Podcast Episode Title: Embracing the Era of Combination Medical Therapy for HFmrEF/HFpEF

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Orly Vardeny: Welcome to the American Heart Association's Heart Failure Podcast Series. This episode is titled, Embracing the Era of Combination Medical Therapy for Heart Failure with Mildly Reduced or Preserved Ejection Fraction.

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00:00:21.520 --> 00:00:28.939
Orly Vardeny: This program has been created and directed by a volunteer planning committee, and is made possible by support from Bayer.

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Orly Vardeny: I'm Orly Vardeny, and I'll be introducing today's discussion.

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Orly Vardeny: I'm a professor of medicine at the Minneapolis VA University of Minnesota.

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Orly Vardeny: And next, I will ask my colleagues to introduce themselves.

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00:00:43.210 --> 00:00:57.629
Steve Greene: So, hi everyone, I'm Dr. Steve Green. I'm a heart failure cardiologist, clinical researcher at Duke University and the Duke Clinical Research Institute, and I'm also our co-director for our guideline-directed medical therapy heart failure clinic. My pleasure to be here.

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00:00:59.430 --> 00:01:14.859
Meg Fraser: I'm Meg Fraser, I'm a nurse practitioner at the University of Minnesota in the Division of Advanced Heart Failure, Transplant, and Mechanical Circulatory Support. I see patients in Advanced Heart Failure Clinic, in the inpatient setting, I do the cardiovascular genetics Clinic, as well as Heart Transplant Clinic.

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00:01:15.510 --> 00:01:17.619
Meg Fraser: It's a pleasure to be here, thank you for inviting me.

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00:01:21.130 --> 00:01:31.140
Orly Vardeny: Great, so I think let's dive into our discussion. To start off with, maybe, Steve, you can take us through what we might consider as pillars

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00:01:31.350 --> 00:01:35.980
Orly Vardeny: Of therapy for heart failure with mildly reduced or preserved ejection fraction.

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00:01:36.660 --> 00:01:54.780
Steve Greene: Yeah, it's a great question, Orly, and you know, pillars, this is a word that we've, you know, historically been using for heart failure with reduced ejection fraction, and in that phenotype, we've been talking about quadruple medical therapy for at least a few years now, but now, you know, it's relatively new

to be thinking about pillars

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00:01:54.780 --> 00:02:04.589
Steve Greene: of therapy for heart failure with mildly reduced or preserved ejection fraction. I'll give you, you know, my definition of what makes a pillar, because people think about a lot of different therapies.

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Steve Greene: for these patients now. So, to me, for heart failure with mildly reduced or preserved ejection fraction.

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Steve Greene: I define a pillar as something that's definitively proven in a clinical trial, at least one clinical trial, to improve either hard clinical outcomes

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00:02:20.310 --> 00:02:30.839
Steve Greene: and or patient-reported quality of life. And to my understanding, I think there's really 3 classes of therapy that kind of meet those criteria in my mind.

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Steve Greene: I mean, the first was, of course, SGLT2 inhibitors, and we've had now multiple clinical trials, Emperor Preserve with empagliflozin to liver with dapagliflozin. There is even patients with mildly reduced or preserved ejection fraction in the Soloist trial with sotagliflozin.

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00:02:48.170 --> 00:02:56.210
Steve Greene: But we've now seen that in these clinical trials, we have hard outcome benefits on cardiovascular death or heart failure, hospitalization.

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Steve Greene: And we also have patient-reported outcomes, so that's SGLT2 inhibitors, is the first pillar.

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Steve Greene: Then, we also have now the nonsteroidal MRA finerenone, which we'll talk more about, and that was at the Fine Arts trial, which was an outcomes trial of more than 6,000 patients with heart failure with mildly reduced or preserved ejection, and finerenone versus placebo yielded a 16% relative risk reduction on cardiovascular death or worsening heart failure.

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00:03:24.140 --> 00:03:27.750
Steve Greene: So that's a definitively positive trial. To me, that's pillar number two.

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00:03:27.770 --> 00:03:40.090
Steve Greene: And then we now have our third class of medicine that we're talking about now, and that's, like, the incretin-based therapies, or the GLP-1 receptor agonists, or the GLP/GIP receptor agonists.

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00:03:40.090 --> 00:03:48.240
Steve Greene: And there's been multiple clinical trials with semaglutide and tirzepatide, and these clinical trials have been in the obese

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Steve Greene: phenotype of HFPEF.

