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RESEARCH ARTICLE

Baseline characteristics of patients enrolled in the EMPACT-MI trial

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Aims Empagliflozin has been shown to reduce the risk of adverse cardiovascular outcomes in patients with type 2 diabetes and in those with heart failure. The impact of empagliflozin in post-acute myocardial infarction (AMI) patients is unknown.

Methods and results The Study to Test the Effect of Empagliflozin on Hospitalization for Heart Failure and Mortality in Patients with Acute Myocardial Infarction (EMPACT-MI) trial screened 6610 participants with AMI and randomized 6522 to empagliflozin or placebo in addition to standard of care. The median (interquartile) age was 64 (56–71) years and 75.1% of patients were male. Major comorbidities included hypertension (69.1%), type 2 diabetes (31.7%), prior myocardial infarction (13.0%), and atrial fibrillation (10.9%). The majority (74.3%) of patients presented with an ST-elevation myocardial infarction. Overall, 56.9% of patients had acute signs or symptoms of congestion requiring treatment and 78.3% had left ventricular systolic dysfunction with ejection fraction <45%. Clinical characteristics, including baseline demographics, rates of revascularization, and cardiovascular medications at discharge were largely comparable to recent trials of the post-AMI population.

Conclusion The EMPACT-MI trial will establish the benefit and risks of empagliflozin treatment in patients with AMI.

Keywords Acute myocardial infarction • Baseline characteristics • Clinical trial • Empagliflozin • Risk of heart failure

Introduction

Despite improvements in therapies, patients with acute myocardial infarction (AMI) are at high risk for mortality and for developing heart failure (HF).[1] This risk is particularly high for patients with reduced left ventricular ejection fraction (LVEF), acute signs and symptoms of congestion at the time of AMI, or with other risk factors such as advanced age, type 2 diabetes (T2D), or chronic kidney disease. A number of drugs that have demonstrated improved outcomes for patients with HF have also proven to be effective in patients post-AMI.[2–7] As a result, post-AMI patients, especially those with a reduced LVEF, are now prescribed a beta-blocker, angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), and mineralocorticoid receptor antagonist (MRA).[8,9] However, not all guideline-directed medical therapies (GDMT) for HF have been proven to be effective in the post-AMI population, as demonstrated by the neutral results of the Prospective ARNI versus ACE Inhibitor Trial to Determine Superiority in

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Reducing HF Events After Myocardial Infarction (PARADISE-MI) trial of angiotensin receptor–neprilysin inhibitor (ARNI) following myocardial infarction.[10]

Sodium–glucose cotransporter 2 inhibitors (SGLT2i), such as empagliflozin, have been shown to improve cardiovascular outcomes in patients with HF with both reduced or preserved LVEF, and to reduce the risk of HF or cardiovascular death in patients with T2D.[11–18] The efficacy of empagliflozin in patients following an AMI is unknown.[19,20] The Study to Test the Effect of Empagliflozin on Hospitalization for Heart Failure and Mortality in Patients With Acute Myocardial Infarction (EMPACT-MI) trial was designed to evaluate the safety and efficacy of empagliflozin versus placebo on top of standard of care following AMI in patients at risk of new-onset HF or mortality.[21] Herein, we describe the baseline characteristics of patients randomized in EMPACT-MI, and compare this population to those from prior trials of HF GDMT in the post-AMI setting.

Methods

Study design

EMPACT-MI (NCT04509674) is a double-blind, randomized, placebo-controlled, event-driven trial designed to assess the superiority of empagliflozin versus placebo in addition to standard of care for the composite endpoint of time to first event of hospitalization for HF or all-cause mortality in patients at high risk for new-onset HF following an AMI. The trial rationale and design have been previously reported.[21] Briefly, patients were eligible for enrolment if they had no history of HF, had been hospitalized with an AMI, and were randomized within 14 days of admission. Patients were required to have either acute signs or symptoms of congestion that required treatment, and/or a depressed LVEF <45% without known chronic HF.

Patients were also required to have at least one additional risk factor, including age ≥65 years, LVEF <35%, estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2, prior AMI, atrial fibrillation, T2D, elevated natriuretic peptide levels (≥1400 pg/ml in sinus rhythm and ≥2800 pg/ml if in atrial fibrillation), uric acid ≥7.5 mg/dl, pulmonary artery systolic pressure ≥40 mmHg, no revascularization for the index AMI, three-vessel coronary artery disease at the time of index AMI, or peripheral artery disease. Patients with a prior diagnosis of chronic HF, cardiogenic shock, or use of intravenous inotropes within 24 h before randomization, systolic blood pressure ≤90 mmHg at randomization, eGFR <20 ml/min/1.73 m^2 or requiring dialysis, or with current or planned open-label use of SGLT2i or combined SGLT-1/2i were excluded.

