Effects of Dapagliflozin on Symptoms, Function and Quality of Life in Patients with Heart Failure: The DAPA-HF Trial

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DAPAHF

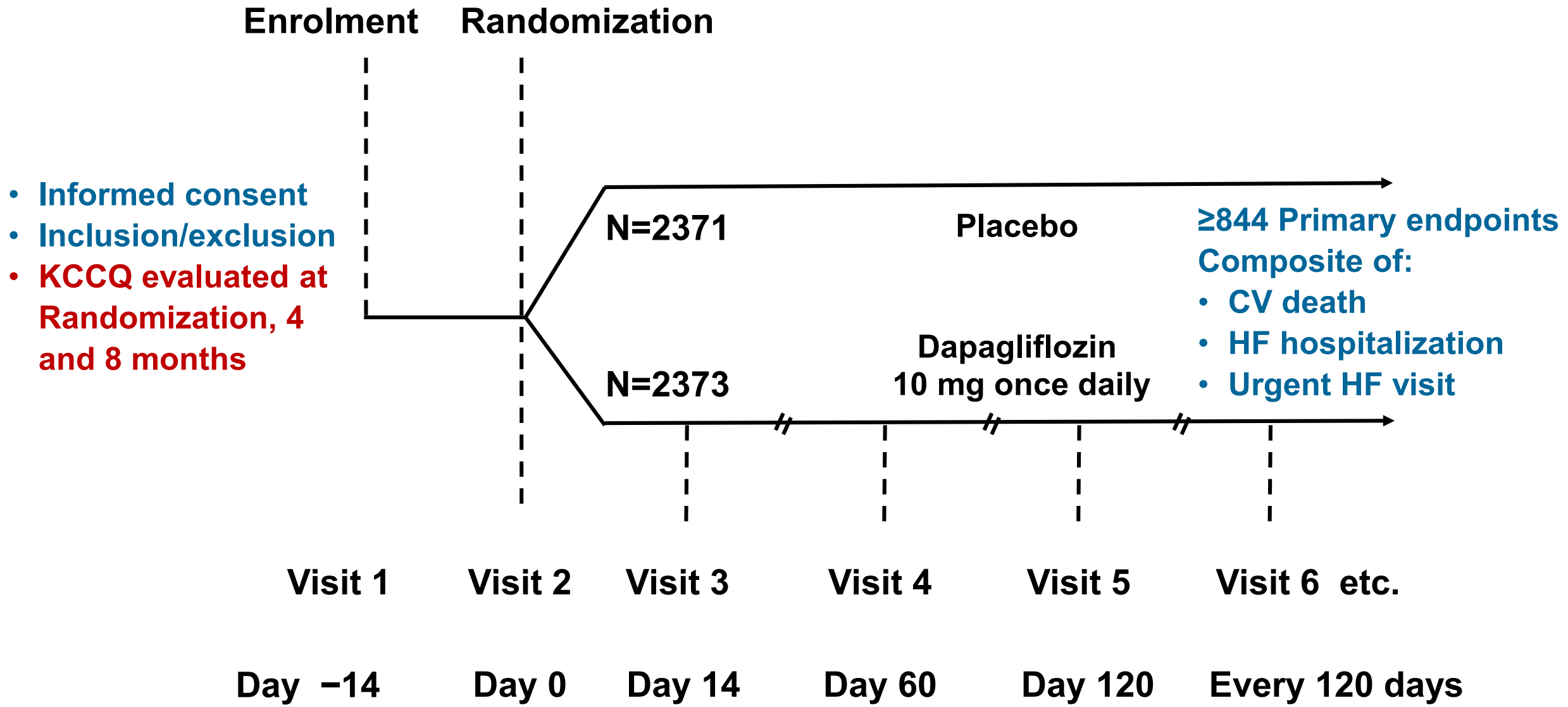
Disclosures

- Research Grants:
  - AstraZeneca, Boehringer Ingelheim
- Consultant/Advisory Board:
  - Amarin, Applied Therapeutics, AstraZeneca, Amgen, Bayer, Boehringer Ingelheim, Eisai, Glytec, GSK, Intarcia, Janssen, Eli Lilly, Merck (Diabetes), Novartis, Novo Nordisk, Sanofi
- DAPA-HF Trial was sponsored by AstraZeneca

Goals of Care in Heart Failure

- Reduce death and hospitalizations
- Improve health status
  - Symptoms
  - Physical Limitations
  - Quality of Life

