Diuretics and "New" Drugs in Acute HF

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Conflict of Interest Disclosures

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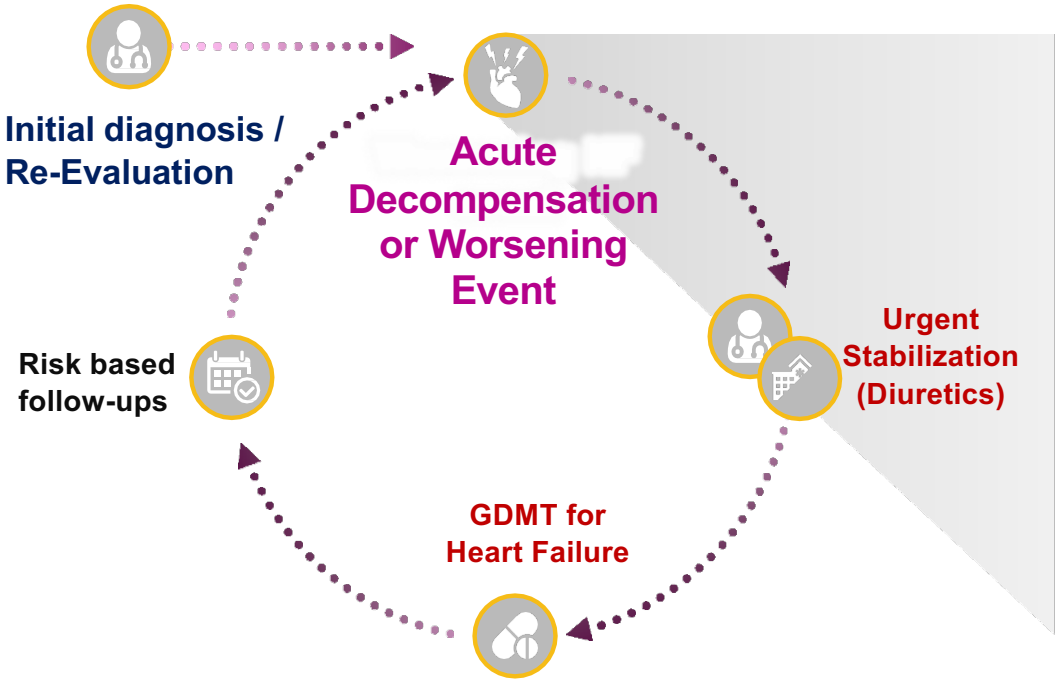
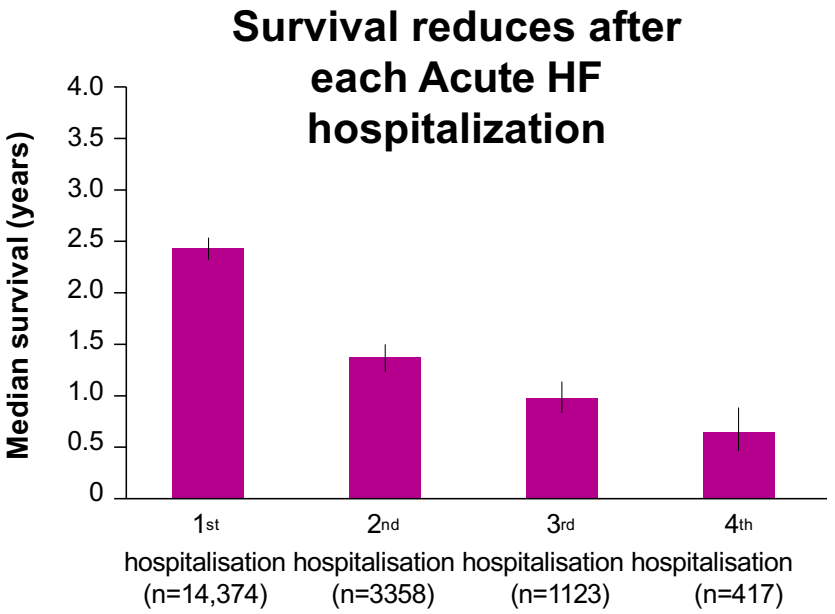
- **Speaker fees**: NovoNordisk, Bayer, Merck

Diuretics and “New” Drugs in HF

- Challenges of acute heart failure
- Escalating diuretics & combination regimen
- Early initiation of GDMT in hospital - including “quadruple therapy” in HFrEF
- “New drugs” in acute heart failure

HF Worsens with Each Acute Decompensation





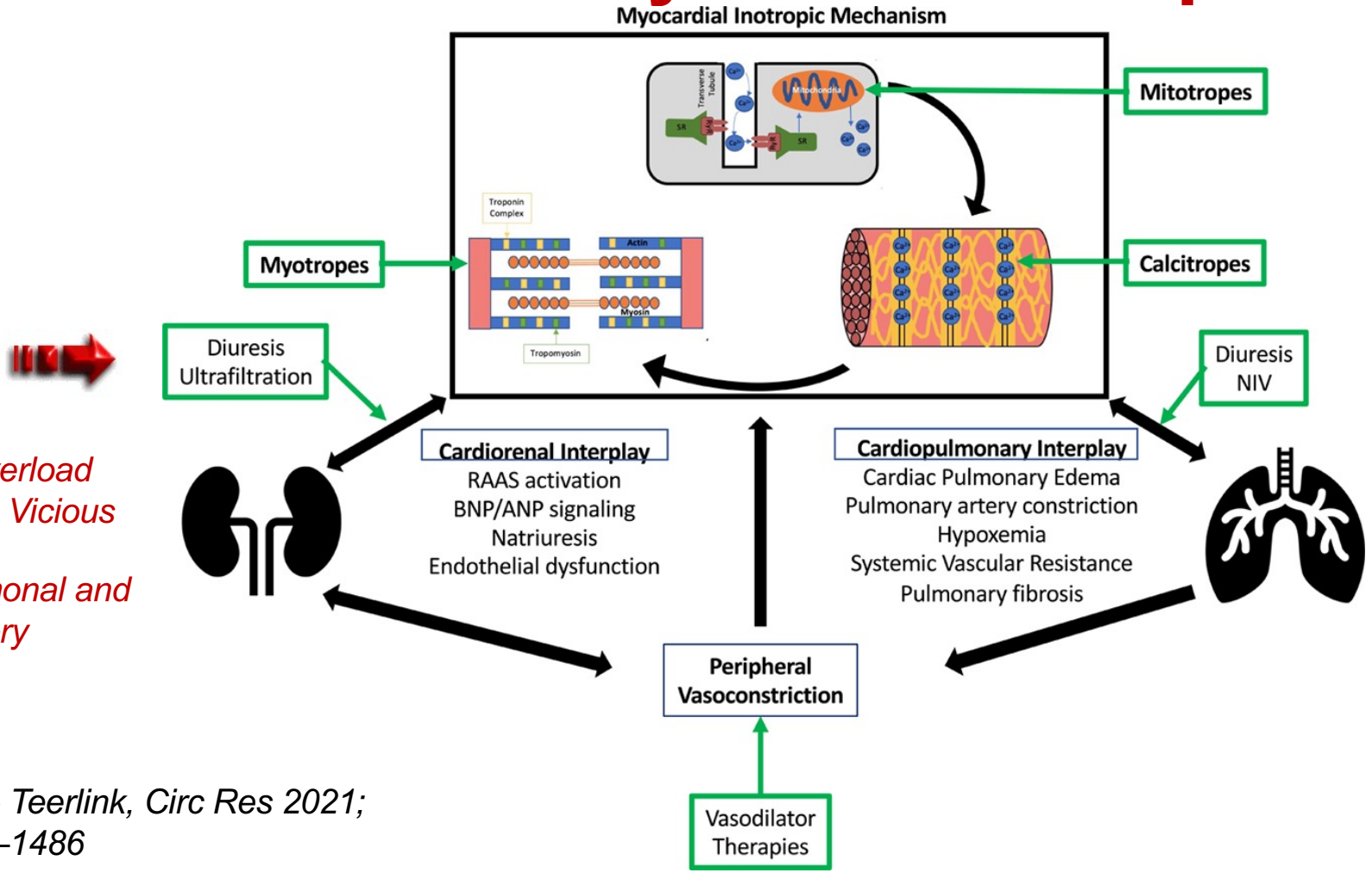
Adapted from Gheorghiade et al. *Am J Cardiol*, 2005 and Cowie et al. *ESC Heart Fail,* 2014.