Eligible patients were randomized 1:1 for treatment with empagliflozin 10 mg daily or placebo while in hospital or after discharge, no later than 14 days after hospital admission for the index AMI. The study drug was given in addition to standard of care treatment for AMI, which was at the discretion of the investigator and/or other treating physician in accordance with local, national, and international guidelines. The primary composite endpoint is time to first hospitalization for HF or all-cause death. The trial design and organizational structure included streamlined elements aiming to increase trial efficiency, reduce burden for patients and investigators, and to increase generalizability of results, including use of clinical and laboratory information readily available during clinical practice for eligibility assessment, remote follow-up for most patient visits, focused collection of safety information, and use of blinded investigator reporting and classifications of events instead of central adjudication. The full list of inclusion and exclusion criteria as well as main trial endpoints, details of trial design, and statistical considerations have been detailed previously.[21]

Comparator trials

The EMPACT-MI patient characteristics were compared with prior AMI trials with HF GDMT, including the Survival and Ventricular Enlargement (SAVE) trial, the Acute Infarction Ramipril Efficacy (AIRE) trial, the Trandolapril Cardiac Evaluation (TRACE) trial, the Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction (CAPRICORN) trial, the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival (EPHESUS) trial, the Valsartan in Acute Myocardial Infarction (VALIANT) and the PARADISE-MI trial.[2–7,10] Qualitatively comparisons were made for demographic and clinical characteristics, cardiovascular metrics, including type of AMI, LVEF, and treatment, including use of antiplatelet drugs, ACEi/ARB/ARNI, beta-blockers, and MRA use, and revascularization.

The full eligibility criteria of these trials have been previously described. Briefly, SAVE compared captopril to placebo in patients with recent AMI and LVEF ≤40% without overt signs or symptoms of HF in 2231 patients.[2,22] AIRE compared ramipril versus placebo in patients with recent AMI and evidence of HF and randomized 2006 patients.[3] TRACE compared trandolapril to placebo in 1749 patients with recent AMI and left ventricular dysfunction (wall motion index ≤1.2, which corresponds to LVEF ~≤35%).[4,23] CAPRICORN compared carvedilol versus placebo in 1959 patients with a LVEF ≤40% following an AMI.[5] EPHESUS compared eplerenone versus placebo in 6632 patients following AMI who had both a LVEF ≤40% and signs of HF and/or T2D.[6] VALIANT compared valsartan versus captopril versus both in 14 703 patients with LVEF ≤35%, HF, or both, following myocardial infarction.[7,24] PARADISE-MI compared sacubitril-valsartan versus ramipril in 5661 patients with recent AMI without a history of HF who either had LVEF ≤40% and/or HF, in addition to at least one additional high-risk feature.[10]

Results

The first patient in EMPACT-MI was randomized on 16 December 2020, and enrolment was completed on 10 March 2023. Overall, 6610 patients were screened, and 6522 patients were randomized at 451 sites in 22 countries, including 4307 (66.0%) in Europe, 864 (13.2%) in North America, 773 (11.9%) in Asia, and 578 (8.9%) in Latin America.

Patient characteristics

The median (interquartile) age of participants was 64 (56–71) years, and 75.1% were male (*Table 1*). Overall, 83.6% of the participants were White, 1.4% ($n = 92$) were Black (including 8.3% [43/517]) of those randomized in the United States), 12.8% were Asian, and 10.3% identified as Hispanic or Latino. Major comorbidities included hypertension (69.1%), T2D (31.7%), prior AMI (13.0%), atrial fibrillation (10.9%), valvular heart disease (6.4%), peripheral artery disease (5.4%), chronic obstructive pulmonary disease (5.1%) and prior stroke/transient ischaemic attack (4.6%).

