Dossier zur Nutzenbewertung gemäß § 35a SGB V

Dapagliflozin (Forxiga®)

AstraZeneca GmbH

Separater Anhang 4-G

Zur Behandlung einer symptomatischen, chronischen Herzinsuffizienz mit erhaltener Ejektionsfraktion

Stand: 17.02.2023

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AstraZeneca
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Analysis	Medication	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)
Medication at baseline	ACEi/ARB	2262/3131 (72.2)	2281/3132 (72.8)
	ARNI	165/3131 (5.3)	136/3132 (4.3)
	Beta Blocker	2592/3131 (82.8)	2585/3132 (82.5)
	Diuretics	2793/3131 (89.2)	2787/3132 (89.0)
	MRA	1340/3131 (42.8)	1327/3132 (42.4)
Medication during study	ACEi/ARB	2394/3131 (76.5)	2451/3132 (78.3)
	ARNI	248/3131 (7.9)	262/3132 (8.4)
	Beta Blocker	2718/3131 (86.8)	2725/3132 (87.0)
	Diuretics	2885/3131 (92.1)	2923/3132 (93.3)
	MRA	1560/3131 (49.8)	1624/3132 (51.9)
Increase in dosing	ACEi/ARB	151/2262 (6.7)	177/2281 (7.8)
	ARNI	20/ 165 (12.1)	6/ 136 (4.4)
	Beta Blocker	211/2592 (8.1)	238/2585 (9.2)
	Diuretics	464/2793 (16.6)	575/2787 (20.6)
	MRA	98/1340 (7.3)	103/1327 (7.8)
Decrease in dosing	ACEi/ARB	195/2262 (8.6)	182/2281 (8.0)
	ARNI	22/ 165 (13.3)	12/ 136 (8.8)
	Beta Blocker	262/2592 (10.1)	260/2585 (10.1)
	Diuretics	366/2793 (13.1)	352/2787 (12.6)
	MRA	95/1340 (7.1)	90/1327 (6.8)
Increase or decrease in dosing	ACEi/ARB	335/2262 (14.8)	344/2281 (15.1)
	ARNI	38/ 165 (23.0)	18/ 136 (13.2)
	Beta Blocker	439/2592 (16.9)	465/2585 (18.0)
	Diuretics	688/2793 (24.6)	759/2787 (27.2)
	MRA	182/1340 (13.6)	181/1327 (13.6)
New initiation	ACEi/ARB	132/ 869 (15.2)	170/ 851 (20.0)
	ARNI	83/2966 (2.8)	126/2996 (4.2)
	Beta Blocker	126/ 539 (23.4)	140/ 547 (25.6)
	Diuretics	92/ 338 (27.2)	136/ 345 (39.4)
	MRA	220/1791 (12.3)	297/1805 (16.5)

Medication at baseline: N defines number of patients in Full Analysis Set.
Medication during study: N defines number of patients in Full Analysis Set.
Increase/Decrease in dosing: N defines number of patients with respective medication given at baseline.
New initiation: N defines number of patients with respective medication not given at baseline.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to composite of CV death, hospitalisation for HF or urgent HF visit
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	512/3131 (16.4)	7.83	610/3132 (19.5)	9.59	0.82 (0.73, 0.92)	0.0008	
Age							0.9283
<= median	247/1545 (16.0)	7.63	306/1604 (19.1)	9.28	0.82 (0.69, 0.97)	0.0208	
> median	265/1586 (16.7)	8.04	304/1528 (19.9)	9.92	0.81 (0.69, 0.96)	0.0133	
Gender							0.8510
Male	317/1767 (17.9)	8.67	367/1749 (21.0)	10.52	0.82 (0.71, 0.96)	0.0110	
Female	195/1364 (14.3)	6.77	243/1383 (17.6)	8.46	0.81 (0.67, 0.97)	0.0242	
Race							0.6434
White	372/2214 (16.8)	7.92	461/2225 (20.7)	10.06	0.79 (0.69, 0.90)	0.0006	
Black or African	21/ 81 (25.9)	13.47	19/ 78 (24.4)	12.43	1.08 (0.58, 2.01)	0.8067	
Asian	97/ 630 (15.4)	7.58	106/ 644 (16.5)	8.30	0.91 (0.69, 1.21)	0.5268	
Other	22/ 206 (10.7)	5.48	24/ 185 (13.0)	6.97	0.83 (0.46, 1.48)	0.5184	
Geographic region							0.8510
Asia	92/ 607 (15.2)	7.47	103/ 619 (16.6)	8.44	0.89 (0.67, 1.18)	0.4051	
Europe and Saudi Arabia	261/1494 (17.5)	7.94	309/1511 (20.5)	9.56	0.83 (0.70, 0.98)	0.0267	
North America	89/ 428 (20.8)	10.74	111/ 423 (26.2)	14.33	0.75 (0.57, 1.00)	0.0479	
Latin America	70/ 602 (11.6)	5.88	87/ 579 (15.0)	7.68	0.78 (0.57, 1.07)	0.1264	
NYHA class at enrolment							0.9213
II	331/2314 (14.3)	6.71	411/2399 (17.1)	8.28	0.81 (0.70, 0.94)	0.0044	
III or IV	181/ 817 (22.2)	11.30	198/ 732 (27.0)	14.20	0.80 (0.65, 0.98)	0.0296	
LVEF at enrolment							0.7240
<= 49	207/1067 (19.4)	9.62	229/1049 (21.8)	11.05	0.87 (0.72, 1.04)	0.1329	
50-59	174/1133 (15.4)	7.20	211/1123 (18.8)	9.10	0.79 (0.65, 0.97)	0.0238	
>= 60	131/ 931 (14.1)	6.65	170/ 960 (17.7)	8.65	0.78 (0.62, 0.98)	0.0300	
NT-proBNP at enrolment							0.6623
<= median	173/1555 (11.1)	5.12	208/1578 (13.2)	6.12	0.84 (0.68, 1.02)	0.0806	
> median	339/1576 (21.5)	10.73	402/1553 (25.9)	13.60	0.79 (0.69, 0.92)	0.0017	
Type 2 Diabetes Medical History							0.8606
Yes	270/1401 (19.3)	9.34	317/1405 (22.6)	11.35	0.83 (0.70, 0.97)	0.0207	
No	242/1730 (14.0)	6.64	293/1727 (17.0)	8.22	0.81 (0.68, 0.96)	0.0145	
Atrial fibrillation or flutter at enrolment ECG							0.9168
Yes	227/1327 (17.1)	8.22	271/1317 (20.6)	10.18	0.81 (0.68, 0.97)	0.0205	
No	285/1803 (15.8)	7.56	339/1814 (18.7)	9.18	0.82 (0.70, 0.96)	0.0147	
BMI (kg/m2) at enrolment							0.1435
< 30	275/1734 (15.9)	7.64	302/1736 (17.4)	8.63	0.89 (0.75, 1.04)	0.1495	
>= 30	236/1395 (16.9)	8.04	308/1392 (22.1)	10.81	0.74 (0.63, 0.88)	0.0007	
Baseline eGFR (mL/min/1.73m^2)							0.7564
< 60	289/1516 (19.1)	9.49	355/1554 (22.8)	11.69	0.81 (0.69, 0.94)	0.0072	
>= 60	223/1615 (13.8)	6.39	255/1577 (16.2)	7.68	0.84 (0.70, 1.00)	0.0549	
SBP at randomisation							0.0278
<= median	280/1568 (17.9)	8.80	300/1590 (18.9)	9.43	0.93 (0.79, 1.10)	0.3956	
> median	232/1563 (14.8)	6.92	310/1542 (20.1)	9.76	0.71 (0.60, 0.85)	0.0001	

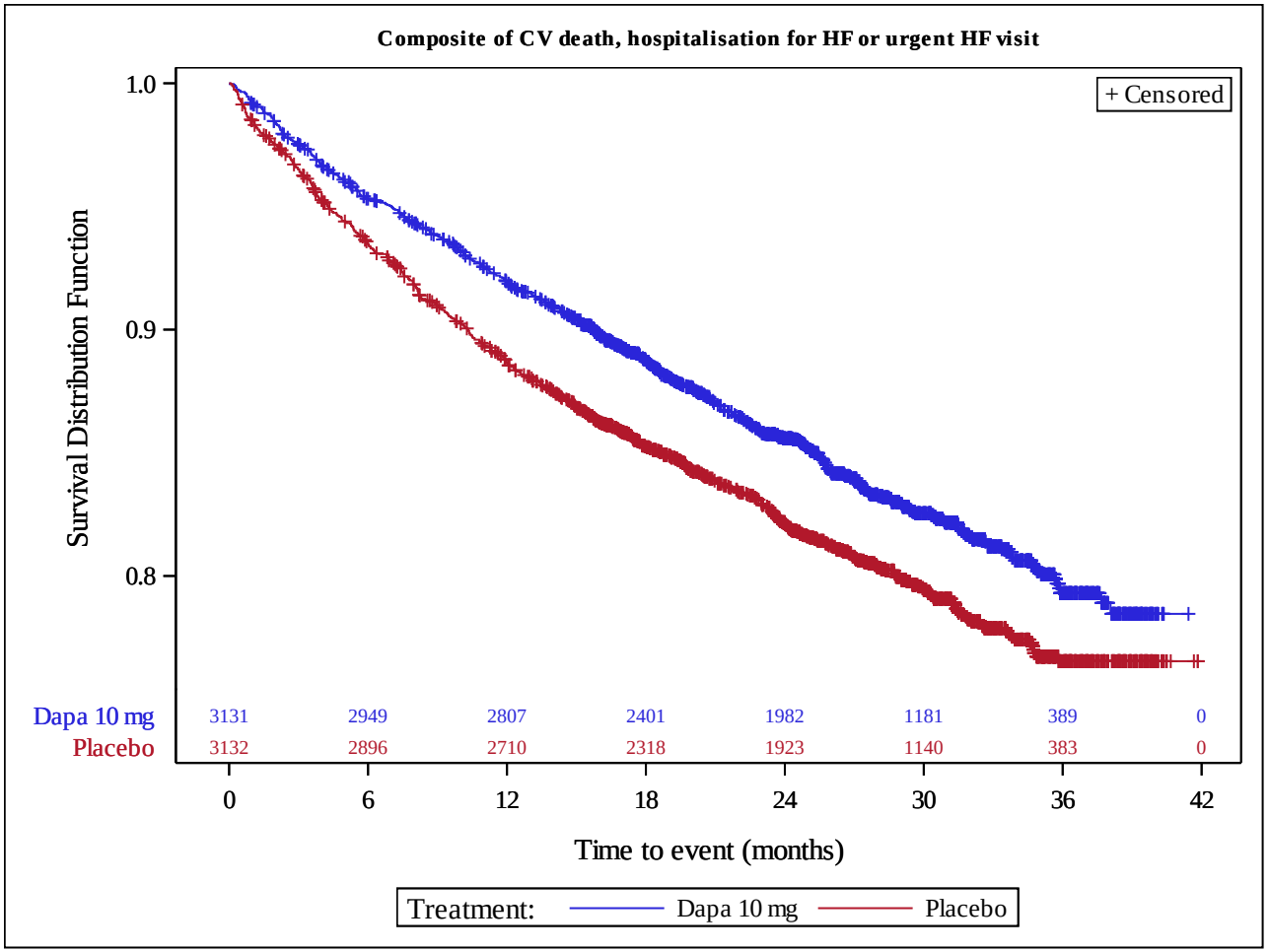
Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to composite of CV death, hospitalisation for HF or urgent HF visit
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.4313
<= 49	207/1067 (19.4)	9.62	229/1049 (21.8)	11.05	0.87 (0.72, 1.04)	0.1329	
>= 50	305/2064 (14.8)	6.96	381/2083 (18.3)	8.89	0.79 (0.68, 0.91)	0.0017	
Randomised during hospitalisation for HF or within 30 days of discharge							0.7091
Yes	93/ 328 (28.4)	15.38	113/ 326 (34.7)	19.75	0.78 (0.60, 1.03)	0.0824	
No	419/2803 (14.9)	7.06	497/2806 (17.7)	8.59	0.82 (0.72, 0.94)	0.0035	
MRAs at baseline							0.2962
Yes	213/1340 (15.9)	7.73	266/1327 (20.0)	10.10	0.76 (0.64, 0.91)	0.0033	
No	299/1791 (16.7)	7.91	344/1805 (19.1)	9.23	0.86 (0.74, 1.01)	0.0658	
ACEi+ARB at baseline							0.7979
Yes	363/2262 (16.0)	7.50	432/2281 (18.9)	9.10	0.83 (0.72, 0.95)	0.0070	
No	149/ 869 (17.1)	8.79	178/ 851 (20.9)	11.04	0.80 (0.64, 1.00)	0.0463	
ARNI at baseline							0.7547
Yes	31/ 165 (18.8)	10.50	31/ 136 (22.8)	13.52	0.74 (0.45, 1.22)	0.2341	
No	481/2966 (16.2)	7.71	579/2996 (19.3)	9.45	0.82 (0.73, 0.92)	0.0012	
Beta Blocker at baseline							0.8490
Yes	410/2592 (15.8)	7.53	485/2585 (18.8)	9.14	0.82 (0.72, 0.94)	0.0036	
No	102/ 539 (18.9)	9.37	125/ 547 (22.9)	11.86	0.79 (0.61, 1.03)	0.0833	
Diuretics at baseline							0.6052
Yes	474/2793 (17.0)	8.14	558/2787 (20.0)	9.89	0.82 (0.73, 0.93)	0.0020	
No	38/ 338 (11.2)	5.32	52/ 345 (15.1)	7.25	0.73 (0.48, 1.12)	0.1490	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to composite of CV death, hospitalisation for HF or urgent HF visit
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

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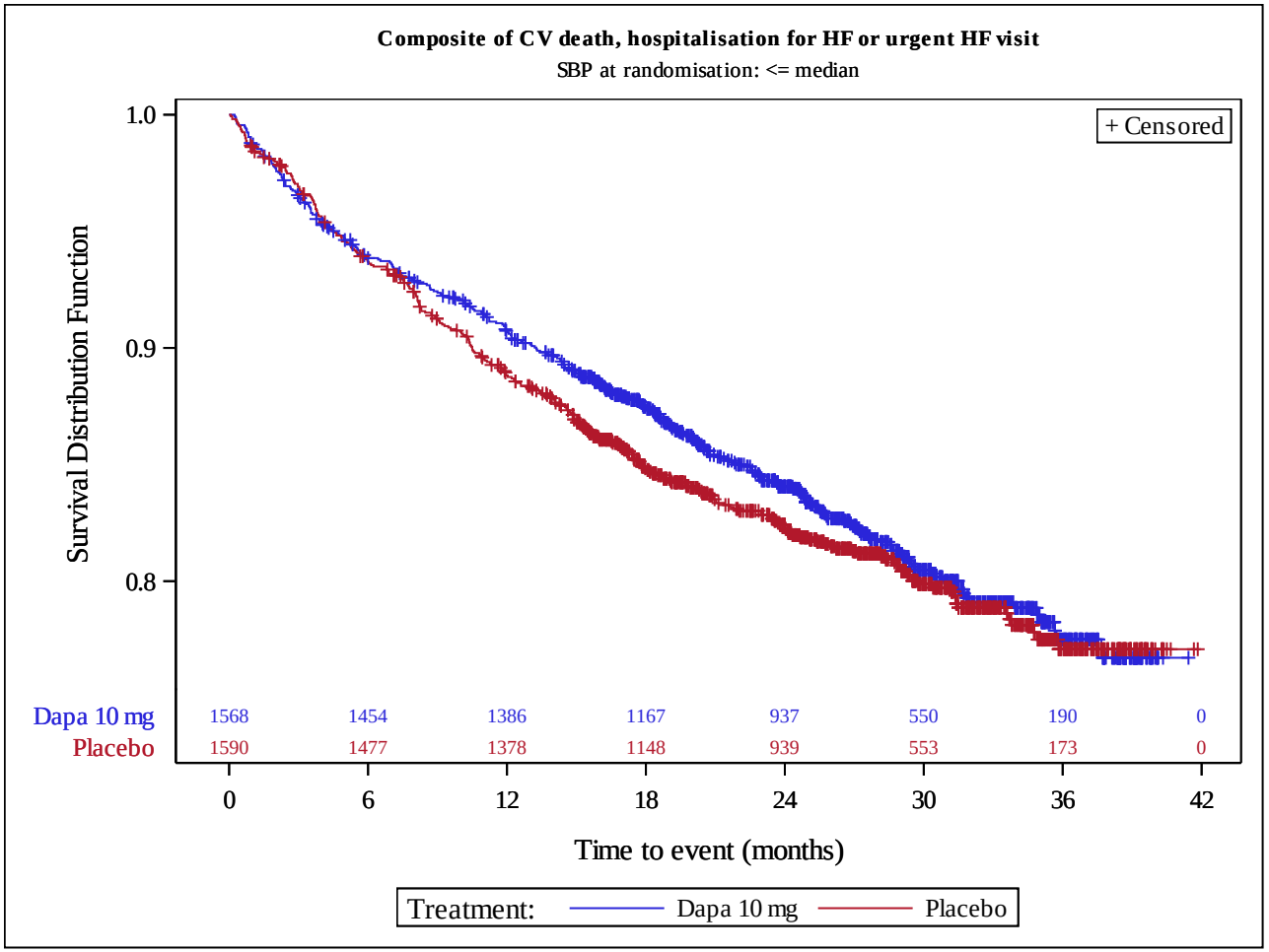

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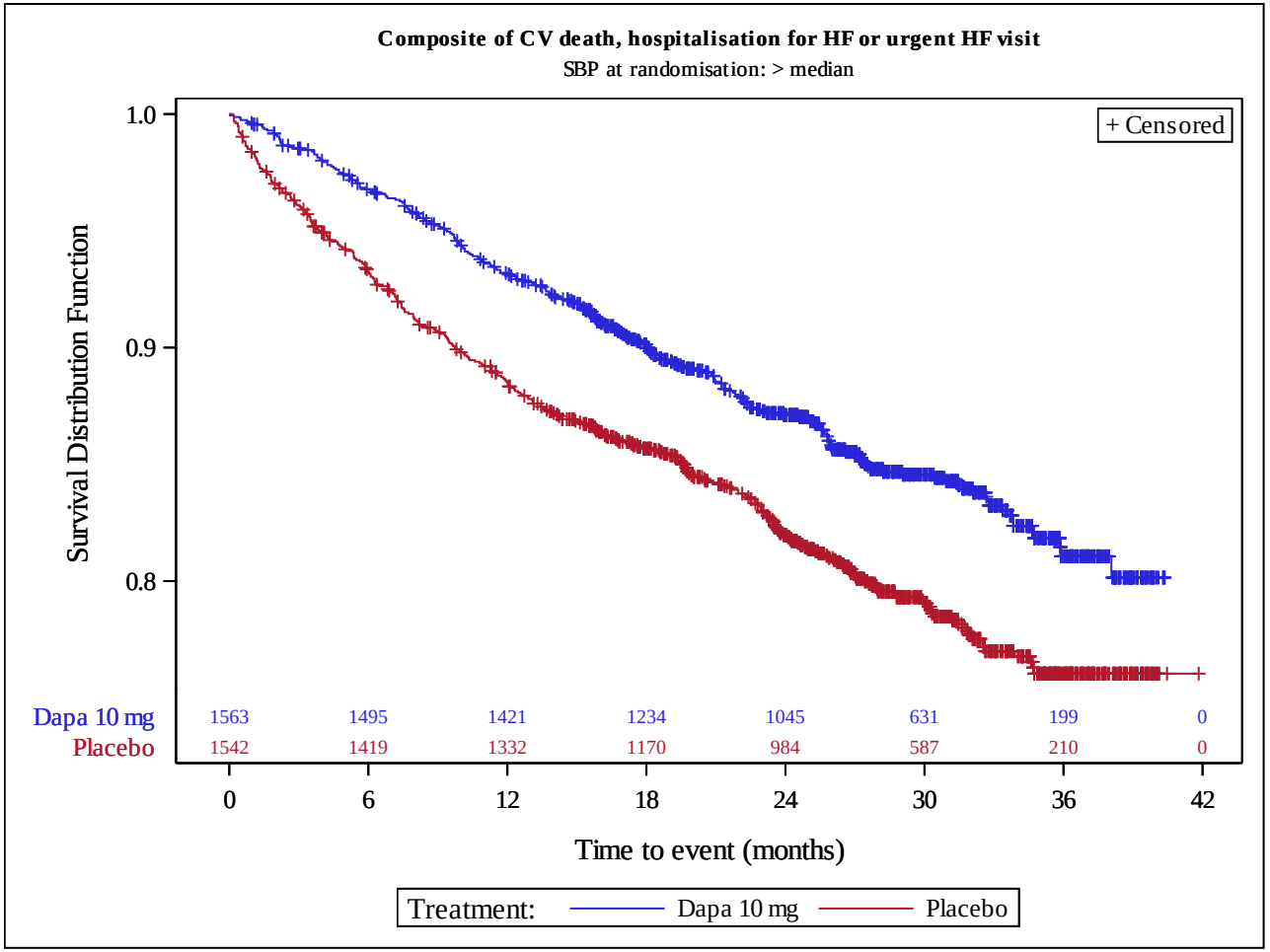

Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to composite of CV death or hospitalisation for HF
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	475/3131 (15.2)	7.21	577/3132 (18.4)	8.98	0.80 (0.71, 0.91)	0.0004	
Age							0.9119
<= median	228/1545 (14.8)	6.97	288/1604 (18.0)	8.63	0.81 (0.68, 0.96)	0.0159	
> median	247/1586 (15.6)	7.44	289/1528 (18.9)	9.35	0.80 (0.67, 0.94)	0.0089	
Gender							0.8332
Male	297/1767 (16.8)	8.05	350/1749 (20.0)	9.93	0.81 (0.69, 0.94)	0.0074	
Female	178/1364 (13.0)	6.14	227/1383 (16.4)	7.82	0.79 (0.65, 0.96)	0.0182	
Race							0.6233
White	343/2214 (15.5)	7.23	436/2225 (19.6)	9.39	0.77 (0.67, 0.89)	0.0003	
Black or African	18/ 81 (22.2)	11.25	17/ 78 (21.8)	10.88	1.05 (0.54, 2.04)	0.8855	
Asian	92/ 630 (14.6)	7.16	100/ 644 (15.5)	7.78	0.92 (0.69, 1.22)	0.5647	
Other	22/ 206 (10.7)	5.48	24/ 185 (13.0)	6.96	0.82 (0.46, 1.47)	0.5155	
Geographic region							0.7865
Asia	87/ 607 (14.3)	7.03	97/ 619 (15.7)	7.90	0.89 (0.67, 1.19)	0.4373	
Europe and Saudi Arabia	239/1494 (16.0)	7.20	289/1511 (19.1)	8.82	0.82 (0.69, 0.97)	0.0194	
North America	84/ 428 (19.6)	10.03	105/ 423 (24.8)	13.36	0.76 (0.57, 1.01)	0.0553	
Latin America	65/ 602 (10.8)	5.45	86/ 579 (14.9)	7.56	0.73 (0.53, 1.01)	0.0601	
NYHA class at enrolment							0.7190
II	301/2314 (13.0)	6.05	389/2399 (16.2)	7.77	0.78 (0.67, 0.91)	0.0012	
III or IV	174/ 817 (21.3)	10.75	187/ 732 (25.5)	13.21	0.82 (0.66, 1.00)	0.0541	
LVEF at enrolment							0.7902
<= 49	193/1067 (18.1)	8.91	220/1049 (21.0)	10.51	0.84 (0.69, 1.02)	0.0818	
50-59	161/1133 (14.2)	6.60	196/1123 (17.5)	8.35	0.79 (0.64, 0.98)	0.0283	
>= 60	121/ 931 (13.0)	6.10	161/ 960 (16.8)	8.10	0.76 (0.60, 0.96)	0.0227	
NT-proBNP at enrolment							0.4638
<= median	162/1555 (10.4)	4.78	194/1578 (12.3)	5.66	0.84 (0.68, 1.04)	0.1086	
> median	313/1576 (19.9)	9.78	383/1553 (24.7)	12.79	0.77 (0.66, 0.89)	0.0005	
Type 2 Diabetes Medical History							0.9015
Yes	248/1401 (17.7)	8.49	298/1405 (21.2)	10.51	0.81 (0.68, 0.96)	0.0138	
No	227/1730 (13.1)	6.19	279/1727 (16.2)	7.77	0.80 (0.67, 0.95)	0.0113	
Atrial fibrillation or flutter at enrolment ECG							0.9103
Yes	212/1327 (16.0)	7.61	258/1317 (19.6)	9.59	0.80 (0.66, 0.96)	0.0143	
No	263/1803 (14.6)	6.92	319/1814 (17.6)	8.54	0.81 (0.69, 0.95)	0.0106	
BMI (kg/m2) at enrolment							0.2793
< 30	256/1734 (14.8)	7.07	292/1736 (16.8)	8.29	0.85 (0.72, 1.01)	0.0650	
>= 30	218/1395 (15.6)	7.34	285/1392 (20.5)	9.84	0.75 (0.63, 0.89)	0.0012	
Baseline eGFR (mL/min/1.73m^2)							0.3748
< 60	266/1516 (17.5)	8.62	342/1554 (22.0)	11.17	0.77 (0.66, 0.90)	0.0013	
>= 60	209/1615 (12.9)	5.96	235/1577 (14.9)	6.99	0.86 (0.71, 1.04)	0.1104	
SBP at randomisation							0.0080
<= median	265/1568 (16.9)	8.25	281/1590 (17.7)	8.73	0.94 (0.80, 1.12)	0.5054	
> median	210/1563 (13.4)	6.21	296/1542 (19.2)	9.22	0.68 (0.57, 0.81)	<.0001	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
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Protocol: D169CC00001
Overall study population
Analysis of time to composite of CV death or hospitalisation for HF
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.5275
<= 49	193/1067 (18.1)	8.91	220/1049 (21.0)	10.51	0.84 (0.69, 1.02)	0.0818	
>= 50	282/2064 (13.7)	6.38	357/2083 (17.1)	8.24	0.78 (0.66, 0.91)	0.0015	
Randomised during hospitalisation for HF or within 30 days of discharge							0.7028
Yes	89/ 328 (27.1)	14.54	110/ 326 (33.7)	19.01	0.77 (0.58, 1.02)	0.0679	
No	386/2803 (13.8)	6.46	467/2806 (16.6)	7.99	0.81 (0.71, 0.93)	0.0022	
MRAs at baseline							0.2338
Yes	197/1340 (14.7)	7.09	254/1327 (19.1)	9.56	0.74 (0.62, 0.89)	0.0017	
No	278/1791 (15.5)	7.30	323/1805 (17.9)	8.57	0.86 (0.73, 1.01)	0.0616	
ACEi+ARB at baseline							0.9635
Yes	331/2262 (14.6)	6.78	405/2281 (17.8)	8.44	0.80 (0.70, 0.93)	0.0033	
No	144/ 869 (16.6)	8.43	172/ 851 (20.2)	10.56	0.80 (0.64, 1.00)	0.0506	
ARNI at baseline							0.9373
Yes	31/ 165 (18.8)	10.50	30/ 136 (22.1)	13.01	0.76 (0.46, 1.26)	0.2871	
No	444/2966 (15.0)	7.05	547/2996 (18.3)	8.83	0.80 (0.71, 0.91)	0.0005	
Beta Blocker at baseline							0.8402
Yes	377/2592 (14.5)	6.86	460/2585 (17.8)	8.58	0.80 (0.70, 0.92)	0.0012	
No	98/ 539 (18.2)	8.95	117/ 547 (21.4)	10.97	0.82 (0.62, 1.07)	0.1411	
Diuretics at baseline							0.6388
Yes	442/2793 (15.8)	7.53	531/2787 (19.1)	9.32	0.81 (0.71, 0.92)	0.0010	
No	33/ 338 (9.8)	4.56	46/ 345 (13.3)	6.32	0.72 (0.46, 1.13)	0.1527	

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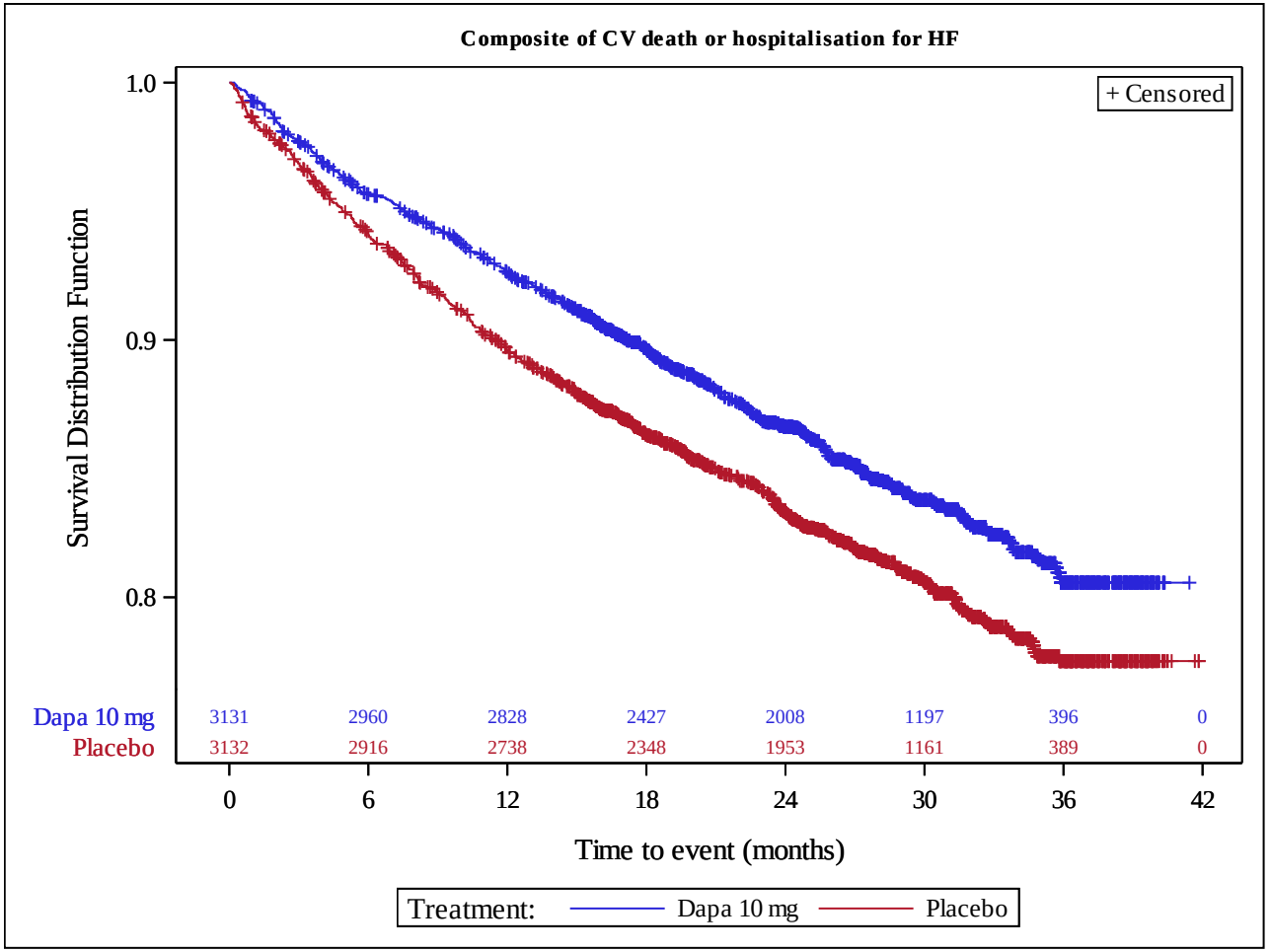
Overall study population
Kaplan Meier Plot of time to composite of CV death or hospitalisation for HF
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

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Kaplan Meier Plot of time to composite of CV death or hospitalisation for HF
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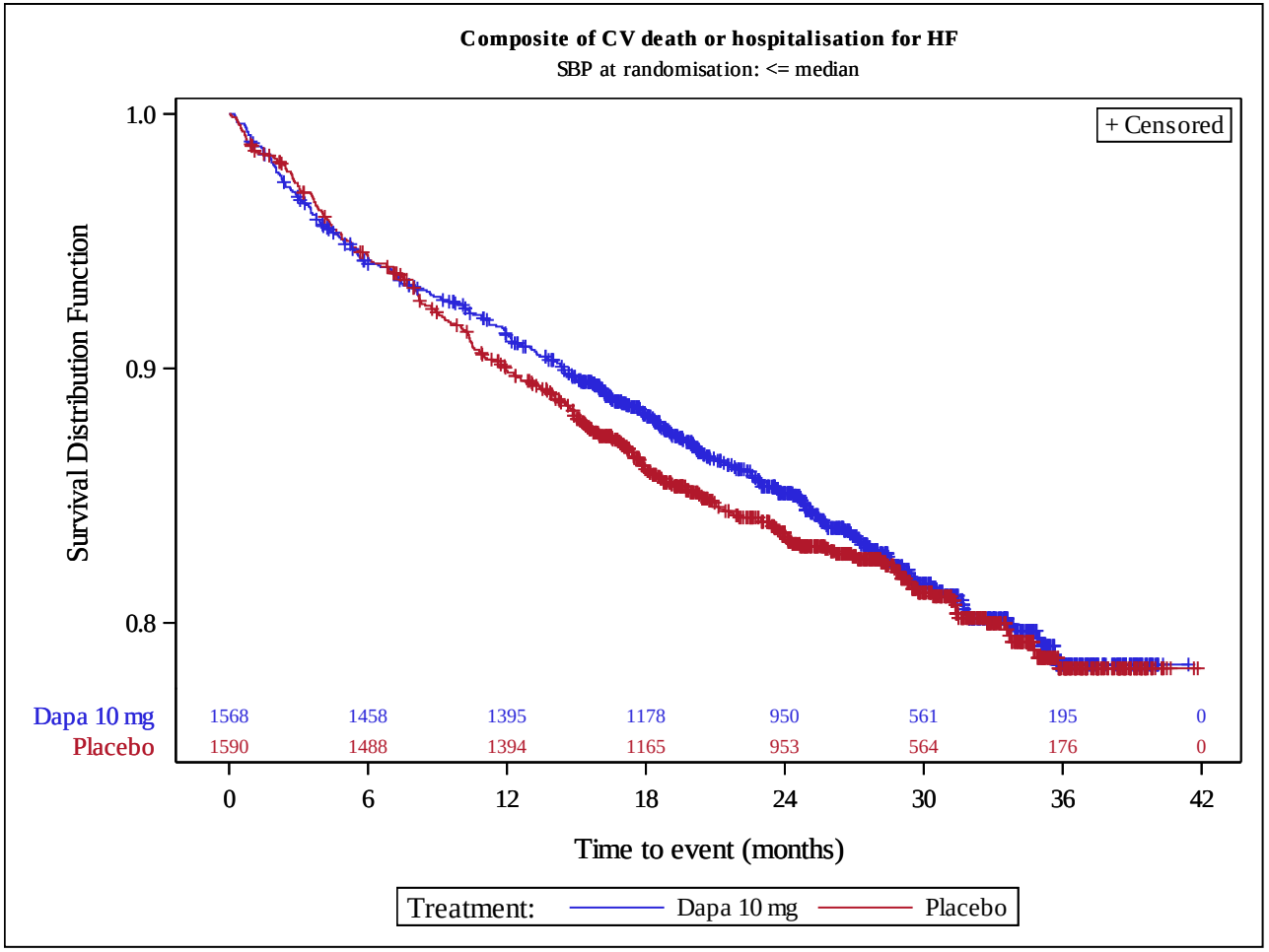

