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Potassium Binders to Optimize GDMT Therapy in HFrEF

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Dr. Kelepouris:
This is Continuing Education with GLC, and I'm Dr. Ellie Kelepouris. Here with me today is Dr. Nihar Desai.

Nihar, we know that optimizing GDMT yields the best outcomes for our patients. Can you review the data behind this?

Dr. Desai:
I think there's a couple of important elements for this. To start off, patients that have reduced EF heart failure really need to be optimized on the 4 sort of foundational pillars of background medical therapy. The evidence to support their use is overwhelming. The benefits come very early; they are very substantial, there's a real urgency, and the stakes are very, very high.

And so when we think about background, sort of guideline-directed medical therapy for our reduced EF heart failure patients, we're, of course, speaking about beta-blockers, about SGLT2 inhibitors, then ACE inhibitors, ARBs or ARNI therapy, and then last but certainly not least, mineralocorticoid receptor antagonist therapy.

Again, if you look kind of cumulatively across all of the clinical trials, all 4 of these therapies have Class I indications in the guidelines, meaning the highest quality and the highest level of evidence to support their use, with very substantial reductions in morbidity and mortality.

I think from there, sort of switch gears a little bit and think about that patient with reduced EF heart failure that then develops hyperkalemia and what are some of the key data on the management of those specific patients for the use of potassium binders specifically as we've been talking about through these cases and these episodes. And I think there are a couple of additional trials that I think are very important for the audience to know about. Two specific ones that I'd like to speak about are the DIAMOND trial and REALIZE-K.

The DIAMOND trial was a study looking at patiromer, one of our modern potassium binders. Similarly, REALIZE-K looked at sodium zirconium cyclosilicate. The designs of the 2 trials were quite similar. They were looking at the association or the impact of using a potassium binder, essentially on the ability to maintain RAASi therapy, specifically mineralocorticoid receptor antagonist therapy.

So you could imagine there's a group of patients with reduced EF heart failure. There's a run-in period where you're intensifying their

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background MRA. Everybody is getting the potassium binder, and then at the point of randomization, half the patients have continuation of their potassium binder, the other half of patients actually have withdrawal of their potassium binder, and then what we're going to look at, of course, are a series of endpoints. But one of the endpoints that we're going to look at is the ability to maintain that MRA therapy.

And so in the DIAMOND study and in REALIZE-K, with the use of patiromer and SZC, respectively, in both of those studies, we saw that there was an increase in the ability to maintain MRA therapy in the potassium binder–receiving patients.

In the REALIZE-K data, when you use sodium zirconium cyclosilicate in REALIZE-K, while you were again able to maintain the spironolactone dosing, there actually ended up being an increase in heart failure hospitalizations in that clinical trial. Now that was a secondary sort of safety endpoint but was included in the clinical trial. And while the exact mechanism of that remains a bit unclear, I do think that we have to come back a little bit to the mechanism of action. There is a sodium load that comes with SZC dosing. There's about 400 mg of sodium for every 5 g of SZC, and whether that was the contributor to that safety signal that was observed in REALIZE-K obviously needs to be teased out further, but that was not observed in the DIAMOND trial with patiromer, and there, of course, we have a calcium-based exchange for the potassium.

And so I think the body of evidence that's relevant for our audience is sort of multifold. Again, just to recap: first, the importance of guideline-directed medical therapy in patients with reduced EF heart failure, overwhelming benefit, overwhelming evidence, Class I indications for all 4 of the therapies that we have talked about. And then in the specific context of managing hyperkalemia, we have clinical trials of the modern potassium binders and some differences there between the DIAMOND study of patiromer and the REALIZE-K study of SZC.

Dr. Kelepouris:
Continuation of GDMT is really critical for mortality benefits in these patients, and the use of potassium binders have really proven to be a very important advance and are part of, really, the guidelines for both kidney management and heart failure.

And the European guidelines state very specifically that instead of decreasing GDMT, adding a potassium binder is very important. I think identifying the phenotypes of patients that are beneficial would be really important, that would benefit. And really the issue of sodium loading and other real-world side effects from these binders need to be taken into account when prescribing to our patients.

Our time is up. We hope you enjoyed this brief overview, and thanks for listening.

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