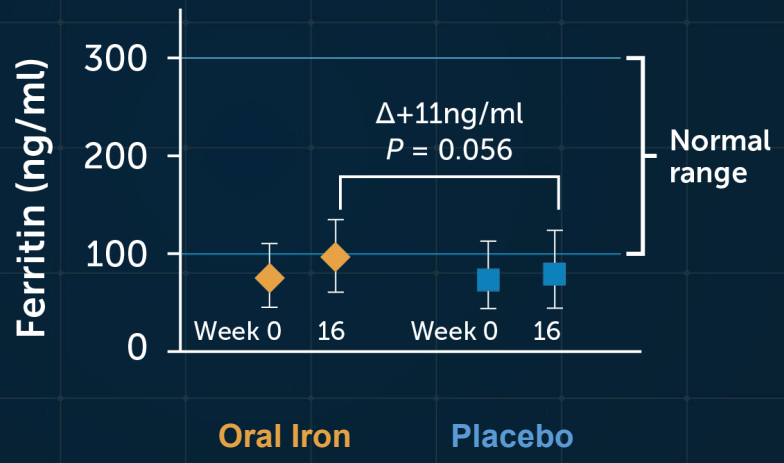
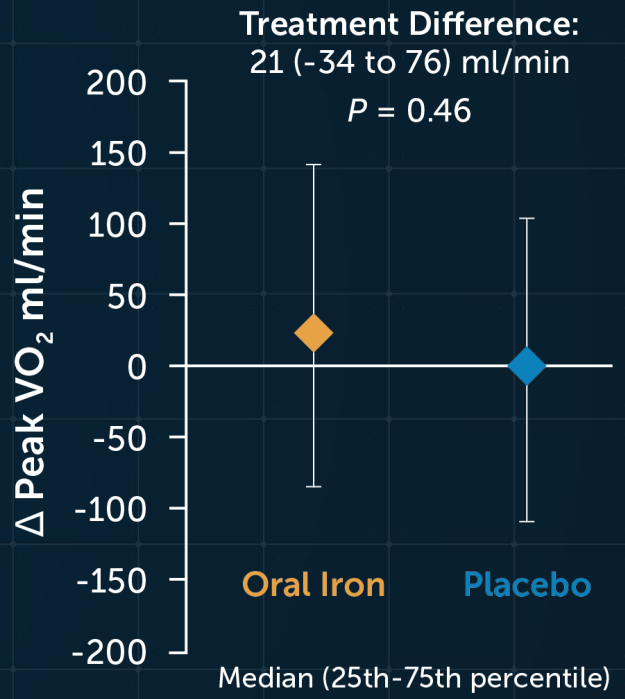
Lack of Benefit with Oral Iron: IRONOUT-HF Study

- Double-blind, randomized, placebo-controlled trial
- Median ferritin levels remained below 100 ng/mL after 16 weeks
- In patients with HFrEF and ID, 150 mg oral iron polysaccharide twice daily **failed to improve exercise capacity, inflammatory markers, and QOL compared to placebo**





HFrEF, heart failure with reduced ejection fraction; ID, iron deficiency; QOL, quality of life; VO_2, volume of oxygen.

Lewis GD, et al. *JAMA*. 2017;317(19):1958-1966.

Prior IV Iron Studies (HFrEF + HFmEF)

Trial	Patients	Time	Primary endpoint
FAIR-HF	459	24	Self-reported patient global assessment and NYHA functional class
CONFIRM-HF	304	52	6-MWD
EFFECT-HF	172	24	Peak VO_2

Improvements in:

