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Reducing Morbidity and Mortality in Patients with CKD in T2D: New Late-Breaking Data

Announcer:
Welcome to CME on ReachMD. This activity, entitled **"Reducing Morbidity and Mortality in Patients with CKD in T2D: New Late-Breaking Data"** is provided by **Medtelligence**.

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Dr. Taub:
Do nonsteroidal mineralocorticoid receptor antagonists, or MRAs, reduce morbidity and mortality in diabetic patients with chronic kidney disease? The FIDELITY pooled analysis findings demonstrated benefits in cardiovascular and kidney outcomes when adding nonsteroidal MRAs to maximally tolerated RAAS (renin-angiotensin-aldosterone system) inhibition.

Today, we're digging deeper with the new FIDELITY subanalysis on mortality and discussing how providers can use these insights to improve outcomes for their patients.

This is CME on ReachMD, and I'm Pam Taub.

Dr. Filippatos:
And I'm Dr. Gerasimos Filippatos.

Dr. Bakris:
And I'm Dr. George Bakris.

Dr. Taub:
Let's get started. Gerasimos, the FIDELITY analysis published earlier this year looked at the combined results of FIDELIO-DKD and FIGARO-DKD. And now we have new mortality data from the subanalysis. What are the findings, and what was the impact of nonsteroidal MRAs?

Dr. Filippatos:
Thank you, Pam. As you pointed out, in the FIDELITY analysis in more than 13,000 patients with chronic kidney disease and diabetes, we found that finerenone demonstrated a significant 14% reduction in the cardiovascular morbidity and mortality, and 23% reduction in the progression of chronic kidney disease.

So we thought that it would be interesting and clinically important to have a subanalysis on the causes of mortality in the FIDELITY pooled analysis. And first of all, what we found is, yes, cardiovascular mortality is the main reason for mortality in these patients in FIDELITY. That includes as you know, a broad spectrum of patients with chronic kidney disease and type 2 diabetes.

The other reasons were malignancy and infections, and the other causes are the minority. And also, as you remember, in the FIDELITY data that you just pointed out, in the primary analysis, we found a numerical decrease in the cardiovascular mortality. And we thought that it would be interesting and important to see what happened to the patients who were on finerenone and then on treatment analysis.

And we found an 18% decrease in the cardiovascular and in the all-cause mortality. And also, we found in the primary analysis a 25% decrease in the sudden death in finerenone versus placebo.

I think this is important for many specialties. And I'm sure that we should come back to this. But what I think is also important, and maybe George could comment more on this, we found that across the whole spectrum of albuminuria, the results were the same, but it appeared that there was an even better effect in those with higher GFR [glomerular filtration rate].

Dr. Bakris:
Yeah, no, that's absolutely true. And I just want to, for the listeners, make it clear what Gerasimos was talking about. That's an N of over 13,000 people. So I think it's important to keep in mind that in this circumstance, this is not a small study. This is a landmark study. And to answer Gerasimos' question, if you want to make a proper diagnosis of kidney disease, you don't just look at the eGFR; you have to look at albuminuria. So you need both components. And as was correctly pointed out, the more albuminuria you have, the greater your risk for cardiovascular cause, and likely you need to think about kidney disease, defined as an eGFR of less than 60, and of course that includes albuminuria being present as a risk factor for cardiovascular disease. So it's important to measure a spot urine albumin creatinine to see exactly what's going on.

Dr. Taub:
Great points. I think as cardiologists there's a lot of biomarkers that we're used to looking at – troponin, natriuretic peptides – and I think this analysis really highlights that we really also have to be looking at eGFR and albuminuria as a potent predictor of cardiovascular outcomes.

Now that we've discussed the FIDELITY subanalysis data, let's review chronic kidney disease with a focus on how overlapping stages and disease progression affect outcomes.

George, when it comes to CKD, what are the risk factors and how can they be modified?

Dr. Bakris:
So risk factors for CKD, there's a long list. But the big ones that people need to be aware of is poorly controlled diabetes. So if you have diabetes, you're immediately at risk. Poor control puts you at even higher risk. Poor control of blood pressure puts you at high risk. And even poor control of cholesterol adds to the risk, too, especially if you have the other conditions. Excessive use of nonsteroidal anti-inflammatory agents, poor hydration. All of those factors increase your risk for having some sort of kidney disease.

Dr. Filippatos:
Pam, let me point it out that – I think we have discussed in the beginning of our conversation, but I still believe that is important. A biomarker, you're a world expert in biomarkers, is UACR [urine albumin-creatinine ratio]. In FIDELITY, 45% of patients have a history of cardiovascular disease. In 45% of patients, they have chronic kidney disease with a GFR above 60. And the only marker, the only biomarker if you prefer, is albuminuria. This 45%, because we're cardiologists, nephrologists, they always measure UACR. Sometimes when we see a patient in our clinic with a GFR of 70 and with a history of a PCI [percutaneous coronary intervention], even if the patient has diabetes, very often we forget to measure UACR. And I think this is important, because now with the results from this new trial, we can answer the question, "So what?" We can do something. So I think George pointed out the risk factor. But UACR is a risk factor, and usually in cardiology, we're not so familiar with this.

Dr. Bakris:
Well, Gerasimos, thank you for bringing that up. Because one of the big points of the FIGARO trial by itself, which is a component of the FIDELITY analysis, the GFRs were higher; they were on average 57. And there was a lot more people with microalbuminuria, or lower levels. And yet, it was that group that had a 36% reduction in progression to dialysis. So yes, you too, as cardiologists can help us prevent dialysis.

