FDA Approves Lenvima Plus Keytruda for Advanced Kidney Cancer

Targeted therapy and immunotherapy combination doubles response rate for people with advanced renal cell carcinoma.

August 12, 2021 By Food and Drug Administration (FDA)

FDA Approves Lenvatinib Plus Pembrolizumab for Advanced Renal Cell Carcinoma

On August 10, 2021, the Food and Drug Administration approved the combination of lenvatinib (Lenvima, Eisai) plus pembrolizumab (Keytruda, Merck) for first-line treatment of adult patients with advanced renal cell carcinoma (RCC).

The efficacy of this combination was investigated in CLEAR (Study 307/KEYNOTE-581; NCT02811861), a multicenter, open-label, randomized phase 3 trial in patients with advanced RCC in the first-line setting. Patients were enrolled regardless of PD-L1 tumor expression status. The efficacy population supporting this approval included patients randomized to lenvatinib plus pembrolizumab (n=355) compared with those randomized to single-agent sunitinib (n=357).

Progression-free survival (PFS), assessed by independent radiologic review according to RECIST 1.1, and overall survival (OS) were the major efficacy endpoints.

Patients receiving pembrolizumab with lenvatinib had a median PFS of 23.9 months (95% CI: 20.8, 27.7) compared with 9.2 months (95% CI: 6.0, 11.0) for those receiving sunitinib (HR 0.39; 95% CI: 0.32, 0.49; $p<0.0001$). Median OS was not reached in either arm (HR 0.66; 95% CI: 0.49, 0.88; $p=0.0049$).

The objective response rates were 71% (95% CI: 66, 76) and 36% (95% CI: 31, 41; $p<0.0001$); complete response rates were 16% and 4% on the combination and sunitinib arms, respectively.

The most common adverse reactions reported in ≥20% of patients who received lenvatinib and pembrolizumab in clinical trials are fatigue, diarrhea, musculoskeletal pain, hypothyroidism, hypertension, stomatitis, decreased appetite, rash, nausea, decreased weight, dysphonia, proteinuria, palmar-plantar erythrodysesthesia syndrome, abdominal pain, hemorrhagic events, vomiting, constipation, hepatotoxicity, headache, and acute kidney injury. Arterial thrombotic events occurred in 5% of patients in CLEAR, including myocardial infarction (3.4%) and cerebrovascular accident (2.3%).

The recommended dosages for patients with advanced RCC are lenvatinib 20 mg orally once daily with pembrolizumab 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks up to 2 years, until disease progression or until unacceptable toxicity.

View full prescribing information for Lenvima.

View full prescribing information for Keytruda.

This review used the Real-Time Oncology Review (RTOR) pilot program, which streamlined data submission prior to the filing of the entire clinical application, and the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment. The FDA approved this application approximately 1 month ahead of the FDA goal date.

This application was granted priority review and breakthrough therapy designation for this indication. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

This announcement was originally published by the Food and Drug Administration on August 10, 2021
