

*Commentary on Sacubtril/Valsartan
Across the Spectrum of Heart Failure*

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Model of Sacubitril/Valsartan Across Low to Preserved EF By Gender

PARADIGM known benefits:

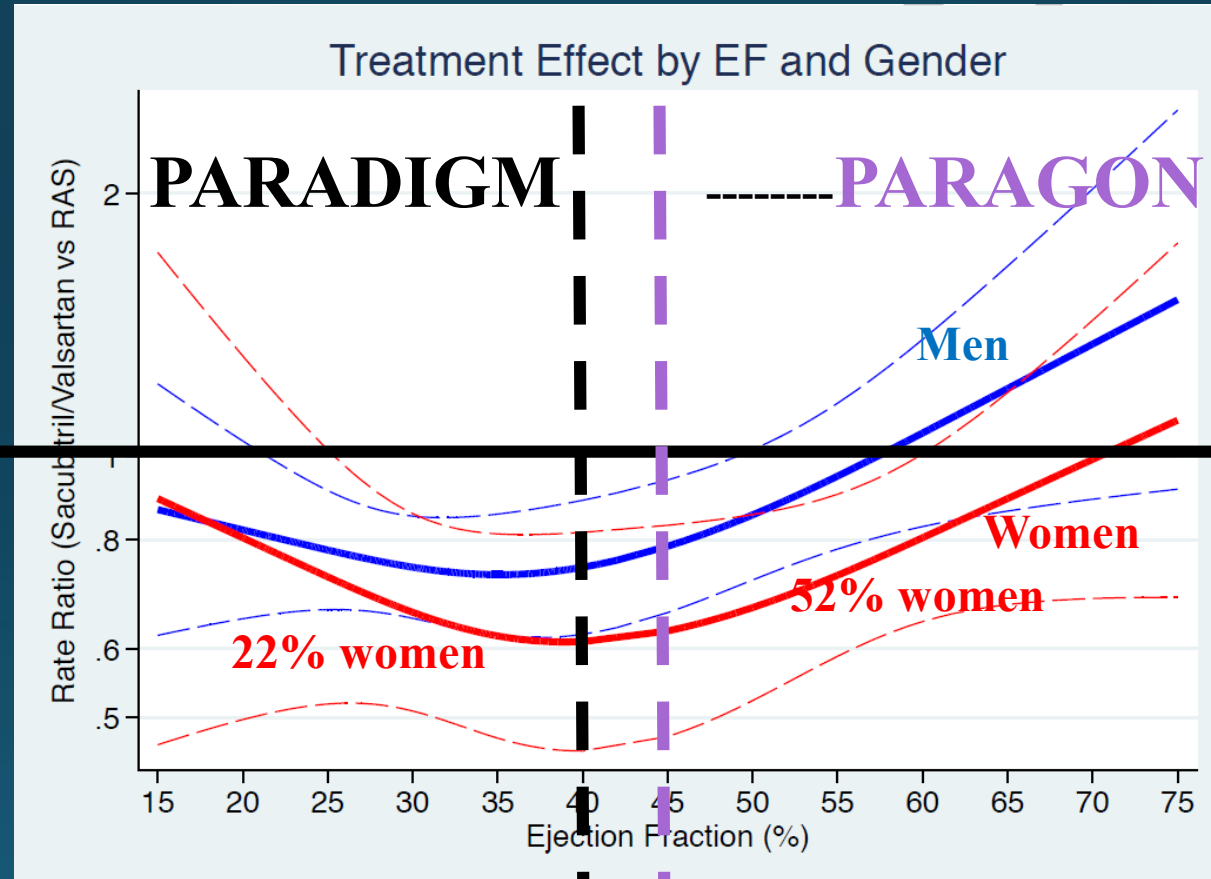
Reduction in mortality
from 19.8 to 17 %

Absolute 2.8%, relative 14%

Reduction in HF hosp
from 15.6 to 12.8 %

Absolute 2.8%, relative 18%

Benefit to Reduce Risk with
Sacubitril/valsartan



RR = 1

Solomon, Vaduganathan, Clagett, Packer, Zile, Swedberg, Rouleau, Pfeffer, Desai, Lund, Kober, Anand, Sweitzer, Linssen, Merkely, Arango, Venereanu, Chen, Senni, Sibilo, Boytsov, Shi, Rizkala, Lefkowitz, McMurray

AHA Late-Breaking Science 2019

Two Different Physiologies? Two Different Targets of Benefit?

