

Clinical trial: Three-drug combination slows progression of advanced kidney cancer

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A targeted kinase inhibitor added to a two-drug immunotherapy combination slowed the progression of advanced kidney cancer in previously untreated patients, according to research led by an oncologist

from Dana-Farber Cancer Institute.

"Patients who received the kinase inhibitor cabozantinib in addition to checkpoint-blockers nivolumab and [ipilimumab](#) experienced significantly improved progression-free survival compared to those who received only nivolumab and ipilimumab," said Toni Choueiri, MD. Choueiri, who is the director of the Lank Center for Genitourinary Cancer at Dana-Farber, is the lead author of the COSMIC-313 study evaluating the combination of cabozantinib with nivolumab and ipilimumab in previously untreated advanced renal cell carcinoma (RCC) of intermediate or poor risk, which was published today, May 10, in the *New England Journal of Medicine*.

Patients treated with the three-drug combination had a 27% lower risk of progression or death compared to those on the two immunotherapy drugs. That progression-free survival (PFS) advantage met the primary endpoint. The median PFS was not yet reached in the three-drug patient group. The median PFS was 11.3 months for patients receiving nivolumab and ipilimumab.

"This is the first study to evaluate a triplet therapy against a contemporary immune-oncology doublet control and it was designed to answer an important question of whether adding cabozantinib to dual checkpoint inhibition can improve outcomes for this patient population," said Choueiri. "The initial findings provide a clear look at the efficacy and safety profile of this triplet therapy and demonstrate a significant [progression-free survival](#) benefit."

The patients have been followed for between 17.7 and 20 months. Overall survival is a secondary endpoint of the COSMIC-313 trial. At this stage of the trial there was no significant survival benefit for the three-drug combination, so the trial will continue to the next analysis of overall survival.

The trial included 855 previously untreated patients with advanced or metastatic renal cell cancer (RCC) who were judged to be at intermediate or poor risk for survival according to the International Metastatic RCC Database Consortium (IMDC) risk model. Nivolumab plus cabozantinib and nivolumab plus ipilimumab are both standard of care first-line treatments of advanced kidney cancer. This is the first phase 3 trial in metastatic renal cell carcinoma to use nivolumab plus ipilimumab as the control arm.

Nivolumab and ipilimumab both work by blocking immune checkpoints, molecular "brakes" that prevent the [immune system](#) from attacking the cancer. Releasing the brakes allows the immune's T cell army to invade the tumors and kill the cancer cells.

Cabozantinib inhibits several [cancer](#)-promoting pathways including MET, VEGFR, and TAM, and "may enhance response to checkpoint inhibitors," said Choueiri, thus providing an additive or synergistic benefit when combined with [nivolumab](#) and ipilimumab.

The data was previously presented at the ESMO Congress 2022 in Paris during the Presidential Symposium.

More information: Cabozantinib plus Nivolumab and Ipilimumab in Renal-Cell Carcinoma, *New England Journal of Medicine* (2023). [DOI: 10.1056/NEJMoa2212851](https://doi.org/10.1056/NEJMoa2212851)

Provided by Dana-Farber Cancer Institute

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