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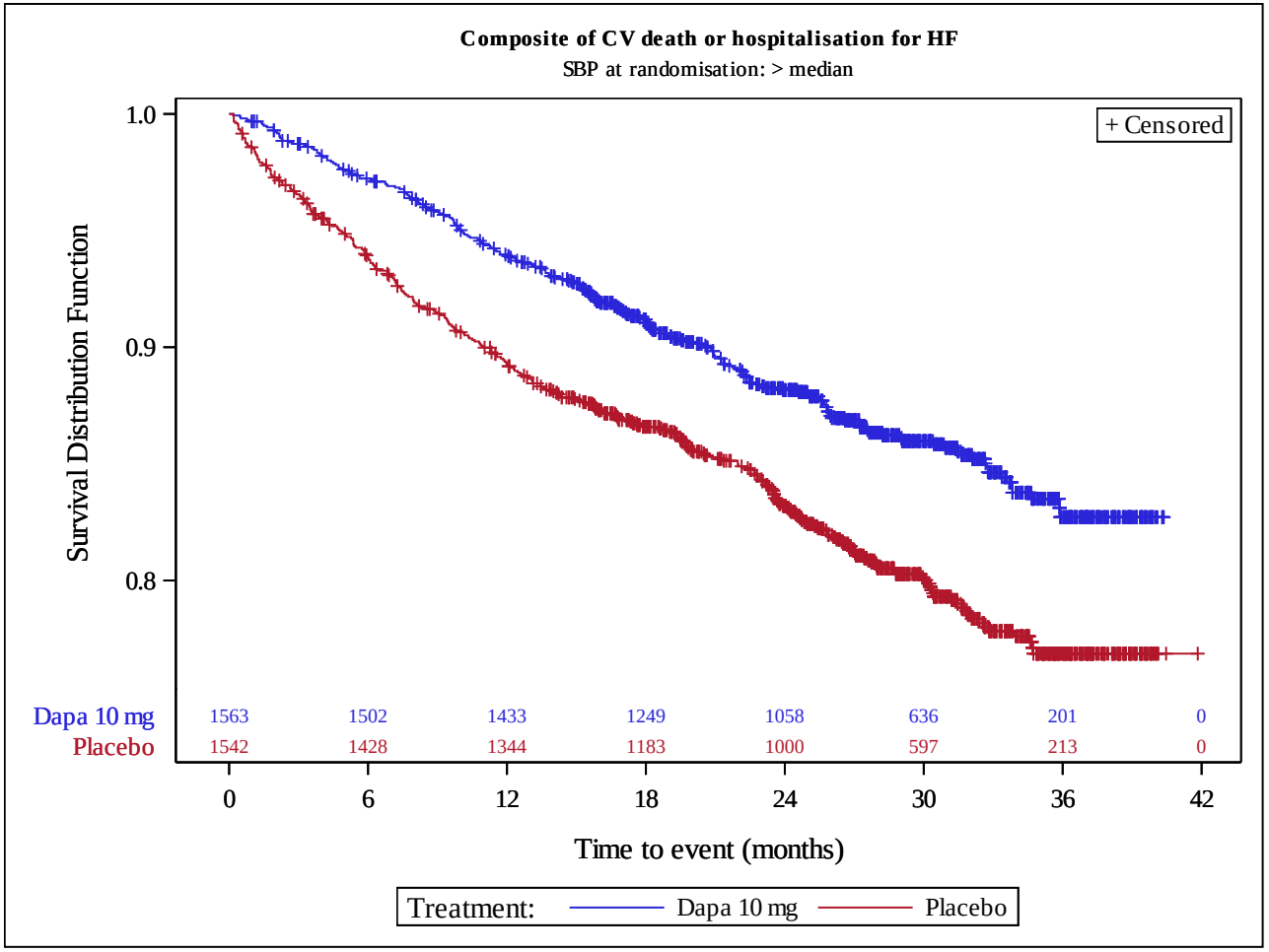
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to composite of CV death or hospitalisation for HF
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to cmposite of all-cause-mortality and hospitalization for HF
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	698/3131 (22.3)	10.59	791/3132 (25.3)	12.31	0.86 (0.78, 0.95)	0.0038	
Age							0.5311
<= median	301/1545 (19.5)	9.21	372/1604 (23.2)	11.15	0.82 (0.71, 0.96)	0.0128	
> median	397/1586 (25.0)	11.95	419/1528 (27.4)	13.56	0.88 (0.77, 1.01)	0.0699	
Gender							0.9976
Male	433/1767 (24.5)	11.74	481/1749 (27.5)	13.64	0.86 (0.75, 0.98)	0.0202	
Female	265/1364 (19.4)	9.13	310/1383 (22.4)	10.68	0.86 (0.73, 1.01)	0.0699	
Race							0.9835
White	516/2214 (23.3)	10.88	589/2225 (26.5)	12.69	0.86 (0.76, 0.96)	0.0102	
Black or African	20/ 81 (24.7)	12.50	25/ 78 (32.1)	16.00	0.78 (0.43, 1.41)	0.4097	
Asian	116/ 630 (18.4)	9.02	132/ 644 (20.5)	10.27	0.88 (0.68, 1.13)	0.3027	
Other	46/ 206 (22.3)	11.46	45/ 185 (24.3)	13.05	0.89 (0.59, 1.35)	0.5905	
Geographic region							0.8028
Asia	108/ 607 (17.8)	8.72	128/ 619 (20.7)	10.42	0.84 (0.65, 1.08)	0.1717	
Europe and Saudi Arabia	353/1494 (23.6)	10.63	395/1511 (26.1)	12.06	0.88 (0.76, 1.01)	0.0779	
North America	108/ 428 (25.2)	12.89	131/ 423 (31.0)	16.67	0.77 (0.60, 1.00)	0.0493	
Latin America	129/ 602 (21.4)	10.81	137/ 579 (23.7)	12.05	0.90 (0.71, 1.15)	0.4036	
NYHA class at enrolment							0.7484
II	453/2314 (19.6)	9.11	543/2399 (22.6)	10.84	0.84 (0.74, 0.95)	0.0058	
III or IV	245/ 817 (30.0)	15.13	247/ 732 (33.7)	17.45	0.87 (0.73, 1.04)	0.1189	
LVEF at enrolment							0.9061
<= 49	269/1067 (25.2)	12.41	293/1049 (27.9)	14.00	0.88 (0.75, 1.04)	0.1373	
50-59	238/1133 (21.0)	9.76	267/1123 (23.8)	11.38	0.86 (0.72, 1.02)	0.0853	
>= 60	191/ 931 (20.5)	9.63	231/ 960 (24.1)	11.63	0.83 (0.69, 1.01)	0.0635	
NT-proBNP at enrolment							0.8952
<= median	245/1555 (15.8)	7.23	289/1578 (18.3)	8.42	0.86 (0.72, 1.01)	0.0737	
> median	453/1576 (28.7)	14.16	502/1553 (32.3)	16.77	0.85 (0.75, 0.96)	0.0099	
Type 2 Diabetes Medical History							0.6645
Yes	352/1401 (25.1)	12.05	406/1405 (28.9)	14.32	0.84 (0.73, 0.97)	0.0172	
No	346/1730 (20.0)	9.43	385/1727 (22.3)	10.72	0.88 (0.76, 1.02)	0.0843	
Atrial fibrillation or flutter at enrolment ECG							0.6334
Yes	314/1327 (23.7)	11.26	344/1317 (26.1)	12.79	0.88 (0.76, 1.03)	0.1150	
No	384/1803 (21.3)	10.10	447/1814 (24.6)	11.97	0.84 (0.73, 0.96)	0.0130	
BMI (kg/m2) at enrolment							0.8036
< 30	377/1734 (21.7)	10.42	422/1736 (24.3)	11.98	0.87 (0.75, 1.00)	0.0448	
>= 30	320/1395 (22.9)	10.78	369/1392 (26.5)	12.74	0.85 (0.73, 0.98)	0.0287	
Baseline eGFR (mL/min/1.73m^2)							0.5598
< 60	396/1516 (26.1)	12.84	465/1554 (29.9)	15.18	0.84 (0.73, 0.96)	0.0110	
>= 60	302/1615 (18.7)	8.61	326/1577 (20.7)	9.70	0.89 (0.76, 1.04)	0.1545	
SBP at randomisation							0.0431
<= median	371/1568 (23.7)	11.55	388/1590 (24.4)	12.06	0.96 (0.83, 1.10)	0.5289	
> median	327/1563 (20.9)	9.67	403/1542 (26.1)	12.56	0.77 (0.67, 0.90)	0.0006	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to cmposite of all-cause-mortality and hospitalization for HF
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.6973
<= 49	269/1067 (25.2)	12.41	293/1049 (27.9)	14.00	0.88 (0.75, 1.04)	0.1373	
>= 50	429/2064 (20.8)	9.70	498/2083 (23.9)	11.49	0.85 (0.74, 0.96)	0.0108	
Randomised during hospitalisation for HF or within 30 days of discharge							0.6671
Yes	113/ 328 (34.5)	18.46	130/ 326 (39.9)	22.46	0.83 (0.64, 1.06)	0.1376	
No	585/2803 (20.9)	9.78	661/2806 (23.6)	11.30	0.87 (0.78, 0.97)	0.0115	
MRAs at baseline							0.5914
Yes	298/1340 (22.2)	10.72	340/1327 (25.6)	12.79	0.83 (0.71, 0.98)	0.0229	
No	400/1791 (22.3)	10.50	451/1805 (25.0)	11.96	0.88 (0.77, 1.01)	0.0680	
ACEi+ARB at baseline							0.5408
Yes	483/2262 (21.4)	9.89	564/2281 (24.7)	11.75	0.84 (0.75, 0.95)	0.0055	
No	215/ 869 (24.7)	12.58	227/ 851 (26.7)	13.94	0.91 (0.75, 1.09)	0.2958	
ARNI at baseline							0.5692
Yes	42/ 165 (25.5)	14.22	42/ 136 (30.9)	18.21	0.74 (0.48, 1.14)	0.1716	
No	656/2966 (22.1)	10.42	749/2996 (25.0)	12.09	0.86 (0.78, 0.96)	0.0058	
Beta Blocker at baseline							0.4807
Yes	570/2592 (22.0)	10.37	634/2585 (24.5)	11.83	0.88 (0.78, 0.98)	0.0216	
No	128/ 539 (23.7)	11.68	157/ 547 (28.7)	14.73	0.79 (0.63, 1.00)	0.0525	
Diuretics at baseline							0.8610
Yes	646/2793 (23.1)	11.01	728/2787 (26.1)	12.77	0.86 (0.77, 0.96)	0.0059	
No	52/ 338 (15.4)	7.19	63/ 345 (18.3)	8.65	0.83 (0.57, 1.20)	0.3176	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
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p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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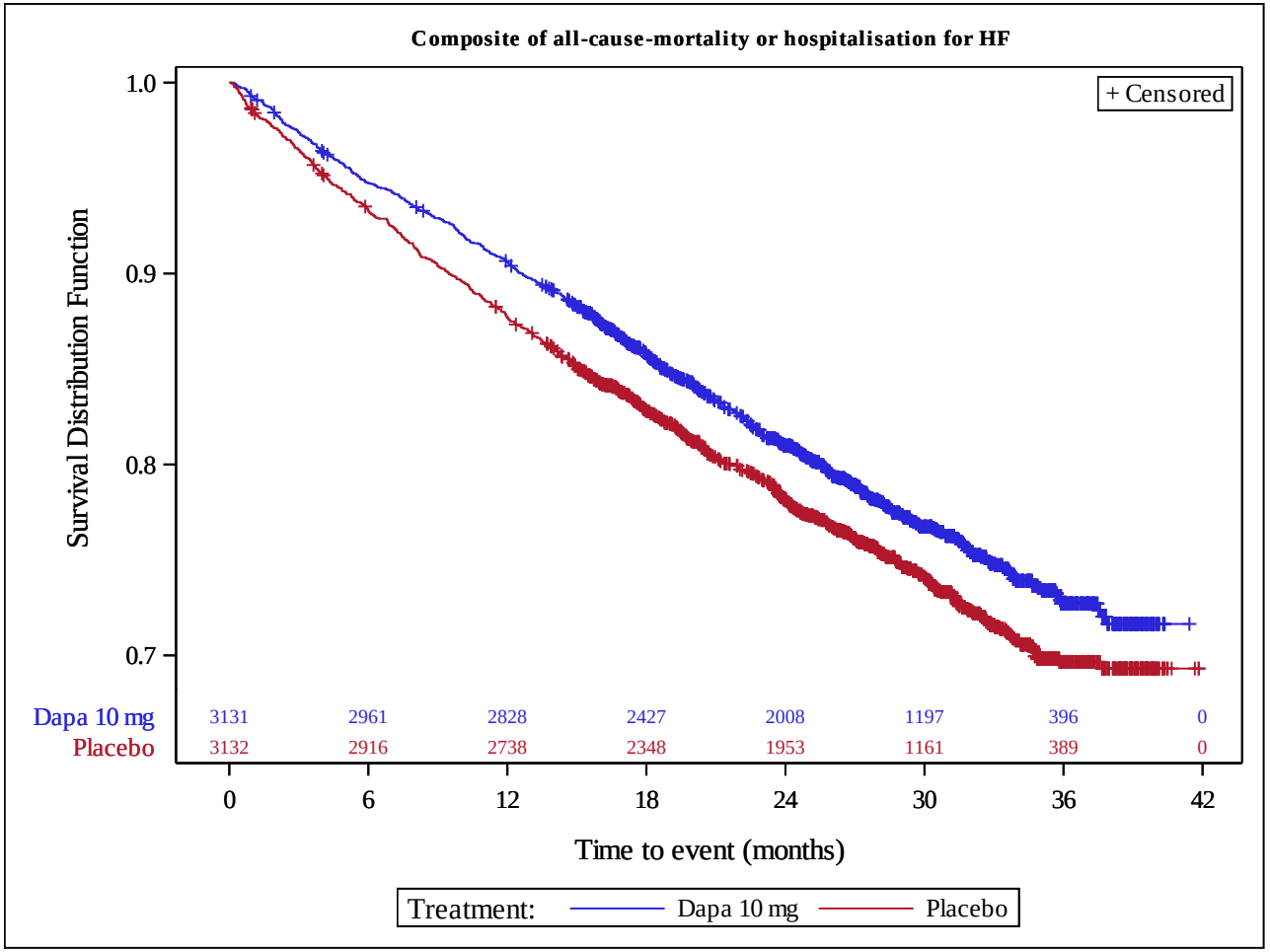
AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to cmposite of all-cause-mortality and hospitalization for HF
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

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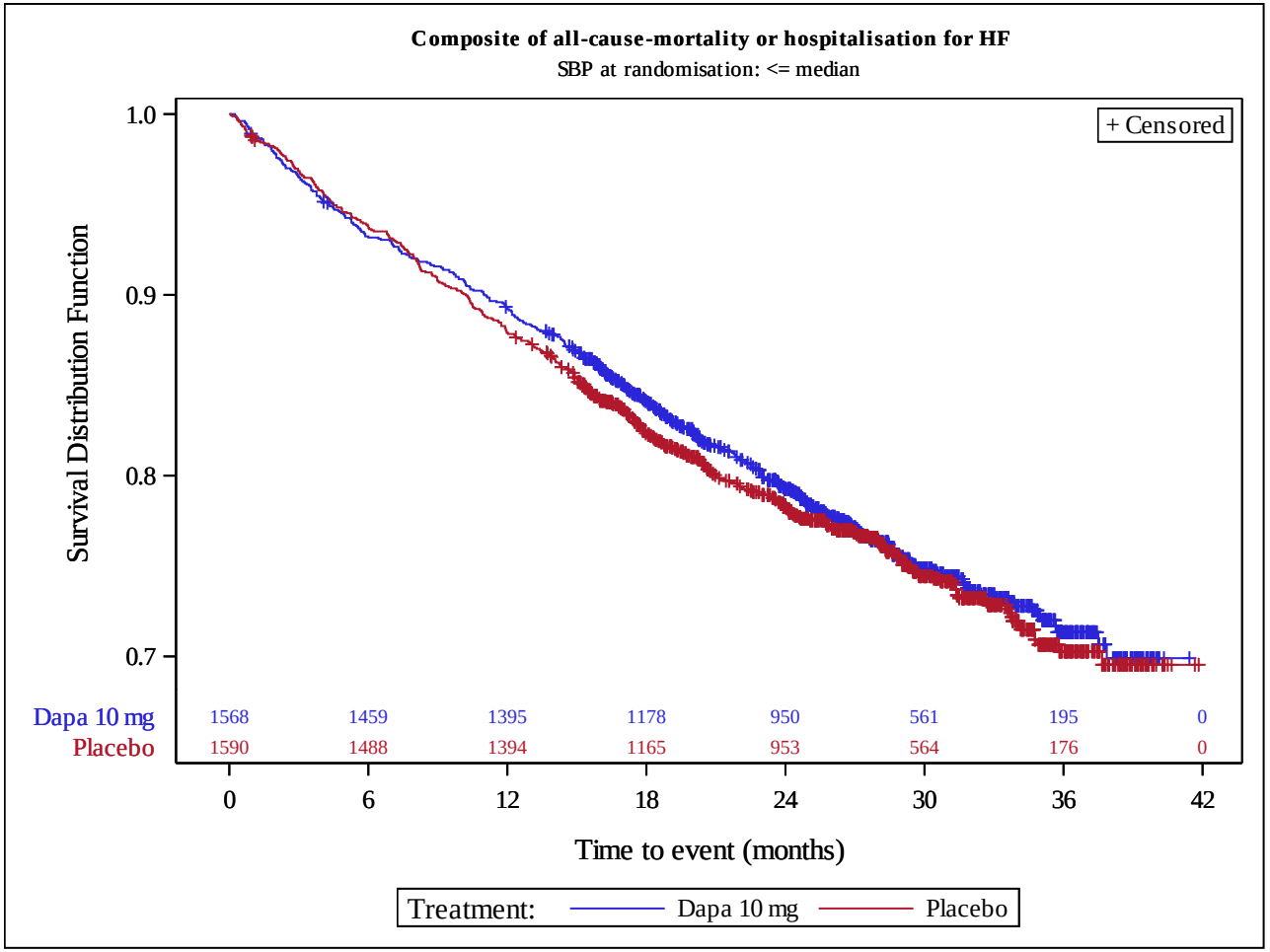

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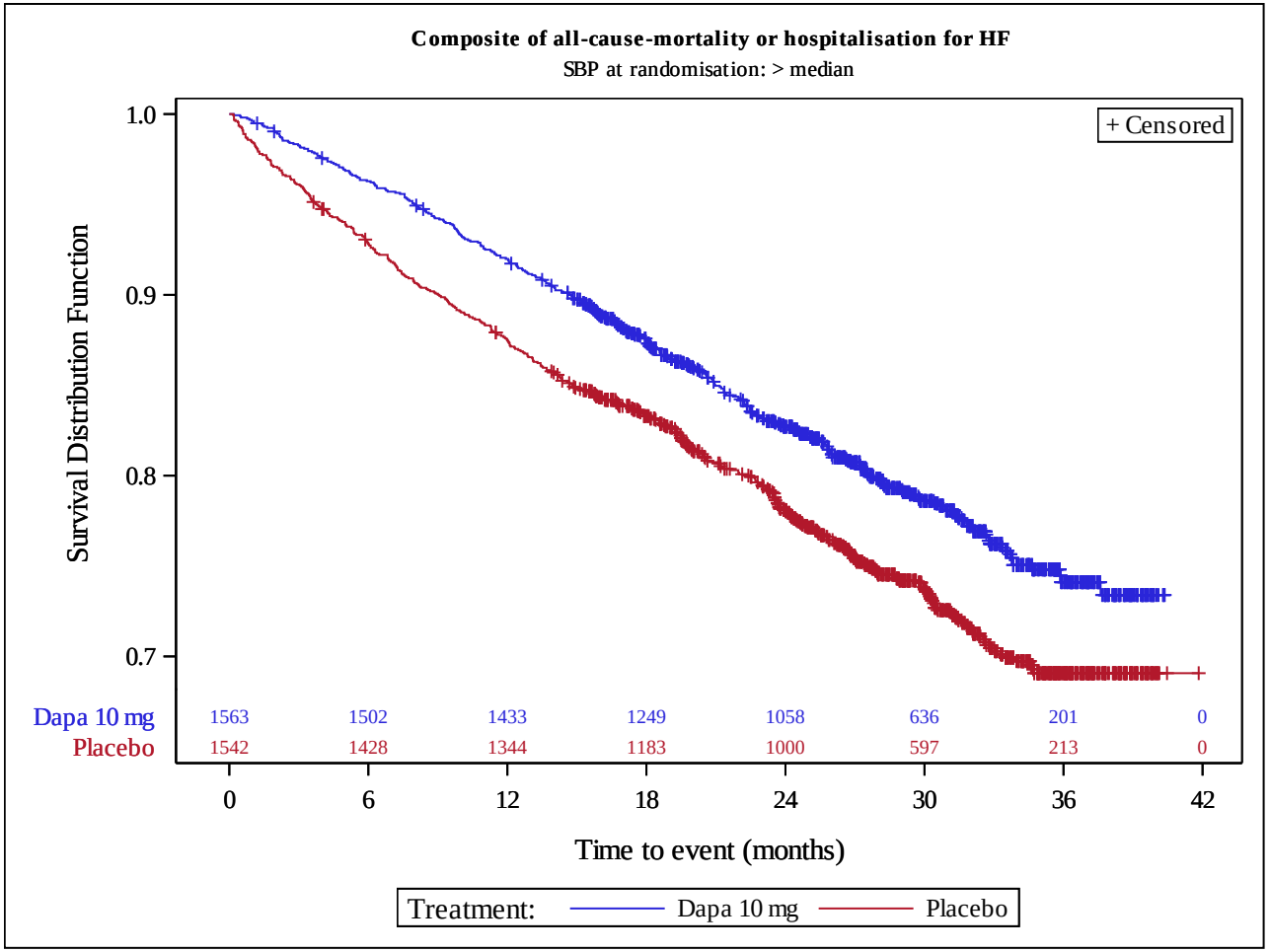
Kaplan Meier Plot of time to cmposite of all-cause-mortality and hospitalization for HF
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to composite of all-cause-mortality, hospitalization for HF or urgent HF visit
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	735/3131 (23.5)	11.25	819/3132 (26.1)	12.88	0.87 (0.79, 0.96)	0.0076	
Age							0.5576
<= median	320/1545 (20.7)	9.88	387/1604 (24.1)	11.74	0.84 (0.72, 0.97)	0.0209	
> median	415/1586 (26.2)	12.59	432/1528 (28.3)	14.10	0.89 (0.78, 1.02)	0.0962	
Gender							0.9614
Male	453/1767 (25.6)	12.40	496/1749 (28.4)	14.22	0.87 (0.76, 0.99)	0.0304	
Female	282/1364 (20.7)	9.79	323/1383 (23.4)	11.25	0.87 (0.75, 1.03)	0.0999	
Race							0.9996
White	545/2214 (24.6)	11.60	610/2225 (27.4)	13.31	0.87 (0.78, 0.98)	0.0192	
Black or African	23/ 81 (28.4)	14.76	26/ 78 (33.3)	17.01	0.86 (0.49, 1.51)	0.5981	
Asian	121/ 630 (19.2)	9.46	138/ 644 (21.4)	10.80	0.87 (0.69, 1.12)	0.2817	
Other	46/ 206 (22.3)	11.46	45/ 185 (24.3)	13.06	0.89 (0.59, 1.35)	0.5913	
Geographic region							0.7048
Asia	113/ 607 (18.6)	9.17	134/ 619 (21.6)	10.98	0.84 (0.65, 1.07)	0.1588	
Europe and Saudi Arabia	375/1494 (25.1)	11.41	411/1511 (27.2)	12.72	0.89 (0.78, 1.03)	0.1193	
North America	113/ 428 (26.4)	13.63	136/ 423 (32.2)	17.56	0.78 (0.61, 1.00)	0.0485	
Latin America	134/ 602 (22.3)	11.26	138/ 579 (23.8)	12.18	0.93 (0.73, 1.18)	0.5562	
NYHA class at enrolment							0.9271
II	483/2314 (20.9)	9.79	561/2399 (23.4)	11.31	0.86 (0.77, 0.98)	0.0190	
III or IV	252/ 817 (30.8)	15.73	257/ 732 (35.1)	18.43	0.86 (0.72, 1.02)	0.0791	
LVEF at enrolment							0.8418
<= 49	283/1067 (26.5)	13.16	300/1049 (28.6)	14.47	0.90 (0.77, 1.06)	0.2246	
50-59	251/1133 (22.2)	10.39	279/1123 (24.8)	12.03	0.86 (0.73, 1.02)	0.0928	
>= 60	201/ 931 (21.6)	10.21	240/ 960 (25.0)	12.21	0.84 (0.70, 1.02)	0.0719	
NT-proBNP at enrolment							0.9469
<= median	256/1555 (16.5)	7.58	300/1578 (19.0)	8.82	0.86 (0.73, 1.01)	0.0705	
> median	479/1576 (30.4)	15.16	519/1553 (33.4)	17.56	0.87 (0.76, 0.98)	0.0227	
Type 2 Diabetes Medical History							0.7854
Yes	374/1401 (26.7)	12.94	420/1405 (29.9)	15.03	0.86 (0.75, 0.99)	0.0347	
No	361/1730 (20.9)	9.90	399/1727 (23.1)	11.19	0.89 (0.77, 1.02)	0.0928	
Atrial fibrillation or flutter at enrolment ECG							0.6700
Yes	329/1327 (24.8)	11.91	356/1317 (27.0)	13.37	0.89 (0.77, 1.04)	0.1452	
No	406/1803 (22.5)	10.77	463/1814 (25.5)	12.54	0.86 (0.75, 0.98)	0.0224	
BMI (kg/m2) at enrolment							0.5915
< 30	396/1734 (22.8)	11.00	431/1736 (24.8)	12.32	0.89 (0.78, 1.02)	0.1012	
>= 30	338/1395 (24.2)	11.52	388/1392 (27.9)	13.61	0.85 (0.73, 0.98)	0.0247	
Baseline eGFR (mL/min/1.73m^2)							0.9218
< 60	419/1516 (27.6)	13.76	476/1554 (30.6)	15.67	0.87 (0.77, 0.99)	0.0417	
>= 60	316/1615 (19.6)	9.05	343/1577 (21.8)	10.33	0.88 (0.76, 1.03)	0.1027	
SBP at randomisation							0.0906
<= median	386/1568 (24.6)	12.13	404/1590 (25.4)	12.69	0.95 (0.83, 1.09)	0.4857	
> median	349/1563 (22.3)	10.41	415/1542 (26.9)	13.06	0.80 (0.69, 0.92)	0.0022	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
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p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to composite of all-cause-mortality, hospitalization for HF or urgent HF visit
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.5804
<= 49	283/1067 (26.5)	13.16	300/1049 (28.6)	14.47	0.90 (0.77, 1.06)	0.2246	
>= 50	452/2064 (21.9)	10.31	519/2083 (24.9)	12.11	0.85 (0.75, 0.97)	0.0135	
Randomised during hospitalisation for HF or within 30 days of discharge							0.6599
Yes	117/ 328 (35.7)	19.35	133/ 326 (40.8)	23.24	0.84 (0.65, 1.07)	0.1576	
No	618/2803 (22.0)	10.42	686/2806 (24.4)	11.85	0.88 (0.79, 0.98)	0.0204	
MRAs at baseline							0.6695
Yes	314/1340 (23.4)	11.39	350/1327 (26.4)	13.29	0.85 (0.73, 0.99)	0.0401	
No	421/1791 (23.5)	11.14	469/1805 (26.0)	12.59	0.89 (0.78, 1.02)	0.0839	
ACEi+ARB at baseline							0.6733
Yes	515/2262 (22.8)	10.64	587/2281 (25.7)	12.37	0.86 (0.76, 0.97)	0.0129	
No	220/ 869 (25.3)	12.98	232/ 851 (27.3)	14.39	0.91 (0.75, 1.09)	0.2937	
ARNI at baseline							0.4331
Yes	42/ 165 (25.5)	14.23	43/ 136 (31.6)	18.75	0.72 (0.47, 1.11)	0.1389	
No	693/2966 (23.4)	11.10	776/2996 (25.9)	12.66	0.88 (0.79, 0.97)	0.0129	
Beta Blocker at baseline							0.2784
Yes	603/2592 (23.3)	11.07	654/2585 (25.3)	12.33	0.90 (0.80, 1.00)	0.0534	
No	132/ 539 (24.5)	12.12	165/ 547 (30.2)	15.65	0.78 (0.62, 0.98)	0.0296	
Diuretics at baseline							0.8411
Yes	678/2793 (24.3)	11.65	751/2787 (26.9)	13.31	0.87 (0.79, 0.97)	0.0116	
No	57/ 338 (16.9)	7.98	68/ 345 (19.7)	9.47	0.84 (0.59, 1.20)	0.3415	

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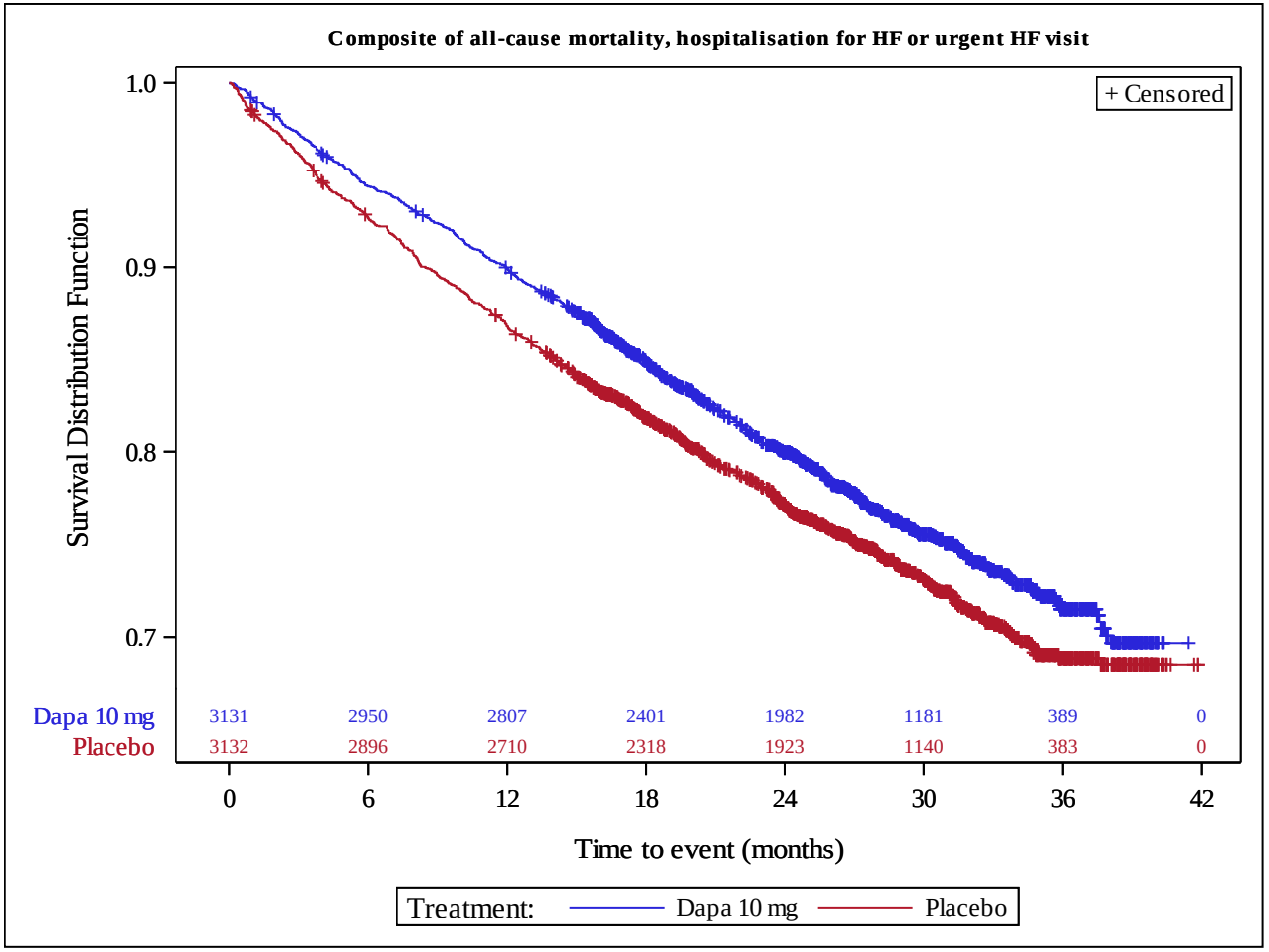


Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to hospitalisation for HF
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	329/3131 (10.5)	4.99	418/3132 (13.3)	6.50	0.77 (0.67, 0.89)	0.0004	
Age							0.7007
<= median	161/1545 (10.4)	4.92	208/1604 (13.0)	6.23	0.79 (0.64, 0.97)	0.0252	
> median	168/1586 (10.6)	5.06	210/1528 (13.7)	6.80	0.75 (0.61, 0.91)	0.0048	
Gender							0.8852
Male	201/1767 (11.4)	5.45	248/1749 (14.2)	7.03	0.77 (0.64, 0.93)	0.0071	
Female	128/1364 (9.4)	4.41	170/1383 (12.3)	5.86	0.76 (0.60, 0.95)	0.0185	
Race							0.5365
White	237/2214 (10.7)	5.00	319/2225 (14.3)	6.87	0.73 (0.62, 0.86)	0.0002	
Black or African	12/ 81 (14.8)	7.50	11/ 78 (14.1)	7.04	1.12 (0.49, 2.54)	0.7916	
Asian	74/ 630 (11.7)	5.76	81/ 644 (12.6)	6.30	0.91 (0.67, 1.25)	0.5723	
Other	6/ 206 (2.9)	1.49	7/ 185 (3.8)	2.03	0.79 (0.27, 2.37)	0.6799	
Geographic region							0.7462
Asia	70/ 607 (11.5)	5.65	78/ 619 (12.6)	6.35	0.89 (0.65, 1.23)	0.4884	
Europe and Saudi Arabia	160/1494 (10.7)	4.82	208/1511 (13.8)	6.35	0.76 (0.62, 0.93)	0.0086	
North America	68/ 428 (15.9)	8.12	88/ 423 (20.8)	11.20	0.73 (0.53, 1.00)	0.0519	
Latin America	31/ 602 (5.1)	2.60	44/ 579 (7.6)	3.87	0.68 (0.43, 1.09)	0.1071	
NYHA class at enrolment							0.2461
II	202/2314 (8.7)	4.06	286/2399 (11.9)	5.71	0.71 (0.60, 0.85)	0.0002	
III or IV	127/ 817 (15.5)	7.85	131/ 732 (17.9)	9.25	0.85 (0.67, 1.09)	0.2012	
LVEF at enrolment							0.6297
<= 49	123/1067 (11.5)	5.68	147/1049 (14.0)	7.02	0.80 (0.63, 1.02)	0.0748	
50-59	110/1133 (9.7)	4.51	152/1123 (13.5)	6.48	0.70 (0.55, 0.89)	0.0040	
>= 60	96/ 931 (10.3)	4.84	119/ 960 (12.4)	5.99	0.82 (0.62, 1.07)	0.1391	
NT-proBNP at enrolment							0.6651
<= median	106/1555 (6.8)	3.13	135/1578 (8.6)	3.94	0.79 (0.61, 1.02)	0.0718	
> median	223/1576 (14.1)	6.97	283/1553 (18.2)	9.45	0.74 (0.62, 0.88)	0.0009	
Type 2 Diabetes Medical History							0.5470
Yes	177/1401 (12.6)	6.06	215/1405 (15.3)	7.59	0.80 (0.66, 0.98)	0.0293	
No	152/1730 (8.8)	4.14	203/1727 (11.8)	5.65	0.73 (0.59, 0.91)	0.0039	
Atrial fibrillation or flutter at enrolment ECG							0.7874
Yes	151/1327 (11.4)	5.42	195/1317 (14.8)	7.25	0.75 (0.61, 0.93)	0.0085	
No	178/1803 (9.9)	4.68	223/1814 (12.3)	5.97	0.78 (0.64, 0.95)	0.0149	
BMI (kg/m2) at enrolment							0.4929
< 30	165/1734 (9.5)	4.56	199/1736 (11.5)	5.65	0.81 (0.66, 0.99)	0.0439	
>= 30	164/1395 (11.8)	5.52	219/1392 (15.7)	7.56	0.73 (0.60, 0.90)	0.0024	
Baseline eGFR (mL/min/1.73m^2)							0.5375
< 60	190/1516 (12.5)	6.16	253/1554 (16.3)	8.26	0.74 (0.62, 0.90)	0.0020	
>= 60	139/1615 (8.6)	3.97	165/1577 (10.5)	4.91	0.81 (0.65, 1.02)	0.0745	
SBP at randomisation							0.0046
<= median	185/1568 (11.8)	5.76	196/1590 (12.3)	6.09	0.95 (0.77, 1.16)	0.5946	
> median	144/1563 (9.2)	4.26	222/1542 (14.4)	6.92	0.62 (0.50, 0.77)	<.0001	

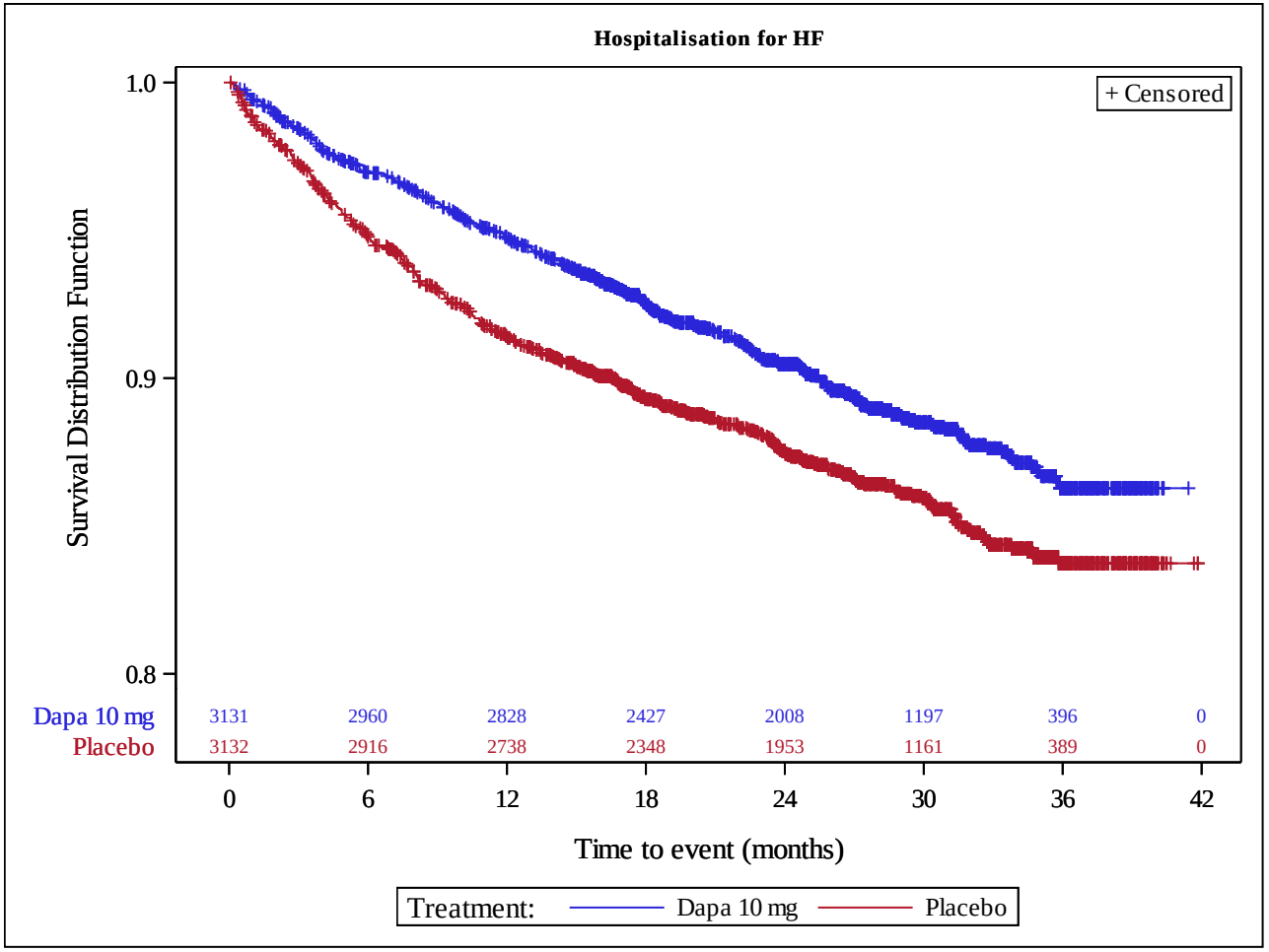
Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to hospitalisation for HF
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.6430
<= 49	123/1067 (11.5)	5.68	147/1049 (14.0)	7.02	0.80 (0.63, 1.02)	0.0748	
>= 50	206/2064 (10.0)	4.66	271/2083 (13.0)	6.25	0.75 (0.62, 0.90)	0.0017	
Randomised during hospitalisation for HF or within 30 days of discharge							0.8991
Yes	66/ 328 (20.1)	10.78	83/ 326 (25.5)	14.34	0.76 (0.55, 1.04)	0.0893	
No	263/2803 (9.4)	4.40	335/2806 (11.9)	5.73	0.77 (0.66, 0.90)	0.0015	
MRAs at baseline							0.2830
Yes	134/1340 (10.0)	4.82	182/1327 (13.7)	6.85	0.71 (0.56, 0.88)	0.0022	
No	195/1791 (10.9)	5.12	236/1805 (13.1)	6.26	0.82 (0.68, 1.00)	0.0466	
ACEi+ARB at baseline							0.7812
Yes	219/2262 (9.7)	4.49	285/2281 (12.5)	5.94	0.76 (0.63, 0.90)	0.0019	
No	110/ 869 (12.7)	6.44	133/ 851 (15.6)	8.17	0.79 (0.61, 1.02)	0.0693	
ARNI at baseline							0.7759
Yes	26/ 165 (15.8)	8.80	24/ 136 (17.6)	10.41	0.79 (0.45, 1.39)	0.4188	
No	303/2966 (10.2)	4.81	394/2996 (13.2)	6.36	0.76 (0.65, 0.88)	0.0003	
Beta Blocker at baseline							0.9305
Yes	262/2592 (10.1)	4.77	331/2585 (12.8)	6.17	0.77 (0.66, 0.91)	0.0018	
No	67/ 539 (12.4)	6.12	87/ 547 (15.9)	8.16	0.75 (0.55, 1.04)	0.0811	
Diuretics at baseline							0.5654
Yes	311/2793 (11.1)	5.30	390/2787 (14.0)	6.84	0.78 (0.67, 0.90)	0.0009	
No	18/ 338 (5.3)	2.49	28/ 345 (8.1)	3.84	0.65 (0.36, 1.18)	0.1557	

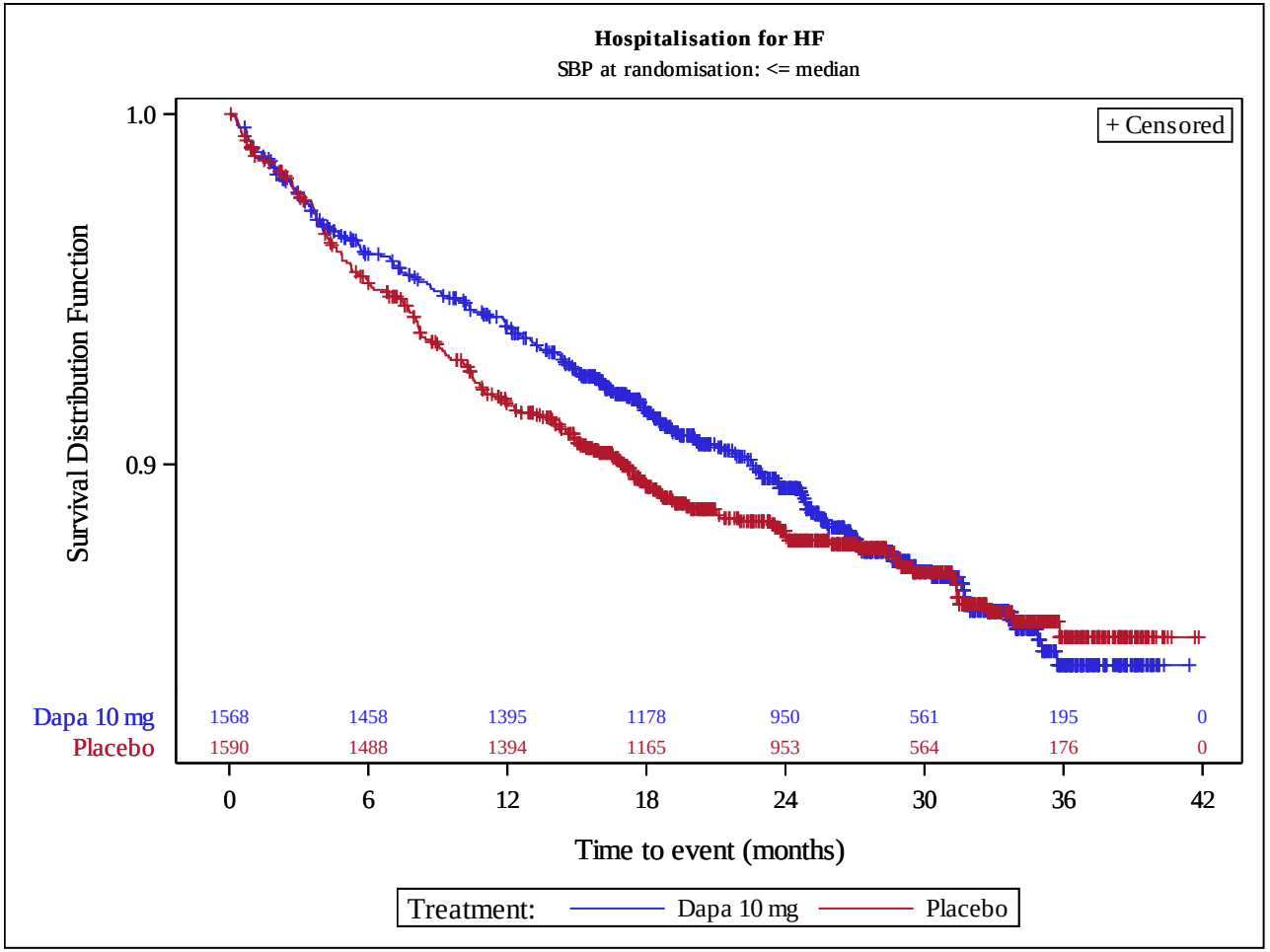
Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to hospitalisation for HF
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to hospitalisation for HF
Full Analysis Set



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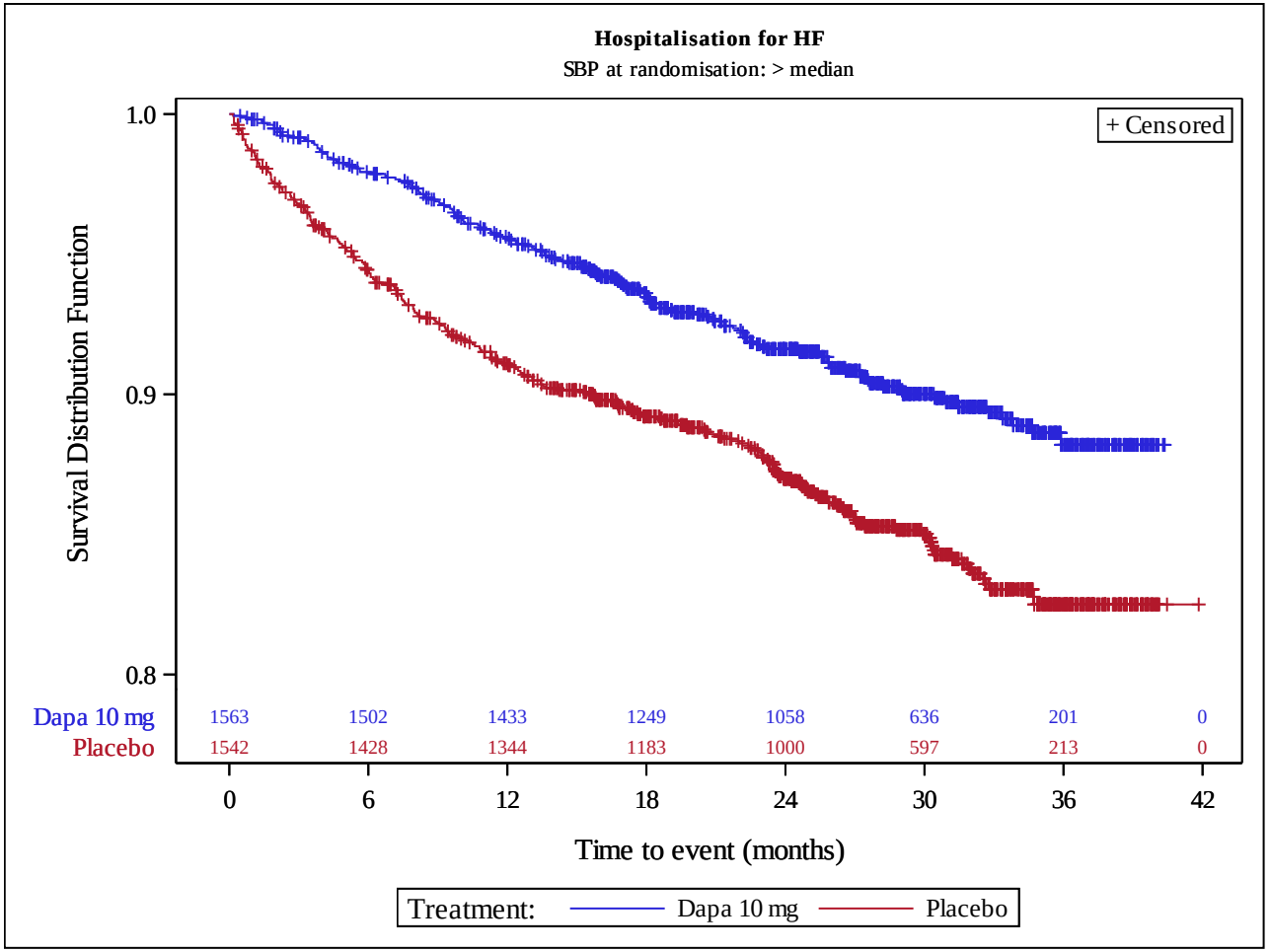
AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to hospitalisation for HF
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to Hospitalisation from any cause
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	1210/3131 (38.6)	21.71	1251/3132 (39.9)	23.22	0.94 (0.86, 1.01)	0.1014	
Age							0.9374
<= median	573/1545 (37.1)	20.64	618/1604 (38.5)	22.00	0.94 (0.84, 1.05)	0.2579	
> median	637/1586 (40.2)	22.77	633/1528 (41.4)	24.54	0.93 (0.83, 1.04)	0.1986	
Gender							0.9734
Male	701/1767 (39.7)	22.69	713/1749 (40.8)	24.31	0.93 (0.84, 1.04)	0.2021	
Female	509/1364 (37.3)	20.49	538/1383 (38.9)	21.91	0.94 (0.83, 1.06)	0.2872	
Race							0.4569
White	873/2214 (39.4)	21.65	896/2225 (40.3)	22.83	0.95 (0.86, 1.04)	0.2518	
Black or African	36/ 81 (44.4)	27.44	35/ 78 (44.9)	28.25	0.99 (0.62, 1.58)	0.9600	
Asian	253/ 630 (40.2)	24.23	284/ 644 (44.1)	28.20	0.86 (0.73, 1.02)	0.0835	
Other	48/ 206 (23.3)	13.16	36/ 185 (19.5)	10.82	1.24 (0.80, 1.92)	0.3283	
Geographic region							0.7503
Asia	243/ 607 (40.0)	24.12	272/ 619 (43.9)	28.20	0.86 (0.72, 1.02)	0.0839	
Europe and Saudi Arabia	580/1494 (38.8)	20.47	597/1511 (39.5)	21.43	0.95 (0.85, 1.07)	0.3847	
North America	215/ 428 (50.2)	33.15	210/ 423 (49.6)	34.02	0.97 (0.80, 1.17)	0.7536	
Latin America	172/ 602 (28.6)	15.87	172/ 579 (29.7)	16.85	0.95 (0.77, 1.17)	0.6349	
NYHA class at enrolment							0.7589
II	872/2314 (37.7)	20.69	929/2399 (38.7)	22.04	0.94 (0.85, 1.03)	0.1724	
III or IV	338/ 817 (41.4)	24.87	321/ 732 (43.9)	27.43	0.92 (0.79, 1.07)	0.2548	
LVEF at enrolment							0.6568
<= 49	415/1067 (38.9)	22.50	413/1049 (39.4)	23.21	0.97 (0.84, 1.11)	0.6267	
50-59	442/1133 (39.0)	21.64	448/1123 (39.9)	22.74	0.95 (0.83, 1.09)	0.4634	
>= 60	353/ 931 (37.9)	20.93	390/ 960 (40.6)	23.79	0.89 (0.77, 1.02)	0.0974	
NT-proBNP at enrolment							0.7578
<= median	539/1555 (34.7)	18.73	572/1578 (36.2)	19.85	0.94 (0.84, 1.06)	0.3317	
> median	671/1576 (42.6)	24.90	679/1553 (43.7)	27.12	0.92 (0.83, 1.03)	0.1358	
Type 2 Diabetes Medical History							0.2464
Yes	594/1401 (42.4)	24.37	635/1405 (45.2)	27.45	0.89 (0.80, 1.00)	0.0460	
No	616/1730 (35.6)	19.65	616/1727 (35.7)	20.03	0.98 (0.88, 1.10)	0.7260	
Atrial fibrillation or flutter at enrolment ECG							0.5645
Yes	531/1327 (40.0)	22.53	532/1317 (40.4)	23.47	0.96 (0.85, 1.08)	0.5162	
No	678/1803 (37.6)	21.09	719/1814 (39.6)	23.06	0.92 (0.83, 1.02)	0.1049	
BMI (kg/m2) at enrolment							0.7170
< 30	643/1734 (37.1)	20.99	674/1736 (38.8)	22.82	0.92 (0.83, 1.03)	0.1392	
>= 30	566/1395 (40.6)	22.58	576/1392 (41.4)	23.75	0.95 (0.85, 1.07)	0.3921	
Baseline eGFR (mL/min/1.73m^2)							0.6989
< 60	650/1516 (42.9)	25.50	694/1554 (44.7)	27.51	0.93 (0.83, 1.03)	0.1585	
>= 60	560/1615 (34.7)	18.52	557/1577 (35.3)	19.45	0.95 (0.85, 1.07)	0.4276	
SBP at randomisation							0.0099
<= median	626/1568 (39.9)	23.07	600/1590 (37.7)	22.09	1.04 (0.93, 1.16)	0.4820	
> median	584/1563 (37.4)	20.42	651/1542 (42.2)	24.37	0.84 (0.75, 0.94)	0.0028	

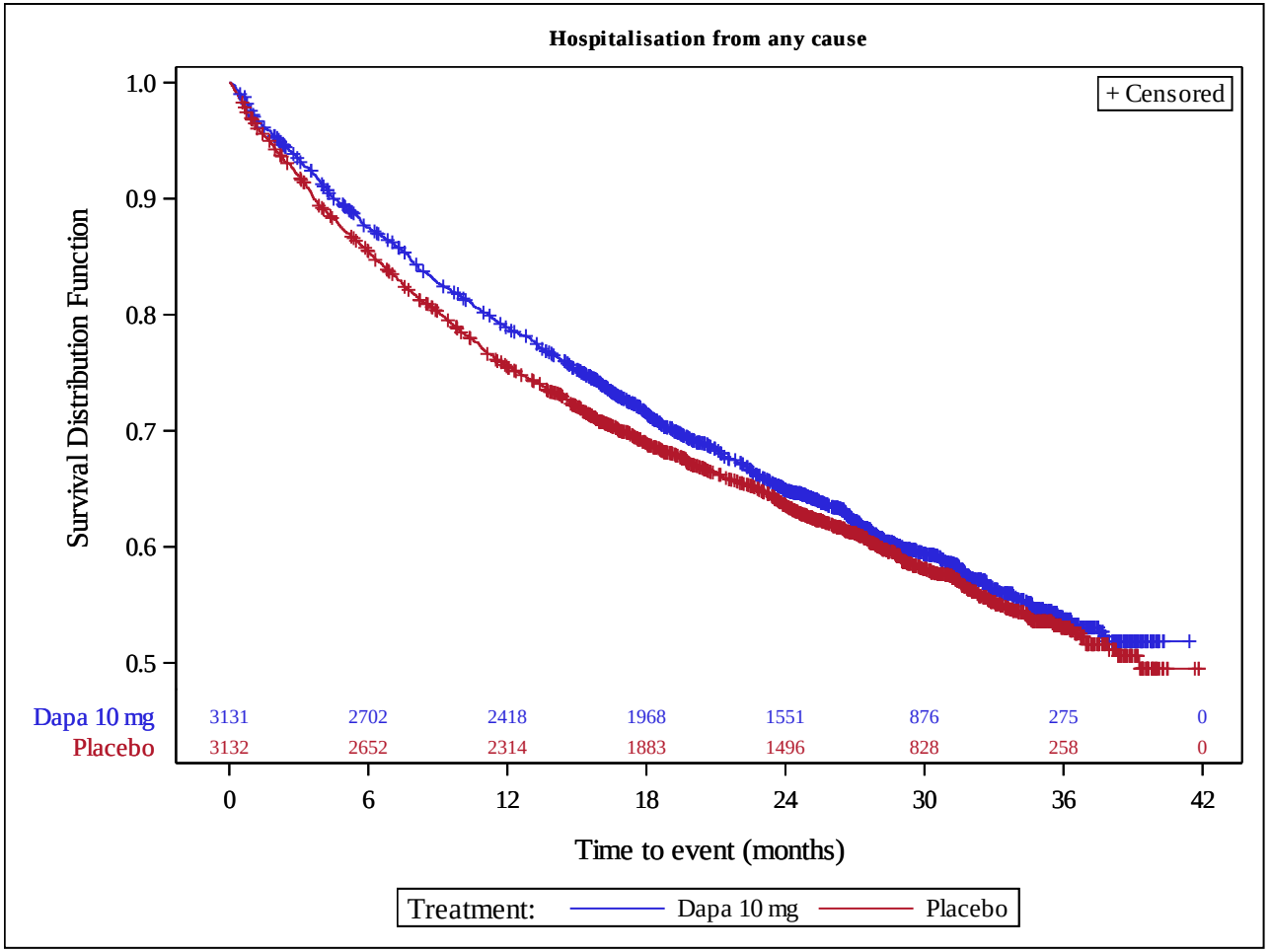
Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to Hospitalisation from any cause
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.5842
<= 49	415/1067 (38.9)	22.50	413/1049 (39.4)	23.21	0.97 (0.84, 1.11)	0.6267	
>= 50	795/2064 (38.5)	21.32	838/2083 (40.2)	23.22	0.92 (0.84, 1.02)	0.0991	
Randomised during hospitalisation for HF or within 30 days of discharge							0.0936
Yes	146/ 328 (44.5)	27.97	169/ 326 (51.8)	36.01	0.79 (0.63, 0.99)	0.0381	
No	1064/2803 (38.0)	21.06	1082/2806 (38.6)	22.00	0.96 (0.88, 1.04)	0.3185	
MRAs at baseline							0.9820
Yes	497/1340 (37.1)	20.97	505/1327 (38.1)	22.18	0.94 (0.83, 1.06)	0.3288	
No	713/1791 (39.8)	22.26	746/1805 (41.3)	23.98	0.94 (0.85, 1.04)	0.2136	
ACEi+ARB at baseline							0.7332
Yes	851/2262 (37.6)	20.49	892/2281 (39.1)	22.13	0.93 (0.84, 1.02)	0.1162	
No	359/ 869 (41.3)	25.27	359/ 851 (42.2)	26.44	0.96 (0.83, 1.11)	0.5716	
ARNI at baseline							0.7943
Yes	64/ 165 (38.8)	25.06	50/ 136 (36.8)	25.02	0.92 (0.63, 1.34)	0.6588	
No	1146/2966 (38.6)	21.55	1201/2996 (40.1)	23.15	0.93 (0.86, 1.01)	0.0930	
Beta Blocker at baseline							0.3555
Yes	995/2592 (38.4)	21.29	1011/2585 (39.1)	22.33	0.95 (0.87, 1.04)	0.2692	
No	215/ 539 (39.9)	23.90	240/ 547 (43.9)	27.88	0.86 (0.72, 1.04)	0.1126	
Diuretics at baseline							0.4158
Yes	1104/2793 (39.5)	22.27	1130/2787 (40.5)	23.57	0.95 (0.87, 1.03)	0.1880	
No	106/ 338 (31.4)	17.20	121/ 345 (35.1)	20.39	0.85 (0.66, 1.11)	0.2361	

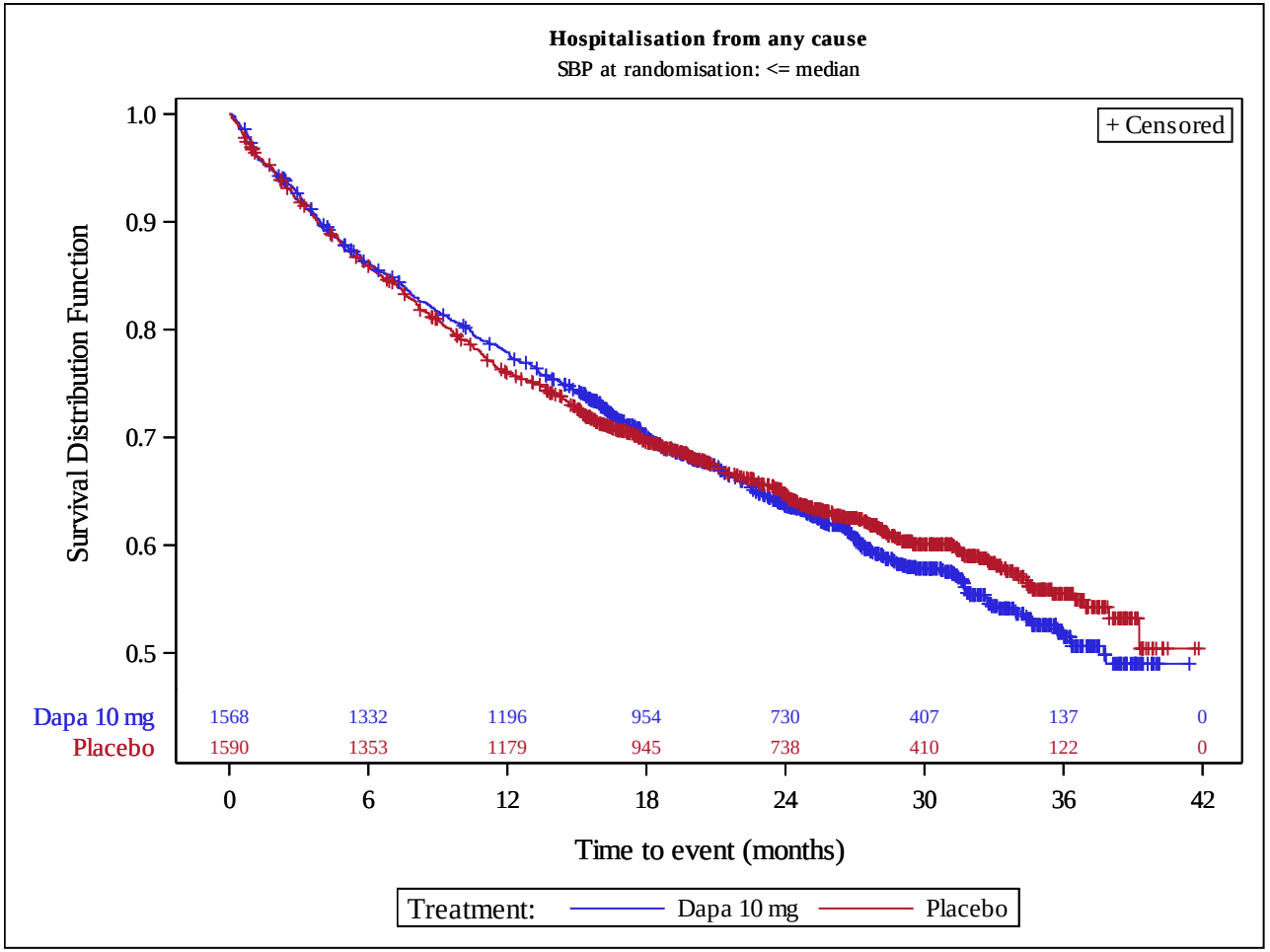
Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to Hospitalisation from any cause
Full Analysis Set



