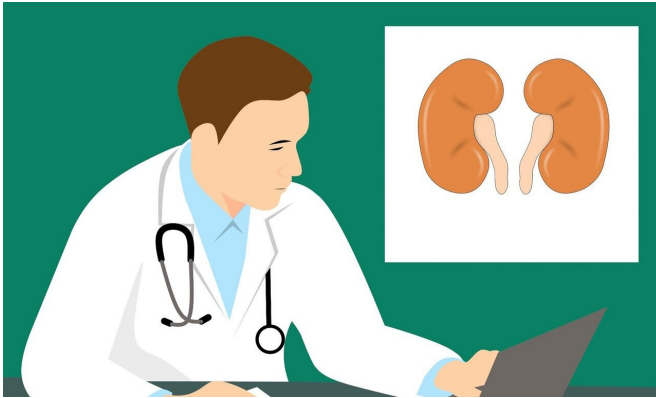


Immunotherapy—targeted drug combination improves survival in advanced kidney cancer

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Patients with advanced kidney cancer, who received a targeted drug combined with a checkpoint-blocker immunotherapy agent had longer survival than patients treated with the standard targeted drug, said an investigator from Dana-Farber Cancer Institute, reporting results from a phase 3 clinical trial.

The survival benefit demonstrates that an [immune checkpoint inhibitor](#) together with a targeted kinase inhibitor drug "is important in the first-line treatment of patients with advanced renal cell carcinoma," said the authors of a study published in *The New England Journal of Medicine* today and simultaneously presented during American Society of Clinical Oncology (ASCO) 2021 Genitourinary Cancers Symposium. The senior author is Toni Choueiri, MD, director of the Lank Center for Genitourinary Oncology at Dana-Farber.

The phase 3 CLEAR study results showed significant benefits from the combination comprised of lenvatinib, an oral kinase inhibitor that targets proteins involved in the formation of

blood vessels supplying a tumor, and [pembrolizumab](#), a checkpoint inhibitor given by infusion that helps the immune system attack the [cancer](#). Another group of patients received a combination of lenvatinib and everolimus, a drug that targets a protein, mTOR.

The comparison drug was [sunitinib](#), an inhibitor that targets multiple kinases and has been the [standard treatment](#) in these patients with [advanced kidney cancer](#), which carries a poor prognosis. However, standard-of-care options now include treatment with immune checkpoint inhibitors, either as a combination of two checkpoint inhibitors or a checkpoint inhibitor plus a kinase inhibitor. These combinations have achieved improved outcomes for advanced kidney cancer patients compared with sunitinib.

The results of the CLEAR study showed that those receiving the combination of lenvatinib and pembrolizumab not only had longer overall survival but also longer [progression-free survival](#)—the period before their disease worsened—and a higher response rate. In addition to lenvatinib plus pembrolizumab, the clinical trial also tested the combination of lenvatinib and everolimus, which is approved for patients with advanced kidney cancer whose disease progresses following sunitinib treatment.

The primary endpoint of the trial was progression-free survival (PFS). Both combinations proved superior to sunitinib alone: lenvatinib/pembrolizumab achieved a median PFS of 23.9 months vs 9.2 for sunitinib; PFS for lenvatinib/everolimus was 14.7 months.

The 24-month overall survival rate was 79.2% with lenvatinib/pembrolizumab, 66.1% with lenvatinib/everolimus, and 70.4% with sunitinib.

The confirmed objective response rate (percentage of patients whose disease shrank) was 71% with lenvatinib/pembrolizumab, 53.5% with lenvatinib/everolimus, and 35.1% with sunitinib. The rate of complete responses—total tumor shrinkage—was 16.1% in patients receiving lenvatinib/pembrolizumab, 9.8% in the lenvatinib plus everolimus group, and 4.2% in the sunitinib group.

"The rate of responses and complete responses, and the progression-free survival were the longest we have seen to date in a phase 3 combination of a targeted VEGF inhibitor and an immune checkpoint inhibitor," said Choueiri. The CLEAR trial is the last of the [clinical trials](#) that were launched to compare immunotherapy and targeted drug combinations to sunitinib, and sunitinib will not be the comparison drug in future trials because the combinations have proven superior in these advanced kidney cancer patients, said Choueiri.

Almost all patients in the CLEAR trial experienced some adverse events from treatment. The most frequent adverse events were diarrhea and hypertension. These side effects led to stopping the treatment in 37.2% of patients in the lenvatinib/pembrolizumab group, and dose reduction of lenvatinib in 68.5% of patients. "Although the combination of lenvatinib and pembrolizumab was associated with some notable side effects, these adverse events are often adequately managed" the researchers said.

More information: Robert Motzer et al, Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma, *New England Journal of Medicine* (2021). [DOI: 10.1056/NEJMoa2035716](#)

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