeal disease are not permitted on study. Patients enrolled to study will be randomized to receive either atezolizumab (1200 mg IV every 3 weeks) plus cabozantinib (60 mg PO daily) or cabozantinib 60 mg PO daily, until unacceptable toxicity or disease progression.

**Endpoints:** The co-primary endpoints of this trial progression free survival (PFS) and overall survival (OS). The secondary outcomes include investigator-assessed PFS, investigator-assessed objective response rate (ORR), independently reviewed ORR, investigator-assessed duration of response (DOR) and independently reviewed DOR, as well as percentage of patients with adverse events.

**Comments:** As an increasing number of options emerge for the initial treatment of mRCC, selection of therapy becomes complicated, especially insofar as subsequent therapy is concerned. The most robust data for treatment after progression on ICI therapy is currently available for cabozantinib. There is also some data regarding the potential to treat with additional ICI therapy after progression on a prior ICI, but these data are limited to single-arm studies. This trial will both better characterize the response to cabozantinib after progression on ICI, and evaluate whether combining atezolizumab with cabozantinib provides benefit to patients previously treated with ICI. The trial allows prior treatment with atezolizumab, but does not allow prior cabozantinib exposure. As a result, this study will exclude those patients treated with nivolumab plus cabozantinib, a recently approved first-line combination treatment, but this is a necessary aspect of evaluating the clinical question at hand.

## **CONFLICT OF INTEREST**

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