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CLINICAL RESEARCH

Baseline Characteristics of Patients With HF With Mildly Reduced and Preserved Ejection Fraction

DELIVER Trial

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ABSTRACT

OBJECTIVES This report describes the baseline clinical profiles and management of DELIVER (Dapagliflozin Evaluation to Improve the Lives of Patients With Preserved Ejection Fraction Heart Failure) trial participants and how these compare with those in other contemporary heart failure with preserved ejection fraction trials.

BACKGROUND The DELIVER trial was designed to evaluate the effects of the sodium-glucose cotransporter–2 inhibitor dapagliflozin on cardiovascular death, heart failure (HF) hospitalization, or urgent HF visits in patients with HF with mildly reduced and preserved left ventricular ejection fraction (LVEF).

METHODS Adults with symptomatic HF and LVEF >40%, with or without type 2 diabetes mellitus, elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels, and evidence of structural heart disease were randomized to dapagliflozin 10 mg once daily or matching placebo.

RESULTS A total of 6,263 patients were randomized (mean age: 72 ± 10 years; 44% women; 45% type 2 diabetes mellitus; 45% with body mass index ≥30 kg/m^2; and 57% with history of atrial fibrillation or flutter). Most participants had New York Heart Association functional class II symptoms (75%). Baseline mean LVEF was 54.2 ± 8.8% and median NT-proBNP of 1,399 pg/mL (IQR: 962 to 2,210 pg/mL) for patients in atrial fibrillation/flutter compared with 716 pg/mL (IQR: 469 to 1,281 pg/mL) in those who were not. Patients in both hospitalized and ambulatory settings were enrolled, including 10% enrolled in-hospital or within 30 days of a hospitalization for HF. Eighteen percent of participants had HF with improved LVEF.

CONCLUSIONS DELIVER is the largest and broadest clinical trial of this population to date and enrolled high-risk, well-treated patients with HF with mildly reduced and preserved LVEF. (Dapagliflozin Evaluation to Improve the Lives of Patients With Preserved Ejection Fraction Heart Failure [NCT03619213]) (J Am Coll Cardiol HF 2022;10:184–197) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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Evidence-based therapeutic options have been limited in patients with heart failure (HF) and left ventricular ejection fraction (LVEF) >40%. Recent guidelines have subdivided this broad group into HF with mildly reduced (LVEF between 40% and 49%) and preserved ejection fraction (LVEF ≥50%). Although the cutoffs used to distinguish these groups are relatively arbitrary, this distinction reflects the growing appreciation that patients in these groups may differ etiologically, phenotypically, and in their responses to treatment. Patients with HF with mildly reduced LVEF may respond similarly to evidence-based therapies that are effective in HF with reduced ejection fraction (HFrEF), whereas expected relative benefits may be attenuated at higher LVEF.[1-3] Moreover, with the use of disease-modifying therapies for patients with LVEF ≤40%, there is a growing pool of patients with HF and an LVEF >40% who have improved from a lower LVEF.[4-6] These patients with HF with improved LVEF have generally been excluded from clinical trials.

The DELIVER (Dapagliflozin Evaluation to Improve the Lives of Patients With Preserved Ejection Fraction Heart Failure) trial will test the hypothesis that dapagliflozin, a sodium-glucose cotransporter (SGLT)-2 inhibitor, would reduce cardiovascular death, HF hospitalization, or urgent HF visits in patients with HF and an LVEF >40%. Unlike prior studies in patients with HF and mildly reduced or preserved LVEF, DELIVER has included patients with HF and improved LVEF and allowed enrollment irrespective of care setting (including during hospitalization). In this report, we describe the baseline clinical characteristics of the 6,263 patients enrolled in DELIVER, and place these data in the context of previous trials of similar patients.

ABBREVIATIONS AND ACRONYMS

AFF = atrial fibrillation/flutter

ARB = angiotensin receptor blocker

BMI = body mass index

HF = heart failure

LVEF = left ventricular ejection fraction

NT-proBNP = N-terminal pro-B type natriuretic peptide

NYHA = New York Heart Association

SGLT-2 = sodium-glucose cotransporter-2

T2DM = type 2 diabetes mellitus

METHODS

STUDY DESIGN. DELIVER is a global, randomized, double-blind, parallel-group, event-driven trial comparing the efficacy and safety of dapagliflozin with placebo in patients with HF and mildly reduced, preserved, or improved LVEF. DELIVER enrolled adults 40 years or older with and without type 2 diabetes mellitus (T2DM), signs and symptoms of HF (New York Heart Association [NYHA] functional class II-IV), LVEF of >40%, elevated concentrations of N-terminal pro-B-type natriuretic peptide (NT-proBNP; degree of elevation depending on presence or absence of atrial fibrillation/flutter [AFF]), and evidence of structural heart disease (increased left atrial size or left ventricular hypertrophy). The most recent LVEF measurement was used to qualify patients for enrollment,

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TABLE 1 Baseline Characteristics by LVEF Group

