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## Do Not Delay: Timing, Triggers, and Identifying the Right Patient for Additional Therapies in HFrEF

### Announcer:

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### Dr. Bauersachs:

This is CE on ReachMD, and I'm Dr. Johann Bauersachs. Here with me today is Dr. Javed Butler. Our topic today is identifying patients with heart failure with reduced ejection fraction on guideline-directed medical therapy who may benefit from added sGC stimulation therapy and when to initiate it.

Javed, which patients would you consider candidates for this intervention?

### Dr. Butler:

Yeah, well, great to be with you, Johann, and a really good question. Life used to be a little bit simpler because we did the VICTORIA trial. That trial was done in patients with worsening heart failure, those that were hospitalized within the past 6 months or required outpatient IV diuretics. And the message was clear that if on medical therapy or breaking through and you develop worsening symptoms requiring escalation of therapy, that's about the time that vericiguat should be started on these patients.

But remember, the reason why we assessed the patients with worsening heart failure is because, for all heart failure therapies, we start either at the earlier part of the spectrum or the later part. But there's no biological reasons to believe that it will not work in all heart failure patients. It was just the first step that we did in worsening heart failure.

Also, there were some signals for cardiovascular mortality benefit, but the trial was not long enough to be able to really discern that. So then the VICTOR trial was designed, which was specifically looking at the patients who did not have worsening heart failure, so that we have sort of the data across the spectrum, but was specifically designed and powered prospectively to address also the question of cardiovascular mortality.

Now, as you know, the trial did not meet its primary endpoint. There was a 7% relative risk reduction, not statistically significant. But as we mentioned, there were 2 aims. One was to look at cardiovascular death, heart failure hospitalization, but the other was to look at CV mortality, and there was a 17% relative risk reduction, which was statistically significant.

Not only that, we found really consistent results in terms of reduction in all-cause mortality, about a 25% relative risk reduction in sudden cardiac death, and about a 29% relative risk reduction in the risk of heart failure-related mortality as well. So we have this really consistent result. We also showed that the trajectory of NT-proBNP was also in favor of vericiguat use, so a lot of sort of consistent data.

So now that we have the data across the spectrum, where do we go from here? Well, few answers are very simple in terms of who is an ideal patient. If you're developing worsening heart failure, no question, you should be on vericiguat. If you are unable to take some medication because of intolerance or side effect or contraindication—remember, for instance, we went down to GFR of 15, whereas MRAs are contraindicated to GFR less than 30, but a lot of people cannot even tolerate less than 45 of GFR. Then, no-brainer, the

person should get vericiguat.

If, for some reason, low blood pressure, other reasons, patient can take the medication but at really small doses, they cannot even get to 50% of the target doses, again, vericiguat.

The bigger question is whether all patients with HFrEF should be getting this therapy. And I can give you my opinion, and that is that if you look at the spectrum of risk, there's a lot of variation that we see in terms of heart failure hospitalization depending on worsening symptoms. But there's a reasonably consistent risk of cardiovascular mortality, which is pretty high and unacceptable. And vericiguat, now that we have this confirmatory data of reduction in the risk of death and also sudden cardiac death, that I think a very strong consideration should be given to the patients, because of this residual risk.

**Dr. Bauersachs:**

Thank you very much, Javed. So it's really important to have all these data together, and I think you did also the meta-analysis of these 2 studies, VICTOR and VICTORIA. And so we have, for the whole spectrum of heart failure, ranging from patients with recent decompensation or a worsening heart failure event to patients that are considered to be stable.

Nevertheless, we all know that heart failure patients, even New York Heart Association Class II, can never be really stable, because also these patients may die without previous heart failure hospitalization. And VICTOR has nicely shown that in these patients, we can reduce cardiovascular mortality and also total mortality with vericiguat.

So I think we have a lot of data now accumulated that in many patients with heart failure, vericiguat confers additional benefit in reducing either mortality or hospitalization or even both.

And I think it's perhaps also worth mentioning that you have a drug which is easy to use. So you can use vericiguat once daily. This is how you do it. You start usually with 2.5 mg, go up to 5, and then to 10 mg. And the VELOCITY trial now also has shown that you even can omit, in most of the patients, the vericiguat 2.5 mg. You can directly start with a 5-mg, and this is tolerated by the vast majority, more than 95%, because the effect on blood pressure is rather low. So you don't see a blood pressure drop when you start with the 5 in the vast majority of patients.

And you also have, I think, an excellent side effect profile. So you don't have a problem with the potassium. You don't have to think about eGFR, because you can go down to 15, as you mentioned.

So in fact, I think we have a drug which is easy to use, which is quite efficient, and which is also helpful for many patients with heart failure with reduced ejection fraction. And you also mentioned that many patients do not tolerate the standard high dosages of HFrEF guideline-directed medical therapy. And in these patients, clearly, we often have the chance to improve outcomes when adding vericiguat, which is an additional principle also, and it's a new principle that adds to more and better medication and better outcomes as compared without vericiguat.

So in my opinion, you really should think about adding vericiguat in your heart failure patients.

And thank you, Javed, very much for the excellent discussion and thank the audience for listening. We hope that this information will be useful in your practice. And our time is up. Thank you very much.

**Announcer:**

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