*Adjustment of and potential addition to current therapy. #After the initial worsening HF event, each subsequent event becomes longer in duration and is separated by shorter intervals due the inability of the heart to fully recover.

HCP, healthcare professional; HF, heart failure.

1. Gheorghiade M et al. *Am J Cardiol*. 2005;96(6A):11G–17G. 2. Cowie MR et al. *ESC Heart Fail*. 2014;1:110–145; 3. Setoguchi S et al. *Am Heart J*. 2007;154:260–206.

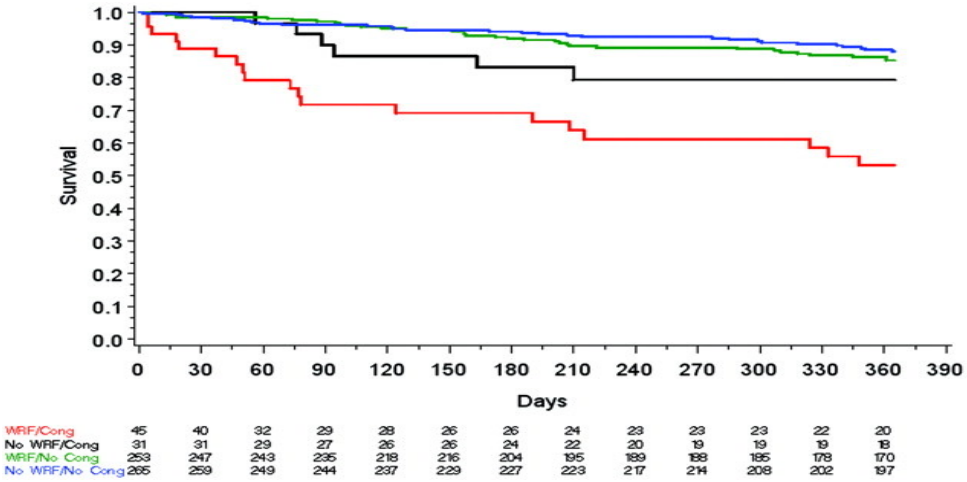
Acute HF – Heart & Systemic Disequilibrium

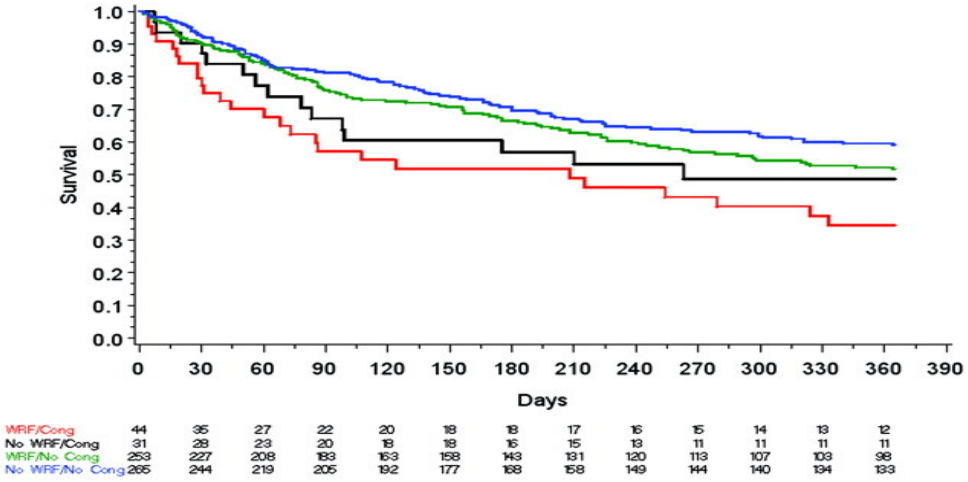


Volume Overload Activates a Vicious Cycle of Neurohormonal and Inflammatory Activation

Njoroge & Teerlink, Circ Res 2021; 128:1468–1486

Don’t underestimate the importance of diuretics - decongestion is really important

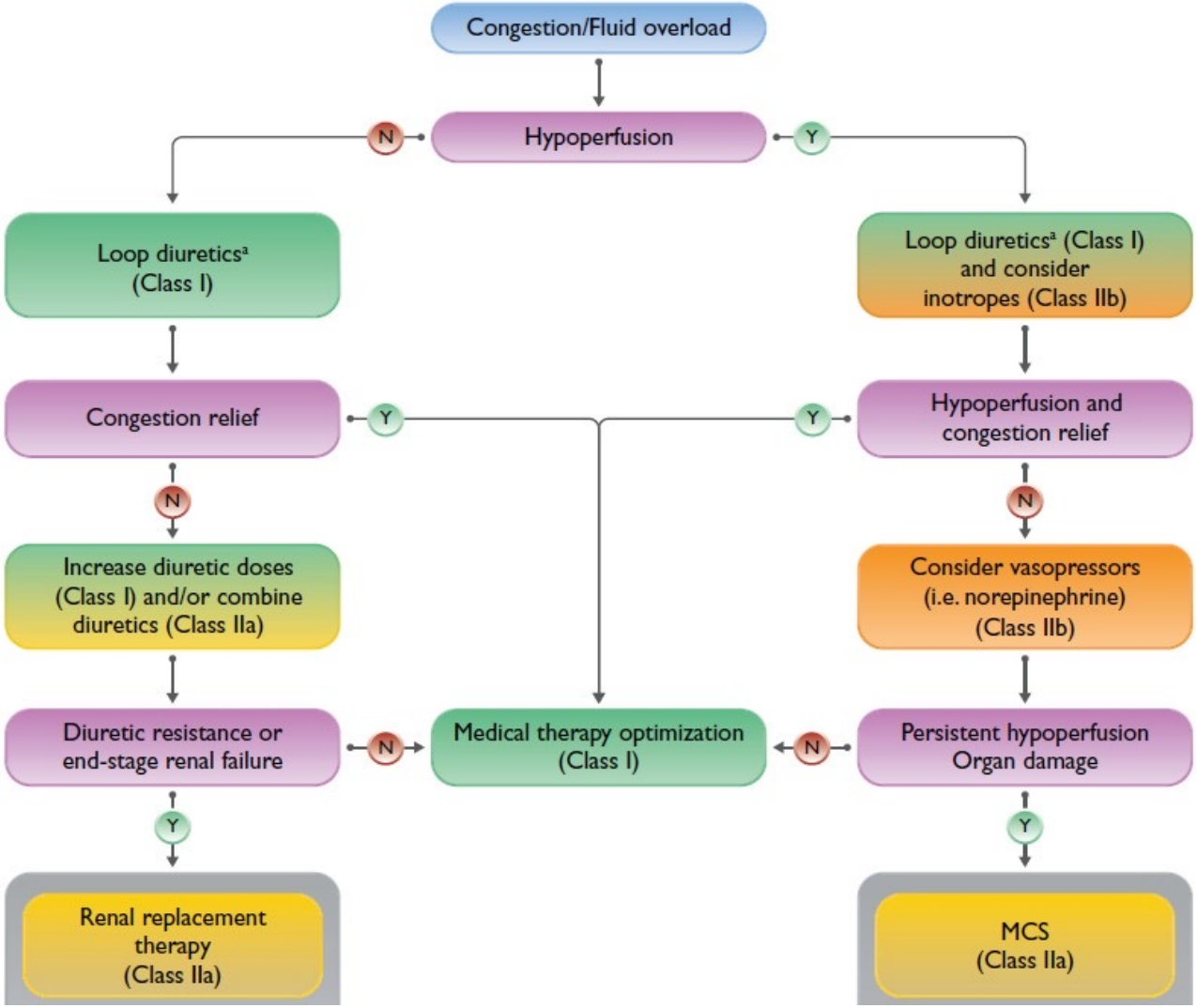




Outcome for 1-year death or urgent heart transplantation (Tx) (left) and for the combined end point of 1-year death, urgent heart transplantation, or heart failure (HF) readmission (right) for the patients subdivided on the basis of the development of worsening renal function (WRF) and on the presence of signs of congestion (Cong) at discharge.