Table 1 Baseline characteristics of patients in the EMPACT-MI and other post-myocardial infarction trials

	SAVE	AIRE	TRACE	CAPRICORN	EPHESUS	VALIANT	PARADISE-MI	EMPACT-MI
Investigational treatment/control	Captopril/ placebo	Ramipril/ placebo	Trandolapril/ placebo	Carvedilol/ placebo	Eplerenone/ placebo	Valsartan/ captopril/both	Sacubitril-valsartan/ ramipril	Empagliflozin/ placebo
Year	1992	1993	1995	2001	2003	2003	2021	2023
No. of patients	2231	1986	1749	1959	6632	14 703	5661	6522
Time from AMI to randomization, days	11	5.4	4.5	NR	7.3	4.9	4.3	5.0 (3.0–8.0)
Male sex	83%	74%	72%	74.%	71%	69%	76%	75.1% (4897)
Age, years	59.4	66	67.5	63	64	65	64	64.0 (56.0–71.0)
Race								
White	89.3%	NR	NR	NR	90.2%	93.5%	75.3%	83.6% (5450)
Black	5.6%	NR	NR	NR	1.1%	2.8%	1.3%	1.4% (92)
Asian	NR	NR	NR	NR	NR	1.0%	16.8%	12.8% (834)
Other (including mixed and missing race)	5.0%	NR	NR	NR	8.7%	2.8%	6.5%	2.2% (146)
Current smoker	53%	NR	48%[a]	33%	NR	31.7%	21.1%	34.1% (2221)
Past medical history								
Hypertension	43%	28%	23%	54%	61%	55.2%	64.9%	69.1% (4504)
Prior AMI	36%	23%	36%	30%	27%	27.7%	16.3%	13.0% (845)
Diabetes[b]	22%	12%	14%	22%	32%	23.1%	42.4%	31.7% (2068)
Prior HF	NR	8%	22%	NR	15%	14.8%	Excluded	Excluded
Index AMI characteristics								
Ejection fraction	31%	NR	30%	32.8%	33%	35.3%	36.5%	40.0[c]
STEMI	84%[d]	63%[d]	66%[d]	NR	NR	66.6%[d]	75.8%	74.3% (4846)
NSTEMI	10%[e]	37%[e]	15%[e]	NR	NR	31.9%[e]	24.2%	25.7% (1675)
Acute congestion at AMI	40%	100%	59%	NR	90%	72%	54%	53.4% (3481)
eGFR, ml/min/1.73 m^2	NR	NR	NR	NR	78.5	NR	71.8	76.1 (20.1)
SBP, mmHg	113	NR	121	121.7	119	122.7	121	120.4 (14.9)
DBP, mmHg	70	NR	76	73.6	72	72.3	74	73.4 (10.0)

Counts are shown as % (*n*) for EMPACT-MI or % for other studies based on number of patients. Continuous variables are shown as median (interquartile range) for age and time from index AMI to randomization for EMPACT-MI, mean (standard deviation) for eGFR, SBP and DBP for EMPACT-MI, and mean for eGFR, time from index AMI to randomization, SBP and DBP for other studies. If other studies presented data by treatment group only and not for the total population, the mean of both treatment groups is shown (rounded).
AMI, acute myocardial infarction; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HF, heart failure; NR, not reported; NSTEMI, non-ST-elevation myocardial infarction; SBP, systolic blood pressure; STEMI, ST-elevation myocardial infarction.
[a]Smokers at admission in the cohort of 1747 with wall motion index ≤1.2.
[b]Only type 2 diabetes for EMPACT-MI.
[c]Mean of lowest ejection fraction during index hospitalization from 4945 (75.8)% of patients with exact ejection fraction data.
[d]Q-wave AMI.
[e]Non-Q wave AMI.

Overall, 56.9% of patients had acute signs or symptoms of congestion requiring treatment and 78.3% had a depressed LVEF <45%, with 35.6% meeting both criteria (*Figure 1*). The most commonly reported lowest LVEF during index hospitalization was 35%–<45%, which was reported for 52.7% of patients. An additional 25.6% of patients had an LVEF <35%, 3.9% had an LVEF <25% and 21.7% had an LVEF of 25%–<35%. An additional 20.9% of patients had a preserved LVEF ≥45% including those with LVEF ≥55% (7%). Data collection requirements in the trial allowed investigators to report patient LVEF either as an exact value or as a range (if no exact value was available). Mean LVEF among patients with reported exact LVEF was 40.0% ($n = 4945$), consistent with the fact that the majority of patients in the trial had an LVEF category of 35%–<45%. Most patients (77.9%) had 1–3 enrichment criteria, with the three most common being age ≥65 years (50.0%), T2D (31.7%) and three-vessel coronary artery disease (31.0%); the prevalence of all enrichment criteria are detailed in *Figure 1*. Most patients (83.2%) were randomized while hospitalized for index AMI with median (interquartile range) time from index AMI to randomization of 5 (3–8) days and the length of index hospitalization was a median of 5 (3–8) days.

