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The 4 Pillars of Treatment in HFrEF: Does Risk of Hyperkalemia Threaten to Topple Them Over?

Announcer:
Welcome to ReachMD. This episode is part of the Global Heart Failure Academy and is brought to you by Medtelligence.

Dr. Kosiborod:
Welcome to the Clinic Minutes Program addressing updates to managing hyperkalemia in patients with heart failure. The 2022 updates to the ACC/AHA/HFSA guidelines for heart failure are the first since 2017, and in the interim, a considerable amount of research and data has been conducted in the care of patients with heart failure, including the impact of optimal renin-angiotensin-aldosterone system inhibition [RAASi] therapy and the management of hyperkalemia in these patients.

This is ReachMD, and I'm Dr. Mikhail Kosiborod, and with me today is my good friend and colleague, Dr. Michael Böhm. Michael it's good to have you with us. Welcome.

Dr. Böhm:
Thank you very much. I'm Michael Böhm from the University of the Saarland. I'm a heart failure specialist and also a co-author of the European guidelines, so the other ones.

Dr. Kosiborod:
Fantastic. So, Michael, let's get into this and try to kind of dissect these new guidelines that we just saw a very short while ago and some of the kind of key considerations that we learned from the guidelines. And maybe before we kind of get into it, you can comment on what stood out for you as something our audience needs to know and was the most notable in those guidelines.

Dr. Böhm:
So, first of all, I mean, there are these recommendations for the guideline-directed medications of first-line medications. So, and **this is sacubitril/valsartan first, which is a tier A1 recommendation**. So, the PARADIGM study was one of the studies that definitely showed the definite evidence, but the American guidelines looked at the totality of evidence and gave them a class 1A recommendation, also taking into considerations a study which looked at the initiation of therapy already in the hospital post-discharge, and that is a PARADIGM-HF study, the TRANSITION study, and others. So, the totality of evidence led the authors to give them the class 1A recommendation, and if that is not maybe affordable, achievable, or intolerant, the sacubitril/valsartan, then of course, there is a road for ACE [angiotensin-converting enzyme] inhibitors and also ARBs [angiotensin receptor blocker] in the case of intolerance. So that is a very concise and clear-cut recommendation.

The second key point are the novelties, of course, and these are the new kids on the block, and these are SGLT2 inhibitors. **They have it here as a tier 1A recommendation** based on the DOPPLER-HF study and the EMPEROR-REDUCE study, and there is novel evidence – and this gets a 2A recommendation already for heart failure with preserved ejection fractions [HFpEF] for empagliflozin, and that is indeed the EMPEROR-Preserved study. So, there is a recommendation now for HFpEF, and I think that is very clear.

Dr. Kosiborod:
And, Michael, maybe a word also on just general attention to optimizing guideline-directed medical therapy [GDMT] across heart failure types, if you will, and certainly in heart failure with reduced ejection fraction [HFrEF]. The guidelines, I think, also spent some time talking about the importance of optimizing GDMT, about doing it as quickly as possible, make sure all of the disease-modifying therapies are started as quickly as possible and up-titrated to appropriate doses, and those doses, of course, provided in the guidelines, and the doses generally that were used in clinical trials that showed benefits. And this requirement or any kind of attention to

sequencing is also removed, indicating that, again, this really should be done; all of the disease-modifying therapies, fundamental therapies, should be started as quickly as possible and up-titrated to max dose as quickly as possible. So, this whole sequencing piece is really no longer at play. And again, that's somewhat similar to European guidelines, I believe, as well.

Dr. Böhm:
Yeah, and this is the most important strategic change has turned out that every other therapy, including the old ones in the trial in beta-blockers, have a significant treatment effect within 1 month. Sometimes as for the SGLT2 inhibitors for 14 to 16 days, that is a very short period of time when it becomes significant. So, any postponing of therapy would cause events and set patients at danger to get an event, and therefore all the guidelines are in agreement to start as early as possible, and also you have the recompensation still in the hospital. So, the transition phase to the outpatient situations to the family doctors is also facilitated. And that is a very important strategic change and message which both guidelines have in common.

Dr. Kosiborod:
For those just tuning in, you're listening to ReachMD. I'm Dr. Mikhail Kosiborod and here with me today is Dr. Michael Böhm. We are discussing key updates to the 2022 ACC/AHA/HFSA guidelines and what this may mean for your practice.

I would also have to say glad to see that the guidelines acknowledged the concept of enablement of a renin-angiotensin-aldosterone system inhibition with use of various strategies including novel potassium binders such as patiromer and sodium zirconium cyclosilicate [ZS-9], acknowledging that there is no outcome data currently, but also bringing it to the forefront with the formal recommendations, level 2b recommendation currently, based on available evidence. But I think the fact that this concept of enablement of GDMT is a clearly recognized in the guidelines as a step forward. Was that your take on this data as well?

Dr. Böhm:
Yeah. Right. That is one of the big problems also in our country, and I think in the States, as well, that if there is hyperkalemia, then indeed, the drugs are continuously withdrawn, and that is wrong, definitely. The European guideline said, okay, they should be intermittently paused, but now there is a clear recommendation in the table for the potassium binding, so that is patiromer and ZS-9, which indeed can enable therapy. And also, it is explicitly stated, which speaks in favor of the specific recommendation, which is given that there are data not yet available to show that this translates into a clinic improvement. However, during the ACC congress this time, the DIAMOND study data will be presented, and this gives another piece of evidence that enabling – at least concerning potassium enabling for these guideline-directed medications – is still possible.

Another point which should be mentioned, I think, anytime that hyperkalemia due to MRA can be also attenuated with sacubitril/valsartan and SGLT2 inhibitors, there are also new data, and indeed together with the potassium binding we might see, hopefully, more people being on the full guideline-directed treatment, in particular, at appropriate doses.

Dr. Kosiborod:
Great. So, Michael, this has been a great conversation. But before we wrap up, can you share your one take-home message with the audience in regards to the new ACC/AHA guidelines and the guidelines across the Atlantic, as well? What do you think is the most important message for the audience to concentrate on?

Dr. Böhm:
So, both guidelines, so that's what they have in common, they share one very important strategic change, and that is that they moved away from the time-consuming up-titration and sequencing of drugs. The 4 guideline-directed groups – beta-blockers, MRA, SGLT2, and sacubitril/valsartan – should be given as fast as possible, even in the hospital after recompensation in the stable patient. I think that is the key message; that's what they have in common.

Also, the American guideline is a little bit more practical than the European one. It gives sacubitril/valsartan a tier 1A recommendation while the European 1B because there is only the PARADIGM trial. So, the American guidelines looked at the totality of treatment. Also, it is highly recommended to all colleagues because it's very nice read with very good schemes, and also good summary of comorbidity including also iron deficiency, the treatment of diabetes, and also other comorbidities like atrial fibrillation. It is very straightforward, and I think the differences are not so big. There are some minor differences, but all across, over the Atlantic on both sides of the ocean, we will have a very similar guideline with very important strategic changes.

Dr. Kosiborod:
Yeah, I think these are very important steps forward, and I think from my standpoint the take-home message is GDMT works, and we need to do whatever we can as quickly as we can to get patients on lifesaving and disease-modifying therapies.

Unfortunately, that's all the time we have today. So, I want to thank our audience for listening and thank you, Michael, for joining me and for sharing all of your valuable insights. It was really great speaking with you today.

Dr. Böhm:
Thank you. Thank you very much. Bye-bye. Stay safe.

Announcer:
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