

Supplementary material

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Table S1. Detailed baseline characteristics of HF-POL patients

Variable	Number of available cases	Values
Social status		
Retired, n (%)	1419	1218 (84.2)
Professionally active, n (%)	1419	184 (12.97)
Education		
Primary, n (%)	923	211 (22.9)
Secondary, n (%)	923	547 (61.4)
Higher, n (%)	923	145 (15.7)
Non-cardiac comorbidities		
Chronic obstructive pulmonary disease, n (%)	1497	220 (14.70)
History of malignancy, n (%)	1497	344 (22.98)
History of depression, n (%)	1497	90 (6.01)
Hypothyroidism, n (%)	1497	208 (13.89)
Hyperthyroidism, n (%)	1497	46 (3.07)
History of procedures		
Artificial heart valve, n (%)	1497	96 (6.41)
Transcatheter aortic valve implantation, n (%)	1497	29 (1.94)
Non-cardiac therapy		
Allopurinol, n (%)	1497	320 (21.38)
Oral antidiabetic agents, n (%)	1497	210 (14.02)

Insulin, n (%)	1497	124 (8.68)
Nonsteroidal anti-inflammatory drugs, n (%)	1497	141 (9.42)
Glucocorticoids, n (%)	1497	140 (9.35)
Systolic blood pressure, mmHg, median (Q1–Q3)	1489	130 (119–1442)
Diastolic blood pressure, mmHg, median (Q1–Q3)	1487	76 (70–83)
Laboratory results		
Hemoglobin, g/dl, median (Q1–Q3)	1409	12 (7.9–13)
Fasting glucose mg/dl, median (Q1–Q3)	1307	107 (94–134)
Glycated hemoglobin, %, median (Q1–Q3)	462	6 (5.6–6.73)
Total cholesterol, mmol/l, median (Q1–Q3)	1014	3.72 (3.08–4.6)
Low-density lipoprotein, mmol/l, median (Q1–Q3)	1026	1.97 (1.47–2.72)
High-density lipoprotein, mmol/l, median (Q1–Q3)	1024	1.17 (0.95–1.48)
Triglycerides, mmol/l, median (Q1–Q3)	1024	1.215 (0.92–1.81)
Urea, mg/dl, median (Q1–Q3)	674	40 (27–57)
Creatinine, mg/dl, median (Q1–Q3)	1398	1.2 (0.95–1.65)
eGFR ml/min/1.73 m², median (Q1–Q3)	1278	56 (43–70.30)
eGFR <30 ml/min/1.73 m², n (%)	1278	110 (8.61)
NT-proBNP, pg/ml, median (Q1–Q3)	1056	1617 (557.5–3936.50)
hsTnT, ng/ml, median (Q1–Q3)	559	30 (15–71)
Ferritin, ng/ml, median (Q1–Q3)	222	145.5 (72–313)
TSAT, %, median (Q1–Q3)	134	16.15 (10.8–24)
TSH, mIU/L, median (Q1–Q3)	963	1.513 (0.99–2.4)
Sodium, mmol/l, median (Q1–Q3)	1397	141 (139–143)
Potassium, mmol/l, median (Q1–Q3)	1402	4.55 (4.1–5)
Uric acid, μmol/L, median (Q1–Q3)	706	404 (300–503)
Electrocardiography		
Sinus rhythm, n (%)	892	540 (60.54)
Atrial fibrillation in electrocardiogram, n (%)	892	289 (32.40)
Pacemaker rhythm, n (%)	892	63 (7.06)
Heart rate, median (Q1–Q3)	900	73 (64–83)
Atrio-ventricular blocs (I/II or III degree), n (%)	901	85 (9.44)
LBBB, n (%)	901	70 (7.77)
QRS ms, median (Q1–Q3)	899	100 (90–120)

QTC, median (Q1–Q3)	497	436 (412–453)
Echocardiography		
Left ventricular mass index, g/m², median (Q1–Q3)	489	107.36 (85.7–132.3)
Tricuspid regurgitation velocity, m/s, median (Q1–Q3)	214	2.6 (2–3.1)
Medium e', cm/s, median (Q1–Q3)	200	6 (4.7–8.1)
Pulmonary arterial systolic pressure, mm Hg, median (Q1–Q3)	665	40 (30–55)
Six minute walk test, m, median (Q1–Q3)	140	295.5 (193–385.5)

Abbreviations: eGFR, estimated glomerular filtration rate; EF, ejection fraction; HF, heart failure; hsTnT, high sensitive troponin T; LBBB, left bundle branch block; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TSAT, transferrin saturation; TSH, thyroid-stimulating hormone

Table S2. Comparison of baseline characteristics studied population with DELIVER [3]