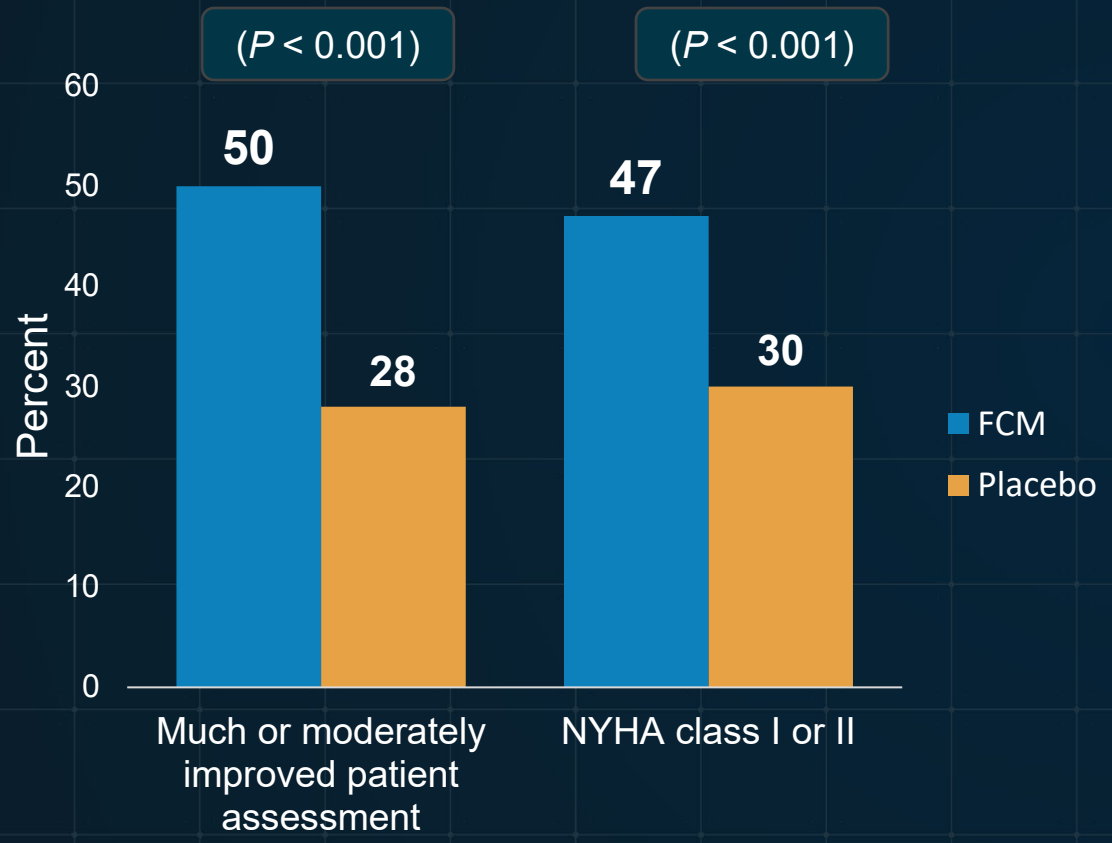
- Patient global assessment
- Functional status (6-MWD, peak VO_2, NYHA class)
- Biomarkers (BNP)
- Reduction in HF hospitalizations

6-MWD, 6-minute walk distance; BNP, brain natriuretic peptide; HF, heart failure; HFmEF, heart failure with mid-range ejection fraction; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; NYHA, New York Heart Association; VO_2, volume of oxygen.

Lewis GD, et al. *Circ Heart Fail*. 2016;9(5):e000345. Anker SD, et al. *N Engl J Med*. 2009;361(25):2436-2448. Ponikowski P, et al. *Eur Heart J*. 2015;36(11):657-668. van Veldhuisen DJ, et al. *Circulation*. 2017;136(15):1374-1383.

FAIR-HF

Trial design: Patients with chronic heart failure and iron deficiency (with or without anemia) were randomized to intravenous iron (ferric carboxymaltose) (n = 304) vs placebo (n = 155) for 24 weeks



Results:

- Primary outcome, Patient Global Assessment at 24 weeks: Much or moderately improved in 50% of the intravenous iron group vs 28% of the placebo group ($P < 0.001$)
- NYHA class I or II at 24 weeks: 47% vs 30% ($P < 0.001$)
- Death: 3.4% vs 5.5% ($P = 0.47$)
- Hospitalization for any cardiovascular cause: 10.4% vs 20.0% ($P = 0.08$)

