Transcript Details

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Is It Time to Change Your Treatment Strategy for Type 2 Diabetes Patients with CV Risks?

Announcer:
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Dr. Cannon:
Well, welcome to Clinical Countdown. I’m Dr. Chris Cannon.

Dr. Dagogo-Jack:
I’m Dr. Sam Dagogo-Jack.

Dr. Cannon:
Well, in this discussion, I’m the bumbling cardiologist, and I know little about diabetes other than it’s really important and I need to get myself up to speed, and so I’m looking forward to talking with you about getting myself up to speed.

Dr. Dagogo-Jack:
All right, Chris, nice try. Your self-deprecating humor calling yourself a bumbling cardiologist does not impress me. I know you’re a smart guy, but you’re not an endocrinologist; that’s for sure.

Dr. Cannon:
Indeed, indeed. Well, that’s why we’re here today on Clinical Countdown: The Type 2 Diabetes edition. We’ll be taking a look at the latest data from the ADA and focusing on the appropriate use of SGLT2 inhibitors in reducing cardiovascular risk in type 2 diabetes. So, you ready, Sam?

Dr. Dagogo-Jack:
You bet I am.

Dr. Cannon:
All right. Well, I think we’ll – first off, we’ll talk about the risk of patients with diabetes. So we often think about the cardiovascular complications, and I always think of myocardial infarction, but that’s not the whole story. What else do we need to think about?

Dr. Dagogo-Jack:
Well, as you know, Chris, patients with type 2 diabetes have several comorbidities that increase their risk for heart disease. They do have a high prevalence of hypertension, of dyslipidemia, especially low HDL, high triglycerides, and small dense LDL particles. And so these background risks do set them up for myocardial infarction, but nearly 50 percent of people with diabetes are at risk for heart failure. So heart failure is an important cardiovascular morbidity that tends to get forgotten amidst the excitement and gimmickry that goes around opening up clogged arteries and heart attacks and MI – that heart failure, quantitatively, is as great a burden, if not greater, than a myocardial infarction in people with diabetes.

Dr. Cannon:
Well, it's very true that beyond MI, heart failure is a huge issue, and I've also come to appreciate that renal dysfunction and advancing renal disease is another key thing to focus on even for me as a cardiologist. And one of the things I've really liked is that the new guidelines in the last year or two from the ADA call us out to say look at the patient profile. Do they have ASCVD? Do they have heart failure? Do they have chronic kidney disease? And, you know, that has been a really wonderful change in the approach. How has that been received in the endocrine community?

Dr. Dagogo-Jack:
I think it's been embraced very enthusiastically because it does provide a clearer roadmap as to what to do with our patients with diabetes. I mean, the diabetic patients have a 2- to 4-fold increased risk of cardiovascular disease, stroke, and heart failure, yet the guidelines had been less than specific in giving clear directions. But right now, a history of prevalent atherosclerotic cardiovascular disease, kidney disease, or heart failure, it makes a patient eligible for early consideration of use of certain drug classes that have randomized control trials evidence that they offer additional benefit beyond glucose lowering.

Dr. Cannon:
Well, you know, it's really nice to see that the focus is shifting really less on glucose lowering. It used to always be just the hemoglobin A1c, but now it's really shifting towards using different classes and how we lower the glucose. Do you want to touch on this class – the SGLT2 inhibitors?

Dr. Dagogo-Jack:
Yes. This is a fascinating class. As you know, people with diabetes excrete large amounts of glucose in the urine. In fact, ancient testing mechanisms involved testing the urine. Thank goodness we now don't have to mess with urine to know the exact blood glucose levels. However, that mechanism of glucose elimination in the urine has provided a therapeutic strategy where – in people with type 2 diabetes, would you believe that some of the glucose that has already been filtered from the blood and destined for elimination in urine get taken back by some receptors? The sodium-glucose co-transporter type 2 receptors take back 90 percent of the filtered glucose in the proximal kidney tubules. So drugs that block that reabsorption help the body get rid of excess sugar, and those drugs that belong to the SGLT2 inhibitor family – and so the expectation was that they would help improve glucose control. But long-term randomized controlled cardiovascular outcome trials now give us almost an unexpected, additional benefit showing that they do reduce body weight; they decrease blood pressure. And now members of the class are very repeatedly and are very – in a very reinforcing manner, demonstrated that they reduce cardiovascular risks, particularly heart failure hospitalization. So we can take this information solidly to the bank that, as a class, these drugs are good for reducing the risk of heart failure hospitalization.

So let's get down to results and review some of the data. Chris, you are very familiar. In fact, you're in the committee that presented these data at the ADA meeting on the latest SGLT2 inhibitor cardiovascular outcomes trial. I believe the name of that trial was VERTIS CV. Can you tell us a little bit more about the design and key results?

Dr. Cannon:
Well, certainly. This was the fourth agent to be tested in a cardiovascular trial in patients with documented atherosclerotic cardiovascular disease – the agent ertugliflozin at one of two doses versus placebo looking primarily for cardiovascular safety. And we didn't see, indeed, a noninferiority, so demonstrating the cardiovascular safety. Then, looking for superiority, we found some trends, but not significant reduction in cardiovascular death or hospitalization for heart failure as a combined endpoint. But hospitalization for heart failure alone was 30 percent lower, and there is also a trend towards reduction in worsening renal dysfunction and significant improvements in the EGFR. And so really, similar-type findings has been seen in the other CV outcomes trials, although some of the P values weren't as strong as in prior trials.

