- Greetings. I'm Dr. Javed Butler. I'm a professor and chairman of the Department of Medicine at University of Mississippi in Jackson, Mississippi. I was the co-principal investigator for the EMPEROR-Preserved trial, and that's the trial we will be discussing today.

Rationale for the Study

So the rationale for EMPEROR-Preserved trial was to assess the impact of empagliflozin on outcomes in patients with heart failure and preserved ejection fraction. Obviously, we know before EMPEROR-Preserved came out, that there was no trial that has ever been a positive for its primary end point. So this was a big unmet need. The study that was presented here at the American Heart Association was focusing on the quality of life outcomes in patients with heart failure and preserved ejection fraction and how it was impacted by the use of empagliflozin. And there are sort of two questions that people ask. One is obviously our patients not only want to live longer and have less hospitalisation, that obviously is very important. But also whether the therapy improves their quality of life and health status. So that's sort of one question. And then the second question is, are there some patients who are just too sick or too healthy at baseline to actually benefit from medical interventions? So what is the impact of health status on clinical outcome and what is the impact of therapy on health status? So these were the two questions that we are asked in this particular study.

Health Status

So the health status was measured with the use of a validated questionnaire called Kansas City Cardiomyopathy Questionnaire. We use the 23-question version. These questions are then divided into three domains. So one domain is related to symptoms, so symptom frequency and symptom burden that is called TSS, total symptom score. If on top of the total symptom score you add physical limitations, then it becomes CSS or clinical summary score. And on top of clinical summary score, if you add other domains like sexual function, social integration, quality of life, then it becomes OSS, overall summary score. So all patients in the trial were asked to fill out this questionnaire at baseline to get an idea where is the starting point, and at three points during the trial. At three points to assess early changes, at eight months to assess intermediate. And then at 12 months to see sustainable changes.

Design and Patient Population

So EMPEROR-Preserved trial included patients, close to 6,000 patients that had a history of heart failure with preserved ejection fraction. Their comorbidities for treated to standard of care, they either needed to have elevation in natriuretic peptide level or a heart failure hospitalisation within the year prior to enrollment, and some evidence of structural heart disease on an echocardiogram, either left atrial enlargement or left ventricular hypertrophy, some sort of structural changes. So history of heart failure with preserved ejection fraction, natriuretic peptide or heart failure hospitalisation, and evidence of structural heart disease. These were the patients that were enrolled and were randomised to either placebo or empagliflozin 10 milligrammes, and were followed for outcomes and see how they do.

Key Findings

So the key findings in the overall trial were presented earlier and have already been published in that empagliflozin reduced the risk of cardiovascular death and heart failure hospitalisation, total heart failure hospitalisation, and preservation of eGFR slope or preservation of renal function. These were three aims for which the trial was tested. Again, what we presented here at the American Heart Association was to focus on health status. So there were two questions that we assessed. One was did the baseline health status affect the benefit from the drug on the patients' outcomes? And the answer was no. We divided the patients on the basis of baseline tertiles of clinical summary score. And whether you started at the lower end of the health status, really not feeling well. Or at the higher end that you were doing sort of okay, or in the middle. None of that matters in all three groups of patients, had benefit in their clinical endpoint of cardiovascular death and heart failure hospitalisation. Now, the second issue was to assess whether empaglifozin improves health status. So again, we saw the benefit. There was a statistically significant improvement early when we first measured at three months. And that was sustained both at 8 months and at 12 months. So early benefit and was sustained. What is the standard in the field of health status and quality of life measurement, is to do something which is called a responder analysis. So what you do is you look at various threshold, 5-point, 10-point, 15-point improvement, or 5-point deterioration. So we measure all of this CSS, TSS, OSS. 5-point, 10-point, 15-point improvement. 3-month, 8-month, 12-month improvement. And the summary is that we consistently showed that with the use of empagliflozin, health status was improved at all threshold, all domains in an all-time points. And patients who were randomised to placebo showed worsening of their health status.

Take-Home Messages

The take home messages are that patients with heart failure and preserved ejection fraction in the absence of a contraindication or intolerance, or some other reason should be treated for clinical endpoints, risk for heart failure hospitalisation, cardiovascular mortality, total heart failure hospitalisation. However, now with this study, we also have the data that we can discuss with their patients that not only should they expect improvement in clinical outcomes, but they should expect improvement in their health status and quality of life as well. The next step obviously is that clinical medicine is a two-front war. First is to generate evidence to know what works, but the second is evidence implementation.

Next Steps

So the next steps are to go through all of these data, see what the guidelines say, and good amount of medical education for our practicing clinicians, doctors, and nurses. And the eventual goal is to have the therapy be implemented to the patients that have the indication for this therapy.