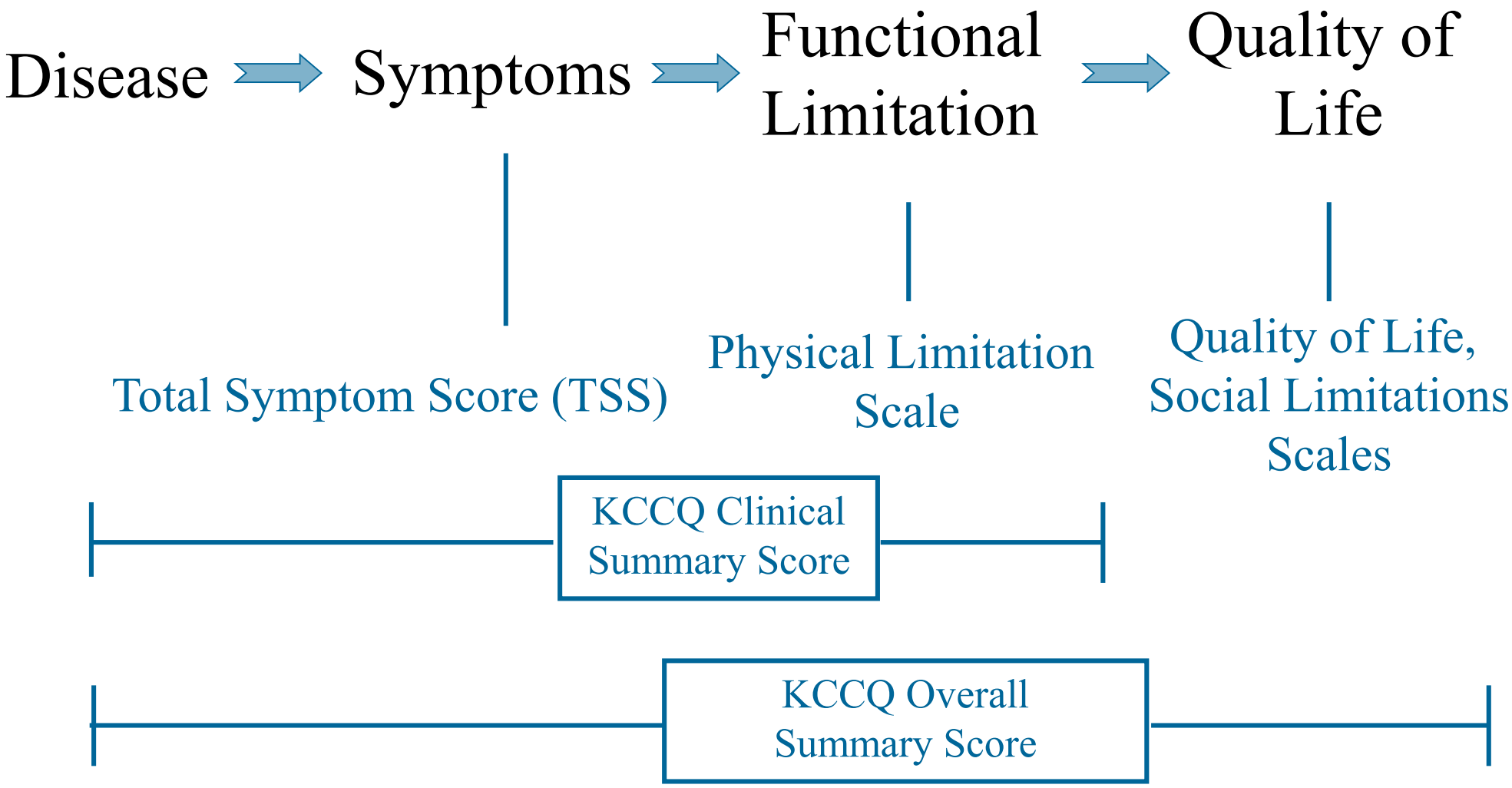
DAPA-HF Design



Kansas City Cardiomyopathy Questionnaire

- 23 items that measure 4 clinical domains
  - Symptoms: Frequency and Severity
  - Physical Limitation
  - Quality of Life
  - Social Limitation
- Represents the *patient's* perspective of their HF
- Scores range 0-100, higher scores reflect better health status
- Established validity, reliability and responsiveness
  - Independently associated with death and hospitalization
- 5-point threshold established as clinically meaningful change

