ダパグリフロジンの有益性が糖尿病を合併しない心不全患者に拡大される(Late breaking Science I)

DAPA-HF試験：ダパグリフロジンはベースラインのHbA1c値に関係なく心不全を改善する

DAPA-HF: Dapagliflozin's improves heart failure outcomes regardless of baseline A1c levels

DAPA-HF試験の新たな解析の結果、SGLT-2阻害薬ダパグリフロジンの有益性が2型糖尿病治療としての効果を超えて拡大されることが示唆された、とAmerican Heart Association's Scientific Sessions 2019で発表された。追跡期間中央値18か月間に、ダパグリフロジン（1日1回10mg）は主要評価項目である心血管死または心不全増悪を、糖尿病を有する患者において25%減少させたのに対し、糖尿病を有さない患者において27%減少させた（p=0.8）。重要なことに、主要評価項目におけるダパグリフロジンの効果は、ベースラインの糖化ヘモグロビン（A1c）値に関わらず実質的に同等であった。その他の結果から、副次的評価項目に対しても同様の有益性が認められた。

Full Text

New analyses of the DAPA-HF trial suggest that the benefits of the SGLT2 inhibitor dapagliflozin extend beyond its effects as a type 2 diabetes therapy according to a Late Breaking Clinical Trial presented at the American Heart Association's Scientific Sessions 2019.

John J.V. McMurray, MD,professor of cardiology at the Institute of Cardiovascular and Medical Sciences at University of Glasgow, Scotland, presented new data that confirm benefits of treatment with dapagliflozin 10 mg once daily in patients with HF with reduced ejection fraction and no type 2 diabetes. Importantly, dapagliflozin's effect on the primary endpoint was virtually the same regardless of baseline glycosylated hemoglobin (A1c) levels.

DAPA-HF (Dapagliflozin And Prevention of Adverse-outcomes in Heart Failure) is an international, multi-center, parallel group, randomized, double-blind trial in patients with heart failure and reduced ejection fraction (LVEF ≤ 40%), with and without T2D, designed to evaluate the effect of Dapagliflozin 10mg, compared with placebo, given once daily in addition to standard of care. The primary composite outcome was time to a worsening heart failure event (hospitalization or equivalent event; i.e. an urgent heart failure visit), or cardiovascular death.

Over a median follow-up of 18 months, dapagliflozin showed benefit for the primary outcome of CV death or worsening HF, with a 27% relative risk reduction in patients without diabetes (HR = 0.73; 95% CI, 0.6-0.88) compared with 25% in patients with diabetes (HR = 0.75; 95% CI, 0.63-0.9; P for interaction = 0.8).

"Even in patients without diabetes, you see very early separation [of the primary outcome curves] — a rapidly developing benefit of dapagliflozin compared to placebo," McMurray said during a press conference.

Additional results presented show similar results for secondary outcomes, including:

- CV death or HF hospitalization: 27% relative risk reduction in patients without diabetes (HR = 0.73; 95% CI, 0.6-0.89) and 25% relative risk reduction in patients with diabetes (HR = 0.75; 95% CI, 0.63-0.9); P for interaction = 0.83.
- Total HF hospitalizations and CV death, including first and repeat hospitalizations: rate ratio = 0.73 (95% CI, 0.59-0.91) in patients without diabetes and 0.77 (95% CI, 0.63-0.94) in patients with diabetes; P for interaction = 0.74.
- Clinically meaningful change (at least 5 points) in Kansas City Cardiomyopathy Questionnaire Total Symptom Score: OR for improvement = 1.12 (95% CI, 1.03-1.22) for patients without diabetes and 1.2 (95% CI, 1.09-1.31) for patients with diabetes; P for interaction = 0.74)
- Worsening renal function, defined as a sustained 50% reduction in estimated glomerular filtration rate, end-stage renal disease or death from renal causes: HR = 0.67 (95% CI, 0.3-1.49) for patients without diabetes and 0.73 (95% CI, 0.39-1.34) for patients with diabetes; P for interaction = 0.86.
- All-cause death: 12% relative reduction in patients without diabetes (HR = 0.88; 95% CI, 0.7-1.12) and 22% relative reduction in patients with diabetes (HR = 0.78; 95% CI, 0.63-0.97); P for interaction = 0.45.

"The relative and absolute risk reductions in death and hospitalization were substantial, clinically important, and consistent in patients with and without type 2 diabetes," McMurray said.

DAPA-HF is the first outcomes trial with an SGLT2 inhibitor investigating the treatment of HF in patients with reduced ejection fraction (HFrEF), with and without type-2 diabetes (T2D). The new analyses showed the consistency of these results across patient subgroups with and without T2D, an early onset of effects, and improvement in patient-reported outcomes of HF-related health status.

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