mixed hATTR phenotype and are to receive specific disease modifying therapies, either Patisiran or Inotersen.

CONCLUSION: Patients with hATTR-CM can display a wide range of neurological symptoms. In this study, we were able to identify a significant number of patients with abnormal neurological tests in the absence of obvious neurologic signs and symptoms suggesting TTR-PN. Therefore, patients with hATTR-CM should be systematically referred to a specialised neurologist for routine assessment.

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ECHOCARDIOGRAPHIC EVALUATION OF LEFT VENTRICULAR REMODELING AFTER VALSARTAN/SACUBITRIL INITIATION IN PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION

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BACKGROUND: In PARADIGM-HF, Valsartan/Sacubitril (ARNI) therapy was shown to reduce morbidity and mortality compared to ace-inhibitor (ACE-I) therapy in Heart Failure with Reduced Ejection Fraction (HFrEF). However, PARADIGM-HF did not report echocardiographic findings which may provide a mechanism for the observed improvement in clinical outcomes. ACE-I, mineralocorticoid receptor antagonist (MRA) and beta-blockers have previously demonstrated favorable left ventricular (LV) remodeling. We sought to analyze echocardiographic markers of cardiac remodeling before and after ARNI therapy.

METHODS AND RESULTS: We conducted a blinded retrospective cohort study at a regional cardiovascular center. All HFrEF patients who had 3 months of stable disease on optimal background therapy with ACE-I, Beta-blocker and MRA (where tolerated) who were newly switched to maximal dose ARNI therapy were screened for inclusion. Only patients who previously had an echocardiogram within 6 months prior to ARNI initiation and a second echocardiogram within 3 to 12 months after initiation were included. Patients who had adjustments to other HFrEF therapies (such as beta-blockers or MRA) between follow-up echocardiograms were excluded from the study. Following inclusion, all echocardiograms (pre and post ARNI initiation) were re-evaluated by a single cardiologist reviewer in a blinded fashion under the same protocol in order to decrease the variability and reviewer bias. LV end systolic volume index (LVESVi) was the pre-specified primary outcome. We screened 252 HFrEF patient charts. 21 patients met inclusion criteria and their echocardiograms were re-evaluated in a blinded manner. The primary reason for exclusion was lack of available pre and post echocardiograms. Mean age was 67 and 81% were male. Prior to ARNI initiation, the mean LVEF was 34%, 67% of patients had ischemic cardiomyopathy and 81% of patients had New York Heart Association class II symptoms. Mean LVESVi was significantly reduced from 49.4 ml/m2 at baseline to 37.4 ml/m2 post-ARNI initiation (mean reduction 11.9 ml/m2, 95% CI -22.2, -1.7). Among secondary outcomes, LVEF was significantly increased by a mean 10.9% (95% CI 5.0, 16.8) and right ventricular systolic pressure was significantly reduced by a mean 6.7 mmHg (95% CI -11.5, -1.9). There was no significant reduction in LV end diastolic volume index (mean reduction -7.1 ml/m2, 95% CI -17.0, 2.8) or significant increase in stroke volume (mean increase 4.6 mL, 95% CI -4.5, 13.7).

CONCLUSION: This study demonstrates significant improvements in multiple echocardiographic parameters following ARNI optimization in HFrEF patients, suggesting favorable LV remodeling. This may provide a mechanistic explanation for the benefits of ARNI therapy in HFrEF.

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EFFECTIVENESS, SAFETY, AND TOLERABILITY OF SACUBITRIL/VALSARTAN OVER 3 YEARS OF FOLLOW-UP IN CANADIAN PRACTICE: INSIGHTS FROM THE PARTHENON REGISTRY

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BACKGROUND: The PARADIGM-HF trial demonstrated the superiority of sacubitril/valsartan over enalapril in reducing the risk of CV death or HF hospitalization in patients with HFrEF. The generalisability of these data as well as safety and medication persistence to unselected, real world patients remained to be evaluated. The PARTHENON (PAtient RegisTry assessing effectiveness and safety of HEart failure treatment with LCZ696 acrOss CaNada) registry study was conducted to evaluate the effects of sacubitril/valsartan use in Canadian patients with HFrEF.

METHODS AND RESULTS: PARTHENON was an observational, naturalistic, multi-centre study of Canadian patients with HFrEF who were initiated on sacubitril/valsartan as per the Canadian label within 3 months prior to study start. Over a 3-year period, 996 patients from 32 community and academic centres across 7 provinces were followed. Total daily dosage of sacubitril/valsartan at initiation and at each annual timepoint are shown in Figure 1. At baseline, most (699/996; 70.2%) were initiated on 100 mg daily. By 12 months, 47.5% of patients (n=401/844) were at the maximum daily dosage of 400 mg, with 26.3% of patients receiving 200 mg daily, and 20.4% receiving 100 mg daily. The observed 3-year all-cause mortality rate was 10.8%, which was lower than the 3-year all-cause mortality rate of 29.0 $\pm$ 13.7% predicted by the MAGGIC risk score; the projected 3-year survival rate of 53.4 $\pm$ 26.4% from the Seattle Heart Failure Model was also lower than the observed 89.2% survival rate. Several a priori defined secondary safety-related endpoints are summarized in Table 1. For patients who experienced an AE, 354 (35.5%) were suspected by the investigator to be related to sacubitril/