

**Supplementary Table 1: A short summary on five selected heart failure trials presented at the 2023 meeting of the European Society of Cardiology**

Study	Setting and design	Patients	N	Follow-up	Comparison	Outcomes	Main Results	Relevance for pharmacists
PUSH-AHF <sup>1</sup>	Single-center, open-label, randomized controlled trial	Acute HF patients requiring IV loop diuretics	310	6 months	Natriuresis--guided vs. standard diuretic therapy	Effect on natriuresis and clinical outcome	Natriuresis-guided approach increased natriuresis (409 vs. 345 mmol, p = 0.0061)  No significant difference in all-cause mortality or HF rehospitalization rates  Safety and feasibility demonstrated	Pragmatic trial in a generalizable acute HF patient population.  A soft endpoint was chosen.  The validation of a previous consensus-derived proposal, is important as there is only very limited guidance on how to use loop diuretics in the acute phase. <sup>2</sup>
ADVOR kidney <sup>3</sup>	Prespecified analysis within the ADVOR trial	Acute HF patients requiring IV loop diuretics	519	3 months	Acetazolamide + IV loop diuretics vs. IV loop diuretics	According to baseline renal function: the acetazolamide effects on decongestion, diuresis, natriuresis estimated glomerular filtration rate and clinical outcome	Acetazolamide retains diuretic efficacy across a broad range of renal function  Increase in worsening renal function with acetazolamide (40.5% vs. 18.9%, p < 0.001), but without impact on creatinine levels or heart failure outcomes	Acetazolamide remains effective. It does not improve hard clinical outcomes per se however. The analysis does show the association between 'dry at discharge' and better HF outcomes. The main takeaway is that IV acetazolamide was associated with a

								shorter hospital stay, and less congestion at discharge.
CASTLE-HTX <sup>4</sup>	Single-center, open-label, randomized controlled trial	Patients with symptomatic AF and end-stage HF	194	18 months	Catheter ablation vs. usual care	Composite of death left ventricular assist device, urgent heart transplant	Reduction of primary outcome in favor of ablation (8% vs. 30%, p<0.001)  Reduced deaths (6% vs. 20%)	Arrhythmia burden is an important determinant of prognosis in patients with AF and HF.  It is unclear to what extent trial findings can be translated to clinical practice due to certain limitations (single-center, unblinded, very large, and very fast risk reductions based on a few events).
HEART-FID <sup>5</sup>	Double-blind, randomized, placebo-controlled trial	Ambulatory HFrEF patients with iron deficiency	3065	12 months	IV iron (ferric carboxymaltose) vs. placebo	Hierarchical composite of death, HF hospitalizations, 6-minute walk distance	No significant difference in the composite primary endpoint  IV iron vs. placebo: Mortality: 8.6% vs. 10.3%, p-value not specified  HF hospitalizations: 297 vs. 332, p-value not specified	After previous trials, it is not completely certain what IV iron holds for HF patients in terms of reducing morbidity, particularly on the current GDMT background.  At a minimum, IV iron improves functionality, and QoL and likely reduces HF

							Modest effect on 6-minute walking distance (p=0.02)  The use of IV iron was safe	readmissions in AHF patients. <sup>6</sup>
STEP-HFpEF <sup>7</sup>	Double-blind, randomized, placebo-controlled trial	HfpEF patients with obesity	529	57 weeks	Semaglutide vs. placebo	Change from baseline in the KCCQ-CSS score and body weight	KCCQ-CSS score change higher in the semaglutide group: (16.6 vs 8.7, p < 0.001)  Greater weight loss in semaglutide group (-13.3% vs. -2.6%, p<0.001)  Improved 6-minute walk distance and NT-proBNP reduction	Some might argue whether this was an obesity study or a 'real' HFpEF investigation.  Patients lost weight and felt better.  The trial was not designed for HF outcomes but importantly did highlight the safety of intentional weight loss in HF (hence, refuting the so-called obesity paradox in HF).

**Abbreviations:** HF: heart failure; IV: intravenous; AF: atrial fibrillation; HFrEF: heart failure with reduced ejection fraction; GDMT: guideline-directed medical therapy; AHF: acute heart failure; HFpEF: heart failure with preserved ejection fraction; KCCQ-CSS: Kansas City Cardiomyopathy Questionnaire - Clinical Summary Score; NT-proBNP: N-terminal prohormone of brain natriuretic peptide.

## References

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