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ns-MRAs and eGFR Slope: The Kidney Perspective

Announcer:
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Dr. Mc Causland:
So this is CME on PACE-CME on ReachMD, and I'm Dr. Finnian Mc Causland. Here with me today is Dr. Csaba Kovesdy.

Let's review the emerging data on nonsteroidal mineralocorticoid receptor antagonists and kidney outcomes in patients with chronic kidney disease, and we'll start with the subanalysis of FOUNTAIN.

Dr. Kovesdy, what are the latest findings?

Dr. Kovesdy:
FOUNTAIN is a platform that provides us a snapshot of information about how finerenone is being used in the real world. So it's data collected from the US, from clinical practices, retrospectively, and the main results of FOUNTAIN were that in about 2,000 patients on finerenone, there was a significant reduction in albuminuria at 4 months and at 12 months of about 33% and 38%, respectively.

Now, our latest analysis dived into this data to try to discern nuances of these finerenone effects in terms of CKD stage. So is there a difference in albuminuria reduction by CKD stage? And interestingly, we found that in patients who had CKD stage 2 of finerenone initiation, there seemed to be more of a reduction in albuminuria than in patients who had more advanced stages.

The other aspect of these secondary analyses were an evaluation of ancillary medications, co-medications, and as we know, the clinical trials examine finerenone in combination with RAS inhibition. But we don't know whether, in real-life practice, providers apply the same rules. And, of course, there is other medications, such as SGLT2 inhibitors or GLP-1 receptor agonists, which are also known to improve kidney outcomes and cardiovascular outcomes.

So the question is, how do healthcare providers apply these therapies concomitantly with finerenone, and what is their impact on albuminuria reduction? And what we found, interestingly, when looking at combinations is that about 1/3 of the patients were on finerenone monotherapy, even though the clinical trials never looked at this therapy without RAS inhibition. And then, on the opposite side of the spectrum, about 10% were on quadruple therapy: RAS inhibition, finerenone, SGLT2 inhibitor, and GLP-1 receptor agonists.

Interestingly, when looking at albuminuria reduction, they were about the same for all combinations. In other words, the finerenone monotherapy achieved largely the same reduction in albuminuria as the combinations, which was somewhat of a surprise. And, again, in retrospective data, we don't know for sure why it's happening, but it certainly tells us about the effectiveness of finerenone in reducing albuminuria.

Lastly, hyperkalemia-wise, again, a dreaded complication of finerenone and other similar medications. These rates were extremely low in this database, about 1%. Okay. Which may have something to do with the definition, which was a chronic hyperkalemia at repeat

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measurements. But certainly, it provides a sense of comfort in terms of finerenone's application in real-world populations and its safety in this context.

Dr. Mc Causland:
So let's turn to the emerging data on kidney outcomes in FIDELITY. What was observed in patients on combination therapy?

Dr. Kovesdy:
The combination of the FIDELIO and FIGARO databases, the so-called FIDELITY cohort, showed fairly similar results. Again, there were about 160 patients in the combined clinical trial population that was on this quadruple therapy. So RAS inhibition, finerenone, SGLT2 inhibitor, GLP-1 receptor agonist.

But overall, at 1 year, there was about a 40% reduction in albuminuria with finerenone alone. And in the quadruple group, the same reduction was 49%. So slightly higher but statistical significance could not be achieved because of the low number of patients in combination therapies. But, again, putting together these two large databases, we see the same message that albuminuria reduction is substantial in both clinical trials and real-world evidence at 4 months, at 1 year, and the addition of other co-medications did not change this substantially.

Dr. Mc Causland:
And so just one other thought in terms of the FIDELITY analysis: they also kind of looked at hyperkalemic risk in that as well, and there was some interesting data in terms of the combination therapies.

Dr. Kovesdy:
While from an effectiveness standpoint, you would look at albuminuria reduction, but the question is how is safety affected? And confirming other studies, this FIDELITY analysis also showed that combining finerenone with an SGLT2 inhibitor lowered the risk of hyperkalemia.

So, again, I call this a marriage made in heaven, where you achieve an additive benefit while the adverse events are being lowered by combining these two agents.

Dr. Mc Causland:
So just another interesting point in the FIDELITY analysis where they looked at the changes in eGFR slope according to the different combination therapies. Could you provide a brief comment on that?

Dr. Kovesdy:
Right. So, of course, ultimately, we want to see a reduction in progression of kidney disease, which we can quantify by looking at the eGFR slopes. And again, the main results of the trial show that the slopes in patients treated with finerenone were shallower, if I could use these words. So they were protective.

When looking at combination regimens, the same protective effect was evident in all of these subgroups treated with other medication. So finerenone seemed to retain the protective effect irrespective of which combination it was part of.

Dr. Mc Causland:
So I think this has been a certainly fascinating conversation, but before we wrap up, Csaba, what is your kind of final take-home message for our listeners?

Dr. Kovesdy:
Yeah. So what we see from these added analyses is bolstering the data that's coming out from these very rigorous, large, randomized controlled trials in the sense that even when we apply finerenone as a cardio-kidney-protective medication in real-world populations, we see similar effects. So the albuminuria reduction is present, and then knowing that albuminuria reduction is a legitimate surrogate endpoint, we can expect probably improved clinical outcomes in these patients.

Dr. Mc Causland:
Fantastic. Well, this was brief, but I'm glad we had the chance to share this recent data with you. Thanks very much for listening.

Dr. Kovesdy:
Thank you and goodbye.

Announcer:
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