Scientific Sessions 2019

Efficacy and Safety of Sacubitril/Valsartan in High-Risk Patients in the PIONEER-HF Trial

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Disclosures

- ***I have no personal disclosures***

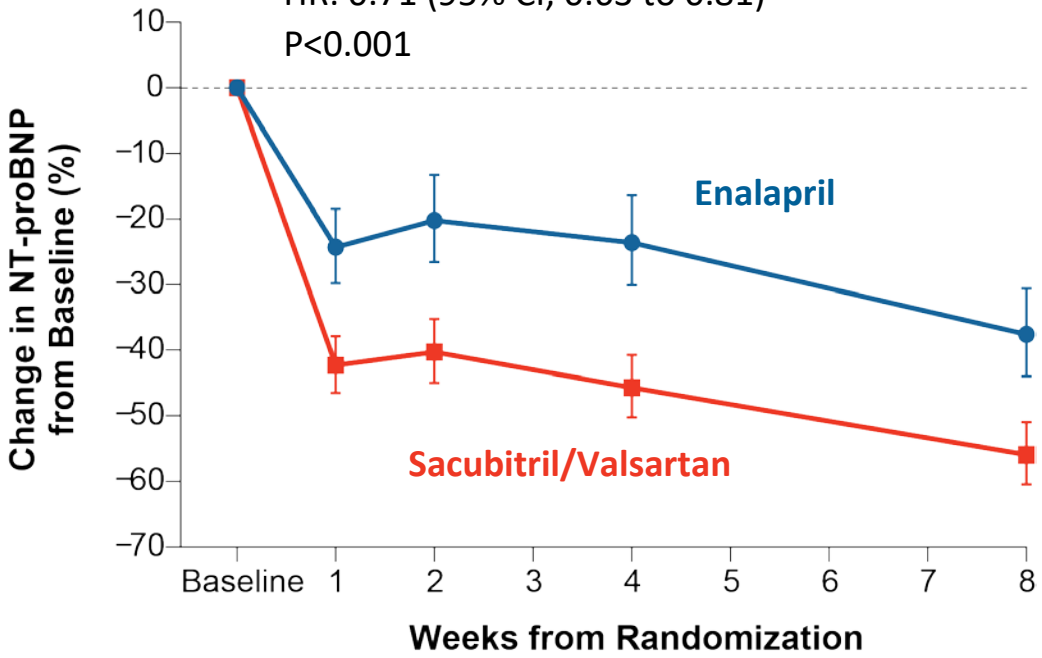
- ***The PIONEER-HF trial was sponsored by Novartis***

Background

- **Pts with ADHF are at high risk for poor outcomes, including complications of therapy**
- **Among pts with HFrEF hospitalized for ADHF, in-hospital initiation of sacubitril/valsartan vs. enalapril was well-tolerated and led to a greater ↓ in NT-proBNP and ↓ rHHF/CVD**

