Title: HFA 23: DAPA-HF and DELIVER: KCCQ in Patients with Varying Ejection Fraction
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I'm Ankeet Bhatt. I'm from the Kaiser Permanente San Francisco Medical Center, San Francisco, California and the United States.

What was the reasoning behind comparing the DAPA-HF and DELIVER Trials?

You know, the reason behind this analysis is that we've now conducted two large randomized clinical trials looking at the effectiveness of dapagliflozin in patients with both heart failure with reduced and preserved ejection fraction. We were interested in whether dapagliflozin also improved how patients feel looking at physical limitations and quality of life in this population, and whether, if, those benefits were consistent across the full spectrum of left ventricular ejection fraction.

What is the current landscape of research into dapagliflozin in 2023?

Yeah, the SGLT2 inhibitors have been an exciting time in heart failure. They've now been studied in patients with reduced ejection fraction less than 40% and preserved ejection fraction those at the higher end of the spectrum. They've also been shown to improve how patients feel in terms of quality of life and functional limitations. What we don't know are a few things which we looked at in this analysis. Specifically, one are the benefits of dapagliflozin consistent amongst those who have lower ejection fractions and those who have higher ejection fractions. To provide some clinical context here, another program of an SGLT2 inhibitor called empagliflozin showed that possibly at the higher end of ejection fraction, the clinical benefits and the quality of life improvements were attenuated with that therapy. We wanted to evaluate that with the SGLT2 inhibitor dapagliflozin.

What was the study design and patient cohort?

So this was a participant-level pooled analysis from two large international randomized clinical trials, the DAPA Heart Failure Study, which enrolled HFrEF patients, and the DELIVER Study, which enrolled patients with heart failure with mildly reduced and preserved ejection fraction. We pooled these data and we looked at a few things. We looked at the mean changes in quality of life as summarized by the Kansas City Cardiomyopathy Questionnaire summary scores.We also looked at the improvements across the full range of ejection fraction as modelled as a continuous variable. And thirdly, we looked at whether the proportion of patients who had meaningful deteriorations or worsening of their clinical status and those who had small, moderate and large improvements in their clinical status when they received dapagliflozin versus placebo.

What are the key findings?

Looking at this pooled analysis, which is just over 11,000 clinical trial participants from both trials, we noted a few things. First, dapagliflozin improved KCCQ across the spectrum of the summary scores that we evaluated, with findings evident at four months post-randomization that appeared consistent at eight months post-randomization. The mean benefits were relatively modest. However, there were significantly fewer clinical deteriorations, a five point decline in KCCQ, and more small, moderate and large improvements in KCCQ with dapagliflozin. In all of these cases, the findings were entirely consistent across the full spectrum of left ventricular ejection fracture. We noted one more thing, and that was that if you model KCCQ as someone approaches a heart failure hospitalization, we see a steep decline in the three months preceding that heart failure hospitalization in which quality of life and symptom status generally decline prior to that heart failure hospitalization. So it's indicative that people feel worse up to three months before they actually experience a clinical event. Again, that was consistent in both DAPA heart failure, reduced ejection fraction and DELIVER mildly reduced and preserved ejection fraction.

How does this analysis shed new light on the findings of both DAPA and DELIVER?

Well, I think this is an exciting time and really pairs nicely with additional data from dedicated, smaller quality of life trials with dapagliflozin who've demonstrated very similar findings and have been recently published.

How should the results of this study be applied to clinical practice?

Yeah, I think this study provides compelling evidence that dapagliflozin not only improves clinical outcomes in patients with heart failure across the spectrum of ejection fraction, something we knew, but also improves quality of life across that same spectrum with no attenuation of benefit at the highest ejection fraction ranges.

What further study is needed?

Yeah, I mean, I think we have a compelling therapy that should benefit patients. It will make them live longer. It'll make them live, we think, better and more and less symptomatically, and we know that there's other downstream benefits of this therapy. The key question, I think, in my mind, and in the mind of others, is how are we now going to ensure that there's optimal implementation of these highly efficacious therapies in routine clinical practice?