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Racial differences in quality of life in patients with heart failure treated with sodium-glucose cotransporter 2 inhibitors: A patient-level meta-analysis of the CHIEF-HF, DEFINE-HF, and PRESERVED-HF trials

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Abstract

Background—Health status outcomes, including symptoms, function, and quality of life, are worse in Black, as compared with White, patients with heart failure (HF). While sodium glucose co-transporter 2-inhibitors (SGLT2i) reduce cardiovascular mortality and improve health status in patients with HF, whether the health status benefit of SGLT2i is similar across races is not established. The objective of this study was to compare the treatment effect of SGLT2i (vs. placebo) on health status in Black compared with White patients with HF.

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Methods—We combined patient-level data from three randomized clinical trials of SGLT2i, DEFINE-HF (n=263), PRESERVED-HF (n=324), and CHIEF-HF (n=448). These three U.S.-based trials enrolled a substantial proportion of Black patients, and each utilized the Kansas City Cardiomyopathy Questionnaire (KCCQ) to measure health status at baseline and after 12 weeks of treatment. Among 1035 total participants, selecting self-identified Black and White patients with complete information yielded a final analytic cohort of 935 patients. The primary endpoint was KCCQ Clinical Summary (CS) score. Twelve-week change in KCCQ with SGLT2i vs. placebo was compared between Black and White patients by testing the interaction between race and treatment using multivariable linear regression models adjusted for trial, baseline KCCQ (as a restricted cubic spline), race, and treatment. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results—Among 935 participants, 236 (25%) self-identified as Black, and 469 (50.2%) were treated with an SGLT2i. Treatment with an SGLT2i, compared with placebo, resulted in CS score improvements at 12 weeks of +4.0 points (95% confidence interval [95%CI] 1.7 to 6.3, p=0.0007) in White patients and +4.7 points (95%CI 0.7 to 8.7, p=0.02) in Black patients with no significant interaction by race and treatment (p=0.76). Other KCCQ scales showed similar results.

Conclusions—Treatment with an SGLT2i resulted in consistent and significant improvements in health status for both Black and White patients with HF.

Keywords

Heart failure; race; health outcomes; SGLT2i; KCCQ

INTRODUCTION

The prevalence of heart failure (HF) is rising in the United States and is projected to affect greater than 8 million people by 2030.[1–3] HF not only markedly shortens patients' survival, but also impairs their health status due to severe symptoms, functional limitations, and impaired quality of life. Over the last decade, several new therapies for HF have dramatically changed the HF treatment landscape. In particular, sodium-glucose cotransporter 2 inhibitors (SGLT2i) have emerged as a treatment that improves patients' health status across the spectrum of HF, including heart failure with reduced ejection fraction (HFrEF), heart failure with mildly reduced ejection fraction (HFmrEF), and heart failure with preserved ejection fraction (HFpEF).[4–9] Thus, the clinical and health status benefits, coupled with a favorable tolerability profile of SGLT2i, represent a new opportunity to improve care for HF, as embraced by recent updates to clinical guidelines.[10,11]

Concordant with the growth of HF has been an increasing focus on the need to address and reduce racial disparities in care and outcomes.[12–14] In the setting of HF, racial differences in the incidence of HF and response to some therapies are known, as are racial disparities in access to care and clinical outcomes.[15–19] Specifically, Black people have higher rates of HF risk factors (including hypertension and diabetes mellitus type 2) when compared with White people. Furthermore, data suggests Black individuals develop HF at higher rates when similar risk factors are present, resulting in nearly twice the incidence of HF in Black

people (4.6 vs. 2.4 per 1000 person-years).[20–23] Importantly, recent real-world data suggest that Black patients with HF suffer from worse health status than their White counterparts, underscoring the need to address racial disparities in care and outcomes.[24]

