Cardio-Renal-Metabolic Overlap, Outcomes, and Treatment with Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

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Background

- Cardio-renal-metabolic (CRM) conditions (ASCVD, CKD, and T2D) commonly coexist with HF.
- The influence of overlapping CRM conditions on clinical outcomes in HFmrEF/HFpEF has not been well-studied.
- Whether the relative and absolute benefits of SGLT2i differ by the extent and type of CRM overlap in this population remains uncertain.

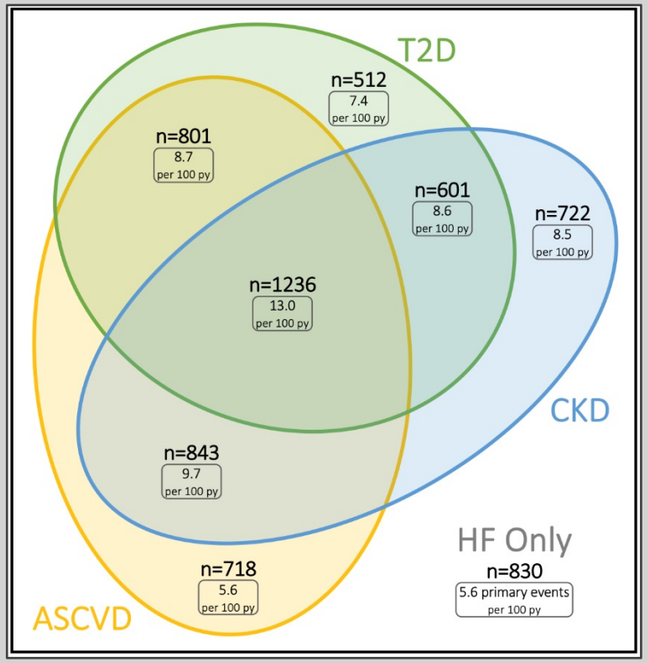
Study Aims

1. To characterize the prevalence and impact of overlapping CRM conditions on outcomes in HFmrEF and HFpEF
2. To determine whether the safety and efficacy of dapagliflozin varies by number of overlapping CRM conditions in HFmrEF and HFpEF

Methods

- DELIVER (Dapagliflozin Evaluation to Improve the Lives of Patients with Preserved Ejection Fraction Heart Failure) evaluated the safety/efficacy of dapagliflozin versus placebo in chronic HF with LVEF >40%.
- In this *post-hoc* analysis, we evaluated the prevalence of comorbid CRM conditions (ASCVD, CKD, T2D), their impact on the primary outcome (cardiovascular death or worsening HF), and both relative and absolute treatment effects of dapagliflozin on the primary outcome and key secondary outcomes by CRM status.

Prevalence of CRM Overlap and Primary Event Rates in DELIVER, by Baseline CRM Status

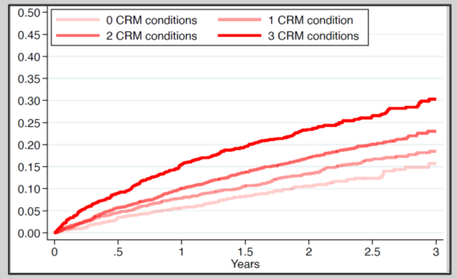


HF only: ~1 in 10 DELIVER participants
HF + ASCVD + CKD + T2D: ~1 in 5 DELIVER participants

Higher CRM overlap associated with:

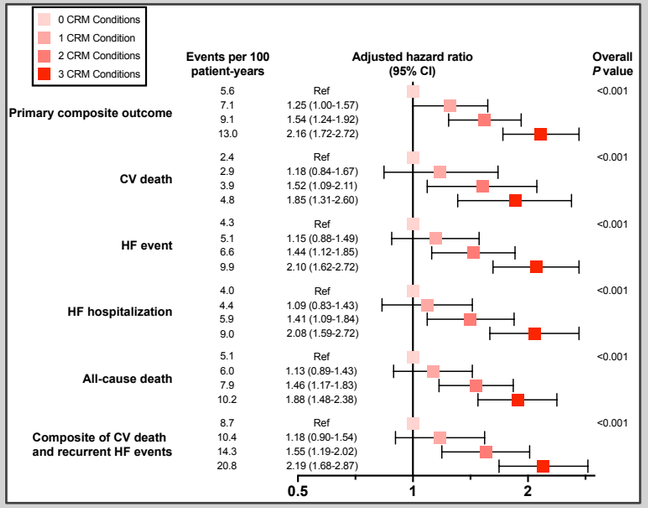
Older age, male sex, higher burden of major CRM risk factors, longer-duration HF, prior HF hospitalization, lower LVEF, and worse baseline health status by NYHA functional class and KCCQ.

Incidence of Primary Outcome by CRM Status



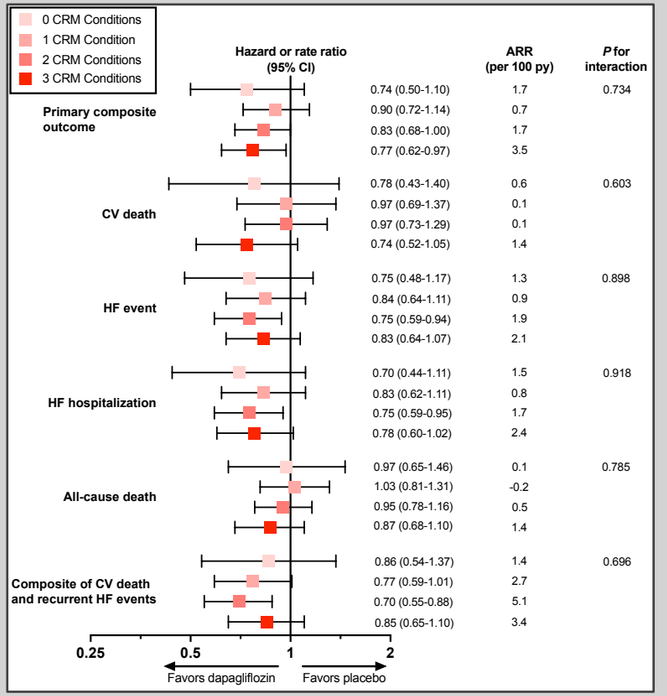
Kaplan-Meier curve for the primary endpoint of CV death or worsening HF, by number of additional CRM conditions at baseline.

Risk of Primary and Secondary Endpoints by Number of Overlapping CRM Conditions



*: Adjusted for baseline age, sex, race, geographic region, and LVEF.

Effect of Dapagliflozin versus Placebo on Primary and Secondary Endpoints, by CRM Status



Any Serious Adverse Event, by CRM Status

Number of Additional CRM Conditions								
0		1		2		3	
Placebo	Dapa	Placebo	Dapa	Placebo	Dapa	Placebo	Dapa
34.3%	36.3%	39.7%	42.4%	49.3%	41.8%	55.0%	53.8%

CRM multimorbidity was common in DELIVER and associated with adverse outcomes. Dapagliflozin was safe and effective across the CRM spectrum, with greater absolute benefits among those with highest CRM overlap. While relatively uncommon, patients with HFmrEF or HFpEF alone and without any other indication for SGLT2i consistently benefited from dapagliflozin. These findings support the expanding focus on integrative strategies to optimize outcomes for patients with overlapping CRM conditions.