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What Are the Emerging Therapies for Managing Gout?

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Johnson:

This is CME on ReachMD. I'm Dr. Richard Johnson, and with me today is Dr. John Botson.

In the last couple years some very major clinical trials have been performed that is changing the way we manage gout, and Dr. Botson has led some of these trials. So, John, give us the insights.

Dr. Botson:

There was one medication approved in 2010 and that was pegloticase. Antidrug antibodies ultimately being the determination of why the medication would stop working, why patients would start to have side effects, infusion reactions, and such. And that led into the MIRROR trial and the MIRROR RCT [randomized clinical trial] trial which then used methotrexate as the immunomodulator. And really, that's been the paradigm shift in how we treat these patients now with these uricases. Now pegloticase is the only one FDA-approved. These uricases have the ability to make the body aware of them and so create these antidrug antibodies. So ultimately, we started using methotrexate. FDA even approved it for use in combination in July of 2022, and it's really been a game changer in how manage these patients. Some of the more recent data showed even over 70% of patients getting treatment with pegloticase have immunomodulation. Essentially everybody, unless they have an absolute contraindication for one of these immunomodulators, really needs to be on it. It's standard of care.

So the MIRROR RCT trial is the one that we've kind of been focusing on, and that one was really a game changer in the fact that baseline pegloticase monotherapy was about 42% of patients that would respond to the medication, and MIRROR RCT showed 71% of the patients would actually respond. And the safety was really what got the FDA to approve this combination, and that was from 30% infusion reactions all the way down to 4%.

And 4% puts pegloticase right along the line with every other IV medication that we use in rheumatology, so very much more manageable, very much safer to be given in your office or in an infusion center.

We've done some studies on mycophenolate, we've done some studies on leflunomide and azathioprine potentially, so I think there's going to be some other options. The COMPARE trial was one that used pegadricase with rapamycin, so this is SEL-212. And so this one basically compared them head-to-head. And those results just recently came out, and they were looking at serum uric acid-lowering abilities at months 3 and 6 to be less than 6. And what they found, maybe unfortunately to the study's opinion, not a statistically significant superiority, but 53% of patients versus 46% of pegloticase. So not statistically different when looking at superiority, around the same as pegloticase. And it should be noted that that's monotherapy, so without the immunomodulation. Gout flares still happened in both of those groups, maybe more so in the SEL-212 molecule.

Dr. Johnson:

Does the methotrexate have any effect in blocking gout flares that occur with lowering uric acid?

Dr. Botson:

There was absolutely no difference in the flare rate with methotrexate or with the patient not being on methotrexate in combination with the pegloticase.

Dr. Johnson:

What is your feeling about the use of methotrexate in chronic kidney disease?

Dr. Botson:

So I'm a big fan of methotrexate, and I don't even think twice about it if it's going down to 40, 45. In the MIRROR trials we would eliminate folks, you know, exclude them if they had an eGFR [estimated glomerular filtration rate] less than 40, but in patients that do get treated with that, it's a short-term treatment. It's 6 months, maybe 9 months of treatment, and, in fact, probably the treatment of the gout probably affects the kidney function as much as an ill effect from methotrexate. So it is still a medication that I think is very viable to use in mild to moderate, I guess, kidney disease.

Dr. Johnson:

Thank you, John. This will wrap it up for today. And thank you all for listening.

Announcer:

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