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

Vincent Chau, PharmD Candidate & Jared Sheley, PharmD, BCPS

Southern Illinois University Edwardsville

Southern Illinois University Edwardsville School of Pharmacy

BACKGROUND

- The 2017 ACC/AHA/HFSA Heart Failure Guidelines recommend patients with chronic heart failure with reduced ejection fraction (HFrEF) tolerating an angiotensin converting enzyme (ACEi) or angiotensin II receptor blocker (ARB) replace the ACEi or ARB with an angiotensin receptor neprilysin inhibitor (ARNI).[1]
- This recommendation is based off the findings of the PARADIGM-HF trial that compared sacubitril/valsartan to enalapril.[2]
- The PARADIGM-HF trial had limitations of strict inclusion criteria and submaximal target dose for enalapril.[2]

OBJECTIVE

- 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

Study Design

- Single-centered, retrospective chart review from December 2017 to May 2019

Inclusion Criteria

- Admitted to the hospital
- Had a diagnosis of HFrEF or had a documented ejection fraction of less than or equal to 40%
- Received either sacubitril/valsartan or an ACEi during the hospital encounter and at discharge

Outcome Measures

- **Primary outcome:**
  - Composite endpoint of cardiovascular death and hospitalizations due to a heart failure exacerbation
- **Secondary outcomes:**
  - Total number of hospitalizations due to a heart failure exacerbation
  - Average time until subsequent hospitalizations
- **Safety outcomes:**
  - Angioedema
  - Hypotension
  - Acute kidney injury

Data Analysis

- Nominal data were analyzed by chi-squared test
- Continuous data were analyzed by unpaired t-test

RESULTS

Table 1: Patient Characteristics

Characteristics	Sacubitril/valsartan n= 77	ACEi n= 77
Age	66.47 ± 13.60	64.21 ± 13.11
Gender		
Male	58/77 (75.3%)	51/77 (66.2%)
Female	19/77 (24.7%)	26/77 (33.8%)
Ethnicity		
Caucasian	57/77 (74.0%)	58/77 (75.3%)
African American	19/77 (24.7%	18/77 (23.4%)
Other	1/77 (1.3%)	1/77 (1.3%)
Co-morbidities		
Atrial fibrillation	38/77 (49.4%)	34/77 (44.2%)
Coronary artery disease	46/77 (59.7%)	42/77 (54.5%)
Diabetes mellitus	39/77 (50.6%)	38/77 (49.4%)
Smoking Status		
Current smoker	7/77 (9.1%)	21/77 (27.3%)
Former smoker	39/77 (50.6%)	30/77 (39.0%)
Never smoked	31/77 (40.3%)	26/77 (33.8%)
Average ejection fraction (%)	28%	28%
NYHA Class		
II	22/77 (28.6%)	12/77 (15.6%)
III	30/77 (39.0%)	33/77 (42.9%)
IV	25/77 (32.5%)	32/77 (41.6%)
CrCl at time of inclusion (mL/min)	70 (71 patients)	67 (76 patients)

Table 2: Guideline-directed medical therapy (GDMT) for heart failure used with average dosage

Medications	Sacubitril/valsartan n= 77	Average Daily Dose (mg)	ACEi n= 77	Average Daily Dose (mg)
Aldosterone antagonist use	31/77 (40.3%)	-	30/77 (39.0%)	-
Sacubitril/valsartan use	77/77 (100%)	116.56 mg	-	-
# of patients at target dose	2/77 (2.6%)	-	-	-
ACEi use	-	-	77/77 (100%)	-
# of patients at target dose			19/77 (24.7%)	-
Lisinopril			72/77 (93.5%)	11.18 mg
Other*			5/77 (6.5%)	-
Beta blocker use	74/77 (96.1%)	-	71/77 (92.2%)	-
GDMT beta blocker†	**73/77 (94.8%)**		**58/77 (75.3%)**	
# of patients at target dose	5/77 (6.5%)	-	2/77 (2.6%)	-
Carvedilol	45/77 (58.4%)	23.19 mg	32/77 (41.6%)	21.09 mg
Metoprolol succinate	28/77 (36.4%)	40.63 mg	26/77 (33.8%)	62.98 mg
Metoprolol tartrate††	1/77 (1.3%)	25 mg	10/77(13.0%)	117.5 mg
Sotalol††	-	-	2/77 (2.6%)	160 mg
Propranolol††	-	-	1/77 (1.3%)	80 mg