Marco Metra et al. Circ Heart Fail. 2012;5:54-62

Management of Acute Heart Failure

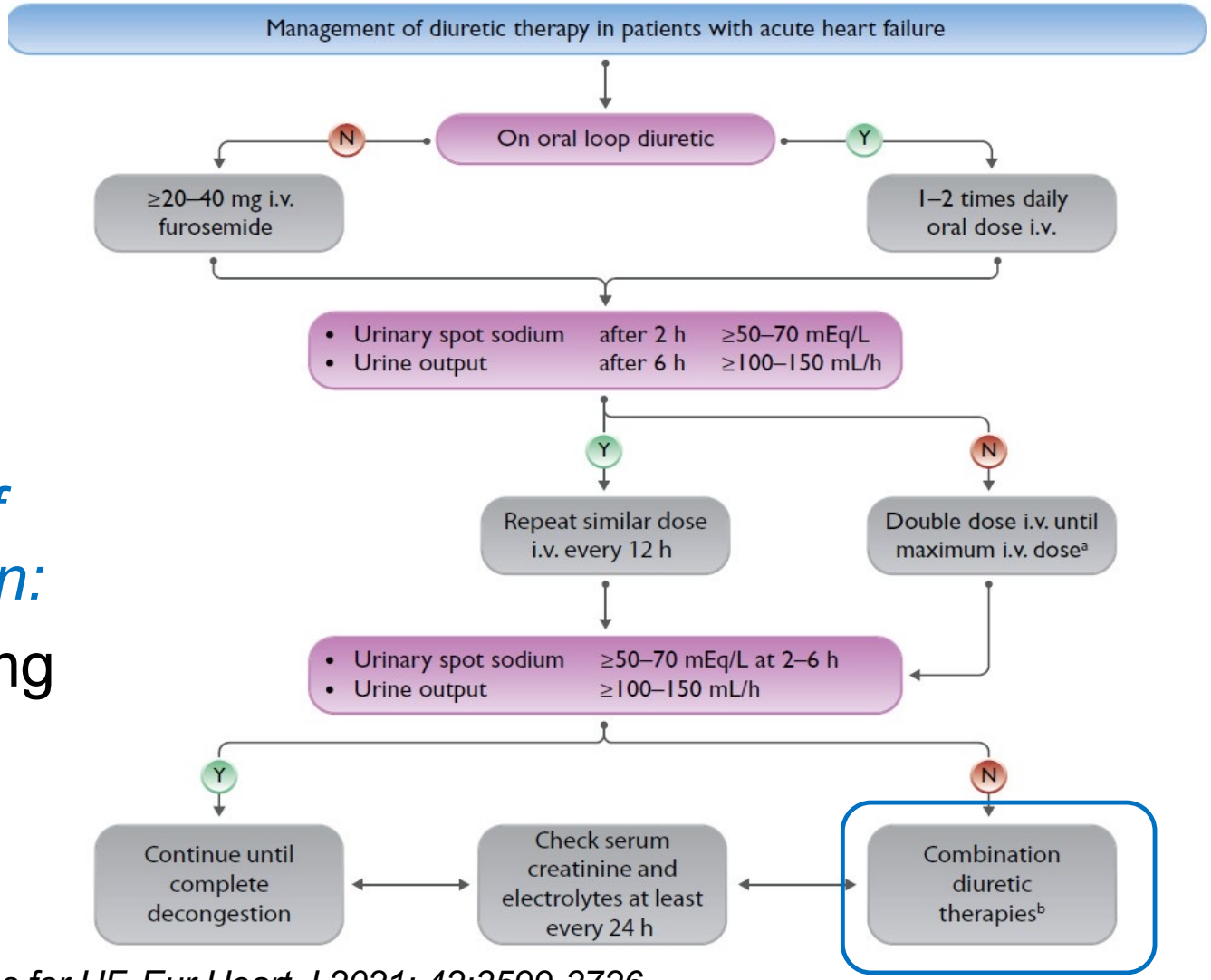


McDonagh et al., 2021 ESC Guidelines for HF, Eur Heart J 2021; 42:3599-3726

Diuretic Rx of Acute Heart Failure

Combine diuretics of different site of action:

- Metolazone 2.5-5 mg
- Thiazides
- Acetazolamide



McDonagh et al., 2021 ESC Guidelines for HF, Eur Heart J 2021; 42:3599-3726

Diuretics and “New” Drugs in HF

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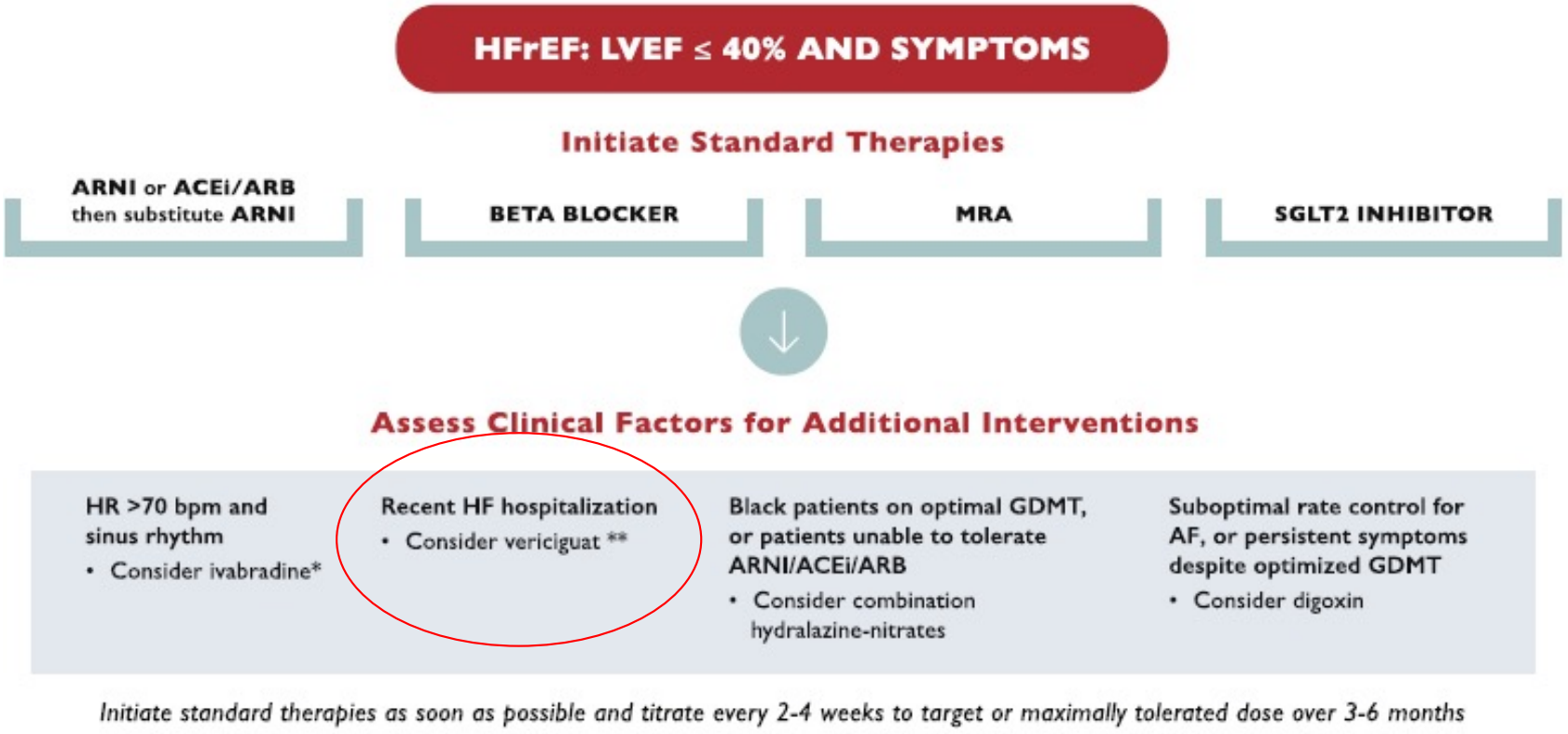
CCS/CHFS 2021 HF Guideline Update



