Lenvima Plus Keytruda Shows Promise for Advanced Liver Cancer

Nearly half of patients treated with the combination saw their tumors shrink in an early study.

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A combination of the targeted therapy Lenvima (lenvatinib) and the immune checkpoint inhibitor Keytruda (pembrolizumab) showed promising antitumor activity in an early study, with 88% of participants either experiencing tumor remission or having stable disease, according to a report at the Digital International Liver Congress.

Over years or decades, chronic hepatitis B or C, heavy alcohol use, fatty liver disease and other causes of liver injury can lead to the development of cirrhosis and hepatocellular carcinoma (HCC), the most common type of liver cancer.

Liver cancer is often diagnosed late and is difficult to treat. It generally responds poorly to traditional chemotherapy, but several targeted therapy and immunotherapy medications have recently been approved for this indication.

Richard Finn, MD, of the David Geffen School of Medicine at the University of California, Los Angeles, presented results from a Phase Ib clinical trial testing the safety and effectiveness of two of these drugs used in combination (ClinicalTrials.gov number NCT03006926).

Lenvima is a multikinase inhibitor that targets VEGF receptors and enzymes that play a role in cancer cell growth and the development of blood vessels that feed tumors. The Food and Drug Administration (FDA) approved Lenvima for first-line HCC treatment in August 2018.

Keytruda is a monoclonal antibody that blocks PD-1, an immune checkpoint on T cells that regulates immune function. Drugs that interfere with the interaction between PD-1 and its binding partner, known as PD-L1, can release the brakes and restore T-cell activity against tumors. Keytruda was approved for liver cancer treatment in November 2018.

The study included 100 people with unresectable, or inoperable, HCC. About 80% were men, and the median age was approximately 66. A majority had cancer that had invaded the portal vein in the liver or had spread elsewhere in the body. They had not yet received systemic therapy for advanced liver cancer.

All participants in this single-arm trial were treated with 8 or 12 milligrams of Lenvima (depending on body weight) taken as a daily pill plus 200 mg of Keytruda given by IV infusion on the first day of each 21-day cycle.

The overall response rate (ORR) was 46% according to modified RECIST criteria, which are commonly used to evaluate immunotherapy. This included 11% with complete remission (CR) and 35% with partial responses (PR). The median response duration was 8.6 months. Another 42% had stable disease without further progression. Just 7% experienced disease progression.

Using traditional RECIST criteria, the ORR was 36%, the CR rate was 1% and the PR rate was again 35%. However, 52% had stable disease, so using either measure, the disease control rate—meaning either remission or no progression—was 88%.

The estimated median progression-free survival time, meaning time to either disease progression or death, was 9.3 months using the modified RECIST and 8.6 months using the traditional RECIST criteria.

Overall survival (OS) data are not yet mature, but the estimated median OS time for the whole group was 22.0 months, with a death rate of 34%. But this varied according to the type of response. Using the modified RECIST criteria, the median OS was just 2.3 months for those with progressive disease (100% death rate), but it could not yet be determined for those with stable disease (36% death rate) or complete or partial response (15% death rate) because a majority were still doing well.

Treatment was generally safe, but side effects were common. About two thirds had severe (Grade 3 or higher) treatment-related adverse events, and three had fatal side effects. The most common side effects overall were hypertension, diarrhea, fatigue, decreased appetite, hypothyroidism, hand and foot syndrome (redness, swelling and pain on the palms of the hands and soles of the feet). The most common severe side effects were hypertension (17%) and AST liver enzyme elevation (11%). About one in five stopped treatment due to adverse events.

Based on these findings, the researchers concluded that Lenvima plus Keytruda had “promising antitumor activity,” and “no new or unexpected toxicities” resulted from combining the two drugs.

To confirm these results in a larger population, the Phase III LEAP-002 trial (NCT03713593) is currently testing Lenvima plus Keytruda versus Lenvima alone as first-line treatment for unresectable HCC. The study has completed enrollment and is awaiting results, Finn said.

Click here to view the presentation.

Click here for full prescribing information for Lenvima.

Click here for full prescribing information for Keytruda.
Click here to learn more about liver cancer.
