



## **Transcript Details**

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/clinical-practice/nephrology/iga-nephropathy-updates-evolving-guidelines-and-practical-strategies/26632/

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IgA Nephropathy Updates: Evolving Guidelines and Practical Strategies

#### Announcer:

Welcome to CME on ReachMD. This activity, titled "IgA Nephropathy Updates: Evolving Guidelines and Practical Strategies" is provided by Medtelligence. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

#### Dr. Latus:

Given that IgA nephropathy is one of the leading causes of kidney failure, early diagnosis and timely intervention are critical. As clinical practice guidelines continue to evolve, clinicians must consider how to best incorporate emerging therapies for proteinuria remission and the preservation of glomerular filtration rate to ultimately improve patient outcomes.

In this session, we will explore this topic using a real-world patient case. This is ReachMD, and I'm Dr. Jörg Latus.

# Dr. Floege:

And I'm Dr. Jürgen Floege.

## Dr. Latus:

To start things off, Jürgen, what can you tell us about the highly anticipated, updated KDIGO guidelines?

## Dr. Floege:

First of all, you still have to wait a little more because we will likely publish them in October or November of this year, but there will be some fundamental changes in there.

First of all, be more liberal with your biopsy. Biopsy earlier. Catch the patient earlier, before damage really builds up. Second of all, you need the biopsy. Third, the biopsy itself, other than giving you the diagnosis and some prognostic information, it shouldn't guide your treatment. That's an important statement.

But I think the most fundamental thing is that we now advocate that we completely reverse what we've done in the past. In the past, we slowly increase treatment, build up supportive treatment, and then thought about steroids or not steroids. We want this to change. We want you—now that we have safe and effective therapies—to start treatment right away and start combination therapy targeting the CKD aspect of the disease—so blood pressure, lifestyle, RAS blockade, possibly sparsentan, the dual endothelin angiotensin blocker. And at the same time, start treating the immune disease—Nefecon, possibly in the future, anti-complement therapies, etc.

This is guided by the fact that patients all too often lost significant kidney function before we really started to treat. And the other big new insight is that even low proteinuria is harmful, it has a prognostic impact, and patients will go to kidney failure at youngish adult age. And that is, of course, something we need to prevent in the future.

## Dr. Latus:

I think it's a very good guideline. We can easily, I believe, implement this guideline in our everyday clinical practice, and maybe you can comment, just a short, about the kidney biopsy and the guidance to choose whether immunosuppression or CKD therapy because that's an issue we all hear. What do you think?

## Dr. Floege:

Very often I do hear that because the MEST score shows this and that I will know. But first of all, that's a snapshot. We know experimentally that even massive inflammatory changes can disappear in a week. Crescents can disappear in a week completely. So





what does a single snapshot in time tell me—number one?

Number two, the MEST score has reproducibility issues. Remember, it's a semi-quantitative eyeballing score.

And third, we have no prospective studies showing ever that you can make decisions based on the biopsy. Don't misunderstand me. The situation is radically different if 50% of your glomeruli are necrotic and have crescents and the creatinine is rising like crazy. But then the clinical course dictates your treatment.

So can you now—having said all this, let's become practical. Give us some guidance and additional perspective using a patient case.

#### Dr. Latus

I would like to present a case of a 46-year-old man. The diagnosis of IgAN was done in 2019. At this time point, eGFR was 72 mL/min, proteinuria was 0.8 g/g, and blood pressure was 145/80.

We put the patient on RAS inhibition of ramipril 5 mg twice a day. And after we got the excellent data from the DAPA-CKD trial, of course we decided to put the patient on dapagliflozin 10 mg once a day.

But in January 2024, the patient presented to my outpatient clinic: eGFR was 46 mL/min, proteinuria was still high with 1.1 g, blood pressure was well controlled with 125/80, and BMI was 21. So of course, we have asked us the question, are we satisfied with the proteinuria? And of course we are not satisfied.

So the question is now, what can we offer to this patient? And, yes, we have the sparsentan data presented in the PROTECT trial. But there was always an ongoing discussion because in the PROTECT trial, the patients were not on a stable SGLT2 inhibition. So the question was, of course, now I have a patient on RASi and SGLT2, the question is, do we have additive effect in this patient when we add, for example, a therapy with sparsentan?

