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## MACE and SGLT2 Inhibitors: Do They Have an Impact?

### Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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### Dr. Bhatt:

This is CME on ReachMD, and I'm Dr. Deepak Bhatt. There are a number of recent publications exploring the impact of SGLT2 inhibitors on cardiovascular risk. Today, we're focusing on their impact on major adverse cardiovascular events, or MACE. So let's get to it.

There is, at this point in time, a ton of data supporting SGLT2 inhibitors as a class in reducing heart failure outcomes and improving kidney outcomes, and that appears due to SGLT2's effect, or more precisely, inhibition of SGLT2's effect on the kidney. But what about SGLT1/2 inhibitors? Well, there's one agent that's available out there right now, and that's sotagliflozin, and it inhibits SGLT2 and has the benefits on heart failure and kidney outcomes that are known for the whole class of agents. But the SGLT1 does appear to provide a bit of extra benefit, and that extra benefit seems to be with respect to MACE.

In particular, in the SCORED trial, which was a randomized trial of sotagliflozin versus placebo in patients with diabetes and chronic kidney disease and excess cardiovascular risk, these sorts of patients were randomized to sotagliflozin or placebo, and there was a significant reduction in heart failure-related events, the primary endpoint of the study. But there was also a significant reduction in both myocardial infarction and a significant reduction in stroke, and that's not been seen with other SGLT2 inhibitors. So it does appear, then, that the SGLT1 action may be accounting for these additional benefits on MACE. SCORED was a high-risk population.

The TRANSFORM trial is looking at primary prevention, albeit higher-risk primary prevention, and examining a variety of different therapies that are approved and available, but using them in ways that go beyond what the current data actually support. And in TRANSFORM, in primary prevention patients, we will be randomizing patients to either receive guideline-concordant care or to receive care that is informed by coronary CT [computed tomography] angiography. And in particular, using an AI-enabled algorithm to help better risk stratify patients based on how much plaque they have or don't have in their coronary arteries on a CT angio. And the idea, then, is in patients that have plaque, to use more intense medical therapy, including agents like sotagliflozin, to see if it might have an effect in preventing plaque progression. We will be analyzing CT angios at baseline and at 2 years in TRANSFORM and, perhaps even more importantly, seeing if there is an impact on actual cardiovascular events, MI, stroke, the need for revascularization, and so forth. So hopefully, this approach that we're studying in TRANSFORM, using an AI-enabled CT angio and the data from it to more precisely estimate a patient's risk and then titrate their medical therapy, will be one that is found to be useful, but we'll see.

But as part of that intensive medical therapy algorithm, sotagliflozin along with agents like bempedoic acid to lower LDL cholesterol, colchicine in patients with elevated C-reactive protein to target inflammation, and a variety of other agents will be tested. So this may potentially, in the case of sotagliflozin, as well as some of these other agents I mentioned, provide novel insights into how drugs may have benefit beyond where they've already been studied and established and have labeling and so forth. So a very exciting trial. We've

already launched it. We've started randomizing, so stay tuned.

So in terms of key takeaways, TRANSFORM will hopefully show us the value of CT angiography in both risk assessment but also guiding medical therapy. As well, it will hopefully help us evaluate the impact of some relatively new drug classes, such as SGLT1/2 inhibitors, sotagliflozin specifically, to see if this type of approach of inhibiting both SGLT1 and 2 helps reduce MACE in a primary prevention population, as it was shown to already do in a SCORED population, that is patients with diabetes, chronic kidney disease, and cardiovascular risk factors.

**Announcer:**

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