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Emerging Evidence: IgAN Disease-Modifying Agents

Announcer:
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Dr. Zhang:
This is CE on ReachMD, and I am Dr. Hong Zhang. Here with me today is Dr. Richard Lafayette. Today, we are looking at the emerging disease-modifying therapies.

Dr. Lafayette, can you review this agent for us?

Dr. Lafayette:
Yeah. It's great to be with you, Hong. Thank you so much. I think we're using a very formal definition for disease modifying here and really talking about agents which directly go after the galactose-deficient IgA and maybe antibodies against galactose-deficient IgA. As you've helped contribute, we know that systemic steroids can in part be disease modifying but may have lots of side effects that targeted steroids, likewise, have been approved globally now and can also help to reduce galactose-deficient IgA. But I think there's even greater excitement now that we've looked at some of these B cell-modifying agents.

We were able to see relatively complete data for APRIL/BAFF reduction with telitacicept just in Chinese patients, where there looked to be a wonderful reduction in galactose-deficient IgA, proteinuria, and stabilization in GFR. But for global trials, it's really exciting that we've now seen the 9- to 12-month data for sibeprenlimab, which as you know is a monoclonal antibody to APRIL, which very efficiently reduces APRIL, in turn reducing plasma cell activity and B-cell maturation, which reduces IgG a little bit, IgA by about two-thirds, reduces IgM, and importantly reduces galactose-deficient IgA by about two-thirds. And in the phase 3 study at 9 to 12 months, we saw that achieved in a very well-tolerated way where safety looked to be quite acceptable. In fact, serious infections were even less numerous in patients getting study drugs, sibeprenlimab versus placebo, and patients seemed to tolerate the injections. And importantly, clinical efficacy seems to be similar to what we saw in their phase 2 trial, that proteinuria rapidly comes down, reaching proteinuria reductions compared to placebo of even greater than 50%, which was sustained out to 12 months. Seeing patients with baseline hematuria have their hematuria go away.

Very similarly for atacicept, which again is both an anti-BAFF and anti-APRIL drug as an IgA fusion protein with the receptor for BAFF and APRIL. Atacicept looked really, really well tolerated as well in their data at 9 months, where patients stayed in the trial. Again, serious adverse events and serious infections were less numerous than among placebo groups. And we again saw proteinuria that was approaching 50% net compared to placebo was closer to about 43%. We saw, again, very, very nice resolution of hematuria among patients who had blood in the urine at baseline. And again, the FDA doesn't allow us to look early at the GFR data, but the atacicept studies had gone out in phase 2 to 96 weeks and shown really nice stability of GFR. And the hope was that we would see similar in

phase 3's.

And I think this is really outstanding data. As you know, in the United States, sibeprenlimab is already now FDA-approved and we're just starting to be able to prescribe that to patients who we think are at risk for progression. Atacicept will have a decision sometime late spring, early summer. And I think these agents really look like they're truly disease modifying, that they have potent effects on reducing proteinuria, that they're well tolerated, and again, we are expecting that their impact on GFR progression is really going to be revolutionary in terms of expecting them to fully stabilize kidney function.

So I think that's what we've seen so far. And back to you, Hong, what do you think about this for your practice and for patients in Asia?

Dr. Zhang:
Yes, thank you, Richard.

A number of therapies that are directed against APRIL or BAFF and APRIL are now in clinical development, as you already described. Some, as you just mentioned, the sibeprenlimab, atacicept, as well as the povetacicept.

Actually, all these phase 3 clinical trials recruited Chinese patients. So we are also awaiting the expected phase 3 study results. The subgroup analysis in different origins will provide more information, I think. Additionally, the phase 3 trial of telitacicept, that is a Chinese company that's produced the product, and the same principle was conducted in China. And the interim analysis data were presented last year at the same time as VISIONARY and ORIGIN. And the results are very similar with these 2 studies.

Dr. Lafayette:
Yeah, I think it's, again, just like you said, I think it's very exciting. So this is really changing therapy. Again, we're really lucky to have the use of SGLT2 inhibitors, endothelin antagonists, to consider steroids, to have complement inhibitors already, so I think this really gives us a chance to take in our patients with IgA nephropathy and give them their very best chance to now move from a disease, which was so likely to have them end up on dialysis, and now to have a good chance of lifelong stability. We will see.

Dr. Zhang:
Yes. Thank you, Dr. Lafayette, for sharing the updated data from emerging therapies in IgA nephropathy. And overall, this data highlights the potential for therapies targeting in IgA nephropathy. And the data from the ongoing phase 3 clinical trials are very exciting. We are excited to wait for the 2-year GFR data.

Well, this was brief, but I'm glad we had the opportunity to share this data with our audience. Thanks for listening.

Dr. Lafayette:
Thank you.

Dr. Zhang:
Thank you.

Announcer:
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