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Steve Greene: So patients with a BMI of 30 or greater, which in real-world practice is the majority of patients with HFpEF, particularly in the United States. And in these clinical trials, I think the thing we can say definitively is that an obese phenotype HFpEF,

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00:04:04.110 --> 00:04:19.859
Steve Greene: These incretin-based therapies improve patient-reported quality of life, and they do so with a huge magnitude of benefit. I think, you know, again, there's signals of potentially improvements in hard clinical outcomes in these clinical trials, but they're generally not powered for that.

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00:04:19.860 --> 00:04:33.509
Steve Greene: But I think the thing we can say for sure is that those therapies really do improve how patients feel, and that's certainly important for patients. So again, to wrap it up, in my mind, these are the three pillars we're dealing with in 2025 for HFpEF.

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00:04:35.800 --> 00:04:46.439
Orly Vardeny: Great. Let's… let's talk about some of the other therapies that maybe don't quite make it to the status of being a pillar.

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Orly Vardeny: but that we still might see, or might even use in select, patient populations. So let's… what are your thoughts about, sacubitril/valsartan?

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Steve Greene: Yeah, that's a great point, because there are other therapies that we've talked about, and I'm going to turn it on you, Orly, have you give your feedback on what, you know, your definition of pillars are and everything.

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Steve Greene: I'll say with sacubitril/valsartan, the reason why I did not include it in one of my personal pillars, even though, in the United States, it is FDA approved for patients with, below normal ejection fraction, so that includes some patients with mildly reduced or preserved ejection fraction.

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Steve Greene: The reason why I didn't put it as a pillar is because I would say it's not, in my mind, definitively proven with a clean

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00:05:31.920 --> 00:05:51.909
Steve Greene: clinical trial. You know, we're using it in the subgroup, it's based on subgroup analysis in the Paragon HF trial, where it seemed to be benefits in those with EF below normal, less than 60% or so. You know, so that's why I don't put it to the threshold of pillar, and there, you know, some nuance to it.

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00:05:51.910 --> 00:05:58.590
Steve Greene: But that's just my personal opinion why I think it's an important therapy, but again, from a prioritization of the cleanest

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00:05:58.590 --> 00:06:09.989
Steve Greene: outcome benefits and or quality of life benefits, I give SGLT2s, non-steroidal MRA, and the incretin-based therapies the priority. But Orly, what do you think about

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Steve Greene: security of all starting in HFpEF, and, you know, what's your take on it?

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00:06:14.990 --> 00:06:26.520
Orly Vardeny: Yeah, I tend to agree with you, Steve, in terms of it's not, as… certainly not as definitive as, SGLT2 inhibitors or non-steroidal

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00:06:26.630 --> 00:06:32.210
Orly Vardeny: MRAs. The Paragon HF trial, sacubitril/valsartan, narrowly missed

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Orly Vardeny: Its primary endpoint of cardiovascular death, or all-cause hospital… or heart failure, or all heart failure hospitalizations.

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00:06:42.270 --> 00:06:51.019
Orly Vardeny: But there was certainly a signal for improving hospitalizations, or even, improving outcomes in

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Orly Vardeny: a few subgroups of patients, as you mentioned, one with EF below normal, another potentially in female patients.

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00:06:57.970 --> 00:07:16.349
Orly Vardeny: But ultimately, I think the evidence for sacubitril/valsartan just doesn't rise to the level of the others. However, we know that patients with heart failure with mildly reduced or preserved ejection fraction often have comorbidities such as hypertension. So if we're looking for an additional therapy that we can use.

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Orly Vardeny: instill a symptomatic, at least New York Heart Association, functional class II patient with mildly reduced or preserved ejection fraction. We have some… we have blood pressure, high blood pressure that we want to tackle, so sacubitril/valsartan is certainly a good option for that.

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00:07:34.100 --> 00:07:52.809
Meg Fraser: And maybe one of you could also comment. I was going to say, the HFpEF population specifically, the comorbidity burden is high, and so not only in hypertension, but in renal disease and diabetes, the benefit of… could you maybe comment on the benefit of just ARB therapy? If you're going to use something for blood pressure, why it might be a good choice?