Most index AMI presentations were ST-elevation MI (STEMI; 74.3%, $n = 4846$). Overall, 58.3% had multi-vessel and 35.0% had single-vessel disease. In total, 89.3% of patients underwent revascularization before randomization, with 88.8% receiving percutaneous revascularization and 0.5% undergoing coronary artery bypass grafting prior to randomization; 10.7% were treated with thrombolytic therapy. Rates of GDMT at discharge were 82.0% for ACEi/ARB/ARNI, 86.0% for beta-blockers, 47.2% for MRAs, with the proportion of patients using dual antiplatelet/antiplatelet plus anticoagulant agents of 93.5% (*Table 2*).

Comparison with other acute myocardial infarction trials

In comparison with selected trials of GDMT following AMI, EMPACT-MI randomized a large number of patients (6522 vs. 1749–14 703 patients). Average patient age (63.6 vs. 59.4–67.5 years) and sex distribution (75.1% vs. 69–82.5% male) were similar. The proportion of participants with STEMI versus non-STEMI were comparable to other trials (74.3% vs. 63–75.8% STEMI). The proportion of patients with a prior history

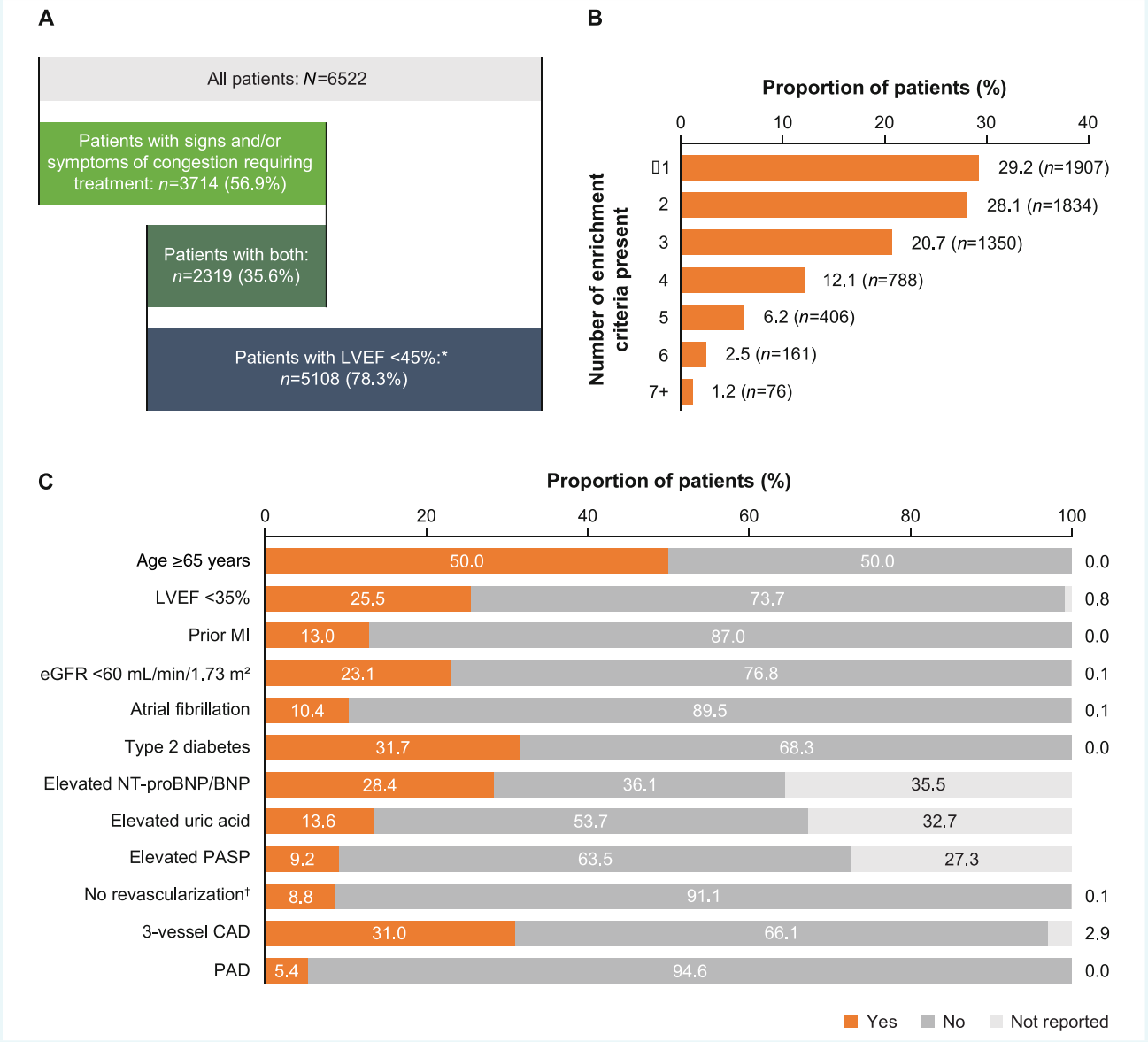

Figure 1 Key characteristics of the EMPACT-MI patient population. (*A*) Patients meeting major inclusion criteria of prevalence of signs/symptoms of congestion requiring treatment, lowest left ventricular ejection fraction (LVEF) <45% during index hospitalization, or both. (*B*) Patient distribution according to number of enrichment criteria at baseline. (*C*) Prevalence of individual enrichment criteria at baseline. BNP, B-type natriuretic peptide; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; NT-proBNP, N-terminal pro- B-type natriuretic peptide; PAD, peripheral artery disease; PASP, pulmonary artery systolic pressure. *53 patients had missing LVEF. †No revascularization for index MI.

of AMI in EMPACT-MI was 13.0% and ranged from 16.3–36% in previous trials. Average time from index AMI to randomization was similar as compared to other trials (5.6 vs. 4.3–7.3 days). Mean LVEF was slightly higher in EMPACT-MI as compared to other trials (40.0% vs. 30–37%).