Despite the disproportionate burden of HF amongst Black people, they are underrepresented in clinical trials due to a range of issues including suboptimal engagement with the healthcare system, insufficient awareness of trials, impaired trust towards clinical trials, and others. [25] Accordingly, whether the health status benefits of SGLT2i are undermined by these health disparities remains insufficiently clear because pivotal trials demonstrating the clinical and health status benefits of SGLT2i enrolled few Black participants. Subgroup analyses of EMPEROR-Reduced (257 (6.9%) Black patients of 3730 total) and DAPA-HF (226 (4.8%) Black patients of 4744 total) showed similar effect amongst Black and White patients treated with an SGLT2i,[4,5] however a meta-analysis of these two trials suggested a potential enhanced benefit among Black people in reducing the primary combined endpoint of cardiovascular death and HF hospitalization.[26,27] On the other hand, subgroup analysis of EMPEROR-Preserved (258 Black participants (4.3%) of 5988 total) suggested a similar impact across races. [8] Neither of these studies has explicitly tested whether the health status benefits are similar in Black and White participants.

To address this gap in knowledge regarding the health status benefits of SGLT2i in Black patients with HF, we conducted a patient-level analysis of data from three clinical trials conducted in the United States that enrolled a substantial proportion of Black patients with HF. To our knowledge, there is no clear physiologic evidence to hypothesize that SGLT2i would have differential effects in Black patients compared with White patients with HF, but given low enrollment rates of Black patients in the landmark clinical trials studying the benefit of SGLT2i in HF we felt this additional investigation was warranted. We specifically sought to quantify the treatment effect of SGLT2i on health status in Black patients compared to White patients, across the full spectrum of ejection fractions (EFs). Quantification of the benefits of SGLT2i in Black patients can aid discussions with patients regarding this treatment and better inform considerations of SGLT2i as means of potentially reducing disparities in health status outcomes.[24]

Methods

Parent Studies and Patients

This study used data from three randomized clinical trials that have been previously reported and are summarized in Supplemental Table 1, including the Dapagliflozin effects on biomarkers, symptoms, and functional status in patients with heart failure with reduced ejection fraction (DEFINE-HF, n=263), the Dapagliflozin in heart failure with preserved ejection fraction clinical trial (PRESERVED-HF, n=324), and the Canagliflozin: Impact on health status, quality of life and functional status in heart failure trial (CHIEF-HF, n=448), which enrolled both individuals with both reduced and preserved EF. Briefly, all were randomized, blinded, parallel-group clinical trials recruiting patients with an established diagnosis of HF. The inclusion criteria of the studies were broadly similar, except for differences by EF; the inclusion criterion in DEFINE-HF was EF ≤40%; PRESERVED-HF required an EF ≥ 45%, and CHIEF-HF had no EF inclusion criteria (although randomization

was stratified by EF >40% or ≤40%). Patients in DEFINE-HF and PRESERVED-HF were randomized to dapagliflozin 10 mg vs. placebo, while CHIEF-HF randomized patients to canagliflozin 100 mg or placebo. All three trials treated patients for 12 weeks and assessed participants' health status with the Kansas City Cardiomyopathy Questionnaire (KCCQ) at baseline and 12 weeks. For the current study, all patients that self-identified as either Black or White race were included. Patients with missing data (race and KCCQ) or those who died prior to completing the 12 week follow-up were excluded. Due to insufficient data on people identifying as other race groups, comparisons were made between participants that self-identified as Black or White races only. All studies were approved by their human studies committees and complied with the Declaration of Helsinki. All participants provided informed consent in the respective studies.

Health Status Outcomes Assessment

The KCCQ was used as the health status outcome for all three trials. The KCCQ is a self-administered, 23-item questionnaire designed to assess patients' perceptions over the previous two weeks across four domains 1) total symptoms (KCCQ-TS scale), 2) physical limitation (KCCQ-PL scale), 3) social limitation (KCCQ-SL scale), and 4) quality of life (KCCQ-QoL scale).[28–30] Combining the KCCQ-TS and KCCQ-PL scales gives the clinical summary score (KCCQ-CS scale) which mirrors the New York Heart Association functional classification. Combining all four scales, the KCCQ-TS, KCCQ-PL, KCCQ-SL, and KCCQ-QoL gives the overall summary score (KCCQ-OS scale) that provides a holistic summary of the patient's health status. Each domain of the KCCQ is scored from 0 to 100, where 0 represents the worst and 100 represents the best health status, with scores of 0–24 representing very poor to poor; 25–49, poor to fair; 50–74, fair to good; and 75–100, good to excellent health status.[31] Additionally, changes in the KCCQ score in increments of 5, 10, and 20 points are associated with clinically relevant small to moderate, moderate to large, large to very large changes from patient and provider perspectives.[31–33] KCCQ score and changes in scores are significantly and independently associated with mortality and hospitalization rates in patients with HF regardless of EF or etiology.[34]