	All DELIVER Participants (n = 6,263)	LVEF 41%-49% (n = 2,111)	LVEF 50%-59% (n = 2,256)	LVEF ≥60% (n = 1,892)	*P* Value
Age, y	71.7 ± 9.6	69.3 ± 9.9	72.2 ± 9.3	73.7 ± 8.8	<0.001
Age groups, y					<0.001
≤65	1,504 (24.0)	703 (33.3)	491 (21.8)	308 (16.3)	
>65–75	2,412 (38.5)	807 (38.2)	906 (40.2)	698 (36.9)	
>75	2,347 (37.5)	601 (28.5)	859 (38.1)	886 (46.8)	
Men	3,516 (56.1)	1,461 (69.2)	1,208 (53.5)	844 (44.6)	<0.001
Race					<0.001
White	4,458 (71.2)	1,555 (73.7)	1,647 (73.0)	1,254 (66.3)	
Asian	1,273 (20.3)	405 (19.2)	415 (18.4)	452 (23.9)	
Black or African American	159 (2.5)	43 (2.0)	60 (2.7)	56 (3.0)	
American Indian or Alaskan Native	189 (3.0)	54 (2.6)	71 (3.1)	63 (3.3)	
Other	184 (2.9)	54 (2.6)	63 (2.8)	67 (3.5)	
Geographic region					<0.001
Europe and Saudi Arabia	3,005 (48.0)	1,101 (52.2)	1,168 (51.8)	734 (38.8)	
Asia	1,226 (19.6)	391 (18.5)	403 (17.9)	431 (22.8)	
Latin America	1,181 (18.9)	424 (20.1)	347 (15.4)	410 (21.7)	
North America	851 (13.6)	195 (9.2)	338 (15.0)	317 (16.8)	
History of AFF	3,548 (56.7)	1,039 (49.2)	1,370 (60.7)	1,138 (60.1)	<0.001
History of stroke	591 (9.4)	181 (8.5)	243 (10.8)	167 (8.8)	0.05
History of hypertension	5,555 (88.7)	1,814 (85.9)	2,035 (90.2)	1,704 (90.1)	<0.001
History of type 2 diabetes	2,807 (44.8)	974 (46.1)	1,009 (44.7)	823 (43.5)	0.33
History of chronic obstructive pulmonary disease	695 (11.1)	243 (11.5)	257 (11.4)	195 (10.3)	0.52
History of noncoronary revascularization	140 (2.2)	59 (2.8)	46 (2.0)	35 (1.9)	0.19
History of sleep apnea	481 (7.7)	128 (6.1)	171 (7.6)	182 (9.6)	<0.001
Prior myocardial infarction	1,631 (26.0)	827 (39.2)	525 (23.3)	278 (14.7)	<0.001
Coronary artery disease	3,160 (50.5)	1,308 (62.0)	1,102 (48.8)	748 (39.5)	<0.001
Atherosclerotic cardiovascular disease	3,548 (56.7)	1,383 (65.5)	1,273 (56.4)	890 (47.0)	<0.001
Smoking status					<0.001
Current	484 (7.7)	223 (10.6)	167 (7.4)	94 (5.0)	
Former	2,261 (36.1)	841 (39.8)	807 (35.8)	612 (32.3)	
Never	3,518 (56.2)	1,047 (49.6)	1,282 (56.8)	1,186 (62.7)	
Baseline body mass index, kg/m^2	29.8 ± 6.1	29.4 ± 5.8	30.2 ± 6.2	29.9 ± 6.4	<0.001
Body mass index groups, kg/m^2					<0.001
<18.5 (underweight)	54 (0.9)	15 (0.7)	13 (0.6)	26 (1.4)	
18.5–24.9 (normal weight)	1,343 (21.5)	482 (22.8)	447 (19.8)	414 (21.9)	
25.0–29.9 (overweight)	2,073 (33.1)	744 (35.2)	744 (33.0)	582 (30.8)	
30.0–34.9 (class I obesity)	1,574 (25.2)	521 (24.7)	568 (25.2)	484 (25.6)	
35.0–39.9 (class II obesity)	798 (12.8)	241 (11.4)	311 (13.8)	246 (13.0)	
≥40 (class III obesity)	415 (6.6)	108 (5.1)	169 (7.5)	138 (7.3)	
Time from diagnosis of HF to enrollment					0.001
0–3 mo	569 (9.1)	156 (7.4)	215 (9.5)	197 (10.4)	
>3–6 mo	592 (9.5)	182 (8.6)	228 (10.1)	180 (9.5)	
>6–12 mo	840 (13.4)	279 (13.2)	315 (14.0)	246 (13.0)	
>1–2 y	995 (15.9)	317 (15.0)	372 (16.5)	305 (16.1)	
>2–5 y	1,569 (25.1)	548 (26.0)	560 (24.8)	461 (24.4)	
>5 y	1,693 (27.1)	626 (29.7)	565 (25.1)	502 (26.5)	
NYHA functional class at baseline					<0.001
I	1 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	
II	4,706 (75.1)	1,496 (71.9)	1,701 (75.4)	1,505 (79.5)	
III	1,537 (24.5)	607 (28.8)	550 (24.4)	380 (20.1)	
IV	19 (0.3)	8 (0.4)	5 (0.2)	6 (0.3)	
Baseline LVEF, %	54.2 ± 8.8	44.8 ± 2.5	53.9 ± 2.8	64.9 ± 4.9	<0.001
Pooled LVEF groups					<0.001
≤40%	4 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	
41%–49%	2,111 (33.7)	2,111 (100)	0 (0.0)	0 (0.0)	
50%–59%	2,256 (36.0)	0 (0.0)	2,256 (100.0)	0 (0.0)	
≥60%	1,892 (30.2)	0 (0.0)	0 (0.0)	1,892 (100.0)	

Continued on the next page

TABLE 1 Continued

	All DELIVER Participants (n = 6,263)	LVEF 41%-49% (n = 2,111)	LVEF 50%-59% (n = 2,256)	LVEF ≥60% (n = 1,892)	*P* Value
Baseline NT-proBNP, pg/mL	1,011.0 (623.0-1,751.0)	1,112.5 (650.0-2,076.0)	1,024.0 (642.0-1,691.0)	912.0 (568.5-1,541.5)	<0.001
NT-proBNP in AFF, pg/mL	1,399.0 (962.0-2,210.0)	1,532.0 (1,017.0-2,642.0)	1,370.5 (942.0-2,112.0)	1,349.0 (943.0-2,095.0)	<0.001
NT-proBNP when no AFF, pg/mL	716.0 (469.0-1,281.0)	846.5 (514.0-1,715.0)	715.0 (468.5-1,205.5)	617.5 (427.0-989.0)	<0.001
Baseline ECG AFF	2,644 (42.2)	758 (35.9)	1,051 (46.6)	834 (44.1)	<0.001
Baseline systolic blood pressure, mm Hg	128.2 ± 15.3	126.3 ± 15.1	129.1 ± 15.2	129.2 ± 15.5	<0.001
Baseline diastolic blood pressure, mm Hg	73.9 ± 10.4	74.4 ± 9.9	74.4 ± 10.5	72.9 ± 10.6	<0.001
Baseline HbA1c, %	6.6 ± 1.4	6.6 ± 1.5	6.6 ± 1.4	6.5 ± 1.3	0.040
Baseline heart rate, beats/min	71.5 ± 11.7	71.8 ± 11.8	71.8 ± 11.7	70.7 ± 11.8	0.010
Baseline creatinine, μmol/L	102.5 ± 31.1	103.9 ± 31.1	101.8 ± 30.8	101.7 ± 31.3	0.09
Baseline eGFR, mL/min per 1.73 m^2	61.0 ± 19.1	63.1 ± 19.6	60.7 ± 18.8	59.0 ± 18.8	<0.001
eGFR ≥60 mL/min per 1.73 m^2	3,138 (50.1)	1,138 (53.9)	1,127 (50.0)	870 (46.0)	<0.001
Loop diuretics	4,528 (72.3)	1,579 (74.8)	1,622 (71.9)	1,324 (70.0)	0.008
ACEi	2,087 (33.3)	849 (40.2)	717 (31.8)	520 (27.5)	<0.001
ARB	2,143 (34.2)	595 (28.2)	771 (34.2)	776 (41.0)	<0.001
ARNI	260 (4.2)	166 (7.9)	67 (3.0)	27 (1.4)	<0.001
β blocker	4,765 (76.1)	1,695 (80.3)	1,677 (74.3)	1,391 (73.5)	<0.001
MRA	2,425 (38.7)	1,024 (48.5)	798 (35.4)	600 (31.7)	<0.001
Pacemaker	661 (10.6)	247 (11.7)	249 (11.0)	165 (8.7)	0.013
ICD	112 (1.8)	72 (3.4)	26 (1.2)	13 (0.7)	<0.001

Values are mean ± SD, n (%), or median (IQR).

