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### Applying Key Updates from ESC/HFA to Managing Heart Failure

Announcer:

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Dr. Fonarow:

In the management of patients with heart failure, rapid initiation and up-titration of foundational medical therapies for heart failure is critical. These include the renin-angiotensin-aldosterone system [RAAS] blockers, beta-blockers, and SGLT2 inhibitors.

To improve outcomes, it's crucial that we avoid unnecessary halting or dose reductions to these medications. This is particularly important in the population of patients that have several comorbid conditions, such as chronic kidney disease or recurrent hyperkalemia, that can commonly be present. So how can we approach the care of patients who have heart failure with multiple comorbidities while maintaining optimal, guideline-directed medical therapy, including renin-angiotensin-aldosterone system inhibitors?

This is CME on ReachMD, and I'm Dr. Gregg Fonarow.

Dr. Coats:

And I'm Dr. Andrew Coats.

Dr. Fonarow:

So, Andrew, thanks for joining, and let's approach this topic by first discussing some of the key updates to the ESC Heart Failure Guidelines that were recently released. So first question is, you know, what were the significant updates, from your perspective, pertaining to the care of patients with heart failure?

Dr. Coats:

Oh, thanks Gregg. And as you know, the European Guidelines updated just this year. It was the first time there'd been an update for 5 years, so an awful lot's happened in that period so that the guidelines covered a lot of new territory. But to me, the take-home messages, the big changes, were the introduction of the concept of 4 foundational drug classes, and of course, they are the established agent, but first of all the group that includes ACE inhibitors, ARBs, or ARNI. Second is the beta-blocker group. Third, the mineralocorticoid receptor antagonist, or MRAs. And fourthly, obviously, the new SGLT2 inhibitor class, now recommended for the treatment of HFrEF [heart failure with reduced ejection fraction]. But the other important change in these guidelines is the increased emphasis on patient profiling, looking at the patient in front of you and optimizing the treatment based on other factors. It may be the level of blood pressure, heart rate, kidney function, the risk of hyperkalemia, and the optimization – so the recognition that you need to take into account patient factors and particularly common comorbidities, such as the presence and severity of CKD, or chronic kidney disease, the risk of hyperkalemia, particularly on the background of other compounding comorbidities, which are common, such as type 2 diabetes. And this means that there's a much greater emphasis on the art of medicine. How do we implement these 4 foundational drug classes? And in that regard, the 2 classes that are commonly called RAASi – renin-angiotensin-aldosterone system inhibitors, including the ACE/ARB/ARNI group and the MRAs – are often limited in practice by the perceived or real risk of CKD and the risk of

hyperkalemia. And too often, we've seen in registries, we're simply underperforming.

So the guidelines are going much further than we've ever seen in a guideline, just saying we really need to look at how we implement guideline-directed medical therapy, and we need to take into account these comorbidities that sometimes in practice lead us to underuse important drug classes, thereby stressing the need to optimize particularly RAASi therapy to obtain the full possible benefit.

Dr. Fonarow:

Yeah, I found it really impressive, that emphasis on those mortality-reducing therapies, and that they should really be utilized together, that they're additive in their therapeutic benefit, and putting greater emphasis on that and less towards, oh, I can just pick my favorite 1 or 2 of the guideline-recommended therapies and be sufficient there. Recognize there may need to be some personalization in the actual up-titration sequencing, but that getting all 4 of these therapies at well-tolerated, guideline-recommended doses, so long as well tolerated being so critically important, and that comorbid conditions are really additional aspects to manage but should not preclude, unless absolutely contraindicated, the use of the therapies, and finding strategies to where the therapies can be efficiently and rapidly initiated and up-titrated, and importantly, adhered to in the longer term and not just backed down or stopped at the first attempt, where there's a little bump in the road. That emphasis in the guidelines is so patient-centered and, I think, so important in discussing additional strategies to improve the tolerability of the medications, so that go fast with the essential medications getting started and doing everything that can be done to ensure that they're maintained while helping to manage the comorbidities and anticipate some of the challenges that may occur and provide effective strategies to overcome those challenges really shine through in the guidelines.

Dr. Coats:

Absolutely. I think they're very important issues.

Dr. Fonarow:

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Gregg Fonarow, and here with me today is Dr. Andrew Coats. We're discussing the key updates from the ESC/HFA Heart Failure Guidelines, and the implications for managing the care of patients with heart failure and multiple comorbid conditions

Dr. Coats:

Gregg, I wonder if I could turn now and ask you what were the guidelines saying about the use of potassium binders to treat hyperkalemia and to make sure that hyperkalemia isn't a problem that interferes in our otherwise optimal treatment of patients with heart failure?