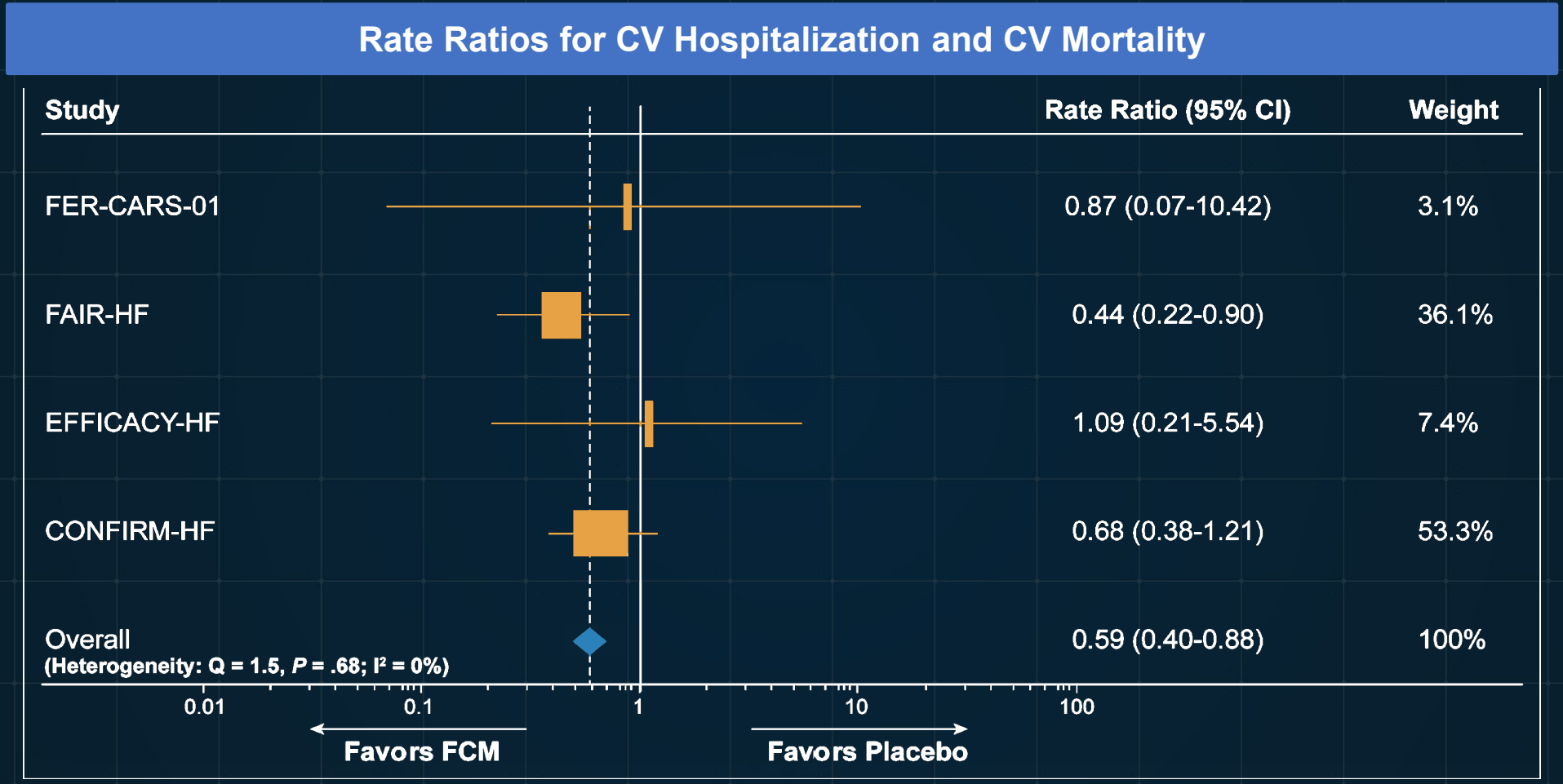
Conclusions:

- Among patients with chronic heart failure and iron deficiency, the use of intravenous iron for 24 weeks was beneficial
- This therapy resulted in improved symptoms and functional capacity
- Intravenous iron appeared to be safe

FCM, ferric carboxymaltose; NYHA, New York Heart Association.

