Adding Immunotherapy to Local Treatment Delays Liver Cancer Progression

Combining Imfinzi and Avastin with TACE led to better treatment outcomes.

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Adding the immune checkpoint inhibitor Imfinzi (durvalumab) and the VEGF inhibitor Avastin (bevacizumab) to transarterial chemoembolization (TACE) led to improved progression-free survival for people with inoperable liver cancer, according to study findings reported at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO GI).

“These results of the EMERALD-1 trial have the potential to establish a new standard of care for the treatment of unresectable hepatocellular carcinoma, a complex disease with poor prognosis, by showing for the first time that adding an immunotherapy-based combination to TACE significantly improved progression-free survival,” ASCO expert Cathy Eng, MD, of Vanderbilt-Ingram Cancer Center, said in a news release.

Over years or decades, chronic hepatitis B or hepatitis C, fatty liver disease, heavy alcohol consumption and other causes of liver injury can lead to liver fibrosis, cirrhosis and hepatocellular carcinoma (HCC), the most common type of liver cancer. HCC is often detected at a late stage and is difficult to treat.

The standard of care for eligible patients with localized liver cancer that can’t be surgically removed is TACE, which delivers chemicals to block blood vessels that supply tumors; chemotherapy drugs or radiation beads may also be delivered directly to the liver. Around 25% of people with HCC are eligible for embolization, but most patients who undergo the procedure experience disease progression within a year. In a previous study, adding the targeted therapy Nexavar (sorafenib) to TACE did not improve survival.

Riccardo Lencioni, MD, of Pisa University School of Medicine in Italy, and colleagues conducted the Phase III EMERALD-1 trial (NCT03778957) to evaluate whether adding two other types of medication would improve outcomes for people undergoing TACE. The study enrolled 616 patients from 18 countries who had unresectable HCC that had not spread beyond the liver.

The study participants were randomly assigned to receive Imfinzi and Avastin plus TACE; Imfinzi

plus TACE without Avastin; or TACE alone. First, they received IV infusions of Imfinzi or a placebo every four weeks plus TACE. After completing TACE, they received Imfinzi alone, Imfinzi plus Avastin or placebos. Imfinzi, a PD-L1 checkpoint inhibitor, is currently approved for HCC treatment in combination with Imjudo (tremelimumab), a CTLA-4 checkpoint inhibitor.

"Research in other studies suggested that TACE would work well with two other types of anticancer therapy: immunotherapy, which attacks tumors using the immune system, and anti-VEGF therapy, which inhibits vascular endothelial growth factor (VEGF)—a protein which, when expressed in tumors, can promote blood flow to the tumor," Lencioni said in the ASCO news release.

People who received both Imfinzi and Avastin plus TACE had longer progression-free survival (PFS) than those who underwent TACE alone. The median PFS time was 15.0 months in the triple therapy group versus 8.2 months in the TACE-only group, representing a 23% reduction in the risk of disease progression or death. The median time to progression doubled in the triple therapy group compared with the TACE-only group (22.0 versus 10.0 months). At 18 months, the PFS rate—meaning the proportion of patients still alive without disease progression—was 43% versus 28%, respectively.

In contrast, the PFS difference between Imfinzi plus TACE without Avastin and TACE alone was not statistically significant (10.0 versus 8.2 months). Nor was the difference in time to progression (11.5 versus 10 months). However, the overall response rate, reflecting tumor shrinkage, was higher in both Imfinzi groups compared with the TAC-only group (44%, 41% and 30%).

Overall survival data is not yet mature, and follow-up is ongoing. Commenting on the study findings, Josep Llovet, MD, PhD, of Mount Sinai School of Medicine and the University of Barcelona, noted that an improvement in progression-free survival does not necessarily predict better overall survival.

Treatment was generally safe, and adverse events were consistent with those seen in other studies of these therapies; no new safety signals were identified. Side effects were common, however, and people who received the triple therapy were about twice as likely to experience severe adverse events (46% compared with 23% in the TACE-only group).

The Imfinzi, Avastin and TACE combination "is the first immune checkpoint inhibitor-based regimen in a global Phase III trial to show statistically significant and clinically meaningful improvement in PFS, versus TACE, in patients with embolization-eligible unresectable HCC," the researchers concluded. Thus, the triple combination "has the potential to set a new standard of care in unresectable HCC."

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