Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/cme/protect-study-in-igan-topline-data/14980/

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

PROTECT Study in IgAN: Topline Data

Announcer:
Welcome to ReachMD. This episode is part of the Global Kidney Academy and is brought to you by Medtelligence.

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

Dr. Barratt:
The PROTECT study is one of the largest interventional studies and the only head-to-head trial in IgA nephropathy. It is a global randomized, multicenter, double-blind, parallel-arm, active-controlled clinical trial evaluating the safety and efficacy of 400 mg of sparsentan compared to 300 mg of irbesartan. The study included 404 patients ages 18 years and up with IgA nephropathy and persistent proteinuria despite receiving at least 50% of the maximum label dose and maximal tolerated dose of an ACE [angiotensin-converting enzyme] or ARB [angiotensin receptor blocker].

Today, I'm highlighting the 2-year topline PROTECT findings that can reshape the landscape of our patients with IgA nephropathy.

This is ReachMD, and I'm Dr. Jonathan Barratt.

So sparsentan is a very interesting drug because it has 2 mechanisms of action in 1. It has an angiotensin receptor-blocking action and an endothelial receptor antagonist action as well. So when you give this drug, you are blocking both the renin-angiotensin system pathway and the endothelial pathway.

The study itself is also unique in that it compares the drug sparsentan against an active control arm. It's the only trial to have done this. And in those patients who received irbesartan, they were titrated up to the maximal label dose, and over 95% of the patients in the active control arm managed to tolerate the top dose of irbesartan.

What we see from the topline data that was presented at the ASN [American Society of Nephrology] is that sparsentan led to a significant reduction in proteinuria that was sustained over the full 2 years of the study. And we know that it's not only the magnitude of proteinuria reduction that impacts on the rate of loss of kidney function, it is the durability of that response as well. So to see the magnitude of reduction that we saw, but also the fact that it was sustained over a 2-year period, it's highly reassuring that this mechanism of action is preserving kidney function in a very and highly relevant way. And indeed, that was reflected in the data we saw from eGFR [estimated glomerular filtration rate] over the 2 years.

So eGFR was assessed using something called total slope and chronic slope. Total slope is the slope of eGFR decline from the beginning of the study through to the 2-year endpoint, whereas chronic slope does not take into account the first 6 weeks of treatment but takes in all eGFR data from 6 weeks through to the end of the study. And it's important to understand the differences because with a drug like sparsentan that has a hemodynamic effect, there can be variability in GFR when you first start the medication. And of course, that variability in GFR can impact on how you statistically model the impact of a drug on long-term slope.

The chronic slope was statistically significant, and the total slope just missed statistical significance. But in both cases, there was an average, approximately a 1 mL/minute/year difference in eGFR slope. And for a 30-year-old patient living with IgA nephropathy who's got another 50 years or so of life, that 1 mL/min/1.73 m^2/year translates to a significant delay in the time to them reaching dialysis.

In terms of safety, this drug was well tolerated. There were no concerns over abnormalities in liver function. That's something clearly that people are aware of following the accelerated approval, but actually there was no liver signal at all in this study. There were very few significant adverse events. There were episodes of hypotension because this drug does reduce blood pressure. But actually, the

number of treatment withdrawals was very small. In fact, there was more treatment withdrawals and more parachuting in of additional therapies in the irbesartan arm because they were clearly doing less well than the patients on sparsentan.

So with this data, I think it's very clear to me that actually this is a valuable addition to renin-angiotensin system inhibition to protect kidneys and to slow the rate of kidney function decline in those patients with persistent proteinuria. I think it's a safe and well-tolerated drug. And I think it's going to be a very useful addition to our drug armamentarium in terms of how we handle these young patients with progressive kidney loss with IgA nephropathy.

So that's all I have time for today. So I want to thank the audience for listening and keeping up with the changing landscape in IgA nephropathy. Thank you.

Announcer:
You have been listening to ReachMD. This activity is provided by Medtelligence.

To download this activity, go to ReachMD.com/Medtelligence. Thank you for listening.