The effect of dapagliflozin across the spectrum of baseline risk: a post-hoc analysis of DAPA-HF

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Funding Acknowledgement: Type of funding source: Private company. Main funding source(s): DAPA-HF was funded by AstraZeneca

Background: In DAPA-HF, compared to placebo, the sodium-glucose co-transporter 2 (SGLT-2) inhibitor, dapagliflozin, reduced the risk of cardiovascular death or worsening heart failure in patients with heart failure with reduced ejection fraction (HFrEF). The majority of patients in DAPA-HF reported mild functional limitation, however there is significant heterogeneity in prognosis among these patients.

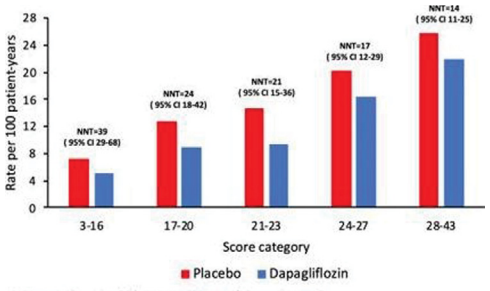
Purpose: To examine the effect of dapagliflozin compared with placebo across the spectrum of baseline risk in DAPA-HF.

Methods: The primary composite outcome of DAPA-HF was time-to-first cardiovascular death or worsening heart failure event (hospitalization for heart failure or outpatient visit requiring intravenous therapy). We examined whether the effect of dapagliflozin was modified by baseline risk, as determined by the MAGGIC (Meta-Analysis Global Group in Chronic Heart Failure) risk score based upon 13 predictive variables giving a potential maximum score of 57. The number needed to treat (NNT) to over a median follow-up of 18.2 months was calculated by applying the overall relative risk reduction in DAPA-HF (26%, 95% CI 15–35) to the proportion of patients with a primary outcome event in the placebo group of each MAGGIC risk score category (defined by quintiles of score).

Results: The MAGGIC risk score was calculable for 4740 of 4744 patients in DAPA-HF. The median score was 22 (range 3–43). The event rate for the primary outcome was 7.2 per 100 patient-years in the lowest risk score quintile and 25.7 in the highest. A 1-point increase in score was associated with an 8% increase in the risk of a primary outcome event ($p<0.001$). Dapagliflozin, compared to placebo, reduced the risk of the primary outcome across quintiles of the MAGGIC risk score (Figure - Interaction p value=0.69) and when the score was analysed as a continuous variable (Interaction p value=0.56). The NNT to prevent one primary event was 39 (95% CI 29–68) in the lowest quintile of risk scores, compared with 14 (11–25) in the highest quintile (Figure).

Similar results were found for the individual components of the primary composite outcome and for all-cause mortality.

Conclusions: DAPA-HF included patients with a wide spectrum of risk. Treatment with dapagliflozin, compared to placebo, reduced the risk of cardiovascular death or worsening heart failure, irrespective of baseline risk as measured by the MAGGIC risk score.



NNT = number needed to treat; CI = confidence interval.