Dr. Fonarow:

Yeah, the guidelines were really impressive in recognizing there really is significant underutilization, particularly of mineralocorticoid receptor antagonists, out of either fear of hyperkalemia or it transiently developing. So there is emphasis and discussion and acknowledging that the data is evolving, that a transient increase in potassium is not a reason to completely and permanently discontinue MRA or ACE inhibitor or sacubitril-valsartan therapy, but instead, consider the options, including taking advantage of the newer agents that can bind potassium, that the maintenance of the mortality-reducing therapies being so critically important. There are ongoing trials and further evidence that would come forward. It is recognized that profound benefits of MRAs, ACE inhibitors, sacubitril-valsartan in reducing hospitalizations and mortality really call for any effective strategy to allow these therapies being maintained while avoiding any excess risk due to hyperkalemia. So this is an important, evolving area in that the guidelines really do go nicely into the discussion of transient rises in potassium really not being a sufficient basis for permanent discontinuation of life-prolonging therapy.

Dr. Coats:

I think that's a really important point. So much in the last few years we've heard of the problems with stopping treatment, particularly with a RAASi, because of short-term potassium increases. And when people looked at the older guidelines, you know, they really said down-titration or stopping. And that was such an easy thing to do. The important thing now is, as you say, these new guidelines are saying, actually, consider using a potassium binder to treat that acute hyperkalemia, and that means maybe you don't need to down-titrate, and that, of course, we all believe would be of major benefit for our patients.

But I guess the next question is how the potassium binders fit in the long-term care of patients with heart failure. If we're constantly thinking of managing short-term hyperkalemia, it's very much the risk of a on/off, stop/start approach. And in a patient where the potassium levels are at the upper end of the desired range when you start, or perhaps they've had multiple episodes, I'm personally thinking that we should consider these agents in the longer term, to iron out, flatten the potassium trajectory, and to prevent subsequent potassium elevations being a barrier, and for patients who simply haven't been able to maintain the appropriate doses of RAASi drugs because of intermittent potassium elevation. So I think we do not need to start thinking about the long-term maintenance strategies of appropriate potassium levels to allow the appropriate guideline-directed medical therapy doses of RAASi and the use of potassium binders in our armamentarium so that we can achieve that long-term, optimal treatment with those 2 important drug classes, the

ARNI/ACE inhibitor/ARB class and the MRAs. And I think that would be a major step forward, and we're going to get some new trials that show how potassium binders will help maintain appropriate potassium levels despite pushing up the doses, and I think that that's going to be the next big question. And I think experts are already saying that the long-term therapy with potassium binders could optimize and improve guideline-directed medical therapy long term for the benefit of our patients.

Dr. Fonarow:

Yeah, I really agree with that, and they allow us to initiate therapy in those patients where previously thought not to be possible due to high baseline elevations in potassium levels. That could really be an important advance for our patients.

Dr. Coats:

So what I take from this, Gregg, is really how important the implementation of our clinical trial results is. It's not enough simply to show that we can treat patients with heart failure with an ACE inhibitor, with an ARNI, with spironolactone or eplerenone – an MRA – and get benefits. We actually need to, now, identify the barriers for up-titration and maintenance, so-called implementation science. And we've got to recognize there are real barriers. You know, they are surmountable, but the issue of, in patients with CKD, potassium levels going up when you first use the RAASi drugs is important, and if we have other treatments, supportive care, potassium binders can ease that. I think it's important we face that head-on, because ultimately, our duty is to protect our patients with heart failure from adverse outcomes, and that means getting the best guideline-directed medical therapy on board and maintained. That's critical. So that's my take-home from this particularly useful talk.

Dr. Fonarow:

Yeah, my take-home is very similar. Each of these 4 foundational medical therapies are truly additive and incremental to each other, and the benefits they offer patients in reduction of heart failure hospitalizations, reduction in cardiovascular death and all-cause mortality are really profound. So it is so important to initiate each of these therapies, maintain and optimize the dose, and not let these potential barriers that arise with comorbid conditions or other challenges get so in the way that they preclude the use of the therapy unless absolutely contraindicated, and that by overcoming those barriers, ensuring patients are well treated, we could really markedly improve clinical outcomes, beyond what we're doing. And we see in study after study, such large gaps in the use as well as dosing of our guideline-recommended therapies, so that emphasis in the ESC guidelines regarding "here are these mortality-reducing therapies," and it is just so important to work on their appropriate and rapid initiation and maintenance. That's such a key take-home message.

Unfortunately, that's all the time we have today, so I want to thank our audience for listening in, and thank you, Dr. Andrew Coats, for joining me, sharing all of your valuable insights. It's been terrific speaking to you today.

Dr. Coats:

Thanks, Gregg. I've had a fantastic opportunity to interact with you, and I think it really is a very exciting time, and I really thank you for this fascinating conversation, so have a great day.

Announcer:

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