MacDonald, Virani, et al., 2021 Update HFrEF, Can J Cardiol 2021; 37:531-46

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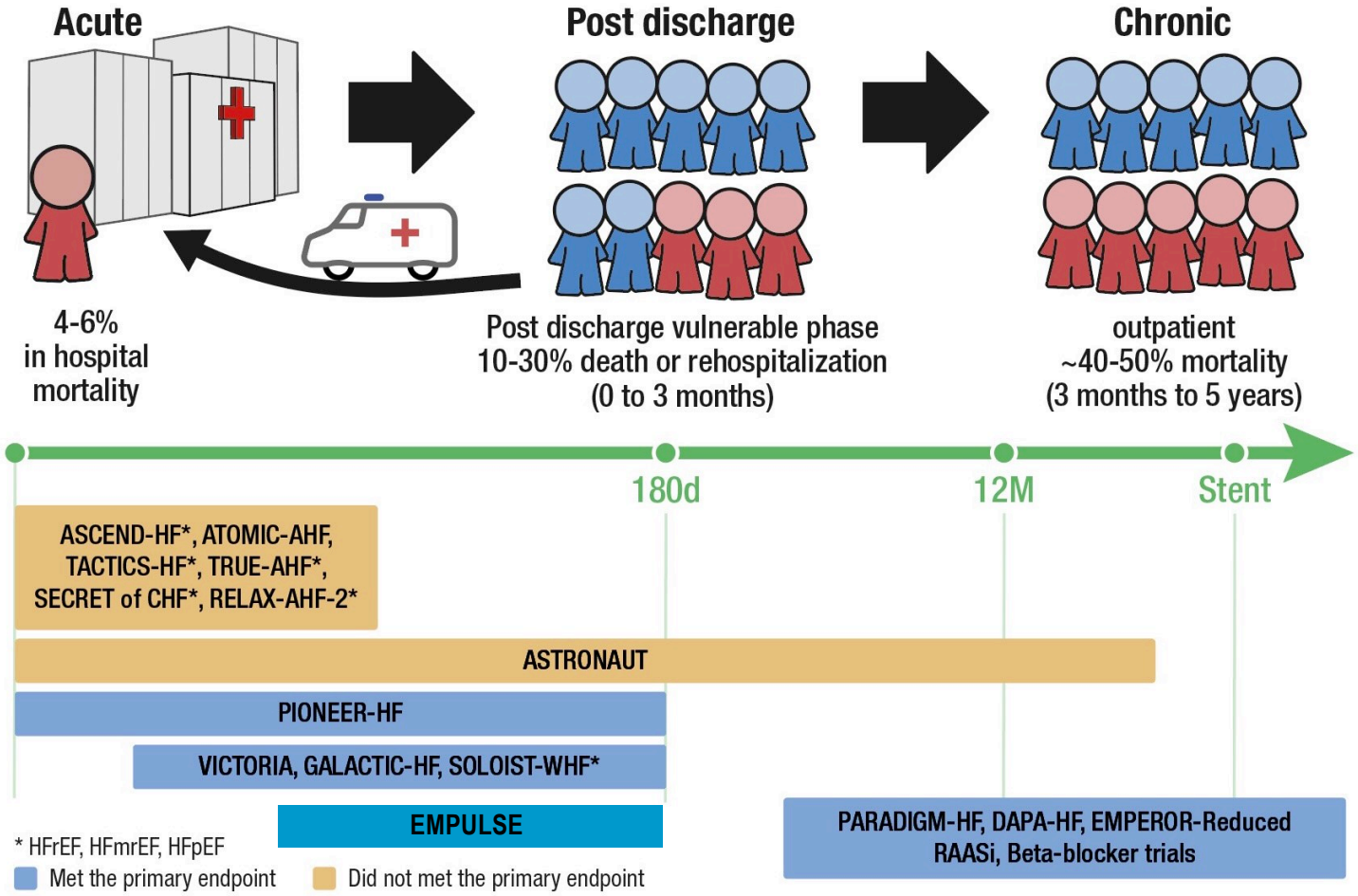
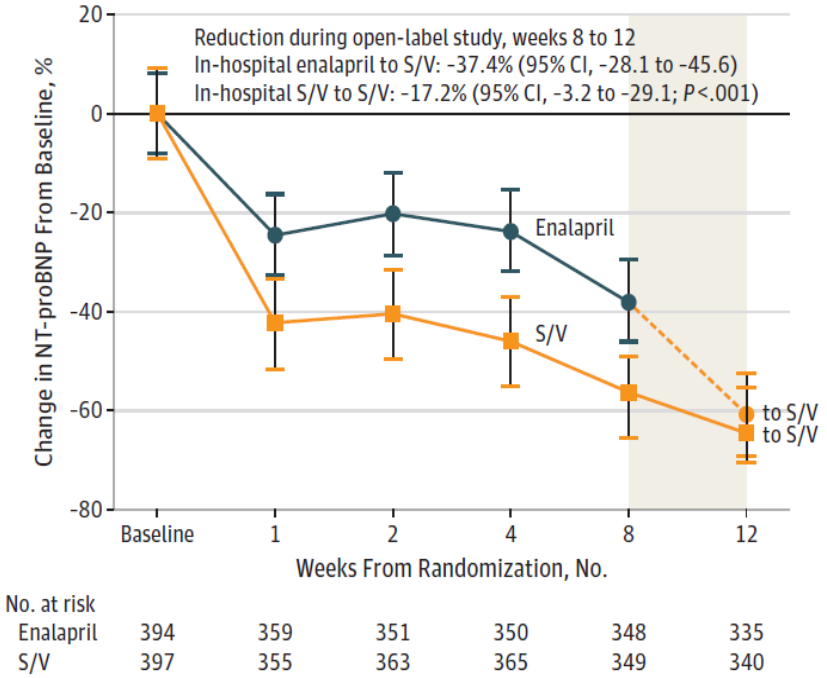
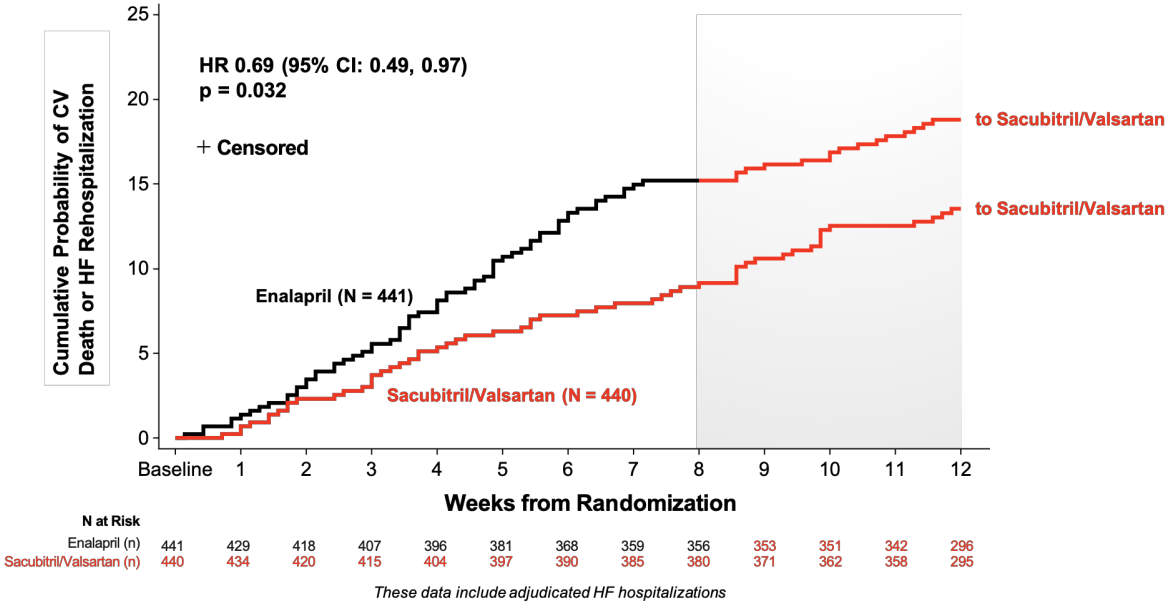
Quadruple Foundational Rx for HFrEF

