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DEARA Versus SOC in FSGS Management: Clinical Trial Insights

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Dr. Tesar:
This is CE on ReachMD, and I'm Vladimir Tesar. Here with me today is Dr. Meghan Sise. Today, we are going to discuss some clinical trials results regarding dual endothelin and angiotensin receptor antagonists for the management of FSGS and how they may compare to current standard of care therapies.

In the beginning, I would like to stress that we have no approved licensed therapy for FSGS. We use, of course, RAAS inhibition, and also there are some data on systemic corticosteroids or other immunosuppressants such as calcineurin inhibitors, but they have limited efficacy and the treatment is associated with sometimes severe adverse events. So there is a great unmet need for new treatment and inhibition of endothelin-A receptor could be a good step forward.

And really, we have now some data on this dual antagonist called sparsentan, which was tested in a phase 2 trial, DUET, showing that there is a significantly greater decrease of proteinuria with sparsentan compared with angiotensin receptor blocker, irbesartan. At 8 weeks only 9% on irbesartan.

And this early positive data stimulated the phase 3 trial, which of course recorded much greater number of patients and there was a long-term follow-up of 108 weeks. And this phase 3 trial largely confirmed what was observed already in phase 2 trial. So there was a much greater proteinuria decrease in sparsentan- compared to irbesartan-treated patients, 50% versus 32%, and a higher rate of remission was defined by different ways.

And this very promising data definitely represent a great hope for the patients with FSGS.

There are some exciting data from DUPLEX trial, which were not yet published, showing that sparsentan compared to irbesartan was much more successful in terms of reaching complete remission, which occurred 2.5 times more in patients treated with sparsentan compared to irbesartan.

And also partial remission, and here, sparsentan was 1.5 times more successful than irbesartan. What is also important is that the remission was very early and the curves of proteinuria separated quite early, at about 6 weeks.

And what is even more important is that reaching a complete remission, or even only partial remission, was clearly translated into long-

term outcomes in terms of ameliorating the risk of progression of chronic kidney disease. For instance, in those patients who reached partial remission, the risk was decreased from 16% to only 3%. And this is, of course, very important.

I have a question to Dr. Sise. What are your thoughts about the potential clinical implication of these data and patients who may benefit?

Dr. Sise:
Yeah, I think DUPLEX is a really important clinical trial. It's large, international, and included patients, as you mentioned, with biopsy-proven FSGS, and the patients were followed for 108 weeks. The difference in proteinuria reduction, partial remission, complete remission was statistically significantly favorable for sparsentan. And the GFR slope favored numerically sparsentan, although it was not statistically significant.

I think key findings here are that the medication is safe and well tolerated with comparable adverse events. And that's really important for a treatment for any chronic illness.

I think future subgroup analyses are warranted, but it seems like patients with early disease, those with high-grade proteinuria are the most likely to benefit from this therapy.

And I think that, although sparsentan is already approved for IgA nephropathy, it is not approved by the FDA yet for FSGS. It's under review. So it's hard to know what will happen, but if it were to be approved, then I do think it would offer a treatment for patients who have persistent proteinuria despite renin-angiotensin-aldosterone blockade, and I think that fact that it's well tolerated would be really important for patients as we try to address their ongoing symptoms and risk of kidney failure.

Dr. Tesar:
Thank you very much. I agree that in FSGS, there is probably even higher unmet need than in IgA nephropathy, where now there are many competitive new drugs which could be used quite soon, or some of them are already available.

Thank you very much for this nice discussion and thanks for listening to us.

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