Immunotherapy Combo Improves Outcomes in Advanced Kidney Cancer

Opdivo plus Cabometyx reduced the risk of death by 40%.

March 11, 2021 By Dana-Farber Cancer Institute

Update: This press release was initially issued on September 19, 2020. It is now updated and was re-issued on March 3, 2021 to reflect the study's publication in The New England Journal of Medicine.

An immunotherapy agent combined with a tyrosine kinase inhibitor drug significantly improved progression-free survival and reduced the risk of death compared to a single agent treatment in advanced kidney cancer patients, according to first results of a phase 3 clinical trial, CheckMate -9ER, published in the New England Journal of Medicine.

Recently, results from that trial led to the approval by the U.S. Food and Drug Administration (FDA) of the combination of nivolumab (OPDIVO®) and cabozantinib (CABOMETYX®) as a first-line treatment for patients with advanced renal cell carcinoma (RCC). CheckMate -9ER evaluated the combination compared to sunitinib, a single agent treatment.

Patients receiving the combination had a higher response rate and superior quality of life, said investigators from Dana-Farber Cancer Institute. The results were previously presented in a Presidential/Plenary Symposium of the European Society for Medical Oncology (ESMO) Virtual Congress 2020.

The first author of the report, Toni Choueiri, MD, director of the Lank Center for Genitourinary Oncology at Dana-Farber, said the combination of nivolumab and cabozantinib achieved significant improvements across all efficacy endpoints, including overall survival, in previously untreated patients with metastatic renal cell carcinoma. The combination was tested against sunitinib in a randomized trial involving 651 patients.

"I'm quite encouraged with the results," said Choueiri, the Jerome and Nancy Kohlberg Professor of Medicine at Harvard Medical School. "The combination treatment demonstrated meaningful efficacy benefits with consistent effects observed across pre-specified subgroups. These results, along with manageable toxicity and superior health-related quality-of-life, highlight this regimen's potential importance among first-line combinations of immunotherapies and tyrosine kinase inhibitors."

Nivolumab is a PD-1 checkpoint inhibitor designed to help the body's immune system recognize and attack cancer cells. Cabozantinib is a small-molecule inhibitor of tyrosine kinases including c-Met and VEGFR2, which are implicated in cancer cell growth. Cabozantinib may also counteract tumor-induced immunosuppression, say the investigators.

The CheckMate -9ER trial data showed that the combination of nivolumab and cabozantinib reduced the risk of death by 40% compared with sunitinib. Median overall survival was not reached in either group, at a median follow-up of 18.1 months. In patients receiving the combination, median progression-free survival – the study's primary endpoint – was doubled compared to those who got sunitinib alone, 16 .6 months vs 8.3 months. The median duration of response was 20.2 months for the combination, vs 11.5 months for sunitinib.

In addition, twice as many patients receiving the combination had a response compared to sunitinib – 56% vs. 27% – and 8% achieved a complete response vs 5% for sunitinib.

The combination was well-tolerated, according to the investigators with less than 5% of patients having to completely discontinue both nivolumab and cabozantinib due to side effects. Patients treated with nivolumab plus cabozantinib reported significantly better health-related quality of life than those treated with sunitinib at most time points, according to a kidney symptom index.

The five-year survival rate for patients with advanced or late-stage metastatic kidney cancer is only 12%, according to the American Cancer Society's 2020 statistics.

This article was originally published on March 3, 2021, by Dana-Farber Cancer Institute. It is republished with permission.