Early Introduction of GDMT in Acute HF Hosp'n



PIONEER-HF Study: Sacubitril-Valsartan in ADHF



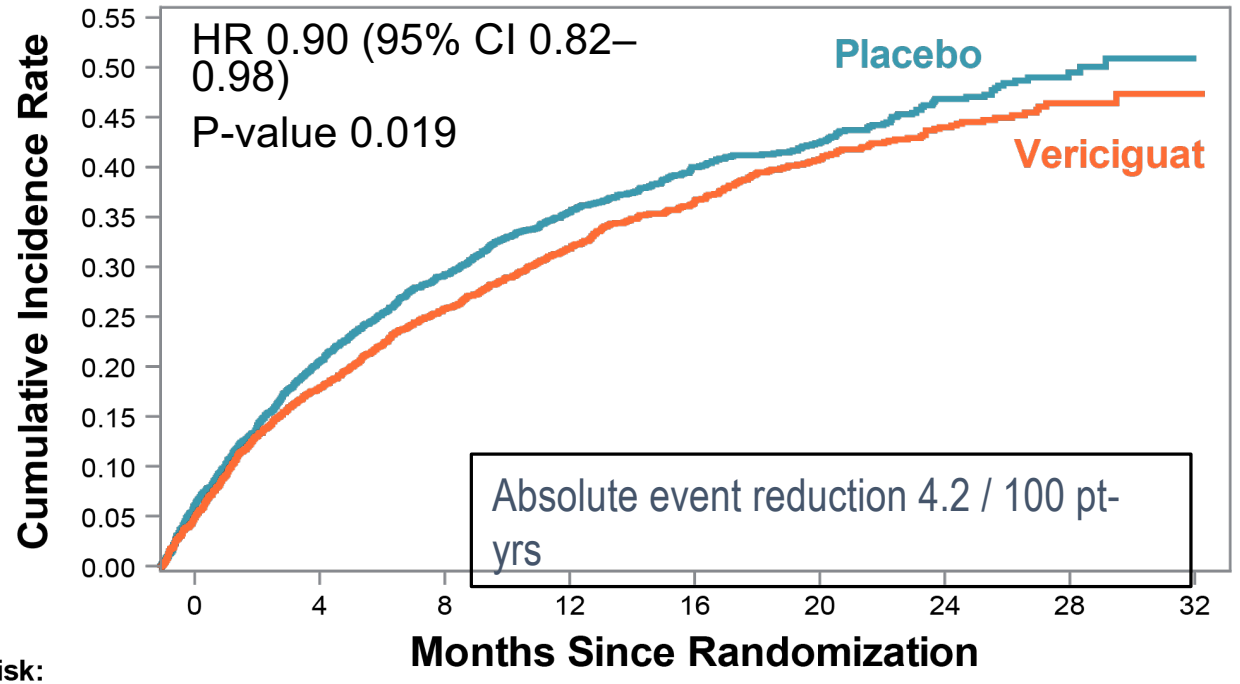


These data include adjudicated HF hospitalizations

- Sacubitril-Valsartan/Enalarpil initiation in hospital
- Open label extension:
  - Further reduction in NTproBNP (both groups)
  - In-hospital sac-val group experienced lower incidence of death or re-hospitalization over 12 weeks follow-up

Velazquez et al, N Engl J Med 2019
Devore et al, JAMA Cardiol 2020

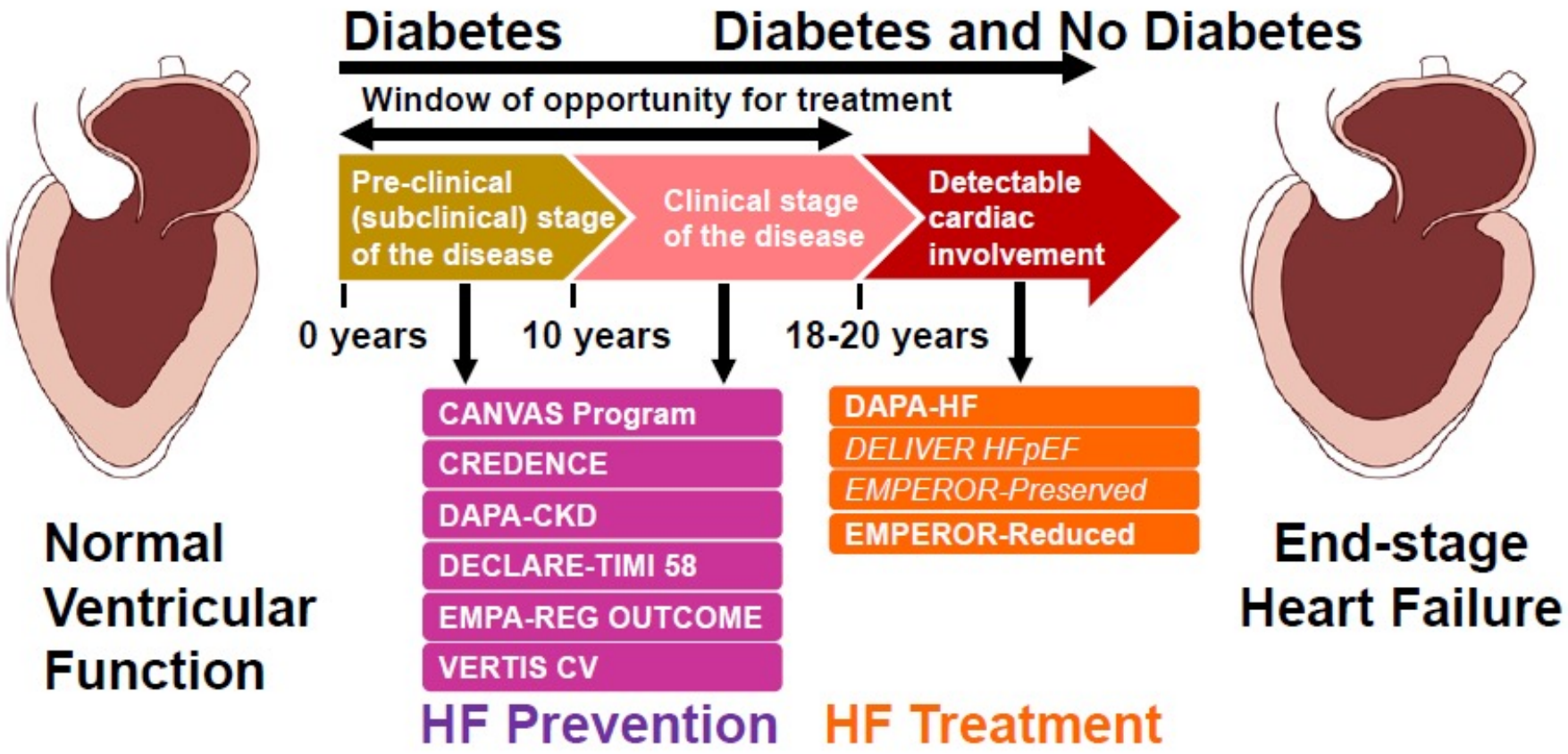
VICTORIA: Vericiguat & Effect on CVD/HFH



Number at Risk:									
Vericiguat	2526	2099	1621	1154	826	577	348	125	1
Placebo	2524	2053	1555	1097	772	559	324	110	0

