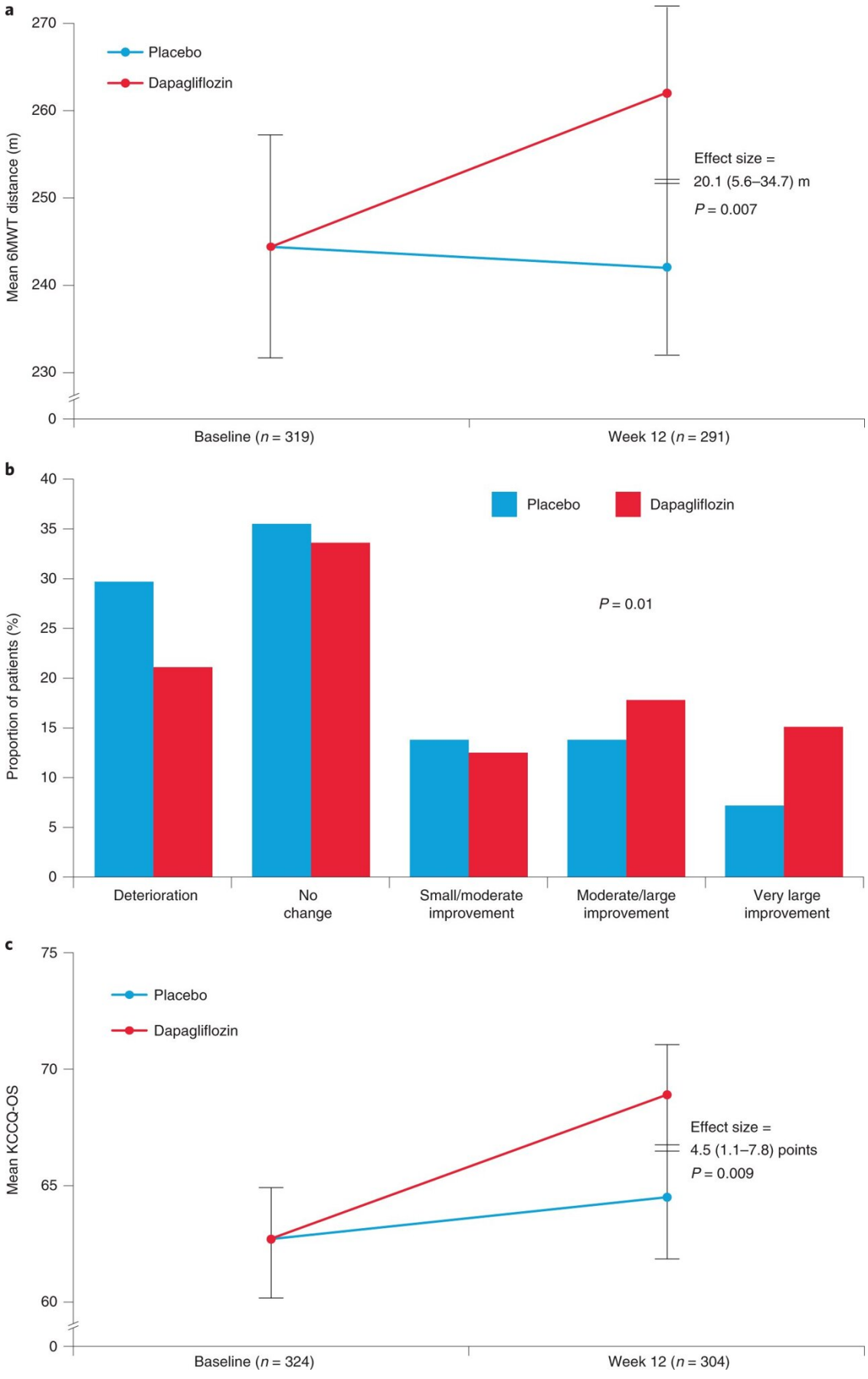
Diabetes drug dapagliflozin may benefit patients with heart failure