Change in NTproBNP

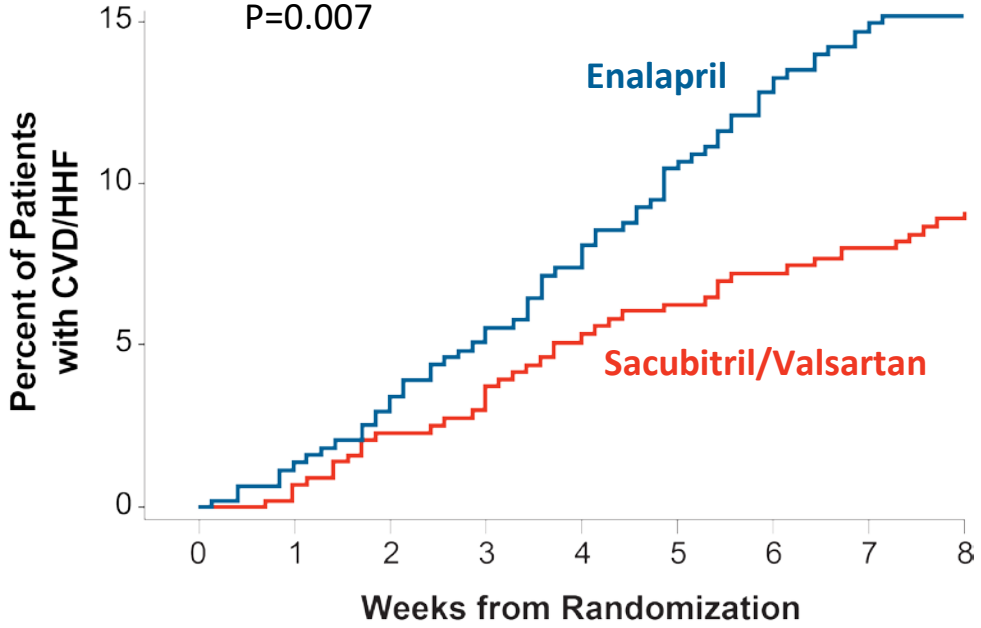
HR: 0.71 (95% CI, 0.63 to 0.81)
P<0.001



Velazquez et al. N Engl J Med 2019;380:539-548

Re-Hospitalization for HF or CV Death

HR: 0.58 (95% CI, 0.39 to 0.87)
P=0.007



Morrow et al. Circulation 2019;139:2285–2288.

Objective

Given heightened clinical concern about in-hospital initiation of sacubitril/valsartan in ***pts at higher risk of complications***, we assessed outcomes in ***selected high-risk subgroups*** in PIONEER-HF

Study Design

N = 881

Hospitalized with ADHF (EF≤40%)

Stabilized while still hospitalized

- SBP ≥100 mmHg in prior 6h; no symptomatic ↓ BP
- No increase in IV diuretics in prior 6h
- No IV vasodilators in prior 6h
- No IV inotropes in prior 24h

Sacubitril/valsartan Target: 97/103 mg twice daily	vs	Enalapril Target: 10 mg twice daily

Evaluate

- NTproBNP
- Safety and tolerability
- Clinical outcomes

In-hospital initiation

Blinded Study Rx for 8 weeks

Velazquez et al. AHJ 2018;198:145-51
Velazquez et al. N Engl J Med 2019;380:539-548

High-Risk Subgroups

Defined in analysis plan

- SBP ≤118 mmHg (median) (n=440)
- LVEF ≤25% (n=573)
- NYHA class III/IV (n=627)
- NT-proBNP concentration >2701 pg/ml (median) (n=440)
- eGFR <60 ml/min/1.73 m^2 (n=455)

Exploratory

- ≥1 additional HHF within the prior year (n=343)
- Admission to the ICU during the index hospitalization (n=96)
- Use of inotropes during the index hospitalization (n=68)

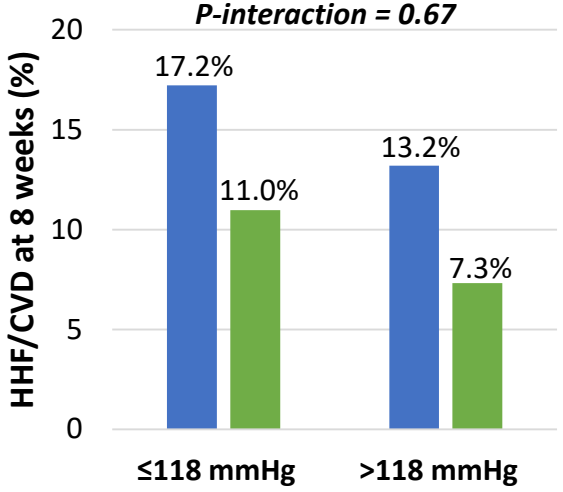
Rehospitalization for HF or CV Death (8 Weeks)

Enalapril
Sacubitril/valsartan

Overall RR (Sacubitril/Valsartan vs. Enalapril) 0.58 (95% CI, 0.39-0.87)