VICTORIA, NEJM 2

The Evolution of SGLT2i in HF Management

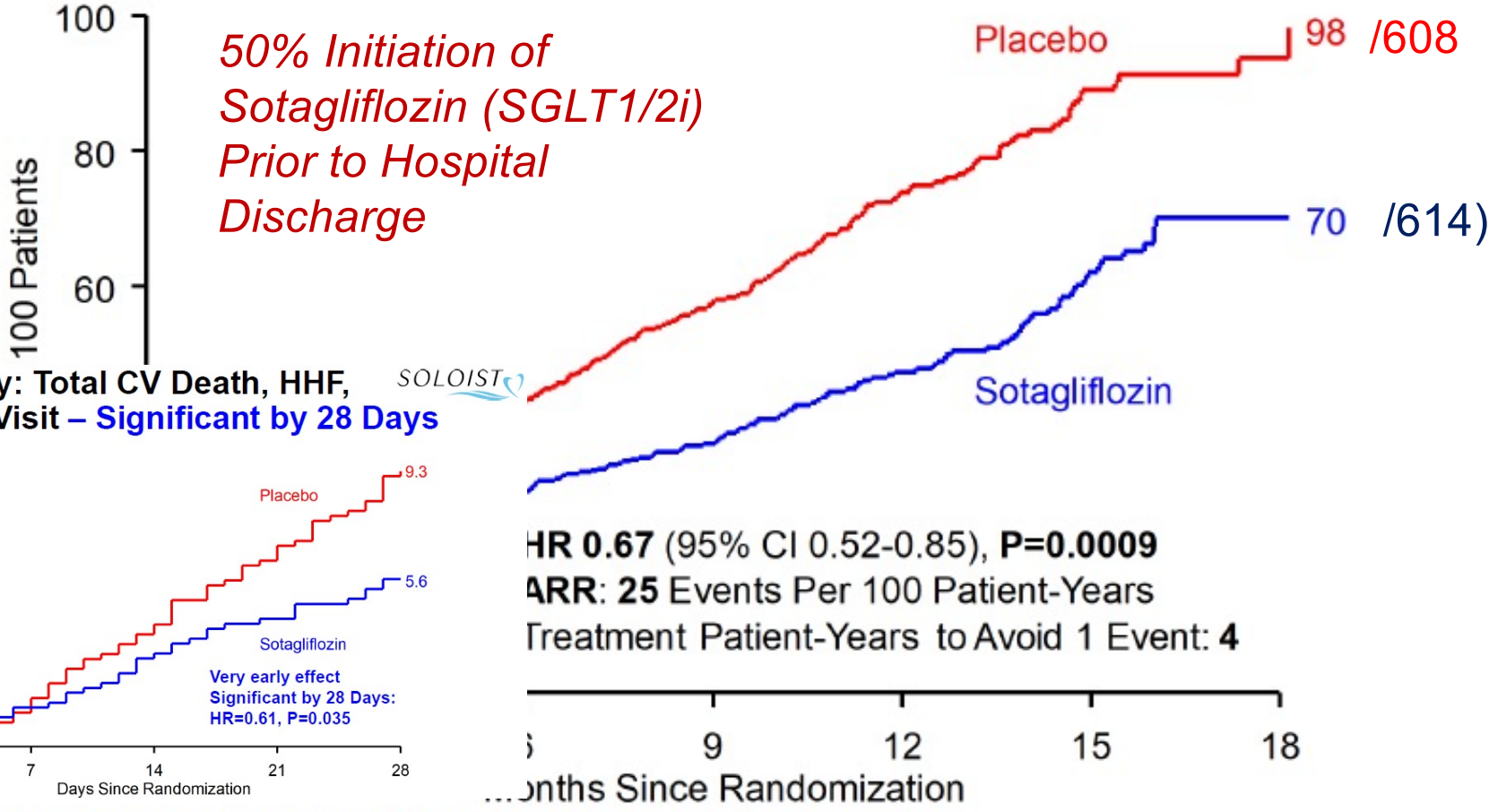


Adapted from Bhatt DL, Verma S, Braunwald E. *Cell Metabolism*. 2019;30:847-849.

Primary Efficacy: Total CV Death, HHF, and Urgent HF Visit

SOLOIST

50% Initiation of Sotagliflozin (SGLT1/2i) Prior to Hospital Discharge



Primary Efficacy: Total CV Death, HHF, and Urgent HF Visit – Significant by 28 Days

SOLOIST

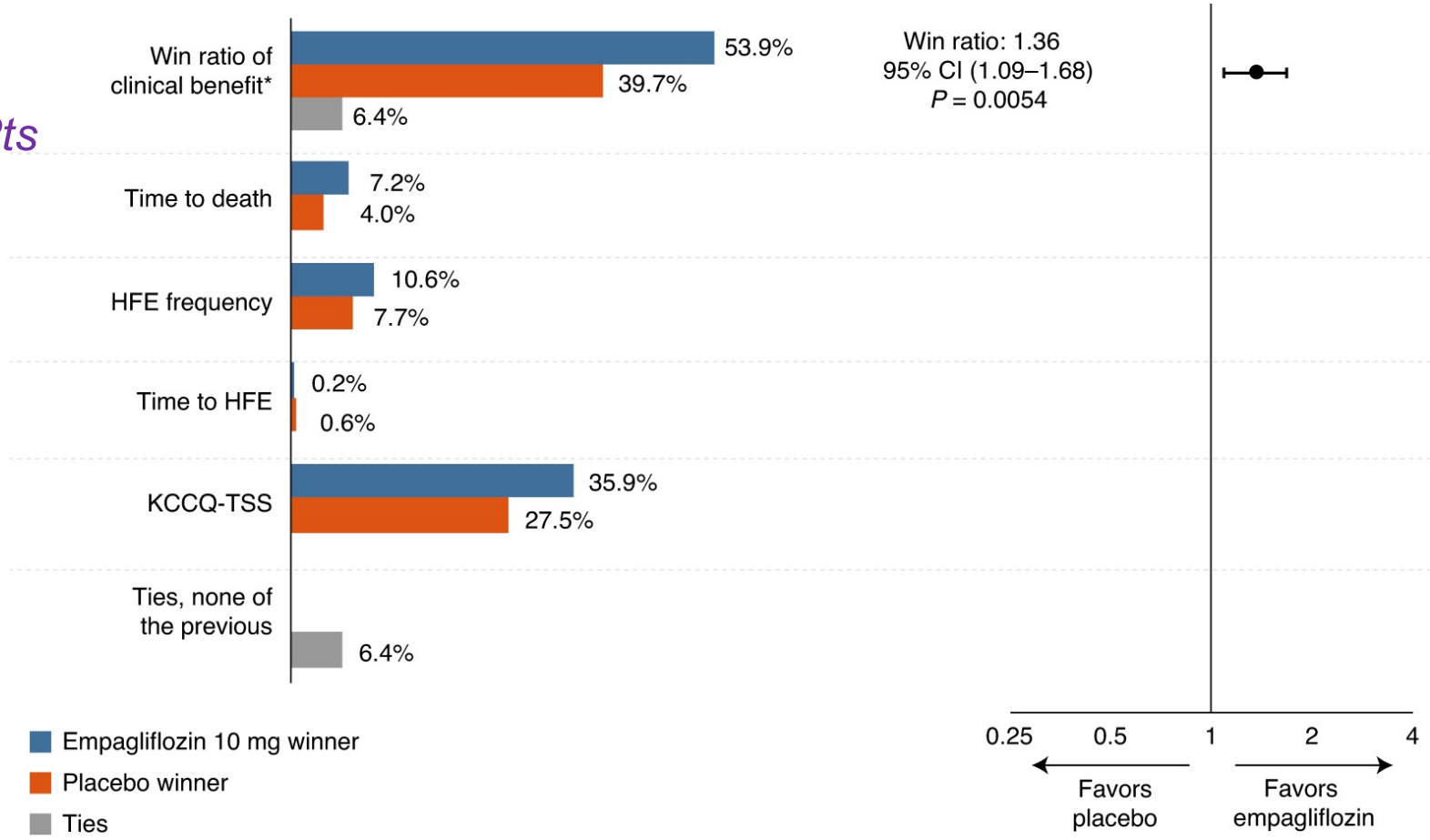
Bhatt DL, Szarek M, Steg PG, et al., and Pitt B. *N Engl J Med.* 2020. Bhatt DL. AHA 2020, virtual.