November 30 2021, by Melissa Rohman


a
Mean 6MWT distance (m)
270
260
250
240
230
0
Placebo
Dapagliflozin
Effect size =
20.1 (5.6–34.7) m
P = 0.007
Baseline (n = 319)
Week 12 (n = 291)
b
Proportion of patients (%)
40
35
30
25
20
15
10
5
0
Placebo
Dapagliflozin
P = 0.01
Deterioration
No change
Small/moderate improvement
Moderate/large improvement
Very large improvement
c
Mean KCCQ-OS
75
70
65
60
0
Placebo
Dapagliflozin
Effect size =
4.5 (1.1–7.8) points
P = 0.009
Baseline (n = 324)
Week 12 (n = 304)

Effects of dapagliflozin on selected secondary endpoints and in supportive responder analysis. a–c, Effects of dapagliflozin on selected secondary endpoints and in supportive responder analysis. Effects of dapagliflozin versus placebo at 12 weeks on 6MWT distance (a), KCCQ-CS responder analysis (b) and KCCQ-OS (c). Data are presented as mean values with 95% CI. a,c, An F-test was used in data analysis; b, a chi-square test was used in data analysis All P values are two-sided, with no adjustments made for multiple comparisons. Credit: DOI: 10.1038/s41591-021-01536-x

Dapagliflozin, a drug commonly used to treat type 2 diabetes, improved symptoms and physical limitations in patients with heart failure with preserved ejection fraction, according to clinical trial results published in *Nature Medicine*.

Sadiya Khan, '09 MD, '14 MSc, '10, '12 GME, assistant professor of Medicine in the Division of Cardiology and of Preventive Medicine in the Division of Epidemiology, and Sanjiv Shah, '00 MD, the Neil J. Stone, MD, Professor and director of the Center for Deep Phenotyping and Precision Therapeutics at the Institute for Augmented Intelligence in Medicine, were co-authors of the study.

Heart failure with preserved ejection fraction (HFpEF) occurs when the heart's lower left chamber is unable to fill with blood properly. The condition accounts for approximately half of all heart failure cases and disproportionally affects older individuals. Patients with HFpEF can experience a host of debilitating symptoms linked to cardiometabolic abnormalities, including physical limitations, impaired cognition and poor quality of life.

Improving patients' health and developing or identifying therapeutic

interventions that not only reduce hospitalization but also improve patient survival is key, according to the authors, but there are currently no available treatments that improve patient survival for patients with HFpEF.

Previous research demonstrated that sodium glucose cotransporter 2 (SGLT2) inhibitors, drugs that inhibit SGLT2 receptor proteins produced by the kidneys and which are currently used to treat type 2 diabetes, reduced risk of cardiovascular death and heart failure-related hospitalization in patients with HFpEF.

In the current clinical trial, the investigators measured patient-reported symptoms, physical limitations and function in patients with HFpEF who were given the SGLT2 inhibitor drug dapagliflozin.

A total of 324 patients with HFpEF from across the U.S. were randomized to receive either dapagliflozin or placebo for 12 weeks and at the end of the trial were evaluated using the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score, a measure of heart failure-related health status.

Patients were also 56.8 percent women, who are more likely to develop HFpEF than men.

"It's important to note the percentage of women that were enrolled in this study because usually women are under-enrolled in clinical trials," Khan said.

The investigators found that the dapagliflozin group demonstrated overall improvement in patient-reported symptoms, physical limitations and exercise function compared to the placebo group. Adverse events were also similar between both groups, according to the authors.

"It was definitely surprising and very exciting to see such a stark difference between the treatment group and the placebo group, that there was this clear separation that happened even over a short period of time," Khan said, adding that next steps will be to investigate dapagliflozin's precise molecular mechanisms that enable its effectiveness.

More information: Michael E. Nassif et al, The SGLT2 inhibitor dapagliflozin in heart failure with preserved ejection fraction: a multicenter randomized trial, *Nature Medicine* (2021). DOI: 10.1038/s41591-021-01536-x

Provided by Northwestern University