NTproBNP over 12 weeks. Key secondary endpoints included functional status based on 6-minute walk test, and change in KCCQ. Exploratory endpoints included hospitalizations for HF and urgent HF visits. **Results:** Enrollment in DEFINE-HF was completed in March 2019, with last visit scheduled in June. Baseline characteristics are consistent with other trials of high risk HFrEF patients, and are shown in the Table. Topline study results will be available in July 2019, in time for presentation at HFSA 2019. **Conclusion:** DEFINE-HF is the first dedicated multicenter randomized double-blind placebo-controlled trial of SGLT-2i in patients with established HFrEF with and without T2D. It will assess whether the SGLT2i dapagliflozin improves HF biomarkers, symptoms and functional status in this high-risk patient population.

Baseline Characteristics	
Male	193 (73.4%)
Age (years)	61.3 ± 11.5
KCCQ-os	67.3 ± 21.5
African American	97 (39.1%)
ICD	164 (62.4%)
NYHA III	91 (35.6%)
Ejection fraction (%)	26.4 ± 8.1
Diabetes	164 (62.4%)
Hx HF hosp	206 (78.3%)
Atrial Fibrillation	104 (39.5%)
NTproBNP (pg/mL)	1936 ± 2272
eGFR (mL/min)	69.2 ± 22.2
ACE/ARB	142 (54.5%)
ARNI	79 (30.0%)
Beta blockers	243 (92.4%)
MRA	155 (58.9%)
Loop diuretics	218 (82.9%)

Effects of Sacubitril-valsartan Compared with Enalapril on Arterial Hemodynamics, Cardiac Remodeling, and Quality of Life in Patients with Heart Failure and Reduced Ejection Fraction

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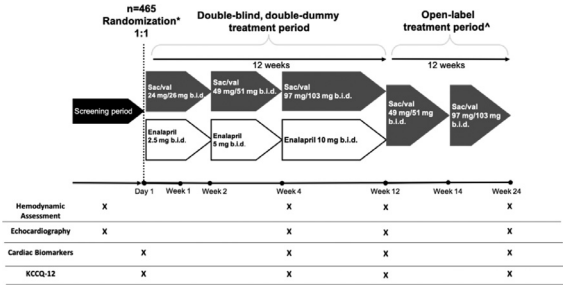
Background: Compared to angiotensin-converting enzyme inhibition alone, angiotensin receptor-neprilysin inhibition reduces cardiovascular mortality and heart failure (HF) hospitalization in patients with HF and reduced ejection fraction (HFrEF). The pathophysiologic mechanisms responsible for these clinical benefits remain unclear but may be related to effects on central hemodynamics and cardiac structure and function. We sought to determine whether treatment of HFrEF with sacubitril/valsartan improves central aortic stiffness, cardiac remodeling, biomarkers of wall stress and injury, and quality of life compared with enalapril. **Methods:** EVALUATE-HF was a prospective, randomized, multicenter, double-blind, double-dummy clinical trial of patients aged 50 or older with chronic HF, NYHA I-III symptoms, and EF of 40% or less. Participants were randomized 1:1 to treatment with sacubitril/valsartan (target dose 97/103 mg twice daily) versus enalapril (target dose 10 mg twice daily) for 12 weeks followed by open-label sacubitril/valsartan for 12 weeks (**Figure**). The primary study outcome was between group difference in change from baseline to week 12 in aortic characteristic impedance (Zc). Other prespecified outcomes included change from baseline to week 12 in levels of cardiac biomarkers and echocardiographic measures of cardiac structure and function as well as change in health-related quality of life assessed by the 12-item Kansas City Cardiomyopathy Questionnaire (KCCQ-12). **Results:** Between August 17, 2016 and January 26, 2019 we randomized 464 participants at 85 sites in the United States, of whom 231 were randomly assigned to sacubitril/valsartan and 233 to enalapril. For the overall population, mean age was 67.3 +/- 9.1 years, mean EF was 34 +/- 10%, median NTproBNP was 584 [IQR 244, 1467], 109 (23.5%) were female, 115 (24.8%) were black, 313 (67.4%) reported NYHA Class 2, and 391 (84.3%) were previously treated with an ACEi or ARB. We will present the primary results of the EVALUATE-HF study as initially submitted to the 2019 European Society of Cardiology Scientific Sessions, including the effects of sacubitril/valsartan compared with enalapril on change from baseline in central aortic stiffness, cardiac biomarkers, cardiac structure and function. We will also present new data regarding the time course and magnitude of changes in quality of life in both treatment groups during study follow up as well as the relationship of these changes to changes in cardiac structure, function, and biomarkers. **Conclusions:** EVALUATE-HF will provide important mechanistic insights into established clinical benefits of sacubitril/valsartan in HFrEF. We will present detailed quality of life outcomes for the first time at HFSA 2019.



Primary Results of the Sensible Medical Innovations Lung Fluid Status Monitor Allows Reducing Readmission Rate of Heart Failure Patients (smile) Trial

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Background: Acute decompensated heart failure (ADHF) is associated with a high rate of readmissions and mortality. Remote dielectric sensing (ReDS) fluid monitoring provides an accurate tool for non-invasive measurement of absolute lung fluid content, providing actionable information and a new tool for managing HF. **Methods:** The SMILE trial was a prospective, multicenter, randomized clinical trial testing the hypothesis that post-discharge HF management guided by frequent in-home ReDS assessment is superior to usual care. Patients with a current hospitalization for ADHF, regardless of the LVEF, were enrolled in 43 US centers. Subjects randomized to the treatment arm were discharged home with the ReDS fluid monitor system and managed using ReDS measurements, according to protocol-defined algorithms. Control patients received usual care, without ReDS. The primary endpoint was recurrent (cumulative) ADHF hospitalizations, analyzed using the Andersen-Gill model with treatment group as the only covariate. Patients were followed for up to 9 months, until the last patient enrolled reached 3 months of follow-up. **Results:** Between October 2015 and October 2017, 268 patients were randomized - 135 to treatment and 133 to control - and followed for 6.1±3.4 months. Patients were aged 68±12 years; 30% were women and 29% had LVEF≥40%. Pre-specified analysis of the per-protocol cohort demonstrated 21 readmissions in 15 ReDS patients compared to 43 readmissions in 34 control patients (HR 0.52, 95% CI [0.31-0.87], P=0.01) or a 48% readmissions reduction (Figure). Subgroup analysis by LVEF < or ≥40% showed similar reductions in ADHF readmissions (RRR 50%, P=0.03 and 46%, P=NS, respectively), with ReDS-guided HF management. Number of days lost to ADHF hospitalization was lower (1.37 vs. 2.62 days, 48% reduction, P=0.006) and time from discharge to first ADHF readmission was longer (HR 0.45, 95% CI [0.25-0.83], P=0.01), for ReDS-guided management. There was no significant difference in mortality between groups. **Conclusions:** The SMILE trial demonstrates a substantial reduction in recurrent ADHF hospitalizations and improvement in other outcome measures in recently discharged ADHF patients managed using daily ReDS assessment of absolute lung fluid content.