PARADIGM LVEF \leq 0.40

- Benefit not dependent on EF ($.30 \pm .06$)
- Equivalent benefit across gender
- Benefit for mortality:
HR = 0.80 CV death, 0.84 all death
- Benefit more obvious in Class I-II
- Benefit apparent regardless of previous hospitalizations

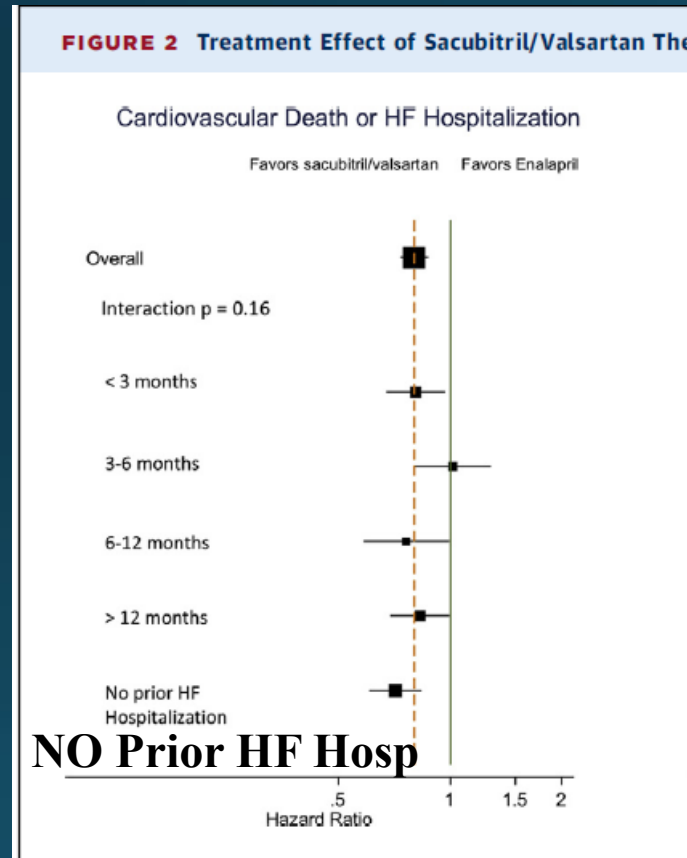
PARAGON LVEF \geq 0.45

- Benefit only if EF \leq 0.57
- **Benefit only in women** (RR = 0.67)
despite lower event rate than men
- **No benefit for mortality even in women** (RR = 1.05)
- Signal of benefit only in Class III-IV
- **Benefit only in patients with prior hospitalization in the previous 6 months**

Differential Impact of Prior HF Hospitalization On Benefit of Sacubitril/Valsartan Across EF

