FIRST LINE THERAPY IN HEART FAILURE: ARNI vs ACE-I/ARB

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12/13/2019

Disclosures
- No conflicts of interest to disclose

Abbreviations
- ACCF/AHA = American College of Cardiology Foundation/American Heart Association
- ACE-I = Angiotensin converting enzyme inhibitor
- ADHF = Acute decompensated heart failure
- ARB = Angiotensin receptor blocker
- ARNI = Angiotensin receptor neprilysin inhibitor
- ANP = Atrial natriuretic peptide
- BNP = B-type or brain natriuretic peptide
- BP = Blood pressure
- CI = Confidence intervals
- CV = Cardiovascular disease
- HF = Heart failure
- HFrEF = Heart failure reserved ejection fraction
- HFpEF = Heart failure preserved ejection fraction
- LVEF = Left ventricular ejection fraction
- NT-proBNP = N terminal pro B natriuretic peptide
- RAAS = Renin angiotensin aldosterone system

Objectives
- Review epidemiology and pharmacologic recommendation of heart failure
- Discuss updated 2017 American Cardiology of College Foundation/American Heart Association (ACCF/AHA) guidelines on its recommendation of angiotensin receptor neprilysin inhibitor (ARNI) and place in therapy
- Compare ACE-Inhibitor and ARNI
- Evaluate literature investigating efficacy and safety of ARNI
- Provide evidence based recommendation on appropriate use of ARNI

Patient Case

- TC is a 58 year old African American male with a PMH of hypertension, diabetes, hyperlipidemia, and asthma. At his office visit 2 days ago, he was diagnosed with HFrEF NYHA II. The physician asked for your recommendation on treatment for this patient.

Patient Case

Current medications:
- Lisinopril 20 mg daily
- Metformin ER 1000 mg BID
- Invokana 100 mg daily
- Rosuvastatin 20 mg daily
- Flovent 110 mcg inhaler 1 puff bid
- Albuterol HFA inhaler 1 puff Q4-6 hours prn

Allergies:
- NKDA
- Father has hypertension

Social history:
- (-) tobacco, (-) alcohol, 1 cup of coffee daily
Patient Case

- Vitals:
  - BP: 126/78 mmHg
  - Pulse: 80 bpm
  - Weight: 86 kg
  - Height: 68 in
  - BMI: 27.4
- Labs:
  - A1C: 6.8%
  - Scr: 1.1 mg/dL
  - K: 4.0 mEq/L
  - Ca: 8.5 mg/dL
  - WBC: 7.4 x 10^9 cells/L
- ECHO:
  - EF: 35%
- Lipid Panel:
  - TC: 163 mg/dL
  - HDL: 31 mg/dL
  - LDL: 96 mg/dL
  - TG: 161 mg/dL

Epidemiology

- Global pandemic
  - 26 million people worldwide
  - 5.8 million people in the United States
- Nearly 1 million hospitalizations per year
  - Common in people over 65
  - About 83% of patients are hospitalized due to an acute HF episode at least once
- 1 in 9 deaths included heart failure as a contributing cause
- Estimated health expenditure of around $31 billion dollars per year

Heart failure

- ACCF/AHA definition: “a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood”
- Common causes: hypertension and coronary artery disease

HFrEF

- Left ventricle is enlarged and heart is not able to pump enough blood to the rest of the body
- Ejection fraction < 40%
- Pharmacologic treatment have demonstrated efficacy

HFpEF

- Heart contract normally but the ventricles are not relaxed and cannot fill up all the way. Results in less blood being pumped to the rest of the body
- Ejection fraction > 50%
- Pharmacologic treatment dependent on comorbidities (HTN, CAD, AF, DM)

Classification

<table>
<thead>
<tr>
<th>NYHA Functional Classification</th>
<th>Acute/Non-acute Stages</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>A</td>
</tr>
<tr>
<td>No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>C</td>
</tr>
<tr>
<td>Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>D</td>
</tr>
<tr>
<td>Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.</td>
<td></td>
</tr>
</tbody>
</table>

BACKGROUND
2013 ACCF/AHA pharmacologic recommendations

HFrEF Stage C
NYHA Class I – IV Treatment

ACE-I or ARB AND beta blocker

2017 ACCF/AHA pharmacologic recommendations

Recommendations for Renin-Angiotensin System inhibition with ACE inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A</td>
<td>ACE-I: A</td>
</tr>
<tr>
<td>I</td>
<td>A</td>
<td>ARB: A</td>
</tr>
<tr>
<td>I</td>
<td>B-R</td>
<td>ARNI: B-R</td>
</tr>
</tbody>
</table>

The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors or ARBs or ARNI in conjunction with evidence-based beta blockers and aldosterone antagonists in selected patients, is recommended for patients with chronic HFrEF to reduce morbidity and mortality.