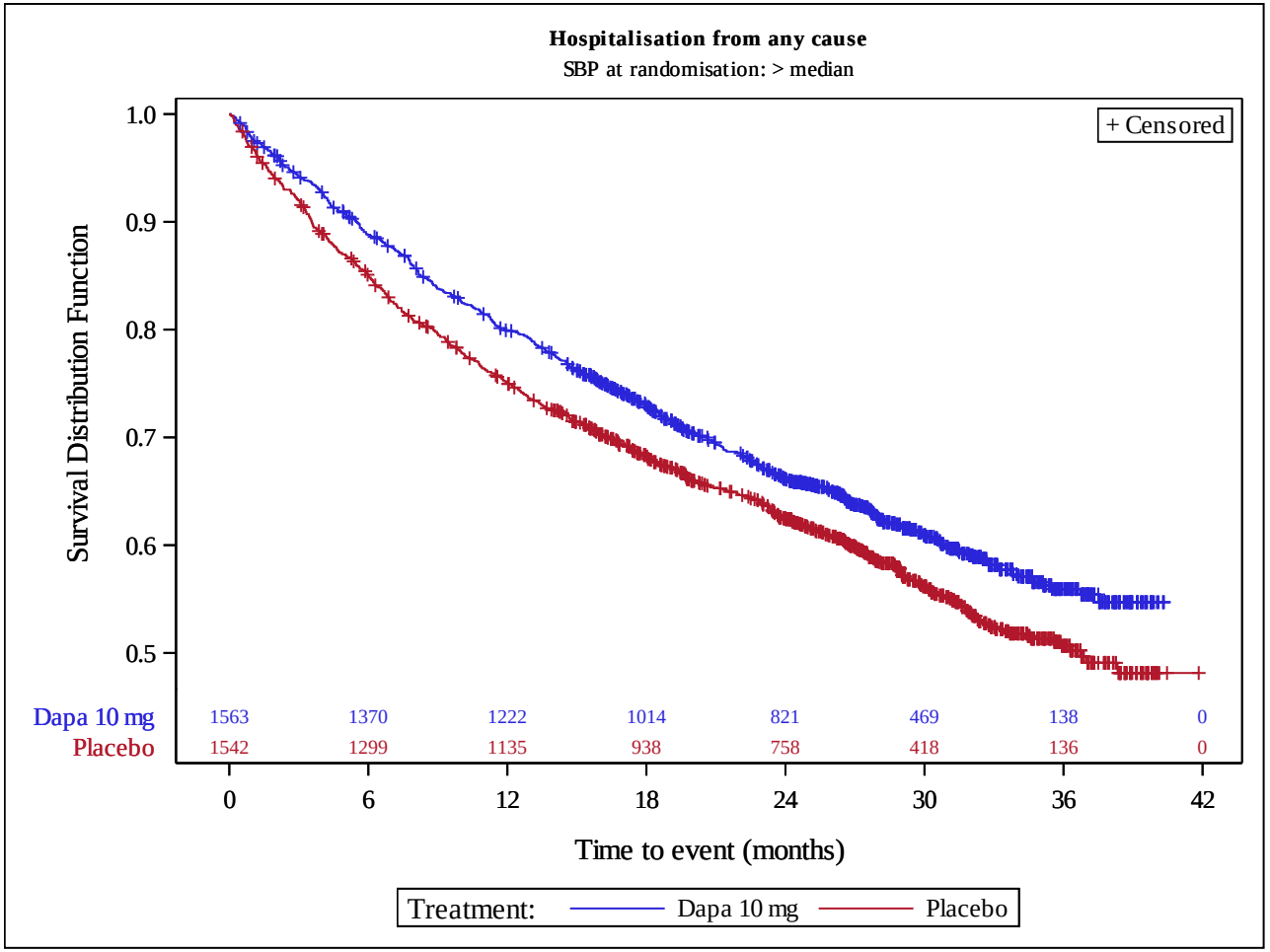
Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to Hospitalisation from any cause
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to Hospitalisation from any cause
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to urgent HF visit
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	60/3131 (1.9)	0.88	78/3132 (2.5)	1.15	0.76 (0.55, 1.07)	0.1159	
Age							0.9216
<= median	29/1545 (1.9)	0.85	40/1604 (2.5)	1.14	0.75 (0.46, 1.21)	0.2337	
> median	31/1586 (2.0)	0.90	38/1528 (2.5)	1.16	0.77 (0.48, 1.24)	0.2874	
Gender							0.8579
Male	37/1767 (2.1)	0.96	46/1749 (2.6)	1.23	0.78 (0.51, 1.20)	0.2621	
Female	23/1364 (1.7)	0.77	32/1383 (2.3)	1.05	0.73 (0.43, 1.25)	0.2548	
Race							0.8855
White	42/2214 (1.9)	0.85	56/2225 (2.5)	1.14	0.75 (0.50, 1.12)	0.1565	
Black or African	6/ 81 (7.4)	3.68	5/ 78 (6.4)	3.08	1.15 (0.35, 3.76)	0.8229	
Asian	11/ 630 (1.7)	0.82	16/ 644 (2.5)	1.18	0.70 (0.32, 1.50)	0.3564	
Other	1/ 206 (0.5)	0.24	1/ 185 (0.5)	0.29	0.99 (0.06, 15.94)	0.9971	
Geographic region							0.7980
Asia	11/ 607 (1.8)	0.85	16/ 619 (2.6)	1.23	0.69 (0.32, 1.48)	0.3399	
Europe and Saudi Arabia	29/1494 (1.9)	0.84	42/1511 (2.8)	1.21	0.69 (0.43, 1.10)	0.1219	
North America	14/ 428 (3.3)	1.57	15/ 423 (3.5)	1.74	0.91 (0.44, 1.89)	0.8001	
Latin America	6/ 602 (1.0)	0.49	5/ 579 (0.9)	0.43	1.21 (0.37, 3.98)	0.7509	
NYHA class at enrolment							0.7437
II	43/2314 (1.9)	0.84	56/2399 (2.3)	1.06	0.79 (0.53, 1.17)	0.2368	
III or IV	17/ 817 (2.1)	0.99	22/ 732 (3.0)	1.44	0.70 (0.37, 1.31)	0.2656	
LVEF at enrolment							0.6137
<= 49	18/1067 (1.7)	0.79	29/1049 (2.8)	1.31	0.60 (0.34, 1.09)	0.0925	
50-59	27/1133 (2.4)	1.08	30/1123 (2.7)	1.21	0.89 (0.53, 1.50)	0.6593	
>= 60	15/ 931 (1.6)	0.72	19/ 960 (2.0)	0.91	0.80 (0.41, 1.57)	0.5126	
NT-proBNP at enrolment							0.3499
<= median	18/1555 (1.2)	0.52	30/1578 (1.9)	0.85	0.60 (0.34, 1.08)	0.0903	
> median	42/1576 (2.7)	1.25	48/1553 (3.1)	1.47	0.85 (0.56, 1.29)	0.4458	
Type 2 Diabetes Medical History							0.9159
Yes	36/1401 (2.6)	1.17	46/1405 (3.3)	1.52	0.77 (0.50, 1.20)	0.2509	
No	24/1730 (1.4)	0.63	32/1727 (1.9)	0.85	0.75 (0.44, 1.27)	0.2807	
Atrial fibrillation or flutter at enrolment ECG							0.7472
Yes	26/1327 (2.0)	0.89	36/1317 (2.7)	1.25	0.72 (0.43, 1.19)	0.1978	
No	34/1803 (1.9)	0.86	42/1814 (2.3)	1.07	0.80 (0.51, 1.26)	0.3401	
BMI (kg/m2) at enrolment							0.0684
< 30	31/1734 (1.8)	0.83	28/1736 (1.6)	0.76	1.09 (0.65, 1.82)	0.7419	
>= 30	29/1395 (2.1)	0.94	50/1392 (3.6)	1.62	0.58 (0.37, 0.91)	0.0192	
Baseline eGFR (mL/min/1.73m^2)							0.1794
< 60	37/1516 (2.4)	1.15	40/1554 (2.6)	1.21	0.94 (0.60, 1.47)	0.7798	
>= 60	23/1615 (1.4)	0.63	38/1577 (2.4)	1.09	0.59 (0.35, 0.99)	0.0444	
SBP at randomisation							0.3755
<= median	27/1568 (1.7)	0.81	41/1590 (2.6)	1.22	0.66 (0.40, 1.07)	0.0913	
> median	33/1563 (2.1)	0.94	37/1542 (2.4)	1.08	0.89 (0.56, 1.43)	0.6334	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
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p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to urgent HF visit
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.3371
<= 49	18/1067 (1.7)	0.79	29/1049 (2.8)	1.31	0.60 (0.34, 1.09)	0.0925	
>= 50	42/2064 (2.0)	0.92	49/2083 (2.4)	1.07	0.86 (0.57, 1.30)	0.4682	
Randomised during hospitalisation for HF or within 30 days of discharge							0.4478
Yes	6/ 328 (1.8)	0.90	11/ 326 (3.4)	1.67	0.51 (0.19, 1.38)	0.1867	
No	54/2803 (1.9)	0.87	67/2806 (2.4)	1.09	0.80 (0.56, 1.15)	0.2235	
MRAs at baseline							0.8983
Yes	22/1340 (1.6)	0.76	27/1327 (2.0)	0.96	0.79 (0.45, 1.39)	0.4094	
No	38/1791 (2.1)	0.96	51/1805 (2.8)	1.29	0.75 (0.50, 1.15)	0.1889	
ACEi+ARB at baseline							0.4263
Yes	49/2262 (2.2)	0.97	60/2281 (2.6)	1.18	0.82 (0.56, 1.20)	0.3085	
No	11/ 869 (1.3)	0.61	18/ 851 (2.1)	1.04	0.60 (0.28, 1.27)	0.1793	
ARNI at baseline							0.1930
Yes	1/ 165 (0.6)	0.32	4/ 136 (2.9)	1.59	0.20 (0.02, 1.76)	0.1456	
No	59/2966 (2.0)	0.90	74/2996 (2.5)	1.13	0.80 (0.57, 1.13)	0.2056	
Beta Blocker at baseline							0.2296
Yes	53/2592 (2.0)	0.93	63/2585 (2.4)	1.11	0.84 (0.58, 1.20)	0.3347	
No	7/ 539 (1.3)	0.61	15/ 547 (2.7)	1.33	0.46 (0.19, 1.14)	0.0927	
Diuretics at baseline							0.3923
Yes	52/2793 (1.9)	0.85	71/2787 (2.5)	1.17	0.72 (0.51, 1.04)	0.0778	
No	8/ 338 (2.4)	1.09	7/ 345 (2.0)	0.94	1.12 (0.40, 3.09)	0.8297	

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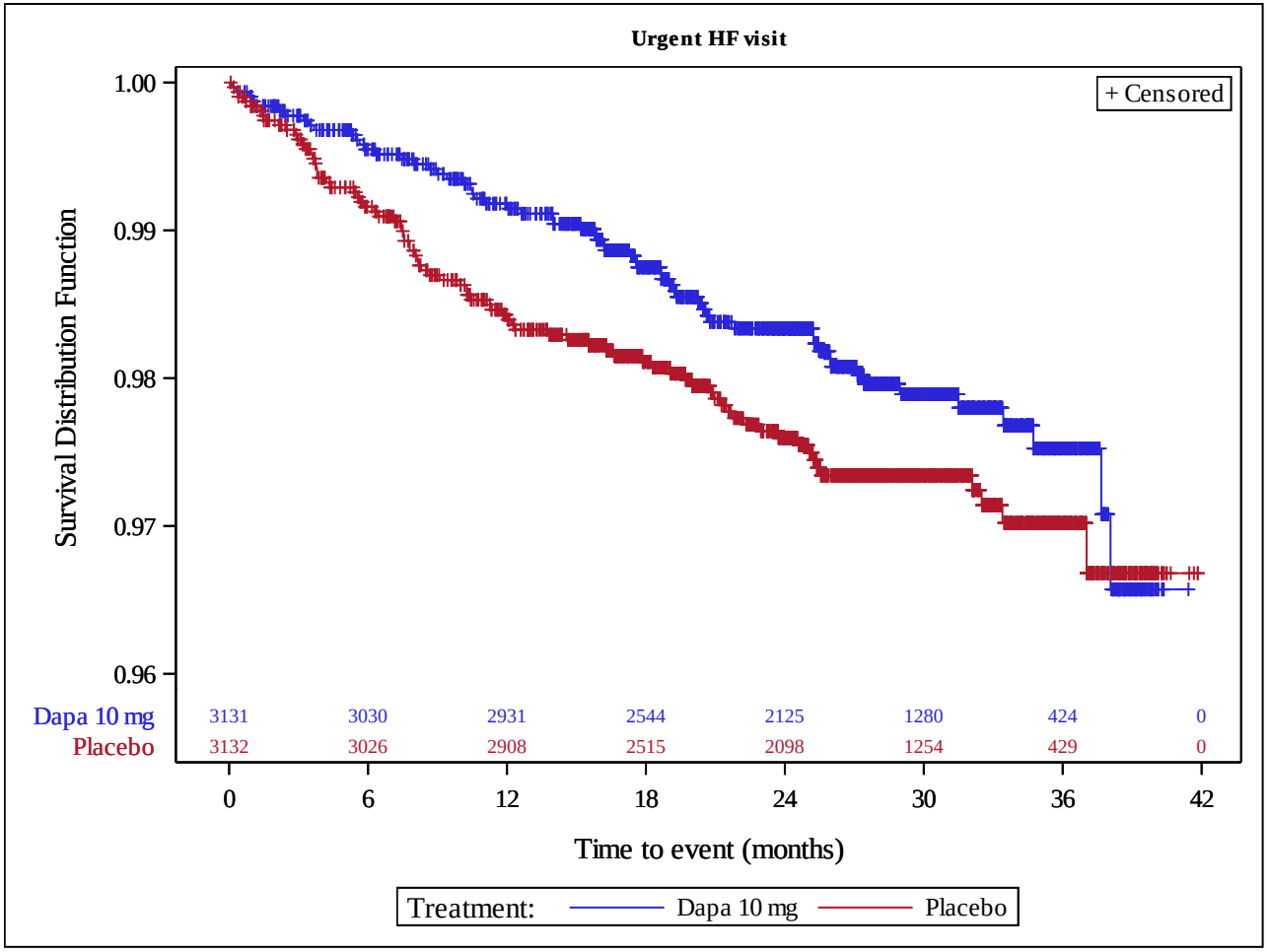
AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to urgent HF visit
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to CV death
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	231/3131 (7.4)	3.33	261/3132 (8.3)	3.77	0.88 (0.74, 1.05)	0.1678	
Age							0.9664
<= median	106/1545 (6.9)	3.08	126/1604 (7.9)	3.51	0.88 (0.68, 1.13)	0.3113	
> median	125/1586 (7.9)	3.58	135/1528 (8.8)	4.05	0.88 (0.69, 1.13)	0.3186	
Gender							0.6637
Male	145/1767 (8.2)	3.72	166/1749 (9.5)	4.35	0.85 (0.68, 1.07)	0.1626	
Female	86/1364 (6.3)	2.83	95/1383 (6.9)	3.06	0.93 (0.69, 1.24)	0.6020	
Race							0.6698
White	172/2214 (7.8)	3.45	201/2225 (9.0)	4.01	0.86 (0.70, 1.05)	0.1477	
Black or African	7/ 81 (8.6)	3.98	7/ 78 (9.0)	4.20	0.93 (0.33, 2.66)	0.8950	
Asian	35/ 630 (5.6)	2.57	32/ 644 (5.0)	2.30	1.12 (0.69, 1.81)	0.6457	
Other	17/ 206 (8.3)	4.14	21/ 185 (11.4)	6.02	0.72 (0.38, 1.36)	0.3088	
Geographic region							0.4117
Asia	32/ 607 (5.3)	2.44	32/ 619 (5.2)	2.41	1.01 (0.62, 1.65)	0.9628	
Europe and Saudi Arabia	126/1494 (8.4)	3.61	131/1511 (8.7)	3.71	0.97 (0.76, 1.24)	0.8214	
North America	29/ 428 (6.8)	3.17	43/ 423 (10.2)	4.86	0.64 (0.40, 1.03)	0.0678	
Latin America	44/ 602 (7.3)	3.61	55/ 579 (9.5)	4.65	0.79 (0.53, 1.17)	0.2376	
NYHA class at enrolment							0.5415
II	149/2314 (6.4)	2.87	170/2399 (7.1)	3.18	0.90 (0.73, 1.13)	0.3697	
III or IV	82/ 817 (10.0)	4.68	91/ 732 (12.4)	5.81	0.80 (0.60, 1.08)	0.1490	
LVEF at enrolment							0.1969
<= 49	101/1067 (9.5)	4.41	115/1049 (11.0)	5.08	0.87 (0.66, 1.13)	0.2920	
50-59	85/1133 (7.5)	3.33	79/1123 (7.0)	3.12	1.07 (0.79, 1.45)	0.6752	
>= 60	45/ 931 (4.8)	2.15	67/ 960 (7.0)	3.15	0.68 (0.47, 1.00)	0.0482	
NT-proBNP at enrolment							0.1600
<= median	82/1555 (5.3)	2.33	80/1578 (5.1)	2.23	1.05 (0.77, 1.43)	0.7627	
> median	149/1576 (9.5)	4.35	181/1553 (11.7)	5.44	0.80 (0.64, 0.99)	0.0438	
Type 2 Diabetes Medical History							0.7274
Yes	110/1401 (7.9)	3.53	128/1405 (9.1)	4.12	0.85 (0.66, 1.10)	0.2260	
No	121/1730 (7.0)	3.17	133/1727 (7.7)	3.48	0.91 (0.71, 1.16)	0.4509	
Atrial fibrillation or flutter at enrolment ECG							0.7302
Yes	103/1327 (7.8)	3.48	112/1317 (8.5)	3.81	0.91 (0.70, 1.20)	0.5130	
No	128/1803 (7.1)	3.22	149/1814 (8.2)	3.74	0.86 (0.68, 1.09)	0.2047	
BMI (kg/m2) at enrolment							0.9758
< 30	134/1734 (7.7)	3.54	151/1736 (8.7)	4.03	0.88 (0.69, 1.10)	0.2612	
>= 30	96/1395 (6.9)	3.05	110/1392 (7.9)	3.47	0.88 (0.67, 1.16)	0.3593	
Baseline eGFR (mL/min/1.73m^2)							0.7394
< 60	129/1516 (8.5)	3.95	153/1554 (9.8)	4.55	0.87 (0.68, 1.09)	0.2261	
>= 60	102/1615 (6.3)	2.78	108/1577 (6.8)	3.04	0.92 (0.70, 1.21)	0.5454	
SBP at randomisation							0.3570
<= median	135/1568 (8.6)	3.98	143/1590 (9.0)	4.16	0.95 (0.75, 1.20)	0.6838	
> median	96/1563 (6.1)	2.71	118/1542 (7.7)	3.38	0.80 (0.61, 1.05)	0.1141	

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Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to CV death
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.8662
<= 49	101/1067 (9.5)	4.41	115/1049 (11.0)	5.08	0.87 (0.66, 1.13)	0.2920	
>= 50	130/2064 (6.3)	2.80	146/2083 (7.0)	3.13	0.89 (0.71, 1.13)	0.3484	
Randomised during hospitalisation for HF or within 30 days of discharge							0.7744
Yes	42/ 328 (12.8)	6.16	49/ 326 (15.0)	7.30	0.85 (0.56, 1.29)	0.4430	
No	189/2803 (6.7)	3.02	212/2806 (7.6)	3.39	0.89 (0.73, 1.09)	0.2538	
MRAs at baseline							0.0854
Yes	99/1340 (7.4)	3.40	130/1327 (9.8)	4.54	0.75 (0.58, 0.97)	0.0302	
No	132/1791 (7.4)	3.28	131/1805 (7.3)	3.23	1.02 (0.80, 1.30)	0.8671	
ACEi+ARB at baseline							0.2230
Yes	171/2262 (7.6)	3.35	183/2281 (8.0)	3.54	0.94 (0.77, 1.16)	0.5946	
No	60/ 869 (6.9)	3.28	78/ 851 (9.2)	4.43	0.75 (0.53, 1.05)	0.0886	
ARNI at baseline							0.5986
Yes	10/ 165 (6.1)	3.12	11/ 136 (8.1)	4.30	0.72 (0.30, 1.70)	0.4522	
No	221/2966 (7.5)	3.34	250/2996 (8.3)	3.75	0.89 (0.74, 1.07)	0.2121	
Beta Blocker at baseline							0.9346
Yes	181/2592 (7.0)	3.14	204/2585 (7.9)	3.54	0.89 (0.72, 1.08)	0.2326	
No	50/ 539 (9.3)	4.30	57/ 547 (10.4)	4.94	0.86 (0.59, 1.26)	0.4416	
Diuretics at baseline							0.6509
Yes	212/2793 (7.6)	3.42	236/2787 (8.5)	3.83	0.89 (0.74, 1.08)	0.2354	
No	19/ 338 (5.6)	2.55	25/ 345 (7.2)	3.30	0.77 (0.42, 1.39)	0.3806	

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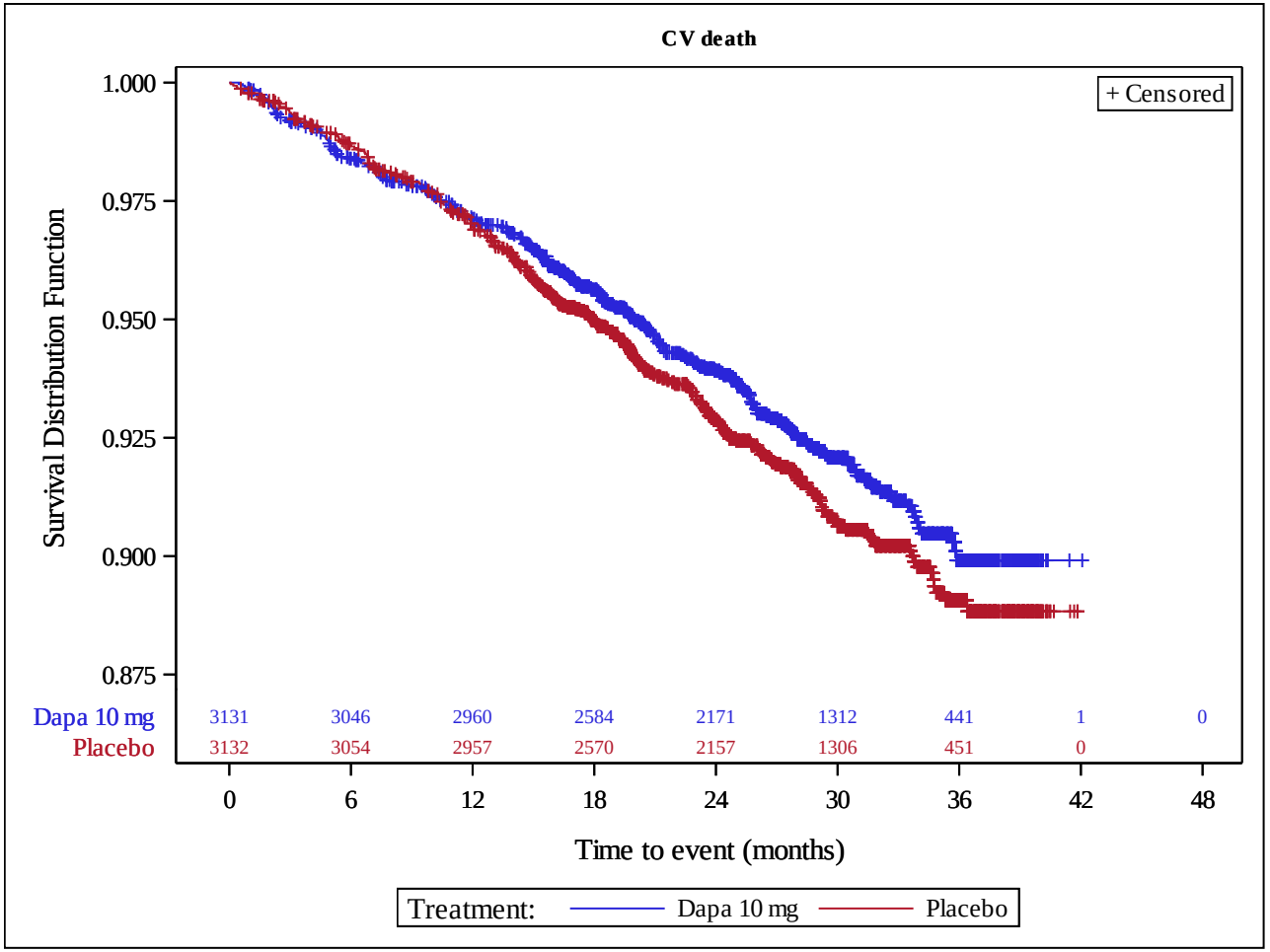
AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to CV death
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to all-cause mortality
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	497/3131 (15.9)	7.16	526/3132 (16.8)	7.59	0.94 (0.83, 1.07)	0.3425	
Age							0.7707
<= median	201/1545 (13.0)	5.83	229/1604 (14.3)	6.38	0.91 (0.76, 1.10)	0.3498	
> median	296/1586 (18.7)	8.46	297/1528 (19.4)	8.89	0.95 (0.81, 1.12)	0.5277	
Gender							0.4871
Male	310/1767 (17.5)	7.94	333/1749 (19.0)	8.71	0.91 (0.78, 1.06)	0.2181	
Female	187/1364 (13.7)	6.15	193/1383 (14.0)	6.21	0.99 (0.81, 1.21)	0.9465	
Race							0.5711
White	379/2214 (17.1)	7.59	399/2225 (17.9)	7.94	0.96 (0.83, 1.10)	0.5211	
Black or African	10/ 81 (12.3)	5.68	16/ 78 (20.5)	9.59	0.61 (0.28, 1.37)	0.2338	
Asian	67/ 630 (10.6)	4.92	68/ 644 (10.6)	4.89	1.00 (0.72, 1.41)	0.9832	
Other	41/ 206 (19.9)	9.98	43/ 185 (23.2)	12.32	0.82 (0.53, 1.25)	0.3556	
Geographic region							0.5440
Asia	59/ 607 (9.7)	4.49	67/ 619 (10.8)	5.04	0.89 (0.62, 1.26)	0.4999	
Europe and Saudi Arabia	266/1494 (17.8)	7.62	267/1511 (17.7)	7.55	1.01 (0.85, 1.19)	0.9461	
North America	62/ 428 (14.5)	6.74	78/ 423 (18.4)	8.77	0.77 (0.55, 1.07)	0.1160	
Latin America	110/ 602 (18.3)	9.02	114/ 579 (19.7)	9.65	0.94 (0.72, 1.22)	0.6233	
NYHA class at enrolment							0.7150
II	321/2314 (13.9)	6.19	362/2399 (15.1)	6.76	0.91 (0.79, 1.06)	0.2422	
III or IV	176/ 817 (21.5)	10.00	164/ 732 (22.4)	10.42	0.96 (0.77, 1.18)	0.6914	
LVEF at enrolment							0.5712
<= 49	195/1067 (18.3)	8.51	206/1049 (19.6)	9.10	0.93 (0.77, 1.14)	0.4927	
50-59	172/1133 (15.2)	6.73	167/1123 (14.9)	6.58	1.02 (0.83, 1.27)	0.8379	
>= 60	130/ 931 (14.0)	6.20	153/ 960 (15.9)	7.18	0.86 (0.68, 1.09)	0.2119	
NT-proBNP at enrolment							0.8963
<= median	175/1555 (11.3)	4.97	189/1578 (12.0)	5.26	0.95 (0.77, 1.16)	0.5948	
> median	322/1576 (20.4)	9.40	337/1553 (21.7)	10.10	0.93 (0.80, 1.08)	0.3475	
Type 2 Diabetes Medical History							0.6797
Yes	240/1401 (17.1)	7.69	260/1405 (18.5)	8.36	0.92 (0.77, 1.09)	0.3329	
No	257/1730 (14.9)	6.72	266/1727 (15.4)	6.96	0.97 (0.81, 1.15)	0.6918	
Atrial fibrillation or flutter at enrolment ECG							0.4691
Yes	224/1327 (16.9)	7.57	225/1317 (17.1)	7.65	0.99 (0.82, 1.19)	0.9348	
No	273/1803 (15.1)	6.85	301/1814 (16.6)	7.55	0.91 (0.77, 1.07)	0.2332	
BMI (kg/m2) at enrolment							0.4231
< 30	276/1734 (15.9)	7.28	303/1736 (17.5)	8.07	0.90 (0.76, 1.06)	0.1952	
>= 30	220/1395 (15.8)	6.98	223/1392 (16.0)	7.03	0.99 (0.83, 1.20)	0.9507	
Baseline eGFR (mL/min/1.73m^2)							0.8277
< 60	291/1516 (19.2)	8.89	311/1554 (20.0)	9.23	0.96 (0.82, 1.13)	0.6071	
>= 60	206/1615 (12.8)	5.61	215/1577 (13.6)	6.04	0.93 (0.77, 1.13)	0.4742	
SBP at randomisation							0.6898
<= median	264/1568 (16.8)	7.77	275/1590 (17.3)	8.00	0.97 (0.82, 1.14)	0.6880	
> median	233/1563 (14.9)	6.57	251/1542 (16.3)	7.18	0.92 (0.77, 1.10)	0.3525	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to all-cause mortality
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.9233
<= 49	195/1067 (18.3)	8.51	206/1049 (19.6)	9.10	0.93 (0.77, 1.14)	0.4927	
>= 50	302/2064 (14.6)	6.49	320/2083 (15.4)	6.85	0.95 (0.81, 1.11)	0.4872	
Randomised during hospitalisation for HF or within 30 days of discharge							0.9489
Yes	77/ 328 (23.5)	11.29	79/ 326 (24.2)	11.74	0.96 (0.70, 1.31)	0.7933	
No	420/2803 (15.0)	6.71	447/2806 (15.9)	7.14	0.94 (0.82, 1.07)	0.3590	
MRAs at baseline							0.6528
Yes	219/1340 (16.3)	7.52	235/1327 (17.7)	8.19	0.91 (0.76, 1.10)	0.3396	
No	278/1791 (15.5)	6.89	291/1805 (16.1)	7.16	0.97 (0.82, 1.14)	0.6871	
ACEi+ARB at baseline							0.6490
Yes	355/2262 (15.7)	6.94	375/2281 (16.4)	7.25	0.96 (0.83, 1.11)	0.5669	
No	142/ 869 (16.3)	7.75	151/ 851 (17.7)	8.56	0.91 (0.72, 1.14)	0.3963	
ARNI at baseline							0.3432
Yes	24/ 165 (14.5)	7.48	26/ 136 (19.1)	10.09	0.73 (0.42, 1.27)	0.2627	
No	473/2966 (15.9)	7.14	500/2996 (16.7)	7.49	0.95 (0.84, 1.08)	0.4522	
Beta Blocker at baseline							0.1960
Yes	411/2592 (15.9)	7.11	419/2585 (16.2)	7.25	0.98 (0.85, 1.12)	0.7622	
No	86/ 539 (16.0)	7.38	107/ 547 (19.6)	9.26	0.79 (0.60, 1.05)	0.1068	
Diuretics at baseline							0.9386
Yes	457/2793 (16.4)	7.37	482/2787 (17.3)	7.81	0.94 (0.83, 1.07)	0.3696	
No	40/ 338 (11.8)	5.36	44/ 345 (12.8)	5.79	0.92 (0.60, 1.41)	0.6989	

