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Cardiovascular Outcomes with Finerenone According to Glycemic Status at Baseline and Prior Treatment with Newer Antidiabetics among Patients with Type 2 Diabetes Mellitus

Dr. Patel:
Hello, this is Manesh Patel. I'm a cardiologist at Duke and presenting some findings from a recently published paper called "Cardiovascular Outcomes with Finerenone According to Glycemic Status at Baseline and Prior Treatment with Newer Antidiabetic Agents in Patients with Type 2 Diabetes Mellitus."

As I stated, I'm a cardiologist and really been interested in the revolution that's going on in our patients who have kidney disease, cardiometabolic disorders or diabetes. And one of the interesting agents is an agent called Finerenone, a nonsteroidal selective mineralocorticoid receptor antagonist, and this agent was recently reported in a journal called "Chronology and Metabolism" and just recently published. And so I think going through this paper has been really important at least for my understanding of the therapeutic.

What the investigators here did is they were trying to determine the cardioprotective effects of Finerenone according to whether or not patients had prior treatment with some of the newer antidiabetic therapies and the glycemic status, or sort of how bad the diabetes was for the patient.

They actually conducted a sort of a systematic literature review and analysis and eventually looked at all clinical trials in PubMed and Cochrane Library from inception to October of 2021 for RCTs that looked at finerenone on major cardiovascular outcomes. And as you can imagine, that this was an interesting and important finding to see what could they see and find in this area. And they went through several papers, as they stated they retrieved over 64 papers in PubMed and they had two people reviewing all of this 64 to 77 reports to see if they were inclusion of finerenone in any active comparator or placebo. And as one can imagine, they actually ended on two trials that are pretty well known in this space. They ended on both the FIGARO-DKD trial and the FIDELIO-DKD trial, and they reviewed those specifically and can be seen in the paper, and what they identify, as you may already know, is that the FIDELIO-DKD and the FIGARO-DKD studies both enrolled subjects with long-standing diabetes and insufficient glycemic control often with either some proteinuria or CKD, and they were mostly overweight, obese individuals. These randomized trials tested finerenone compared to placebo and looked at cardiovascular outcomes. And I think in the evolving world of clinical care, many want to know how does that compare to the care that we're providing our patients now? So in table one of this paper, you can identify that, in fact, these were fairly large studies, you know, FIDELIO-DKD was 5,674 patients and FIGARO-DKD was 7,352 patients. And importantly, you know, these patients had diabetes over 14 years or 16 years in these studies. There are 64, 65-year-old patients with the mean hemoglobin A1C around 7.7 and about 45% of the patients had prior cardiovascular disease. Importantly, thinking about their baseline therapies, it was evident that looking at these data, that these patients had some baseline use of GLP-1 and SGLT-2 inhibitors. The GLP-1 therapies were used in 6.9% of the patients in FIDELIO-DKD, and 7.5% of the individuals in FIGARO-DKD. The SGLT- inhibitors were used in 4.6% of the patients in FIDELIO-DKD and 8.4% of the patients in FIGARO-DKD.

And I think the most telling figure from the paper potentially the most important slide to look at is, I'll call it the forest plot of the outcomes in cardiovascular benefit in patients based on the hemoglobin A1C status. And they break down hemoglobin A1C as greater than 7.5 or less than 7.5, and it's evident looking at the combined finerenone data that there is a benefit with a hazard rate issue of 0.87 or a risk

ratio of 0.87 for finerenone whether or not the patient has a hemoglobin A1C greater than or less than 7.5%. And so, again, a pretty robust finding showing us that finerenone, this nonsteroidal mineralocorticoid receptor antagonist is a valuable therapy in these patients because it does reduce cardiovascular events and broadly patients with diabetes, and some proteinuria at risk for worse than kidney disease. And these patients have a 13% risk reduction as highlighted by this figure. And that's consistent amongst both the hemoglobin A1C status, but it's also present and not modified by whether or not a patient was in a GLP-1 or SGLT-2.

And so the authors, I think, conclude that finerenone provides significant cardiovascular benefit for patients with type 2 diabetes, especially those who are obese, and the glycemic status and the newer anti-diabetic agents don't seem to have any modification on that or any existing superior cardioprotective effect that's seen above once it's seen in the trials. Now these are small numbers and caution is, obviously, this a subgroup analysis but again, the overall trial findings are consistent across the diabetes, level of diabetes or hemoglobin A1C and prior agents. And I guess the clinical questions that we're all going to be struggling with is as more of these therapies come on board, how do we pick and choose these therapies? And I think these data highlight that in addition to our patients with diabetes that are getting a variety of other agents for diabetes, therapies like finerenone might be standard therapies we think about for patients with diabetes and kidney disease as they prevent cardiovascular events, and maybe different mechanistically and additively to some other therapies that we're using. Thank you for listening. This is Manesh Patel describing this paper on the cardiovascular outcomes of Finerenone according to glycemic status for DukeHeart On the Go.