Efruxifermin Improves Liver Cirrhosis in People With MASH

The fibroblast growth factor analog reduced liver scarring in about a third of people with fatty liver disease and cirrhosis.

May 12, 2025 By Liz Highleyman

Efruxifermin, a fibroblast growth factor analog, led to regression of liver fibrosis in people with metabolic dysfunction-associated steatohepatitis (MASH) and compensated cirrhosis, Akero Therapeutics announced this week. If approved, it could become the first medication for people with the most advanced stage of fibrosis due to fatty liver disease.

A mid-stage study found that 29% of people who received once-weekly 50 milligram injections of efruxifermin experienced at least a one-stage improvement in fibrosis with no worsening of MASH. These topline results have not yet been presented at a medical conference or reported in a peer-reviewed journal.

[Update: Study results were presented at the European Association for the Study of the Liver (EASL) Congress in May and published in The New England Journal of Medicine.]

“Until today, we’ve not had the prospect of an effective treatment for compensated cirrhosis due to MASH, which is associated with high rates of short-term morbidity and mortality,” principal investigator Mazen Nourredin, MD, of Houston Methodist Hospital, said in a news release. “Now we have reason to be optimistic about the future potential of efruxifermin as a much-needed treatment for cirrhosis, if approved.”

MASH, the new name for non-alcoholic steatohepatitis (NASH), and its earlier stage, metabolic dysfunction-associated steatotic liver disease (MASLD), are leading causes of advanced liver disease worldwide. Over time, the buildup of fat in the liver can lead to fibrosis (scar tissue), cirrhosis, liver cancer and the need for a liver transplant. Estimates suggest that around a third of people in the United States have MASLD, and about 5% have MASH.

The new terminology emphasizes the link with obesity, diabetes and other metabolic conditions. Last year, the Food and Drug Administration (FDA) approved the first medication for NASH, Rezdiffra (resmetirom), but management still largely relies on lifestyle changes such as weight loss and exercise. Rezdiffra is indicated for people with moderate to advanced liver fibrosis (Stage F2 or F3), but not those who have already progressed to cirrhosis (Stage F4).

Developing treatments for fatty liver disease has proved challenging, as the FDA's dual benchmark of MASH improvement without worsening fibrosis and fibrosis improvement without worsening MASH has been difficult to meet. Numerous drug candidates that work by various mechanisms have looked promising in early clinical trials, only to fail in larger studies.

Efruxifermin appeared to be on that path as well in October 2023, when 36-week results from the primary analysis of the Phase IIb SYMMETRY trial did not reach the threshold for statistical significance. But more obvious benefits emerged with longer follow-up.

Fibroblast growth factor analogs mimic a natural hormone that regulates metabolism. Early studies showed that efruxifermin appears to reduce fat storage in the liver, decrease inflammation, increase insulin sensitivity and improve lipid levels. Other candidates in this drug class include NGM Bio's aldafermin and 89bio's pegazofermin.

MASH and Cirrhosis

SYMMETRY enrolled 182 adults with compensated cirrhosis due to MASH. Obesity and type 2 diabetes were common, and nearly a third were taking GLP-1 agonist weight-loss medications such as semaglutide (Ozempic, Wegovy) or tirzepatide (Monjuaro, Zepbound). They were randomly assigned to receive weekly subcutaneous injections of one two doses of efruxifermin (28 or 50 mg) or a placebo, and they underwent liver biopsies at study entry, 36 weeks and 96 weeks.

In a 96-week intention-to-treat analysis including all treated participants, 29% of patients treated with 50 mg efruxifermin saw at least a one-stage improvement in fibrosis with no worsening of MASH, compared with 21% of those on the 28 mg dose and 12% of placebo recipients. In this analysis, missing 96-week biopsies were considered failures.

Looking just at the 134 patients with paired biopsies at baseline and 96 weeks, the corresponding response rates jumped to 39%, 29% and 15%, respectively. The benefits of the higher efruxifermin dose were statistically significant in both analyses. The 39% response rate in the 50 mg efruxifermin group far exceeds the 24% rate seen at 36 weeks, showing that improvement increases over time.

An even greater 96-week response was seen in the subgroup of 97 patients with follow-up biopsies who were not taking a GLP-1 agonist at baseline: 45% of 50 mg efruxifermin recipients and 17% of placebo recipients experienced fibrosis regression without worsening MASH. This shows that the improvement with efruxifermin can't be attributed to the weight-loss meds, which also help reduce liver fat.

People treated with efruxifermin also saw significantly greater improvements in liver stiffness according to FibroScan imaging and noninvasive biomarkers of liver injury.

Efruxifermin was reported to be "generally well-tolerated," according to Akero. Across both dose groups, the most frequent adverse events were transient mild to moderate gastrointestinal side

effects (diarrhea, nausea and increased appetite). There were no drug-related serious adverse events. Some people using the higher dose of efruxifermin experienced reduced bone mineral density, but the number of fractures was similar in the placebo group.

Earlier-Stage Fibrosis

A study presented at the AASLD Liver Meeting in November showed that efruxifermin is also effective for people with less advanced liver disease.

The Phase IIb HARMONY trial enrolled 128 people with Stage F2 or F3 fibrosis considered to have "at-risk" MASH. Here too, obesity and type 2 diabetes were common. They were randomly assigned to receive 28 mg or 50 mg efruxifermin or a placebo once weekly, and had liver biopsies at baseline, 24 weeks and 96 weeks.

Previously reported results showed that among participants with paired biopsies, 41% of those taking the higher dose of efruxifermin experienced at least a one-stage improvement in fibrosis with no worsening of MASH, compared with 20% in the placebo group.

Again, longer treatment led to continued improvement. At 96 weeks, the corresponding response rates were 75% and 24%, respectively. What's more, 36% in the high-dose efruxifermin group saw at least a two-stage improvement in fibrosis, compared with just 3% in the placebo group. At the 96-week mark, 30% of patients in the high-dose group showed near-complete disease reversal, with little or no fibrosis and liver fat normalization, and 46% were no longer considered to have at-risk MASH.

Efruxifermin is now being tested in ongoing Phase III studies. Earlier this month, Akero announced completion of enrollment in the blinded portion of the SYNCHRONY trial, a real-world study of people with any stage of fibrosis or cirrhosis and suspected or confirmed MASLD or MASH not diagnosed by biopsy.

Click here for more news about fatty liver disease.
