Medical trial meets one primary endpoint in heart failure with preserved ejection fraction

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Sacubitril/valsartan reduces NT-proBNP, a biomarker predictive of long-term clinical outcomes in heart failure, but does not improve functional capacity compared to individualized background therapy in patients with heart failure with preserved ejection fraction. That's the main finding of the PARALLAX trial presented in a Hot Line session today at ESC Congress 2020.

Heart failure with preserved ejection fraction (HFpEF) affects approximately half of patients with heart failure. Prevalence is expected to rise with the aging population and increased rates of risk factors such as hypertension, diabetes, obesity and atrial fibrillation. Patients are often highly symptomatic, with shortness of breath, reduced ability to exercise, impaired quality of life, and frequent rehospitalisations.

There is currently no approved therapy to reduce morbidity and mortality in patients with HFpEF. Treatment recommendations mainly focus on symptom relief with diuretics and treating comorbidities, typically with inhibitors of the renin-angiotensin system (RAS) including angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs).

The PARAGON-HF outcome trial suggested that sacubitril/valsartan may reduce heart failure hospitalisations in HFpEF patients compared to valsartan (an ARB). However, in daily practice, not all HFpEF patients receive an ARB. Many take an ACE inhibitor, and some no RAS inhibitor at all.

PARALLAX therefore tested the effects of sacubitril/valsartan versus optimal individualized background therapy, which could be the ACE inhibitor enalapril, the ARB valsartan, or placebo. The co-primary endpoints were chosen to assess heart failure severity and functional capacity: 1) change from baseline to 12 weeks in plasma N-terminal pro B-type natriuretic peptide (NT-proBNP); and 2) change in six-minute walk distance from baseline to 24 weeks.

A total of 2,572 HFpEF patients were randomly allocated to sacubitril/valsartan or their current RAS medication (enalapril, valsartan or placebo if they were not taking a RAS inhibitor). Patients in the trial had a mean age of 73 years and 51% were women. The mean left ventricular ejection fraction at baseline was 56%.

The trial met the first primary endpoint: after 12 weeks, patients treated with sacubitril/valsartan showed a highly significant 16.4% greater reduction in NT-proBNP than patients treated with optimal individualized medical therapy (p