In patients with chronic symptomatic HFrEF NYHA Class II or III who tolerate and ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.

COMPARISON OF ACE-I VS ARNI

Target pathways of heart failure

RAAS

- Sodium and water retention
- Vasoconstriction
- Increased aldosterone level
- Increased sympathetic tone
- Cardiac remodeling

Counter-regulates the upregulation of RAAS

Natriuretic peptide system

- Causes direct vasodilation
- Increases glomerular filtration rate

Natriuretic peptide system

MEDICATIONS:
- ACE-I
- ARB

MEDICATION:
- Neprilysin inhibitor

ACE-Inhibitor

- Standard of therapy for almost 30 years in patients with heart failure
- Reduces hospitalization and mortality
- Trials that demonstrated its efficacy:
  - CONSENSUS (1987)
  - SOLVD (1991)
  - SAVE (1993)

ACE-Inhibitor

Mechanism of action

Targets RAAS
- Inhibits conversion of angiotensin I to angiotensin II
- Prevents vasoconstriction and raises vasodilation
ACE-Inhibitors

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial dose</th>
<th>Target dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>6.25-25 mg TID</td>
<td>50 mg TID</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5 mg BID</td>
<td>10-20 mg BID</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>5-10 mg daily</td>
<td>40 mg daily</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5-5 mg daily</td>
<td>20-40 mg daily</td>
</tr>
<tr>
<td>Perindopril</td>
<td>2 mg daily</td>
<td>16 mg daily</td>
</tr>
<tr>
<td>Quinapril</td>
<td>5 mg BID</td>
<td>20 mg BID</td>
</tr>
<tr>
<td>Ramipril</td>
<td>1.25-2.5 mg daily</td>
<td>30 mg daily</td>
</tr>
<tr>
<td>Trandolapril</td>
<td>1 mg daily</td>
<td>4 mg daily</td>
</tr>
</tbody>
</table>

ARNI

- One drug in this class: Entresto® (Sacubitril/valsartan)
  - Sacubitril: neprilysin inhibitor
  - Valsartan: Inhibits RAAS

ARNI: Mechanism of Action

- **Neprilysin inhibitor: Sacubitril**
  - Increases bioavailability of natriuretic peptides (ANP, BNP, CNP)
  - Promotes natriuresis, vasodilation, diuresis, and prevents cardiac hypertrophy

- **ARB: Valsartan**
  - Targets RAAS
  - Prevents vasoconstriction
  - Decreases aldosterone secretion and renal absorption of sodium
- Aim of its design was to inhibit neprilysin while blocking the adverse effects of RAAS and reduce bradykinin potentiation

Entresto®

- Formerly called LCZ696
- FDA approved July 2015
- Indicated to reduce the risk of death and hospitalization in patients with chronic heart failure (NYHA class II-IV) and reduced ejection fraction

Entresto®: Formulation

- Taken orally twice daily
- Valsartan component is more bioavailable

Entresto®: Titration

- Do not need to wait to start Entresto® if patient had not started an ACE-i or ARB or switching from an ARB
- High dose ACE-i or high dose ARB
  - With 36 hours before starting Entresto®
  - Titrate to AFxV/1.5 mg twice daily at scheduled follow up in 2-4 weeks

- Low dose ACE-i or low dose ARB
  - Wait 36 hours before starting Entresto®
  - Titrate to AFxV/1 mg twice daily at scheduled follow up in 2-4 weeks

- Titrate to target dose (37.5/75 mg twice daily as tolerated)
Side effects
- Hypotension
- Hyperkalemia
- Dizziness
- Increased serum creatinine
- Cough

Contraindications with Entresto®
- Angioedema to ACE-I or ARB
- Past use of ACE-I within 36 hours
- Allergic reaction to sacubitril or valsartan or any of the ingredients in Entresto®
- Have diabetes and take a medication that contains aliskiren

SHOULD ARNI REPLACE ACE-I/ARB AS FIRST LINE THERAPY?