Mapping the KCCQ Scales



Statistical Analysis

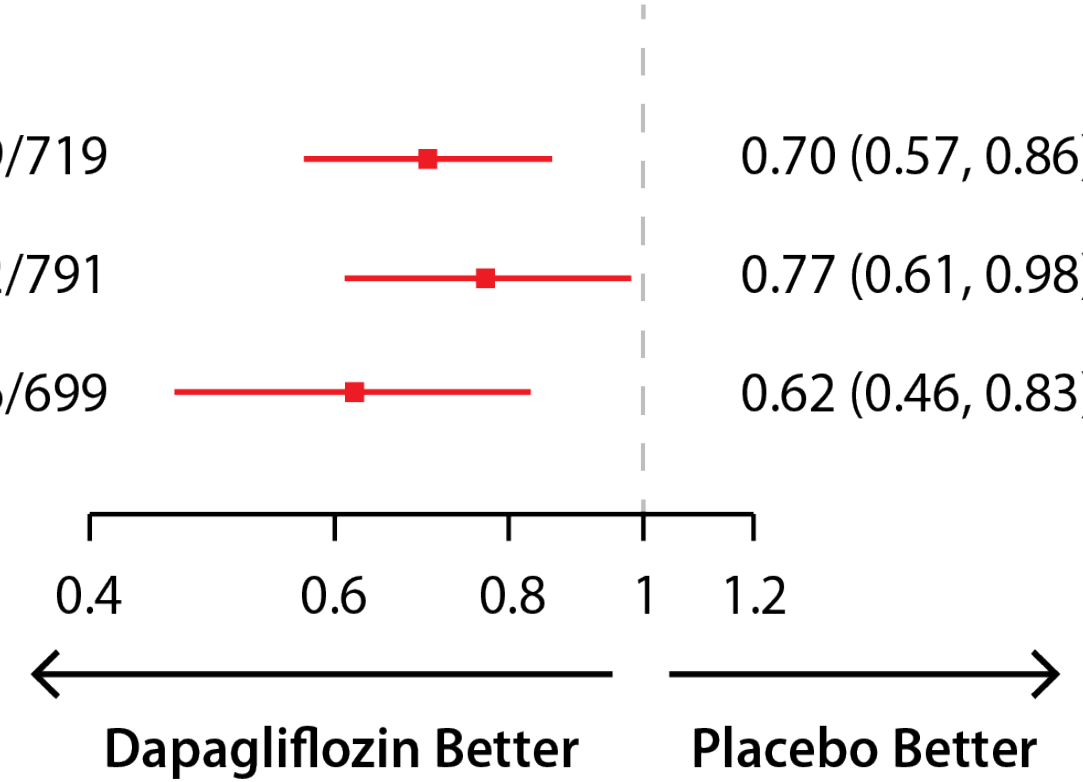
- Patients divided based on baseline KCCQ-TSS tertiles
- Effects of dapagliflozin on clinical outcomes across the KCCQ tertiles evaluated using Cox proportional-hazards models
- Between-group differences in mean KCCQ-TSS, CSS and OSS at 4 and 8 months assessed by using mixed models for repeated measures, adjusted for baseline KCCQ
- Responder analyses examined proportions of patients with a deterioration, and clinically meaningful improvements in KCCQ at 8 months (≥5 point [at least small], ≥10 point [at least moderate], and ≥15 point [large] change)

Baseline Characteristics

KCCQ-TSS at Baseline	Tertile 1 (N=1,487)	Tertile 2 (N=1,564)	Tertile 3 (N=1,392)	Total (N=4,443)	p for trend
Age (years)	65.8	66.4	66.8	66.3	0.007
Male	72.2%	78.0%	83.3%	77.7%	<0.001
White Race	79.0%	73.0%	62.1%	71.6%	<0.001
NT-proBNP (pg/mL)	1716	1389	1292	1432	<0.001
NYHA Class III/IV	49.9%	29.4%	18.2%	32.6%	<0.001
T2DM	45.9%	39.5%	40.7%	42.0%	0.004
Atrial fibrillation	44.0%	36.8%	35.4%	38.8%	<0.001
ACE-I/ARB/ARNI	94.2%	94.8%	93.7%	94.3%	0.544
Diuretic	96.2%	94.0%	90.5%	93.6%	<0.001
Beta blocker	96.3%	96.3%	96.0%	96.2%	0.653
MRA	73.8%	71.5%	67.0%	70.9%	<0.001

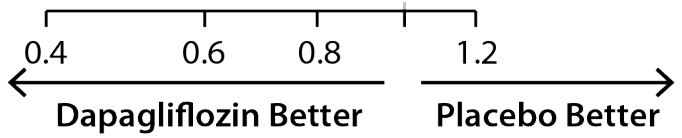
Effects of Dapagliflozin on Primary Endpoint by KCCQ Tertiles

Cardiovascular Death, Hospitalization for HF or Urgent HF Visit	Dapagliflozin	Placebo	HR (95% CI)	p-value for Interaction
≤65.6 (n=1487)	162/768	209/719	0.70 (0.57, 0.86)	
65.7-87.5 (n=1564)	119/773	152/791	0.77 (0.61, 0.98)	0.52
>87.5 (n=1392)	73/693	116/699	0.62 (0.46, 0.83)	