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00:07:54.530 --> 00:08:10.700

Steve Greene: Yeah, I think that's a very, great comment, Meg. I mean, yeah, for patients with chronic kidney disease, it's, like, really a very important therapy to be on RASI, therapy. And the other thing I'll say that, like, Orly kind of picked up on, you know, Paragon HF

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00:08:10.700 --> 00:08:22.800
Steve Greene: you know, it was an active comparator. So, you know, sacubitril/valsartan versus placebo was not the comparator here. It was versus an active comparator with valsartan. So, I do think of it as, important for our patients with

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Steve Greene: HFpEF to have their blood pressure well-controlled.

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Steve Greene: ARB, or maybe preferentially Arnie, does a better job of that. But then also, you, you know, mentioned there's data that says that really the majority of HFpEF patients might have some variation of chronic kidney disease.

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00:08:36.720 --> 00:08:50.929
Steve Greene: So again, treating the whole patient, not just the HFpEF, is certainly the way to go. And, for those reasons, I think a lot of people are… should probably be on a RASI therapy with their HFpEF, whether you're treating the HFpEF,

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00:08:50.930 --> 00:09:05.150
Steve Greene: Or just, it's for something else, but it's a HFpEF patient. To me, it's kind of, you know, doesn't really… doesn't 6 to 1, half a dozen, but, I think it's a great point, though, that a lot of these patients have comorbidities, like hypertension or CKD, that are gonna make us think about RASI's anyway.

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Steve Greene: I want to ask the group, though, about, steroidal MRA.

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Steve Greene: Because that's something else that, you know, before Fine Arts, you know, we were already talking about, you know, the TopCAT trial from years ago, and in the United States, we have, spironolactone, steroidal MRA is a Class 2B indication.

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Steve Greene: So what are your thoughts on steroidal MRA, and how do you put finerenone in the context of what we know from TopCat?

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Orly Vardeny: Yeah, that's a… that's a really great question, and fraught with controversy because of the TopCAT trial, that, as you alluded to, was a neutral trial, but there was some study integrity

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Orly Vardeny: Issues, or study conduct issues in a few regions of the, of the study.

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Orly Vardeny: And so we are not,

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Orly Vardeny: the results of the TopCAT trial are not as straightforward, whereas if you just took the Americas, the primary endpoint would have been positive, but the overall trial was neutral. At the end of the day, the guideline committee gave a 2b recommendation for the use of steroidal MRAs, like spironolactone.

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Orly Vardeny: Because now that we have Fine Arts, HF, and finer known data that are, relatively, or that are definitive or are stronger, then…

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Orly Vardeny: what I would say is that the finerenone would

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00:10:34.920 --> 00:10:37.150
Orly Vardeny: Rise to my first choice.

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Orly Vardeny: as an MRA for use in mildly reduced or preserved ejection fraction. However, not everyone can afford it, and there are access issues, so we need to think about that, and if that's the case, then spironolactone

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Orly Vardeny: can be a very viable alternative to finerenone if we can't use finerenone. But what are your thoughts?

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00:10:58.790 --> 00:11:18.619
Meg Fraser: The way that I look at MRAs in this patient population, I think most of these patients are on a loop diuretic, and so if you're on a loop diuretic in potassium, my thought, you know, has always been, why not be on an MRA instead of potassium? I think it provides, you know, a stable potassium sparing effect.

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00:11:18.620 --> 00:11:43.390
Meg Fraser: you know, a lot of patients are under the misconception that it is going to work like a diuretic in their case, too, so it's a lot of, kind of, counseling with patients and explaining the rationale, but as we know, patients hate swelling potassium, and so the way that I look at it in this population is, you know, while the data is not as strong as some of these other agents, if I have a HFpEF patient, that's on a loop diuretic, I'm using spironolactone or eplerenone in that case

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Meg Fraser: case in an effort to get them off potassium supplements.

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00:11:47.310 --> 00:11:52.989
Steve Greene: I couldn't agree more, Meg. I mean, yeah, one of the pills I hate seeing on med lists is potassium supplements.

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Steve Greene: Now.

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00:11:54.700 --> 00:12:12.160
Steve Greene: I think, you know, in terms of, in my mind, you know, finerenone versus spironolactone, I mean, I clearly think finerenone, I call it definitively proven, and I think no matter what your… with spironolactone, no matter what your, you know, stance is on TopCat, I think we can say, respectfully, there's some level of uncertainty.

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00:12:12.160 --> 00:12:22.759
Steve Greene: with how well spironolactone, or if it works at all in half-peer, some level of uncertainty. You know, Arlie, you mentioned the post-hoc analysis from the Americas and whatnot.

