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METEORIC-HF: The Effect of Omecamtiv Mecarbil on Exercise Tolerance in Patients With Chronic Heart Failure and Reduced Ejection Fraction

Dr. Felker:
Hello, this is Michael Felker from Duke University and the Duke Clinical Research Institute. It's my pleasure today to talk about the results of the METEORIC-HF trial recently presented at the American College of Cardiology.

Exercise intolerance is a cardinal manifestation of heart failure, but it is not improved by current medical therapies even those that improve cardiac outcomes. Omecamtiv mecarbil is a novel selective cardiac myosin activator that increases cardiac performance and improves outcomes in patients with heart failure and reduced ejection fraction as seen in the GALACTIC-HF trial. In METEORIC, we tested the hypothesis that omecamtiv mecarbil can improve exercise capacity in patients with heart failure and reduced ejection fraction of HFrEF. METEORIC was a double-blind, placebo-controlled, multi-center, randomized clinical trial. Patients with heart failure and reduced exercise capacity were screened using cardiopulmonary exercise testing. Those that had documented reduced exercise capacity and a strong exercise effort were randomized to either omecamtiv mecarbil using a dosing regimen identical to that that was used in GALACTIC or placebo. Patients were treated for 20 weeks and had a follow-up CPET performed at the end of the study. Patients were randomized two to one such that two times as many patients got omecamtiv mecarbil as placebo.

Key inclusion criteria included NYHA class II to III heart failure, an ejection fraction less than or equal to 35%, and patients needed to be on maximally tolerated background heart failure therapy. Importantly, as I mentioned earlier, they needed to have a documented CPET result where their peak VO2 measure of exercise capacity was less than or equal to 75% of their age-predicted normal, and they needed a respiratory exchange ratio on that CPET of greater or equal to 1.05, suggesting an excellent effort on the test.

Baseline characteristics were well-balanced between the groups. The patients had a mean age of 64. Most were men. Most had ischemic heart disease. They predominantly had NYHA class II and moderately elevated natriuretic peptides. Importantly, background medical therapy was excellent with very good use of beta blockers, ARNi, MRA corticoid receptor antagonists and device therapy.

The primary endpoint was change in pVO2 from baseline to 20 weeks. When we looked at this difference between omecamtiv mecarbil-treated patients and placebo-treated patients, there was no significant difference between the two groups with a least-square mean difference of negative 0.45, which favored numerically placebo, but again, not statistically significant p-value of 0.13.

Secondary endpoints which measured change in workload, change in ventilatory efficiency during exercise, and change actigraphy using a wearable activity monitor again, showed no clinically important difference between the groups.

So in conclusion, in well-treated patients with chronic HFrEF, omecamtiv mecarbil did not improve measures of exercise capacity over 20 weeks of treatment compared to placebo. Consistent with prior studies, overall safety was comparable to placebo, and we did not identify any new safety signals related to peak exercise. And importantly, identifying medical therapies that can safely improve exercise capacity in heart failure with reduced ejection fraction remains an unmet challenge. Thank you very much.