Dr. Dagogo-Jack:
Interesting. So in addition to the VERTIS CV, which happens to be the latest trial among the SGLT2 inhibitors, there are other trials that have been conducted with members of the class. I recall – so there's, like, DECLARE-TIMI, CREDENCE, EMPA-REG, which was I believe the earliest of these studies. So would you say that there is a trend toward a class effect among members of the SGLT2 family with regard to reducing cardiovascular risk?

Dr. Cannon:
Well, this was a really nice analysis that Darren McGuire led – a formal meta-analysis with all the prior big trials – and the pattern was very similar to what we saw in VERTIS CV versus the overall meta-analysis. And so in that, there was a reduction in MACE of about 10 percent, so CV death and minor stroke, and then also a reduction in heart failure that was very consistent – about a 30 to 35 percent reduction. Cardiovascular death alone had a very slight trend, but overall across the five trials lower. And then improvement in kidney function also improved. So really substantial benefits across many different clinical endpoints of this class of drugs and largely similar

across all the different agents in the different trials.

Dr. Dagogo-Jack:
I do agree that the meta-analysis do support a class effect, and as I recall for MACE events, the full estimate would be an expectation that risk would be reduced by about 10 to 15 percent. And a comparable range of about 10 percent proved risk reduction for CV death and a whopping 30 percent risk reduction for heart failure, so these are very reassuring and consistent data. So the question is, given these benefits demonstrated by members of the class, how aggressive should we really be when starting patients on SGLT2 inhibitors and because of their diabetes management?

Dr. Cannon:
Well, this is, I think, a – what I've come away as a call to action that, you know, again, as my bumbling cardiologist, I need to get involved. I've traditionally not – said, "Oh, go see your primary care doctor you'll follow up with," but, you know, here there are benefits on all these different cardiovascular endpoints. And so with this seen in all these trials that it says, you know, we've got to start doing this on each patient who comes to us.

Dr. Cannon:
All right, Sam. So now we're moving into our lightning rundown, so we'll each have 60 seconds to talk about key topics, and you're up first. So, the topic is how do we solve the collaborative care model amongst us all?

Dr. Dagogo-Jack:
With regard to optimization of cardiovascular health in patients with diabetes, the collaborative care model is the best approach. It involves the use of a structured, multicomponent, multidisciplinary, evidence-based approach to select and optimize certain drugs that would deliver significant risk reductions. So SGLT2 inhibitors have been shown to decrease weight, blood pressure, blood glucose, and cardiovascular risk. Therefore, the creation is we should prescribe it, and I think that decision support and a collaborative team with the primary care physician engaging the endocrinologist and cardiovascular specialist should all lead to earlier realization that exposure of people at risk to SGLT2 inhibitor is the best way to lock in the long-term benefits of reduction in cardiovascular outcomes.

Dr. Cannon:
Well, for the SGLT2 inhibitors, the effects and the side effects that have been seen really do seem to be similar across the entire class with just slight variations. So, interestingly, there isn't much of a reason to choose one agent over another, I don't think, but the key is to choose the class. There are lots of patients who will benefit from this, having atherosclerotic cardiovascular disease, heart failure, chronic kidney disease – that's like two-thirds of our cardiology practice, of course, in patients with diabetes that we really have to think about how can we add this in a collaborative way to the care of our patients.

Dr. Dagogo-Jack:
Excellent, and I believe that in light of the current body of evidence, guideline writers better pay heed and make sure that the guidelines are up to date. I can predict – or I do foresee that there would be a reinforcement of the current practice of segmenting our diabetic patients very early on to those who already have evidence of atherosclerotic cardiovascular disease, prior history of heart failure, or chronic kidney disease so that such people can have earlier exposure to treatment with medications that have been demonstrated to reduce those risks. I think that would be an important reinforcement of existing guidelines. It may also be that since the DAPA-HF showed evidence of a risk reduction in heart failure and death in people who did not even have diabetes, consideration may be given to enabling more proximal introduction of these agents in people with diabetes without waiting for them to actually have had an event – a cardiovascular event. I think that may be a direction to consider.

Dr. Cannon:
Well, this has been a really fun discussion, Sam. So what would be your one key takeaway?

Dr. Dagogo-Jack:
The key takeaway is that type 2 diabetes, cardiovascular disease, heart failure, and chronic kidney disease are intertwined, mutually reinforced in comorbidities, and parsimonious approach in selecting drugs that hit many of these targets while lowering blood glucose would be smart medicine.

Dr. Cannon:
Well, my key takeaway is that I've got to get with it, and it's time to implement all of these terrific benefits. And so each patient with diabetes who I see, I have to risk stratify and really try and work in a collaborative way to get these beneficial treatments to them. So that's it. We're out of time, and thank you very much for joining us and until next time.

Dr. Dagogo-Jack:
Bye.

Announcer:
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