EMPULSE – Empagliflozin in ADHF

N = 530 ADHF Pts

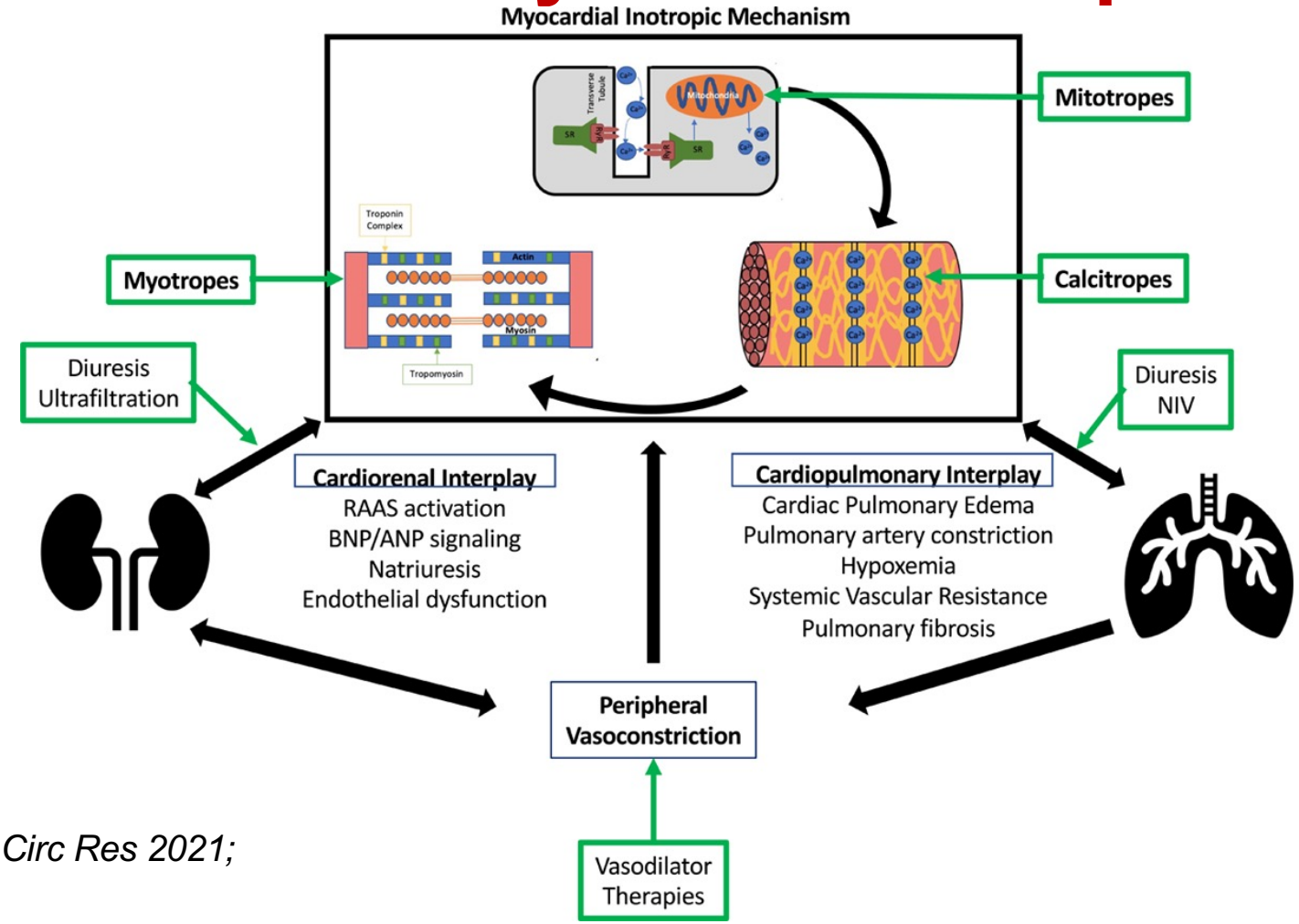
Empa Initiation following stabilization

Follow Up = 90 days



Voors AA, Ponikowski P, et al., Nature Med 2022; 28:568-574

Acute HF – Heart & Systemic Disequilibrium

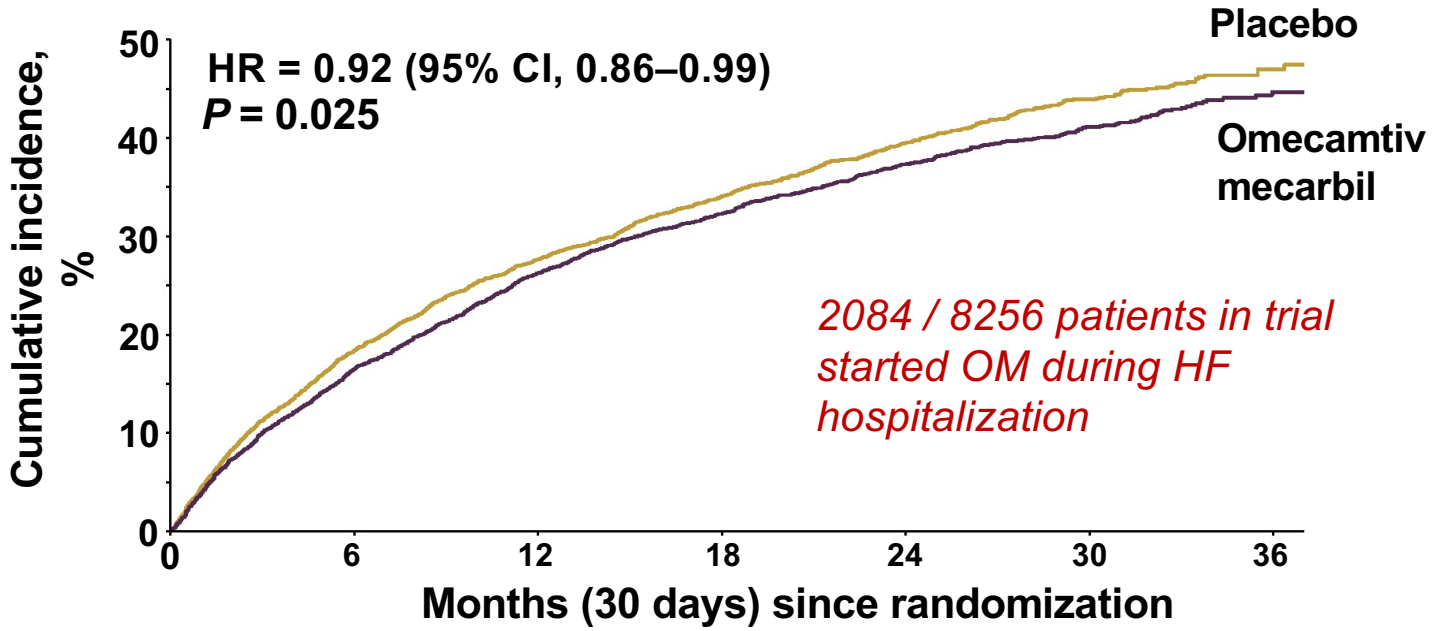


Njoroge & Teerlink, Circ Res 2021; 128:1468–1486

GALACTIC-HF: Omecativ mecarbil in HF

Primary Composite Endpoint

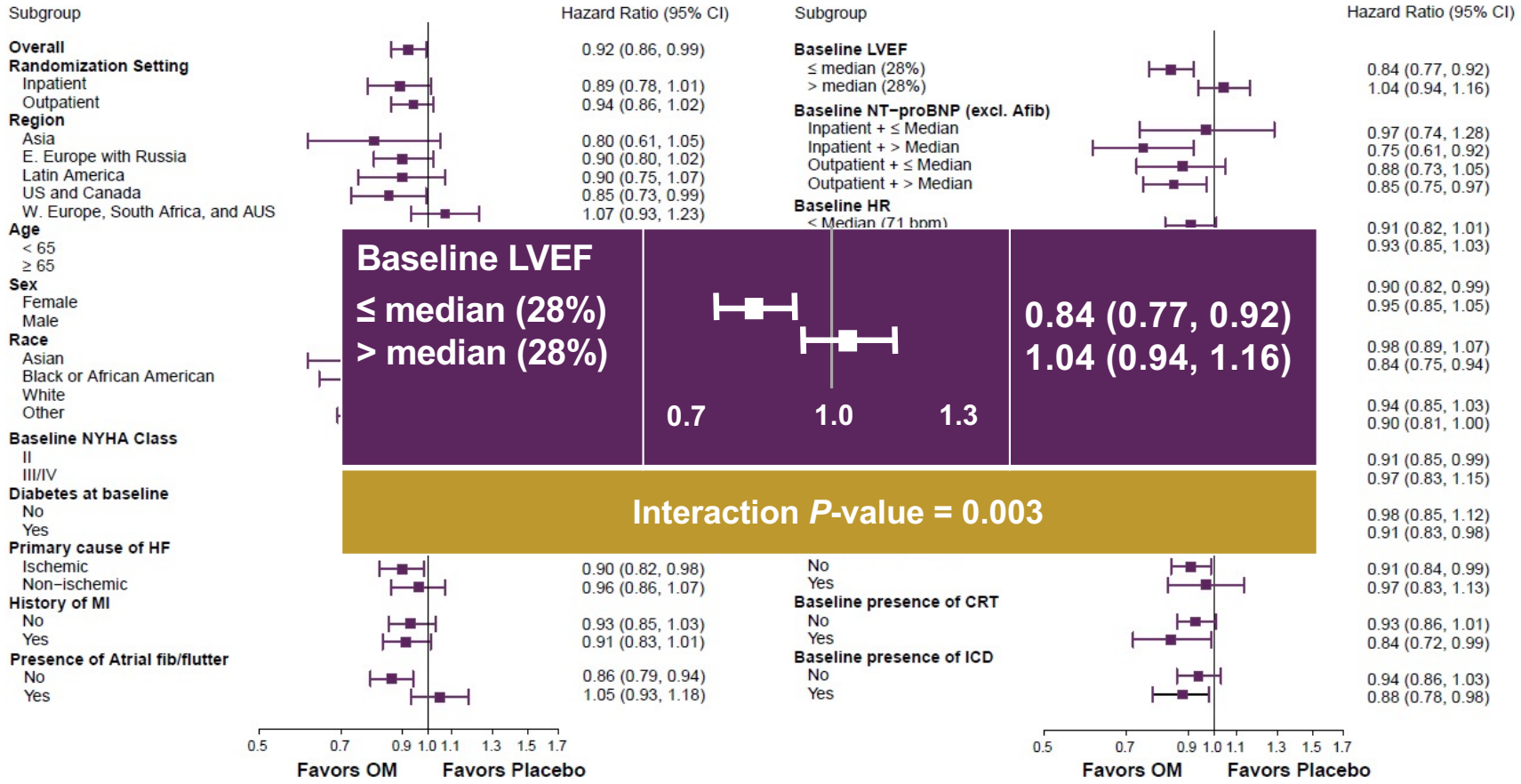
Time to First Heart Failure Event or Cardiovascular Death