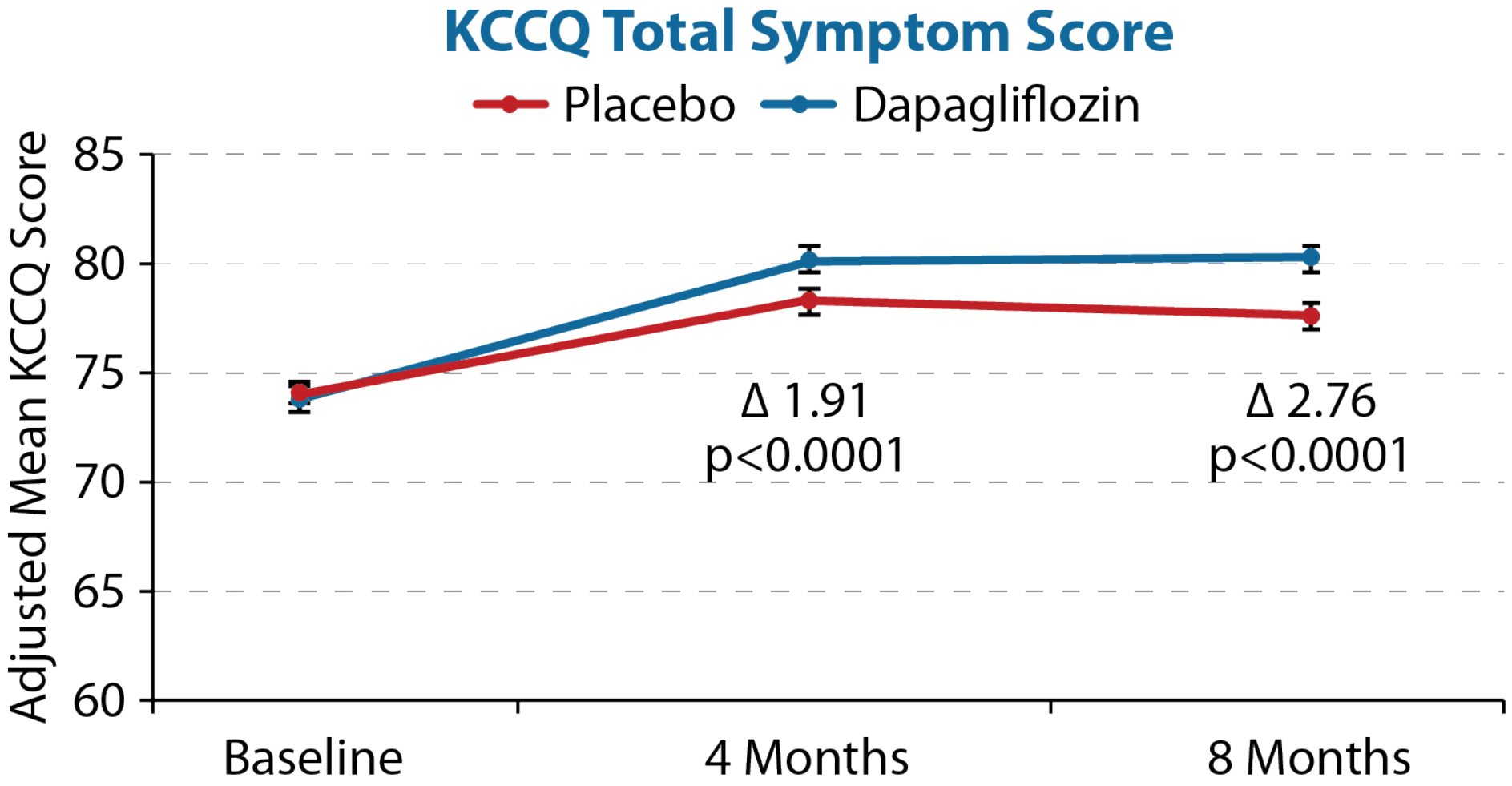


Effects of Dapagliflozin on Secondary Endpoints by KCCQ Tertiles

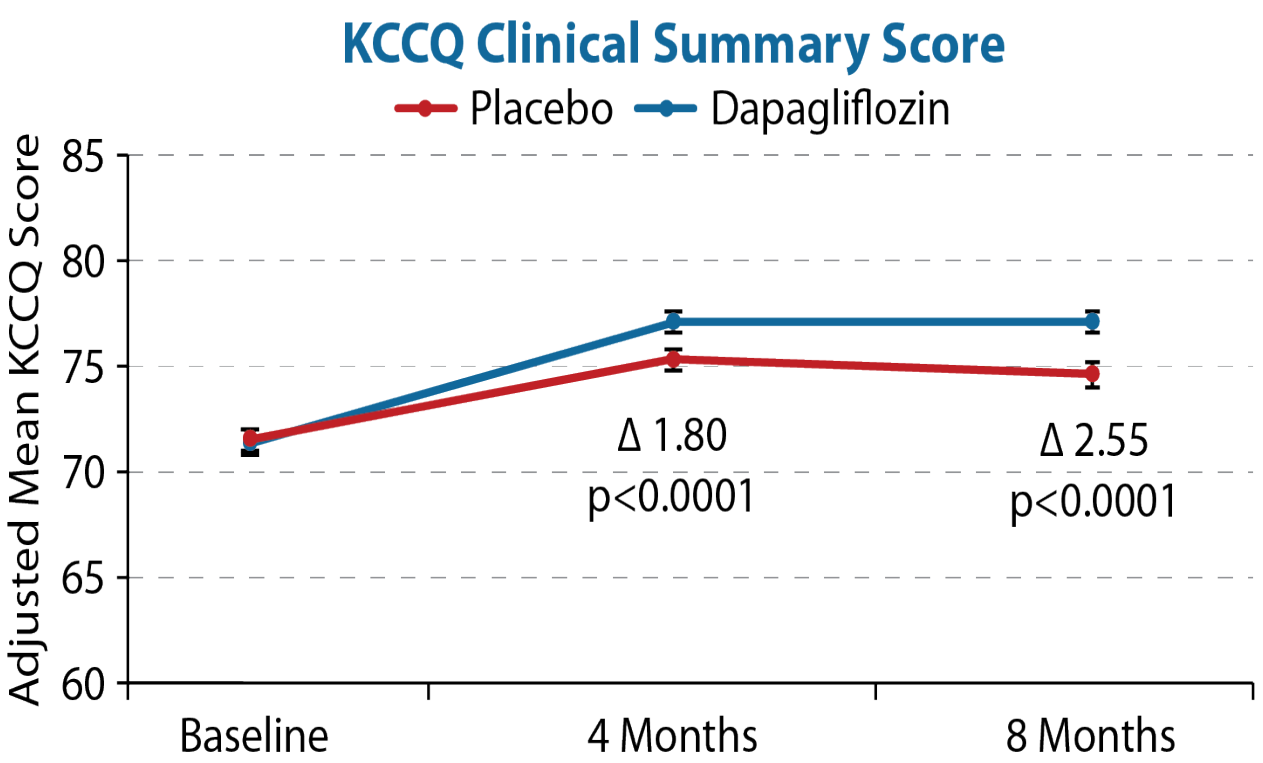
Outcome	Dapagliflozin	Placebo	HR (95% CI)	p for interaction
CV Death or Hospitalization for HF				0.53
≤65.6 (n=1487)	160/768	205/719	0.71 (0.57, 0.87)	
65.7-87.5 (n=1564)	118/773	150/791	0.77 (0.61, 0.99)	
>87.5 (n=1392)	73/693	115/699	0.62 (0.46, 0.83)	
Hospitalization for HF or Urgent HF Visit				0.38
≤65.6 (n=1487)	99/768	134/719	0.67 (0.51, 0.86)	
65.7-87.5 (n=1564)	78/773	101/791	0.76 (0.56, 1.02)	
>87.5 (n=1392)	43/693	78/699	0.54 (0.37, 0.78)	
Hospitalization for HF				0.40
≤65.6 (n=1487)	96/768	130/719	0.67 (0.51, 0.87)	
65.7-87.5 (n=1564)	76/773	98/791	0.76 (0.56, 1.03)	
>87.5 (n=1392)	43/693	77/699	0.55 (0.38, 0.79)	
Cardiovascular Death				0.82
≤65.6 (n=1487)	107/768	121/719	0.84 (0.64, 1.09)	
65.7-87.5 (n=1564)	63/773	81/791	0.78 (0.56, 1.09)	
>87.5 (n=1392)	39/693	54/699	0.72 (0.48, 1.09)	
Death from Any Cause				0.45
≤65.6 (n=1487)	134/768	142/719	0.89 (0.70, 1.13)	
65.7-87.5 (n=1564)	76/773	99/791	0.77 (0.57, 1.04)	
>87.5 (n=1392)	46/693	67/699	0.68 (0.47, 0.99)	