Statistical Analyses

A total of 1035 patients participated in the three trials, of which we excluded those missing information for race or marked as "other" race (n=37), baseline clinical summary score (n=1), or 12-week clinical summary score (n=62, of which 11 were due to death), leaving a final sample of 935 participants (Figure 1). Continuous variables are described as mean and standard deviation and compared using the Students T-Test, while categorical variables are described as proportions and compared with chi-square or Fisher's exact tests, as appropriate. The primary analysis compared the change in clinical summary score (baseline to 12 weeks) by treatment arm (SGLT2i vs. placebo) and tested the interaction of treatment by race, using multivariable linear regression. Models included treatment, race, the interaction effect of treatment and race, and were also adjusted for trial and baseline KCCQ score (as a restricted cubic spline term). In similar models, each domain of KCCQ (TS, PL, SL, QoL) and total summary score were also tested. Responder analyses were conducted examining proportions of patients with deterioration (change <−5 points), no improvement (change −5 to <5 points), small to moderate improvement (change 5 to <10 points),

moderate to large improvement (change 10 to <20 points), and very large improvement (change ≥20 points) in KCCQ-CS and KCCQ-OS scales at the end of treatment period by race. Only those with a score ≤ 80 at baseline in the individual domains were included in the responder analyses with n=785 for the KCCQ-CS scale and n=738 for the KCCQ-OS scale. Approximately a quarter of those included in each scale were Black participants. A 2-sided alpha less than 0.05 was used to establish significance. All analyses were performed using SAS v9.4 (SAS Institute, Cary, North Carolina).

Results

Among the 935 participants included in the analyses, 236 self-identified as Black (25%) and 469 (50.2%) were randomized to SGLT2i. Table 1 describes the baseline characteristics, overall and stratified by race and treatment assignment. The mean age was 65.1 ± 12.3 years and 537 (56.4%) were male. The two treatment arms were well-balanced in all baseline characteristics, overall and within race subgroups. Compared with White trial participants, Black participants tended to be younger (mean age 60.3±11.4 vs 66.7±12.2 years, p<0.001), were more often female (53% vs. 41%, p=0.001), and more often had reduced EF (48.3% vs 40.8%; p=0.043), but had similar prevalence of diabetes mellitus type 2 (77.3% vs. 74.6%, p =0.40).

Baseline Health Status

The baseline and 12-week KCCQ scores by race, by treatment, and both race and treatment are shown in Supplemental Table 2. Raw baseline KCCQ scores were similar when comparing Black and White participants across all domains except physical limitations where Black patients had worse baseline values (55.8 ± 25.3 vs. 59.8 ± 22.2, p=0.02). However, adjusted for age, sex, and trial, Black patients had significantly worse baseline KCCQ scores in OS, CS, PL, and SL domains when compared to White patients (all p<0.015, Supplemental Table 5). When considering treatment assignment in the overall study cohort, the KCCQ-CS score was similar in the SGLT2i compared to placebo arms (61.6 ± 20.9 vs. 61.2 ± 20.7, p=0.77). When stratified by race and then comparing across treatment arms (SGLT2i vs. placebo), there again was no significant difference in baseline KCCQ-CS scores within either race group.