ACEi = angiotensin-converting enzyme inhibitor; AFF = atrial fibrillation/flutter; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HbA1c = hemoglobin A1c; HF = heart failure; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal pro-B natriuretic peptide; NYHA = New York Heart Association.

provided it was >40% and made within the previous 12 months (by echocardiogram or cardiac magnetic resonance imaging). Patients with an LVEF <40% before the qualifying LVEF measurement could be included. Patients who experienced a recent acute cardiac event or underwent a cardiac procedure that may influence left ventricular function were required to have qualifying cardiac imaging at least 12 weeks later. Patients were enrolled as both outpatients and as inpatients in the setting of a hospitalization for worsening HF. Patients were considered to have improved LVEF if they had previously had a known LVEF <40%. The primary endpoint for the trial is a composite of cardiovascular death or worsening HF event (either an HF hospitalization or an urgent HF visit). The trial is event-driven and will stop when approximately 1,117 primary adjudicated events have been reached. The study was approved by institutional review boards or ethics committees at individual study sites, and all patients signed written informed consent. The details of the study design have been published and the trial is registered with ClinicalTrials.gov (NCT03619213).[7]

CONCOMITANT MEDICAL THERAPIES. Study investigators were encouraged to treat patients according to local recommendations, including those for hypertension and T2DM, if present. Patients receiving SGLT2 inhibitors within 4 weeks of randomization or with prior SGLT2 inhibitor intolerance were ineligible for the trial.

BASELINE DATA COLLECTION AND ANALYSIS. Detailed baseline data including demographics, medical history, concomitant medications, cardiac procedures, physical exam, vital signs, quality of life, electrocardiography, and laboratory assessment were collected at enrollment before randomization. To describe patient-level characteristics, we divided patients into 3 separate LVEF groups (49% or less, between 50% and 59%, and 60% or greater). We also examined characteristics according to recency of prior hospitalization for HF. Each of these analyses was consistent with prespecified subgroups of interest. Because DELIVER enrolled a large proportion of patients with improved LVEF, we compared patients with and without improved LVEF. All between-group comparisons were made using Student's *t*-tests or analysis of variance for continuous variables and chi square tests for categorical variables. Statistical analyses were performed using STATA version 16.1.

COMPARISON WITH OTHER CONTEMPORARY HF TRIALS. Baseline characteristics in DELIVER were contextualized alongside other trials enrolling patients with HF with mildly reduced or preserved LVEF including CHARM (Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity),

TABLE 2 Baseline Characteristics by Recency of Prior Heart Failure Hospitalization

	No Prior Hospitalization (n = 3,727)	>1 y (n = 903)	3–12 mo (n = 632)	30 d – 3 mo (n = 346)	<30 d (n = 655)	*P* Value
Age, y	71.7 ± 9.4	72.5 ± 9.3	70.8 ± 10.3	71.0 ± 10.7	71.9 ± 9.1	0.008
Age groups, y						0.001
≤65	906 (24.3)	184 (20.4)	169 (26.7)	105 (30.3)	140 (21.4)	
>65–75	1,419 (38.1)	357 (39.5)	248 (39.2)	111 (32.1)	277 (42.3)	
>75	1,402 (37.6)	362 (40.1)	215 (34.0)	130 (37.6)	238 (36.3)	
Men	2,074 (55.6)	531 (58.8)	368 (58.2)	205 (59.2)	335 (51.6)	0.027
Race						<0.001
White	2,591 (69.5)	634 (70.2)	456 (72.3)	252 (72.8)	519 (80.0)	
Asian	703 (18.9)	241 (26.7)	146 (23.1)	75 (21.7)	107 (16.5)	
Black or African American	93 (2.5)	25 (2.8)	14 (2.2)	12 (3.5)	15 (2.3)	
American Indian or Alaskan Native	169 (4.5)	1 (0.1)	8 (1.3)	6 (1.7)	5 (0.8)	
Other	171 (4.6)	2 (0.2)	7 (1.1)	1 (0.3)	3 (0.5)	
Geographic region						<0.001
Europe and Saudi Arabia	1,581 (42.4)	460 (51.0)	337 (53.4)	183 (52.9)	439 (67.6)	
Asia	670 (18.0)	236 (26.2)	141 (22.3)	72 (20.8)	106 (16.3)	
Latin America	975 (26.2)	33 (3.7)	61 (9.7)	34 (9.8)	76 (11.7)	
North America	500 (13.4)	174 (19.3)	92 (14.6)	57 (16.5)	28 (4.3)	
History of AFF	1,954 (52.4)	566 (62.7)	370 (58.5)	223 (64.5)	435 (66.4)	<0.001
History of stroke	317 (8.5)	102 (11.3)	56 (8.9)	26 (7.5)	90 (13.7)	<0.001
History of hypertension	3,284 (88.1)	812 (89.9)	548 (86.7)	302 (87.3)	609 (93.0)	0.001
History of type 2 diabetes	1,635 (43.9)	416 (46.1)	292 (46.2)	144 (41.6)	320 (48.9)	0.09
History of chronic obstructive pulmonary disease	343 (9.2)	155 (17.2)	64 (10.1)	44 (12.7)	89 (13.6)	<0.001
History of noncoronary revascularization	82 (2.2)	14 (1.6)	23 (3.6)	4 (1.2)	17 (2.6)	0.042
History of sleep apnea	271 (7.3)	105 (11.6)	50 (7.9)	23 (6.6)	32 (4.9)	<0.001
Prior myocardial infarction	937 (25.1)	257 (28.5)	193 (30.5)	71 (20.5)	173 (26.4)	0.002
Coronary artery disease	1,765 (47.4)	517 (57.3)	371 (58.7)	153 (44.2)	354 (54.0)	<0.001
Atherosclerotic cardiovascular disease	1,994 (53.5)	571 (63.2)	405 (64.1)	182 (52.6)	396 (60.5)	<0.001
Smoking status						<0.001
Current	280 (7.5)	81 (9.0)	57 (9.0)	20 (5.8)	46 (7.0)	
Former	1,374 (36.9)	364 (40.3)	232 (36.7)	110 (31.8)	181 (27.6)	
Never	2,073 (55.6)	458 (50.7)	343 (54.3)	216 (62.4)	428 (65.3)	
Baseline body mass index, kg/m^2	30.0 ± 6.0	29.6 ± 6.3	29.6 ± 6.4	29.6 ± 6.3	29.8 ± 6.1	0.43
Body mass index groups, kg/m^2						0.44
<18.5 (underweight)	29 (0.8)	8 (0.9)	8 (1.3)	4 (1.2)	5 (0.8)	
18.5–24.9 (normal weight)	757 (20.3)	211 (23.4)	139 (22.0)	81 (23.4)	155 (23.7)	
25.0–29.9 (overweight)	1,257 (33.7)	288 (32.0)	222 (35.1)	112 (32.4)	194 (29.7)	
30.0–34.9 (class I obesity)	950 (25.5)	219 (24.3)	145 (22.9)	79 (22.8)	181 (27.7)	
35.0–39.9 (class II obesity)	490 (13.2)	113 (12.6)	69 (10.9)	47 (13.6)	79 (12.1)	
≥40 (class III obesity)	242 (6.5)	61 (6.8)	49 (7.8)	23 (6.6)	40 (6.1)	
Time from diagnosis of HF to enrollment						<0.001
0–3 mo	336 (9.0)	5 (0.6)	14 (2.2)	100 (29.0)	114 (17.4)	
>3–6 mo	347 (9.3)	10 (1.1)	141 (22.3)	36 (10.4)	58 (8.9)	
>6–12 mo	531 (14.3)	18 (2.0)	185 (29.3)	36 (10.4)	70 (10.7)	
>1– 2 y	633 (17.0)	146 (16.2)	78 (12.4)	39 (11.3)	99 (15.1)	
>2–5 y	911 (24.4)	332 (36.8)	95 (15.1)	64 (18.6)	167 (25.5)	
>5 y	968 (26.0)	391 (43.3)	118 (18.7)	70 (20.3)	146 (22.3)	
NYHA functional class at baseline						<0.001
I	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
II	3,001 (80.5)	695 (77.0)	448 (70.9)	225 (65.0)	333 (51.5)	
III	722 (19.4)	205 (22.7)	180 (28.5)	119 (34.4)	311 (47.5)	
IV	3 (0.1)	3 (0.3)	4 (0.6)	2 (0.6)	7 (1.1)	