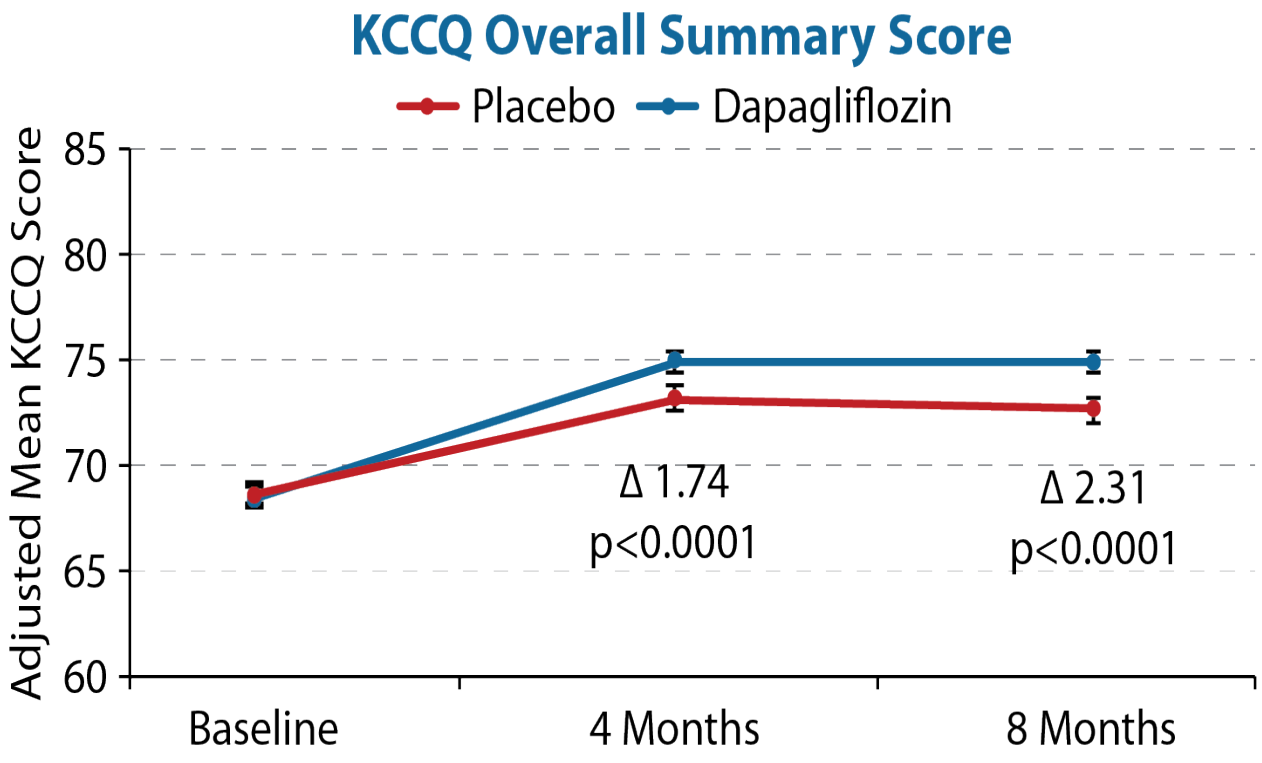


Effect of Dapagliflozin on KCCQ Total Symptom Score at 4 and 8 months



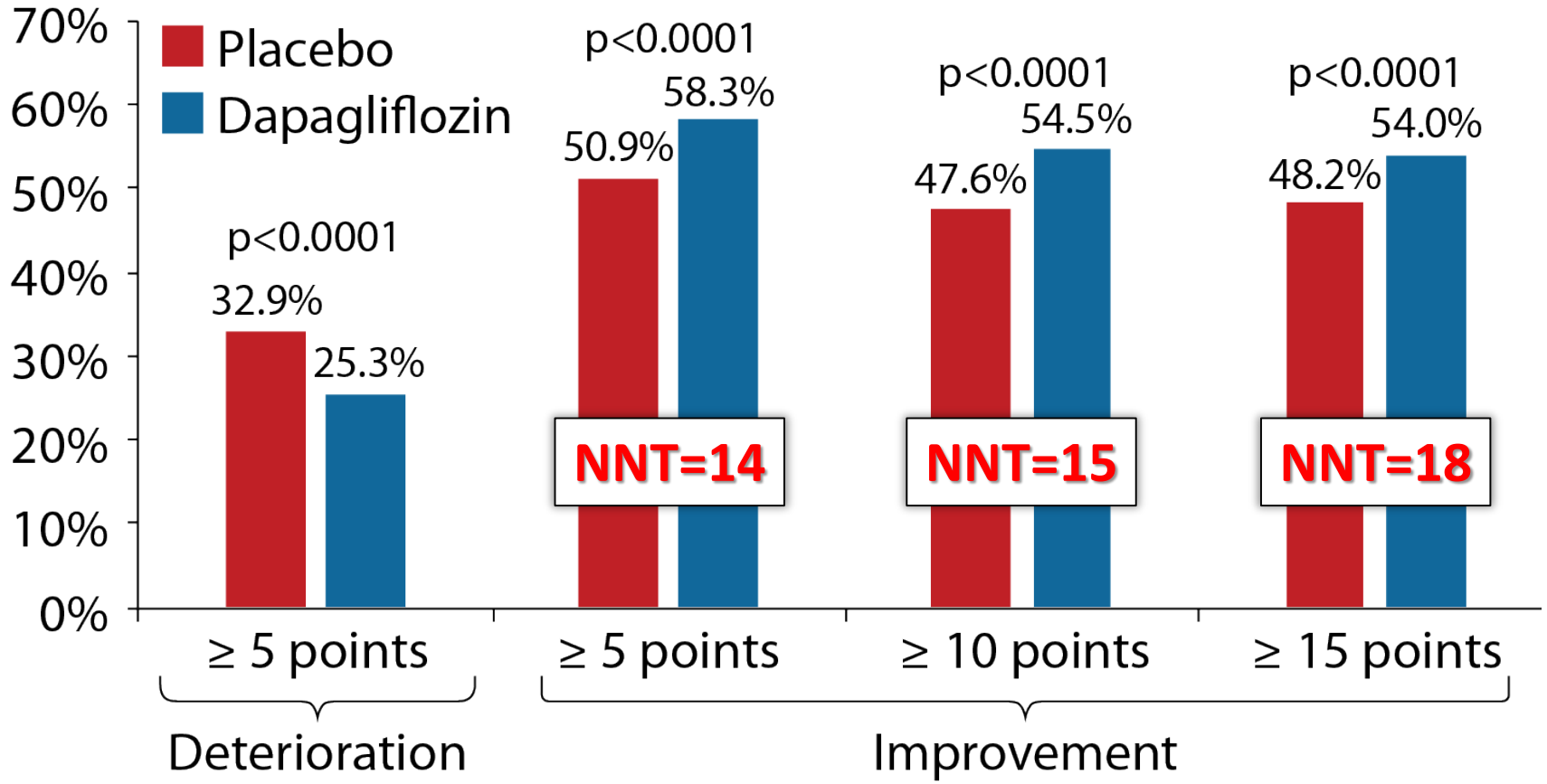
Effect of Dapagliflozin on KCCQ Clinical Summary Score and Overall Summary Score at 4 and 8 months