Impact of SGLT2 inhibition on Health Status in Black compared to White Patients

The primary results of multivariable linear regression analysis of treatment effect and race are shown in Table 2. The effect of SGLT2i (compared to placebo) on 12 week change in CS was not statistically different between White and Black participants. Among Black HF patients (n=236, 123 SGLT2i vs. 113 placebo) the change in CS score due to treatment with SGLT2i was +4.7 points (95% confidence interval: 0.7 to 8.7, p=0.02), while among White patients (n=699, 346 SGLT2i vs. 353 placebo) the treatment effect was +4.0 points (95% confidence interval: 1.7 to 6.3, p=0.0007); with no significant race*treatment interaction (p interaction=0.76). Changes in the other domains of the KCCQ are also summarized in Table 2 and showed a similar pattern of health status benefit in both races without any significant interaction by race (all p for interaction > 0.44). We also tested three-way interactions of race, ejection fraction category and treatment, as well as race, diabetes status, and treatment

on the outcome of change in CS. Neither was statistically significant (both p for interaction > 0.3).

In the responder analysis, similar patterns were seen regardless of race, with greater proportions of both White and Black participants treated with SGLT2i (vs placebo) having small-moderate, moderate-large, or very large increases in the KCCQ-CS and KCCQ-OS scores, and placebo-treated patients having relatively more frequent deterioration, as shown in Figure 2A and 2B.

Discussion

A critical challenge confronting US healthcare is to address racial disparities in care and outcomes, underscoring the importance of examining racial differences in the benefits of novel therapies. Given the emerging evidence of the benefits of SGLT2i on the treatment of patients with HF, this study combined data from three randomized trials to create the largest reported cohort of Black patients, treated with an SGLT2i vs placebo, to explore potential racial differences in patient-reported health status outcomes. These data demonstrate a consistent health status benefit of SGLT2i in Black and White patients that were both statistically significant. To our knowledge, this is the first study to demonstrate a significant improvement in short-term quality of life in Black patients with HF (across the entire range of EF) treated with SGLT2i. These data are critically important since much of the impact of HF lies in health status impairment (poor quality of life, severe symptoms, and functional limitation) and not simply survival.

The findings of this study support and extend the existing literature on SGLT2i in HF. Data from EMPEROR-Reduced and DAPA-HF, summarized in a meta-analysis by Zannad et al, [26] demonstrated a substantial reduction in the composite outcome of hospitalization due to HF or cardiovascular death in those treated with an SGLT2i compared with placebo and thereby suggested a potentially greater benefit in Black patients. However, data from EMPEROR-Preserved showed similar effects in clinical benefit across racial groups. [8] While the impact of SGLT2i on reducing clinical events in HF is important, there is scarce data on the health status benefits of SGLT2i by race, which is a critically important outcome from patients' perspectives.[35,36] For example, the DELIVER trial showed in patients with HFmrEF and HFpEF, the use of dapagliflozin vs placebo improved the KCCQ-TS score. However, the trial enrolled few black patients (n=159/6263, 2.5%). [9,37] An important characteristic of the current study is that the health status benefits of SGLT2i are apparent within three months, and these shorter-term improvements in symptoms and physical limitations are especially appreciable to patients.

These findings have important clinical implications; SGLT2i should be embraced for treatment of individuals with HF regardless of race, given the robust health status benefit from this class of treatment. However, implementing this could be challenging, particularly for Black patients with HF who have, on average, worse health status. One of the key barriers is likely cost. Fortunately, recent studies have reported favorable coverage decisions regarding SGLT2i by most health insurance plans, including Medicaid.[38,39] Despite this, the out-of-pocket costs for some patients are higher than other generically-available guideline-

directed medical therapies, which may represent an obstacle to their use. Additional barriers to implementing wider SGLT2i use among Black patients are likely to be encountered when considering the disproportionate burden of social determinants of health (SDoH) in Black persons in the U.S., with noted disparities in the availability of health insurance, financial resources, health literacy, and access to quality healthcare.[14,40,41] Specific to HF, despite the availability of many treatments proven to reduce the progression of HF, successful implementation of therapies among patients in need remains a major public health and societal challenge and adverse SDoH are a known contributor to cardiometabolic disease among Black adults. [12,42,43] In this context, simply waiting for prescription of SGLT2i through the typical course of medical care may not be an effective strategy [44] since it does not overcome the underlying critical barriers related to access, bias, or poor engagement with the healthcare system. These practical barriers can make conventional routes for medical care less effective, a dynamic clearly demonstrated regarding blood pressure control.[12,42] Development and implementation of methods to overcome such barriers and ensure systematic application of these agents to those who are likely to benefit deserves further exploration and encouragement. These could include standardization or algorithm-based care, innovative, team-based coordinated delivery models that proactively engage vulnerable populations, or other novel interventions to enhance access to treatment.[45]