Past medical history was comparable between EMPACT-MI and a contemporary trial of post-MI patients, PARADISE-MI (hypertension 69.1% vs. 64.9% and prior MI 13.0% and 16.3%, respectively). In older trials, hypertension was less (23–61%) and prior MI was more (22–36%) common. Compared with PARADISE-MI, fewer patients in EMPACT-MI had T2D (31.7% vs. 42.4%) and more were current smokers (34.1% vs. 21.1%). Management post-AMI was similar in EMPACT-MI compared to PARADISE-MI, including revascularization (88.8% vs. 90.6%) and use of dual antiplatelet/antiplatelet plus anticoagulant agents (90% vs. 92.2%), statins (94.7% vs. 94.9%), beta-blockers (86.0% vs. 85.3%) and MRA (47.2% vs. 41.3%) at discharge. Patients enrolled in earlier trials were less likely to receive these therapies, and in many cases use was not reported as they were not standard at the time (online supplementary *Table S1*).

Table 2 Patient therapies at discharge of hospitalization for index myocardial infarction in the EMPACT-MI trial ($n = 6522$)

	Rates of prescribed therapy, % (*n*)
Renin–angiotensin modulator	82.0 (5346)
Angiotensin-converting enzyme inhibitor	58.3 (3801)
Angiotensin receptor blocker[a]	18.5 (1205)
Angiotensin receptor–neprilysin inhibitor	6.5 (422)
Beta-blocker	86.0 (5607)
Mineralocorticoid receptor antagonists	47.2 (3081)
Loop or high ceiling diuretics	37.8 (2464)
Any diuretic	64.7 (4218)
Antiplatelet therapy	97.9 (6388)
Acetylsalicylic acid	92.9 (6058)
$P2Y_{12}$ inhibitor	95.0 (6198)
Vitamin K antagonist	3.1 (199)
Direct oral anticoagulant	10.0 (649)
Dual antiplatelet or antiplatelet plus anticoagulation therapy	93.5 (6100)
Dual antiplatelet therapy[b]	90.0 (5869)
Antiplatelet plus oral anticoagulation therapy[c]	12.6 (821)
Statin	94.7 (6179)

[a]Excluding valsartan when taken with sacubitril, because sacubitril/valsartan is shown as angiotensin receptor–neprilysin inhibitor.
[b]Includes patients receiving dual antiplatelet therapy ($P2Y_{12}$ inhibitor and acetylsalicylic acid).
[c]Includes patients receiving at least one antiplatelet agent and oral anticoagulant (vitamin K antagonist or direct oral anticoagulant).