LITERATURE REVIEW

Angiotensin-Nephrilysin Inhibition versus Enalapril in Heart Failure
PARADIGM-HF TRIAL
Murray et al (2014)

McMurray et al (2014)
- Multicenter, randomized, double blind, active-controlled study
- Took place in 1043 centers from December 2009 to November 2012
- Completed early due to compelling efficacy of Entresto® (LCZ696) in patients with HF and reduced EF
**Objective:**
- Evaluate the efficacy and safety of LCZ696 compared to enalapril on morbidity and mortality in patients with chronic heart failure (NYHA II – IV and EF ≤ 35%)

**Intervention:**
- LCZ696 200 mg twice daily
  - Based off valsartan component
  - 200 mg dose of LCZ696 is equivalent to 160 mg of valsartan
- Enalapril 10 mg twice daily

**Inclusion criteria**
- Diagnosis of CHF NYHA class II–IV and reduced ejection fraction ≤ 35% and elevated BNP
- Patients must be on an ACE-I or ARB at a stable dose of at least enalapril 10 mg/day or equivalent for at least 4 weeks

**Exclusion criteria**
- History of hypersensitivity or allergy to any of the study drugs
- Known history of angioedema
- Previous history of intolerance to recommended target doses of ACE-I or ARB
- Current acute decompensated heart failure

**Baseline characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LCZ696 (N=4387)</th>
<th>Enalapril (N=4312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.8 ± 11.5</td>
<td>63.8 ± 11.5</td>
</tr>
<tr>
<td>Race or ethnic group – no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2703 (66)</td>
<td>2781 (66)</td>
</tr>
<tr>
<td>Black</td>
<td>211 (5.1)</td>
<td>215 (5.1)</td>
</tr>
<tr>
<td>Serum creatinine – mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.13 ± 0.3</td>
<td>1.12 ± 0.3</td>
</tr>
<tr>
<td>NYHA Class – no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>180 (4.3)</td>
<td>209 (5.0)</td>
</tr>
<tr>
<td>II</td>
<td>2998 (72.6)</td>
<td>2912 (68.0)</td>
</tr>
<tr>
<td>III</td>
<td>930 (23.3)</td>
<td>1069 (24.8)</td>
</tr>
<tr>
<td>IV</td>
<td>33 (0.8)</td>
<td>27 (0.6)</td>
</tr>
</tbody>
</table>

**Primary outcome**
- Cardiovascular death
- Heart failure hospitalization

**Secondary outcome**
- All cause mortality
McMurray et al (2014)

### Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>LCZ696 (N=4187)</th>
<th>Enalapril (N=4212)</th>
<th>Hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from CV causes or first hospitalization for worsening heart failure</td>
<td>894 (21.4)</td>
<td>1151 (27.0)</td>
<td>0.8 (0.73-0.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospitalization for worsening heart failure</td>
<td>400 (9.6)</td>
<td>514 (12.1)</td>
<td>0.79 (0.70-0.88)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Primary composite outcomes – no. (%)**

<table>
<thead>
<tr>
<th>Primary composite outcomes</th>
<th>LCZ696</th>
<th>Enalapril</th>
<th>Hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from CV causes or first hospitalization for worsening heart failure</td>
<td>914 (21.8)</td>
<td>1117 (26.5)</td>
<td>0.8 (0.73-0.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death from CV disease</td>
<td>558 (13.3)</td>
<td>693 (16.5)</td>
<td>0.8 (0.71-0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>First hospitalization for worsening heart failure</td>
<td>537 (12.8)</td>
<td>658 (15.6)</td>
<td>0.79 (0.71-0.89)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Secondary outcomes – no. (%)**

<table>
<thead>
<tr>
<th>Secondary outcomes</th>
<th>LCZ696</th>
<th>Enalapril</th>
<th>Hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from any cause</td>
<td>711 (17.0)</td>
<td>835 (19.8)</td>
<td>0.84 (0.76-0.93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Decline in renal function</td>
<td>94 (2.2)</td>
<td>108 (2.6)</td>
<td>0.86 (0.65-1.13)</td>
<td>0.28</td>
</tr>
</tbody>
</table>

### Adverse events

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>LCZ696 (N=4187)</th>
<th>Enalapril (N=4212)</th>
<th>Hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>588 (14.0)</td>
<td>388 (9.2)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptomatic with SBP &lt; 90 mmHg</td>
<td>112 (2.7)</td>
<td>59 (1.4)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Elevated serum creatinine - no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 2.5 mg/dL</td>
<td>139 (3.3)</td>
<td>188 (4.5)</td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>&gt; 3.0 mg/dL</td>
<td>63 (1.5)</td>
<td>63 (2.0)</td>
<td></td>
<td>0.10</td>
</tr>
</tbody>
</table>

