PARALLAX: Sacubitril/Valsartan versus Individualized RAAS Blockade in Patients with HFpEF

Purpose: To evaluate the effect of sacubitril/valsartan (S/V) in comparison to individualized medical therapy (IMT) for cardiovascular and related co-morbidities on NT-proBNP, functional capacity, symptoms, and quality of life in patients with HF and ejection fraction (EF) >40%

Trial Design: N=2566, 24 week randomized, double blind parallel-group, active controlled, or placebo-controlled trial in patients with LVEF >40%, New York Heart Association (NYHA) class II–IV symptoms, elevated NT- proBNP, and evidence of structural heart disease. The optimal individualized background therapy was either ACE inhibitor enalapril, ARB valsartan or placebo.

Primary Endpoints: Change in plasma NT-proBNP concentration from baseline to 12 weeks and the change from baseline in functional capacity (6 min walk distance) at 24 weeks

Secondary: Quality of life (Kansas City Cardiomyopathy Questionnaire; KCCQ) and NYHA functional class

Exploratory endpoints: Change in eGFR, HF hospitalization and HF death

	Sacubitril/ Valsartan	Individualized Medical Therapy	P value
Adjusted geometric mean ratio of NT-proBNP at Week 12 vs baseline	0.83 (N=1203) Adjusted geometric mean ratio at Week 12 (S/V vs IMT): 0.84	0.98 (N=1216)	p<0.0001
6-minute Walk Distance at 24 weeks vs baseline	Adjusted Mean change= 9.7m (5.4,14.0)	Adjusted Mean change=12.2m (7.9, 16.5)	P=0.79
KCCQ-CSS at week 24 (LSM change from baseline)	12.3 (95% CI 11.3-13.4) LSM difference (S/V vs IMT): 0.52(-0.93,1.97)	11.8 (95% CI 10.8-12.8)	P=0.48
NYHA class- change from baseline at Week 24	OR (95% CI) (S/V vs IMT): 1.01 (.075,1.37)		P=0.93
First Hospitalization due to HF	HR (95% CI): 0.49 (0.30,0.81)		P=0.005
Composite of time to death due to cardiac failure or HF hospitalization	HR (95% CI): 0.64 (0.42,0.97)		P=0.034

Results: Sacubitril/Valsartan demonstrated significant reduction in NT-proBNP, though no additional benefits on NYHA class and 6min walk distance. Quality of life improved after 4 weeks but no longer after 24 weeks. There was reduced HF hospitalizations and slowed the decline in renal function compared to IMT. The results are consistent with the findings from PARAGON-HF (LVEF≥45%).

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