Dr. Taub:
Well, we like targeting numbers. We aim for low LDLs; we have blood pressure targets. And now I think we can really have a target in terms of reduction of UACR by 30%, based on the guidelines.

Dr. Bakris:
Very good that you brought that up, Pam. The most recent ADA guidelines clearly states with a high level of evidence that you need to reduce albuminuria by 30% if it's greater than 300.

Dr. Taub:
For those of you just tuning in, you're listening to CME on ReachMD. I'm Dr. Pam Taub, and here today with me are Dr. Gerasimos Filippatos and George Bakris. We're reviewing results of the FIDELITY subanalysis on the use of nonsteroidal MRAs in patients with

chronic kidney disease and type 2 diabetes.

Okay, Gerasimos, how do we put all of this incredible data into clinical practice? Considering that there are many different types of clinicians who encounter the patient with CKD and type 2 diabetes, how do we select the patient that's going to get the most benefit from nonsteroidal MRA therapy?

Dr. Filippatos:
Thank you, Pam. I think that it is clear, also from our previous discussion, that the group of patients that we see in the FIDELITY pooled analysis is being seen by nephrologists, cardiologists, internists, and primary care physicians. And it is clear why. Because 40% of patients, they have a history of cardiovascular disease. All patients, they have diabetes, but these are patients with a broad spectrum of chronic kidney disease.

So many of these patients, of this 45% of these 13,000 patients with a history of cardiovascular disease, in 45%, they have a GFR above 60 and are being seen by cardiologists. And usually in cardiology, and I'm sure that you do the same, despite the fact that you are a world expert in biomarkers, when we see a patient with a history of PCI, a GFR of 70, even with a history of diabetes, it's not in our routine clinical practice to measure the UACR. Now I think that we should do this. And this is a broad spectrum of patients because we have something to offer, a new therapy, and I think this was clear from the data that we present today, but also from the previous publications. I don't know if in nephrology, George, that things are different, if the selection should be different of patients.

Dr. Bakris:
Well, yes, you made a very important point. And I want to re-emphasize it and actually add some perspective to it. The FIGARO trial, which was a major component of the FIDELITY analysis, had people with mostly microalbuminuria and a GFR of 57 as an average. In that study, the group with microalbuminuria actually had a 36% reduction in progression to dialysis. So this is something the cardiologists have control more than we have control.

Dr. Taub:
I think you bring up really good points about how the combination of eGFR and assessment of microalbuminuria is very synergistic in really predicting both renal and cardiovascular outcomes. The other thing is cardiologists love targets. We're very used to LDL targets, blood pressure targets. Now we can really focus on the target of reducing UACR by 30% if it's over 300, with multiple different agents available to us, including finerenone.

Dr. Bakris:
Right, and that number comes from the most recent ADA [American Diabetes Association] clinical practice guidelines published in this year, in 2022, where it specifically says that your goal should be to reduce albuminuria by greater than 30% if it's greater than 300.

Dr. Taub:
And another important point is, you pointed out earlier, microalbuminuria is a measure of inflammation. And inflammation is a big driver of atherosclerotic cardiovascular disease. And now we have an agent, finerenone, that selectively, it really impacts both inflammation and fibrosis. So I feel like all the organs are starting to come together.

Dr. Bakris:
Well, there's always been, as I affectionately call it, especially when I talk to primary care physicians, you need to think of the heart and the kidney as a spousal relationship. And so what's good for one, is generally good for the other, and they try to help each other. But if one is in trouble, the other one will try to help, but there's a limited amount of things that they can do.

So you want, ideally, to have, as we were talking about earlier, really, in heart failure, you have these pillars of therapy that you can use because you've tested them all and together, they give you better outcomes than any one alone.

Now in nephrology, for the first time, we have 3 pillars of therapy. We never had this before. We had RAAS blockers; that was it. And those were ineffectively used. So now, the goal is to get all 3 of these used and actually, Gerasimos, to your point, SGLT2s alleviate or attenuate the hyperkalemia risk of finerenone. So there's a host of reasons other than outcomes to be using the combination of the 3.

Dr. Taub:
Well, I love the spousal analogy between the heart and kidney, and let's hope they never get divorced and they always work together.

Well, this has been a fascinating conversation. And before we wrap up, Gerasimos and George, do you have any take-home messages that you would like to convey to the audience?

Dr. Filippatos:
Yes, I think it's clear when you see a patient, always, with diabetes and chronic kidney disease, don't think that does not have chronic

kidney disease until you evaluate, as cardiologists, both the eGFR and UACR.

Dr. Bakris:
You heard it here, folks. A cardiologist is saying measure albuminuria along with eGFR. So I want to emphasize that big time. And I want you to understand that you need to know how to read kidney signals. So if you're seeing albuminuria, it's not just that it's a risk factor for heart disease, but also, you have to figure out that if you're reducing it, you are going to benefit both the heart and the kidney.

Dr. Taub:
Well, unfortunately, that's all the time that we have today. So I want to thank our audience for listening. And a special thank you to Gerasimos and George for joining me and sharing all of your valuable insights and expertise. It was great speaking to both of you today.

Dr. Bakris:
Thank you, Pam.

Dr. Filippatos:
Thank you, Pam. Thank you.

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