* (2 ramipril, 1 captopril, 1 enalapril, 1 quinapril)
† statistically significant, p = 0.0006
†† Not a GDMT medication for HFrEF

Table 3: Primary and Secondary Efficacy Outcomes

Outcome	Sacubitril/valsartan n =77	ACEi N= 77	p-value
Primary composite outcome			
CV Death or hospitalizations due to HF	22/77 (28.6%)	27/77 (35.1%)	0.489
CV Death	5/77 (6.5%)	7/77 (9.1%)	0.765
Hospitalized due to HF	19/77 (24.7%)	25/77 (32.5%)	0.373
Secondary Outcomes			
Total # of hospitalizations due to HF	31 hospitalizations	42 hospitalizations	0.353
Average time until subsequent hospitalizations due to HF	78.8 days	100.7 days	0.401

Figure 1: Primary Outcome

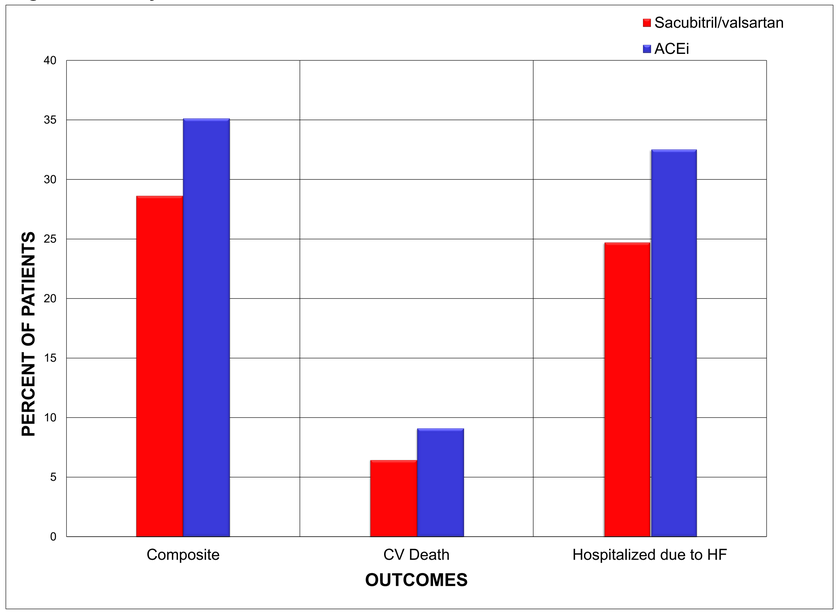

Table 4: Safety Outcomes

Outcome	Sacubitril/valsartan n =77	ACEi N= 77	p-value
Safety Outcome (composite)	29/77 (37.7%)	33/77 (42.9%)	0.622
Hypotension	23/77 (29.9%)	21/77 (27.3%)	
Acute kidney injury	14/77 (18.2%)	21/77 (27.3%)	
Angioedema	0/77 (0%)	1/77 (1.3%)	

LIMITATIONS

- An initial goal was to compare efficacy outcomes when sacubitril/valsartan and ACEi has reached target dose; however, there were not many patients that achieved target dose.
- There were more patients on GDMT beta blockers for HFrEF in the sacubitril/valsartan group compared to ACEi group (p = 0.0006).
- Unable to determine when medications were initiated and titrated based off a chart review from a hospital; ambulatory care clinic chart review may provide clearer clinical picture.

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 patients from HSHS St. Elizabeth's Hospital with HFrEF.
- Further research is warranted to assess outcomes between these treatments in real world setting, including assessing potential effects of attempted titration to target dosing.

CONTACT / DISCLOSURES

- Vincent Chau: Nothing to Disclose; vchau@siue.edu
- Jared Sheley: Nothing to Disclose

References:

1. Yancy CW, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Card Fail. 2017 Aug;23(8):628-651.
2. McMurray JJ, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014 Sep 11;371(11):993-1004.