

Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

Abstract

BACKGROUND

Sodium–glucose cotransporter 2 (SGLT2) inhibitors reduce the risk of hospitalization for heart failure and cardiovascular death among patients with chronic heart failure and a left ventricular ejection fraction of 40% or less. Whether SGLT2 inhibitors are effective in patients with a higher left ventricular ejection fraction remains less certain.

METHODS

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RESEARCH SUMMARY

Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

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CLINICAL PROBLEM

Clinical guidelines recommend the use of sodium–glucose cotransporter 2 (SGLT2) inhibitors in patients with chronic heart failure and a reduced ejection fraction (a left ventricular ejection fraction of $\leq 40\%$), but the benefits in patients with a higher ejection fraction are less certain.

Dapagliflozin
10 mg daily
Usual therapy



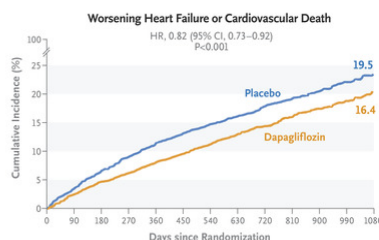
Placebo
Daily
Usual therapy



CLINICAL TRIAL

Design: An international, double-blind, randomized, placebo-controlled trial examined the efficacy and safety of the SGLT2 inhibitor dapagliflozin in patients with stabilized heart failure and a mildly reduced or preserved ejection fraction.

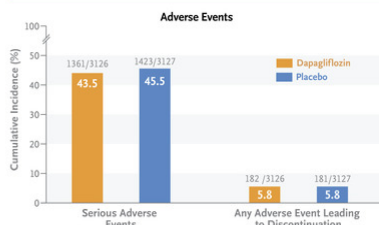
Intervention: 6263 patients 40 years of age or older with a left ventricular ejection fraction of more than 40% were assigned to receive either dapagliflozin (10 mg once daily) or placebo, in addition to usual therapy. The primary outcome was a composite of worsening heart failure (an unplanned hospitalization for heart failure or an urgent visit for heart failure) or cardiovascular death.



RESULTS

Efficacy: Overall, during a median follow-up of 2.3 years, a primary-outcome event occurred in significantly fewer patients in the dapagliflozin group than in the placebo group. A similar benefit was observed in a subgroup of patients with a left ventricular ejection fraction of less than 60%.

Safety: The incidence of serious adverse events was similar in the two groups.



LIMITATIONS AND REMAINING QUESTIONS

- Less than 5% of the patients enrolled were Black.
- All the subgroups were underpowered, so findings within subgroups should be interpreted with caution.
- Trials in higher-risk populations, or of longer duration, are needed to better assess the benefits of dapagliflozin with respect to mortality.

CONCLUSIONS

The SGLT2 inhibitor dapagliflozin reduced the risk of worsening heart failure or cardiovascular death among patients with heart failure and a mildly reduced or preserved ejection fraction, with no excess of adverse events.

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We randomly assigned 6263 patients with heart failure and a left ventricular ejection fraction of more than 40% to receive dapagliflozin (at a dose of 10 mg once daily) or matching placebo, in addition to usual therapy. The primary outcome was a composite of worsening heart failure (which was defined as either an unplanned hospitalization for heart failure or an urgent visit for heart failure) or cardiovascular death, as assessed in a time-to-event analysis.

RESULTS

Over a median of 2.3 years, the primary outcome occurred in 512 of 3131 patients (16.4%) in the dapagliflozin group and in 610 of 3132 patients (19.5%) in the placebo group (hazard ratio, 0.82; 95% confidence interval [CI], 0.73 to 0.92; $P < 0.001$). Worsening heart failure occurred in 368 patients (11.8%) in the dapagliflozin group and in 455 patients (14.5%) in the placebo group (hazard ratio, 0.79; 95% CI, 0.69 to 0.91); cardiovascular death occurred in 231 patients (7.4%) and 261 patients (8.3%), respectively (hazard ratio, 0.88; 95% CI, 0.74 to 1.05). Total events and symptom burden were lower in the dapagliflozin group than in the placebo group. Results were similar among patients with a left ventricular ejection fraction of 60% or more and those with a left ventricular ejection fraction of less than 60%, and results were similar in prespecified subgroups, including patients with or without diabetes. The incidence of adverse events was similar in the two groups.

CONCLUSIONS

Dapagliflozin reduced the combined risk of worsening heart failure or cardiovascular death among patients with heart failure and a mildly reduced or preserved ejection fraction.