Continued on the next page

TABLE 2 Continued

	No Prior Hospitalization (n = 3,727)	>1 y (n = 903)	3-12 mo (n = 632)	30 d - 3 mo (n = 346)	<30 d (n = 655)	*P* Value
Baseline LVEF, %	55.0 ± 8.9	53.2 ± 8.5	53.0 ± 8.7	53.4 ± 8.4	52.5 ± 8.2	<0.001
Pooled LVEF groups, %						<0.001
≤40	3 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	
41-49	1,125 (30.2)	349 (38.6)	253 (40.0)	125 (36.1)	259 (39.9)	
50-59	1,334 (35.8)	311 (34.4)	232 (36.7)	128 (37.0)	250 (38.2)	
≥60	1,264 (33.9)	243 (26.9)	146 (23.0)	93 (26.9)	146 (22.3)	
Baseline NT-proBNP, pg/mL	937.0 (581.0-1,594.0)	1,022.0 (640.0-1,663.0)	1,094.0 (643.5-1,980.0)	1,321.0 (716.0-2,496.0)	1,283.0 (737.0-2,414.0)	<0.001
NT-proBNP in AFF, pg/mL	1,307.0 (924.0-2,014.0)	1,374.0 (967.0-2,210.0)	1,637.0 (1,078.0-2,578.0)	1,790.0 (1,228.0-2,742.0)	1,647.0 (1,040.0-2,629.0)	<0.001
NT-proBNP when no AFF, pg/mL	687.5 (452.0-1,188.0)	692.0 (471.0-1,181.0)	759.0 (494.5-1,377.0)	946.0 (477.0-1,851.0)	855.0 (526.0-1,914.0)	<0.001
Baseline ECG AFF	1,488 (39.9)	423 (46.8)	263 (41.7)	148 (42.8)	322 (49.2)	<0.001
Baseline systolic blood pressure, mm Hg	128.6 ± 15.2	128.7 ± 15.9	127.5 ± 15.4	126.1 ± 15.6	127.2 ± 15.0	0.005
Baseline diastolic blood pressure, mm Hg	73.8 ± 10.3	74.1 ± 10.7	73.8 ± 10.2	74.0 ± 11.1	74.7 ± 9.8	0.32
Baseline HbA1c, %	6.5 ± 1.4	6.6 ± 1.3	6.7 ± 1.5	6.7 ± 1.4	6.7 ± 1.4	0.015
Baseline heart rate, beats/min	71.0 ± 11.7	72.1 ± 11.5	71.1 ± 11.4	72.1 ± 12.4	73.4 ± 12.3	<0.001
Baseline creatinine, μmol/L	100.2 ± 30.3	105.2 ± 32.2	105.5 ± 30.8	106.7 ± 32.6	106.4 ± 32.2	<0.001
Baseline eGFR, mL/min/1.73 m^2	62.3 ± 19.1	59.5 ± 18.9	59.7 ± 19.1	59.5 ± 19.9	57.7 ± 18.8	<0.001
eGFR <60 mL/min/1.73 m^2	1,979 (53.1)	428 (47.4)	297 (47.0)	162 (46.8)	272 (41.5)	<0.001
Loop diuretic agents	2,436 (65.4)	717 (79.4)	532 (84.2)	304 (87.9)	539 (82.3)	<0.001
ACEi	1,126 (32.0)	354 (39.2)	240 (38.0)	143 (41.3)	224 (34.2)	<0.001
ARB	1,388 (37.2)	259 (28.7)	185 (29.3)	93 (26.9)	218 (33.3)	<0.001
ARNI	133 (3.6)	47 (5.2)	29 (4.6)	27 (7.8)	24 (3.7)	0.001
β-blockers	2,702 (72.5)	750 (83.1)	527 (83.4)	264 (76.3)	522 (79.7)	<0.001
MRA	1,287 (34.5)	354 (39.2)	299 (47.3)	163 (47.1)	322 (49.2)	<0.001
Pacemaker	375 (10.1)	110 (12.2)	59 (9.3)	35 (10.1)	82 (12.5)	0.12
ICD	63 (1.7)	25 (2.8)	12 (1.9)	5 (1.4)	7 (1.1)	0.12

Values are mean ± SD, median (%), or median (IQR).
Abbreviations as in Table 1.

