Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/advances-in-the-treatment-of-pbc-part-2/29115/

Released: 11/08/2024
Valid until: 11/08/2025
Time needed to complete: 54m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Advances in the Treatment of PBC: Part 2

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Kowdley:
This is CME on ReachMD, and I'm Dr. Kris Kowdley, Director at Liver Institute Northwest, and Professor at Elson S. Floyd College of Medicine, Washington State University. In this brief lecture, I will review the clinical data from the phase 3 ELATIVE trial which investigated elafibranor in PBC. I'll review elafibranor and its mechanism of action, the results in terms of efficacy, safety, and effect on pruritus in this trial.

So ELATIVE was a phase 3, randomized, placebo-controlled trial that was double-blind in nature and investigated elafibranor at a dose of 80 mg versus placebo in patients with PBC who had an alkaline phosphatase greater than 1.67 times upper limit of normal and had a bilirubin that could be elevated but needed to be less than 2. Now, for patients who met the criteria for inclusion, they were randomized 2:1 to elafibranor or placebo. And the response was a composite endpoint based on the proportion of patients who achieved an alkaline phosphatase less than 1.67 times upper limit of normal, maintained a normal bilirubin level, and had at least a 15% reduction.

Now in this study, the results show that elafibranor achieved this result in 51% of patients treated with elafibranor at 80 mg, compared to only 4% of patients treated with placebo, which resulted in a 47% placebo-corrected response rate of patients achieving this result. And that was highly statistically significant. When we look at the degree of reduction in alkaline phosphatase, it was around 40% or thereabouts. So a marked reduction in alkaline phosphatase was seen in the elafibranor-treated patients, and the reduction in alkaline phosphatase began very quickly after treatment was initiated and was maintained throughout the course of the trial. Now, the other features of elafibranor therapy that were attractive was that 15% of patients achieved normalization of alkaline phosphatase compared to no patients treated with placebo.

And as we were discussing now, in the treatment of PBC, our goal is increasingly to try and achieve normal alkaline phosphatase rather than achieve an alkaline phosphatase that remains elevated with treatment. So this is encouraging and would suggest that the ideal treatment goal can be achieved in a substantial percentage of patients.

Now, elafibranor did have some side effects which are expected for the class of drug that it is. So elafibranor is a PPAR-alpha/delta dual agonist. And these drugs seem to have significant efficacy in terms of having anti-inflammatory effects, potentially improving metabolic profile, and more importantly, reducing bile acid production and increasing bile acid secretion. And this combination, of course, is very attractive for a chronic cholestatic liver disease where damage to the bile ducts leads to both increased bile acid production and increased bile acid leakage into the liver parenchyma where they can cause injury and then recruit immunologic cells to cause further injury, eventually leading to fibrosis. There's also evidence that elafibranor may have antifibrotic effects.

One of the attractive things about elafibranor therapy was that it did not exacerbate pruritus. Although the pruritus score using Worst

Itch-NRS was reduced in patients who were treated compared to placebo, this reduction was not statistically significant among those who had moderate to severe pruritus. However, exploratory endpoints using other measures of pruritus, such as PBC-40 and 5-D Itch, suggested that there could be some benefit.

Some adverse events that were reported in higher proportion of elafibranor patients compared to placebo patients included weight gain and fractures. Occasionally, patients may be at risk for increased CPK and should be monitored for muscle injury. And GI symptoms are more common in patients treated with elafibranor than placebo. So clinicians need to monitor patients for these side effects and follow them carefully over the course of treatment.

So in summary, elafibranor appears to be an effective second-line therapy for patients with PBC with a high degree of efficacy in achieving the primary composite endpoint of improvement in alkaline phosphatase and maintaining normal bilirubin, and has a side effect profile that's acceptable in my view, and can be managed with appropriate education and monitoring.

Thank you for your attention. I hope this information will be helpful in your practice.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/Prova. Thank you for listening.