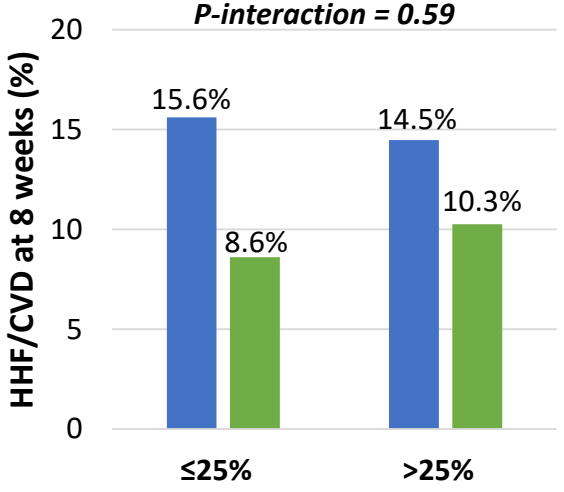
SBP at randomization

P-interaction = 0.67



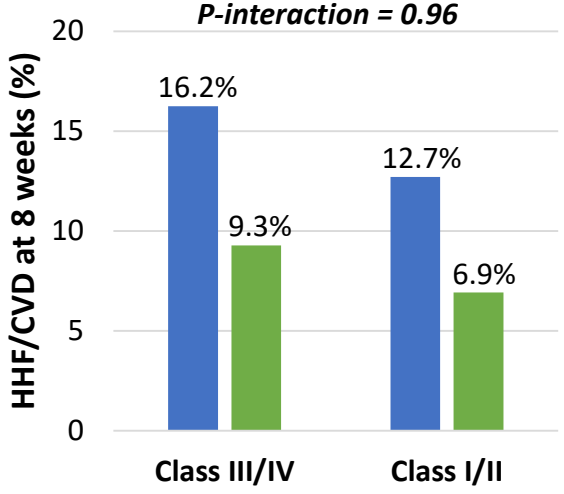
LVEF at screening

P-interaction = 0.59



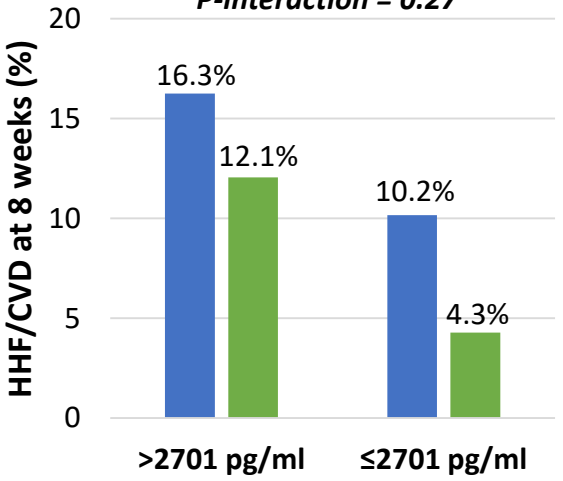
NYHA class at randomization

P-interaction = 0.96



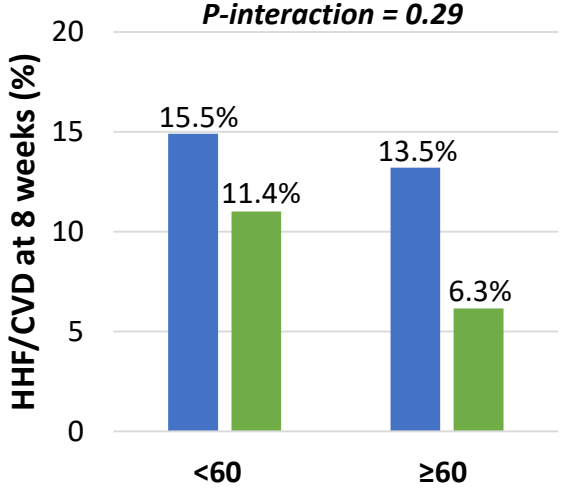
NT-proBNP at randomization

P-interaction = 0.27



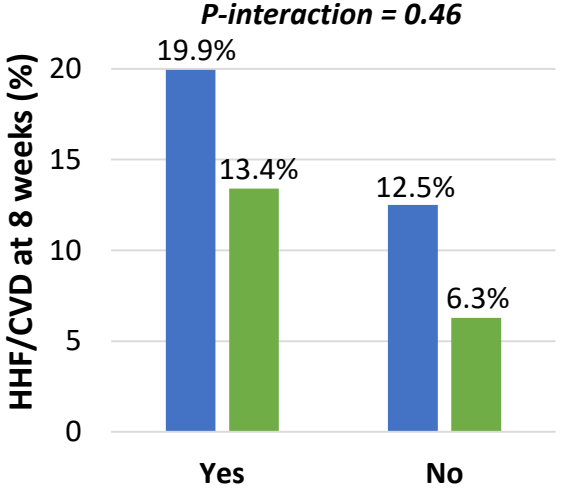
eGFR at randomization

P-interaction = 0.29



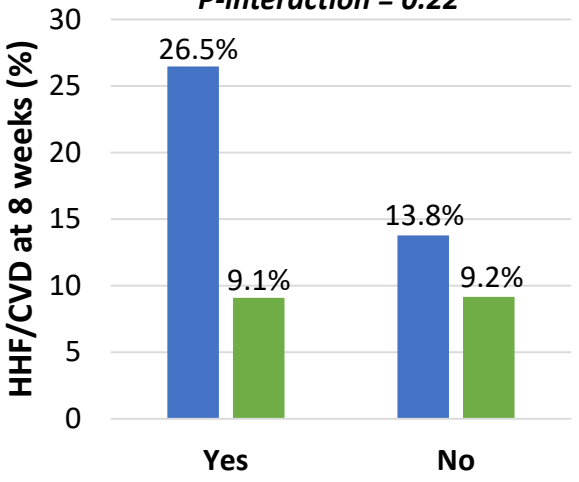
HF hospitalization in past year

