Amino-terminal pro-B type natriuretic peptide in the Canagliflozin Cardiovascular Assessment Study (CANVAS).

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Introduction: Among patients with type 2 diabetes (T2D) and high cardiovascular (CV) risk, compared to placebo, treatment with canagliflozin significantly reduced risk for hospitalized heart failure (HHF) or CV death, with a non-significant trend toward lower risk for all-cause death. Amino-terminal pro-B type natriuretic peptide (NT-proBNP) concentrations ≥125 pg/mL are associated with HF diagnosis and may predict risk.

Hypothesis: Patients in CANVAS will have NT-proBNP levels consistent with a high risk population. Concentrations of NT-proBNP will be affected by canagliflozin treatment and prognosticate outcomes.

Methods: NT-proBNP was measured in 3587, 2918, and 995 participants at baseline, 1 year and 6 years, respectively. Distribution of NT-proBNP concentrations was assessed. Effects of treatment with canagliflozin on NT-proBNP was evaluated. Ability of baseline NT-proBNP concentrations to predict HHF, HHF/CV death, or all-cause death during a mean follow up of 226 weeks was calculated.

Results: At baseline, study participants (mean age 62.7 years, 13% with prior HF) had a median NT-proBNP of 91 pg/mL; 39.3% had an NT-proBNP concentration ≥125 pg/mL. Concentrations of NT-proBNP were higher in those with a history of HF compared to those without (187 vs 81 pg/mL); however, substantial overlap of NT-proBNP distribution between these two groups was present. During follow up, NT-proBNP increased in the placebo arm; in contrast, treatment with canagliflozin resulted in less NT-proBNP change by 1 year (β = -0.118 [95% confidence intervals -0.170, -0.065]; P <.001), with lower concentrations of NT-proBNP at 1 and 6 years in patients treated with canagliflozin compared to placebo (both P <0.001). In adjusted models, baseline NT-proBNP ≥125 pg/mL was substantially prognostic for subsequent HHF (hazard ratio [HR] 5.07 [2.18, 11.8]; P < .001), HHF/CV death (HR 4.91 [2.84, 8.48]; P < .001) and all-cause death (HR 4.46 [2.42, 8.19]; P < .001). No interaction between biomarker and treatment was detected. Compared to those with NT-proBNP <125 pg/mL, allocation to canagliflozin vs placebo was associated with similar relative (but greater absolute) reduction of risk for HHF, HHF/CV death and all-cause death.

Conclusions: A significant percentage of patients in CANVAS had higher NT-proBNP concentrations despite lacking history of HF. Treatment with canagliflozin reduced NT-proBNP. Elevated NT-proBNP identified a patient with T2D at high risk for CV events or death.