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00:12:22.830 --> 00:12:44.510
Steve Greene: So again, it's suggestive. Obviously, it was enough for the guidelines to give it a Class 2b week recommendation for use, but I think scientifically, speaking, to me, there's no question that the science, as stands today, is stronger and definitive for fi finerenone nerinone, whereas it's not definitive for spironolactone. And we'll see, there's ongoing clinical trials.

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00:12:44.590 --> 00:13:01.499
Steve Greene: With spironolactone and HFpEF, going on, and we'll see if those either are positive and kind of buff up, you know, the standing of spironolactone in the guidelines and in our minds, or if they're neutral, you know, it means that maybe spironolactone falls out of our thinking altogether as an efficacious therapy for,

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00:13:01.760 --> 00:13:18.890
Steve Greene: Perhaps PEF, but I mean, practically speaking, what I do is I try to prioritize non-steroidal MRA, finerenone, and then I do use spironolactone if non-steroidal MRA is not feasible, whether it's because of, you know, cost, access, or something else. But I do think, scientifically.

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00:13:18.890 --> 00:13:22.300
Steve Greene: We should go with the definitively proven option, if at all possible.

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Steve Greene: I want to kind of, you know, now that we've talked about our stance on pillars and what makes or breaks the threshold for being labeled a pillar, you know, let's talk about really, like, the elephant in the room here, and that's, like, implementation. You know, for so long, you know, in HFpEF,

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Steve Greene: we really had no evidence-based therapy, so implementation really wasn't our focal point. It was just diuretics and optimized comorbidities and all the implementation talk was going on in the REF world.

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00:13:52.610 --> 00:14:01.330
Steve Greene: But now we have this situation, now we have multiple evidence-based therapies we were just discussing, and, you know, we're trying to figure out what's the best way to get our patients

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00:14:01.330 --> 00:14:14.030

Steve Greene: all the therapies they need and are eligible for. So, Meg, I'll throw it to you first. I mean, what do you think in terms of just kind of practical strategies for implementing these therapies, and what makes sense in your mind?

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00:14:14.260 --> 00:14:30.440
Meg Fraser: Yeah, so this is, a topic I feel pretty strongly about, and I'm gonna describe it kind of the opposite way, or one of the barriers to starting, GDMT in the HFrEF population, or these pillars in the PEF and heart failure with mildly reduced population, and I think there's

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00:14:30.480 --> 00:14:49.990
Meg Fraser: sort of… the way I think about it is there's five major barriers. So, one, what I would call soft blood pressures. I think we don't say hypotension, we say soft blood pressures is often something you'll see. Number two, acute kidney injury or creatinine bumps. Number three, I would say this high potassium, and I'm putting this in air quotes for people who can't see me.

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00:14:49.990 --> 00:15:09.800
Meg Fraser: Insurance issues or cost coverage, and then lastly, but perhaps most importantly, is clinical inertia. So, I think if we tackle one at a time, you know, low blood pressures, and this is more so in the HFrEF population, but we certainly tolerate some low blood pressures, in an effort to get patients on medical therapy, but as we know.

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Meg Fraser: as it relates to spironolactone, this is commonly a comment that I'll see in charts is, you know, deferring MRAs because of blood pressure, but as you know from the Rales trial, the initiation of spironolactone should not significantly impact blood pressure, and if it does, it's possible that patient is just over-diuresed. So, some interventions from that first barrier, you know, reassessing diuretics and clinical congestion status.

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Meg Fraser: There are ways to stagger timing, split dosing, and I'm a big fan of, you know, making sure that we're optimizing blood pressure in a way that, you know, patients are not on other blood pressure affecting medications that they're not getting benefit for.

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Meg Fraser: And then for AKI, we see this a lot, too, is I think there's a lack of awareness of the impact of RNI and SGLT inhibitors with the expected decrease in GFR and the actual benefit to the kidneys in the long term. For hyperkalemia, I think there's something about the number 5 that really freaks people out with potassium. Like, 5.0.

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00:16:08.960 --> 00:16:25.969
Meg Fraser: And people get squirrely and stop some of these therapies, but I think it's important to know that a potassium of 5 is normal, and Orly, you actually published this in Circ, but, you know, the addition of MRAs, the benefit is still there, even with modest hyperkalemia, in terms of mortality.