Clinically Meaningful Change in KCCQ: Dapagliflozin vs. Placebo

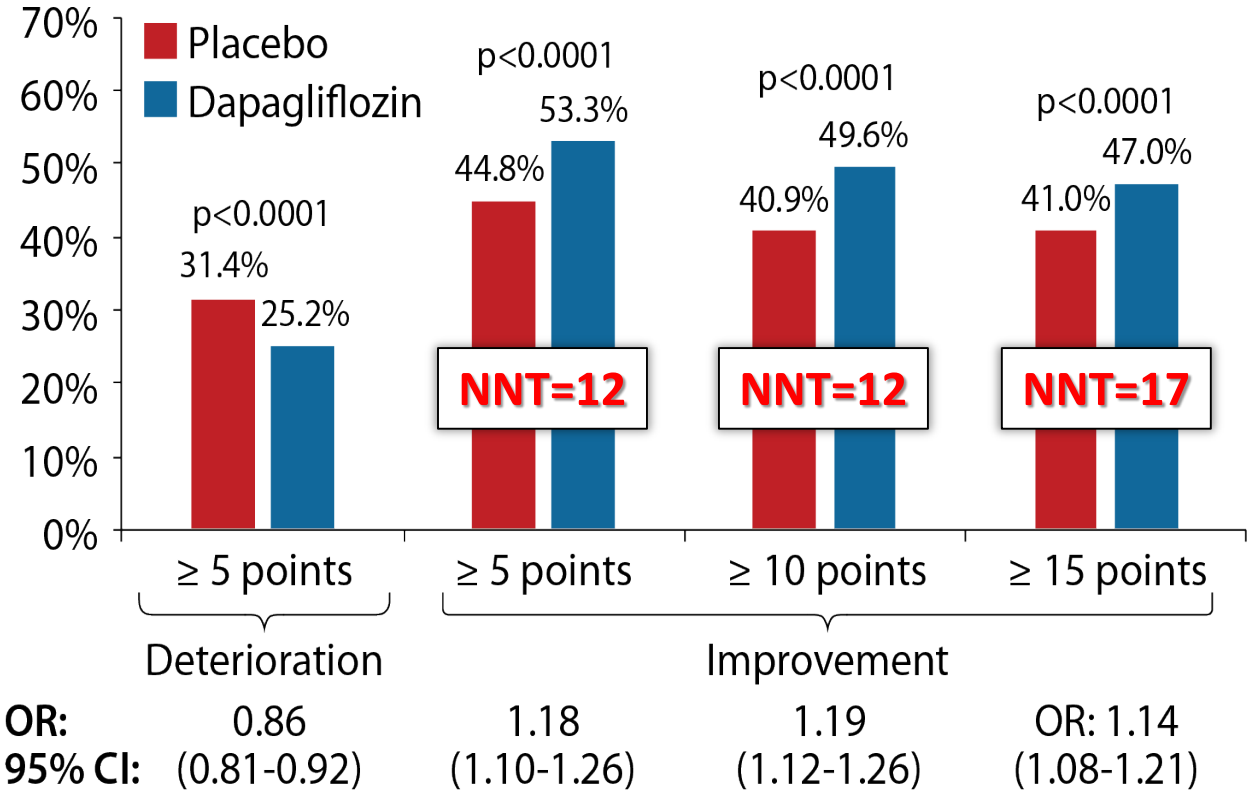
KCCQ Total Symptom Score



OR:	0.84	1.15	1.15	1.14
95% CI:	(0.78, 0.90)	(1.08-1.23)	(1.08-1.22)	(1.07-1.22)

