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/programs/frontlines-iga-nephropathy/early-combination-therapy-iga-nephropathy/60617/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Early Combination Therapy in IgA Nephropathy

Announcer:
This is *On the Frontlines of IgA Nephropathy* on ReachMD. Here's your host, Dr. Gates Colbert.

Dr. Colbert:
You're listening to *On the Frontlines of IgA Nephropathy* on ReachMD, and I'm Dr. Gates Colbert. Joining me to discuss the shift toward earlier treatment in patients with IgA nephropathy, or IgAN for short, is Dr. Sayna Norouzi. She's an Associate Professor of Medicine and Clinical Nephrologist at Loma Linda University Medical Center in California. She's also the Founder and Director of the Glomerular Diseases Clinic at Loma Linda and serves as the Director of the GlomCon Glomerular Diseases Fellowship Program. Dr. Norouzi, we're so glad to have you here today.

Dr. Norouzi:
Thank you so much for having me here, and thank you for the kind introduction, Dr. Colbert.

Dr. Colbert:
Well, let's dive right in. For years, IgA nephropathy treatment has followed a pretty stepwise approach: start with supportive care, then consider immune-targeted therapy if patients remain at high risk. But how has that approach changed, and what's been driving the move toward earlier treatment?

Dr. Norouzi:
As you know, for years and years, we were taught that IgA nephropathy is a disease that is okay to monitor, control the blood pressure, and change the patient's lifestyle for, and hopefully they're not going to progress to end-stage kidney disease.

But since the RaDaR study came out, our understanding of IgA nephropathy changed. We now know that our patients with IgAN are going to be at risk of ending up on dialysis or transplant throughout their lifetime. We might not be their nephrologist at the time that they're dealing with a complication, but it doesn't mean that they're not going to face complications in the future.

A lot of my patients in the clinic, when they come in, they're really young. They're in their 20s and 30s, and they might not have a lot of symptoms. They feel fine, and someone had told them that they have blood in the urine. They do a kidney biopsy, and they get diagnosed with IgA nephropathy.

Us telling them that they need to take multiple medications to prevent complications in the future could be a barrier. But, because of what we know might happen to our patients and the tools that we have for our patients, the practice has changed. Now, we know that we have to act now, especially for higher-risk patients, to prevent complications for them.

Dr. Colbert:
Now, once you've decided to treat earlier, why is it important to address the immune-driven disease process and protect kidney function at the same time, instead of thinking about those as separate treatment goals?

Dr. Norouzi:
Patients with IgA nephropathy have different phenotypes, and some patients might come in and they've been diagnosed with IgA nephropathy maybe 10 years ago, and they don't have a lot of symptoms. They haven't had hematuria for a long time. Their proteinuria is less than 300, and they have a stable eGFR. These patients have a different phenotype than patients that come in and they have higher proteinuria levels. They have hematuria on and off, and you see some degree of CKD on their labs.

And unfortunately, most of the patients, when they get to the nephrology clinics, already have some degree of CKD. It rarely happens

that you get the referral for the first time—when the patient is experiencing hematuria—to a nephrologist. It can happen, but the majority of patients that we see at the time in the United States, at least—because we do not screen, for example, hematuria, etc.—they do have some degree of CKD at the time.

So, depending on many factors—like if the patient is younger, they have protein in the urine, they have hematuria on and off, they've already lost part of their kidney function—these patients, in my opinion, are at high risk of ending up on dialysis or needing transplant in the future. And not only are these patients going to benefit from CKD care, but I really want to go after the pathophysiology of IgA nephropathy and treat my patients to the core. I don't want to suppress the proteinuria using ACE inhibitors or SGLT2 inhibitors, or even newer medications as sparsentan and atrasentan, and then not go after the pathophysiology of IgA nephropathy with some medications such as B-cell medications or complement inhibitors as well.

So I have really long discussions with my patients when they come in about their treatment options and the thought process behind doing multiple medications at the same time. And I can tell you that about 99 percent of my patients, once they understand their options and the risks of taking the medications versus not taking the medications, they usually opt in for taking multiple medications to bring down the risks.

Dr. Colbert:
So when you're seeing someone who's newly diagnosed with IgA nephropathy, what tells you they may benefit from starting both immune-targeted and kidney protective therapy early?

Dr. Norouzi:
Basically, their phenotype. If you think that your patient is considered high risk, considering the amount of protein that they have in their urine, the hematuria—and I know that the data is controversial, but it's something; it's a piece of information that actually helps you to make decision about how risky your patient is in terms of ending up on dialysis or transplant—their eGFR trajectory over time, how they responded to previous medications if they've taken any medications in the past, how many flares they've had, how old they are, and what degree of CKD they have at the time… Overall, if you consider these patients at high risk, then the recommendation is to start both medications at the same time.

So you consider one of the medications on the CKD care part, which include ACE inhibitors or ARB, and then that could be in addition to atrasentan, or, instead of ACE and ARB, you can consider sparsentan. With SGLT2 inhibitors, I think it's kind of a routine practice at this point, and it's very accepted based on the data that we have to start SGLT2 inhibitors for these patients as well.

But at the same time, we discuss one of the medications that goes after the pathophysiology of the IgA nephropathy as well. And those medications are going to be the B-cell medications and complement inhibitors, and, as you know, we do have two FDA-approved B-cell medications, APRIL inhibitors, and then we do have APRIL/BAFF inhibitors as well. In terms of complement inhibitors, we do have iptacopan as the FDA-approved medication as well. And the first medication that got the FDA approval that could be under the umbrella of the B-cell medications is delayed-release budesonide.