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Meg Fraser: And then insurance coverage, you know, this can certainly be true less and less so as a lot of these therapies are becoming generic, but…

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Meg Fraser: That's why I feel the inpatient initiation of some of these therapies are the perfect time to attempt. We can start prior authorizations early in the hospitalization. At the University of Minnesota, we are lucky enough to have a pharmacy liaison consult, so early on, we can, within 10 minutes, get an idea on what a copay might look like, start the prior authorization early, and work towards that. And I think

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00:16:56.870 --> 00:17:02.439
Meg Fraser: Reassessment is really important when it comes to this particular barrier. Sometimes that

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00:17:02.440 --> 00:17:05.829
Meg Fraser: Comment lives in the chart for years, that insurance didn't cover

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Meg Fraser: and RD therapy, but, you know, it hasn't been reassessed. And then, again, the good old, if you're an inpatient, deferring to outpatient, or deferring to PCP, or patient is stable, so not adding additional therapies, you know, we know from

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Meg Fraser: Multiple trials and some really good recent papers that failure to continue, initiate, or switch medical therapies in this population has increased with

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00:17:30.700 --> 00:17:41.229
Meg Fraser: Associated with an increase of readmission, mortality, decreased medication adherence, and an increased likelihood of never being started, when these therapies are not started in the hospital.

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00:17:41.230 --> 00:17:53.040
Meg Fraser: So, I… I think I… hopefully I addressed, and let me know if you guys can think of other barriers, but that's kind of how I think of things, and I think the inpatient setting is a really good time to consider these therapies. You've got a…

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00:17:53.100 --> 00:18:07.139
Meg Fraser: captive audience, can answer questions. When you're in clinic and trying to convince patients to start new therapies, especially when they're feeling so well, it's really quite tough. And so that's always kind of been my… my…

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Meg Fraser: Attempt at addressing barriers for these therapies.

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00:18:11.420 --> 00:18:35.059
Steve Greene: I mean, so many pearls there, Meg, and that's a great list, and I think the thing that, you know, I always pick up on is what you said towards the end about the clinical inertia piece, and how, you know, kicking the can down the road, you know, usually equates to the patient never getting on the therapy at all, or at best, only after a very substantial delay, where they're then needlessly exposed to clinical risk in the meantime.

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Steve Greene: But, you know, Orly, from your mind, you know, what are some of the, you know, practical

ways to help overcome those barriers that Meg, you know, talked about, and, you know, get people on? Now, not just one evidence-based therapy, but trying to get multiple evidence-based therapies on board?

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00:18:54.280 --> 00:19:08.599
Orly Vardeny: Yeah, and I think, while there's so many great, pearls there, and I think one of the things that we need to… to focus in on is the patient and letting them know that there are… that there are multiple therapies.

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00:19:08.820 --> 00:19:14.959
Orly Vardeny: In heart failure with mildly reduced or preserved ejection fraction, and that we need to use multiple therapies

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Orly Vardeny: because they each act in a different way. They have, differing mechanisms, so I always describe it to patients as… it's like a target that you're trying to hit from different angles. Each one has a distinct mechanism that is beneficial.

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00:19:32.290 --> 00:19:37.290
Orly Vardeny: And something that I also try to reinforce is the fact that

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00:19:37.430 --> 00:19:51.139
Orly Vardeny: for a lot of these therapies, especially SGLT2 inhibitors, and even non-steroidal MRAs, the time to benefit, or the time where we will see a significant

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00:19:51.480 --> 00:19:54.709
Orly Vardeny: Effective, response is short.

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Orly Vardeny: In the order of days to weeks.

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00:19:58.870 --> 00:20:04.359
Orly Vardeny: And so the longer we wait to put, to start these therapies.

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00:20:04.500 --> 00:20:12.110
Orly Vardeny: Then the more… the longer we place patients at risk for having these adverse clinical events.

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Orly Vardeny: And so, the way to think about it is… and sometimes I get asked a lot, what's the hurry?

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00:20:18.780 --> 00:20:25.950
Orly Vardeny: Why… why is there this rush to start therapies quickly, or even simultaneously?

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00:20:26.100 --> 00:20:28.640
Orly Vardeny: And the… we need to…

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00:20:28.720 --> 00:20:46.679
Orly Vardeny: make the medical community and even patients, aware that there is a hurry because of the time to benefit is so short, and so therefore we want to minimize the time that the patient is left at this increased risk for negative outcomes. Steve, what's your take on that?