Our findings should be considered in the context of several potential limitations. First, we lacked extensive medical history and laboratory data in one trial (CHIEF-HF) due to its novel design (fully decentralized without in-person visits and with streamlined data collection), which in turn limited our ability to further adjust the racial differences in treatment effect for other comorbid conditions (other than DM) or laboratory markers. It is worth noting that previous studies, including DEFINE and PRESERVED, examined renal function and other medications, and found no interaction with SGLT2i effect. On the other hand, the potential modifiers of effects of SGLT2i of highest interest are diabetes and EF category, which were previously noted not to impact SGLT2i benefit and which we found to have no significant interaction with race and SGLT2i treatment in terms of health status benefit. Finally, while all three trials used different KCCQ domains as their primary outcome, all collected the KCCQ prospectively and in the same rigorous manner so that this study could calculate all of the scores directly from the collected data.

Conclusion

Treatment with SGLT2i improves health status in Black patients with HF as early as 12 weeks. This benefit was similar to that found among White patients and extended across a variety of health status domains including symptom burden, physical and social limitations, and quality of life. These agents should be used with confidence among Black patients with HF and efforts to ensure equitable access to these treatments have the potential to improve the health status of Black and White patients with HF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Non-standard Abbreviations and Acronyms

EF	Ejection Fraction
HF	Heart Failure
HFrEF	Heart Failure with reduced Ejection Fraction
HFmrEF	Heart Failure with mildly reduced Ejection Fraction
HFpEF	Heart Failure with preserved Ejection Fraction
SGLT2i	Sodium Glucose co-Transporter 2-Inhibitors
EMPEROR-Reduced	Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction
DAPA-HF	Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure
EMPEROR-Preserved	Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Preserved Ejection Fraction
DEFINE-HF	Dapagliflozin effects on biomarkers, symptoms, and functional status in patients with heart failure with reduced ejection fraction
PRESERVED-HF	Dapagliflozin in heart failure with preserved ejection fraction
CHIEF-HF	Canagliflozin: Impact on health status, quality of life and functional status in heart failure
KCCQ	Kansas City Cardiomyopathy Questionnaire

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CLINICAL PERSPECTIVE

What is new?

- In a patient-level meta-analysis of three randomized clinical trials, we explicitly demonstrated SGLT2i improves health status in both Black and White patients with heart failure to a similar degree, as early as 12-weeks after initiation, and irrespective of ejection fraction category.

What are the clinical implications?

- In Black patients with heart failure, who on average have more compromised health status, SGLT2i therapy can be prescribed with confidence to improve health status.
- Additional efforts to ensure widened and equitable access to SGLT2i for patients with heart failure are justified.

