Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/optimizing-outcomes-evidence-based-strategies-for-treating-patients-with-heart-failure-with-mildly-reduced-or-preserved-left-ventricular-ejection-fraction/29905/

Released: 10/01/2025
Valid until: 10/01/2026
Time needed to complete: 15 Minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Optimizing Outcomes: Evidence-Based Strategies for Treating Patients With Heart Failure With Mildly Reduced or Preserved Left Ventricular Ejection Fraction

Announcer:
Welcome to CE on ReachMD. This activity, titled “Optimizing Outcomes: Evidence-Based Strategies for Treating Patients With Heart Failure With Mildly Reduced or Preserved Left Ventricular Ejection Fraction” is provided by Medcon International.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Solomon:
Hello, this is CE on ReachMD, and I’m Dr. Scott Solomon from Harvard Medical School and Brigham and Women’s Hospital in Boston.

Dr. McMurray:
And I’m Dr. John McMurry from the University of Glasgow in Scotland in the UK.

Dr. Solomon:
Today, we're going to be talking about the application of nonsteroidal MRA therapy and how to choose the right patients for this therapy. There's a lot of new evidence now based on the FINEARTS-HF trial. We're going to be hearing about finerenone, and we're going to be thinking about which patients might be the appropriate patients for this new therapy. And I'd like to start by illustrating this with a case.

So let's talk about a 76-year-old woman who had a visit to her primary care physician, has mentioned that she has symptoms of occasional shortness of breath on exertion and swelling of her ankles. And on deeper questioning, she's become dyspneic with one flight of stairs and occasionally doing housework. She denies orthopnea or paroxysmal nocturnal dyspnea or chest pain.

Her past medical history is noted for paroxysmal atrial fibrillation, although she's currently noted to be in sinus rhythm. She has a history of hypertension, and she's recently been diagnosed with diabetes. On physical exam, she has a blood pressure of 138/70, a heart rate of 66, and mild peripheral edema. Currently, she's on the following medications: valsartan for hypertension, metoprolol for atrial fibrillation, and metformin 1 g twice daily for her diabetes.

Her primary care physician then orders some labs and sends her to a cardiologist for further consultation. And when she's seen by the cardiologist, her exam is essentially unchanged, but now he has some labs back. And the NT-proBNP is 640, the GFR is 52, the hemoglobin A1c is 6.8%. She has no evidence of anemia, acute coronary syndrome, significant valvular disease, but echocardiography does confirm a left ventricular ejection fraction of 54% and left atrial enlargement.

So, John, what do you think about this patient? And how might you think about incorporating any new therapies into her regimen?

Dr. McMurray:
Very interesting case and, I would say, very typical and somebody I think we can help a lot because, in fact, this woman has really an indication for 2 new treatments. One, not so new, an SGLT2 inhibitor. I'm surprised she's not on that. She's got type 2 diabetes; she's got chronic kidney disease. She's a good candidate for that. And of course, the picture you've painted is a very clear picture of heart failure

with preserved ejection fraction. She's got typical signs and symptoms. She's got structural heart disease, left atrial enlargement. She's got elevated natriuretic peptides. She's got peripheral edema. She's got HFpEF and, therefore, has an indication for an SGLT2 inhibitor for that reason as well.

But the new treatment, the new indication is, of course, finerenone. She has an indication for finerenone based on having diabetic kidney disease. So we've got 2 large trials showing that finerenone reduced not just cardiovascular risk, but risk of progression to end-stage kidney disease in patients like yours.

But I think the trial that we want to talk about today is FINEARTS-HF, and your patient would have been a perfect patient for FINEARTS-HF.

And what we showed in FINEARTS-HF is that a woman like your patient, on average, was less likely to experience the primary outcome, which was cardiovascular death or a worsening heart failure event.

In fact, there was a highly significant 16% reduction in the risk of that composite outcome, and that's another reason why we would want to treat her with finerenone.

Finerenone is already recommended for patients like yours, for example, in the Japanese heart failure guidelines and in the new international iCARDIO guidelines, and we imagine that indication will be extended, really, across the world in the not-too-distant future.

Dr. Solomon:
So here's an important question about how we actually use this new therapy. And in this woman, she has a GFR of 52. In FINEARTS-HF, we had a dosing strategy based on GFR. If the GFR was under 60, they were targeted to 20 mg of finerenone. If it was over 60, they were targeted to 40 mg of finerenone.

In the diabetic kidney disease trials, however, they only reached a maximum of 20 mg. So I'm assuming, both because of her diabetes and because her GFR was under 52, this is a woman who we would target to 20 mg.

Dr. McMurray:
Absolutely, her target dose is 20. And of course, we wouldn't start in her case with 20; we would start with 10, and we would check both her kidney function and her potassium within 4 weeks. And then, depending on what we find, we would then consider increasing her dose to 20 mg. So assuming her potassium didn't exceed 5 mmol, assuming her eGFR had not decreased by more than 30%, we could increase her finerenone dose to the target of 20 mg per day.

Dr. Solomon:
And, John, you mentioned the use of an SGLT2 inhibitor, which she's not on now. She's got several indications, obviously, for the use of an SGLT2 inhibitor. Is there any reason that a patient can't be on both?

Dr. McMurray:
We believe they work in completely different ways. And we actually have good evidence that their benefits are additive. And unusually, we can sort of look at that question in 2 directions.

So of course, we had a subgroup of patients in FINEARTS-HF who were on baseline SGLT2 inhibitor treatment, and they got just as much benefit from adding finerenone as patients who were not on baseline SGLT2 inhibitor treatment.