And yes, I believe we have evidence. We published this paper last year in *CKJ*, and we investigated 23 patients presenting with a full dose of RAS inhibition. So 75% of our patients had a maximum label dose of RASi, and they were still on an SGLT2 inhibitor, and proteinuria was more than 1 g, and eGFR was around about 42 mL/min.

Do we have any additive effects when we add sparsentan in this patient? And, yes, you can see in our study, UPCR significantly decreased after 14 weeks, equivalent to a relative reduction in proteinuria up to 62%, which is a very good and very promising result.

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Jörg Latus, and here with me today is Dr. Jürgen Floege. We're discussing how to integrate emerging therapies in IqA nephropathy in context of evolving clinical practice guidelines.

So going back to the goals we have, we should put our patient in complete remission. When we look in our patient population, high-risk population, you can see complete remission was achieved in 35% of our patients after we added sparsentan to a stable SGLT2 inhibitor therapy. Partial remission was achieved in 52% of our patients. And we look to the proteinuria reduction, 87% of our patients had a proteinuria reduction of at least 50% when we added sparsentan to a treatment with SGLT2.

When we go into safety results, there was well-tolerated sparsentan in our patient population, with no evidence of serious adverse events, and there were no new signals.

So there was the SPARTACUS trial presented. It was the interim analysis presented last year at the Kidney Week, showing a 40% reduction when you add sparsentan to a stable SGLT2 inhibitor patient population.

And now at the ERA, the full analysis was published with a reduction of 60% of proteinuria when you add sparsentan to SGLT2. So in the same range that we saw in our real-world evidence.

So now I think we have evidence that we can tell, yes, there is additive effect when you add sparsentan to an SGLT2 inhibitor therapy. So we did. We treated our patient with sparsentan. And as you can see, in April 2025, the eGFR was 43 mL/min, and proteinuria decreased to 0.3 g/g.

So before we wrap up, Jürgen, do we have any comments about this case?

## Dr. Floege:

Yeah, I mean, a practical question. GFR dropped a tiny little bit when you added sparsentan. Is that an acute drop, which then stabilizes? Or is it just continuous?

## Dr. Latus:

It's stabilizing. So you have the small decrease of eGFR, but later on, when we look at the eGFR data, even in our small cohort of





patients, there was preserved eGFR.

## Dr. Floege:

And blood pressure was unchanged. I think that is a key aspect. Here, he didn't faint, and you achieved a dramatic reduction in proteinuria. And I think that is a very particular practical aspect. This is not just a more potent blood pressure drug, but this is blocking two systems that really drive proteinuria.

#### Dr Latus

And the SPARTAN data are coming up with sparsentan as a first use, and you can see there was a decrease of inflammatory markers in the urine. So it's, of course, more than only hemodynamic effects.

#### Dr. Floege:

Yeah. Even though the very rapid antiproteinuric response, to me, suggests there's something about glomerular—intraglomerular hemodynamics.

## Dr. Latus:

Completely right.

So now I would like to summarize. The diagnosis of IgAN requires a biopsy. I think that's fundamental. We need a biopsy. We need a diagnosis, otherwise we could not treat our patients in the right manner.

We have to achieve a proteinuria, and that's really low. We have to achieve a proteinuria below 0.3 g, or let's say, or below 0.5 g/g. And to achieve this goal—and this is clearly stated in the draft of the guideline—some patients need multi-target therapy to achieve this goal.

Now we have new drugs available, and when we go to sparsentan, sparsentan has shown efficacy in clinical trials. And now we have real-world studies that even in patients still on an SGLT2 inhibitor, you have additive effects when we talk about reduction of proteinuria and eGFR.

And now we need further studies. We have to look for combination therapies like Nefecon and SGLT2 inhibitors. And then of course the emerging therapies should be considered. And I think this was a clear statement from you, we need biomarker research to identify the patient who might benefit from a—more like therapy would be with the autoimmune disease or the CKD, so we need much more biomarker research.

## Dr. Floege:

Catch them early, do a biopsy, treat them early, and get them to full remission. When I'm 90 years old, which is not too far away, I don't want to see patients with IgA on dialysis anymore.

Thank you.

## Dr. Latus:

So I would like to thank you, the audience, for listening, and thank Dr. Jürgen Floege for sharing your valuable insights.

## Dr. Floege

Thank you from my side as well, and goodbye.

## Announcer:

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