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Optimizing IgAN Care: Sparsentan's Role Amid the Latest KDIGO Guideline Updates

Announcer:
You're listening to ReachMD. This activity, titled "Optimizing IgAN Care: Sparsentan's Role Amid the Latest KDIGO Guideline Updates" is provided by Medtelligence.

Dr. Floege:
After much anticipation, we now have the updated KDIGO guideline for IgA nephropathy and IgA vasculitis. Let's explore the changes and their potential impact on patient outcomes. This is ReachMD, and I'm Dr. Jürgen Floege, and I'm happy that on September 18, 2025, the revised KIDGO IgA nephropathy guideline was finally published, long-awaited. And these are the key points.

First of all, considerations regarding the diagnosis. We still, in 2025, have no validated serum or urine biomarkers for the diagnosis, so you still need a biopsy. And in fact, we advocate for a more liberal biopsy policy starting at a proteinuria of 0.5 grams per day or higher if IgA nephropathy is a possible diagnosis, because now we can do something to these patients. Once the diagnosis is made, assess for secondary causes, and if you have a primary IgA nephropathy, do determine the MEST-C score.

Then comes assessing of prognosis. Because patients, if they have a proteinuria above 0.5 grams per day, are at risk, and this is new in the guideline, we advocate to reduce their proteinuria to almost physiological levels, if not physiological levels. So, below 0.5 grams per day, ideally to below 0.3. But of course, the key goal of therapy, and this is the new guideline, is to slow down the loss of kidney function to the physiological state. In people like me, this would be a milliliter per minute per year for most adults for the rest of the patient's life. Now, that is a big statement because now we're talking decades.

The only validated biomarker to help guide clinical decisions, at present at least, is still urine protein excretion. And as I said, ideally you want full remission, no proteinuria anymore.

This is the algorithm of the new KDIGO guideline, which is probably the most cited figure of all. And the key element in that algorithm is the top line. We now advocate for a simultaneous treatment initiation targeting both the immune aspect, the inflammatory immunologic aspect of the disease, and the generic CKD aspect of the disease. Because by the time that we do see patients in practice, most, if not all of them, have established CKD and many have already lost very significant amounts of kidney function. And don't forget cardiovascular risk evaluation and protection.

And then we have boxed the treatment approaches under these two big aims, realizing that this is in part artificial, realizing that some of this is arguable but it helps you sort the approach in your mind of what to do. And I will focus on the generic CKD aspect for the time being, which of course includes lifestyle modification and so far, RAS blockade, which should be up-titrated as much as possible, plus an SGLT2 inhibitor. And sparsentan, which is shown here. A dual blocker of both the endothelin type A receptor and the angiotensin type 2 receptor. So, this replaces an angiotensin receptor blocker, because now you have 2 in 1, and I will show you that is a very effective combination in one single molecule.

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This is the PROTECT Phase 3 trial, and the first notable thing is that if you compare the red line, which was high-dose irbesartan, literally everybody was on high-dose irbesartan. There was a small proteinuria drop, so it's good to be in a trial, even if you're in the control arm. But if you compare that to the green line, sparsentan 400 mg, you see the immediate rapid drop in proteinuria of 40 to 50% and that clearly implies to me, if it happens so fast, that this is likely something on intraglomerular hemodynamics that accounts for this potent antiproteinuric action.

In terms of GFR course, we found that with sparsentan, the GFR loss per year on average was a milliliter per minute less than with irbesartan. And if you then, finally – and of course, this is what I'm really interested in – look at the time to reach the composite kidney endpoint of 40% GFR loss, kidney failure, or all-cause mortality, you see this marked separation of the two curves, which starts at about half a year, and then the curves really diverge in the long run.

Side effects: Sparsentan doesn't really do much to systemic blood pressure. And if you look at the trial data, the average blood pressure, systolic, is essentially identical. Diastolic, there are very few millimeters mercury less diastolic pressure, but it is not a massive antihypertensive additive effect.

Very importantly, there was at best, a minimal edema signal, but this was not really a problem in this trial. Anemia was a little bit more common. There were no liver toxicity signs.

So, the new KDIGO recommendation now says: Where approved, patients who are at risk for progressive loss of kidney function with IgA nephropathy should be treated with sparsentan.

It's a 2B recommendation, and sparsentan should replace, rather than being prescribed together with a RAS blocker. So, it simply doesn't make sense to combine it; it needs to be replaced.

Here's another study, a very recent one, an interim analysis of the SPARTAN trial. In SPARTAN, newly diagnosed patients with IgA nephropathy were not placed on a RAS blocker first, but rather went directly on sparsentan. And again, it nicely confirms what we would have expected. Within 4 weeks, you had a 60% reduction in proteinuria, confirming once again, sparsentan's enormous antiproteinuric potential.

In the SPARTACUS trial, patients were already on a RAS blocker and an SGLT2 inhibitor, and same picture again, within 4 weeks, proteinuria falls by 50%. Same safety profile, no new signal in SPARTACUS when you add it on top of an SGLT2 inhibitor. And here is, essentially, once again, and this will be the last time I show you the same, the same, the same. This is the German observational trial where, again, SGLT2 inhibitor and RAS blocker was switched to SGLT2 and sparsentan, and you had this rapid lowering of proteinuria within just a few weeks.

So, to sum up, in the KDIGO guidelines, we have a fairly radical paradigm shift in that we propose to treat the immune side and the CKD side in parallel. I didn't go into any detail of the immune treatment, but in the CKD side, we now have so much more than we had in the past. Optimize your RAS blocker, that we've always done, but we have an SGLT2 and we have sparsentan. And I think that's an important message – it's safe and effective to combine an SGLT2 with the sparsentan. So, I think we now have an increasingly good armamentarium to treat our patients at risk of progressive IgA nephropathy.

That's all the time we have today. So, I want to thank the audience for listening and keeping up with how to optimize IgA nephropathy care using the latest KDIGO guideline update.

Announcer:
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