Transcript Details

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Targeting Epicardial Adipose Tissue in Patients With HFpEF Without Diabetes: Sotagliflozin Effect From SOTA-P-CARDIA Trial Sub-Analysis

Announcer:
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Dr. Badimon:
Hello and greetings. This is ReachMD, and I am Juan Badimon, professor of medicine at the Icahn School of Medicine at Mount Sinai in New York City. Today, I will present data from a specified sub-analysis of the SOTA-P-CARDIA trial, focusing on the effects of sotagliflozin on different adipose tissues.

The SOTA-P-CARDIA trial is a mechanistic, single-site, randomized, placebo-controlled study designed to evaluate the effects of the dual SGLT1/2 inhibitor sotagliflozin in non-diabetic patients with heart failure and preserved ejection fraction. Patients were randomized to receive either sotagliflozin or placebo for a period of 6 months.

The cardiorenal benefits of the selective SGLT2 inhibitor in heart failure patients has been very well established by several large randomized clinical trials. In fact, these agents have become 1 of the 4 pillars for the treatment of heart failure patients independently of the ejection fraction values or glycemic status. However, those benefits were obtained without reductions in atherothrombotic events, namely myocardial infarctions and strokes. On the other hand, 2 randomized clinical trials, the SCORED and the SOLOIST, have demonstrated the benefits of the dual SGLT1/2 inhibitor, sotagliflozin, on diabetic patients.

Of interest, sotagliflozin was associated with approximately 30% of reduction in MIs and stroke. However, since most of the patients of these trials were diabetics, there was limited evidence on the effects of sotagliflozin in a non-diabetic population.

Going back again, as an introduction to the main SOTA-CARDIA, the objective were to study the effects of sotagliflozin on cardiac function and structure, and this was assessed by cardiac MRI, as well as on the quality of life and functional capacity using the KCC questionnaire and the 6-minute walking test in comparison with the placebo control group.

Here, in the slide, you can see the results, and basically, we have already reported that the administration of sotagliflozin to heart failure patients with preserved ejection fraction and no diabetics was associated with a significant improvement in cardiac structure and function alongside symptoms and markers of congestion as well as the quality of life and physical activity. Regarding the peak VO2, as you can see, there were a marked trend towards benefits, but we did not reach statistical significance.

However, today, I will focus on a different aspect of the trial. Why we did this sub-analysis? Because given the close interaction between adiposity and heart failure, today, we did a pre-specified sub-analysis in order to investigate the effect of sotagliflozin on the different adipose tissues compared versus placebo.

Again, MRI was used to assess the changes in adipose deposits. And why is this important? Because traditionally, obesity has been diagnosed by the BMI or by measuring the waist circumference of the subject. While these parameters have a good predictive value,

they do not offer a lot of information regarding the location or the magnitude of the adipose tissues. In fact, the adipose tissues can be classified into 3 major deposits: subcutaneous, visceral, and epicardial adipose tissues. Today, we know that not all the fat is created equal, and in fact, they significantly differ in their biological and metabolic activity.

Subcutaneous adipose tissues are associated with hyperplasia, hypertrophy, and they are insulin sensitive. The adipose tissue is pro-inflammatory and is associated with an increased cardiometabolic risk.

On the other hand, the epicardial adipose tissues, because of its close relation and location with the myocardium and the coronary arteries, allow for an endocrine and paracrine cross-talk. Under physiological conditions, epicardial adipose tissues offer a protective effect by releasing immunomodulatory and anti-inflammatory cytokines such as adiponectin, omentin, or interleukin-10.

However, under pathological conditions—and when I say pathological conditions, I mean obesity, diabetes, heart failure, or established cardiovascular disease—it undergoes structural and metabolic changes, and then this protective benefit releases pro-inflammatory mediator, and adipokines such as the TNF-alpha, interleukin-6, interleukin-1β, and at the same time reduce the release of protective adipokine.

Why is this so important? Because obesity and diabetes are strong and independent risk factors for heart failure, cardiovascular disease, and stroke. But what is terrible is that the most recent estimates given by the CDC indicates that approximately 25% of Americans will have diabetes and more than 30% will be obese in the year 2030. So those risk factors can be considered a growing evidence.

What are the studies? As you can see in this figure, our data, they show that 6 months of sotagliflozin administration to non-diabetic heart failure patients with preserved ejection fraction was associated with a significant reduction on the epicardial adipose tissue, but of interest without changes in the subcutaneous and visceral adipose deposits as compared versus the placebo control group. Interestingly, we also observed a marked reduction in the hepatic fat content. However, it did not reach statistical significance.

But one of the points that is very important to consider is that this selective effect on the epicardial adipose tissue was observed in a non-diabetic population. And remember, that usually the non-diabetics are leaner than the diabetic population. Why is it so important, this effect on reduction of the excess epicardial adipose tissue is because so far, all the therapeutic interventions that have been able to reduce epicardial adipose tissues, such as the SGLT2s and the ELP-1 receptor antagonists, have also demonstrated benefits on clinical outcomes on the heart failure patients. This observation seems to highlight the potential therapeutic target of the epicardial adipose tissue in the treatment of the heart failure patients with preserved ejection fraction.

In conclusion, I think that our data showing the benefits in cardiac structure and function, quality of life, combined with the last data presented on the selective reduction on the epicardial adipose tissue strongly suggests that the dual SGLT1 and 2 inhibitor, like sotagliflozin, should be considered a novel and alternative therapeutic option for the control and management of heart failure patients.

So stay tuned because more data are coming with these new agents are the dual SGLT1/2 inhibitors. Thank you for having me and the opportunity of sharing our data with you. Thanks.

Announcer:
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