Transcript: DELIVER Results – Scott Solomon, MD

So the class of drugs known as SGLT2 inhibitors have been shown to reduce morbidity and mortality in patients with heart failure, and reduced ejection fraction, so patients with heart failure with an LVEF less than or equal to 40%, and their use has been strongly recommended in current clinical practice guidelines. But unfortunately, few pharmacologic treatments have been available for patients who have mildly reduced or preserved ejection fraction, in other words, left ventricular ejection fraction of over 40%.

There has been one trial presented a year ago at the ESC, the EMPEROR-Preserved trial, which showed a reduction in cardiovascular death or heart failure hospitalization with empagliflozin in this population, but significant uncertainty remained regarding efficacy in several groups of patients, including those patients at the highest end of the ejection fraction range, where there's been concern about attenuation of the treatment benefit.

Those patients who are initiated on drug either during or shortly after a hospitalization where limited data are available, and those patients who had had a previously reduced ejection fraction that had improved to over 40%. And this group has been excluded from prior trials. So we designed the delivered trial to answer many of these questions.

We enrolled patients who had heart failure, had an injection fraction of over 40%, who had evidence of structural heart disease, evidence of natural peptide elevation. And they could be either ambulatory or hospitalized for heart failure. They were randomized to dapagliflozin, 10 milligrams once a day or placebo.

And it turned out that we randomized 6,263 patients. It's the largest as well as the broadest inclusion heart failure with mildly reduced and preserved ejection fraction. Study patients were randomized to dapagliflozin or placebo. At the end of the study, survival status was known on all but two patients in each group.

The main findings of this study were a 18% overall reduction in the primary endpoint, which was cardiovascular death or worsening heart failure. Worsening heart failure consisting of either a heart failure hospitalization or an urgent heart failure visit.

In addition, we saw significant reduction in worsening heart failure alone. We did not see significant reduction in cardiovascular death alone, that was reduced by 12%, but it wasn't statistically significant. We saw essentially the same results, regardless of whether the patient's left ventricular ejection fraction was less than 60% or above 60%.

In fact, we didn't see any heterogeneity with respect to ejection fraction and the patients at the upper end of the range derived as much benefit as patients at the lower end of the range. We also saw benefit in the patients who were recently hospitalized, and we saw benefit in the patients who had improved ejection fraction. In other words, those people who had ejection fraction that was below 40% at one point, and then had improved to over 40% by the time of enrollment.

With respect to all prespecified subgroups, we saw basically consistency of our treatment effect. We also saw a reduction in total heart failure events and cardiovascular death by 23%. And we saw a significant improvement in the Kansas City Cardiomyopathy Questionnaire total symptom score, which is a measure of symptom burden. This was improved by 2.4 points.

With respect to safety, we saw virtually identical numbers of serious adverse events and adverse events leading to discontinuation in the dapagliflozin and the placebo group. And when we looked at specific adverse events of interest like amputation and diabetic ketoacidosis hypoglycemia, they were very low and almost identical in the two groups.

So we concluded in this largest and most inclusive trial of heart failure with mildly reduced and preserved ejection fraction, that treatment with dapagliflozin resulted in a lower risk of a primary composite of cardiovascular death and worsening heart failure.

In addition, we were able to show that dapagliflozin resulted in improved symptoms as measured by the KCCQ total symptom score. These findings were consistent across all of our pre-specified subgroups but particularly in those defined by ejection fraction with no evidence of attenuation at that highest end of the ejection fraction spectrum. We saw benefit in recently hospitalized patients, in patients with heart failure with improved ejection fraction. And serious adverse events and adverse events leading to discontinuation were very similar between the dapagliflozin and placebo groups.

So overall, we believe that these data provide strong evidence to support the use of SGLT2 inhibitors as foundational therapy in patients with heart failure, regardless of ejection fraction.