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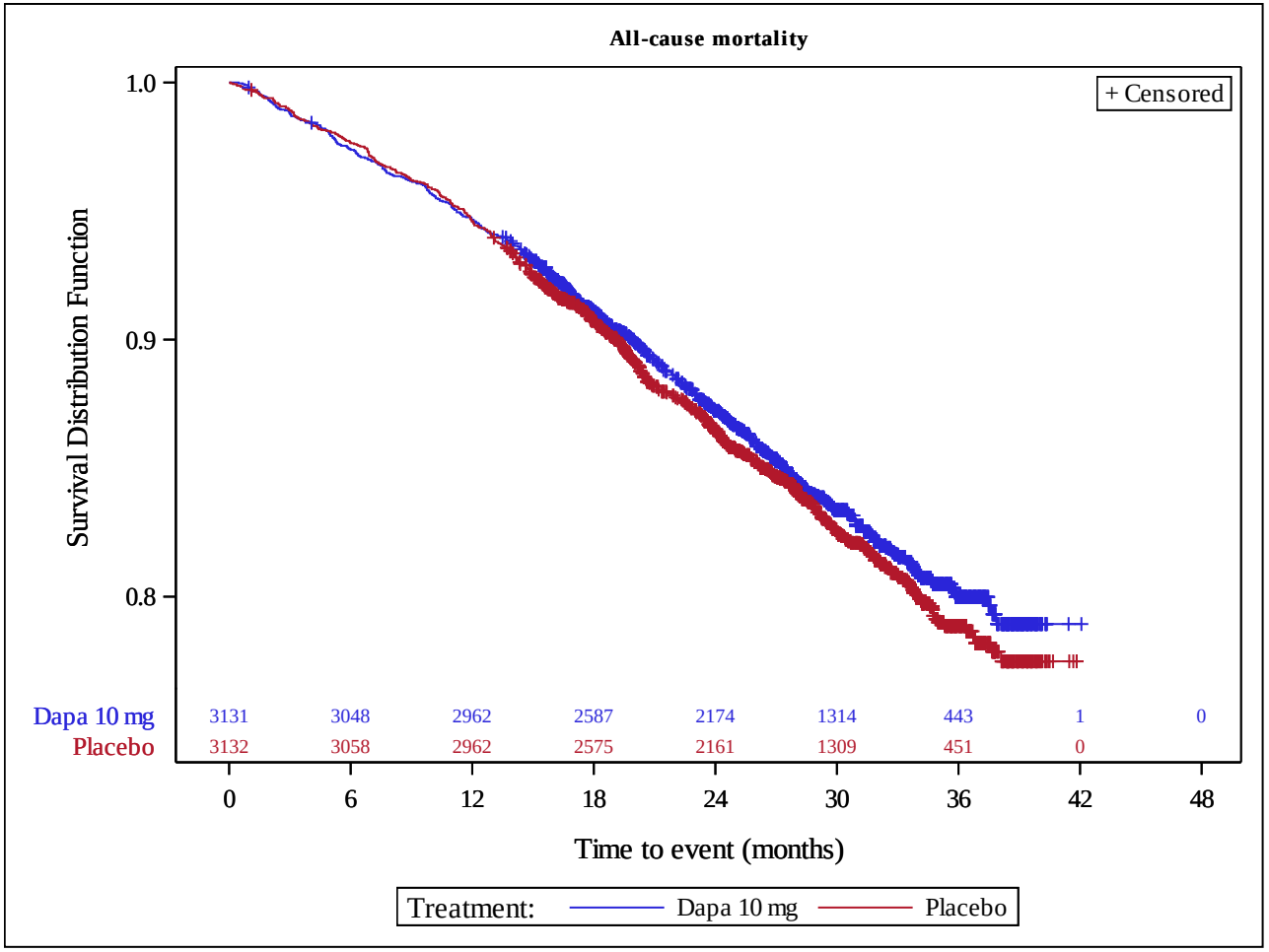
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to all-cause mortality
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to the first occurrence of >=50% sustained decline in eGFR
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	44/3131 (1.4)	0.95	46/3132 (1.5)	0.98	0.96 (0.63, 1.45)	0.8298	
Age							0.0855
<= median	23/1545 (1.5)	1.02	33/1604 (2.1)	1.38	0.73 (0.43, 1.24)	0.2423	
> median	21/1586 (1.3)	0.89	13/1528 (0.9)	0.57	1.56 (0.78, 3.12)	0.2082	
Gender							0.3295
Male	20/1767 (1.1)	0.75	24/1749 (1.4)	0.91	0.75 (0.41, 1.36)	0.3398	
Female	24/1364 (1.8)	1.23	22/1383 (1.6)	1.08	1.17 (0.65, 2.09)	0.5977	
Race							0.9299
White	31/2214 (1.4)	0.95	30/2225 (1.3)	0.90	1.04 (0.63, 1.71)	0.8851	
Black or African	0/ 81 (0.0)	0.00	3/ 78 (3.8)	2.89	NE		
Asian	10/ 630 (1.6)	1.02	9/ 644 (1.4)	0.90	1.16 (0.47, 2.85)	0.7504	
Other	3/ 206 (1.5)	1.15	4/ 185 (2.2)	1.79	0.69 (0.15, 3.11)	0.6323	
Geographic region							0.7640
Asia	8/ 607 (1.3)	0.84	7/ 619 (1.1)	0.72	1.20 (0.43, 3.30)	0.7288	
Europe and Saudi Arabia	20/1494 (1.3)	0.85	16/1511 (1.1)	0.67	1.18 (0.61, 2.28)	0.6212	
North America	5/ 428 (1.2)	0.91	8/ 423 (1.9)	1.51	0.68 (0.22, 2.11)	0.5006	
Latin America	11/ 602 (1.8)	1.43	15/ 579 (2.6)	1.91	0.80 (0.37, 1.75)	0.5786	
NYHA class at enrolment							0.4797
II	33/2314 (1.4)	0.95	32/2399 (1.3)	0.89	1.06 (0.65, 1.73)	0.8013	
III or IV	11/ 817 (1.3)	0.96	14/ 732 (1.9)	1.31	0.75 (0.34, 1.65)	0.4714	
LVEF at enrolment							0.4995
<= 49	16/1067 (1.5)	1.05	12/1049 (1.1)	0.78	1.35 (0.64, 2.87)	0.4276	
50-59	17/1133 (1.5)	0.99	22/1123 (2.0)	1.30	0.76 (0.40, 1.43)	0.3936	
>= 60	11/ 931 (1.2)	0.79	12/ 960 (1.3)	0.83	0.94 (0.41, 2.13)	0.8800	
NT-proBNP at enrolment							0.1945
<= median	15/1555 (1.0)	0.65	22/1578 (1.4)	0.93	0.67 (0.35, 1.30)	0.2375	
> median	29/1576 (1.8)	1.25	24/1553 (1.5)	1.04	1.21 (0.70, 2.07)	0.4961	
Type 2 Diabetes Medical History							0.4035
Yes	27/1401 (1.9)	1.31	32/1405 (2.3)	1.54	0.84 (0.50, 1.41)	0.5115	
No	17/1730 (1.0)	0.66	14/1727 (0.8)	0.54	1.23 (0.61, 2.50)	0.5615	
Atrial fibrillation or flutter at enrolment ECG							0.7655
Yes	15/1327 (1.1)	0.74	16/1317 (1.2)	0.80	0.86 (0.42, 1.75)	0.6763	
No	29/1803 (1.6)	1.11	30/1814 (1.7)	1.12	1.01 (0.61, 1.68)	0.9729	
BMI (kg/m2) at enrolment							0.2230
< 30	24/1734 (1.4)	0.93	19/1736 (1.1)	0.72	1.25 (0.68, 2.28)	0.4738	
>= 30	20/1395 (1.4)	0.98	27/1392 (1.9)	1.32	0.74 (0.42, 1.33)	0.3136	
Baseline eGFR (mL/min/1.73m^2)							0.8588
< 60	22/1516 (1.5)	1.01	25/1554 (1.6)	1.10	0.92 (0.52, 1.64)	0.7875	
>= 60	22/1615 (1.4)	0.90	21/1577 (1.3)	0.87	0.96 (0.52, 1.75)	0.8825	
SBP at randomisation							0.7871
<= median	19/1568 (1.2)	0.83	20/1590 (1.3)	0.86	0.92 (0.49, 1.73)	0.8034	
> median	25/1563 (1.6)	1.07	26/1542 (1.7)	1.11	1.03 (0.59, 1.78)	0.9238	

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p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to the first occurrence of >=50% sustained decline in eGFR
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.2680
<= 49	16/1067 (1.5)	1.05	12/1049 (1.1)	0.78	1.35 (0.64, 2.87)	0.4276	
>= 50	28/2064 (1.4)	0.90	34/2083 (1.6)	1.09	0.82 (0.50, 1.35)	0.4348	
Randomised during hospitalisation for HF or within 30 days of discharge							0.8070
Yes	8/ 328 (2.4)	1.88	9/ 326 (2.8)	2.10	0.86 (0.33, 2.23)	0.7529	
No	36/2803 (1.3)	0.86	37/2806 (1.3)	0.87	0.97 (0.62, 1.54)	0.9132	
MRAs at baseline							0.1522
Yes	22/1340 (1.6)	1.12	16/1327 (1.2)	0.82	1.35 (0.71, 2.57)	0.3608	
No	22/1791 (1.2)	0.83	30/1805 (1.7)	1.11	0.72 (0.41, 1.25)	0.2369	
ACEi+ARB at baseline							0.0643
Yes	39/2262 (1.7)	1.14	34/2281 (1.5)	0.97	1.16 (0.73, 1.84)	0.5233	
No	5/ 869 (0.6)	0.41	12/ 851 (1.4)	1.03	0.41 (0.14, 1.16)	0.0924	
ARNI at baseline							1.0000
Yes	0/ 165 (0.0)	0.00	0/ 136 (0.0)	0.00	NE		
No	44/2966 (1.5)	0.99	46/2996 (1.5)	1.02	0.97 (0.64, 1.46)	0.8793	
Beta Blocker at baseline							0.4285
Yes	37/2592 (1.4)	0.96	36/2585 (1.4)	0.92	1.04 (0.65, 1.64)	0.8779	
No	7/ 539 (1.3)	0.91	10/ 547 (1.8)	1.32	0.66 (0.25, 1.73)	0.3959	
Diuretics at baseline							0.8759
Yes	40/2793 (1.4)	0.97	42/2787 (1.5)	1.01	0.94 (0.61, 1.45)	0.7900	
No	4/ 338 (1.2)	0.83	4/ 345 (1.2)	0.78	1.00 (0.25, 4.00)	0.9958	

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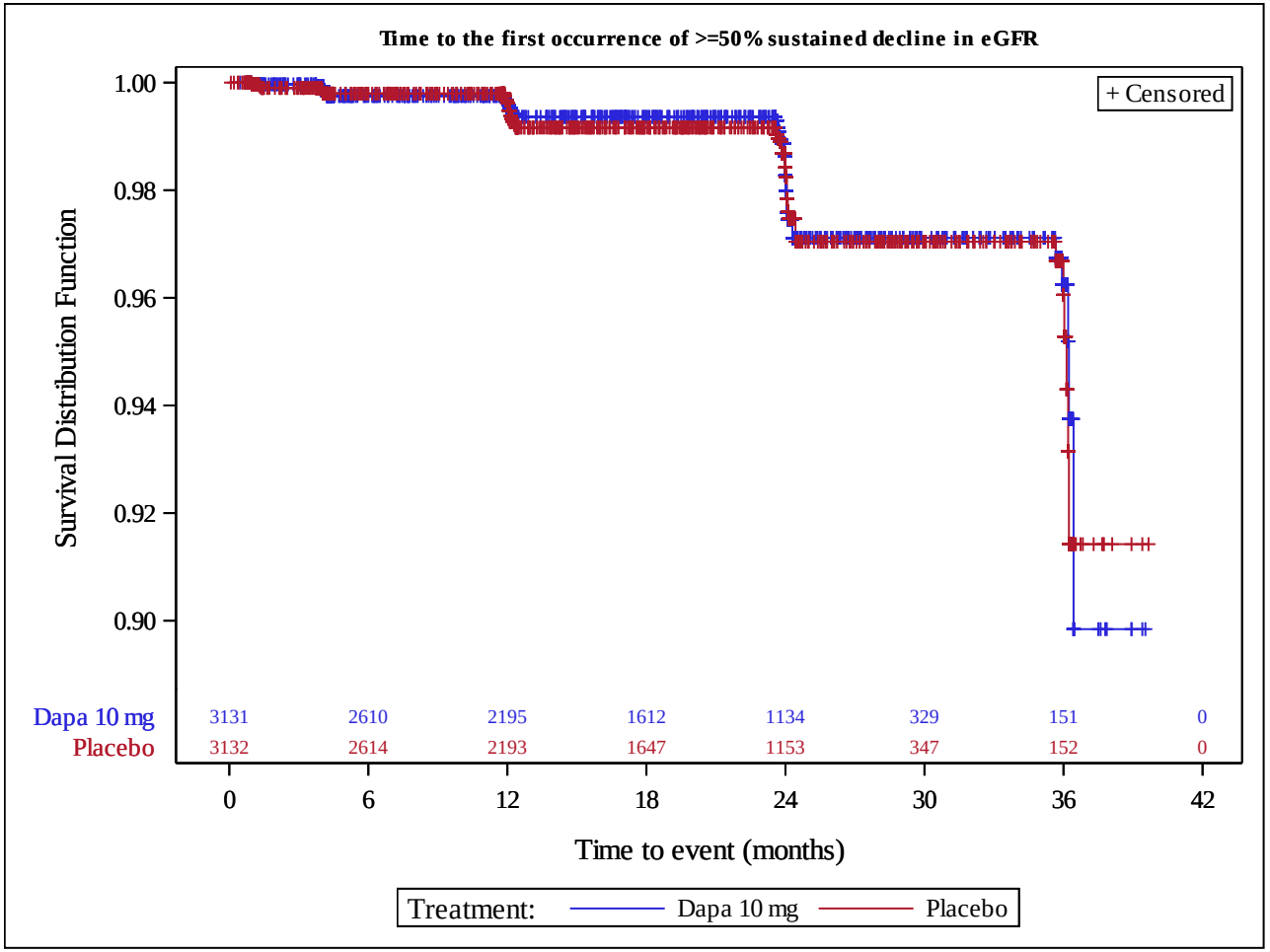
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to the first occurrence of >=50% sustained decline in eGFR
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to first myocardial infarction (MI)
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	83/3131 (2.7)	1.21	81/3132 (2.6)	1.19	1.02 (0.75, 1.39)	0.8904	
Age							0.3075
<= median	42/1545 (2.7)	1.24	49/1604 (3.1)	1.39	0.89 (0.59, 1.34)	0.5725	
> median	41/1586 (2.6)	1.19	32/1528 (2.1)	0.97	1.23 (0.77, 1.95)	0.3855	
Gender							0.4758
Male	51/1767 (2.9)	1.33	53/1749 (3.0)	1.41	0.94 (0.64, 1.38)	0.7397	
Female	32/1364 (2.3)	1.07	28/1383 (2.0)	0.91	1.18 (0.71, 1.97)	0.5148	
Race							0.1706
White	59/2214 (2.7)	1.20	68/2225 (3.1)	1.37	0.87 (0.61, 1.24)	0.4399	
Black or African	5/ 81 (6.2)	2.98	1/ 78 (1.3)	0.60	4.78 (0.56, 40.92)	0.1537	
Asian	14/ 630 (2.2)	1.04	7/ 644 (1.1)	0.51	2.03 (0.82, 5.02)	0.1275	
Other	5/ 206 (2.4)	1.22	5/ 185 (2.7)	1.43	0.91 (0.26, 3.15)	0.8826	
Geographic region							0.1300
Asia	11/ 607 (1.8)	0.85	5/ 619 (0.8)	0.38	2.23 (0.78, 6.42)	0.1366	
Europe and Saudi Arabia	36/1494 (2.4)	1.04	32/1511 (2.1)	0.92	1.13 (0.70, 1.83)	0.6041	
North America	26/ 428 (6.1)	2.94	24/ 423 (5.7)	2.79	1.06 (0.61, 1.84)	0.8459	
Latin America	10/ 602 (1.7)	0.82	20/ 579 (3.5)	1.71	0.50 (0.23, 1.07)	0.0754	
NYHA class at enrolment							0.9788
II	65/2314 (2.8)	1.27	65/2399 (2.7)	1.23	1.03 (0.73, 1.45)	0.8680	
III or IV	18/ 817 (2.2)	1.04	16/ 732 (2.2)	1.03	1.02 (0.52, 2.00)	0.9557	
LVEF at enrolment							0.5576
<= 49	32/1067 (3.0)	1.41	37/1049 (3.5)	1.67	0.85 (0.53, 1.36)	0.4859	
50-59	32/1133 (2.8)	1.27	26/1123 (2.3)	1.03	1.23 (0.73, 2.07)	0.4296	
>= 60	19/ 931 (2.0)	0.92	18/ 960 (1.9)	0.86	1.09 (0.57, 2.07)	0.8022	
NT-proBNP at enrolment							0.2614
<= median	36/1555 (2.3)	1.04	43/1578 (2.7)	1.21	0.85 (0.55, 1.32)	0.4681	
> median	47/1576 (3.0)	1.39	38/1553 (2.4)	1.15	1.21 (0.79, 1.85)	0.3847	
Type 2 Diabetes Medical History							0.3852
Yes	50/1401 (3.6)	1.63	54/1405 (3.8)	1.77	0.92 (0.63, 1.35)	0.6785	
No	33/1730 (1.9)	0.87	27/1727 (1.6)	0.71	1.22 (0.74, 2.04)	0.4351	
Atrial fibrillation or flutter at enrolment ECG							0.4158
Yes	23/1327 (1.7)	0.78	18/1317 (1.4)	0.62	1.27 (0.69, 2.36)	0.4457	
No	60/1803 (3.3)	1.53	63/1814 (3.5)	1.61	0.95 (0.67, 1.35)	0.7734	
BMI (kg/m2) at enrolment							0.4871
< 30	44/1734 (2.5)	1.17	38/1736 (2.2)	1.03	1.13 (0.74, 1.75)	0.5686	
>= 30	39/1395 (2.8)	1.26	43/1392 (3.1)	1.37	0.92 (0.59, 1.41)	0.6908	
Baseline eGFR (mL/min/1.73m^2)							0.3576
< 60	46/1516 (3.0)	1.43	40/1554 (2.6)	1.20	1.17 (0.76, 1.78)	0.4769	
>= 60	37/1615 (2.3)	1.02	41/1577 (2.6)	1.17	0.87 (0.56, 1.36)	0.5556	
SBP at randomisation							0.5976
<= median	36/1568 (2.3)	1.07	32/1590 (2.0)	0.94	1.12 (0.70, 1.80)	0.6415	
> median	47/1563 (3.0)	1.35	49/1542 (3.2)	1.42	0.95 (0.64, 1.42)	0.8049	

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p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to first myocardial infarction (MI)
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.2988
<= 49	32/1067 (3.0)	1.41	37/1049 (3.5)	1.67	0.85 (0.53, 1.36)	0.4859	
>= 50	51/2064 (2.5)	1.11	44/2083 (2.1)	0.95	1.17 (0.78, 1.75)	0.4400	
Randomised during hospitalisation for HF or within 30 days of discharge							0.6783
Yes	5/ 328 (1.5)	0.74	6/ 326 (1.8)	0.90	0.81 (0.25, 2.66)	0.7295	
No	78/2803 (2.8)	1.26	75/2806 (2.7)	1.22	1.04 (0.76, 1.43)	0.8023	
MRAs at baseline							0.9580
Yes	31/1340 (2.3)	1.08	29/1327 (2.2)	1.02	1.04 (0.62, 1.72)	0.8886	
No	52/1791 (2.9)	1.31	52/1805 (2.9)	1.30	1.02 (0.69, 1.50)	0.9220	
ACEi+ARB at baseline							0.3188
Yes	64/2262 (2.8)	1.27	68/2281 (3.0)	1.34	0.95 (0.67, 1.33)	0.7630	
No	19/ 869 (2.2)	1.06	13/ 851 (1.5)	0.74	1.42 (0.70, 2.87)	0.3308	
ARNI at baseline							0.4249
Yes	3/ 165 (1.8)	0.95	4/ 136 (2.9)	1.59	0.58 (0.13, 2.60)	0.4746	
No	80/2966 (2.7)	1.22	77/2996 (2.6)	1.17	1.05 (0.77, 1.43)	0.7686	
Beta Blocker at baseline							0.1897
Yes	71/2592 (2.7)	1.25	63/2585 (2.4)	1.10	1.13 (0.80, 1.58)	0.4927	
No	12/ 539 (2.2)	1.04	18/ 547 (3.3)	1.59	0.66 (0.32, 1.36)	0.2573	
Diuretics at baseline							0.6251
Yes	73/2793 (2.6)	1.19	69/2787 (2.5)	1.13	1.05 (0.76, 1.46)	0.7565	
No	10/ 338 (3.0)	1.36	12/ 345 (3.5)	1.61	0.84 (0.36, 1.95)	0.6909	

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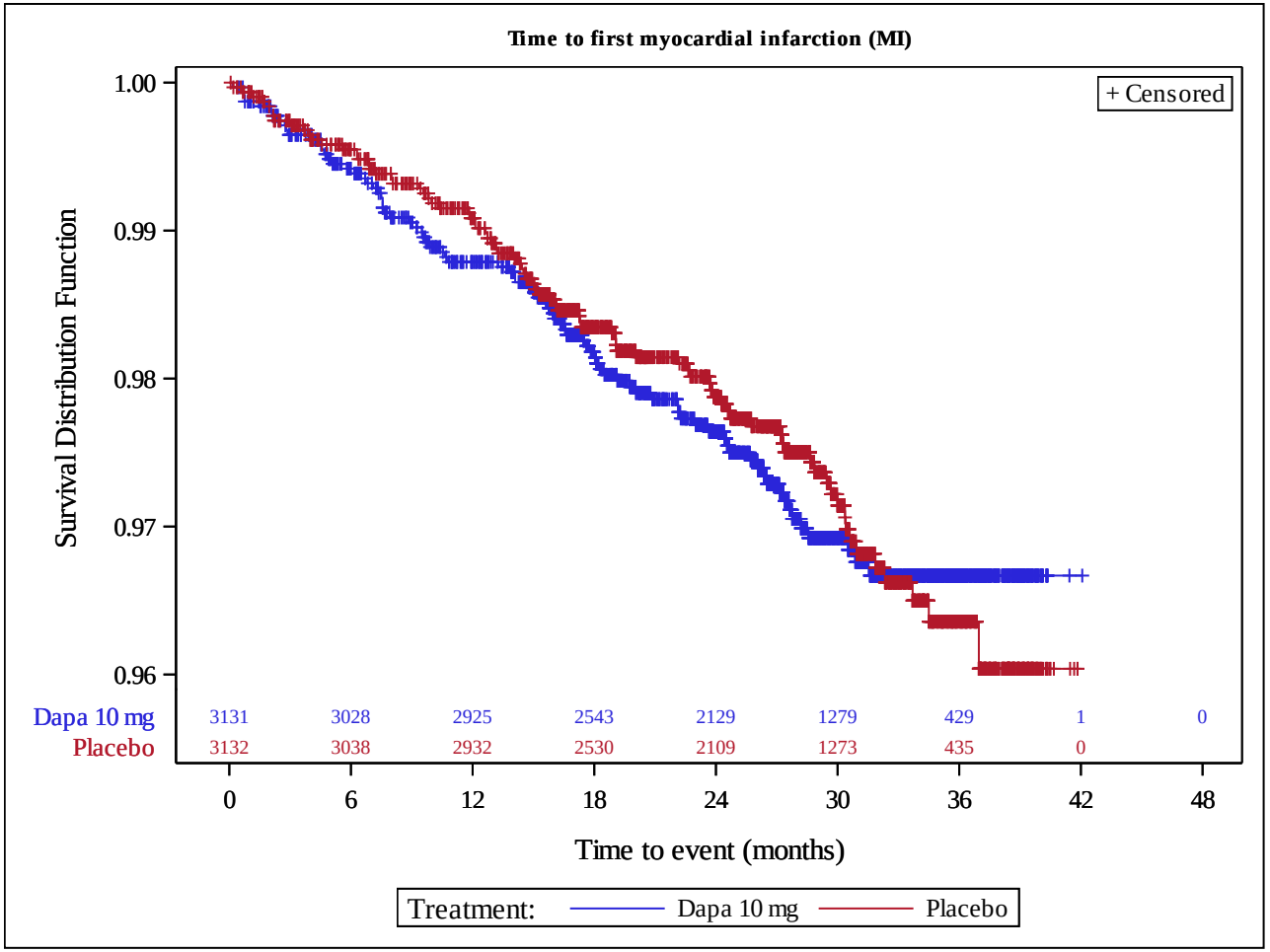
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to first myocardial infarction (MI)
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to fatal myocardial infarction (MI)
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	12/3131 (0.4)	0.17	15/3132 (0.5)	0.22	0.80 (0.37, 1.70)	0.5595	
Age							0.1138
<= median	4/1545 (0.3)	0.12	10/1604 (0.6)	0.28	0.42 (0.13, 1.33)	0.1392	
> median	8/1586 (0.5)	0.23	5/1528 (0.3)	0.15	1.52 (0.50, 4.65)	0.4619	
Gender							0.6211
Male	7/1767 (0.4)	0.18	10/1749 (0.6)	0.26	0.69 (0.26, 1.80)	0.4461	
Female	5/1364 (0.4)	0.16	5/1383 (0.4)	0.16	1.02 (0.30, 3.53)	0.9721	
Race							0.8720
White	10/2214 (0.5)	0.20	12/2225 (0.5)	0.24	0.84 (0.36, 1.94)	0.6794	
Black or African	0/ 81 (0.0)	0.00	0/ 78 (0.0)	0.00	NE		
Asian	1/ 630 (0.2)	0.07	0/ 644 (0.0)	0.00	NE		
Other	1/ 206 (0.5)	0.24	3/ 185 (1.6)	0.86	0.31 (0.03, 2.97)	0.3091	
Geographic region							0.5041
Asia	1/ 607 (0.2)	0.08	0/ 619 (0.0)	0.00	NE		
Europe and Saudi Arabia	7/1494 (0.5)	0.20	5/1511 (0.3)	0.14	1.41 (0.45, 4.44)	0.5588	
North America	2/ 428 (0.5)	0.22	5/ 423 (1.2)	0.57	0.38 (0.07, 1.98)	0.2533	
Latin America	2/ 602 (0.3)	0.16	5/ 579 (0.9)	0.42	0.40 (0.08, 2.06)	0.2724	
NYHA class at enrolment							0.1451
II	6/2314 (0.3)	0.12	12/2399 (0.5)	0.22	0.51 (0.19, 1.37)	0.1828	
III or IV	6/ 817 (0.7)	0.34	3/ 732 (0.4)	0.19	1.80 (0.45, 7.20)	0.4059	
LVEF at enrolment							0.0908
<= 49	4/1067 (0.4)	0.17	5/1049 (0.5)	0.22	0.78 (0.21, 2.92)	0.7165	
50-59	7/1133 (0.6)	0.27	3/1123 (0.3)	0.12	2.32 (0.60, 8.98)	0.2224	
>= 60	1/ 931 (0.1)	0.05	7/ 960 (0.7)	0.33	0.15 (0.02, 1.19)	0.0727	
NT-proBNP at enrolment							0.1630
<= median	3/1555 (0.2)	0.09	8/1578 (0.5)	0.22	0.38 (0.10, 1.44)	0.1557	
> median	9/1576 (0.6)	0.26	7/1553 (0.5)	0.21	1.24 (0.46, 3.34)	0.6658	
Type 2 Diabetes Medical History							0.1083
Yes	6/1401 (0.4)	0.19	12/1405 (0.9)	0.39	0.50 (0.19, 1.33)	0.1640	
No	6/1730 (0.3)	0.16	3/1727 (0.2)	0.08	2.00 (0.50, 8.01)	0.3257	
Atrial fibrillation or flutter at enrolment ECG							0.2302
Yes	5/1327 (0.4)	0.17	3/1317 (0.2)	0.10	1.67 (0.40, 6.98)	0.4835	
No	7/1803 (0.4)	0.18	12/1814 (0.7)	0.30	0.58 (0.23, 1.48)	0.2575	
BMI (kg/m2) at enrolment							0.3603
< 30	7/1734 (0.4)	0.18	6/1736 (0.3)	0.16	1.15 (0.39, 3.43)	0.7987	
>= 30	5/1395 (0.4)	0.16	9/1392 (0.6)	0.28	0.56 (0.19, 1.66)	0.2951	
Baseline eGFR (mL/min/1.73m^2)							0.8880
< 60	5/1516 (0.3)	0.15	6/1554 (0.4)	0.18	0.83 (0.25, 2.73)	0.7625	
>= 60	7/1615 (0.4)	0.19	9/1577 (0.6)	0.25	0.76 (0.28, 2.03)	0.5774	
SBP at randomisation							0.0166
<= median	9/1568 (0.6)	0.27	4/1590 (0.3)	0.12	2.27 (0.70, 7.39)	0.1716	
> median	3/1563 (0.2)	0.08	11/1542 (0.7)	0.32	0.27 (0.08, 0.97)	0.0455	

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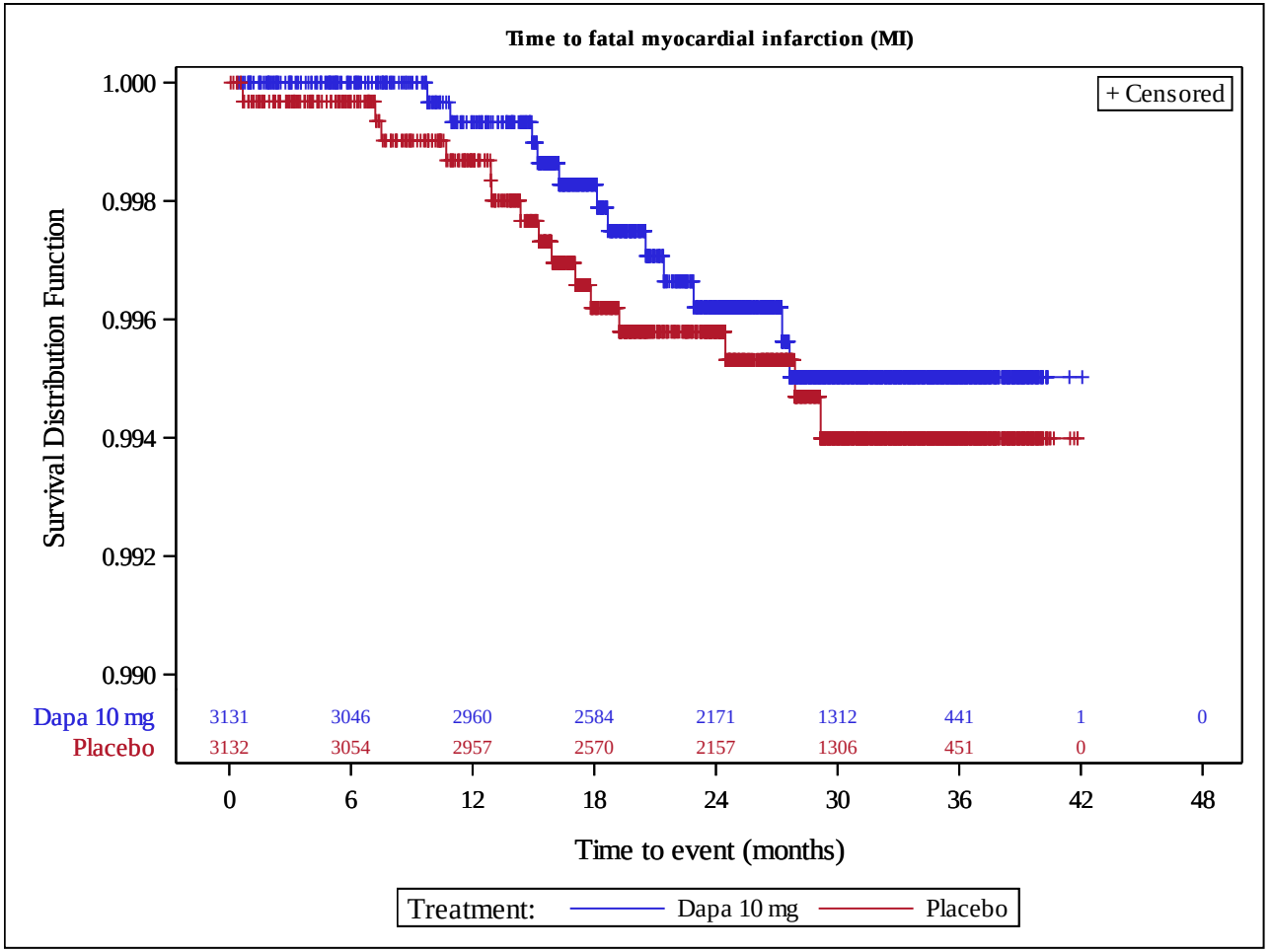
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to fatal myocardial infarction (MI)
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.9694
<= 49	4/1067 (0.4)	0.17	5/1049 (0.5)	0.22	0.78 (0.21, 2.92)	0.7165	
>= 50	8/2064 (0.4)	0.17	10/2083 (0.5)	0.21	0.81 (0.32, 2.04)	0.6497	
Randomised during hospitalisation for HF or within 30 days of discharge							0.8958
Yes	1/ 328 (0.3)	0.15	1/ 326 (0.3)	0.15	0.93 (0.06, 14.80)	0.9565	
No	11/2803 (0.4)	0.18	14/2806 (0.5)	0.22	0.79 (0.36, 1.73)	0.5527	
MRAs at baseline							0.6934
Yes	5/1340 (0.4)	0.17	5/1327 (0.4)	0.17	0.99 (0.29, 3.43)	0.9895	
No	7/1791 (0.4)	0.17	10/1805 (0.6)	0.25	0.71 (0.27, 1.88)	0.4960	
ACEi+ARB at baseline							0.8954
Yes	11/2262 (0.5)	0.22	14/2281 (0.6)	0.27	0.79 (0.36, 1.75)	0.5645	
No	1/ 869 (0.1)	0.05	1/ 851 (0.1)	0.06	0.99 (0.06, 15.79)	0.9930	
ARNI at baseline							0.9998
Yes	0/ 165 (0.0)	0.00	0/ 136 (0.0)	0.00	NE		
No	12/2966 (0.4)	0.18	15/2996 (0.5)	0.22	0.81 (0.38, 1.73)	0.5840	
Beta Blocker at baseline							0.9223
Yes	9/2592 (0.3)	0.16	11/2585 (0.4)	0.19	0.82 (0.34, 1.97)	0.6501	
No	3/ 539 (0.6)	0.26	4/ 547 (0.7)	0.35	0.75 (0.17, 3.37)	0.7114	
Diuretics at baseline							0.6860
Yes	11/2793 (0.4)	0.18	13/2787 (0.5)	0.21	0.84 (0.38, 1.88)	0.6746	
No	1/ 338 (0.3)	0.13	2/ 345 (0.6)	0.26	0.47 (0.04, 5.22)	0.5414	