Discussion

Sodium–glucose cotransporter 2 inhibitors have proven effective at reducing the risk of death and hospitalization for HF across a wide spectrum of patients; however, their efficacy has not yet been assessed following AMI. EMPACT-MI will be the first trial to assess SGLT2i use, specifically empagliflozin, on a composite of time to first hospitalization for HF or all-cause death in a high-risk population of AMI patients with no history of HF. As a pragmatic trial, EMPACT-MI included post-AMI patients at risk for future HF across a wide spectrum of relevant characteristics including a wide range of acute signs or symptoms of congestion, the entire spectrum of LVEF (including patients with depressed or preserved LVEF post-AMI), and a range of additional risk factors including high-risk comorbidities, severe vascular disease, and severely depressed LVEF, which will help ensure broad applicability of the findings of EMPACT-MI to patients following AMI in practice (*Figure 1*). In comparison to other post-AMI trials (*Table 3*), EMPACT-MI enrolled patients with a broader range of risk factors, including symptoms and not only signs of congestion, and allowed for patients with either reduced LVEF or signs or symptoms of congestion to be included, rather than universally requiring a specific single risk factor. The EMPACT-MI population therefore represents patients from the entire range of LVEF, and as a result mean LVEF in EMPACT-MI is slightly higher than what has been reported in prior post-AMI trials.

The ongoing study Dapagliflozin Effects on Cardiovascular Events in Patients with an Acute Heart Attack (DAPA-MI) will also evaluate the impact of an SGLT2i on patients following AMI.[25] Though baseline demographic data are not yet available for this trial, enrolment criteria suggest that it will include a different, and perhaps lower-risk, population (*Table 4*). DAPA-MI has enrolled 4017 patients and excluded those with a history of T2D. Patients were eligible for DAPA-MI if they had any evidence of cardiac dysfunction following AMI. Patients with a history of HF were eligible for enrolment in DAPA-MI provided that their LVEF prior to index hospitalization for AMI was not <40% and they had not been hospitalized for HF within the last year. In contrast, just under a third of patients enrolled in EMPACT-MI have T2D, patients are required

Table 3 Previous heart failure risk factors across past trials

	SAVE	AIRE	TRACE	CAPRICORN	EPHESUS	VALIANT	PARADISE-MI
Acute heat failure risk features	Ejection fraction ≤40%	Clinical evidence of heart failure	Ejection fraction ≤35%	Ejection fraction ≤40%	Ejection fraction ≤40% with clinical or radiological evidence of pulmonary congestion (not mandatory for patients with diabetes)	Ejection fraction ≤35% and/or clinical or radiological signs of symptoms of heart failure	Ejection fraction ≤40% and/or clinical or radiological evidence of pulmonary congestion
Additional risk factors required	None	None	None	None	None	None	At least one of: age ≥70 years, diabetes, prior MI, estimated glomerular filtration rate <60 ml/min/1.73 m^2, atrial fibrillation, ejection fraction <30%, Killip class III or IV heart failure, STEMI without reperfusion within 24 h
Pre-existing heart failure	Permitted	Permitted	Permitted	Permitted	Permitted	Permitted	Exclusionary

MI, myocardial infarction; STEMI, ST-elevation myocardial infarction.

Table 4 Key similarities and differences between the DAPA-MI and EMPACT-MI trials

	DAPA-MI	EMPACT-MI
Trial size	4017	6522
Key inclusion criteria	Confirmed AMI within 7–10 days Evidence of impaired regional or global LV function at any time during index MI hospitalization or definitive evidence on ECG of Q-wave MI	Diagnosis of acute spontaneous MI with randomization within 14 days after hospital admission High-risk for future HF with Either Clinical evidence of congestion (symptoms [e.g. dyspnoea, decreased exercise tolerance, fatigue] or signs [e.g. pulmonary rales, crackles or crepitations, elevated jugular venous pressure, congestion on chest X-ray]) requiring treatment and/or LVEF <45% And at least one additional risk factor Age ≥65 years, LVEF <35%, eGFR <60 ml/min/1.73 m^2, prior MI, AF, T2D, elevated NT-proBNP, elevated uric acid, elevated PASP, no revascularization for the index MI, three- vessel CAD, peripheral artery disease
Key exclusion criteria	Chronic symptomatic HF with a prior HHF within the last year and known reduced ejection fraction (LVEF ≤40%), documented before the current MI hospitalization T2D and T1D	Previously diagnosed chronic heart failure, T1D
Primary endpoint	Hierarchical composite endpoint of 1. Death (cardiovascular death, then non-cardiovascular death) 2. HHF (adjudicated, then investigator-reported) 3. Non-fatal AMI 4. Atrial fibrillation/flutter 5. New-onset T2D 6. Last visit NYHA class 7. Weight loss ≥5% body mass	Time to first HHF or all-cause death