**Hypotension – no. (%)**

### Presenter’s critiques

- **Strengths**
  - Randomized, double blind, controlled trial
  - Large sample size

- **Limitations**
  - Enalapril dose is not at max targeted dose compared to LCZ696
  - Dosing schedule of the study would not be applicable to all populations

### Angiotensin-Neprilysin Inhibition in Acute Decompensated Heart Failure

**PIONEER HF**

Velazquez et al (2018)

- **Background**
  - Patients enrolled from May 2016 to May 2018 at 129 participating centers in the United States
- **Design**
  - Randomized, double-blinded 8 week trial
Velazquez et al. (2018)

Objective
- To assess in-hospital initiation of sacubitril/valsartan vs enalapril on the time-averaged percentage change of NT-proBNP from baseline in patients who have been stabilized following hospitalizations for ADHF and reduced ejection fraction < 40%.

Intervention
- Sacubitril/valsartan
  - Minimum dose 24/26 mg
  - Titrated to max dose 97/103 mg twice daily
- Enalapril
  - Minimum dose 2.5 mg
  - Titrated to max dose 10 mg twice daily
  - Dosing dependent on systolic blood pressure

Inclusion criteria
- Currently hospitalized for ADHF with signs and symptoms of fluid overload
- Left ventricular ejection fraction < 40%
- Elevated NT-proBNP > 1600 pg/mL or BNP > 400 pg/mL during current hospitalization
- Hypersensitivity or angioedema with an ACE-I or ARB
- Currently taking sacubitril/valsartan or any use within the past 30 days
- eGFR < 30 mL/min/1.73 m²
- Serum potassium > 5.2 mEq/L at screening

Exclusion criteria
- Hypersensitivity or angioedema with an ACE-I or ARB
- Currently taking sacubitril/valsartan or any use within the past 30 days
- eGFR < 30 mL/min/1.73 m²
- Serum potassium > 5.2 mEq/L at screening

Efficacy outcome
- Time averaged proportional change from baseline in NT-proBNP

Safety outcome
- Rates of worsening renal function, hyperkalemia, symptomatic hypotension, and angioedema

Baseline characteristics (N=881)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sacubitril-valsartan (N=440)</th>
<th>Enalapril (N=441)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>61</td>
<td>63</td>
</tr>
<tr>
<td>Race – no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>261 (59.3%)</td>
<td>254 (57.6%)</td>
</tr>
<tr>
<td>Black</td>
<td>158 (35.9%)</td>
<td>158 (35.8%)</td>
</tr>
<tr>
<td>NT-proBNP at randomization (pg/mL)</td>
<td>2883</td>
<td>2536</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>1.28</td>
<td>1.27</td>
</tr>
<tr>
<td>Serum potassium (mmol/L)</td>
<td>4.2</td>
<td>4.25</td>
</tr>
</tbody>
</table>
Time averaged reduction in the NT-proBNP concentration was significantly greater in the sacubitril/valsartan group:
Percent change was -46.7% vs -25.3% (sacubitril/valsartan vs enalapril) at week 4
CI: 0.63 to 0.81, p < 0.001

<table>
<thead>
<tr>
<th>Outcomes - no. (%)</th>
<th>Sacubitril-valsartan (N=440)</th>
<th>Enalapril (N=441)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worsening renal function</td>
<td>60 (13.6)</td>
<td>65 (14.7)</td>
<td>0.93 [0.67 to 1.28]</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>51 (11.6)</td>
<td>41 (9.3)</td>
<td>1.25 [0.84 to 1.84]</td>
</tr>
<tr>
<td>Symptomatic hypotension</td>
<td>66 (15.0)</td>
<td>56 (12.7)</td>
<td>1.18 [0.85 to 1.64]</td>
</tr>
<tr>
<td>Angioedema</td>
<td>1 (0.2)</td>
<td>6 (1.4)</td>
<td>0.17 [0.02 to 1.38]</td>
</tr>
</tbody>
</table>

**Presenter’s critiques**

- **Strengths**
  - Randomized, controlled trial
  - Similar baseline characteristics
  - Pertinent patient population
- **Limitations**
  - Short duration
  - Follow up on hospitalization rate