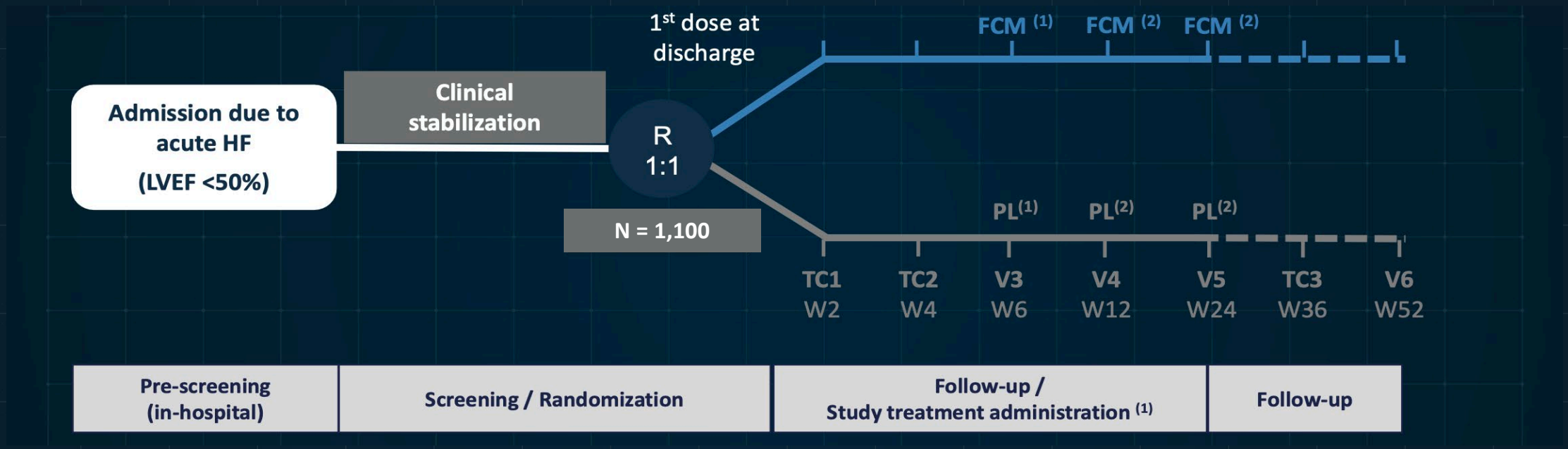
Anker SD, et al. *N Engl J Med.* 2009;361(25):2436-2448.

Individual Patient Data Meta-Analysis



CV, cardiovascular; FCM, ferric carboxymaltose.
Adapted from Anker SD, et al. *Eur J Heart Fail*. 2018;20(1):125-133.

AFFIRM-AHF Study Design



- IV ferric carboxymaltose (FCM)
- Composite of recurrent events of HF hospitalization and cardiovascular death
- 1,132 patients
- Acute HF EF <50%

[1]Adminstered dose of study treatment based on iron need as assessed at the baseline visit.

[2]Study treatment administered only if iron deficiency persisted.

EF, ejection fraction; FCM, ferric carboxymaltose; HF, heart failure; LVEF, left ventricular ejection fraction; PL, placebo; R, randomization; TC, telephone contact; V, visit; W, week.

Ponikowski P, et al. *Eur J Heart Fail*. 2019;21(12):1651-1658.