Variable	DELIVER (SGLT2i and placebo) n = 6263	HF-POL n = 1497	P-value
Age, mean (SD)	71.65 (9.57)	73.74 (11.65)	<0.001
Female sex, n (%)	2747 (43.86)	711 (47.49)	0.01
NYHA			<0.001
II, n (%)	4713 (75.26)	532 (35.54)	
III+IV, n (%)	1549 (24.74)	698 (46.63)	
Mean left ventricular ejection fraction — %, mean (SD)	54.15 (8.77)	50.74 (6.61)	<0.001
Cardiovascular history — no. (%)			
History of coronary artery disease, n (%)	3160 (50.5)	607 (40.55)	<0.001
Atrial fibrillation,	2644 (42.22)	732 (48.90)	<0.001

n (%)			
Diabetes mellitus (type 2), n (%)	2806 (44.80)	559 (37.34)	<0.001
Hypertension, n (%)	5553 (88.66)	1265 (84.50)	<0.001
Previous left ventricular ejection fraction ≤40%, n (%)	1151 (18.38)	218 (14.56)	<0.001
Mean eGFR — ml/min/1.73 m², mean (SD)	61 (19.00)	59.84 (28.99)	0.17
eGFR<60 ml/min/1.73 m² — n/total n (%)	1851 (29.55)	827/1278 (64.7)	<0.001
BMI			0.36
<30, n (%)	3740 (55.46)	776 (56.81)	
≥30, n (%)	2787 (44.54)	590 (43.19)	
Systolic blood pressure			0.001
≤128 mm Hg, n (%)	3158 (50.42)	679 (45.75)	
>128 mm Hg, n (%)	3105 (49.58)	805 (54.25)	
NT-proBNP			<0.001
≤1011 pg/ml, n (%)	3133 (50.03)	377 (35.70)	
>1011 pg/ml, n (%)	3129 (49.97)	679 (64.30)	
Therapy			
ACEi +ARB, n (%)	4490 (72)	1037 (69)	0.06
LBA, n (%)	4765 (76)	1213 (81)	<0.001
MRA, n (%)	2425 (39)	690 (46)	<0.001
ICD or CRT-D, n (%)	112 (1.79)	76 (5.08)	<0.001
Pacemaker, n (%)	661 (10.55)	222 (14.83)	<0.001

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BMI, body mass index; CRT-D, cardiac resynchronisation therapy defibrillator; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter-defibrillator; LBA beta blockers; MRA, mineralocorticoid receptor antagonists; NTproBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; SD, standard deviation; SGLT2i, sodium-glucose cotransporter type 2 inhibitors

Table S3. Comparison of baseline characteristics the studied population with Emperor-Preserved [4]

Variable	EMPEROR-Preserved (placebo + empagliflozin) n = 5988	HF-POL n = 1497	P-value
Age, mean (SD)	71.85 (9.45)	73.74 (11.65)	<0.001
Female sex, n (%)	2676 (44.7)	711 (47.49)	0.05
NYHA			<0.001
II, n (%)	4883 (81.5)	532 (35.54)	
III+IV, n (%)	1101 (18.4)	698 (46.63)	
BMI, mean (SD)	29.83 (5.85)	29.44 (5.97)	0.03
Heart beat — beats per minute, mean (SD)	70.35 (11.90)	77.33 (28.66)	<0.001
Mean left ventricular ejection fraction %, mean (SD)	54.35 (8.8)	50.74 (6.61)	<0.001
Heart failure category, n (%)			<0.001
Ischemic, n (%)	2117 (35.4)	607 (40.55)	
Nonischemic, n (%)	3870 (64.6)	890 (59.45)	
Cardiovascular history, n (%)			
Hospitalization for heart failure during	1369 (22.9)	441 (29.46)	<0.001

previous 12 months, n (%)			
Atrial fibrillation, n (%)	3057 (51.1)	732 (48.90)	0.14
Diabetes mellitus (type 2), n (%)	2938 (49.1)	559 (37.34)	<0.001
Hypertension, n (%)	5424 (90.6)	1265 (84.50)	<0.001
Mean eGFR — ml/min/1.73 m², mean (SD)	60.60 (19.85)	59.84 (28.99)	0.37
eGFR<60 ml/min/1.73 m² — n/total n (%)	2988/5986 (49.9)	827/1278 (64.7)	<0.001
Therapy			
ACEI +ARB, n (%)	4850 (81)	1037 (69)	<0.001
LBA, n (%)	5150 (86)	1213 (81)	<0.001
MRA, n (%)	2216 (37)	690 (46)	<0.001
ICD or CRT-D, n (%)	240 (4.01)	76 (5.08)	0.07

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BMI, body mass index; CRT-D, cardiac resynchronisation therapy defibrillator, eGFR, estimated glomerular filtration rate, ICD, implantable cardioverter defibrillator; LBA, beta blockers; MRA, mineralocorticoid receptor antagonists; NT-proBNP, N-terminal pro-B-type natriuretic peptide NYHA, New York Heart Association

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