And of course, Scott, in DELIVER, we had a lot of patients who were on background MRA therapy, and when they had an SGLT2 inhibitor added, they got as much benefit as people who were not on background MRA therapy. So we looked at that interaction in both directions; there's clearly additive benefits.

And not only that, but actually the main thing that we're concerned about with MRAs, which is hyperkalemia—we know that SGLT2 inhibitors reduce the risk of hyperkalemia. So there's sort of synergies both in terms of benefits and in terms of safety. So this woman has a lot of reasons to be on both of those treatments.

Dr. Solomon:
So, John, you say it is both safe and efficacious to give this patient both of these drugs, but would you give them at the same time?

Dr. McMurray:
Interesting question. So I think it depends a little bit on the patient. So I frequently start both treatments simultaneously, but I'm more likely to do that in somebody who has maybe more normal eGFR, somebody who's got a higher blood pressure. In somebody with a very low eGFR, so the indication for finerenone and SGLT2 inhibitors is eGFR above 25 mL per minute—so if their eGFR was 30 mL per minute or 32 mL per minute, I probably wouldn't start both simultaneously.

But in somebody whose eGFR is 50-odd, or 60, above 60 mL per minute, and their blood pressure is reasonable, then I often do start the treatments simultaneously, because there's a very low risk of any major deterioration in kidney function, you're minimizing the risk of hyperkalemia. And of course, both of these treatments act very quickly, so there's a reason to try and get them started as soon as possible.

Dr. Solomon:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Scott Solomon. I'm here today with Dr. John McMurray, and we're discussing the new indication for finerenone in heart failure and how it might be implemented in clinical practice using patient case vignettes.

Let me ask you about some of the other comorbidities this patient has and whether there's any role for finerenone in the treatment of those. For example, the patient does have hypertension, currently being treated with valsartan, and finerenone obviously can lower blood pressure. This patient has a history of paroxysmal atrial fibrillation, and obviously, also, this patient has some metabolic problems. She has diabetes. We've discovered from the FINEARTS trial that there may be benefit for all of these other comorbidities. Would you want to expand on those?

Dr. McMurray:
Yeah, very good point. So let's start with atrial fibrillation.

So we saw a very strong trend to reduction in new-onset atrial fibrillation in FINEARTS-HF, and in the pooled analysis of all the large finerenone trials, that was a significant benefit of finerenone.

So I think we do think that MRAs are protective against at least development of atrial fibrillation. Maybe not surprising, given the benefit in terms of reducing the risk of hyperkalemia, reducing fibrosis, perhaps in the atria, which might be a causal mechanism for atrial fibrillation. So that's certainly relevant.

In terms of the metabolic disturbances then, we also saw—and I think this was remarkable—a significant reduction in new-onset diabetes with finerenone, something that actually we haven't seen with other MRAs. Indeed, with spironolactone, we've seen the opposite of that. So that's one of those interesting things that maybe, maybe points to something different between finerenone and the older steroidal MRAs.

And then in terms of hypertension, well, it's difficult because heart failure is slightly different than hypertension. And MRAs in heart failure seem to have really a very modest effect on lowering blood pressure. And in fact, actually, finerenone hasn't an indication for reducing blood pressure, and we didn't see much symptomatic hypotension in the FINEARTS-HF trial.

Dr. Solomon:
Well, let me ask you a slightly provocative question. You mentioned steroidal MRAs. We've been using therapies for many, many years now, but would it be fair to say that we lack the robust data in patients with ejection fraction over 40% that we now have with this nonsteroidal MRA?

Dr. McMurray:
Oh, I think we definitely do. So obviously, we have the TOPCAT trial, which overall was neutral. And yes, there was a retrospective subgroup analysis suggesting that there was benefit in people enrolled in the Americas. And there's a plausible hypothesis behind that analysis, but at the end of the day, we have definitive evidence for finerenone. We don't have definitive evidence for spironolactone. So I think at the moment, our recommendation would be use the treatment that's proven efficacy, and at the moment, that is finerenone.

Dr. Solomon:
John, with respect to the FINEARTS-HF data, is there evidence for consistency in all the major subgroups? And in particular, did the patients with ejection fraction at the lower or upper end of the spectrum benefit? Did patients with and without atrial fibrillation benefit? Did patients with and without diabetes benefit to the same extent?

Dr. McMurray:
The good news is, yes, we saw consistency, really, in all the subgroups we looked at. And maybe the most remarkable one was across the spectrum of ejection fraction. I'm not sure we were certain we would see that, but we did.

We didn't see any apparently greater benefit in people with a lower ejection fraction. We didn't see any apparent lesser benefit in people with a more normal or completely normal ejection fraction. And patients with paroxysmal and persistent atrial fibrillation had exactly the same benefit as people in sinus rhythm. And there was, again, no difference in the relative risk reduction in people with and without diabetes and indeed in people with prediabetes.

Dr. Solomon:
Well, John, this has been a great discussion. But before we wrap up, maybe we can ask if there are any final take-home messages that you want to leave for the audience.

Dr. McMurray:
Well, I think the important thing is that we now have a second pillar of therapy for patients with heart failure and preserved ejection fraction. And as you and I know, Scott, we've been trying for 20 years to find an effective treatment.

Dr. Solomon:
We're certainly looking forward to what the new guidelines on both sides of the Atlantic say about finerenone in the context of heart failure with mildly reduced or preserved ejection fraction.

So that's all the time we have for today. I'd love to thank the audience, and of course, my colleague and friend, Dr. McMurray, for joining me.

Dr. McMurray:
It's always a pleasure to speak to you, Scott.

Announcer:
You have been listening to CE on ReachMD. This activity is provided by Medcon International .

To receive your free CE credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.