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Title: *Comparison of Angiotensin Converting Enzyme Inhibitor vs. Sacubitril/valsartan in Patients with Heart Failure with Reduced Ejection Fraction: A Retrospective Study*

Abstract

Purpose: The 2017 ACC/AHA/HFSA Heart Failure Guidelines recommend patients with chronic symptomatic heart failure with reduced ejection fraction (HFrEF) tolerating an angiotensin converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB) replace the ACEi or ARB with an angiotensin receptor-neprilysin inhibitor (ARNI). This is based off of the PARADIGM-HF trial that compared sacubitril/valsartan vs. enalapril 10 mg twice daily. The study's limitations include strict inclusion criteria and submaximal target dose for enalapril. The purpose of this study is to further evaluate morbidity and mortality outcomes between sacubitril/valsartan and ACEi in patients with HFrEF in a real-world setting.

Methods: We performed a single-center retrospective chart review to compare clinical outcomes with treatment of ACEi vs. valsartan/sacubitril in patients hospitalized with HFrEF from December 2017 to May 2019. The protocol was approved by institutional and university institutional review boards. Data was collected from the electronic health record and was inputted into Microsoft Excel. A separate coding sheet was utilized to keep protected health information private. Patients were included if they were admitted to the hospital, had a diagnosis of heart failure with reduced ejection fraction (HFrEF) and received either sacubitril/valsartan or an ACEi during the hospital encounter and at discharge. Data was collected in 77 patients in the sacubitril/valsartan group and 77 patients in the ACEi group, matched by month of admission. The primary outcome was a composite endpoint of cardiovascular death and hospitalizations due to HF exacerbation. Secondary outcomes were total number of hospitalizations due to a heart failure exacerbation and average time to subsequent hospitalizations. Safety outcomes were angioedema, hypotension, and acute kidney injury. The nominal data were analyzed by chi-squared test and continuous data were analyzed by unpaired t-test.

Results: Seventy-seven patients were included in each group. There were 28.6% of patients in the sacubitril/valsartan group and 35.1% patients in the ACEi group who experienced the primary outcome ($p = 0.489$). The incidence of cardiovascular death was 6.5% in the sacubitril/valsartan group and 9.1% in the ACEi group ($p = 0.765$); all-cause mortality rates were 9.1% in sacubitril/valsartan group and 10.4% in the ACEi group ($p = 1.000$). The incidence of hospitalization due to a heart failure exacerbation was 24.7% in the sacubitril/valsartan group and 32.5% in the ACEi group ($p = 0.373$). The total number of subsequent hospitalizations due to a heart failure exacerbation after being included in the study was 31 hospitalizations (0.40 hospitalizations per patient) in the sacubitril/valsartan group and 42 hospitalizations (0.55 hospitalizations per patient) in the ACEi group ($p = 0.353$). Of the patients who were hospitalized due to a heart failure exacerbation, the average time to hospitalization was 78.8 days in the sacubitril/valsartan group and 100.7 days in the ACEi group ($p = 0.401$). There were 37.7% of patients in the sacubitril/valsartan group and 42.9% of patients in the ACEi group who experienced at least one of the safety outcomes ($p = 0.622$).

Conclusion: Sacubitril/valsartan did not result in a significantly lower rate of cardiovascular deaths and hospitalizations due to a heart failure exacerbation compared to ACEi in our real-world group of patients with HFrEF. There was no statistically significant difference in rates of adverse events between the two

groups. Further research is warranted to assess outcomes between these treatments in a real-world setting, including assessing potential effects of attempted titration to target dosing.