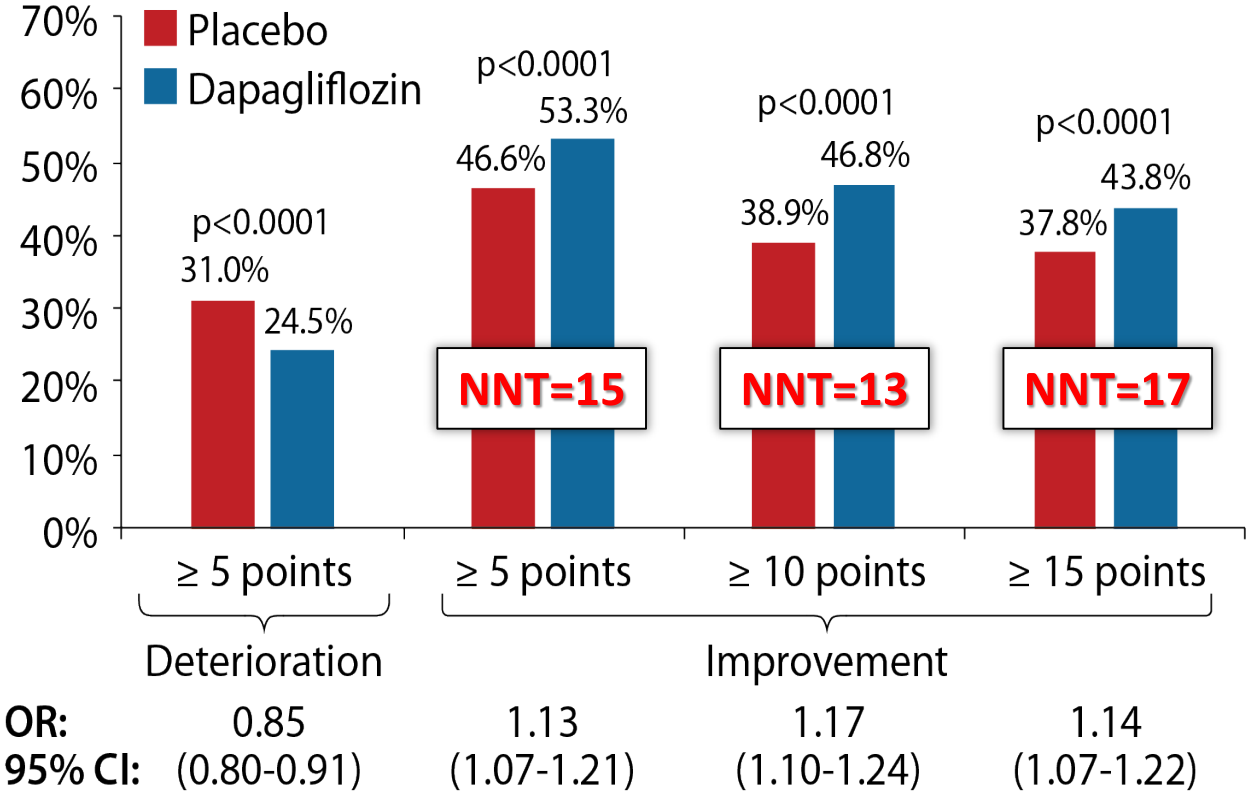
Clinically Meaningful Change in KCCQ: Dapagliflozin vs. Placebo

KCCQ Clinical Summary Score



OR:	0.86	1.18	1.19	OR: 1.14
95% CI:	(0.81-0.92)	(1.10-1.26)	(1.12-1.26)	(1.08-1.21)

KCCQ Overall Summary Score



OR:	0.85	1.13	1.17	1.14
95% CI:	(0.80-0.91)	(1.07-1.21)	(1.10-1.24)	(1.07-1.22)

Conclusions

- Dapagliflozin improved all key clinical outcomes, including CV death and worsening HF, to a similar extent across the entire range of KCCQ at baseline
- Dapagliflozin improved all major components of KCCQ - effects amplified over time
- Fewer dapagliflozin-treated patients had significant deterioration, and more experienced small, moderate and large clinically meaningful improvements across all key domains of KCCQ
- Effects were substantial, with NNT ranging between 12 and 18 when compared to placebo after just 8 months of treatment
- Dapagliflozin offers a new approach to improving symptoms, functional limitations and quality of life in patients with HFrEF

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Effects of dapagliflozin on symptoms, function and quality of life in patients with heart failure and reduced ejection fraction: results from the DAPA-HF Trial

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