Does Opdivo Improve Survival for Newly Treated Liver Cancer?

Phase III study misses statistical threshold, but the immunotherapy appears to show some benefit.

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The checkpoint inhibitor Opdivo (nivolumab) did not significantly improve overall survival compared with the standard targeted therapy Nexavar (sorafenib) in a late-stage trial, but it did show signals of "promising efficacy," according to a Bristol-Myers Squibb announcement.

Over years or decades, chronic hepatitis B or C, heavy alcohol use and other causes of liver injury can lead to the development of liver cirrhosis and hepatocellular carcinoma (HCC), the most common type of primary liver cancer. HCC is often detected late and is difficult to treat, making it one of the leading causes of cancer death worldwide.

The liver cancer field is evolving rapidly, and Opdivo is just one of several immunotherapies and targeted therapies being tested alone or in combination regimens at various stages of the disease. Opdivo was approved in 2017 for liver cancer patients who had previously tried Nexavar. In the past year, the Food and Drug Administration has given the nod to another checkpoint inhibitor, Keytruda (pembrolizumab), as well as to two new targeted drugs, Lenvima (lenvatinib) and Cabometyx (cabozantinib).

Opdivo and Keytruda help the immune system recognize and attack cancer. These monoclonal antibodies block the PD-1 immune checkpoint receptor on T cells, which plays a role in regulating immune function. Some tumors can hijack PD-1 to turn off immune responses against them; checkpoint blockers release the brakes and restore T-cell activity.

The Phase III CheckMate-459 study aimed to show whether Opdivo matches Nexavar as first-line treatment for people with inoperable liver cancer. Most patients who try Nexavar, which targets a kinase protein that promotes cell growth and blood vessel development, eventually experience disease progression or develop unacceptable side effects.

A previous Phase I/II study, CheckMate-040, showed that Opdivo led to complete or partial tumor shrinkage in about 20% of liver cancer patients, regardless of prior treatment status. However, the quarter of participants who had not previously tried Nexavar had a median overall survival time of about 29 months, compared with 16 months for treatment-experienced patients, suggesting

Opdivo might be more effective in the first-line setting.

CheckMate-459 included 1,009 participants with HCC who were starting systemic treatment for the first time. They had well-preserved liver function (Child-Pugh Class A) and liver tumors that could not be surgically removed or treated with local therapies. They were randomly assigned to receive Opdivo or Nexavar until they experienced disease progression or unacceptable toxicity.

Bristol-Myers Squibb announced this week that Opdivo did not lead to a statistically significant improvement in overall survival compared with Nexavar, meaning the difference between the two drugs could have been driven by chance. But Opdivo did show a "clear trend" toward longer survival, meaning it had a numerical advantage that didn't meet the statistical threshold.

Treatment with Opdivo was generally safe and well tolerated with no new safety concerns or unexpected side effects not seen in earlier studies, the company said.

"We are encouraged by the promising efficacy and safety trends seen with Opdivo in CheckMate-459, especially as HCC is a devastating and difficult-to-treat cancer, for which there have been no significant advances over sorafenib, a standard treatment, in more than a decade," said study investigator Bruno Sangro, MD, of Clínica Universidad de Navarra in Pamplona, Spain.

The company said full results from the study would be presented at an upcoming medical conference, which could be the AASLD Liver Meeting in Boston in November.

Click here for full prescribing information for Opdivo.

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