I-PRESERVE (Irbesartan in Heart Failure With Preserved Ejection Fraction), TOPCAT (Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist), PARAGON-HF (Prospective Comparison of ARNI with ARB Global Outcomes in HF with Preserved Ejection Fraction), and EMPEROR-Preserved (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure with Preserved Ejection Fraction).[8-12]

RESULTS

Between August 27, 2018, and December 30, 2020, we screened 10,420 patients from 353 sites across 20 countries for enrollment. The primary reasons for screen failure included failure to meet NT-proBNP criteria (n = 3,373 of 4,157; 81%), failure to meet other inclusion criteria (n = 582 of 4,157; 14%), and participant withdrawal (n = 169 of 4,157; 4%). Overall, 6,263 patients who fulfilled the inclusion and exclusion criteria were randomized to receive dapagliflozin 10 mg once daily or placebo. The baseline characteristics of randomized patients are shown in Table 1. Overall, patients were elderly, with a mean age of 72 ± 10 years, 56% were men, and the majority were White. Most had NYHA functional class II symptoms (75%). Mean Kansas City Cardiomyopathy Questionnaire total symptom score, overall summary score, and clinical summary score were 70.0, 66.6, and 68.3, respectively, consistent with moderate symptomatic impairment. Overall, 40% of patients had a prior HF hospitalization, and 10% were enrolled either in-hospital or within 30 days of a hospitalization for HF.

Comorbidities were common, including a history of hypertension (89%), T2DM (45%), and coronary artery disease (51%). Mean body mass index (BMI) was 29.8 ± 6.1 kg/m^2 and 45% of patients were obese (BMI ≥30 kg/m^2). Overall, 57% of participants had a history of AFF, and 42% had AFF on their electrocardiogram at enrollment. The mean LVEF was 54.2 ± 8.8%, and the median NT-proBNP was 1,399 (IQR: 962

TABLE 3 Baseline Characteristics by Improved LVEF

	LVEF Always >40% (n = 5,107)	Prior LVEF ≤40% (n = 1,156)	*P* Value
Age, y	72.0 ± 9.4	70.1 ± 10.0	<0.001
Age groups, y			<0.001
≤65	1,160 (22.7)	344 (29.8)	
>65-75	1,975 (38.7)	437 (37.8)	
>75	1,972 (38.6)	375 (32.4)	
Men	2,741 (53.7)	775 (67.0)	<0.001
Race			<0.001
White	3,680 (72.1)	778 (67.3)	
Asian	980 (19.2)	293 (25.3)	
Black or African American	123 (2.4)	36 (3.1)	
American Indian or Alaskan Native	168 (3.3)	21 (1.8)	
Other	156 (3.1)	28 (2.4)	
Geographic region			<0.001
Europe and Saudi Arabia	2,522 (49.4)	483 (41.8)	
Asia	939 (18.4)	287 (24.8)	
Latin America	982 (19.2)	199 (17.2)	
North America	664 (13.0)	187 (16.2)	
History of AFF	2,954 (57.8)	594 (51.4)	<0.001
History of stroke	495 (9.7)	96 (8.3)	0.14
History of hypertension	4,571 (89.5)	984 (85.1)	<0.001
History of type 2 diabetes	2,277 (44.6)	530 (45.8)	0.44
History of chronic obstructive pulmonary disease	546 (10.7)	149 (12.9)	0.031
History of noncoronary revascularization	115 (2.3)	25 (2.2)	0.86
History of sleep apnea	385 (7.5)	96 (8.3)	0.37
Prior myocardial infarction	1,234 (24.2)	397 (34.3)	<0.001
Coronary artery disease	2,481 (48.6)	679 (58.7)	<0.001
Atherosclerotic cardiovascular disease	2,814 (55.1)	733 (63.4)	<0.001
Smoking status			<0.001
Current	366 (7.2)	118 (10.2)	
Former	1,758 (34.4)	503 (43.5)	
Never	2,983 (58.4)	535 (46.3)	
Baseline body mass index, kg/m^2	29.9 ± 6.1	29.4 ± 6.0	0.006
Body mass index group, kg/m^2			0.045
<18.5 (underweight)	46 (0.9)	8 (0.7)	
18.5-24.9 (normal weight)	1,057 (20.7)	286 (24.8)	
25.0-29.9 (overweight)	1,698 (33.3)	375 (32.5)	
30.0-34.9 (class I obesity)	1,288 (25.2)	286 (24.8)	
35.0-39.9 (class II obesity)	663 (13.0)	135 (11.7)	
≥40 (class III obesity)	350 (6.9)	65 (5.6)	
Time from diagnosis of HF to enrollment			<0.001
0-3 mo	508 (10.0)	61 (5.3)	
>1-2 y	845 (16.6)	150 (13.0)	
>2-5 y	1,218 (23.9)	351 (30.4)	
>3-6 mo	520 (10.2)	72 (6.2)	
>5 y	1,285 (25.2)	408 (35.3)	
>6-12 mo	726 (14.2)	114 (9.9)	
NYHA functional class at baseline			<0.001
I	1 (0.0)	0 (0.0)	
II	3,784 (74.1)	922 (79.8)	
III	1,307 (25.6)	230 (19.9)	
IV	15 (0.3)	4 (0.3)	
Baseline LVEF, %	55.0 ± 8.6	50.5 ± 8.3	<0.001
Pooled LVEF group, %			<0.001
≤40	3 (0.1)	1 (0.1)	
41-49	1,484 (29.1)	627 (54.2)	
50-59	1,928 (37.8)	328 (28.4)	
≥60	1,692 (33.1)	200 (17.3)	

Continued on the next page

TABLE 3 Continued

	LVEF Always >40% (n = 5,107)	Prior LVEF ≤40% (n = 1,156)	*P* Value
Baseline NT-proBNP, pg/mL	1,012.0 (623.0-1,753.0)	1,008.0 (621.0-1,733.0)	0.98
NT-proBNP in AFF, pg/mL	1,399.0 (954.0-2,193.0)	1,398.5 (987.0-2,324.0)	0.55
NT-proBNP when no AFF, pg/mL	708.0 (460.0-1,260.0)	740.5 (488.0-1,355.0)	0.035
Baseline ECG AFF	2,218 (43.4)	426 (36.9)	<0.001
Baseline systolic blood pressure, mm Hg	128.5 ± 15.0	127.2 ± 16.7	0.013
Baseline diastolic blood pressure, mm Hg	74.0 ± 10.3	73.5 ± 10.6	0.08
Baseline HbA1c, %	6.6 ± 1.4	6.6 ± 1.4	0.49
Baseline heart rate, beats/min	71.7 ± 11.7	70.8 ± 12.1	0.019
Baseline creatinine, μmol/L	101.9 ± 30.9	104.9 ± 31.6	0.004
Baseline eGFR, mL/min per 1.73 m^2	60.8 ± 19.1	61.9 ± 19.2	0.10
eGFR <60 mL/min per 1.73 m^2	2,542 (49.8)	596 (51.6)	0.28
Loop diuretics	3,679 (75.0)	849 (73.4)	0.34
ACEi	1,659 (32.5)	428 (37.0)	0.003
ARB	1,805 (35.3)	338 (29.2)	<0.001
ARNI	126 (2.5)	134 (11.6)	<0.001
β-blockers	3,821 (74.8)	944 (81.7)	<0.001
MRA	1,868 (36.6)	557 (48.2)	<0.001
Pacemaker	542 (10.6)	119 (10.3)	0.75
ICD	52 (1.0)	60 (5.2)	<0.001

Values are mean ± SD, n (%), or median (IQR).
Abbreviations as in Table 1.

to 2,210) pg/mL for patients with AFF compared with 716 (IQR: 469 to 1,281) pg/mL in those without AFF. Mean blood pressure was 128 ± 15/ 74 ± 10 mm Hg, and mean heart rate was 71.5 ± 11.7 beats/min. The mean estimated glomerular filtration rate (eGFR) was 61 ± 19 mL/min per 1.73 m^2.