AF, atrial fibrillation; AMI, acute myocardial infarction; CAD, coronary artery disease; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; HF, heart failure; HHF, hospitalization for heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; T1D, type 1 diabetes; T2D, type 2 diabetes.

to have either LVEF <45% and/or signs or symptoms of congestion requiring treatment, and inclusion of patients with prior diagnosis of HF is not permitted. Unlike EMPACT-MI, whose primary endpoint is a composite of time to first hospitalization for HF or all-cause death, DAPA-MI will use a hierarchical endpoint that includes not only these clinical events but also non-fatal AMI, atrial fibrillation/flutter, occurrence of T2D, last visit New York Heart Association class, and occurrence of weight loss ≥5%.

Importantly, >80% of patients in EMPACT-MI were randomized while still hospitalized for their index AMI. Real-world data have shown that rates of GDMT titration after discharge are often not optimal, and recent initiatives have emphasized the importance of in-hospital initiation of therapies when possible.[26] The results of EMPACT-MI will provide important data on the safety and efficacy of initiating empagliflozin for high-risk patients during index hospitalization.[27,28] Rates of appropriate background medical therapy were high in EMPACT-MI, allowing for the assessment of benefit of empagliflozin in patients already optimally managed with available therapies.

Compared to prior trials of HF GDMT in the post-AMI population, patients in EMPACT-MI had similar baseline characteristics, including age and sex. Comorbidities, including frequency of prior MI, were like PARADISE-MI, the most contemporary trial of GDMT in patients post-AMI, but with fewer T2D patients and more current smokers randomized in EMPACT-MI. Patients in EMPACT-MI additionally had a similar distribution of STEMI versus non-STEMI patients and time between index myocardial infarction and randomization as compared to other trials. As expected, given the wide timespan of almost 30 years over which these trials were conducted, it is not surprising that rates of revascularization, and of background medical therapy, were lower in the AIRE, EPHESUS, and CAPRICORN trials. Indeed, these trials are in part responsible for the guidelines that now recommend these GDMT in patients following AMI. However, rates of both revascularization

and medical therapy, including HF GDMT, antiplatelets, and statins were similar across EMPACT-MI and PARADISE-MI, suggesting that patients were similarly optimized for both recent trials.

EMPACT-MI only randomized 92 (1.4% of total) patients who identified as Black, though this proportion was higher (8.3%) in the United States, where about half (43/92) of all Black patients were randomized. This is like both PARADISE-MI (1.3% overall, 9.3% of North American enrolment), and EPHESUS (1% overall). Similarly to other AMI trials, about a quarter of participants were female, and 10.3% identified as Hispanic or Latino. EMPACT-MI implemented efforts to increase diversity during the trial, including the addition of sites with a more diverse make-up, focused discussions, and training sessions on improving diversity for national leaders and investigators, and individual work with the sites for evaluation of barriers and implementation of individual site-specific actions. We recognize that Black, female, and Hispanic or Latino patients remain unrepresented in EMPACT-MI, as has historically been the case with cardiovascular outcome trials in general. Ongoing efforts are needed to better understand the complex issues surrounding diversity in enrolment and to improve representation of all patients in trials across multiple metrics including age, race, sex, and ethnicity.[29,30] Further efforts to understand the underpinnings that lead to underrepresentation of certain demographic groups in clinical research hold promise to improve on the current status.[31]

In conclusion, EMPACT-MI has enrolled a population of patients with largely similar baseline demographics as compared to prior trials of GDMT in the post-AMI population, including age, sex, and type of myocardial infarction. Patients have largely similar rates of comorbidities, background GDMT, statin and antiplatelet therapy, and revascularization, compared to PARADISE-MI, the most recent post-AMI trial of GDMT. EMPACT-MI will be the first large randomized controlled trial of SGLT2i that will evaluate the effect of empagliflozin on the clinically meaningful composite outcome of time to first HF hospitalization or all-cause death in high-risk patients following an AMI.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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