Cyramza Improves Survival for People With Liver Cancer

Study shows VEGF inhibitor is effective for patients with a biomarker of poor prognosis.

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Cyramza (ramucirumab), which slows tumor growth by blocking blood vessel formation, increased overall survival and progression-free survival in liver cancer patients with a specific biomarker, according to Phase III study results announced this week by Eli Lilly and Company.

The findings come from the REACH-2 trial, which tested Cyramza as a second-line treatment for people with hepatocellular carcinoma (HCC) who had high levels of alpha-fetoprotein (AFP), a biomarker associated with poor prognosis. The new results have not yet been presented at a scientific conference or published in a medical journal.

Hepatocellular carcinoma is a type of primary liver cancer that can develop after long-term chronic hepatitis B or C infection, heavy alcohol use, fatty liver disease or other causes of liver injury. It is often diagnosed at a late stage and is difficult to treat, making it the second leading cause of cancer-related death worldwide.

Early-stage liver cancer may be treated with surgery or local chemotherapy. Nexavar (sorafenib) is standard first-line therapy for more advanced or metastatic (spread beyond the liver) HCC. After the first treatment fails, expected survival is typically around three to five months, according to Lilly.

“Advanced liver cancer is an aggressive disease that has a poor prognosis—and for those that have elevated AFP levels, the prognosis is even more dismal,” Lilly senior vice president Levi Garraway, MD, said in the company press release. “The expected survival of these patients is only a few months following first-line treatment if they don’t go onto second-line therapy. For this reason, Lilly is encouraged by the results of REACH-2 and the potential for Cyramza to benefit patients in this setting.”

Cyramza interferes with vascular endothelial growth factor (VEGF), a protein that stimulates blood vessel production—a process known as angiogenesis. By blocking the VEGF 2 receptor, the drug prevents the development of new blood vessels needed to feed a growing tumor. Cyramza is currently approved by the Food and Drug Administration for the treatment of advanced stomach cancer, colorectal cancer and non-small-cell lung cancer.

REACH-2 is a randomized clinical trial that has enrolled 292 people with HCC in 20 countries in North America, Asia, Europe and Latin America. Participants either experienced disease progression while taking Nexavar or were unable to tolerate it. They were randomly assigned to receive Cyramza administered by IV infusion every two weeks or a placebo, both with the best supportive care.

Patients in REACH-2 had high AFP levels, at least 400 nanograms per milliliter. AFP is a protein produced by the fetal liver and by certain types of tumors. A level below 10 ng/ml is considered normal. Elevated AFP levels, as measured by a blood test, are used as a screening tool for liver cancer; among people with HCC, higher levels are associated with worse outcomes. About half of people with advanced HCC have high AFP, according to Lilly.

The original REACH trial also tested Cyramza as second-line therapy for people who progressed on or couldn't tolerate Nexavar, but it did not select participants based on AFP levels. That study did not show a significant survival benefit for Cyramza overall, but survival nearly doubled in a predefined subgroup of patients with high AFP, leading researchers to design a new trial focused on that group.

Although Lilly did not provide detailed results from REACH-2 in its press release, the company said the trial had met its primary endpoint of improved overall survival as well as a secondary endpoint of progression-free survival, meaning participants were still alive with no worsening of disease.

The safety profile of Cyramza was consistent with prior studies, with no new or unexpected adverse events, according to the announcement. The only severe adverse events occurring in at least 5 percent of patients were high blood pressure and low sodium levels.

Lilly said detailed data from REACH-2 will be presented at an upcoming conference, suggesting that full results may become available at the American Society of Clinical Oncology (ASCO) annual meeting in June or at another meeting later this year. The company indicated that it plans to request approval of Cyramza for HCC in mid-2018. Earlier phase trials are underway to test Cyramza in combination with immunotherapy.

Click here to read Eli Lilly's press release about the study.