The majority of patients (67%) were taking angiotensin-converting enzyme inhibitors (ACEis) or angiotensin receptor blockers (ARBs) at enrollment, 4% were taking sacubitril/valsartan. β-blockers were prescribed in 76% and mineralocorticoid receptor antagonists (MRAs) in 39%. Overall, 45% of patients had T2DM (mean glycated hemoglobin was 7.5 ± 1.6%). In this subgroup, insulin was used in 28%, sulfonylureas in 21%, dipeptidyl-peptidase 4 inhibitors in 16%, and glucagon-like peptide-1 receptor agonists in 2%.

Table 1 also shows clinical characteristics by prespecified LVEF subgroups. The lowest LVEF group had a higher proportion of younger individuals and men and a notably higher proportion of patients with coronary artery disease. Patients with a lower LVEF had slightly higher NYHA functional class and NT-proBNP levels and were less likely to be in AFF at baseline. The use of ACEis and angiotensin receptor-neprilysin inhibitors (ARNIs) was higher in the lowest LVEF group, and patients in this group were substantially more likely to be treated with an MRA.

A total of 3,727 (60%) of patients had never had a prior HF hospitalization, 655 patients (10%) had been hospitalized for HF within 30 days of enrollment, and 1,001 patients (16%) had been hospitalized within 90 days of enrollment (Table 2). Patients with more recent hospitalization had worse NYHA functional class at baseline, slightly lower LVEF, higher NT-proBNP, and lower eGFR, were more likely to be in AFF at baseline, and more likely to be treated with MRAs compared with patients with no prior hospitalization.

Patients with improved LVEF (Table 3), defined as those who met entry criteria but who had had a prior LVEF <40%, comprised 18% of the study population. Compared to those without improved LVEF, these patients were slightly younger, and were substantially more likely to be men and Asian. Patients with an improved LVEF were more likely to have a history of myocardial infarction and less likely to have AFF. These patients also had longer-standing HF, were less likely to have been recently hospitalized for HF, and had a more favorable NYHA functional class distribution. Although patients with an improved LVEF had a lower mean LVEF than other patients and more were in the LVEF category of 41% to 49%, baseline NT-proBNP was similar to patients without improved LVEF. Patients with improved LVEF had substantially higher baseline use of an ARNI (12% vs 3%), MRA

TABLE 4 Comparison of Baseline Characteristics in Various Trials in Heart Failure With LVEF >40%

	DELIVER (n = 6,263)	EMPEROR-Preserved (n = 5,988)	PARAGON-HF (n = 4,822)	TOPCAT-Americas (n = 1,767)	I-PRESERVE (n = 4,128)	CHARM-Preserved (n = 3,023)
Age, y	72 ± 10	72 ± 9	73 ± 8	72 (64 to 79)	72 ± 7	67 ± 11
Women, %	44	45	52	50	60	40
NYHA functional class, %						
II	75	82	77	59	22	61
III	25	18	27	35	77	38
IV	0.3	0.3	0.6	1	3	2
Hypertension, %	89	90	96	90	89	64
Type 2 diabetes, %	45	49	43	45	27	28
COPD, %	11	13	14			
Smoker, %	8	7	7	7		14
History of MI, %	26	29	22	20	23.5	44
History of AFF, %	56	52	52	42	29	29
AFF at screening, %	42	35	32	34	29	29
Stroke, %	9 (stroke/TIA)	10	10	9	10	9
Prior HF hospitalization, %						
Within 6 mo						
Within 12 mo	26	23	48			
Any prior hospitalization	40			59	23	68
Subacute	10					
LVEF, mean %	54	54	58	58	60	54
eGFR, mean mL/min/1.73 m^2	61	61	62	61	73	72
NT-proBNP, median, pg/mL	1,011	974	885	900	339	–
ACEi, %	33	40	40	50	26	19
ARB, %	34	39	45	31	–	–
ARNI, %	4	2	–	–	–	–
MRA, %	39	37	24	–	15	12

Values are mean ± SD or n.
COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; TIA = transient ischemic attack; other abbreviations as in Table 1.

(48% vs 37%), and implantable cardioverter-defibrillator (ICD) (5% vs 1%).

COMPARISON WITH OTHER HF WITH PRESERVED EJECTION FRACTION TRIALS. The clinical characteristics of participants in DELIVER are well-aligned with those of EMPEROR-Preserved, PARAGON-HF, and the Americas region of TOPCAT with similar age and sex distribution (Table 4). Enrollment of Asian participants was higher in DELIVER (20%) compared with EMPEROR-Preserved (14%), PARAGON-HF (13%), and other prior trials. Most individuals in each of these trials were NYHA functional class II. Comorbidities were common including hypertension and T2DM across these trials, and history of AFF was highest compared with prior trials. Mean LVEF was lower (54%) than in TOPCAT, I-PRESERVE, and PARAGON-HF, and comparable to that of participants in EMPEROR-Preserved and CHARM-Preserved. Median NT-proBNP levels (1,011 pg/mL) were generally higher than in prior trials including EMPEROR-Preserved (974 pg/mL), PARAGON-HF (885 pg/mL), and TOPCAT Americas (900 pg/mL). MRA use was higher than in any prior HF with preserved ejection fraction (HFpEF) trial (39% compared with 37% in EMPEROR-Preserved and 24% in PARAGON-HF). Similarly, ARNI was used in more individuals (4%) than in EMPEROR-Preserved (2%) (Figure 1).

