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Advances in the Treatment of PBC: Part 1

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

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Dr. Hirschfield:
Hello. This is CME on ReachMD, and I'm Dr. Gideon Hirschfield. I've been involved in the development of drugs including seladelpar. And in this mini lecture, I will review the clinical data from the phase 3 RESPONSE trial which evaluated seladelpar in primary biliary cholangitis. Seladelpar is a highly selective PPAR delta agonist. It is dosed at a dose of 10 mg daily. There have been a number of phase 2 and phase 3 clinical trials demonstrating the benefit of seladelpar for the potent treatment of primary biliary cholangitis, including biochemical response and an improvement in pruritus.

The pivotal clinical trial was the RESPONSE trial. This was a phase 3 clinical trial that provides safety, biochemical efficacy, symptom efficacy in a population of patients with primary biliary cholangitis who are in need of second-line treatments. The study was placebo controlled. The average age of participants was 56.6 years, and 128 patients received seladelpar and 65 patients received placebo. The study duration during which the drug was given in a placebo-controlled manner was 12 months, but there is a long-term safety extension. At baseline, the alkaline phosphatase was 315, and at least 15% of patients had cirrhosis. This was a phase 3 registration study which was designed to look at potency, safety, and symptoms. Patients were recruited if the alkaline phosphatase was, in essence, over 1.67 times the upper limit of normal. And seladelpar was dosed at 10 mg daily.

The composite endpoint was assessed at 12 months; 6 out of 10 patients met the composite endpoint when treated with seladelpar as compared to placebo. There was a 42.4% drop in alkaline phosphatase when receiving seladelpar as compared to placebo; 1 in 4, 25% of patients had already normalized their alk phos after 12 months.

In this study, a key predetermined secondary endpoint was improvement in pruritus in those patients with moderate to severe pruritus at baseline. Seladelpar demonstrated highly significant improvements in pruritus for this key secondary endpoint, as well as other pruritus endpoints in other analyses.

During the duration of the study, and to date, there were no new significant safety concerns, and seladelpar was dosed safely, and most patients entered the long-term safety extension. Further studies are now ongoing to look at the long-term benefits of seladelpar. And there's now data for seladelpar use over more than 2 years, where normalization rates of alkaline phosphatase are reaching between up to 40%, improvements in pruritus are continuing to be evident, and no new safety signals have been described.

Furthermore, there are now ongoing endpoint studies of seladelpar looking to demonstrate clinical endpoints as well as the potent effects on biochemistry and symptoms.

Therefore, when looking at seladelpar in PBC and in particular the RESPONSE trial, my key takeaways today are, therefore, the new therapies are very exciting. Seladelpar in a phase 3 randomized controlled clinical trial led to 6 out of 10 patients meeting the composite

endpoint, a 40% drop in alkaline phosphatase, 1 in 4 patients normalizing their alk phos at 12 months, and importantly, a key secondary endpoint was statistically met with robust analysis of improvement in pruritus when seladelpar was compared to placebo. All in, very exciting for patients living with PBC.

Unfortunately, our time is up, so I thank you for tuning in.

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