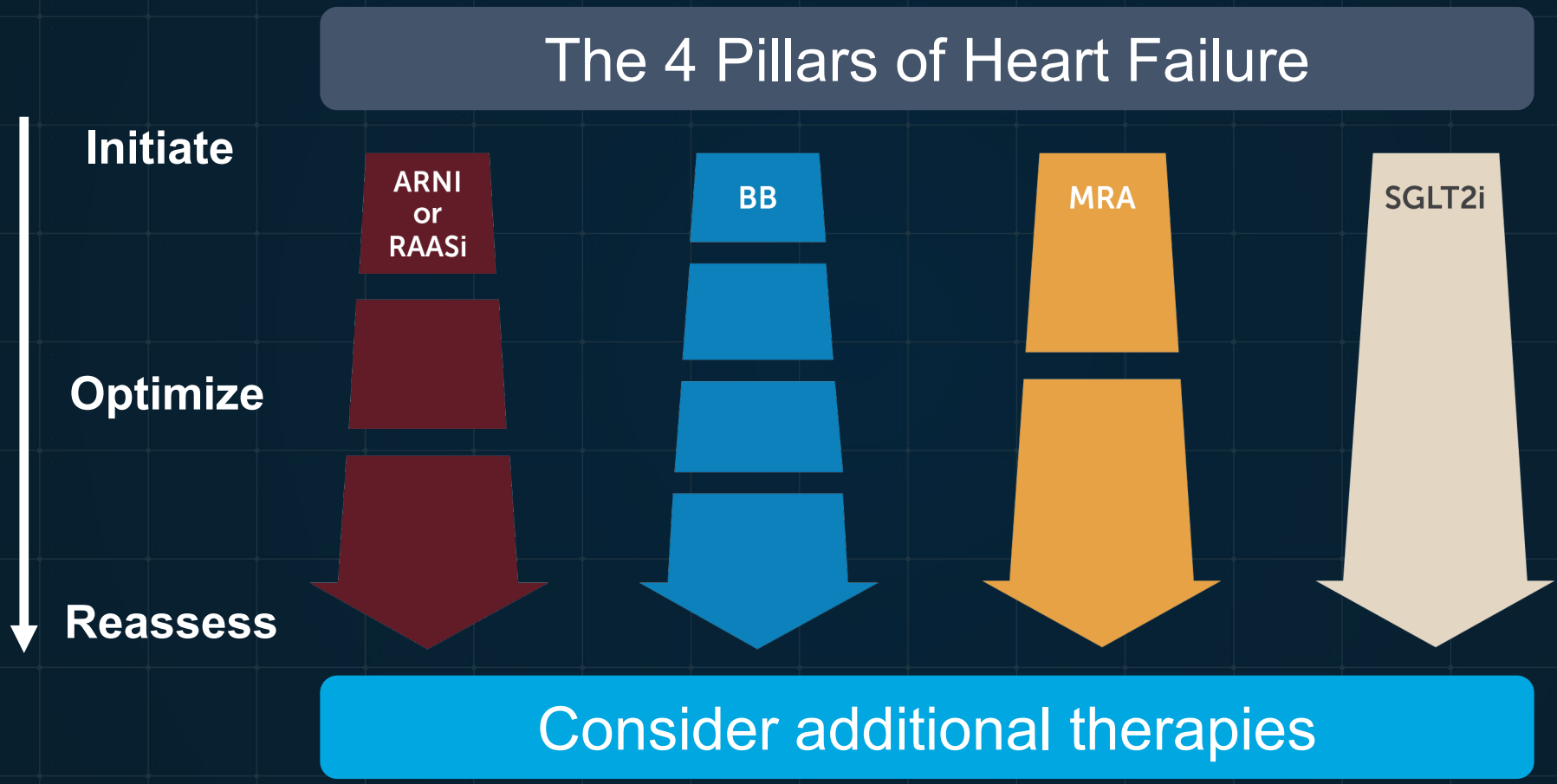
Comparison of IV Iron Studies (Heart Failure)

Study Name	AFFIRM-AHF	HEART-FID
# of Patients	1,132	3,014
Diagnosis	Acute HF EF < 50%	Chronic HF EF ≤ 40%
Recruitment	Hospital	Outpatient
Study Arm	Ferric carboxymaltose	Ferric carboxymaltose
Definition of Iron Deficiency	Serum ferritin < 100 ng/mL, or 100-299 ng/mL if TSAT <20%	Serum ferritin < 100 ng/mL, or 100-299 ng/mL if TSAT <20%
Duration	52 weeks	Event driven + 12 mos last patient
Primary Endpoint	HF hospitalizations + CV death	All-cause mortality + total HF hospitalizations through 12 mos and 6-month 6-MWD
Anticipated Completion Date	**Completed**	**Completed**

6-MWD, 6-minute walk distance; CV, cardiovascular; EF, ejection fraction; HF, heart failure; IV, intravenous TSAT, transferrin saturation.

von Haehling S, et al. *JACC Heart Fail.* 2019;7(1):36-46.