**Januzzi et al (2018)**

- Patients with HFrEF were enrolled in 78 outpatient sites in the United States
- Enrollment began October 2016 and follow up was completed on October 2018

**Association of Change in N-Terminal Pro-B-Type Natriuretic Peptide Following Initiation of Sacubitril-Valsartan Treatment With Cardiac Structure and Function in Patients With Heart Failure With Reduced Ejection Fraction**

PROVE HF


**Inclusion criteria**
- NYHA Class II to IV
- LVEF < 40% within the past 6 months

**Exclusion criteria**
- Hypersensitivity or history of angioedema
- Requirement of treatment with an ACE-I or ARB
- Current or prior treatment with sacubitril/valsartan

**Primary endpoint**
- Correlation between changes in the concentration of NT-proBNP and cardiac remodeling

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1,013 patients screened
794 patients completed screening
794 continued into open-label treatment phase
654 patients completed the study

---


Baseline characteristics (N=794)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sacubitril-Valsalan – no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65.1 (12.4)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>568 (71.5)</td>
</tr>
<tr>
<td>Female</td>
<td>226 (28.5)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>581 (73.4)</td>
</tr>
<tr>
<td>Black</td>
<td>180 (22.7)</td>
</tr>
<tr>
<td>Asian</td>
<td>6 (0.8)</td>
</tr>
<tr>
<td>Other</td>
<td>25 (3.2)</td>
</tr>
<tr>
<td>NT-proBNP pg/mL (median)</td>
<td>816 (332-1822)</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline value, median</th>
<th>6-mo value, Median</th>
<th>Mean change from baseline at 6 months</th>
<th>12-mo value, Median</th>
<th>Mean change from baseline at 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF, %</td>
<td>28.2</td>
<td>34.1</td>
<td>5.2</td>
<td>37.8</td>
<td>9.4</td>
</tr>
</tbody>
</table>
Presenter’s critiques

• Strengths
  – Followed sacubitril/valsartan titrating guidelines

• Limitations
  – Observational, open label design
  – Did not have all echocardiograph measurements since patients dropped out

Cost

• Entresto®
  – 24/26 mg (each): $10.18
  – 49/51 mg (each): $10.18
  – 97/103 mg (each): $10.18

• Enalapril
  – 2.5 mg (each): $0.52 - $1.46
  – 5 mg (each): $0.67 - $1.85
  – 10 mg (each): $0.70 - $1.94
  – 20 mg (each): $1.00 - $2.77

Clinical adoption remains slow

• Less than 3% of patients with HFrEF were receiving the drug as of 2016
• Study analyzed 2818 Medicare Part D plans to determine what barriers could be to adopting this medication
  – 100% covered Entresto® (1069 required prior authorizations)
  – Cost sharing was $57 for Entresto® vs $2-$5 for ACE-I, ARB, B-blocker, diuretic

Barriers

• Out of pocket costs
• Non-formulary
• Prior authorization requirements
• Adherence
TC is a 58 year old African American male with a PMH of hypertension, diabetes, hyperlipidemia, and asthma. At his office visit 2 days ago, he was diagnosed with HFrEF NYHA II. The physician asked for your recommendation on treatment for this patient.

Patient Case

Current medications:
- Lisinopril 20 mg daily
- Metformin ER 1000 mg BID
- Invokana 100 mg once daily
- Rosuvastatin 20 mg daily
- Flovent 110 mcg inhaler 1 puff bid
- Albuterol HFA inhaler 1 puff Q4-6 hours prn

Allergies:
- NKDA

Family history:
- Father has hypertension

Social history:
- (-) tobacco, (-) alcohol, 1 cup of coffee daily

WHAT WOULD YOU RECOMMEND?

Conclusion

Consider using ARNI in patients who have been stable on an ACE-I or ARB with HFrEF and are symptomatic due to decreased hospitalization and improved mortality rates as directed by guidelines.

More studies would be beneficial in strengthening its efficacy in initiating ARNI in other patient populations.

Cost can be a limiting factor for some patients.

Pipeline studies

PARALLAX HF
- Objective: Demonstrate the superiority of LCZ696 over individualized medical therapy comorbidities in reducing NT-pro BNP and HF symptoms in patients with HFrEF

PARADISE-AMI
- Objective: Evaluate the safety and efficacy of LCZ696 compared to ramipril in reducing the composite endpoints of CV death, HF hospitalization, and outpatient HF in post AMI patients.
References