I discuss all of these options with my patients: the risks, the possible side effects, the benefits, the route of administration as well, which is important, because some patients might choose an oral medication, and they might choose a tablet over a subcutaneous injection that they have to do at home. And then once I discuss all of these details, we come up with a decision together. Usually, my patients end up taking multiple medications at the same time, at least in the beginning, and I follow them up closely, and our goal is basically going to be remission.

Dr. Colbert:
For those just joining us, this is *On the Frontlines of IgA Nephropathy* on ReachMD. I'm Dr. Gates Colbert, and I'm speaking with Dr. Sayna Norouzi about the rationale for earlier simultaneous treatment in IgA nepropathy.

So, Dr. Norouzi, the updated KDIGO 2025 recommendations put more focus on things like reducing proteinuria over time and preserving kidney function. How are those goals shaping the way you make treatment decisions today?

Dr. Norouzi:
I completely agree with new KDIGO guidelines. We have to evolve our practices as we are getting more medications available to our patients as well. So now we have a better understanding of IgA nephropathy pathophysiology. Now we know more about the possible prognosis of our patients, especially higher-risk patients. So we have to react to the data that we have, and we have to change our practices, right? And I'm really happy that KDIGO actually released a new update after their first update as well to include the B-cell medications.

So if you look at the newly drafted KDIGO guidelines, they actually aim for eGFR loss of less than one per year, which is ideal. Basically,

if you're controlling the disease and bringing down the proteinuria to less than 300, then you really don't want to see a huge drop in the kidney function over time. So if you believe that your patient is continuing to lose eGFR despite the treatment options that you've discussed and you've started your patients, then you're not achieving your goal. Because at the end of the day, we want to preserve the kidney function for our patients, and if the eGFR is dropping, obviously we are not achieving our goals.

At the same time, we do have some surrogate biomarkers such as urine protein-to-creatinine ratio, and KDIGO is actually emphasizing this biomarker more than any other biomarkers at this point. And it's really easy to actually check in real life and in our daily practice. So if the proteinuria is coming down, you're going into remission, and uPCR is less than 300, that's a really good sign, and that's reassuring that you are actually moving towards a remission state. But it's not actually everything; you're going to look at multiple endpoints for these patients and urine protein-to-creatinine ratio is just one of them.

Dr. Colbert:
Even with this shift toward earlier treatment, are there still patients where a more stepwise approach makes sense? What helps you decide which path is the right one?

Dr. Norouzi:
This is a really good question. I actually have a clinic in China as well, where I accepted a faculty position. And while I was practicing there, I noticed that the phenotype of patients with IgA nephropathy can be really different, even between and among different races in terms of when and how soon you diagnose these patients, and again, the degree of CKD.

So, for example, in China, as I was seeing patients, a lot of patients did not have a lot of proteinuria, but their eGFR had been dropping really fast. So these patients are considered high risk, right? As long as eGFR is dropping—you see the eGFR trajectory is actually dropping really fast—and you don't find any other reasons rather than IgA nephropathy driving the eGFR loss, it makes me become aggressive about treating these patients.

But then, at the same time, you see some patients that come in—and I have a handful of these patients in my clinic—who have been diagnosed with IgA nephropathy many, many years ago. They never had proteinuria more than 300 milligrams. Their hematuria rarely happens. Their eGFR is perfect, like it's been, for example, fluctuating between 95 and 100. And maybe they've been taking low-dose lisinopril for a while, and their blood pressure is well controlled. They're trying to be healthy. For these patients, you do not have a reason to become aggressive at this point, as long as you're following them closely and their kidney function is stable.

I always tell my patients that the with kind of disease that we are dealing with, you can always have flares for multiple reasons. And not having a flare for a long time doesn't mean that you're not going to have it in the future as well. So close follow-ups are really important for our patients here, and I usually check their labs at least every three to four months and make sure that their blood pressure is not going up. I always tell them that if anything is changing, if something stressful happens, if you get an infection and all of a sudden you see some swelling on your legs or you feel tired more than usual, I really want to repeat your labs and make sure that if you're going into a flare, we can act on it, because we do have options.

But for these patients who are already in remission and they are at goal, we do not have to become super aggressive about them and do multiple medications at the same time.

Dr. Colbert:
Before we wrap up, Dr. Norouzi, do you have any final thoughts you'd like to leave with our audience?

Dr. Norouzi:
One of the things that I'm really actually passionate about these days is that, since I get a lot of late referrals for IgA nephropathy, I really want to find a way to fix that. And I think one of them could be coming from our primary care physicians' offices. Maybe we should look into hematuria or proteinuria. And one of the studies that we're working on with the IgAN Foundation these days is actually doing a urine dipstick on healthy individuals of a younger population to see if that could be a feasible or cost-effective way to just start a process.

The way that we are practicing right now—because of the newer options that we have and because of the changes that we can do at this point—it's not like five years ago, where, even if they came to our office, we weren't making huge changes. This is so different, and we want to catch these patients as soon as possible, and we want to prevent progression of CKD.

In my opinion, there is a huge difference between ending up on dialysis in your 50s versus 60s versus 70s. And at this point, we are hopeful about this. We are hopeful about delaying complications for our patients, and we just have to work closely with our primary care physicians to get earlier referrals, catch these patients earlier, and help them to achieve their goals as well.

Dr. Colbert:
That's a great comment for us to think on as we come to the end of today's program. And I want to thank my guest, Dr. Sayna Norouzi,

for sharing her perspective on how earlier intervention is changing IgAN care. Dr. Norouzi, it was great having you on the program.

Dr. Norouzi:
It was a great conversation. Thank you so much for having me.

Announcer:
You've been listening to *On the Frontlines of IgA Nephropathy* on ReachMD. To access this and other episodes in our series, visit *On the Frontlines of IgA Nephropathy* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.