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/innovations-in-igan-care-examining-the-evolving-treatment-landscape/26941/

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

Innovations in IgAN Care: Examining the Evolving Treatment Landscape

Announcer:
Welcome to *On the Frontlines of IgAN* on ReachMD. On this episode, we'll discuss the evolving treatment landscape for immunoglobulin A nephropathy, or IgAN for short, with Dr. Jonathan Barratt. He's the Mayer Professor of Renal Medicine at the College of Life Sciences University of Leicester, while also serving as a committee member for the International IgA Nephropathy Network. Here's Dr. Barratt now.

Dr. Barratt:
There are a lot of exciting new developments coming in IgA nephropathy. We've had the first drugs ever approved for the treatment of IgA nephropathy. We've had Nefecon; we have now had sparsentan; and in the last couple of weeks, we had a drug called iptacopan. I would expect, in actual fact, we're going to have another two drugs approved each year for the next three or four years.

When we think about these new drugs, it's important to think about their mechanism of action. And so we have new drugs that are capable of suppressing the fundamental immunology of the disease by reducing the level of pathogenic forms of IgA and IgA immune complexes, and so Nefecon is able to do that. We have data from clinical trials suggesting other drugs that specifically target B-cells and plasma cells are capable of doing this as well, and here I'm talking about drugs that target CD38 depletion, so depletion of plasma cells, and we have early phase 2 data suggesting efficacy of those drugs. And then we have a range of drugs that are regarded as B-cell modulators that target the signaling of BAFF and APRIL, two cytokines that are important in B-cell and plasma cell survival and proliferation. And here we have a range of phase 2 and phase 3 studies that are currently ongoing. We don't have phase 3 data yet, but we have drugs such as sibeprenlimab and zigakibart, which block APRIL signaling, and we have drugs like atacicept, telitacicept, and povetacicept, which target both BAFF and APRIL signaling. And collectively, what we've seen so far in phase 2 studies is that these drugs are capable of suppressing proteinuria and preserving kidney function and also reducing those levels of pathogenic IgA in the circulation. So those are a group of drugs that look very exciting.

We also then have a group of drugs that target activation of the complement system, and these are novel ways of controlling inflammation within the kidneys. And we've had the first complement inhibitor that's been approved for the treatment of IgA nephropathy, and that's iptacopan, which inhibits factor B of the alternative pathway. And we've seen that that approach reduces proteinuria in patients with IgA nephropathy in the phase 3 APPLAUSE study, and we're waiting to see its impact on change in GFR. And then we have a range of other complement inhibitors that are currently in either phase 2 or phase 3, either targeting the alternative pathway or the final common pathway, and these drugs are going to complement the B-cell-directed therapies and allow us to switch off the production of those damaging IgA complexes but at the same time block the inflammation that is ongoing in the kidney, so this offers a really exciting opportunity to control this disease from two different angles.

And then, of course, we have to accept that patients with IgA nephropathy will come to us already having sustained significant kidney damage because these patients often present late. And so we have a whole range of drugs that allow us to manage those CKD complications of IgA nephropathy. We've always had renin-angiotensin system blockers. We've now got SGLT2 inhibitors. We've got the dual endothelin angiotensin receptor antagonist bosentan, which is now approved to treat IgA nephropathy. And we're going to have endothelin receptor antagonists, which you can combine with any renin-angiotensin system inhibitor, drugs like atrasentan, which are likely to be approved in the very near future.

And then, of course, we have other agents that are being developed to manage CKD, like the GLP-1 receptor agonists, the mineralocorticoid receptor antagonists, and the aldosterone synthase inhibitors, so lots of excitement both in terms of new drugs that we

can potentially manage the immunology of the IgA nephropathy disease but also new drugs that help us better manage general CKD, and we're going to be using these in combination in the future. And my hope is that no patient with IgA nephropathy will progress to kidney failure when we're able to access these drugs and use them in combination.

Announcer:
That was Dr. Jonathan Barratt talking about how the treatment landscape for IgA nephropathy has evolved in recent years. To access this and other episodes in our series, visit *On the Frontlines of IgAN* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!