Alcoholic Hepatitis Drug Shows Promise

In a Phase IIa trial, the drug DUR-928 was associated with numerous positive outcomes after 28 days.

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DUR-928, an experimental treatment for alcoholic hepatitis under development by DURECT, was associated with numerous positive outcomes, including a reduction of biomarkers linked to poor prognosis and a 100% survival rate, after 28 days in a recent mid-stage trial.

Alcoholic hepatitis is highly fatal, with 28% of those diagnosed with the condition dying within one month. Effective treatments for the disorder are seriously lacking.

DUR-928 is an endogenous epigenetic regulator that promotes a reduction in lipid synthesis, inhibits inflammation and cell death and stimulates the regeneration of liver cells.

Tarek I. Hassanein, MD, of the Southern California Research Center, presented findings from the open-label, dose-escalation multicenter study of DUR-928 given to 19 people with moderate or severe alcoholic hepatitis at The Liver Meeting, the Annual Meeting of the American Association for the Study of Liver Diseases, this week in Boston.

The participants received intravenous DUR-928 at three different doses. Eight people (four with moderate alcoholic hepatitis and four with severe alcoholic hepatitis) received 30 milligrams of DUR-928; seven people (three moderate and four severe) received 90 mg; and four people (all severe) received 150 mg.

A total of 57.9% of the participants were male, the median age was 41 years old and 89.5% were white.

The study looked at three major outcomes: change in Lille scores, MELD scores and bilirubin.

After being discharged on the second day of the study, one participant did not return for the study's follow-up visits scheduled for days 7 and 28. Consequently, the analyses based on these three outcomes included 18 participants.

Lille scores help determine the prognosis and response of people with alcoholic hepatitis seven days after treatment. A lower score means a better prognosis. Those with a score below 0.45 have a six-month survival rate of 85%,while those with a score above that threshold have a 25% six-

month survival rate.

Based on Lille scores, all of those in the 30 mg and 90 mg DUR-928 dosing groups responded to treatment.

The median Lille score at the 28-day mark was 0.10. By comparison, the median score in a cohort of 15 people treated for alcoholic hepatitis with the standard of care at the University of Louisville was 0.41.

The study authors also compared the results of those treated with DUR-928 with cohorts from several published studies in which the participants had similar baseline values on various liver tests and were treated with the standard of care with or without corticosteroids. Posttreatment Lille scores were significantly lower in the DUR-928 study compared with those in these cohorts. Such comparisons should be approached with caution, however, because they derive from studies of different cohorts conducted at different times.

Comparing the eight people with severe alcoholic hepatitis who were treated with 30 mg or 90 mg of DUR-928 against 13 well-matched people with severe alcoholic hepatitis in the University of Louisville study, the researchers found that while all of those in the DUR-928 study survived 28 days, three of those in the other study died by that point in time.

Bilirubin levels in the blood are an indicator of liver function, with elevated levels meaning poorer function. In the new study, the participants who began with a median bilirubin level of 14.2 had a significant reduction by day 7. Among those with an elevated bilirubin at the study's outset, meaning greater than 8 milligrams per deciliter, the median reduction was 25% by day 7 and 48% by day 28.

MELD scores assess the severity and prognosis of liver disease and are used to prioritize candidates for liver transplants. A score of 11 to 20 indicates a moderate case; a score of 21 to 30 indicates a severe case. So lower scores mean a better prognosis.

The median reduction in MELD score by day 28 was more than 2 points. Among those who started the study with elevated bilirubin, the median reduction in MELD was 5 points.

DUR-928 was well tolerated at all the doses tested. None of the participants experienced drug-related serious adverse health events. Three adverse health events were deemed possibly related to DUR-928, including one case of moderate generalized itching, one mild rash and one Grade 2 alkaline phosphatase elevation.

None of the participants discontinued treatment, withdrew from the study early or terminated treatment or participation in the study because of adverse health events.

DURECT is planning to run a double-blind, placebo-controlled Phase IIb clinical trial evaluating DUR-928 in individuals with alcoholic hepatitis starting mid-2021. Initial results from that study will likely be available in 2022.

To read the study abstract, click here.

To read a press release about the study, click here.

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