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Emerging Therapies in IgAN: Who Could Benefit the Most?

Announcer:
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Dr. Zhang:
This is CE on ReachMD, and I'm Dr. Hong Zhang. Here with me today is Dr. Richard Lafayette. In another episode, we discussed the phase 3 data from disease-modifying agents, namely sibeprenlimab and atacicept. Today, we are focusing on the subgroup data from these trials.

Dr. Lafayette, what do our listeners need to know about the data from this subgroup analysis?

Dr. Lafayette:
Yeah, thanks, Hong. As we discussed in the other episode, it's really exciting to see the data from the phase 3 sibeprenlimab study and the phase 3 atacicept to really align and show that these agents were well tolerated, they were very safe, and they dramatically reduced proteinuria, dramatically reduced hematuria similarly to what was seen in their phase 2 studies, where both of the agents also controlled disease progression to an extent we haven't experienced before among high-risk patients with IgA nephropathy.

What's really remarkable is that these agents appear to work in each and every subgroup that was analyzed in these studies. And just to review to date, in the sibeprenlimab study, they really looked at age as a variable. They looked at baseline proteinuria, baseline kidney function, time from kidney biopsy, presence of hematuria, and really couldn't find, within the baseline demographics, anything that really differentiated the patients. Furthermore, whether they were from Asia, Europe, Latin America, US, it just didn't matter their place of origin. And this is really important to know that these agents can be used broadly among patients at the highest risk, the lowest risk, and early in disease and in late disease. And we still may need to wait until we see whether or not there's enough pathology data to see whether that's true based on what their baseline biopsy was. But as you know, the biopsies could be a long time from the beginning of the study.

Similarly, for atacicept, they looked at similar subgroup analysis of age, gender, race, baseline proteinuria, GFR, presence or absence of hematuria, and again, none of it really made a difference. They still saw proteinuria reduction of 40% to 50%, hematuria reduction, again suggesting that these agents are broadly applicable to our patients with IgA nephropathy, globally, early, late, mild, or more severe proteinuria, early disease, late disease based on kidney function, and it's just really, really exciting.

I think we all want to try to personalize our therapies for those patients who could benefit from them the most, but right now, it's really hard to choose because it looks like everyone's benefiting similarly, at least those patients who are in the trial.

So I'll turn it back to you, Hong, for what you think about whether these are really universal therapies or maybe there is a group that we should really focus the therapy for.

Dr. Zhang:
I think I agree with you that, actually, in the telitacicept with the baseline and the follow-up is very similar with these 2 studies. And the little bit of difference is in Chinese patients, the renal biopsy time for the randomization is shorter. And that's eGFR is a little bit higher than these 2 studies. That means the patient may have that early stage of the disease. That's maybe because we didn't do a head-to-head to compare.

But as you know, IgA nephropathy displays very heavy heterogenicity in clinical pathology manifestations. And the treatment is also different, and the prognosis is also different in different populations so far in the literature. And that's a published cohort study from China, from Japan, and from Korea that indicates, compared with the non-Asian population, that the East Asian IgA nephropathy patients have more aggressive clinical and pathological features, at least in that cohort study.

But I think there's a variation in biopsy practice and the disease stage at the diagnosis, and there's a comorbidity. I think that the co-existing disease may confound our cross-regional comparison. So international clinical trials will provide the clinical, very critical platform to clarify the ethnicity and the geography relating to these parties, I think.

So it's also to access the therapeutic response to the interventions. So I think that's a very great opportunity and maybe in the future we can combine different clinical trials and really answer this question.

Dr. Lafayette:
Yeah, I completely agree. I think, the early data is what it is. It looks like this is universally good across the globe for every type of IgA nephropathy patient who was eligible for these kinds of trials. But further studies based on other biomarker data, pathology data, are definitely necessary, and maybe we can still personalize it. But for now, it's just wonderful data and a great breakthrough.

Dr. Zhang:
Yes. So, well, that was a lot of data in just a few short minutes. Return again anytime for a refresher. And thanks for listening.

Announcer:
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