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00:20:47.410 --> 00:21:06.559
Steve Greene: Yeah, I mean, Orly, I couldn't have said it better myself. I mean, you know, we talk about, yeah, what's the rush? I mean, let's just consider a few fundamental pieces of information here. So, one is that all of heart failure, but including mildly reduced or preserved ejection fraction patients, I mean, the reality is, this is a prognosis comparable to a cancer.

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00:21:07.260 --> 00:21:21.090
Steve Greene: You know, and there's no such thing as a low-risk heart failure patient. No such thing as a low-risk HFpEF patient. Just to put some context about this, when you look in, you know, real-world data, you know, patients hospitalized for HFpEF, which again.

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Steve Greene: is, you know, really the majority of heart failure hospitalizations these days are for patients with HFpEF. You know, 1 out of 4 of them are passed away within 1 year of going home from that hospitalization. You know, 3 out of 10 are approximately re-hospitalized for heart failure within 1 year, and, you know, 1 out of 2 are hospitalized for any reason.

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Steve Greene: So those are the kind of event rates you're dealing with, and we use phrases like high risk through all these different fields of medicine, but not all high-risk conditions are created equal, and we need to really appreciate this huge, absolute risks that we're dealing with with HFpEF. Again, a prognosis comparable to many forms of cancer. So that's the reality of what we're dealing with.

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00:22:00.020 --> 00:22:14.539
Steve Greene: So then we say, well, of course we need to hurry with our therapy, and of course we need to hurry with therapies that work quickly, as you so elegantly said, Orly. I mean, when you have prognosis like we're talking about, and you have therapies that work within days to weeks of starting.

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00:22:14.540 --> 00:22:22.619
Steve Greene: them, including reduction in hard clinical events with SGLT2s and non-serial MRA. Yes, we owe it to our patients to get these

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00:22:22.840 --> 00:22:24.799
Steve Greene: On board as quickly as possible.

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Steve Greene: And then when you also consider that these therapies are fully additive.

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00:22:29.120 --> 00:22:53.860
Steve Greene: to each other. So what I mean by that is, it's not like, well, once you're on an SGLT2 inhibitor, there's no extra benefit by adding a non-steroidal MRA. It's quite the opposite. It's fully incremental. The relative risk reductions are consistent regardless of background therapy. You know, just like incretin-based

therapies, whether someone's on an MRA or not already, the same improvements in quality of life, statistically speaking.

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00:22:54.150 --> 00:23:01.959
Steve Greene: So again, I say we need to have some level of humility for understanding what we're dealing with when it comes with HFpEF.

119
00:23:02.010 --> 00:23:19.909
Steve Greene: the morbidity and mortality and hospitalization risks. We need to use every tool in our toolbox to get these therapies on board ASAP. And then the other thing I'll say, before I turn it back to you guys, is we need to learn from what went wrong with HFrEF implementation, right? You know.

120
00:23:19.910 --> 00:23:31.279
Steve Greene: We talk about multiple pillars, and, you know, we almost get distracted with questions over, oh, what's the right sequence? You know, which one should we start first, and which one should go second, and all this.

121
00:23:31.530 --> 00:23:40.989
Steve Greene: And we also think, well, gosh, we can only start one medicine at a time because there's some unwritten rule in the heart failure handbook where we said you're only allowed to make one medicine at a time changes.

122
00:23:41.360 --> 00:23:55.790
Steve Greene: I think we've learned that is a wrong approach. And myself and others, and now even the guidelines, have talked about it's okay and encouraged to think about simultaneous or rapid sequence initiation.

123
00:23:55.790 --> 00:24:08.169
Steve Greene: We need to start more than one medicine at the same time. Learn from what we do in hypertension and diabetes and other fields, to recognize there's risks of omission by leaving people off therapy

124
00:24:08.280 --> 00:24:24.990
Steve Greene: That's… that's dangerous, in the sense, compared to people thinking starting two medicines at the same time could be potentially dangerous. I think, you know, in terms of rapid sequence and whatnot, people debate, oh, well, do you need to start all of them out on exactly the same day, or can you wait a week in between, and all this kind of stuff?

125
00:24:25.510 --> 00:24:26.580
Steve Greene: To me.

126
00:24:26.880 --> 00:24:42.449
Steve Greene: I'm not gonna necessarily split hairs, and I think the faster the better, but I think we need to agree on what's the wrong answer. The wrong answer is you have a patient in HFPEF clinic today, and they're not on any evidence-based therapies, and you start one therapy today, and you say, I'm gonna see you back in 6 months, and we'll talk again.

