Characteristics, Outcomes and Treatment Response With Dapagliflozin Across the Range of Ejection Fraction in People With HF and a History of CABG Surgery: A Pooled Analysis From DAPA-HF and DELIVER

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Introduction

- There is limited outcome data on patients with a history of CABG surgery and heart failure (HF).
- The placebo-controlled DAPA-HF and DELIVER trials evaluated the impact of the sodium-glucose cotransporter-2 (SGLT2) inhibitor dapagliflozin (10 mg QD), on top of recommended therapy, in patients with HF with reduced ejection fraction (HFrEF; LVEF ≤40%) and mildly reduced/preserved ejection fraction (HFmrEF/HFpEF; LVEF >40%), respectively).
- This pooled analysis (N=11,007) of the DAPA-HF (n=4,744) and DELIVER (n=6,263) trials compared the baseline characteristics as well as efficacy and safety of dapagliflozin in patients with and without a CABG history.

Methods

- Key Inclusion Criteria
  (A) NYHA II-IV ♦ (B) LVEF ≤40% (DAPA-HF) or >40% (DELIVER) ♦ (C) Elevated NT-proBNP
- Key Exclusion Criteria
  (A) Systolic BP <95 mmHg ♦ (B) eGFR <30 mL/min/1.73m^2 (DAPA-HF) or <25 mL/min/1.73m^2 (DELIVER) ♦ (C) Type 1 diabetes
- Primary Outcome
  Composite of worsening HF or CV death
  - *Worsening HF = hospitalization or urgent visit with intravenous therapy for HF*
  - *CV death includes undetermined deaths*
- Modelling
  - *Stratified by diabetes status and trial and adjusted for treatment assignment and HF hospitalization (except for all-cause death)*
  - *Diabetes defined as investigator-recorded history or baseline HbA1c ≥6.5%*

Conflicts of interest
The DAPA-HF and DELIVER trials were funded by AstraZeneca. SV has received research grants and/or speaking honoraria from AstraZeneca. JJVM's employer, the University of Glasgow, has been remunerated by AstraZeneca for their time working on the DAPA-HF and DELIVER trials.

Results

Baseline Characteristics of the Pooled DAPA-HF and DELIVER Cohorts

	No CABG n=9,431	CABG n=1,576
Age (years)	69.2±10.7	70.4±8.8
Female	3529 (37.4)	327 (20.7)
Duration of HF >5 years	2836 (30.1)	711 (45.1)
LVEF (%)	44.6±14.1	41.8±12.9
LVEF <40%	3947 (41.9)	800 (50.8)
eGFR (mL/min/1.73m^2)	63.7±19.5	59.4±18.1
KCCQ-TSs	71.5±22.2	71.9±21.2
T2DM	3911 (41.5)	878 (55.7)
Previous PCI	2614 (27.7)	722 (45.8)
Previous MI	2712 (28.8)	1019 (64.7)
Statin Therapy	5842 (61.9)	1373 (87.1)
Antiplatelet Therapy	4115 (43.6)	1107 (70.2)
ICD/CRT-D	1095 (11.6)	315 (20.0)

Data are expressed as mean±SD or n (%).

Among the 11,007 patients, ~14% had a prior history of CABG and were characterized by a higher proportion of men, lower eGFR and LVEF, and higher rates of prior MI, PCTA, T2DM, antiplatelet and statin therapy.

Adverse Events

	Placebo	Dapagliflozin
Discontinuation due to AE		
No CABG History	242 (5.2%)	247 (5.2%)
CABG History	55 (6.8%)	47 (6.1%)
Volume depletion		
No CABG History	161 (3.4%)	185 (3.9%)
CABG History	38 (4.7%)	42 (5.5%)
Renal AE		
No CABG History	202 (4.3%)	192 (4.1%)
CABG History	59 (7.3%)	45 (5.9%)

Data are expressed as n (%).

AE rates and tolerability were similar between the dapagliflozin and placebo groups.

Key Outcomes of the Pooled DAPA-HF and DELIVER Cohorts

	No CABG n=9,431	CABG n=1,576	$P_{interaction}$
Worsening HF or CV death	0.79 (0.72-0.87)	0.78 (0.63-0.96)	0.88
Worsening HF	0.76 (0.68-0.86)	0.68 (0.53-0.87)	0.48
HF hospitalization	0.74 (0.66-0.84)	0.71 (0.55-0.92)	0.87
CV death	0.84 (0.74-0.96)	0.95 (0.72-1.26)	0.49
MI, stroke, or CV death	0.90 (0.81-1.01)	0.89 (0.70-1.13)	0.89
All cause death	0.91 (0.82-1.01)	0.86 (0.68-1.08)	0.58
Total HF hospitalizations and CV death	0.77 (0.69-0.86)	0.72 (0.56-0.94)	0.69

Data are expressed as HR (95% CI) except for Total HF hospitalizations and CV death which are presented as RR (95% CI).

Dapagliflozin consistently reduced the primary and key secondary endpoints in patients with and without a history of CABG across the entire spectrum of LVEF.

Patients with HF and a CABG history were at higher risk of experiencing HF outcomes (values expressed as adjusted hazard ratio [aHR] [95% CI])

Primary outcome	*1.21 (1.08-1.36)*
CV death	*1.22 (1.04-1.42)*
All-cause death	*1.22 (1.07-1.38)*
HF hospitalization	*1.31 (1.14-1.51)*
Total HF event	*1.38 (1.20-1.59)*
MACE	*1.34 (1.17-1.52)*

Conclusions

In patients with HF

- A prior history of CABG was associated with higher rates of CV outcomes and mortality compared to those without a history of CABG
- The efficacy and safety of dapagliflozin was similar in the presence and absence of a history of CABG.