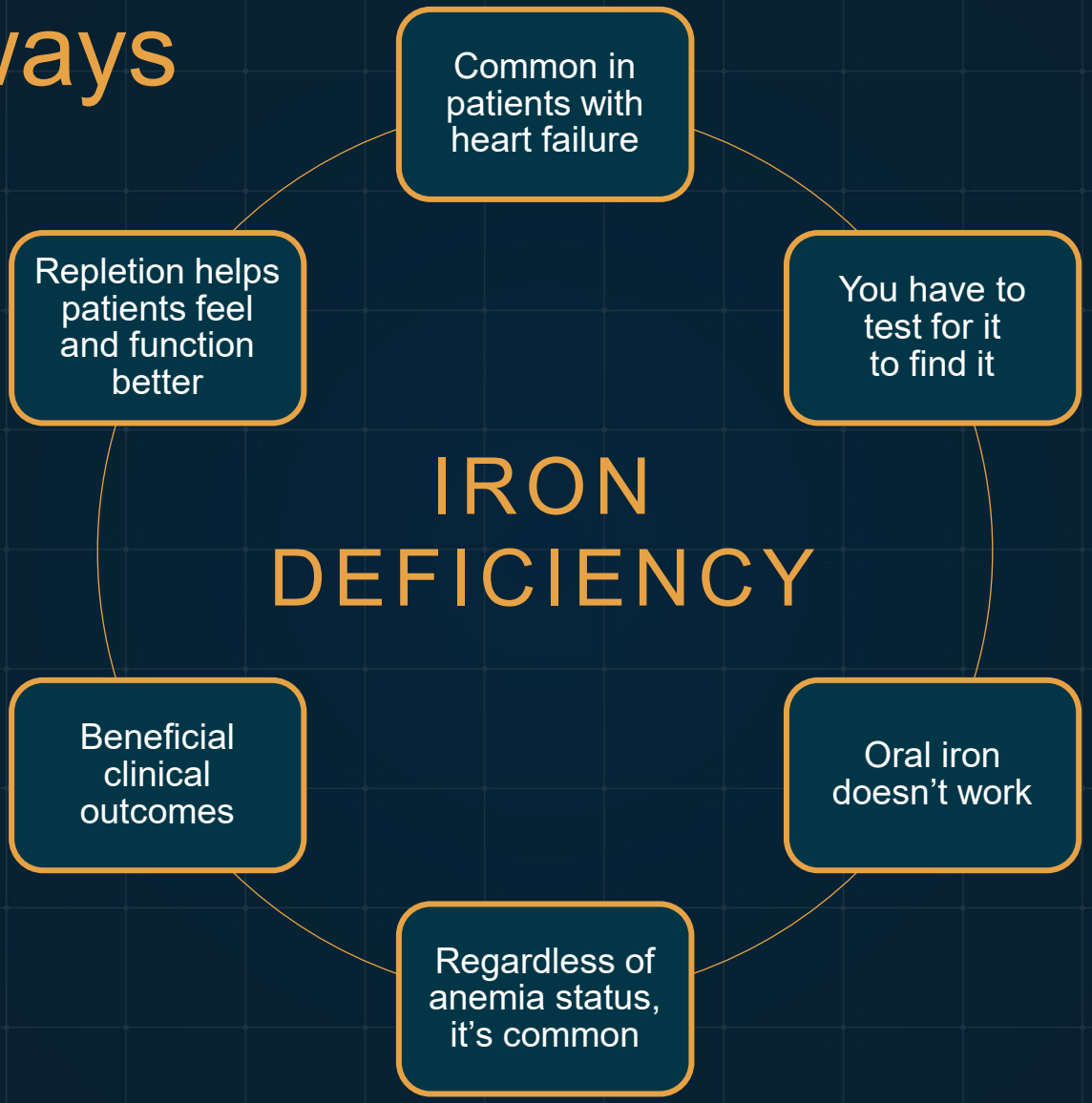
Initiation and Optimization of the 4 Pillars of Heart Failure



ARNI, angiotensin receptor-neprilysin inhibitor; BB, beta-blocker; MRA, mineralocorticoid receptor antagonist; RAASi, renin-angiotensin-aldosterone system inhibitor; SGLT2i, sodium glucose transporter type 2 inhibitor.

Adapted from Straw S, et al. *Open Heart*. 2021;8(1):e001585.

Key Takeaways



Key Takeaways: Piotr Ponikowski, MD

"…read the guidelines and implement IV iron therapy for iron-deficient patients with heart failure for them to live better, to reduce hospital admissions…"