127

00:24:42.650 --> 00:24:46.149
Steve Greene: That is unequivocally the wrong answer.

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00:24:46.480 --> 00:24:57.870
Steve Greene: And we need to move beyond that, and myself advocate, again, for simultaneous and or rapid sequence within one to two weeks of getting at least low doses of all the different therapies on board.

129
00:24:58.350 --> 00:25:04.319
Meg Fraser: And I think it's really important to set expectations with the patient as well. So a new diagnosis of either of these things, or…

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00:25:04.520 --> 00:25:22.670
Meg Fraser: you know, when you're patient-facing, up front saying, these are the… these are the therapies that we're gonna get you on. This is why we use each one, they target different things, they're all used in an effort to do XYZ, but setting that expectation goes such a far way, for adherence and, you know.

131
00:25:22.670 --> 00:25:43.410
Meg Fraser: not uncommonly, patients will say, I'm not interested in starting new medical therapy, and so I think at the very beginning of a diagnosis, or when you have somebody in front of you, really setting that expectation about, this is our goal for medical therapy. I have a question as we sort of wrap up here for either of you. So, you know, in clinic, when we're talking to patients about starting new therapies, I used to sort of

132
00:25:43.410 --> 00:25:45.260
Meg Fraser: Even bring up,

133
00:25:45.580 --> 00:26:03.240
Meg Fraser: you know, I used to have sort of a script for why we use all these different agents, and in this new era of HFpEF, what… if I'm… if I'm a patient, how do you explain to me, you know, in maybe one sentence, the role or the purpose of each of the medical therapies that we're going to be suggesting? What's… what's sort of your script that you've…

134
00:26:04.090 --> 00:26:05.100
Meg Fraser: been using.

135
00:26:05.680 --> 00:26:11.159
Orly Vardeny: Yeah, so I'll tackle this first, and then, Steve, please weigh in.

136
00:26:11.300 --> 00:26:19.270
Orly Vardeny: But I try to keep things fairly straightforward, when I'm explaining the exact mechanism.

137
00:26:19.330 --> 00:26:32.539
Orly Vardeny: to… to patients. So, I say that each one, each class has a different mechanism. One of them, like the SGLT2 inhibitors, or… I start off by saying all of them work in different ways.

138
00:26:32.630 --> 00:26:47.159

Orly Vardeny: To help your heart work more efficiently and prevent the negative effects from some of the chemicals that are circulating that may be damaging your heart or your blood vessels.

139
00:26:47.230 --> 00:27:01.030
Orly Vardeny: And so, what I try to do is say one therapy, like the SGLT2 inhibitors, while we traditionally use this in patients with diabetes to lower blood sugar, we found that it's very effective at improving

140
00:27:01.170 --> 00:27:14.770
Orly Vardeny: outcomes or in prolonging survival and reducing the risk for going into the hospital in patients with heart failure in both HFrEF as well as heart failure with mildly reduced or preserved ejection fraction.

141
00:27:15.320 --> 00:27:24.610
Orly Vardeny: And then for the MRAs, whether steroidal or non-steroidal, I say that one thing that we know is damaging to the heart is this scar tissue that can form.

142
00:27:24.760 --> 00:27:36.539
Orly Vardeny: from some of these processes that go awry in heart failure, and that MRAs can negate some of that… some of those negative effects, negative structural effects that can happen.

143
00:27:36.780 --> 00:27:38.080
Orly Vardeny: In the heart.

144
00:27:38.330 --> 00:27:49.269
Orly Vardeny: But Steve, what else would you say? What else do you add to that? And then, of course, GLP-1 receptor agonists with respect to reducing appetite and lowering, weight.

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00:27:49.960 --> 00:27:58.890
Orly Vardeny: in certain, populations with HFpEF, but really helping people feel better and having more energy.

146
00:27:59.860 --> 00:28:00.470
Orly Vardeny: Alright, now…

147
00:28:00.470 --> 00:28:03.470
Steve Greene: Yeah, I think that… no, I think that's… those were all,

148
00:28:03.470 --> 00:28:20.739
Steve Greene: Great words of wisdom, Orly. I'll tell you… so, for most of my patients, they don't necessarily care about the very specific mechanism of each individual agent, and that goes for HFrEF or HFpEF, but the way I try to phrase it is, like, you know, I have a new diagnosis of heart failure, whether it's REF or PEF in my office.