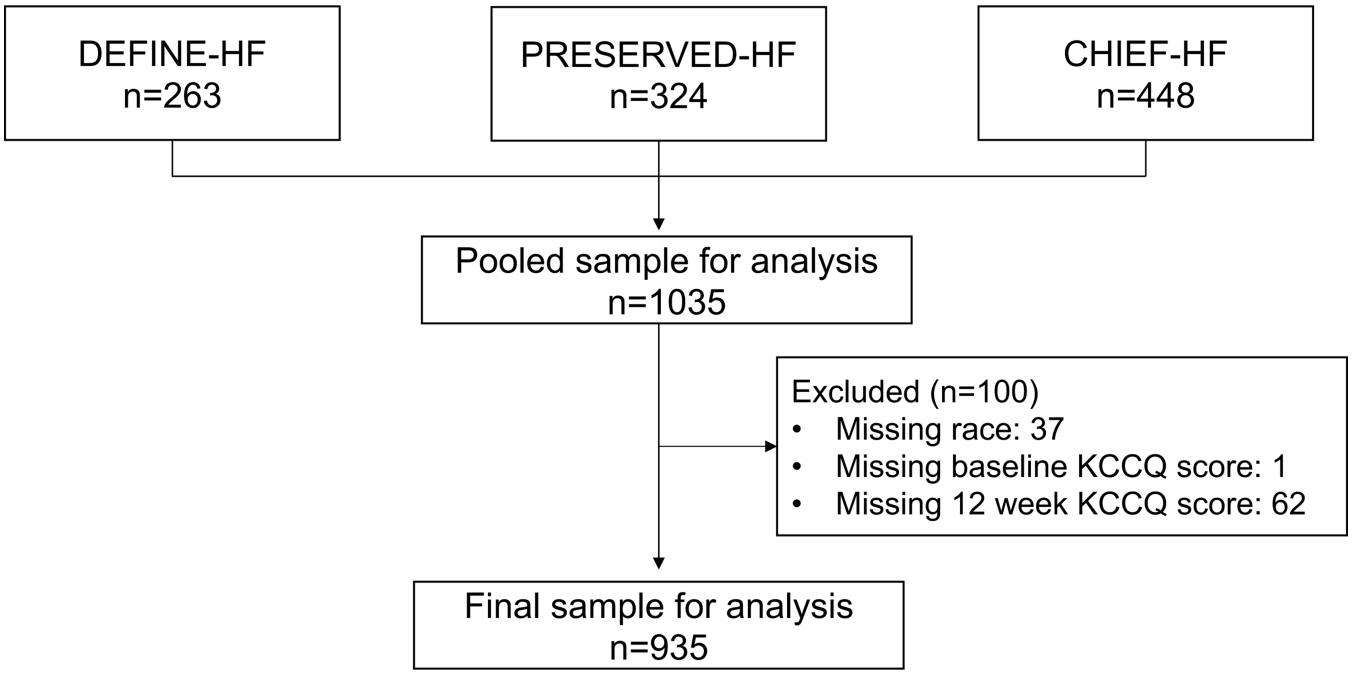

Figure 1:
Consort diagram showing the process for obtaining the sample for analysis. KCCQ, Kansas City Cardiomyopathy Questionnaire