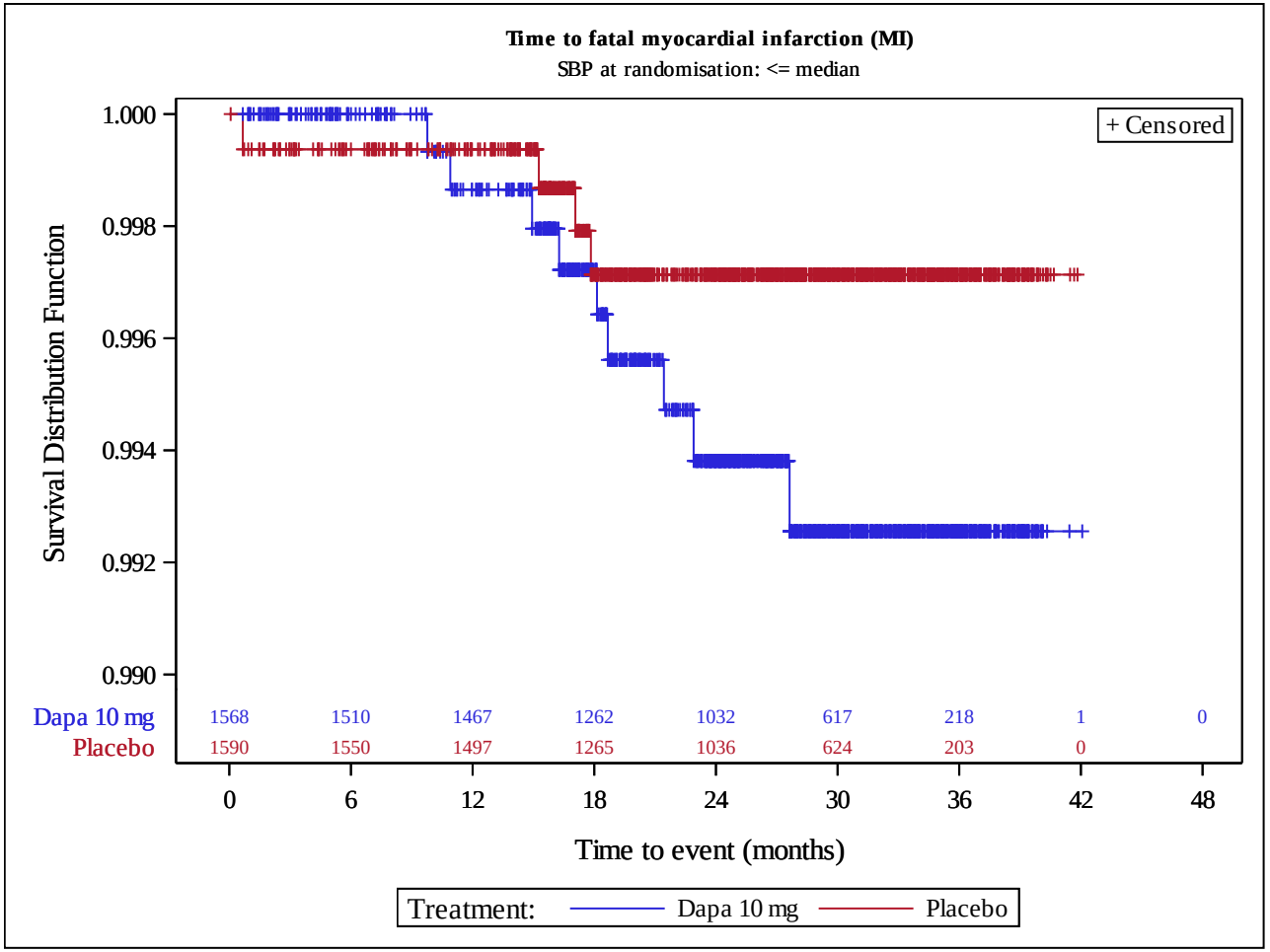
Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to fatal myocardial infarction (MI)
Full Analysis Set



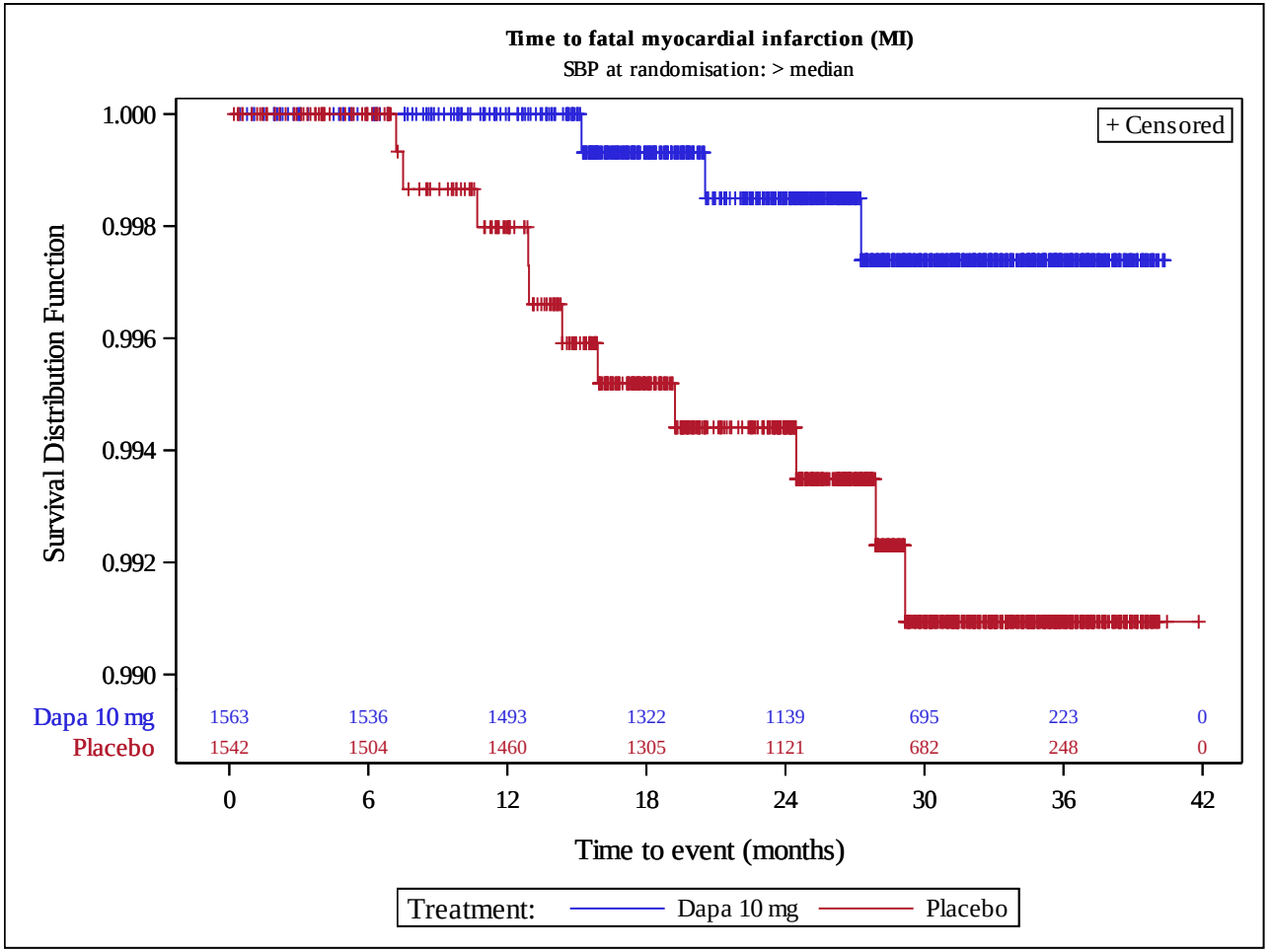
Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to fatal myocardial infarction (MI)
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to fatal myocardial infarction (MI)
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to first stroke of any cause
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	115/3131 (3.7)	1.68	109/3132 (3.5)	1.60	1.05 (0.81, 1.37)	0.7059	
Age							0.9579
<= median	55/1545 (3.6)	1.62	54/1604 (3.4)	1.53	1.06 (0.73, 1.54)	0.7746	
> median	60/1586 (3.8)	1.74	55/1528 (3.6)	1.67	1.04 (0.72, 1.50)	0.8323	
Gender							0.9411
Male	60/1767 (3.4)	1.57	55/1749 (3.1)	1.47	1.07 (0.74, 1.54)	0.7345	
Female	55/1364 (4.0)	1.84	54/1383 (3.9)	1.76	1.04 (0.72, 1.52)	0.8231	
Race							0.4991
White	74/2214 (3.3)	1.50	68/2225 (3.1)	1.37	1.09 (0.79, 1.52)	0.5938	
Black or African	6/ 81 (7.4)	3.62	4/ 78 (5.1)	2.48	1.41 (0.40, 5.01)	0.5948	
Asian	25/ 630 (4.0)	1.87	32/ 644 (5.0)	2.37	0.79 (0.47, 1.33)	0.3704	
Other	10/ 206 (4.9)	2.52	5/ 185 (2.7)	1.44	1.75 (0.60, 5.17)	0.3084	
Geographic region							0.4305
Asia	23/ 607 (3.8)	1.79	30/ 619 (4.8)	2.32	0.77 (0.44, 1.32)	0.3347	
Europe and Saudi Arabia	49/1494 (3.3)	1.42	47/1511 (3.1)	1.35	1.05 (0.70, 1.57)	0.8147	
North America	20/ 428 (4.7)	2.25	12/ 423 (2.8)	1.39	1.60 (0.78, 3.27)	0.2000	
Latin America	23/ 602 (3.8)	1.92	20/ 579 (3.5)	1.72	1.11 (0.61, 2.03)	0.7304	
NYHA class at enrolment							0.2428
II	87/2314 (3.8)	1.70	78/2399 (3.3)	1.48	1.15 (0.85, 1.56)	0.3683	
III or IV	28/ 817 (3.4)	1.63	31/ 732 (4.2)	2.02	0.81 (0.48, 1.35)	0.4133	
LVEF at enrolment							0.1826
<= 49	37/1067 (3.5)	1.64	39/1049 (3.7)	1.76	0.93 (0.59, 1.46)	0.7553	
50-59	48/1133 (4.2)	1.91	33/1123 (2.9)	1.32	1.46 (0.94, 2.27)	0.0958	
>= 60	30/ 931 (3.2)	1.45	37/ 960 (3.9)	1.78	0.81 (0.50, 1.32)	0.4017	
NT-proBNP at enrolment							0.2379
<= median	50/1555 (3.2)	1.44	57/1578 (3.6)	1.62	0.89 (0.61, 1.30)	0.5460	
> median	65/1576 (4.1)	1.93	52/1553 (3.3)	1.58	1.22 (0.85, 1.76)	0.2860	
Type 2 Diabetes Medical History							0.7652
Yes	57/1401 (4.1)	1.86	56/1405 (4.0)	1.84	1.01 (0.70, 1.46)	0.9519	
No	58/1730 (3.4)	1.54	53/1727 (3.1)	1.41	1.10 (0.75, 1.59)	0.6313	
Atrial fibrillation or flutter at enrolment ECG							0.1642
Yes	56/1327 (4.2)	1.93	43/1317 (3.3)	1.49	1.30 (0.87, 1.93)	0.1985	
No	59/1803 (3.3)	1.51	66/1814 (3.6)	1.69	0.89 (0.63, 1.27)	0.5238	
BMI (kg/m2) at enrolment							0.8230
< 30	67/1734 (3.9)	1.80	62/1736 (3.6)	1.68	1.07 (0.76, 1.51)	0.6980	
>= 30	47/1395 (3.4)	1.52	47/1392 (3.4)	1.51	1.01 (0.67, 1.51)	0.9687	
Baseline eGFR (mL/min/1.73m^2)							0.5183
< 60	57/1516 (3.8)	1.77	60/1554 (3.9)	1.82	0.97 (0.67, 1.39)	0.8579	
>= 60	58/1615 (3.6)	1.61	49/1577 (3.1)	1.40	1.15 (0.79, 1.68)	0.4705	
SBP at randomisation							0.9930
<= median	49/1568 (3.1)	1.46	47/1590 (3.0)	1.39	1.05 (0.70, 1.56)	0.8222	
> median	66/1563 (4.2)	1.90	62/1542 (4.0)	1.81	1.05 (0.74, 1.49)	0.7822	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to first stroke of any cause
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.5109
<= 49	37/1067 (3.5)	1.64	39/1049 (3.7)	1.76	0.93 (0.59, 1.46)	0.7553	
>= 50	78/2064 (3.8)	1.71	70/2083 (3.4)	1.53	1.12 (0.81, 1.55)	0.4948	
Randomised during hospitalisation for HF or within 30 days of discharge							0.0757
Yes	11/ 328 (3.4)	1.64	19/ 326 (5.8)	2.89	0.57 (0.27, 1.19)	0.1343	
No	104/2803 (3.7)	1.69	90/2806 (3.2)	1.46	1.16 (0.87, 1.53)	0.3159	
MRAs at baseline							0.5942
Yes	47/1340 (3.5)	1.64	40/1327 (3.0)	1.41	1.16 (0.76, 1.77)	0.4937	
No	68/1791 (3.8)	1.71	69/1805 (3.8)	1.73	1.00 (0.71, 1.39)	0.9777	
ACEi+ARB at baseline							0.8013
Yes	84/2262 (3.7)	1.67	79/2281 (3.5)	1.56	1.07 (0.79, 1.46)	0.6500	
No	31/ 869 (3.6)	1.73	30/ 851 (3.5)	1.73	1.00 (0.60, 1.65)	0.9866	
ARNI at baseline							0.3258
Yes	4/ 165 (2.4)	1.27	1/ 136 (0.7)	0.39	2.76 (0.31, 24.97)	0.3652	
No	111/2966 (3.7)	1.70	108/2996 (3.6)	1.65	1.04 (0.79, 1.35)	0.7979	
Beta Blocker at baseline							0.4660
Yes	95/2592 (3.7)	1.67	86/2585 (3.3)	1.52	1.10 (0.82, 1.48)	0.5123	
No	20/ 539 (3.7)	1.75	23/ 547 (4.2)	2.03	0.86 (0.47, 1.57)	0.6272	
Diuretics at baseline							0.1868
Yes	102/2793 (3.7)	1.67	102/2787 (3.7)	1.68	0.99 (0.76, 1.31)	0.9659	
No	13/ 338 (3.8)	1.78	7/ 345 (2.0)	0.93	1.91 (0.76, 4.79)	0.1670	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
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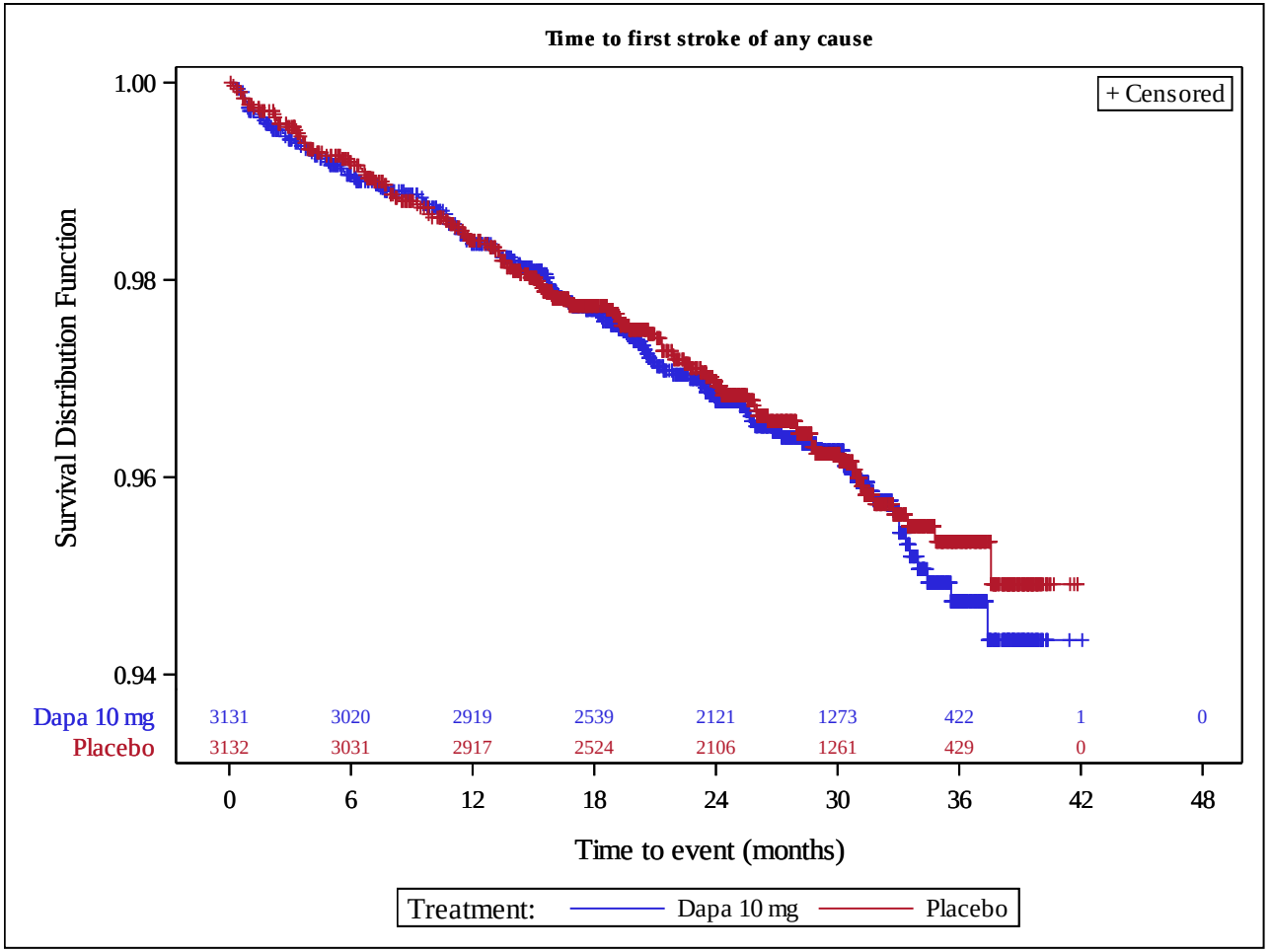
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to first stroke of any cause
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to fatal stroke of any cause
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	28/3131 (0.9)	0.40	25/3132 (0.8)	0.36	1.12 (0.65, 1.92)	0.6822	
Age							0.1283
<= median	13/1545 (0.8)	0.38	7/1604 (0.4)	0.20	1.93 (0.77, 4.85)	0.1593	
> median	15/1586 (0.9)	0.43	18/1528 (1.2)	0.54	0.79 (0.40, 1.58)	0.5113	
Gender							0.2089
Male	14/1767 (0.8)	0.36	8/1749 (0.5)	0.21	1.73 (0.73, 4.12)	0.2165	
Female	14/1364 (1.0)	0.46	17/1383 (1.2)	0.55	0.84 (0.42, 1.71)	0.6351	
Race							0.9998
White	19/2214 (0.9)	0.38	18/2225 (0.8)	0.36	1.07 (0.56, 2.03)	0.8478	
Black or African	1/ 81 (1.2)	0.57	0/ 78 (0.0)	0.00	NE		
Asian	4/ 630 (0.6)	0.29	4/ 644 (0.6)	0.29	1.04 (0.26, 4.14)	0.9602	
Other	4/ 206 (1.9)	0.97	3/ 185 (1.6)	0.86	1.19 (0.27, 5.34)	0.8182	
Geographic region							0.8579
Asia	4/ 607 (0.7)	0.30	4/ 619 (0.6)	0.30	1.02 (0.25, 4.07)	0.9791	
Europe and Saudi Arabia	14/1494 (0.9)	0.40	14/1511 (0.9)	0.40	1.02 (0.48, 2.13)	0.9650	
North America	3/ 428 (0.7)	0.33	1/ 423 (0.2)	0.11	2.93 (0.31, 28.21)	0.3512	
Latin America	7/ 602 (1.2)	0.57	6/ 579 (1.0)	0.51	1.09 (0.36, 3.23)	0.8833	
NYHA class at enrolment							0.1599
II	23/2314 (1.0)	0.44	17/2399 (0.7)	0.32	1.40 (0.75, 2.62)	0.2920	
III or IV	5/ 817 (0.6)	0.29	8/ 732 (1.1)	0.51	0.56 (0.18, 1.73)	0.3156	
LVEF at enrolment							0.2841
<= 49	8/1067 (0.7)	0.35	9/1049 (0.9)	0.40	0.88 (0.34, 2.27)	0.7872	
50-59	16/1133 (1.4)	0.63	9/1123 (0.8)	0.35	1.77 (0.78, 4.00)	0.1722	
>= 60	4/ 931 (0.4)	0.19	7/ 960 (0.7)	0.33	0.59 (0.17, 2.00)	0.3947	
NT-proBNP at enrolment							0.2043
<= median	11/1555 (0.7)	0.31	6/1578 (0.4)	0.17	1.88 (0.69, 5.08)	0.2142	
> median	17/1576 (1.1)	0.50	19/1553 (1.2)	0.57	0.87 (0.45, 1.67)	0.6747	
Type 2 Diabetes Medical History							0.4702
Yes	14/1401 (1.0)	0.45	10/1405 (0.7)	0.32	1.40 (0.62, 3.14)	0.4214	
No	14/1730 (0.8)	0.37	15/1727 (0.9)	0.39	0.93 (0.45, 1.93)	0.8481	
Atrial fibrillation or flutter at enrolment ECG							0.7540
Yes	18/1327 (1.4)	0.61	15/1317 (1.1)	0.51	1.19 (0.60, 2.37)	0.6110	
No	10/1803 (0.6)	0.25	10/1814 (0.6)	0.25	1.00 (0.42, 2.40)	1.0000	
BMI (kg/m2) at enrolment							0.8845
< 30	18/1734 (1.0)	0.48	17/1736 (1.0)	0.45	1.05 (0.54, 2.03)	0.8917	
>= 30	9/1395 (0.6)	0.29	8/1392 (0.6)	0.25	1.14 (0.44, 2.96)	0.7837	
Baseline eGFR (mL/min/1.73m^2)							0.7170
< 60	15/1516 (1.0)	0.46	15/1554 (1.0)	0.45	1.03 (0.50, 2.10)	0.9439	
>= 60	13/1615 (0.8)	0.35	10/1577 (0.6)	0.28	1.25 (0.55, 2.86)	0.5895	
SBP at randomisation							0.5298
<= median	13/1568 (0.8)	0.38	14/1590 (0.9)	0.41	0.94 (0.44, 2.00)	0.8697	
> median	15/1563 (1.0)	0.42	11/1542 (0.7)	0.32	1.33 (0.61, 2.90)	0.4688	

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Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to fatal stroke of any cause
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.5445
<= 49	8/1067 (0.7)	0.35	9/1049 (0.9)	0.40	0.88 (0.34, 2.27)	0.7872	
>= 50	20/2064 (1.0)	0.43	16/2083 (0.8)	0.34	1.26 (0.65, 2.42)	0.4959	
Randomised during hospitalisation for HF or within 30 days of discharge							0.1220
Yes	4/ 328 (1.2)	0.59	8/ 326 (2.5)	1.19	0.51 (0.15, 1.69)	0.2689	
No	24/2803 (0.9)	0.38	17/2806 (0.6)	0.27	1.42 (0.76, 2.64)	0.2715	
MRAs at baseline							0.6617
Yes	13/1340 (1.0)	0.45	10/1327 (0.8)	0.35	1.28 (0.56, 2.92)	0.5560	
No	15/1791 (0.8)	0.37	15/1805 (0.8)	0.37	1.01 (0.49, 2.06)	0.9864	
ACEi+ARB at baseline							0.7485
Yes	21/2262 (0.9)	0.41	18/2281 (0.8)	0.35	1.18 (0.63, 2.22)	0.6043	
No	7/ 869 (0.8)	0.38	7/ 851 (0.8)	0.40	0.97 (0.34, 2.78)	0.9618	
ARNI at baseline							0.9657
Yes	1/ 165 (0.6)	0.31	0/ 136 (0.0)	0.00	NE		
No	27/2966 (0.9)	0.41	25/2996 (0.8)	0.37	1.09 (0.63, 1.88)	0.7560	
Beta Blocker at baseline							0.2375
Yes	23/2592 (0.9)	0.40	17/2585 (0.7)	0.29	1.35 (0.72, 2.53)	0.3467	
No	5/ 539 (0.9)	0.43	8/ 547 (1.5)	0.69	0.62 (0.20, 1.89)	0.3965	
Diuretics at baseline							0.9218
Yes	26/2793 (0.9)	0.42	23/2787 (0.8)	0.37	1.13 (0.64, 1.98)	0.6753	
No	2/ 338 (0.6)	0.27	2/ 345 (0.6)	0.26	1.02 (0.14, 7.26)	0.9816	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
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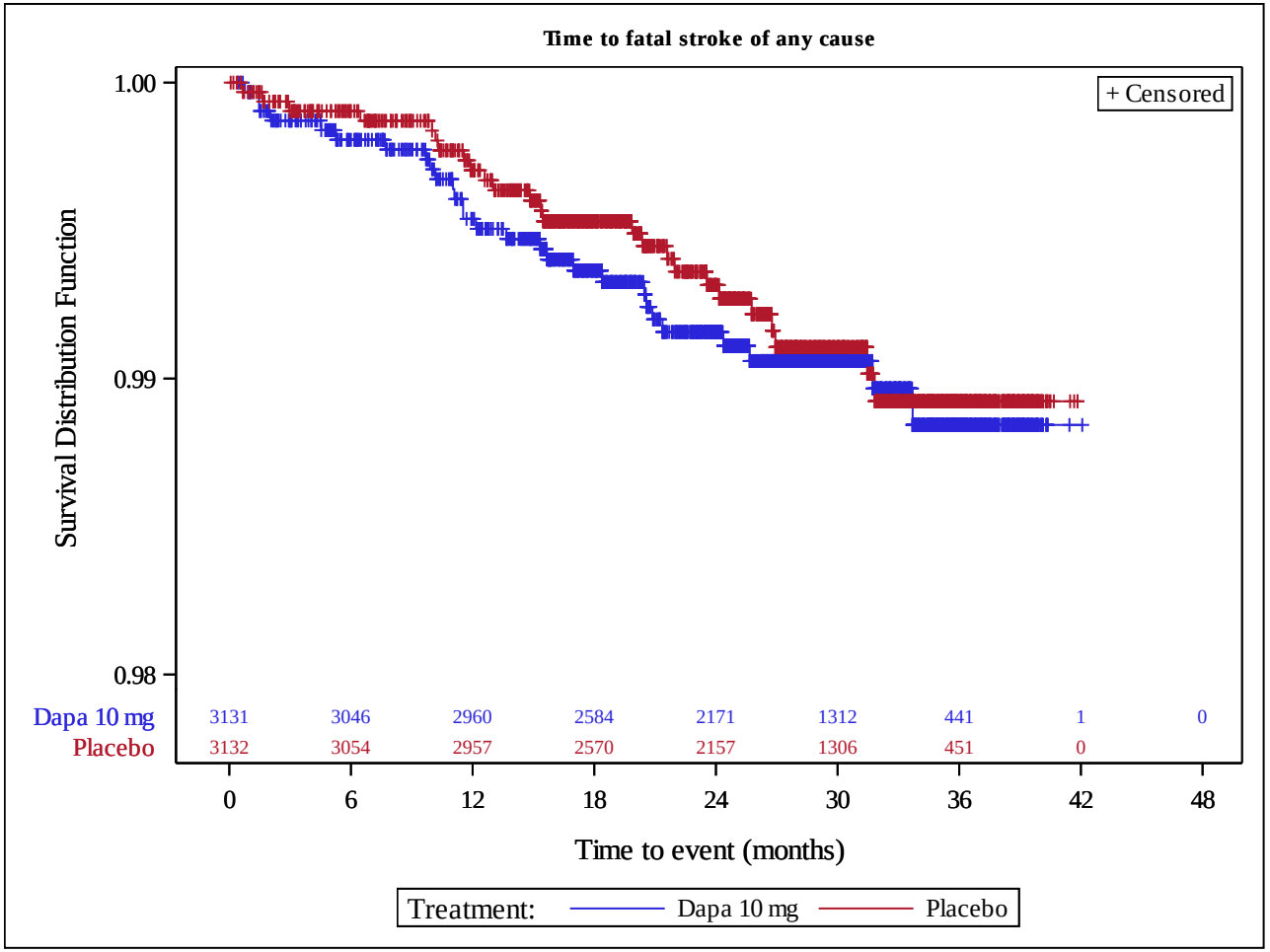
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to fatal stroke of any cause
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to first occurrence of doubling of serum-creatinin-levels accompanied by eGFR <=45 ml/min/1.73m^2
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
Overall	35/3131 (1.1)	0.76	36/3132 (1.1)	0.77	0.98 (0.62, 1.56)	0.9320	
Age							0.8957
<= median	23/1545 (1.5)	1.02	25/1604 (1.6)	1.04	0.98 (0.56, 1.73)	0.9483	
> median	12/1586 (0.8)	0.51	11/1528 (0.7)	0.48	1.04 (0.46, 2.35)	0.9291	
Gender							0.3845
Male	19/1767 (1.1)	0.71	15/1749 (0.9)	0.57	1.21 (0.61, 2.38)	0.5857	
Female	16/1364 (1.2)	0.82	21/1383 (1.5)	1.03	0.80 (0.42, 1.53)	0.4948	
Race							0.9186
White	24/2214 (1.1)	0.73	24/2225 (1.1)	0.72	1.01 (0.57, 1.78)	0.9718	
Black or African	1/ 81 (1.2)	0.96	2/ 78 (2.6)	1.93	0.32 (0.03, 3.76)	0.3632	
Asian	7/ 630 (1.1)	0.71	8/ 644 (1.2)	0.80	0.91 (0.33, 2.52)	0.8581	
Other	3/ 206 (1.5)	1.17	2/ 185 (1.1)	0.89	1.47 (0.24, 8.84)	0.6757	
Geographic region							0.9536
Asia	7/ 607 (1.2)	0.73	8/ 619 (1.3)	0.83	0.90 (0.33, 2.49)	0.8433	
Europe and Saudi Arabia	14/1494 (0.9)	0.59	13/1511 (0.9)	0.55	1.05 (0.49, 2.24)	0.8915	
North America	7/ 428 (1.6)	1.28	6/ 423 (1.4)	1.13	1.19 (0.40, 3.54)	0.7596	
Latin America	7/ 602 (1.2)	0.91	9/ 579 (1.6)	1.15	0.84 (0.31, 2.25)	0.7259	
NYHA class at enrolment							0.4095
II	24/2314 (1.0)	0.69	22/2399 (0.9)	0.61	1.13 (0.63, 2.01)	0.6835	
III or IV	11/ 817 (1.3)	0.96	14/ 732 (1.9)	1.32	0.73 (0.33, 1.60)	0.4300	
LVEF at enrolment							0.4252
<= 49	11/1067 (1.0)	0.73	7/1049 (0.7)	0.45	1.58 (0.61, 4.09)	0.3418	
50-59	17/1133 (1.5)	1.00	18/1123 (1.6)	1.07	0.94 (0.48, 1.82)	0.8443	
>= 60	7/ 931 (0.8)	0.50	11/ 960 (1.1)	0.77	0.66 (0.26, 1.71)	0.3949	
NT-proBNP at enrolment							0.1305
<= median	12/1555 (0.8)	0.52	19/1578 (1.2)	0.80	0.65 (0.32, 1.34)	0.2430	
> median	23/1576 (1.5)	0.99	17/1553 (1.1)	0.74	1.35 (0.72, 2.52)	0.3534	
Type 2 Diabetes Medical History							0.8902
Yes	22/1401 (1.6)	1.07	22/1405 (1.6)	1.06	1.01 (0.56, 1.82)	0.9863	
No	13/1730 (0.8)	0.51	14/1727 (0.8)	0.54	0.94 (0.44, 1.99)	0.8672	
Atrial fibrillation or flutter at enrolment ECG							0.9823
Yes	12/1327 (0.9)	0.60	12/1317 (0.9)	0.60	0.96 (0.43, 2.13)	0.9121	
No	23/1803 (1.3)	0.88	24/1814 (1.3)	0.90	0.99 (0.56, 1.76)	0.9740	
BMI (kg/m2) at enrolment							0.7543
< 30	16/1734 (0.9)	0.62	15/1736 (0.9)	0.57	1.05 (0.52, 2.13)	0.8864	
>= 30	19/1395 (1.4)	0.94	21/1392 (1.5)	1.03	0.92 (0.49, 1.71)	0.7941	
Baseline eGFR (mL/min/1.73m^2)							0.9842
< 60	20/1516 (1.3)	0.92	21/1554 (1.4)	0.93	0.98 (0.53, 1.81)	0.9532	
>= 60	15/1615 (0.9)	0.61	15/1577 (1.0)	0.63	0.97 (0.47, 1.98)	0.9278	
SBP at randomisation							0.7935
<= median	16/1568 (1.0)	0.70	15/1590 (0.9)	0.65	1.08 (0.53, 2.18)	0.8310	
> median	19/1563 (1.2)	0.81	21/1542 (1.4)	0.89	0.94 (0.51, 1.76)	0.8560	

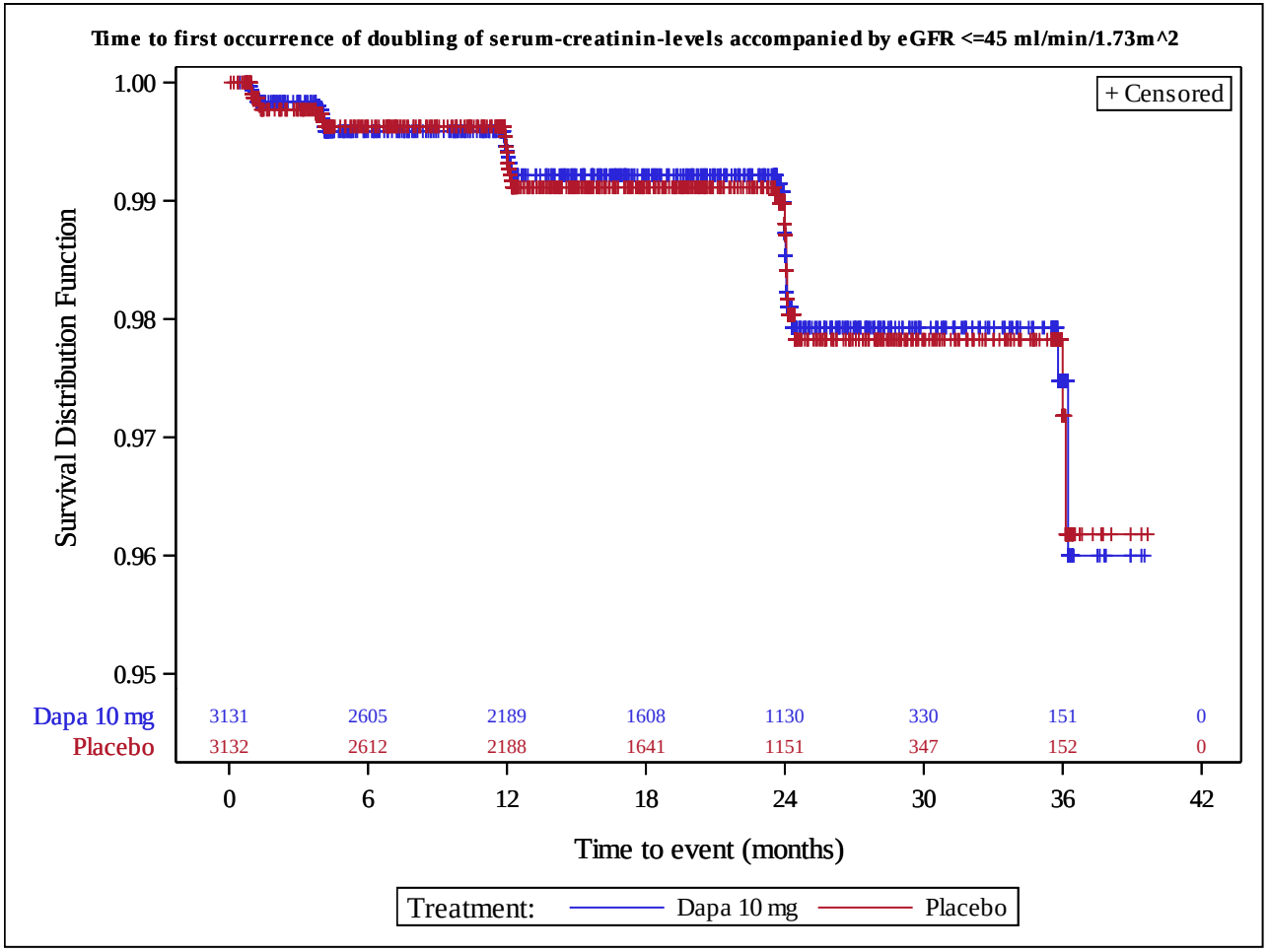
Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of time to first occurrence of doubling of serum-creatinin-levels accompanied by eGFR <=45 ml/min/1.73m^2
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Hazard Ratio (95% CI)	p-Value	p-Value for interaction
LVEF at enrolment 2							0.2428
<= 49	11/1067 (1.0)	0.73	7/1049 (0.7)	0.45	1.58 (0.61, 4.09)	0.3418	
>= 50	24/2064 (1.2)	0.77	29/2083 (1.4)	0.93	0.83 (0.48, 1.43)	0.5030	
Randomised during hospitalisation for HF or within 30 days of discharge							0.7398
Yes	7/ 328 (2.1)	1.67	6/ 326 (1.8)	1.40	1.17 (0.39, 3.47)	0.7839	
No	28/2803 (1.0)	0.67	30/2806 (1.1)	0.71	0.94 (0.56, 1.58)	0.8239	
MRAs at baseline							0.1333
Yes	16/1340 (1.2)	0.82	10/1327 (0.8)	0.51	1.60 (0.72, 3.52)	0.2470	
No	19/1791 (1.1)	0.72	26/1805 (1.4)	0.96	0.74 (0.41, 1.34)	0.3256	
ACEi+ARB at baseline							0.1475
Yes	30/2262 (1.3)	0.88	26/2281 (1.1)	0.74	1.18 (0.70, 1.99)	0.5438	
No	5/ 869 (0.6)	0.41	10/ 851 (1.2)	0.86	0.50 (0.17, 1.45)	0.2008	
ARNI at baseline							0.9621
Yes	1/ 165 (0.6)	0.50	0/ 136 (0.0)	0.00	NE		
No	34/2966 (1.1)	0.77	36/2996 (1.2)	0.80	0.96 (0.60, 1.54)	0.8705	
Beta Blocker at baseline							0.4063
Yes	28/2592 (1.1)	0.73	26/2585 (1.0)	0.67	1.09 (0.64, 1.86)	0.7445	
No	7/ 539 (1.3)	0.91	10/ 547 (1.8)	1.32	0.68 (0.26, 1.78)	0.4262	
Diuretics at baseline							0.6007
Yes	32/2793 (1.1)	0.77	34/2787 (1.2)	0.82	0.95 (0.58, 1.53)	0.8217	
No	3/ 338 (0.9)	0.62	2/ 345 (0.6)	0.39	1.57 (0.26, 9.39)	0.6226	

Event rates are presented as the number of subjects with event per 100 patient years of follow-up.
Hazard ratio for Dapa 10mg vs placebo, confidence intervals and 2-sided p-value are calculated from Cox proportional hazards model (Wald statistic) stratified by T2DM status at randomization, with factor for treatment group.
p-Value for interaction from Cox proportional hazards model stratified by T2DM status at randomization, with factors for the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).