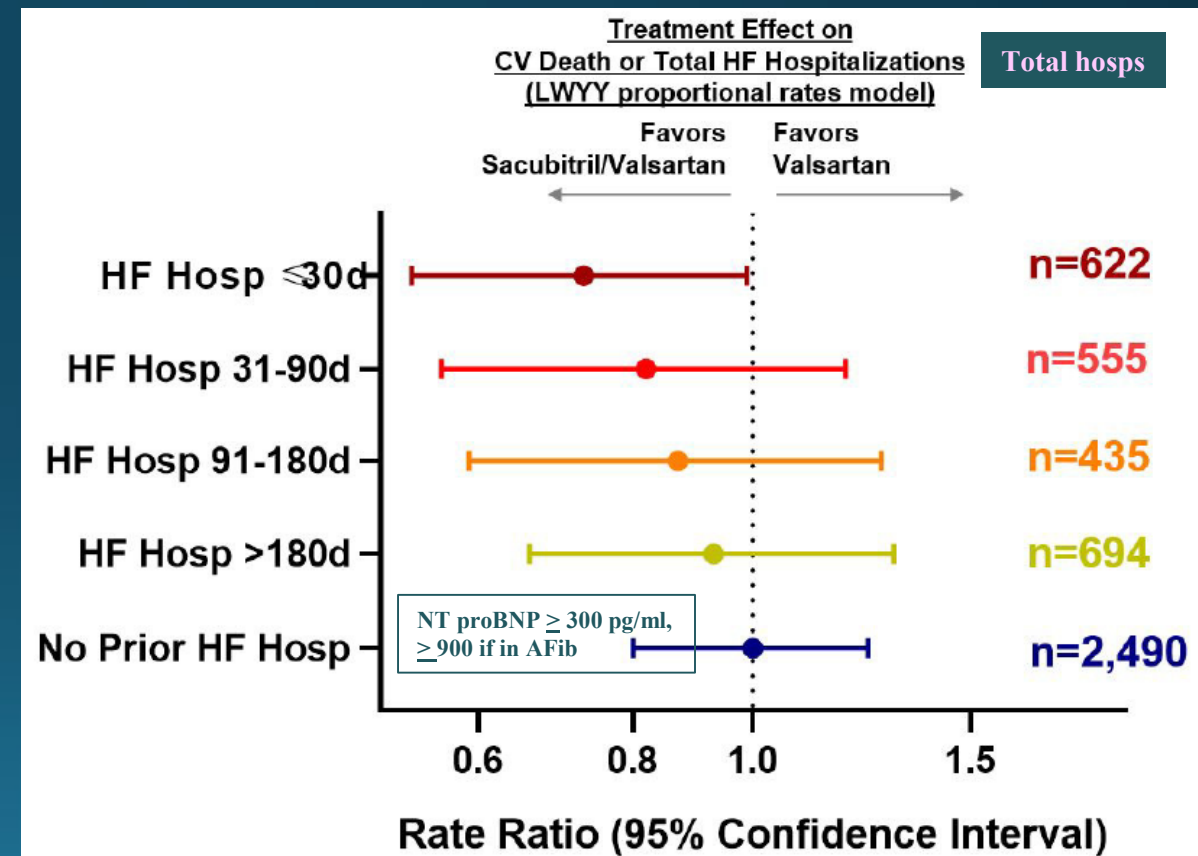
PARADIGM Trial

Equal Benefit Without Prior Hospitalization



PARAGON Trial

Only Benefit Is After Recent Hospitalization

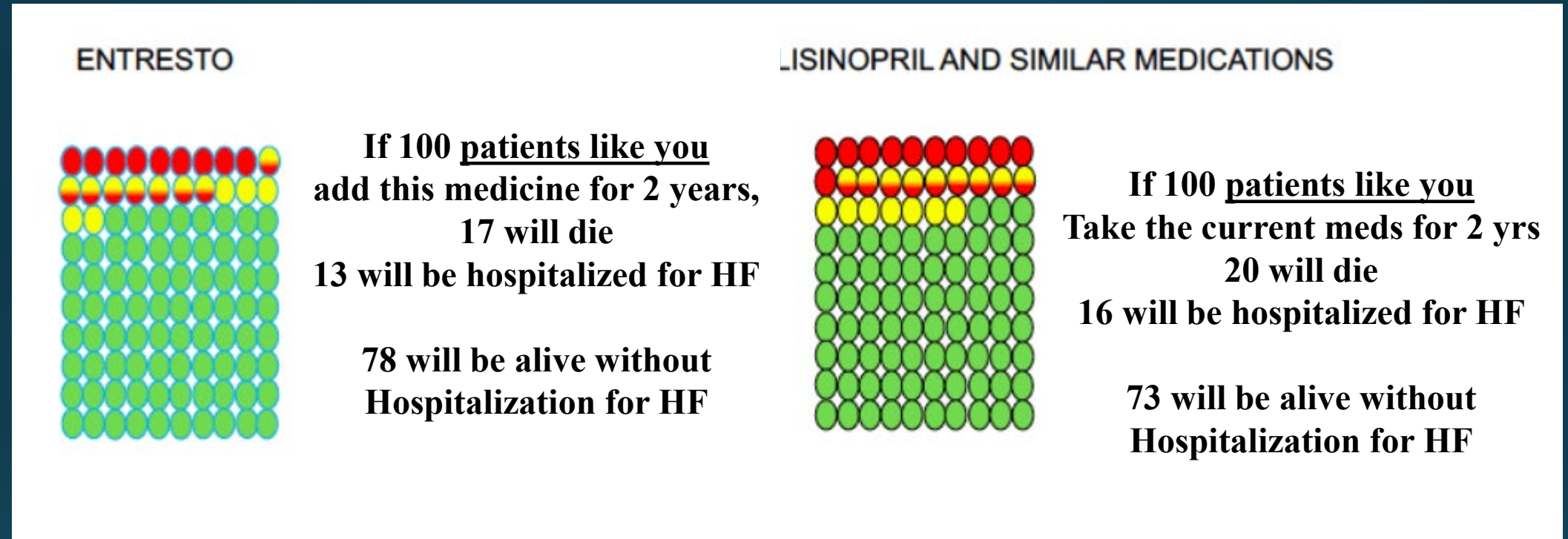


Targets for Therapy with Sacubitril/Valsartan

	Heart failure with Low EF and LV dilation	"Heart failure with Preserved EF"	
Prior HF hospitalization: Symptoms and signs of congestion treated with IV diuretics	Decrease hospitalizations Decrease mortality	Decrease hospitalizations <u>No</u> impact on mortality	Hospitalizations for congestion may be similar across EF
No prior congestion leading to hospitalization	<i>Fewer events, but still impact to</i> Decrease hospitalizations Decrease mortality	No benefit	Disease progression and cardiac mortality may present better targets in low EF than in preserved EF.

NIH Heart Failure Network trials of HFpEF,
Very few events in pts without prior HF hosp
Reddy ...Borlaug, Redfield et al AHA 2019

Shared Decision-Making For Patients Like You About Sacubitril/Valsartan for Low EF HF



If the new medicine cost you
an additional \$5 / month,
would you want it?

92% definitely or probably yes

If it cost you an additional \$ 100/month?

43% definitely or probably yes