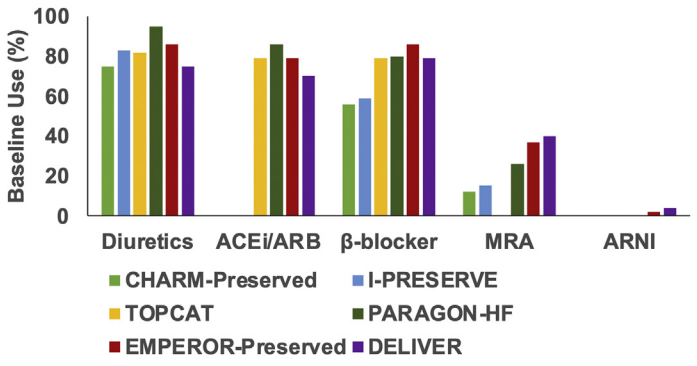
DISCUSSION

DELIVER is the largest, broadest, and most contemporary trial to date to evaluate patients with HF with mildly reduced and preserved LVEF and the only one of these trials to include a broader population including improved LVEF and hospitalized (or very recently hospitalized) patients (Central Illustration). Compared with other recent trials, DELIVER enrolled a population likely to be at higher risk because of greater comorbid disease burden, lower LVEF, and higher NT-proBNP levels. Together, DELIVER and EMPEROR-Preserved will expand the evidence base for SGLT2 inhibitor use in patients with HF and a higher LVEF. However, DELIVER will include understudied patient groups such as recently hospitalized patients and, uniquely, those with improved LVEF.

DELIVER was specifically designed to acknowledge heterogeneity in the HF population at the higher end of the LVEF spectrum. The study is powered for a dual primary analysis assessing the efficacy of dapagliflozin in the full population and among those with LVEF <60%, approximating a "normal" LVEF. Importantly, recently presented data from a pooled individual patient level analysis of the EMPEROR-Reduced and EMPEROR-Preserved studies have shown that the SGLT2 inhibitor empagliflozin reduced first and repeated HF hospitalizations in HF across the lower LVEF spectrum including the LVEF 40% to 60% range, with attenuation of benefit in those with LVEF >65%.[13-15] Although the exact cutoffs that define a normal LVEF are not well established and may differ by sex, patients with HF and a normal and "supra-normal" LVEF appear to be phenotypically distinct from those with a mildly reduced LVEF.[16] For example, more than one-half of those with HF with mildly reduced LVEF had a history of coronary artery disease and more than one-quarter had experienced a prior myocardial infarction, compared to 39.5% and 14.7% of patients, respectively, with an LVEF ≥60%. In addition, important demographic differences are apparent with patients with HF with mildly reduced LVEF and are more likely to be men and younger than those with higher LVEF. The updated 2021 European Society of Cardiology guidelines have now included treatment recommendations for this cohort of HF with mildly reduced LVEF, which include renin-angiotensin-system inhibitors, an ARNI, β-blockers, and MRAs (Class IIb recommendations).[17] DELIVER participants with LVEF 41% to 49% had high background use of these medical therapies (68% on ACEi/ARBs, 8% on ARNI, >80% on β-blockers, and 49% on MRA). MRA use has steadily increased among patients with HF with mildly reduced and preserved LVEF over time in clinical practice since the TOPCAT trial, and background use of MRAs was similarly high in EMPEROR-Preserved.[13,18] As such, DELIVER is well positioned to evaluate the treatment effects of dapagliflozin in people with HF and mildly reduced LVEF on the background of other recommended therapies.

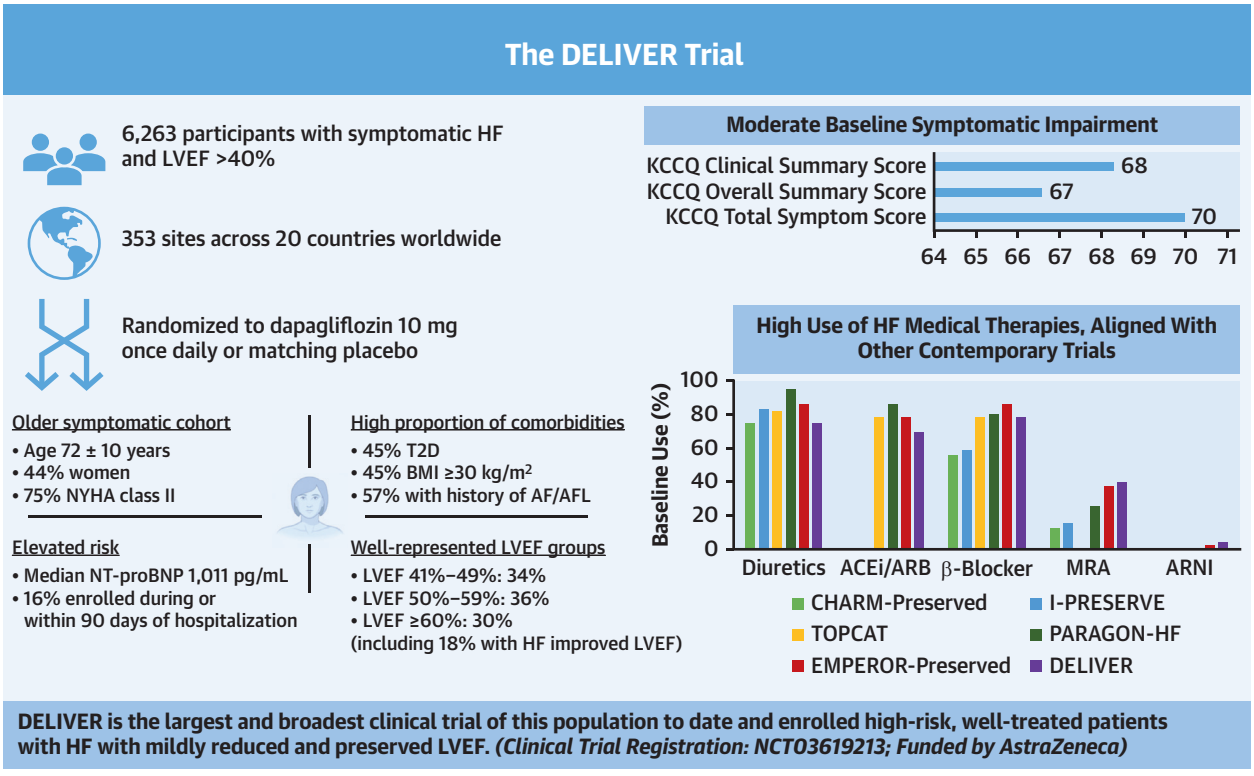
DELIVER allowed broad eligibility independent of care setting as long as participants were stable and off intravenous HF therapies for at least 12 hours before enrollment. Nearly 1,000 participants in the DELIVER trial were actively hospitalized or were within 90 days of hospitalization at the time of enrollment. These individuals had measures suggesting greater HF severity and are expected to face increased recurrent HF events. Few previous clinical trials have enrolled individuals hospitalized for HFpEF. For instance, PARAGON-HF allowed screening in the hospital, but randomization during hospitalization was not permitted, and the run-in period resulted in patients not being randomized until they were at least 30 days post hospitalization.[19] A dedicated clinical trial of 800 participants is underway to understand the effects of sacubitril/valsartan in this high-risk recently hospitalized population (Changes in NT-proBNP and Outcomes, Safety, and Tolerability in HFpEF Patients With Acute Decompensated Heart Failure [ADHF] Who Have Been Stabilized During Hospitalization and Initiated In-hospital or Within 30 Days Post-discharge [PARAGLIDE-HF]; NCT03988634). The SOLOIST-WHF (Effect of Sotagliflozin on Cardiovascular Events in Patients With Type 2 Diabetes Post Worsening Heart Failure) trial showed that sotagliflozin reduced total worsening HF events and cardiovascular death when initiated before or shortly after discharge among patients with T2DM and worsening HF, irrespective of LVEF.[20] Because of early termination of the trial, smaller than targeted sample sizes were achieved, and only 256 individuals with HF with LVEF ≥50% were enrolled. Notably, recent acute decompensated HF requiring intravenous HF therapies or mechanical support was an exclusion criterion in EMPEROR-Preserved.[21] As the hospitalization may be an optimal site for implementation of SGLT2 inhibitors, DELIVER