AstraZeneca
Protocol: D169CC00001
Overall study population
Kaplan Meier Plot of time to first occurrence of doubling of serum-creatinin-levels accompanied by eGFR <=45 ml/min/1.73m^2
Full Analysis Set



Kaplan-Meier Plots for subgroups are only generated if test for interaction is significant (alpha=0.05).

AstraZeneca
Protocol: D169CC00001
Overall study population
Number of hospitalisations
Full Analysis Set

Analysis		Dapa 10 mg (N=3131) n (%)	Placebo (N=3132) n (%)
Number of HF Hospitalisation	1	224 (7.2)	271 (8.7)
	2	60 (1.9)	82 (2.6)
	3	34 (1.1)	33 (1.1)
	>=4	11 (0.4)	32 (1.0)
Number of Hospitalisation from any cause	1	709 (22.6)	683 (21.8)
	2	271 (8.7)	285 (9.1)
	3	103 (3.3)	133 (4.2)
	>=4	127 (4.1)	150 (4.8)

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of recurrent HF hospitalisations
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Dapa 10 mg (N=3131) Event rate	Placebo (N=3132) n/ N (%)	Placebo (N=3132) Event rate	Rate Ratio (95% CI)	p-Value	p-Value for interaction
Overall	508/3131 (16.2)	7.34	707/3132 (22.6)	10.25	0.72 (0.60, 0.85)	0.0002	
Age							0.9373
<= median	238/1545 (15.4)	6.93	344/1604 (21.4)	9.62	0.72 (0.56, 0.93)	0.0108	
> median	270/1586 (17.0)	7.75	363/1528 (23.8)	10.92	0.71 (0.56, 0.90)	0.0048	
Gender							0.9238
Male	313/1767 (17.7)	8.05	430/1749 (24.6)	11.31	0.71 (0.57, 0.89)	0.0032	
Female	195/1364 (14.3)	6.43	277/1383 (20.0)	8.94	0.72 (0.55, 0.94)	0.0169	
Race							0.4326
White	352/2214 (15.9)	7.07	530/2225 (23.8)	10.58	0.67 (0.55, 0.82)	<.0001	
Black or African	26/ 81 (32.1)	15.13	29/ 78 (37.2)	17.44	0.86 (0.30, 2.51)	0.7885	
Asian	124/ 630 (19.7)	9.15	137/ 644 (21.3)	9.97	0.91 (0.64, 1.31)	0.6180	
Other	6/ 206 (2.9)	1.47	11/ 185 (5.9)	3.15	0.51 (0.15, 1.72)	0.2742	
Geographic region							0.6934
Asia	114/ 607 (18.8)	8.73	134/ 619 (21.6)	10.20	0.85 (0.59, 1.23)	0.3991	
Europe and Saudi Arabia	244/1494 (16.3)	7.00	343/1511 (22.7)	9.72	0.72 (0.56, 0.91)	0.0071	
North America	113/ 428 (26.4)	12.44	179/ 423 (42.3)	20.38	0.61 (0.41, 0.92)	0.0170	
Latin America	37/ 602 (6.1)	3.04	51/ 579 (8.8)	4.32	0.72 (0.44, 1.16)	0.1730	
NYHA class at enrolment							0.1349
II	307/2314 (13.3)	5.94	492/2399 (20.5)	9.22	0.64 (0.52, 0.80)	<.0001	
III or IV	201/ 817 (24.6)	11.51	214/ 732 (29.2)	13.68	0.85 (0.64, 1.12)	0.2442	
LVEF at enrolment							0.4512
<= 49	199/1067 (18.7)	8.70	263/1049 (25.1)	11.66	0.74 (0.55, 1.00)	0.0500	
50-59	161/1133 (14.2)	6.33	258/1123 (23.0)	10.20	0.62 (0.47, 0.82)	0.0010	
>= 60	148/ 931 (15.9)	7.09	186/ 960 (19.4)	8.79	0.81 (0.59, 1.12)	0.1966	
NT-proBNP at enrolment							0.4875
<= median	165/1555 (10.6)	4.70	216/1578 (13.7)	6.03	0.78 (0.57, 1.06)	0.1126	
> median	343/1576 (21.8)	10.06	491/1553 (31.6)	14.80	0.68 (0.55, 0.84)	0.0003	
Type 2 Diabetes Medical History							0.2360
Yes	289/1401 (20.6)	9.31	365/1405 (26.0)	11.80	0.79 (0.62, 1.01)	0.0567	
No	219/1730 (12.7)	5.74	342/1727 (19.8)	8.98	0.64 (0.50, 0.82)	0.0004	
Atrial fibrillation or flutter at enrolment ECG							0.5681
Yes	226/1327 (17.0)	7.67	332/1317 (25.2)	11.35	0.68 (0.53, 0.87)	0.0022	
No	282/1803 (15.6)	7.11	375/1814 (20.7)	9.44	0.75 (0.59, 0.96)	0.0202	
BMI (kg/m2) at enrolment							0.2194
< 30	252/1734 (14.5)	6.67	309/1736 (17.8)	8.29	0.81 (0.63, 1.03)	0.0850	
>= 30	256/1395 (18.4)	8.16	398/1392 (28.6)	12.59	0.65 (0.51, 0.83)	0.0005	
Baseline eGFR (mL/min/1.73m^2)							0.7592
< 60	305/1516 (20.1)	9.36	441/1554 (28.4)	13.16	0.71 (0.57, 0.88)	0.0018	
>= 60	203/1615 (12.6)	5.55	266/1577 (16.9)	7.50	0.75 (0.56, 0.99)	0.0448	
SBP at randomisation							0.0711
<= median	283/1568 (18.0)	8.36	339/1590 (21.3)	9.91	0.84 (0.66, 1.08)	0.1706	
> median	225/1563 (14.4)	6.37	368/1542 (23.9)	10.58	0.61 (0.47, 0.78)	0.0001	
LVEF at enrolment 2							0.7454
<= 49	199/1067 (18.7)	8.70	263/1049 (25.1)	11.66	0.74 (0.55, 1.00)	0.0500	
>= 50	309/2064 (15.0)	6.67	444/2083 (21.3)	9.56	0.70 (0.57, 0.86)	0.0010	

Event rates are presented as the number of events per 100 patient years of follow-up.
Rate ratio for Dapa 10 mg vs placebo, CI and 2-sided p-value are calculated from the LWYY (Lin Wei Yang Ying) proportional rates model stratified by T2DM status at randomisation, with a factor for treatment group as a covariate.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of recurrent HF hospitalisations
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Rate Ratio (95% CI)	p-Value	p-Value for interaction
Randomised during hospitalisation for HF or within 30 days of discharge							0.5571
Yes	112/ 328 (34.1)	16.54	170/ 326 (52.1)	25.35	0.65 (0.43, 0.98)	0.0393	
No	396/2803 (14.1)	6.35	537/2806 (19.1)	8.62	0.74 (0.61, 0.89)	0.0015	
MRAs at baseline							0.2928
Yes	201/1340 (15.0)	6.92	306/1327 (23.1)	10.70	0.64 (0.49, 0.85)	0.0017	
No	307/1791 (17.1)	7.65	401/1805 (22.2)	9.93	0.78 (0.62, 0.97)	0.0275	
ACEi+ARB at baseline							0.8549
Yes	324/2262 (14.3)	6.35	464/2281 (20.3)	9.02	0.71 (0.57, 0.87)	0.0013	
No	184/ 869 (21.2)	10.12	243/ 851 (28.6)	13.83	0.73 (0.54, 0.98)	0.0394	
ARNI at baseline							0.5763
Yes	46/ 165 (27.9)	14.50	42/ 136 (30.9)	16.52	0.81 (0.44, 1.52)	0.5211	
No	462/2966 (15.6)	7.00	665/2996 (22.2)	10.01	0.70 (0.59, 0.84)	0.0001	
Beta Blocker at baseline							0.2223
Yes	421/2592 (16.2)	7.32	557/2585 (21.5)	9.69	0.75 (0.62, 0.92)	0.0045	
No	87/ 539 (16.1)	7.49	150/ 547 (27.4)	13.04	0.58 (0.40, 0.84)	0.0040	
Diuretics at baseline							0.9086
Yes	473/2793 (16.9)	7.66	655/2787 (23.5)	10.66	0.72 (0.60, 0.86)	0.0003	
No	35/ 338 (10.4)	4.72	52/ 345 (15.1)	6.89	0.69 (0.33, 1.45)	0.3242	

Event rates are presented as the number of events per 100 patient years of follow-up.
Rate ratio for Dapa 10 mg vs placebo, CI and 2-sided p-value are calculated from the LWYY (Lin Wei Yang Ying) proportional rates model stratified by T2DM status at randomisation, with a factor for treatment group as a covariate.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of recurrent hospitalisations from any cause
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Rate Ratio (95% CI)	p-Value	p-Value for interaction
Overall	2224/3131 (71.0)	32.15	2479/3132 (79.2)	35.92	0.90 (0.82, 0.98)	0.0154	
Age							0.8588
<= median	1059/1545 (68.5)	30.84	1224/1604 (76.3)	34.22	0.90 (0.79, 1.02)	0.1103	
> median	1165/1586 (73.5)	33.45	1255/1528 (82.1)	37.76	0.89 (0.78, 1.00)	0.0555	
Gender							0.4127
Male	1288/1767 (72.9)	33.14	1452/1749 (83.0)	38.18	0.87 (0.77, 0.97)	0.0170	
Female	936/1364 (68.6)	30.88	1027/1383 (74.3)	33.15	0.93 (0.81, 1.07)	0.3345	
Race							0.7201
White	1549/2214 (70.0)	31.10	1755/2225 (78.9)	35.02	0.89 (0.80, 0.99)	0.0269	
Black or African	83/ 81 (102.5)	48.31	87/ 78 (111.5)	52.31	0.92 (0.52, 1.62)	0.7682	
Asian	513/ 630 (81.4)	37.84	581/ 644 (90.2)	42.30	0.89 (0.74, 1.07)	0.2219	
Other	79/ 206 (38.3)	19.30	56/ 185 (30.3)	16.04	1.24 (0.73, 2.11)	0.4294	
Geographic region							0.9863
Asia	484/ 607 (79.7)	37.05	559/ 619 (90.3)	42.57	0.87 (0.72, 1.05)	0.1378	
Europe and Saudi Arabia	1006/1494 (67.3)	28.86	1120/1511 (74.1)	31.75	0.91 (0.80, 1.03)	0.1210	
North America	489/ 428 (114.3)	53.85	532/ 423 (125.8)	60.57	0.89 (0.72, 1.11)	0.2948	
Latin America	245/ 602 (40.7)	20.12	268/ 579 (46.3)	22.68	0.89 (0.71, 1.13)	0.3332	
NYHA class at enrolment							0.2222
II	1536/2314 (66.4)	29.71	1843/2399 (76.8)	34.55	0.86 (0.77, 0.95)	0.0046	
III or IV	688/ 817 (84.2)	39.39	635/ 732 (86.7)	40.59	0.97 (0.82, 1.15)	0.7533	
LVEF at enrolment							0.7287
<= 49	750/1067 (70.3)	32.79	808/1049 (77.0)	35.82	0.91 (0.78, 1.07)	0.2656	
50-59	820/1133 (72.4)	32.25	887/1123 (79.0)	35.06	0.92 (0.80, 1.06)	0.2635	
>= 60	654/ 931 (70.2)	31.33	784/ 960 (81.7)	37.07	0.85 (0.72, 1.00)	0.0497	
NT-proBNP at enrolment							0.6269
<= median	950/1555 (61.1)	27.08	1059/1578 (67.1)	29.58	0.91 (0.80, 1.04)	0.1859	
> median	1274/1576 (80.8)	37.36	1420/1553 (91.4)	42.80	0.87 (0.78, 0.99)	0.0292	
Type 2 Diabetes Medical History							0.6466
Yes	1195/1401 (85.3)	38.48	1305/1405 (92.9)	42.18	0.91 (0.80, 1.04)	0.1568	
No	1029/1730 (59.5)	26.99	1174/1727 (68.0)	30.84	0.88 (0.77, 0.99)	0.0375	
Atrial fibrillation or flutter at enrolment ECG							0.7234
Yes	921/1327 (69.4)	31.25	1044/1317 (79.3)	35.69	0.88 (0.77, 1.00)	0.0540	
No	1302/1803 (72.2)	32.81	1435/1814 (79.1)	36.13	0.91 (0.80, 1.02)	0.1126	
BMI (kg/m2) at enrolment							0.9954
< 30	1153/1734 (66.5)	30.52	1273/1736 (73.3)	34.13	0.89 (0.79, 1.01)	0.0691	
>= 30	1070/1395 (76.7)	34.12	1205/1392 (86.6)	38.11	0.89 (0.78, 1.02)	0.1022	
Baseline eGFR (mL/min/1.73m^2)							0.9497
< 60	1291/1516 (85.2)	39.61	1471/1554 (94.7)	43.89	0.90 (0.79, 1.01)	0.0730	
>= 60	933/1615 (57.8)	25.51	1008/1577 (63.9)	28.42	0.90 (0.79, 1.03)	0.1215	
SBP at randomisation							0.2044
<= median	1118/1568 (71.3)	33.02	1183/1590 (74.4)	34.58	0.95 (0.84, 1.08)	0.4500	
> median	1106/1563 (70.8)	31.32	1296/1542 (84.0)	37.25	0.85 (0.75, 0.96)	0.0104	
LVEF at enrolment 2							0.7710
<= 49	750/1067 (70.3)	32.79	808/1049 (77.0)	35.82	0.91 (0.78, 1.07)	0.2656	
>= 50	1474/2064 (71.4)	31.84	1671/2083 (80.2)	35.97	0.89 (0.80, 0.99)	0.0289	

Event rates are presented as the number of events per 100 patient years of follow-up.
Rate ratio for Dapa 10 mg vs placebo, CI and 2-sided p-value are calculated from the LWYY (Lin Wei Yang Ying) proportional rates model stratified by T2DM status at randomisation, with a factor for treatment group as a covariate.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of recurrent hospitalisations from any cause
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	 Event rate	Placebo (N=3132) n/ N (%)	 Event rate	Rate Ratio (95% CI)	p-Value	p-Value for interaction
Randomised during hospitalisation for HF or within 30 days of discharge							0.1913
Yes	315/ 328 (96.0)	46.51	404/ 326 (123.9)	60.24	0.76 (0.59, 0.99)	0.0396	
No	1909/2803 (68.1)	30.59	2075/2806 (73.9)	33.31	0.92 (0.84, 1.01)	0.0818	
MRAs at baseline							0.6903
Yes	897/1340 (66.9)	30.87	1001/1327 (75.4)	34.99	0.88 (0.76, 1.01)	0.0724	
No	1327/1791 (74.1)	33.08	1478/1805 (81.9)	36.59	0.91 (0.81, 1.02)	0.1087	
ACEi+ARB at baseline							0.6597
Yes	1529/2262 (67.6)	29.98	1705/2281 (74.7)	33.15	0.91 (0.82, 1.01)	0.0641	
No	695/ 869 (80.0)	38.24	774/ 851 (91.0)	44.06	0.87 (0.73, 1.03)	0.0991	
ARNI at baseline							0.9323
Yes	118/ 165 (71.5)	37.19	101/ 136 (74.3)	39.73	0.88 (0.58, 1.34)	0.5592	
No	2106/2966 (71.0)	31.91	2378/2996 (79.4)	35.78	0.89 (0.81, 0.98)	0.0156	
Beta Blocker at baseline							0.5400
Yes	1795/2592 (69.3)	31.19	1973/2585 (76.3)	34.31	0.91 (0.82, 1.00)	0.0545	
No	429/ 539 (79.6)	36.92	506/ 547 (92.5)	43.99	0.84 (0.68, 1.04)	0.1093	
Diuretics at baseline							0.5220
Yes	2037/2793 (72.9)	32.99	2245/2787 (80.6)	36.53	0.90 (0.82, 0.99)	0.0330	
No	187/ 338 (55.3)	25.20	234/ 345 (67.8)	31.00	0.81 (0.60, 1.10)	0.1798	

Event rates are presented as the number of events per 100 patient years of follow-up.
Rate ratio for Dapa 10 mg vs placebo, CI and 2-sided p-value are calculated from the LWYY (Lin Wei Yang Ying) proportional rates model stratified by T2DM status at randomisation, with a factor for treatment group as a covariate.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Dapa 10 mg (N=3131) Compliance	Placebo (N=3132) n/ N#	Placebo (N=3132) Compliance
Clinical Summary Score	Visit 2 (Baseline)	2901/3131	92.65%	2886/3132	92.15%
	Visit 3 (1 Month)	2675/3130	85.46%	2678/3128	85.61%
	Visit 4 (4 Months)	2455/3087	79.53%	2434/3087	78.85%
	Visit 5 (8 Months)	2241/3030	73.96%	2246/3032	74.08%
	Study Closure Visit	2159/2621	82.37%	2154/2599	82.88%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)		Placebo (N=3132)	
	Visit	n/ N#	Compliance	n/ N#	Compliance
Overall Summary Score	Visit 2 (Baseline)	2901/3131	92.65%	2886/3132	92.15%
	Visit 3 (1 Month)	2675/3130	85.46%	2678/3128	85.61%
	Visit 4 (4 Months)	2455/3087	79.53%	2434/3087	78.85%
	Visit 5 (8 Months)	2241/3030	73.96%	2246/3032	74.08%
	Study Closure Visit	2159/2621	82.37%	2154/2599	82.88%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Compliance	Placebo (N=3132) n/ N#	Compliance
Physical Limitation	Visit 2 (Baseline)	2859/3131	91.31%	2850/3132	91.00%
	Visit 3 (1 Month)	2622/3130	83.77%	2629/3128	84.05%
	Visit 4 (4 Months)	2406/3087	77.94%	2398/3087	77.68%
	Visit 5 (8 Months)	2188/3030	72.21%	2202/3032	72.63%
	Study Closure Visit	2096/2621	79.97%	2093/2599	80.53%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Dapa 10 mg (N=3131) Compliance	Placebo (N=3132) n/ N#	Placebo (N=3132) Compliance
Quality of Life	Visit 2 (Baseline)	2901/3131	92.65%	2886/3132	92.15%
	Visit 3 (1 Month)	2675/3130	85.46%	2678/3128	85.61%
	Visit 4 (4 Months)	2455/3087	79.53%	2434/3087	78.85%
	Visit 5 (8 Months)	2241/3030	73.96%	2246/3032	74.08%
	Study Closure Visit	2159/2621	82.37%	2154/2599	82.88%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Dapa 10 mg (N=3131) Compliance	Placebo (N=3132) n/ N#	Placebo (N=3132) Compliance
Symptom Burden	Visit 2 (Baseline)	2901/3131	92.65%	2886/3132	92.15%
	Visit 3 (1 Month)	2675/3130	85.46%	2678/3128	85.61%
	Visit 4 (4 Months)	2455/3087	79.53%	2434/3087	78.85%
	Visit 5 (8 Months)	2241/3030	73.96%	2246/3032	74.08%
	Study Closure Visit	2159/2621	82.37%	2154/2599	82.88%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Dapa 10 mg (N=3131) Compliance	Placebo (N=3132) n/ N#	Placebo (N=3132) Compliance
Self Efficacy	Visit 2 (Baseline)	2901/3131	92.65%	2886/3132	92.15%
	Visit 3 (1 Month)	2675/3130	85.46%	2678/3128	85.61%
	Visit 4 (4 Months)	2455/3087	79.53%	2434/3087	78.85%
	Visit 5 (8 Months)	2241/3030	73.96%	2246/3032	74.08%
	Study Closure Visit	2159/2621	82.37%	2154/2599	82.88%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Dapa 10 mg (N=3131) Compliance	Placebo (N=3132) n/ N#	Placebo (N=3132) Compliance
Symptom Frequency	Visit 2 (Baseline)	2901/3131	92.65%	2886/3132	92.15%
	Visit 3 (1 Month)	2675/3130	85.46%	2678/3128	85.61%
	Visit 4 (4 Months)	2455/3087	79.53%	2434/3087	78.85%
	Visit 5 (8 Months)	2241/3030	73.96%	2246/3032	74.08%
	Study Closure Visit	2159/2621	82.37%	2154/2599	82.88%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Dapa 10 mg (N=3131) Compliance	Placebo (N=3132) n/ N#	Placebo (N=3132) Compliance
Social Limitation	Visit 2 (Baseline)	2743/3131	87.61%	2732/3132	87.23%
	Visit 3 (1 Month)	2524/3130	80.64%	2533/3128	80.98%
	Visit 4 (4 Months)	2301/3087	74.54%	2276/3087	73.73%
	Visit 5 (8 Months)	2082/3030	68.71%	2084/3032	68.73%
	Study Closure Visit	1949/2621	74.36%	1952/2599	75.11%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Dapa 10 mg (N=3131) Compliance	Placebo (N=3132) n/ N#	Placebo (N=3132) Compliance
Symptom Stability	Visit 2 (Baseline)	2901/3131	92.65%	2886/3132	92.15%
	Visit 3 (1 Month)	2675/3130	85.46%	2678/3128	85.61%
	Visit 4 (4 Months)	2455/3087	79.53%	2434/3087	78.85%
	Visit 5 (8 Months)	2241/3030	73.96%	2246/3032	74.08%
	Study Closure Visit	2159/2621	82.37%	2154/2599	82.88%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of KCCQ scores by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Compliance	Placebo (N=3132) n/ N#	Compliance
Total Symptom Score	Visit 2 (Baseline)	2901/3131	92.65%	2886/3132	92.15%
	Visit 3 (1 Month)	2675/3130	85.46%	2678/3128	85.61%
	Visit 4 (4 Months)	2455/3087	79.53%	2434/3087	78.85%
	Visit 5 (8 Months)	2241/3030	73.96%	2246/3032	74.08%
	Study Closure Visit	2159/2621	82.37%	2154/2599	82.88%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of KCCQ scores at baseline
Full Analysis Set

		Dapa 10 mg (N=3131)	Placebo (N=3132)
		n (%)	n (%)
Clinical Summary Score	n	2901	2886
	15-85 points	2154 (74.3)	2162 (74.9)
	<=15 points	20 (0.7)	19 (0.7)
	>=85 points	727 (25.1)	705 (24.4)
Overall Summary Score	n	2901	2886
	15-85 points	2236 (77.1)	2253 (78.1)
	<=15 points	28 (1.0)	16 (0.6)
	>=85 points	637 (22.0)	617 (21.4)
Total Symptom Score	n	2901	2886
	15-85 points	1970 (67.9)	2002 (69.4)
	<=15 points	38 (1.3)	30 (1.0)
	>=85 points	893 (30.8)	854 (29.6)

n is the number of patients with non-missing values at baseline.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Clinical Summary Score	Visit 2 (Baseline)	2901	68.02 (21.13)			2886	68.67 (20.24)		
	Visit 3 (1 Month)	2675	74.55 (18.99)	2638	6.45 (15.66)	2678	73.32 (19.10)	2637	4.47 (15.49)
	Visit 4 (4 Months)	2455	75.64 (18.93)	2416	6.90 (17.54)	2434	74.25 (19.13)	2392	4.98 (17.05)
	Visit 5 (8 Months)	2241	76.65 (18.35)	2207	7.11 (17.77)	2246	74.41 (19.57)	2204	4.68 (18.17)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Overall Summary Score	Visit 2 (Baseline)	2901	66.28 (20.74)			2886	66.99 (19.73)		
	Visit 3 (1 Month)	2675	72.59 (18.52)	2638	6.21 (14.89)	2678	71.52 (18.74)	2637	4.35 (14.62)
	Visit 4 (4 Months)	2455	73.86 (18.65)	2416	6.84 (16.95)	2434	72.86 (18.63)	2392	5.26 (16.20)
	Visit 5 (8 Months)	2241	75.06 (17.92)	2207	7.27 (17.62)	2246	72.98 (19.18)	2204	5.02 (17.13)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Physical Limitation	Visit 2 (Baseline)	2859	64.41 (23.66)			2850	65.47 (23.00)		
	Visit 3 (1 Month)	2622	69.19 (22.64)	2561	4.55 (19.30)	2629	68.37 (22.50)	2566	2.74 (18.16)
	Visit 4 (4 Months)	2406	70.43 (22.67)	2342	5.02 (20.23)	2398	69.14 (22.66)	2338	3.21 (19.60)
	Visit 5 (8 Months)	2188	71.22 (22.34)	2133	5.08 (21.10)	2202	69.27 (22.63)	2144	2.92 (20.33)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Quality of Life	Visit 2 (Baseline)	2901	60.60 (23.63)			2886	61.80 (22.49)		
	Visit 3 (1 Month)	2675	66.89 (21.06)	2638	6.20 (19.69)	2678	66.04 (21.63)	2637	4.03 (19.26)
	Visit 4 (4 Months)	2455	68.32 (21.54)	2416	7.01 (21.41)	2434	68.14 (21.14)	2392	5.68 (20.99)
	Visit 5 (8 Months)	2241	69.91 (20.69)	2207	7.94 (22.27)	2246	68.47 (21.34)	2204	5.96 (20.56)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Symptom Burden	Visit 2 (Baseline)	2901	70.90 (23.36)			2886	71.56 (22.44)		
	Visit 3 (1 Month)	2675	78.58 (20.34)	2638	7.59 (19.30)	2678	77.23 (20.66)	2637	5.51 (19.05)
	Visit 4 (4 Months)	2455	79.56 (19.99)	2416	7.96 (21.20)	2434	78.10 (20.55)	2392	5.84 (20.68)
	Visit 5 (8 Months)	2241	80.37 (19.73)	2207	7.76 (21.15)	2246	78.24 (20.92)	2204	5.52 (21.77)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Self Efficacy	Visit 2 (Baseline)	2901	73.09 (23.14)			2886	73.05 (23.49)		
	Visit 3 (1 Month)	2675	77.35 (21.04)	2638	4.60 (21.20)	2678	77.80 (20.68)	2637	4.90 (22.19)
	Visit 4 (4 Months)	2455	79.06 (20.13)	2416	5.87 (22.23)	2434	78.54 (20.02)	2392	5.46 (22.25)
	Visit 5 (8 Months)	2241	79.76 (19.86)	2207	7.04 (23.36)	2246	79.19 (19.60)	2204	6.66 (23.02)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Symptom Frequency	Visit 2 (Baseline)	2901	68.71 (23.88)			2886	68.96 (23.19)		
	Visit 3 (1 Month)	2675	75.72 (20.98)	2638	7.01 (19.58)	2678	74.24 (21.62)	2637	5.10 (19.48)
	Visit 4 (4 Months)	2455	76.75 (20.91)	2416	7.53 (21.29)	2434	75.38 (21.26)	2392	5.86 (20.87)
	Visit 5 (8 Months)	2241	78.13 (19.90)	2207	8.18 (21.17)	2246	75.50 (22.02)	2204	5.51 (22.59)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Social Limitation	Visit 2 (Baseline)	2743	66.67 (26.93)			2732	66.92 (25.95)		
	Visit 3 (1 Month)	2524	72.27 (24.54)	2398	5.42 (22.35)	2533	71.64 (24.71)	2395	4.48 (21.73)
	Visit 4 (4 Months)	2301	74.20 (24.23)	2171	6.26 (24.29)	2276	73.34 (24.05)	2144	5.70 (22.74)
	Visit 5 (8 Months)	2082	75.45 (23.39)	1966	6.93 (25.76)	2084	73.13 (24.61)	1963	4.91 (24.13)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Symptom Stability	Visit 2 (Baseline)	2901	54.30 (18.18)			2886	54.57 (18.41)		
	Visit 3 (1 Month)	2675	60.27 (19.52)	2638	6.07 (24.42)	2678	58.84 (19.41)	2637	4.19 (24.43)
	Visit 4 (4 Months)	2455	58.82 (20.01)	2416	4.72 (25.02)	2434	57.72 (19.78)	2392	2.80 (25.21)
	Visit 5 (8 Months)	2241	57.99 (19.52)	2207	3.61 (24.82)	2246	56.98 (20.20)	2204	2.26 (25.42)

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of KCCQ scores by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Total Symptom Score	Visit 2 (Baseline)	2901	69.80 (22.62)			2886	70.26 (21.71)		
	Visit 3 (1 Month)	2675	77.15 (19.71)	2638	7.30 (17.86)	2678	75.74 (20.18)	2637	5.30 (17.71)
	Visit 4 (4 Months)	2455	78.16 (19.52)	2416	7.75 (19.85)	2434	76.74 (19.98)	2392	5.85 (19.23)
	Visit 5 (8 Months)	2241	79.25 (18.85)	2207	7.97 (19.70)	2246	76.87 (20.60)	2204	5.51 (20.72)

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Clinical Summary Score	Visit 3 (1 Month)		6.08 (0.27)		4.31 (0.27)	1.76 (1.03, 2.50)	<.0001	0.13 (0.08, 0.18)
	Visit 4 (4 Months)		6.83 (0.30)		4.89 (0.30)	1.93 (1.11, 2.76)	<.0001	0.13 (0.08, 0.19)
	Visit 5 (8 Months)		6.99 (0.32)		4.70 (0.32)	2.30 (1.41, 3.19)	<.0001	0.15 (0.09, 0.21)
	OVERALL	2801	6.63 (0.23)	2805	4.63 (0.23)	2.00 (1.36, 2.64)	<.0001	0.16 (0.11, 0.22)

N displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
OVERALL row displays model estimates over time.
LS Means and difference of LS Means estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Overall Summary Score	Visit 3 (1 Month)		5.85 (0.25)		4.23 (0.25)	1.62 (0.92, 2.32)	<.0001	0.12 (0.07, 0.18)
	Visit 4 (4 Months)		6.76 (0.29)		5.19 (0.29)	1.56 (0.76, 2.36)	0.0001	0.11 (0.05, 0.17)
	Visit 5 (8 Months)		7.10 (0.31)		5.02 (0.31)	2.07 (1.21, 2.94)	<.0001	0.14 (0.08, 0.20)
	OVERALL	2801	6.57 (0.23)	2805	4.81 (0.23)	1.75 (1.12, 2.38)	<.0001	0.15 (0.09, 0.20)

N displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
OVERALL row displays model estimates over time.
LS Means and difference of LS Means estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Physical Limitation	Visit 3 (1 Month)		4.15 (0.33)		2.63 (0.33)	1.53 (0.61, 2.44)	0.0011	0.09 (0.04, 0.15)
	Visit 4 (4 Months)		4.84 (0.36)		3.13 (0.36)	1.71 (0.71, 2.70)	0.0008	0.10 (0.04, 0.16)
	Visit 5 (8 Months)		4.85 (0.39)		2.90 (0.39)	1.95 (0.88, 3.02)	0.0003	0.11 (0.05, 0.17)
	OVERALL	2750	4.61 (0.28)	2758	2.88 (0.28)	1.73 (0.95, 2.51)	<.0001	0.12 (0.06, 0.17)

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OVERALL row displays model estimates over time.
LS Means and difference of LS Means estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.