149
00:28:20.740 --> 00:28:22.970
Steve Greene: And I tell them, well, I mean.

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00:28:22.970 --> 00:28:29.550
Steve Greene: we have to take this seriously, because to most patients, I do try to be open and say, you know, if left untreated.

151
00:28:29.550 --> 00:28:41.069
Steve Greene: This is a prognosis comparable to a cancer, but… so that's the part we need to take seriously, but here's the good news. The good news is, we have multiple agents, definitively proven.

152
00:28:41.410 --> 00:28:42.730
Steve Greene: to help you

153
00:28:42.760 --> 00:28:58.619
Steve Greene: reduce your clinical outcome risk, and feel better. And it's my job to be your coach to try to get these on as quickly and safely as possible. And I, you know, since I've already kind of introduced the cancer analogy, I call, like, our GDMTs, like, PEF, for example.

154
00:28:58.620 --> 00:29:09.849
Steve Greene: I'm gonna call them chemotherapy. These are kind of like our chemotherapies. They're, like, directly trying to target the heart muscle and the underlying condition. And then I'm gonna contrast that with loop diuretic, for example.

155
00:29:09.850 --> 00:29:24.920
Steve Greene: Loop diuretic, I say, it's not going to necessarily make you… it's not proven to make you live longer, feel better, stay out of the hospital. We use it to, you know, to use as much… use as little as we can get away with. The analogy I say there is, like, let's say you break your arm.

156
00:29:25.260 --> 00:29:30.970
Steve Greene: You know, I can make your arm feel really good by just giving you pain medicine, but you still have a broken arm.

157
00:29:31.170 --> 00:29:51.610
Steve Greene: We can make heart failure patients feel really good in the short term by just giving them, you know, lots of loop diuretic and keeping their volume status good, but we don't really do them any favors in terms of their long-term prognosis. So that's why we gotta fix the broken arm, or just kind of fix the heart as best as possible, and that's where we use the chemotherapy that directly tries to target the underlying problem.

158
00:29:51.630 --> 00:29:59.200
Steve Greene: And I think people get that because, you know, my patients then will understand that, yes, the loop diuretic is not their most important heart failure medicine.

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00:29:59.530 --> 00:30:15.150
Steve Greene: And again, the good news is we want to try to use as little of that as we can get away with, and also, importantly, not sacrifice the proven GDMTs for the sake of loop diuretics. That's one of the traps that I see trainees and other clinicians fall into all the time.

160
00:30:15.150 --> 00:30:28.280

Steve Greene: Where, you know, the patient's feeling okay, but the JVP's up a little bit, and the blood pressure's marginal, creatinine's marginal, and they're gonna prioritize, you know, giving more and more loop diuretic and leaving people off the evidence-based therapies.

161
00:30:28.330 --> 00:30:37.539
Steve Greene: In contrast, we need to do everything we can to scratch and claw and get the evidence-based therapies on board and, you know, minimize, to the extent possible, the loop diuretic.

162
00:30:37.930 --> 00:30:48.659
Meg Fraser: I don't know about the two of you, but I feel like in this… with these newer, I won't say new, but newer agents, there's some of the first medications that I feel like patients are feeling better, and early. Yep.

163
00:30:48.660 --> 00:31:10.169
Meg Fraser: you know, for… for a while, you know, titrating medical therapy, you would do it, and, you know, you knew the outcomes were there, but some of these agents, you, more than ever before, I feel like patients are feeling better. And you're able to minimize your loop diuretic, to your point, because they just are, you know, have such a synergistic effect, and so it's a fun time to be in heart failure.

164
00:31:10.880 --> 00:31:25.219
Steve Greene: Yes, couldn't agree more. I mean, if you fix the… I mean, if you fix the underlying issue, you know, patients are gonna feel better, and then they're naturally going to require less and less diuretic, if you make the underlying heart function better. So, yeah, totally agree.

165
00:31:32.500 --> 00:31:50.230
Orly Vardeny: All right, I wanted to really thank you both for joining us for this conversation, and as we wrap up, a reminder that this episode is part of the American Heart Association's Heart Failure Podcast Series, and that more episodes can be found at learn.heart.org.

166
00:31:50.480 --> 00:31:52.970
Orly Vardeny: Thank you so much, everyone. Take care.