Glycerol Phenylbutyrate Reduces Hepatic Encephalopathy Events and Ammonia Levels Compared to Placebo in a Phase 2 Trial

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Phase 2 trial results published in the March issue of Hepatology, a journal of the American Association for the Study of Liver Diseases, suggests the potential for Glycerol Phenylbutyrate (GPB) to reduce hepatic encephalopathy episodes in patients with cirrhosis, with a safety profile similar to placebo.

Patients with hepatic encephalopathy experience neuropsychiatric symptoms that may range from mild confusion to coma. There is conflicting evidence on the link between elevated blood ammonia and hepatic encephalopathy. Poorly-absorbable disaccharides and antibiotics are currently used to treat encephalopathy and are generally believed to act by reducing ammonia production in the intestine.

“GPB is approved to treat urea cycle defects that prevent the removal of ammonia from the body,” explains Dr. Bruce F. Scharschmidt, Sr. VP & Chief Medical Officer with Hyperion Therapeutics in San Francisco, CA. “Our trial was the first to investigate the efficacy of a direct ammonia lowering agent in patients with cirrhosis and hepatic encephalopathy.”

This phase 2 clinical trial enrolled 178 cirrhosis patients, including 59 who were already taking rifaximin. Participants who had two or more hepatic encephalopathy events within the six months prior to the trial were included. The trial aim was to determine the proportion of patients with hepatic encephalopathy taking 6mL GBP twice daily compared to placebo.

Results show that the percentage of patients who experienced hepatic encephalopathy events was significantly reduced among patients randomized to GPB versus placebo at 21% vs. 36%, respectively. Total hepatic encephalopathy events were lower in patients taking the medication (35) versus placebo (57). Hospitalizations due to hepatic encephalopathy tended to be less frequent among patients taking GPB at 13 compared to those in the placebo group at 25.

The trial results also indicate that ammonia levels in the blood of patients on GPB were lower than subjects not taking the medication. “Our findings provide evidence that elevated blood ammonia plays an important role in the development of hepatic encephalopathy,” concludes Dr. Scharschmidt. “GPB reduced the risk of hepatic encephalopathy in patients with cirrhosis and further investigation of its therapeutic potential for patients with hepatic encephalopathy is warranted.”

In a related editorial published in Hepatology, Dr. Meritxell Ventura-Cots with the Hospital Vall Hebron in Barcelona, Spain writes, “The study by Rockey et al. shows that GPB improves the outcome among cirrhotic patients with highly recurrent hepatic encephalopathy. The new drug avoids the risk of sodium overload, was well tolerated and had a good safety profile.”