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Beyond RAASi and Approved Therapies: The Unmet Needs in IgAN

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Dr. Rizk:
This is CE on ReachMD, and I'm Dr. Dana Rizk. Here with me today is Dr. Hong Zhang. And our topic today is unmet clinical needs in IgA nephropathy.

Dr. Zhang, we have real-world and registry-based evidence from China and Japan that demonstrate the frequent failure to achieve guideline-recommended proteinuria targets with standard of care alone. Can you elaborate on this information for us?

Dr. Zhang:
Thank you, Dana. So that's a standard of care-based comprehensive strategy centered on the optimal RAS inhibitor that is fundamental to prevent IgA nephropathy progression and related complication. However, the real world and the registry-based evidence from China and Japan consistently highlight that the standard of care alone is often insufficient to achieve guideline-recommended proteinuria targets. The data from China National IgA Registry, that's a very big sample size of over 3,000, has indicated that 40% to 60% of patients on maximal tolerated RAS inhibitor still have proteinuria over 1 g/day after 2 years of follow-up.

And a subset of patients even have proteinuria over 2 g/day. They are associated with 3- to 5-fold higher ESKD risk over 5 to 10 years. So that's Chinese data. And regarding Japanese data, that also found that Japan's IgA registry, and that's a regional cohort, reported similar trends. That is 35% to 55% of patients on optimal RAS inhibitor do not achieve proteinuria less than 1 g/day. And it's also noticed that up to 20% of those with initial partial response, that means the proteinuria reduction over 30%, they also experience a rebound within 3 years. So that's underscoring RAS inhibitor limitation in long-term disease control. I think that's the information.

So per KDIGO guideline, systemic corticosteroids is an option for high-risk progressive IgA nephropathy patients based on the TESTING trial that confirmed its efficacy in reducing proteinuria and delaying ESKD.

However, the safety concerns and the patient barriers, especially in younger patients, limit its clinical application. So patients treated with corticosteroids have to face higher steroid-related adverse events and a lifetime risk. So that means there are a lot of unmet needs. Fortunately, in more recent years, new agents such as atrasentan, sparsentan, Nefecon, as well as iptacopan were approved in IgA nephropathy treatment. I think that has improved the situation of lack of novel agents for clinical treatment of IgA nephropathy.

Dr. Rizk:

Yeah, and I think not achieving guideline-recommended proteinuria level may be even more dramatic now that the proteinuria recommendation is to reduce it to less than 0.5 g/day, so it's going to be really quite hard for these Asian populations that you just described.

Dr. Zhang:
Yeah, I think that IgA nephropathy is indicative of immune-mediated chronic progressive glomerular disease. And as an immuno–mediated chronic disease, KDIGO guideline management requires targeting of disease-specific drivers of nephron loss under the system response to IgA nephropathy-induced nephron injury. So that's a comprehensive approach that's incorporating novel agent testing in a pathogenesis-based clinical trial, bringing new prospect for our patient.

Dr. Rizk:
Yeah, absolutely. So patients are going to need more than one drug to do so.

Dr. Zhang:
Sure.

Dr. Rizk:
So with that, our time is up. Thank you for a great discussion, Dr. Zhang, and thanks to our audience for tuning in.

Dr. Zhang:
Thank you.

Announcer:
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