FIGURE 1 Background Medical Therapy in DELIVER



ACEi/ARB were not permitted initially and proportion of users were restricted in CHARM-Preserved and I-PRESERVE. ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; CHARM-Preserved = Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity; DELIVER = Dapagliflozin Evaluation to Improve the Lives of Patients With Preserved Ejection Fraction Heart Failure; EMPEROR-Preserved = Empagliflozin Outcome Trial in Patients With Chronic Heart Failure with Preserved Ejection Fraction; I-PRESERVE = Irbesartan in Heart Failure With Preserved Ejection Fraction; MRA = mineralocorticoid receptor antagonist; PARAGON-HF = Prospective Comparison of ARNI with ARB Global Outcomes in HF with Preserved Ejection Fraction; TOPCAT = Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist

CENTRAL ILLUSTRATION **Baseline Characteristics of Participants Enrolled in DELIVER**



DELIVER is the largest and broadest clinical trial of this population to date and enrolled high-risk, well-treated patients with HF with mildly reduced and preserved LVEF. ***(Clinical Trial Registration: NCT03619213; Funded by AstraZeneca)***

Solomon, S.D. et al. J Am Coll Cardiol HF. 2022;10(3):184-197.

DELIVER is a global randomized, double-blind, parallel-group, event-driven trial comparing the efficacy and safety of dapagliflozin with placebo in patients with heart failure (HF) and mildly reduced, preserved, or improved left ventricular ejection fraction (LVEF). AF/AFL = atrial fibrillation/atrial flutter; BMI = body mass index; CHARM-Preserved = Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity; DELIVER = Dapagliflozin Evaluation to Improve the Lives of Patients With Preserved Ejection Fraction Heart Failure; EMPEROR-Preserved = Empagliflozin Outcome Trial in Patients With Chronic Heart Failure with Preserved Ejection Fraction; I-PRESERVE = Irbesartan in Heart Failure With Preserved Ejection Fraction; NT-proBNP = N-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association; PARAGON-HF = Prospective Comparison of ARNI with ARB Global Outcomes in HF with Preserved Ejection Fraction; T2D = type 2 diabetes; TOPCAT = Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist

will inform the feasibility of this approach during this high-risk transitional care period, and provide further data on the role of inpatient and early postdischarge SGLT2 inhibitor use in patients with HF.

With advances and increasing uptake of disease-modifying medical and device therapies for HFrEF, a growing proportion of patients are expected to experience longitudinal improvement in LVEF. Although there are limited high-quality contemporary studies evaluating the natural history of HF with improved LVEF, these patients appear to face a relatively lower risk of clinical events compared with those with HFrEF.[5] However, despite improvement in LVEF and health status, some patients with HF with improved LVEF face risks of recurrent declines in left ventricular function and HF events.[22,23] Patients with HF with improved LVEF have been previously excluded from clinical trials of HF. In trials of HFrEF, these patients would not meet treatment eligibility. In trials of HFpEF, including EMPEROR-Preserved, patients with any prior LVEF ≤40% have been excluded.[21] As such, definitive clinical practice recommendations are lacking for this cohort. DELIVER will assess for consistency of the treatment effect in these patients.

DELIVER has enrolled a global cohort of participants. Notably, 1 in 5 patients in DELIVER were enrolled from Asia, which represents the highest proportion from this region in any global trial of this population. Trends toward higher enrollment from Asian countries in recent HFpEF trials are in part driven by site location and enrollment activity, and also reflective of the high population-level burden of HF in this region. In prior trials and registries, Asian patients with HFpEF have had a unique profile

(younger, leaner, but with higher relative event rates).[24,25] In light of this globalization of trial sites, 14% of trial participants were enrolled from North America, which may partially explain the relatively lower enrollment of Black participants (<5%) in the overall trial, although the proportion of Black adults in the United States (14.3%) was representative of the population. As Black adults face a disproportionate burden of HF in the United States, more in-depth assessment of the effects of SGLT2 inhibition in this at-risk population is needed.[26]

STUDY LIMITATIONS. Limitations of this baseline trial description should be acknowledged. Although no consensus definition is widely accepted to define HF with improved LVEF, patients enrolled in DELIVER had evidence of signs and symptoms of HF and some degree of functional limitation by design and thus do not denote complete recovery. Furthermore, in patients with a prior LVEF ≤40%, the precise prior LVEF was not collected, thus limiting the ability to ascertain the magnitude of the improvement.

CONCLUSIONS

DELIVER is the largest and broadest randomized clinical trial conducted to date in this population, and is poised to expand understanding of the treatment effects of SGLT2 inhibitors in patients with HFpEF, including in groups that have been understudied in prior trials. Prespecified pooled data from the Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) and DELIVER assessed in an individual patient-level meta-analysis will offer additional perspective on the effects of dapagliflozin in HF across the full spectrum of LVEF. Trial results of DELIVER will be available in 2022.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The DELIVER trial will test the hypothesis that dapagliflozin, an SGLT2 inhibitor, would reduce cardiovascular death, HF hospitalization, or urgent HF visits in 6,263 patients with HF and an LVEF >40%.

TRANSLATIONAL OUTLOOK: DELIVER is the largest and broadest randomized clinical trial conducted to date in this population and enrolled high-risk, well-treated patients with HF with mildly reduced and preserved LVEF. Unlike prior studies in this population, DELIVER has included patients with HF with improved LVEF and allowed enrollment irrespective of care setting (including during hospitalization).

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