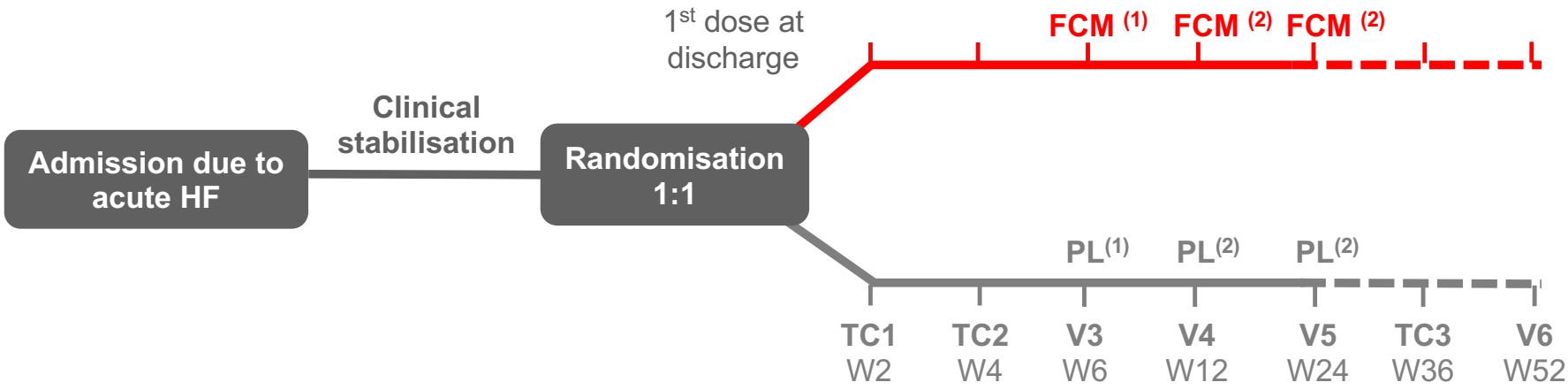
Patients at risk, n							
Placebo	4112	3310	2889	2102	1349	647	141
Omecamtiv mecarbil	4120	3391	2953	2158	1430	700	164

GALACTIC-HF: Omecativ mecarbil in HF

Primary Outcome: Subgroup Results



AFFIRM-AHF Trial: Ferric CarboxyMaltose in AHF



[1] The repletion dose of study treatment will be administered based on the iron need assessed at the baseline visit

[2] Study treatment to be administered only if iron deficiency persisted

PL, placebo; TC, telephone contact; V, visit; W, week.

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

Eligibility Criteria for AFFIRM-AHF Iron Defic Trial

Inclusion criteria	Exclusion criteria
Hospitalisation for acute HF confirmed by signs/symptoms of acute HF and elevated natriuretic peptide (BNP or NT-proBNP) levels	Clinical evidence of ACS, TIA, or stroke within 30 days
Iron deficiency: serum ferritin <100 ng/mL OR serum ferritin 100-299 ng/mL and TSAT <20%	CABG, PTCA, cardiac device implantation (including CRT) within 30 days
Left ventricular ejection fraction <50% not older than 12 months prior to randomization	Hb <8 g/dL[a] or >15 g/dL
	Active infection requiring anti-microbial treatment during an index hospitalisation
	ESA, i.v. iron or blood transfusion administered in last 3 months and oral iron (>100 mg/day) in previous 4 weeks

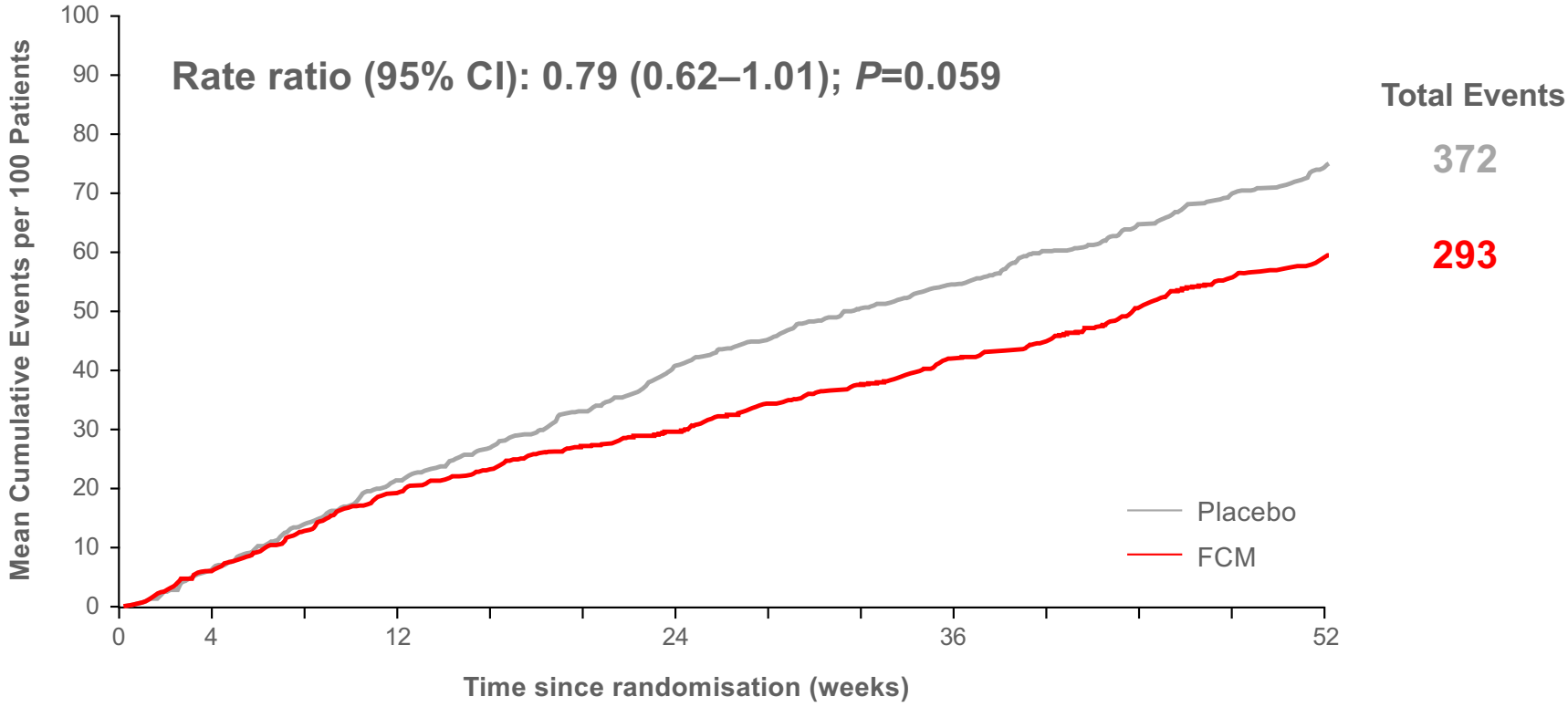
[a]<10 g/dL for sites in The Netherlands, Spain and Singapore.

ACS, acute coronary syndrome; BNP, B-type natriuretic peptide; CABG, coronary artery bypass grafting; CRT, cardiac resynchronization therapy; ESA, erythropoiesis stimulating agent; Hb, haemoglobin; i.v., intravenous; NT-proBNP, N-terminal-pro hormone BNP; PTCA, Percutaneous transluminal coronary angioplasty; TIA, transient ischemic attack; TSAT, transferrin saturation.

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

AFFIRM-AHF Trial: Ferric CarboxyMaltose in AHF

Primary Endpoint:
Total HF Hospitalisations and CV Death



Summary: Diuretics & “New” Drugs in HF

- ADHF = HF progression & worse outcomes
- Effective decongestion with diuretics still cornerstone, effective in combination
- Early in-hospital initiation of GDMT highly efficacious – Sac-Val ± SGLT1/2i ± Vericiguat
- Other Rx: Omecativ mecarbil / Iron (FCM)


Thank You!
Merci!
SEA CLOUD