ダパグリフロジンは糖尿病だけでなく心不全も治療する

DAPA-HF試験：ダパグリフロジンは心不全患者の死亡および入院を減少させる

DAPA-HF: Dapagliflozin reduces death and hospitalization in patients with heart failure

ダパグリフロジンは、糖尿病の有無にかかわらず駆出率の低下した心不全患者の死亡および入院を減少させた、とのDAPA-HF試験のレイトブレイキングの結果がESC Congress 2019 のHot Line Session で発表された。追跡期間中央値18.2か月の間に、一次エンドポイントを発現したのはダパグリフロジン群で16.3% であり、プラセボ群では21.2% であった（p<0.00001）。一次エンドポイントの構成要素はさらに、個別に解析された。ダパグリフロジン投与群の10% およびプラセボ投与群の13.7% が初回の心不全増悪を経験した（p<0.00004）。心血管系が原因で死亡したのは、それぞれ9.6% および11.5% であった（p=0.029）。

Full Text

Dapagliflozin reduces death and hospitalization in patients with heart failure and reduced ejection fraction with and without diabetes. The late breaking results of the DAPA-HF trial are presented in a Hot Line Session at ESC Congress 2019 together with the World Congress of Cardiology.

Principal investigator Professor John McMurray of the University of Glasgow, UK said: "The most important finding of all is the benefit in patients without diabetes. This is truly a treatment for heart failure and not just a drug for diabetes."

Sodium-glucose cotransporter 2 (SGLT2) inhibitors including dapagliflozin reduce the risk of developing heart failure in patients with type 2 diabetes. The DAPA-HF trial investigated whether dapagliflozin was also useful in treating established heart failure, even in patients without diabetes.

The trial enrolled 4,744 patients with heart failure and reduced ejection fraction in 20 countries and randomly allocated them to either dapagliflozin 10 mg once daily or matching placebo. The primary endpoint was the composite of a first episode of worsening heart failure (hospitalization for heart failure or an urgent heart failure visit requiring intravenous therapy) or death from cardiovascular causes.

The allocated treatments were given on top of standard care: 94% received an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker or angiotensin receptor–neprilysin inhibitor; 96% took a beta-blocker; and 71% took a mineralocorticoid receptor antagonist.

Over a median follow-up of 18.2 months, the primary outcome occurred in 386 of 2,373 patients (16.3%) in the dapagliflozin group and in 502 of 2,371 patients (21.2%) in the placebo group (hazard ratio [HR] 0.74; 95% confidence interval [CI] 0.65–0.85; p<0.00001).

The components of the primary outcome were also analyzed separately. A total of 237 patients (10.0%) receiving dapagliflozin and 326 patients (13.7%) receiving placebo experienced a first episode of worsening heart failure (HR 0.70; 95% CI 0.59–0.83; p<0.00004) and 227 (9.6%) and 273 (11.5%), respectively, died from cardiovascular causes (HR 0.82; 95% CI 0.69–0.98; p=0.029).

Regarding side effects, 178 patients (7.5%) in the dapagliflozin group had an adverse event related to volume depletion compared to 162 (6.8%) in the placebo group, with no significant difference between groups. Adverse events related to renal dysfunction occurred in 153 patients (6.5%) in the dapagliflozin group versus 170 patients (7.2%) in the placebo group, with no significant difference between groups. Major hypoglycemia and lower limb amputation and fracture were infrequent and occurred at similar rates in the two treatment groups.

Prof McMurray said: "Adverse events rarely required the discontinuation of treatment. There was no notable excess of any serious adverse event in the dapagliflozin group."

He concluded: "The trial shows that dapagliflozin reduces death and hospitalization, and improves health- related quality of life, in patients with heart failure and reduced ejection fraction, with and without diabetes. The clinical implications are potentially huge – few drugs achieve these results in heart failure and dapagliflozin does even when added to excellent standard therapy."

The DAPA-HF trial was funded by AstraZeneca. Professor McMurray's employer, Glasgow University, was paid by AstraZeneca for his role as Principal Investigator in the DAPA-HF trial with dapagliflozin.

Conference News