P-interaction = 0.46



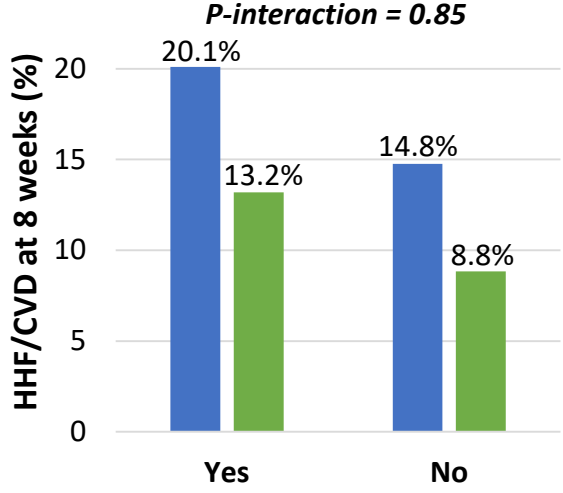
ICU admission for ADHF

P-interaction = 0.22



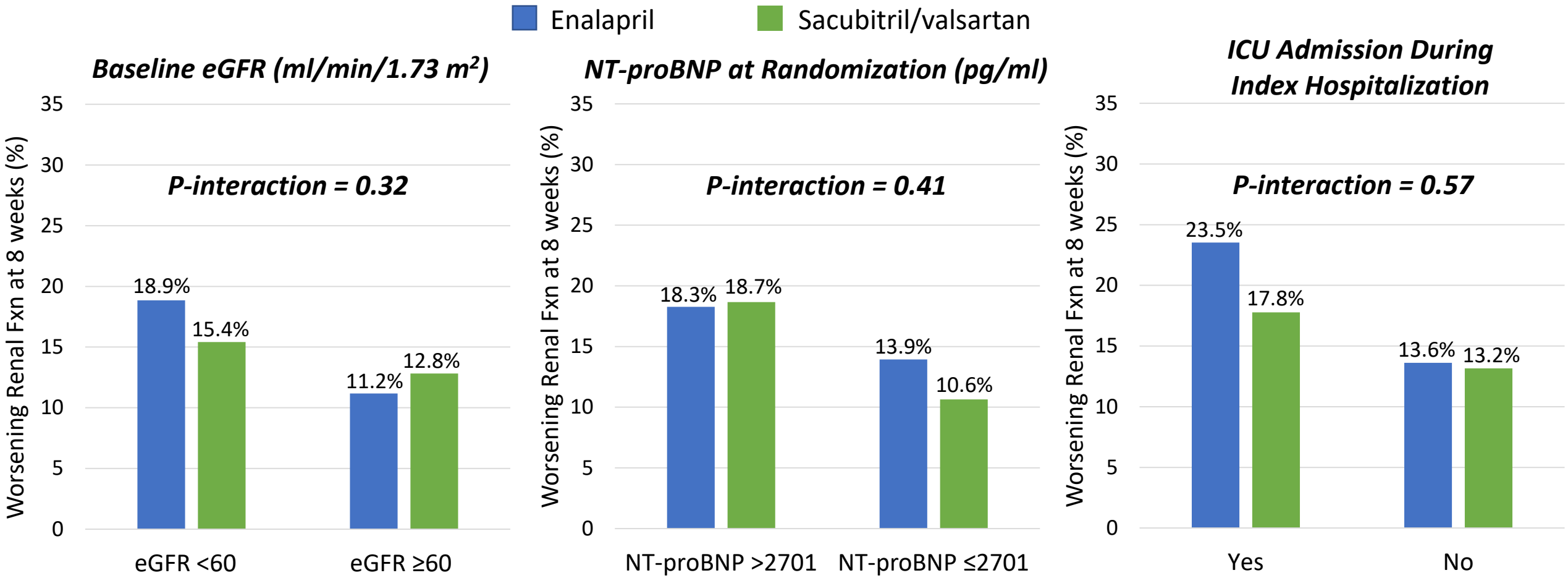
On inotropes during admission

P-interaction = 0.85



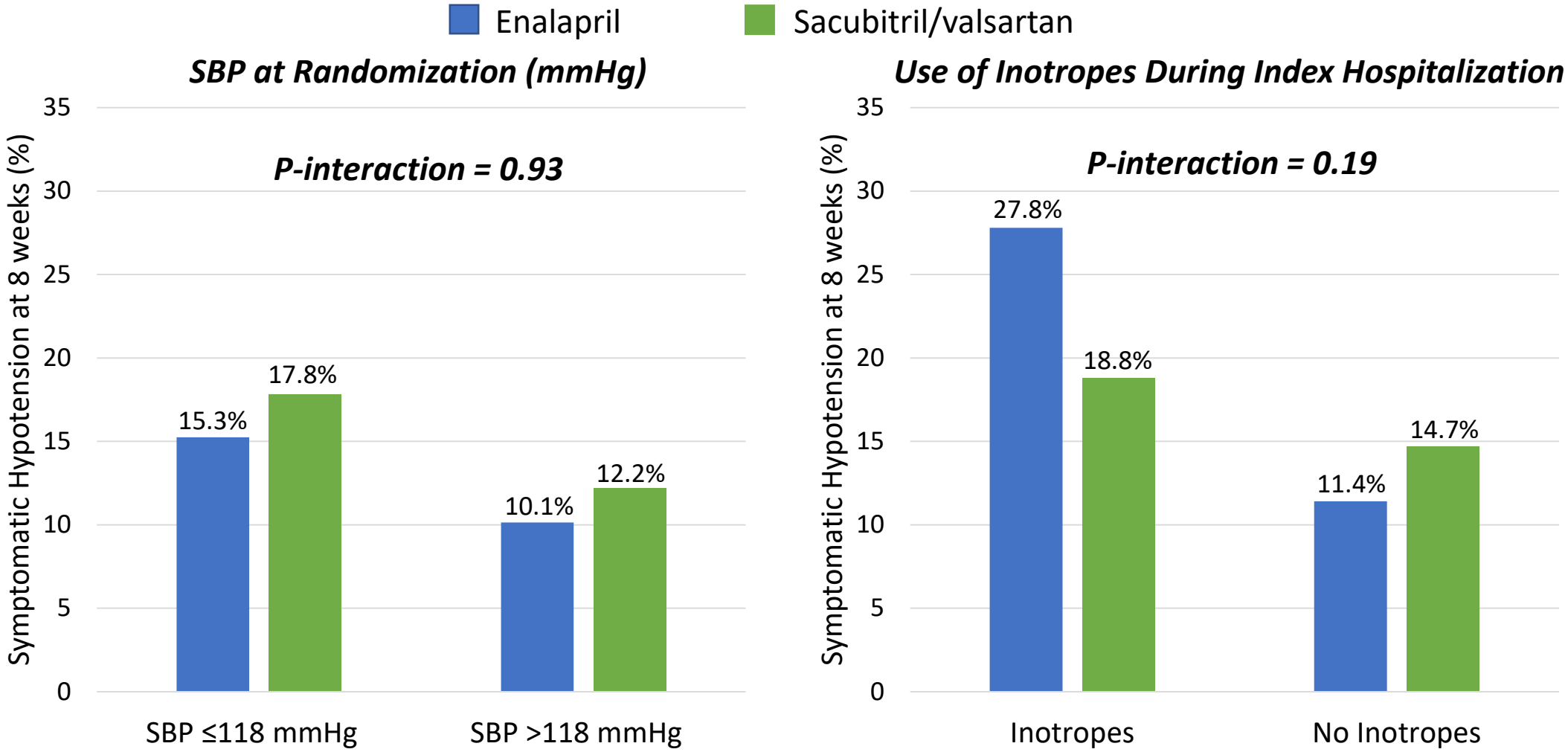
Worsening Renal Function through 8 Weeks

Overall RR (Sacubitril/Valsartan vs. Enalapril) 0.93 (95% CI, 0.67-1.28)



Symptomatic Hypotension through 8 Weeks

Overall RR (Sacubitril/Valsartan vs. Enalapril) 1.18 (95% CI, 0.85-1.64)



Summary

- In HFrEF patients hospitalized with ADHF at potentially higher risk of complications, there was a robust treatment effect and no evidence of lack of tolerability of sacubitril/valsartan vs. enalapril

- Consistent with the overall trial result, these data support in-hospital initiation of sacubitril/valsartan in even the most vulnerable patients with HFrEF who are stabilized during hospitalization for ADHF

Thank you!

American Heart Association.
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