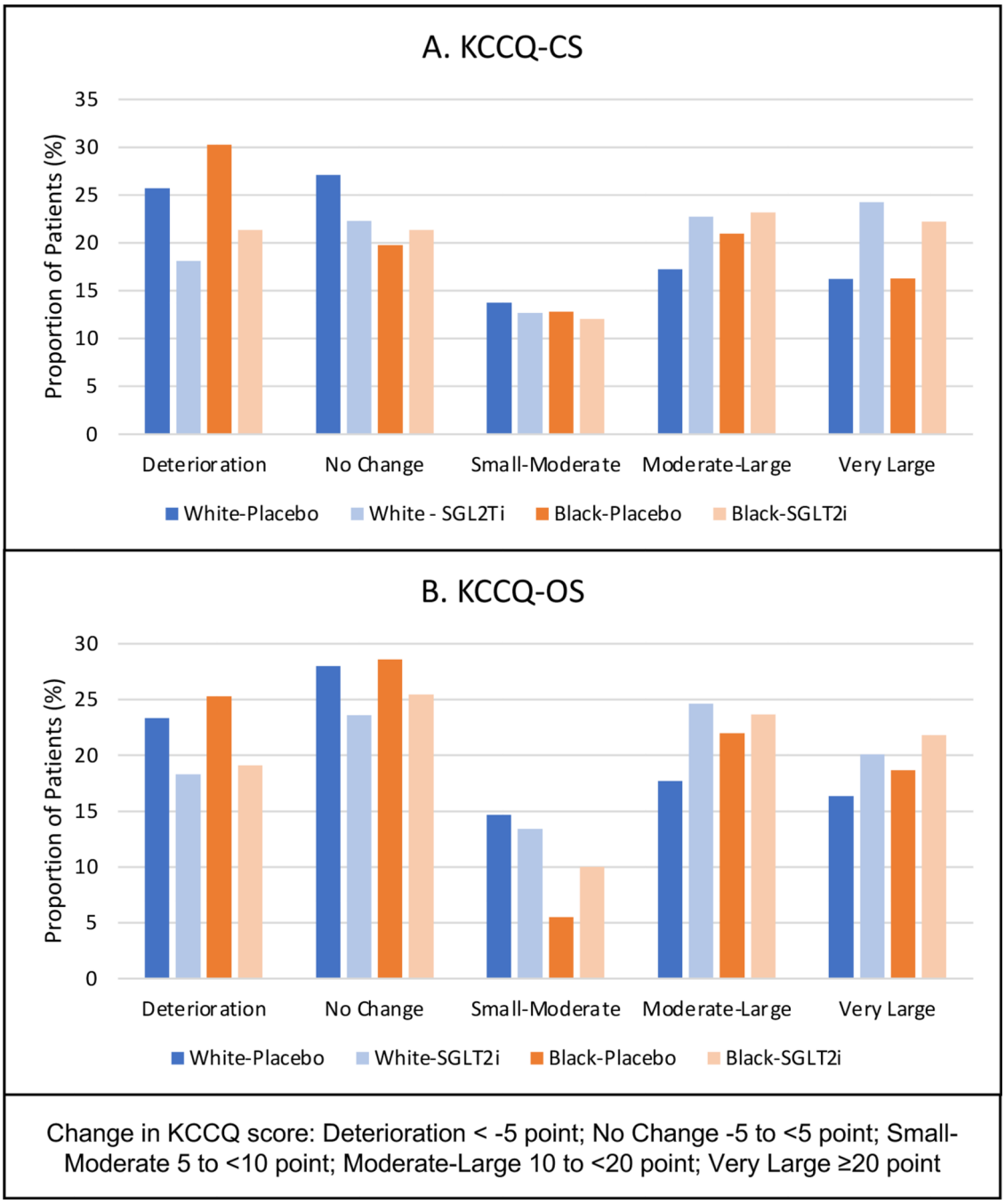

Figure 2:

Responder analysis of changes in the Kansas City Cardiomyopathy Questionnaire (KCCQ), A. Clinically Summary (KCCQ-CS) score, and B. Overall Summary (KCCQ-OS) score at the end of 12 weeks in SGLT2i and placebo arms amongst White and Black participants.

Table 1.

Baseline characteristics of patients by race and treatment category recruited to DEFINE-HF, PRESERVED-HF, and CHIEF-HF

