Cyramza Extends Liver Cancer Survival

Twice as many patients were still alive 18 months after starting treatment.

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Cyramza (ramucirumab), a type of targeted therapy that slows tumor growth, led to improved overall survival and delayed disease progression in people with hepatocellular carcinoma (HCC), according to study results presented at the American Society of Clinical Oncology annual meeting last month in Chicago.

Second-line treatment with Cyramza extended the median survival by only about a month compared with placebo in the REACH-2 trial, but the proportion of patients who were still alive 18 months after starting therapy more than doubled, from about 11 percent to 25 percent.

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 liver cirrhosis and hepatocellular carcinoma, a cancer that starts in the liver. Liver cancer is often detected late when it is difficult to treat, making it a leading cause of cancer death worldwide.

Traditional chemotherapy does not work very well against liver cancer, but targeted therapies known as multi-kinase inhibitors, which target pathways involved in cell proliferation and blood vessel formation, have shown promise.

The kinase inhibitor Nexavar (sorafenib) is approved by the Food and Drug Administration (FDA) for first-line HCC treatment, but it often does not work and most patients experience disease progression. Stivarga (regorafenib), a similar type of drug, was recently approved for second-line HCC treatment after the first therapy fails. Last September, the FDA approved the immune checkpoint inhibitor Opdivo (nivolumab) for HCC.

Cyramza is a monoclonal antibody that interferes with angiogenesis, or blood vessel formation. By blocking activation of vascular endothelial growth factor receptor 2 (VEGFR2), it prevents the development of new blood vessels needed to supply a growing tumor.

A previous trial found that although Cyramza did not improve overall survival among people with advanced HCC as a whole, it did lead to a significant survival benefit for those with highly elevated alpha-fetoprotein (AFP), a biomarker used for liver cancer screening.

Andrew Zhu, MD, of Massachusetts General Hospital in Boston, presented findings from REACH-2,

a follow-up study focusing on people with advanced HCC who had elevated AFP (400 nanograms per milliliter or higher) and had been previously treated with Nexavar but stopped because of disease progression or side effects.

The study included 292 participants in 20 countries in North America, Latin America, Europe and Asia. Most were men and the median age was 64. They had liver cancer that was not considered treatable with local therapies or that recurred after such treatment. Nearly three quarters had metastatic cancer that had spread beyond the liver. More than a third had HCC related to hepatitis B, 26 percent had hepatitis C and 24 percent had a history of heavy alcohol use.

Participants were randomly assigned to receive intravenous infusions of Cyramza or placebo every two weeks, along with the best supportive care.

The median overall survival duration was 8.5 months in the Cyramza arm versus 7.3 months in the placebo arm, Zhu reported. Although this difference was small, it was statistically significant, meaning it was probably not attributable to chance alone.

At 12 months after starting treatment, 36.8 percent of people who received Cyramza and 30.3 percent of placebo recipients were still alive, which was not a significant difference. But the difference was greater and became statistically significant by 18 months, at which point survival rates were 24.5 percent and 11.3 percent, respectively.

The median progression-free survival duration, meaning participants were still alive without worsening of disease, was 2.8 months in the Cyramza arm compared with 1.6 months in the placebo arm, also a significant difference.

Overall response rates, meaning complete or partial tumor shrinkage, were 4.6 percent with Cyramza versus 1.1 percent in the placebo group. None of the participants had a complete response. Looking at the disease control rate, meaning either tumor shrinkage or stable disease, Cyramza performed significantly better than the placebo: 59.9 percent versus 38.9 percent, respectively.

Treatment with ramucirumab was generally safe and tolerable, though side effects were common. Rates of discontinuation as a result of treatment-related adverse events were 10.7 percent with Cyramza and 3.2 percent in the placebo group; about a third of Cyramza recipients adjusted their dose because of side effects. The most notable treatment-related adverse event in the Cyramza group was high blood pressure.

Based on these findings, the researches concluded, "REACH-2 is the first positive study in a biomarker-selected patient population, demonstrating a significant and meaningful overall survival benefit and favorable safety profile in HCC patients with baseline AFP $\geq$400 ng/ml, a population associated with poor prognosis."

Click here to read the ASCO study abstract.