Immunotherapy Plus Targeted Therapy Combo Shrinks Liver Tumors

A triple regimen of Opdivo, Yervoy and Cabometyx showed good antitumor activity, but severe side effects were common.

February 21, 2020 By Liz Highleyman

A triple combination of two immune checkpoint blockers plus a targeted kinase inhibitor led to better responses than a double regimen in people with advanced liver cancer, according to a study presented at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium last month in San Francisco. However, adding more drugs also increased side effects, and more research is needed to weigh the risks and benefits of this approach.

Hepatocellular carcinoma (HCC), the most common type of liver cancer, is often detected late and is difficult to treat. Although it generally does not respond well to conventional chemotherapy, several new immunotherapies and targeted therapies have been approved for HCC in recent years.

Thomas Yau, MD, of the University of Hong Kong, presented the latest findings from the Phase I/II CheckMate 040 trial, which evaluated the PD-1 checkpoint inhibitor Opdivo (nivolumab) alone and in various combinations in people with advanced HCC. This analysis compared a double regimen of Opdivo plus Yervoy (ipilimumab) versus a triple regimen of Opdivo, Yervoy and Cabometyx (cabozantinib).

Opdivo is a PD-1 checkpoint inhibitor that helps the immune system fight cancer. Some tumors can hijack the PD-1 receptor on T cells to turn these cells off; PD-1 blockers release the brakes and restore T-cell activity. Yervoy is a different type of checkpoint inhibitor that blocks CTLA-4, which suppresses T-cell replication. Cabometyx is a multikinase inhibitor that blocks several enzymes that play a role in cancer cell growth and blood vessel development.

This analysis included 71 people with locally advanced or metastatic liver cancer. Nearly 90% were men, about 70% were white, 25% were Asian, and the median age was about 66. Most had compensated liver disease with well-preserved liver function. More than half had cancer that had spread beyond their liver. More people in the triple therapy group (66%) compared with the double therapy group (53%) had previously used Nexavar (sorafenib), a standard-of-care targeted therapy.

The participants were randomly assigned to one of two regimens, with treatment continuing until they experienced disease progression or unacceptable side effects:

- Doublet: 240 milligrams Opdivo by IV infusion every two weeks + 40 mg Cabometyx tablets once daily
- Triplet: 3 mg/kg Opdivo every two weeks + 1 mg/kg Yervoy by IV infusion every six weeks + 40 mg Cabometyx tablets once daily.

The median duration of treatment was about seven months and the median follow-up time was about 19 months. Yau reported that 19% of patients in the doublet group and 29% in the triplet group were still on treatment. A majority of people who stopped did so because of disease progression.

The overall response rate, meaning complete or partial tumor shrinkage, was 19% in the doublet group versus 29% in the triplet group. All were partial responses according to the study investigators, although a blinded review deemed one patient in the doublet group and two in the triplet group to have complete remission. Stable disease rates, meaning no further progression, were 56% and 54%, respectively. Disease progression occurred in 22% and 11%, respectively.

The median progression-free survival (PFS) time, meaning patients were still alive without worsening of their disease, was 5.4 months in the doublet group and 6.8 months in the triplet group. The median overall survival time was 21.5 months in the doublet group but was not reached in the triplet group. At 15 months, the overall survival rates were 64% and 70%, respectively.

In comparison, previously reported CheckMate 040 results for Nexavar-experienced people treated with Opdivo plus Yervoy without Cabometyx showed an overall response rate of 32% and a median overall survival time of 22.8 months. This was substantially better than earlier results showing an overall response rate of about 14% and a median survival time of about 16 months for Nexavar-experienced patients treated with Opdivo alone, although these numbers were higher for people who had not previously used Nexavar.

But the major drawback of adding more drugs to a regimen—aside from the increased cost—is the risk of more side effects, and that was in fact seen in this study.

While treatment was generally safe, 47% of people receiving the double regimen and 71% of those taking the triple regimen experienced severe (Grade 3 or 4) side effects. The most common severe side effects were high blood pressure, diarrhea and hand-foot syndrome (redness, swelling and pain on the palms and soles of the feet), along with elevated liver enzyme and lipase levels.

Checkpoint inhibitors can cause a strong immune reaction that damages healthy organs; the most common severe immune-mediated side effect was liver inflammation. Four people (11%) in the doublet group and seven (20%) in the triplet group stopped treatment due to drug-related adverse

events. Yet overall, side effects were “manageable and reversible,” Yau said.

Based on these findings, the study authors concluded, “Investigation with longer duration of follow-up would be necessary to better characterize the benefit-risk ratio of the doublet and triplet combinations.”

Click here to read the study abstract.

Click here to learn more about liver cancer.

© 2026 Smart + Strong All Rights Reserved.
http://beta.docker.cancerhealth.com/article/immunotherapy-targeted-therapy-combo-shrinks-liver-tumors