	All n = 935			All n = 935			White n = 699 (74.8%)			Black n = 236 (25.2%)		
	SGLT2i n = 469	Placebo n = 466	P-value	White n = 699	Black n = 236	P-value	SGLT2i n = 346	Placebo n = 353	P-value	SGLT2i n = 123	Placebo n = 113	P-value
Age, years	65.0 ± 12.2	65.1 ± 12.5	0.91	66.7 ± 12.3	60.3 ± 11.4	< 0.001	66.7 ± 12.3	66.7 ± 12.2	0.99	60.4 ± 10.7	60.3 ± 12.1	0.93
Sex												
Male	261 (55.7%)	266 (57.1%)	0.66	415 (59.4%)	112 (47.5%)	0.001	202 (58.4%)	213 (60.3%)	0.60	59 (48%)	53 (46.9%)	0.87
Female	208 (44.3%)	200 (44.7%)		284 (40.6%)	124 (52.5%)		144 (41.6%)	140 (39.7%)		64 (52%)	60 (53.1%)	
Diabetes Mellitus Type 2												
Yes	357 (76.1%)	359 (77%)	0.74	540 (77.3%)	176 (74.6%)	0.40	264 (76.3%)	276 (78.2%)	0.55	93 (75.6%)	83 (73.5%)	0.70
No	112 (23.9%)	107 (23%)		159 (22.7%)	60 (25.4%)		82 (23.7%)	77 (21.8%)		30 (24.4%)	30 (26.5%)	
Ejection Fraction												
Reduced	269 (57.4%)	267 (57.3%)	0.99	285 (40.8%)	114 (48.3%)	0.04	203 (58.7%)	211 (59.8%)	0.77	66 (53.7%)	56 (49.6%)	0.53
Preserved	200 (42.6%)	199 (42.7%)		414 (59.2%)	122 (51.7%)		143 (41.3%)	142 (40.2%)		57 (46.3%)	57 (50.4%)	
Baseline KCCQ Score												
Clinical Summary Score	61.6 ± 20.9	61.2 ± 20.7	0.77	61.9 ± 20.3	59.9 ± 22.0	0.19	62.9 ± 20.5	61.0 ± 20.1	0.20	57.9 ± 21.6	62.0 ± 22.4	0.15
Overall Summary Score	59.4 ± 20.9	59.1 ± 20.7	0.79	59.6 ± 20.6	58.3 ± 21.6	0.42	60.6 ± 20.6	58.6 ± 20.5	0.18	56.1 ± 21.5	60.7 ± 21.5	0.10
Total Symptom Score	64.3 ± 22.3	63.5 ± 22.6	0.59	63.9 ± 21.9	63.9 ± 24.0	0.99	65.3 ± 21.6	62.5 + 22.1	0.09	61.4 ± 23.9	66.7 ± 23.9	0.10
Physical Limitation Score *a*	58.9 ± 23.4	58.7 ± 22.8	0.93	59.8 ± 22.2	55.8 ± 25.3	0.02	60.5 ± 22.6	59.1 ± 21.8	0.43	54.3 ± 24.9	57.4 ± 25.7	0.36
Social Limitation Score *b*	58.3 ± 27.1	58.3 ± 26.6	0.97	58.8 ± 26.1	56.9 ± 28.9	0.37	59.8 ± 26.2	57.7 ± 26.0	0.31	54.2 ± 29.3	59.9 ± 28.4	0.14
Quality of Life Score	55.5 ± 24.3	55.4 ± 24.2	0.99	55.1 ± 24.2	56.4 ± 24.3	0.47	55.9 ± 24.0	54.3 ± 24.5	0.38	54.1 ± 25.3	58.9 ± 23.0	0.13

Continuous variables are expressed as mean ± standard deviation and compared using Student's T-testCategorical variables are expressed as n (%) and compared using chi-square or Fisher's exact test

[a] Missing 9 observations for baseline KCCQ physical limitation score

[b] Missing 33 observations for baseline KCCQ social limitation score

KCCQ, Kansas City Cardiomyopathy Questionnaire; SGLT2i, sodium glucose cotransporter-2 inhibitors

Table 2.

Association between treatment, change in KCCQ scores, and race in DEFINE-HF, PRESERVED-HF, and CHIEF-HF

KCCQ Domain [a]	Black Patients		White Patients		Race*Treatment	
	Treatment Effect Difference (SGLT2i vs placebo)	P-value	Treatment Effect Difference (SGLT2i vs placebo)	P-value	Treatment Effect Difference (White vs Black)	P-value
Clinical Summary Score	4.71 (0.74 to 8.68)	0.02	3.99 (1.69 to 6.29)	0.0007	−0.7 (−5.3, 3.9)	0.76
Overall Summary Score	4.66 (0.65 to 8.66)	0.02	3.01 (0.68 to 5.34)	0.01	−1.6 (−6.3, 3.0)	0.49
Total Symptom Score	4.92 (0.56 to 9.27)	0.03	4.56 (2.04 to 7.09)	0.0004	−0.4 (−5.4, 4.7)	0.89
Physical Limitation Score	4.04 (−0.71 to 8.8)	0.10	3.62 (0.85 to 6.38)	0.01	−0.4 (−5.9, 5.1)	0.88
Social Limitation Score	2.87 (−2.75 to 8.5)	0.32	1.78 (−1.45 to 5.01)	0.28	−1.1 (−7.6, 5.4)	0.74
Quality of Life Score	4.98 (0.07 to 9.88)	0.05	2.77 (−0.07 to 5.62)	0.06	−2.2 (−7.9, 3.5)	0.45

[a] Models adjusted for trial, baseline KCCQ scores (as a restricted cubic spline), race, treatment category, and interaction effect of race and treatment

KCCQ, Kansas City Cardiomyopathy Questionnaire; SGLT2i, sodium glucose cotransporter-2 inhibitors