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Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Quality of Life	Visit 3 (1 Month)		5.67 (0.33)		4.12 (0.33)	1.55 (0.65, 2.45)	0.0008	0.09 (0.04, 0.15)
	Visit 4 (4 Months)		6.77 (0.36)		5.86 (0.36)	0.91 (-0.09, 1.91)	0.0750	0.05 (-0.01, 0.11)
	Visit 5 (8 Months)		7.67 (0.37)		6.16 (0.37)	1.52 (0.48, 2.55)	0.0042	0.09 (0.03, 0.15)
	OVERALL	2801	6.70 (0.28)	2805	5.38 (0.28)	1.32 (0.56, 2.09)	0.0007	0.09 (0.04, 0.14)

N displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
OVERALL row displays model estimates over time.
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Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Symptom Burden	Visit 3 (1 Month)		7.09 (0.31)		5.29 (0.31)	1.79 (0.92, 2.67)	<.0001	0.11 (0.06, 0.17)
	Visit 4 (4 Months)		7.88 (0.35)		5.81 (0.35)	2.07 (1.11, 3.03)	<.0001	0.12 (0.07, 0.18)
	Visit 5 (8 Months)		7.77 (0.37)		5.62 (0.37)	2.15 (1.13, 3.17)	<.0001	0.12 (0.07, 0.18)
	OVERALL	2801	7.58 (0.26)	2805	5.57 (0.26)	2.00 (1.28, 2.73)	<.0001	0.14 (0.09, 0.20)

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LS Means and difference of LS Means estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.

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Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Self Efficacy	Visit 3 (1 Month)		4.56 (0.35)		4.92 (0.35)	-0.36 (-1.32, 0.59)	0.4576	-0.02 (-0.07, 0.03)
	Visit 4 (4 Months)		5.94 (0.35)		5.56 (0.36)	0.38 (-0.60, 1.37)	0.4468	0.02 (-0.03, 0.08)
	Visit 5 (8 Months)		6.83 (0.37)		6.41 (0.37)	0.43 (-0.61, 1.46)	0.4215	0.02 (-0.03, 0.08)
	OVERALL	2801	5.78 (0.26)	2805	5.63 (0.26)	0.15 (-0.59, 0.88)	0.6915	0.01 (-0.04, 0.06)

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Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Symptom Frequency	Visit 3 (1 Month)		6.68 (0.32)		4.90 (0.32)	1.79 (0.89, 2.68)	<.0001	0.11 (0.05, 0.16)
	Visit 4 (4 Months)		7.46 (0.35)		5.75 (0.35)	1.71 (0.73, 2.68)	0.0006	0.10 (0.04, 0.16)
	Visit 5 (8 Months)		8.11 (0.38)		5.56 (0.38)	2.55 (1.51, 3.60)	<.0001	0.14 (0.09, 0.20)
	OVERALL	2801	7.42 (0.27)	2805	5.40 (0.27)	2.01 (1.27, 2.76)	<.0001	0.14 (0.09, 0.19)

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Analysis of change from baseline of KCCQ scores
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	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Social Limitation	Visit 3 (1 Month)		5.09 (0.39)		4.17 (0.39)	0.92 (-0.16, 2.00)	0.0963	0.05 (-0.01, 0.10)
	Visit 4 (4 Months)		6.12 (0.42)		5.47 (0.42)	0.65 (-0.52, 1.82)	0.2760	0.03 (-0.03, 0.09)
	Visit 5 (8 Months)		6.76 (0.46)		4.98 (0.46)	1.78 (0.51, 3.06)	0.0062	0.09 (0.02, 0.15)
	OVERALL	2625	5.99 (0.33)	2625	4.87 (0.33)	1.12 (0.21, 2.02)	0.0159	0.07 (0.01, 0.12)

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Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Symptom Stability	Visit 3 (1 Month)		5.82 (0.37)		4.21 (0.37)	1.60 (0.57, 2.63)	0.0024	0.08 (0.03, 0.14)
	Visit 4 (4 Months)		4.40 (0.40)		3.09 (0.40)	1.31 (0.20, 2.42)	0.0205	0.07 (0.01, 0.12)
	Visit 5 (8 Months)		3.42 (0.42)		2.48 (0.42)	0.94 (-0.22, 2.10)	0.1131	0.05 (-0.01, 0.11)
	OVERALL	2801	4.55 (0.27)	2805	3.26 (0.27)	1.28 (0.53, 2.03)	0.0008	0.09 (0.04, 0.14)

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Overall study population
Analysis of change from baseline of KCCQ scores
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Total Symptom Score	Visit 3 (1 Month)		6.91 (0.30)		5.10 (0.30)	1.81 (0.99, 2.62)	<.0001	0.12 (0.06, 0.17)
	Visit 4 (4 Months)		7.68 (0.33)		5.77 (0.33)	1.91 (1.01, 2.82)	<.0001	0.12 (0.06, 0.18)
	Visit 5 (8 Months)		7.93 (0.35)		5.57 (0.35)	2.36 (1.39, 3.32)	<.0001	0.14 (0.08, 0.20)
	OVERALL	2801	7.51 (0.25)	2805	5.48 (0.25)	2.02 (1.33, 2.72)	<.0001	0.15 (0.10, 0.20)

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LS Means and difference of LS Means estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Clinical Summary Score	Age												0.5130
	<= median	1443	69.20 (21.49)	1394	7.25 (0.32)	1507	68.93 (20.60)	1471	5.40 (0.32)	1.84 (0.95, 2.73)	<.0001	0.15 (0.08, 0.23)	
	> median	1458	66.85 (20.70)	1407	6.04 (0.33)	1379	68.38 (19.86)	1334	3.76 (0.34)	2.27 (1.35, 3.20)	<.0001	0.18 (0.11, 0.26)	
	Gender												0.6097
	Male	1691	71.30 (20.43)	1630	6.13 (0.30)	1648	71.87 (19.93)	1608	4.30 (0.30)	1.83 (1.01, 2.66)	<.0001	0.15 (0.08, 0.22)	
	Female	1210	63.44 (21.24)	1171	7.29 (0.37)	1238	64.39 (19.88)	1197	5.12 (0.36)	2.17 (1.16, 3.19)	<.0001	0.17 (0.09, 0.25)	
	Race												0.6593
	White	2087	65.55 (20.26)	2006	7.14 (0.28)	2094	66.44 (19.52)	2032	5.02 (0.28)	2.12 (1.35, 2.89)	<.0001	0.17 (0.11, 0.23)	
	Black or African	69	60.39 (24.36)	64	7.93 (1.94)	71	60.70 (21.27)	70	7.47 (1.88)	0.46 (-4.88, 5.80)	0.8652	0.03 (-0.31, 0.37)	
	Asian	563	80.11 (19.29)	555	3.47 (0.47)	562	80.35 (17.47)	551	2.15 (0.47)	1.31 (0.01, 2.61)	0.0476	0.12 (0.00, 0.24)	
	Other	182	61.82 (21.38)	176	11.81 (0.91)	159	60.18 (22.32)	152	9.27 (0.99)	2.54 (-0.11, 5.18)	0.0601	0.21 (-0.01, 0.43)	
	Geographic region												0.3513
	Asia	544	80.36 (19.26)	536	3.51 (0.47)	544	80.97 (17.12)	536	2.14 (0.47)	1.37 (0.06, 2.68)	0.0403	0.13 (0.01, 0.25)	
	Europe and Saudi Arabia	1395	66.31 (19.17)	1341	6.63 (0.31)	1420	67.18 (18.81)	1381	4.96 (0.31)	1.67 (0.80, 2.54)	0.0002	0.14 (0.07, 0.22)	
	North America	408	62.70 (21.99)	393	5.54 (0.67)	395	63.47 (20.65)	376	2.87 (0.68)	2.66 (0.79, 4.54)	0.0055	0.20 (0.06, 0.34)	
	Latin America	554	64.13 (22.37)	531	11.29 (0.59)	527	63.86 (21.57)	512	8.28 (0.60)	3.01 (1.35, 4.67)	0.0004	0.22 (0.10, 0.34)	
	NYHA class at enrolment												0.0603
	II	2155	72.04 (19.60)	2083	5.72 (0.26)	2218	72.02 (19.05)	2165	4.02 (0.25)	1.70 (0.99, 2.40)	<.0001	0.15 (0.08, 0.21)	
	III or IV	746	56.42 (21.11)	718	9.70 (0.51)	667	57.49 (20.11)	639	6.45 (0.54)	3.25 (1.79, 4.70)	<.0001	0.24 (0.13, 0.34)	
	LVEF at enrolment												0.4638
	<= 49	1002	69.63 (21.01)	959	6.83 (0.38)	981	68.79 (20.47)	950	5.19 (0.38)	1.64 (0.58, 2.70)	0.0024	0.14 (0.05, 0.23)	
	50-59	1051	67.37 (21.47)	1017	6.29 (0.39)	1033	68.44 (19.75)	1009	4.41 (0.39)	1.87 (0.79, 2.95)	0.0007	0.15 (0.06, 0.24)	
	>= 60	848	66.92 (20.74)	825	6.86 (0.44)	872	68.79 (20.58)	846	4.22 (0.44)	2.63 (1.42, 3.85)	<.0001	0.21 (0.11, 0.30)	
	NT-proBNP at enrolment												0.4107
	<= median	1443	69.88 (20.35)	1396	5.84 (0.32)	1442	70.06 (19.75)	1409	4.12 (0.32)	1.72 (0.83, 2.61)	0.0002	0.14 (0.07, 0.22)	
	> median	1458	66.18 (21.72)	1405	7.41 (0.33)	1443	67.31 (20.61)	1395	5.15 (0.33)	2.26 (1.33, 3.18)	<.0001	0.18 (0.11, 0.25)	
	Type 2 Diabetes Medical History												0.0174
	Yes	1276	66.76 (21.34)	1231	7.37 (0.36)	1281	66.68 (20.85)	1243	4.50 (0.36)	2.87 (1.88, 3.87)	<.0001	0.23 (0.15, 0.31)	
	No	1625	69.01 (20.91)	1570	6.05 (0.30)	1605	70.25 (19.61)	1562	4.75 (0.30)	1.29 (0.46, 2.13)	0.0025	0.11 (0.04, 0.18)	
	Atrial fibrillation or flutter at enrolment ECG												0.5147
	Yes	1234	67.41 (21.21)	1185	6.92 (0.36)	1222	67.89 (20.03)	1188	4.67 (0.36)	2.25 (1.26, 3.24)	<.0001	0.18 (0.10, 0.26)	
	No	1667	68.47 (21.06)	1616	6.42 (0.30)	1664	69.23 (20.39)	1617	4.61 (0.30)	1.82 (0.97, 2.66)	<.0001	0.15 (0.08, 0.22)	
	BMI (kg/m2) at enrolment												0.8776
	< 30	1595	71.96 (20.44)	1547	5.93 (0.30)	1592	72.42 (19.48)	1541	3.89 (0.30)	2.04 (1.21, 2.86)	<.0001	0.17 (0.10, 0.24)	
	>= 30	1305	63.22 (20.96)	1253	7.51 (0.36)	1291	64.07 (20.24)	1261	5.57 (0.36)	1.93 (0.93, 2.94)	0.0002	0.15 (0.07, 0.23)	
	Baseline eGFR (mL/min/1.73m^2)												0.9653
	< 60	1391	66.44 (20.94)	1338	6.45 (0.35)	1416	66.96 (20.64)	1377	4.48 (0.34)	1.98 (1.02, 2.93)	<.0001	0.16 (0.08, 0.23)	
	>= 60	1510	69.48 (21.20)	1463	6.77 (0.31)	1469	70.34 (19.70)	1427	4.82 (0.31)	1.95 (1.08, 2.81)	<.0001	0.16 (0.09, 0.24)	
	SBP at randomisation												0.1048
	<= median	1457	67.81 (21.20)	1405	6.24 (0.33)	1459	69.63 (20.46)	1420	4.76 (0.33)	1.48 (0.56, 2.40)	0.0016	0.12 (0.05, 0.19)	
	> median	1444	68.24 (21.06)	1396	7.03 (0.32)	1427	67.68 (19.98)	1385	4.49 (0.33)	2.55 (1.65, 3.44)	<.0001	0.21 (0.14, 0.29)	

Repeated measures analysis displays overall results.
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LSMeans and difference of LSMeans estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.
p-Value for interaction from test for heterogeneity of the differences of LSMeans in the subgroups using Cochrane`s Q statistic.

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Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Clinical Summary Score	LVEF at enrolment 2												0.4071
	<= 49	1002	69.63 (21.01)	959	6.83 (0.38)	981	68.79 (20.47)	950	5.19 (0.38)	1.64 (0.58, 2.70)	0.0024	0.14 (0.05, 0.23)	
	>= 50	1899	67.17 (21.14)	1842	6.54 (0.29)	1905	68.60 (20.13)	1855	4.34 (0.29)	2.20 (1.40, 3.01)	<.0001	0.18 (0.11, 0.24)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.4451
	Yes	300	60.25 (21.25)	280	11.45 (0.80)	294	59.20 (19.59)	281	10.22 (0.79)	1.23 (-0.98, 3.43)	0.2744	0.09 (-0.07, 0.26)	
	No	2601	68.92 (20.93)	2521	6.13 (0.24)	2592	69.74 (20.04)	2524	4.01 (0.24)	2.12 (1.45, 2.79)	<.0001	0.17 (0.12, 0.23)	
	MRAs at baseline												0.9706
	Yes	1246	68.19 (21.54)	1216	6.34 (0.34)	1239	68.88 (20.46)	1210	4.36 (0.35)	1.99 (1.03, 2.94)	<.0001	0.17 (0.09, 0.25)	
	No	1655	67.89 (20.82)	1585	6.86 (0.31)	1647	68.50 (20.08)	1595	4.85 (0.31)	2.01 (1.14, 2.88)	<.0001	0.16 (0.09, 0.23)	
	ACEi+ARB at baseline												0.0326
	Yes	2102	67.31 (21.26)	2037	7.20 (0.27)	2105	68.29 (20.34)	2059	4.77 (0.27)	2.43 (1.69, 3.17)	<.0001	0.20 (0.14, 0.26)	
	No	799	69.88 (20.68)	764	5.12 (0.46)	781	69.68 (19.97)	746	4.30 (0.46)	0.82 (-0.46, 2.10)	0.2073	0.06 (-0.04, 0.17)	
	ARNI at baseline												0.3769
	Yes	156	76.92 (18.71)	149	3.49 (0.92)	126	75.33 (17.64)	125	2.69 (1.01)	0.80 (-1.88, 3.49)	0.5554	0.07 (-0.17, 0.31)	
	No	2745	67.51 (21.15)	2652	6.79 (0.24)	2760	68.36 (20.31)	2680	4.75 (0.24)	2.04 (1.38, 2.71)	<.0001	0.17 (0.11, 0.22)	
	Beta Blocker at baseline												0.5935
	Yes	2410	67.61 (20.97)	2327	6.59 (0.26)	2397	68.77 (19.97)	2330	4.66 (0.25)	1.93 (1.22, 2.63)	<.0001	0.16 (0.10, 0.21)	
	No	491	70.02 (21.78)	474	6.86 (0.55)	489	68.15 (21.56)	475	4.47 (0.56)	2.39 (0.84, 3.94)	0.0025	0.20 (0.07, 0.32)	
	Diuretics at baseline												0.7456
	Yes	2592	67.65 (21.06)	2500	6.72 (0.25)	2577	68.05 (20.34)	2504	4.75 (0.25)	1.98 (1.29, 2.67)	<.0001	0.16 (0.10, 0.21)	
	No	309	71.16 (21.49)	301	5.96 (0.62)	309	73.84 (18.62)	301	3.67 (0.62)	2.28 (0.56, 4.01)	0.0095	0.21 (0.05, 0.37)	

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Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Overall Summary Score	Age												0.3555
	<= median	1443	66.96 (20.86)	1394	7.17 (0.32)	1507	66.81 (19.99)	1471	5.67 (0.31)	1.51 (0.63, 2.38)	0.0008	0.13 (0.05, 0.20)	
	> median	1458	65.61 (20.60)	1407	5.97 (0.32)	1379	67.19 (19.45)	1334	3.87 (0.33)	2.10 (1.20, 2.99)	<.0001	0.18 (0.10, 0.25)	
	Gender												0.3460
	Male	1691	69.22 (19.98)	1630	6.07 (0.29)	1648	69.82 (19.45)	1608	4.60 (0.30)	1.47 (0.66, 2.29)	0.0004	0.12 (0.06, 0.19)	
	Female	1210	62.17 (21.08)	1171	7.23 (0.35)	1238	63.22 (19.49)	1197	5.14 (0.35)	2.08 (1.11, 3.06)	<.0001	0.17 (0.09, 0.25)	
	Race												0.4533
	White	2087	64.32 (20.02)	2006	7.05 (0.27)	2094	65.39 (19.22)	2032	5.04 (0.27)	2.01 (1.26, 2.76)	<.0001	0.17 (0.10, 0.23)	
	Black or African	69	59.33 (23.70)	64	7.85 (1.87)	71	59.77 (21.02)	70	7.42 (1.81)	0.43 (-4.72, 5.57)	0.8702	0.03 (-0.31, 0.37)	
	Asian	563	76.70 (19.55)	555	3.61 (0.46)	562	76.62 (17.64)	551	2.77 (0.47)	0.84 (-0.45, 2.13)	0.2012	0.08 (-0.04, 0.19)	
	Other	182	59.14 (20.56)	176	11.36 (0.86)	159	57.32 (20.82)	152	9.86 (0.94)	1.50 (-1.00, 4.00)	0.2379	0.13 (-0.09, 0.35)	
	Geographic region												0.3741
	Asia	544	76.86 (19.53)	536	3.64 (0.47)	544	77.15 (17.40)	536	2.74 (0.47)	0.90 (-0.40, 2.20)	0.1734	0.08 (-0.04, 0.20)	
	Europe and Saudi Arabia	1395	64.90 (18.69)	1341	6.46 (0.31)	1420	65.97 (18.36)	1381	4.88 (0.30)	1.58 (0.74, 2.42)	0.0002	0.14 (0.07, 0.22)	
	North America	408	62.65 (22.35)	393	5.81 (0.66)	395	63.13 (20.85)	376	3.53 (0.67)	2.28 (0.43, 4.13)	0.0156	0.17 (0.03, 0.32)	
	Latin America	554	62.03 (22.13)	531	10.95 (0.58)	527	62.16 (21.06)	512	8.33 (0.59)	2.62 (0.99, 4.25)	0.0017	0.19 (0.07, 0.32)	
	NYHA class at enrolment												0.0311
	II	2155	70.35 (19.28)	2083	5.67 (0.25)	2218	70.40 (18.47)	2165	4.28 (0.24)	1.39 (0.71, 2.08)	<.0001	0.12 (0.06, 0.18)	
	III or IV	746	54.51 (20.31)	718	9.55 (0.50)	667	55.62 (19.55)	639	6.41 (0.53)	3.14 (1.71, 4.57)	<.0001	0.23 (0.13, 0.34)	
	LVEF at enrolment												0.2130
	<= 49	1002	67.03 (20.35)	959	6.74 (0.37)	981	66.22 (19.93)	950	5.73 (0.38)	1.01 (-0.03, 2.05)	0.0571	0.09 (-0.00, 0.18)	
	50-59	1051	65.68 (21.36)	1017	6.41 (0.38)	1033	67.04 (19.34)	1009	4.36 (0.38)	2.04 (0.98, 3.10)	0.0002	0.17 (0.08, 0.26)	
	>= 60	848	66.12 (20.40)	825	6.59 (0.43)	872	67.81 (19.97)	846	4.29 (0.42)	2.30 (1.12, 3.47)	0.0001	0.19 (0.09, 0.28)	
	NT-proBNP at enrolment												0.5029
	<= median	1443	67.98 (19.95)	1396	5.93 (0.31)	1442	68.34 (19.03)	1409	4.40 (0.31)	1.53 (0.67, 2.39)	0.0005	0.13 (0.06, 0.21)	
	> median	1458	64.59 (21.36)	1405	7.19 (0.33)	1443	65.67 (20.30)	1395	5.23 (0.33)	1.96 (1.05, 2.87)	<.0001	0.16 (0.09, 0.23)	
	Type 2 Diabetes Medical History												0.0029
	Yes	1276	65.13 (20.80)	1231	7.24 (0.35)	1281	65.29 (20.20)	1243	4.42 (0.35)	2.82 (1.86, 3.78)	<.0001	0.23 (0.15, 0.31)	
	No	1625	67.18 (20.65)	1570	6.03 (0.30)	1605	68.35 (19.25)	1562	5.13 (0.30)	0.90 (0.07, 1.72)	0.0332	0.08 (0.01, 0.15)	
	Atrial fibrillation or flutter at enrolment ECG												0.2885
	Yes	1234	65.84 (20.99)	1185	6.82 (0.35)	1222	66.55 (19.57)	1188	4.67 (0.35)	2.15 (1.18, 3.13)	<.0001	0.18 (0.10, 0.26)	
	No	1667	66.60 (20.55)	1616	6.38 (0.30)	1664	67.31 (19.85)	1617	4.92 (0.30)	1.46 (0.64, 2.28)	0.0005	0.12 (0.05, 0.19)	
	BMI (kg/m2) at enrolment												0.5505
	< 30	1595	69.46 (20.21)	1547	5.93 (0.29)	1592	70.16 (19.14)	1541	4.35 (0.29)	1.58 (0.77, 2.39)	0.0001	0.14 (0.07, 0.21)	
	>= 30	1305	62.40 (20.72)	1253	7.37 (0.35)	1291	63.12 (19.78)	1261	5.40 (0.35)	1.96 (0.98, 2.94)	<.0001	0.16 (0.08, 0.23)	
	Baseline eGFR (mL/min/1.73m^2)												0.8972
	< 60	1391	65.05 (20.56)	1338	6.37 (0.34)	1416	65.53 (20.21)	1377	4.61 (0.33)	1.76 (0.83, 2.68)	0.0002	0.14 (0.07, 0.22)	
	>= 60	1510	67.41 (20.84)	1463	6.73 (0.30)	1469	68.42 (19.15)	1427	5.05 (0.31)	1.68 (0.83, 2.53)	0.0001	0.14 (0.07, 0.22)	
	SBP at randomisation												0.1215
	<= median	1457	65.77 (20.84)	1405	6.38 (0.33)	1459	67.54 (19.94)	1420	5.11 (0.32)	1.27 (0.37, 2.17)	0.0059	0.10 (0.03, 0.18)	
	> median	1444	66.79 (20.62)	1396	6.76 (0.31)	1427	66.43 (19.51)	1385	4.49 (0.32)	2.26 (1.39, 3.13)	<.0001	0.19 (0.12, 0.27)	

Repeated measures analysis displays overall results.
N* displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
LSMeans and difference of LSMeans estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.
p-Value for interaction from test for heterogeneity of the differences of LSMeans in the subgroups using Cochrane`s Q statistic.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Overall Summary Score	LVEF at enrolment 2												0.0850
	<= 49	1002	67.03 (20.35)	959	6.74 (0.37)	981	66.22 (19.93)	950	5.73 (0.38)	1.01 (-0.03, 2.05)	0.0571	0.09 (-0.00, 0.18)	
	>= 50	1899	65.88 (20.93)	1842	6.49 (0.28)	1905	67.39 (19.63)	1855	4.34 (0.28)	2.15 (1.37, 2.94)	<.0001	0.18 (0.11, 0.24)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.5619
	Yes	300	57.81 (20.36)	280	11.46 (0.79)	294	57.52 (19.26)	281	10.30 (0.78)	1.17 (-1.02, 3.36)	0.2945	0.09 (-0.08, 0.25)	
	No	2601	67.25 (20.56)	2521	6.05 (0.23)	2592	68.07 (19.50)	2524	4.21 (0.24)	1.84 (1.19, 2.50)	<.0001	0.16 (0.10, 0.21)	
	MRAs at baseline												0.7087
	Yes	1246	65.99 (20.82)	1216	6.30 (0.34)	1239	66.58 (19.88)	1210	4.68 (0.34)	1.62 (0.67, 2.57)	0.0008	0.14 (0.06, 0.22)	
	No	1655	66.49 (20.68)	1585	6.78 (0.30)	1647	67.30 (19.62)	1595	4.92 (0.30)	1.86 (1.02, 2.70)	<.0001	0.15 (0.08, 0.22)	
	ACEi+ARB at baseline												0.0264
	Yes	2102	65.79 (20.85)	2037	7.08 (0.26)	2105	66.70 (19.76)	2059	4.88 (0.26)	2.19 (1.47, 2.92)	<.0001	0.19 (0.12, 0.25)	
	No	799	67.57 (20.39)	764	5.22 (0.45)	781	67.77 (19.65)	746	4.66 (0.46)	0.56 (-0.70, 1.81)	0.3842	0.04 (-0.06, 0.15)	
	ARNI at baseline												0.3143
	Yes	156	72.39 (18.72)	149	3.62 (0.90)	126	72.32 (16.72)	125	3.18 (0.98)	0.44 (-2.18, 3.06)	0.7425	0.04 (-0.20, 0.28)	
	No	2745	65.93 (20.79)	2652	6.72 (0.23)	2760	66.75 (19.83)	2680	4.91 (0.23)	1.82 (1.17, 2.46)	<.0001	0.15 (0.10, 0.20)	
	Beta Blocker at baseline												0.3284
	Yes	2410	65.92 (20.60)	2327	6.45 (0.25)	2397	67.13 (19.51)	2330	4.83 (0.25)	1.62 (0.93, 2.31)	<.0001	0.13 (0.08, 0.19)	
	No	491	68.03 (21.33)	474	7.16 (0.54)	489	66.30 (20.78)	475	4.72 (0.55)	2.44 (0.93, 3.96)	0.0016	0.21 (0.08, 0.33)	
	Diuretics at baseline												0.9978
	Yes	2592	66.02 (20.68)	2500	6.62 (0.24)	2577	66.49 (19.88)	2504	4.86 (0.24)	1.77 (1.09, 2.44)	<.0001	0.15 (0.09, 0.20)	
	No	309	68.43 (21.13)	301	6.17 (0.61)	309	71.16 (17.92)	301	4.40 (0.61)	1.76 (0.07, 3.46)	0.0414	0.17 (0.01, 0.33)	

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Physical Limitation	Age												0.2329
	<= median	1431	66.67 (23.43)	1382	5.13 (0.38)	1494	66.60 (22.71)	1456	3.78 (0.37)	1.35 (0.30, 2.39)	0.0115	0.09 (0.02, 0.17)	
	> median	1428	62.16 (23.68)	1368	4.13 (0.41)	1356	64.22 (23.25)	1302	1.84 (0.42)	2.29 (1.15, 3.44)	<.0001	0.15 (0.08, 0.23)	
	Gender												0.6218
	Male	1681	68.70 (22.66)	1611	3.97 (0.36)	1627	69.48 (22.11)	1583	2.46 (0.36)	1.51 (0.51, 2.51)	0.0030	0.11 (0.04, 0.17)	
	Female	1178	58.30 (23.72)	1139	5.45 (0.44)	1223	60.13 (23.08)	1175	3.54 (0.44)	1.91 (0.69, 3.13)	0.0022	0.13 (0.05, 0.21)	
	Race												0.7813
	White	2055	61.51 (22.51)	1970	4.94 (0.33)	2069	62.58 (22.13)	1998	3.23 (0.33)	1.70 (0.78, 2.62)	0.0003	0.12 (0.05, 0.18)	
	Black or African	68	58.04 (27.85)	63	3.06 (2.40)	68	58.86 (24.99)	66	4.53 (2.36)	-1.47 (-8.13, 5.20)	0.6639	-0.08 (-0.42, 0.27)	
	Asian	558	78.19 (22.32)	548	3.01 (0.56)	558	80.12 (19.26)	546	1.00 (0.56)	2.01 (0.46, 3.57)	0.0110	0.15 (0.04, 0.27)	
	Other	178	57.14 (23.07)	169	7.84 (1.14)	155	54.22 (23.60)	148	6.49 (1.23)	1.35 (-1.95, 4.66)	0.4206	0.09 (-0.13, 0.31)	
	Geographic region												0.8255
	Asia	540	78.61 (22.21)	530	3.07 (0.56)	540	80.60 (19.05)	531	1.05 (0.56)	2.01 (0.46, 3.57)	0.0113	0.16 (0.04, 0.28)	
	Europe and Saudi Arabia	1378	62.44 (21.22)	1323	4.39 (0.38)	1405	63.20 (21.51)	1360	3.02 (0.38)	1.38 (0.33, 2.42)	0.0101	0.10 (0.02, 0.18)	
	North America	401	58.94 (24.47)	386	3.44 (0.81)	384	61.19 (22.59)	362	1.42 (0.83)	2.01 (-0.27, 4.30)	0.0836	0.13 (-0.02, 0.27)	
	Latin America	540	59.33 (24.90)	511	8.30 (0.73)	521	59.05 (24.29)	505	6.02 (0.74)	2.28 (0.24, 4.32)	0.0288	0.14 (0.01, 0.26)	
	NYHA class at enrolment												0.3807
	II	2126	68.18 (22.41)	2046	4.13 (0.31)	2196	68.60 (22.05)	2136	2.52 (0.31)	1.62 (0.75, 2.48)	0.0002	0.11 (0.05, 0.17)	
	III or IV	733	53.49 (23.81)	704	6.37 (0.59)	653	54.95 (23.02)	621	3.90 (0.63)	2.47 (0.77, 4.16)	0.0043	0.16 (0.05, 0.27)	
	LVEF at enrolment												0.2497
	<= 49	987	66.64 (22.83)	944	4.50 (0.47)	973	65.56 (22.61)	939	3.56 (0.47)	0.94 (-0.35, 2.23)	0.1530	0.07 (-0.02, 0.16)	
	50-59	1038	63.69 (23.88)	1001	3.96 (0.47)	1015	65.63 (22.84)	988	2.23 (0.47)	1.73 (0.42, 3.03)	0.0096	0.12 (0.03, 0.20)	
	>= 60	834	62.68 (24.17)	805	5.51 (0.53)	862	65.18 (23.62)	831	2.92 (0.52)	2.59 (1.14, 4.05)	0.0005	0.17 (0.08, 0.27)	
	NT-proBNP at enrolment												0.8301
	<= median	1425	66.19 (23.53)	1371	4.30 (0.39)	1427	66.86 (22.81)	1389	2.66 (0.39)	1.64 (0.56, 2.72)	0.0030	0.11 (0.04, 0.19)	
	> median	1434	62.64 (23.66)	1379	4.93 (0.40)	1422	64.09 (23.09)	1368	3.12 (0.40)	1.81 (0.70, 2.93)	0.0015	0.12 (0.05, 0.20)	
	Type 2 Diabetes Medical History												0.3261
	Yes	1261	63.38 (23.88)	1213	4.89 (0.43)	1261	63.38 (23.46)	1219	2.73 (0.43)	2.16 (0.98, 3.34)	0.0004	0.15 (0.07, 0.22)	
	No	1598	65.23 (23.46)	1537	4.39 (0.37)	1589	67.13 (22.49)	1539	3.01 (0.37)	1.38 (0.35, 2.40)	0.0087	0.09 (0.02, 0.17)	
	Atrial fibrillation or flutter at enrolment ECG												0.6555
	Yes	1214	63.92 (23.60)	1164	4.63 (0.43)	1203	64.60 (22.82)	1164	2.69 (0.43)	1.94 (0.74, 3.14)	0.0015	0.13 (0.05, 0.21)	
	No	1645	64.78 (23.71)	1586	4.61 (0.37)	1647	66.11 (23.11)	1594	3.03 (0.37)	1.58 (0.56, 2.60)	0.0024	0.11 (0.04, 0.18)	
	BMI (kg/m2) at enrolment												0.1268
	< 30	1577	68.50 (23.27)	1520	4.41 (0.37)	1573	69.21 (22.54)	1517	2.15 (0.37)	2.26 (1.24, 3.28)	<.0001	0.16 (0.09, 0.23)	
	>= 30	1281	59.40 (23.17)	1229	4.85 (0.43)	1274	60.93 (22.70)	1238	3.81 (0.43)	1.04 (-0.14, 2.23)	0.0850	0.07 (-0.01, 0.15)	
	Baseline eGFR (mL/min/1.73m^2)												0.9717
	< 60	1365	62.07 (23.73)	1307	4.64 (0.42)	1392	62.88 (23.87)	1345	2.93 (0.41)	1.71 (0.56, 2.86)	0.0036	0.11 (0.04, 0.19)	
	>= 60	1494	66.55 (23.40)	1443	4.56 (0.38)	1457	67.98 (21.82)	1412	2.88 (0.38)	1.68 (0.63, 2.73)	0.0017	0.12 (0.04, 0.19)	
	SBP at randomisation												0.4035
	<= median	1434	63.80 (23.65)	1376	4.66 (0.40)	1437	66.41 (23.39)	1395	3.23 (0.40)	1.43 (0.32, 2.54)	0.0114	0.10 (0.02, 0.17)	
	> median	1425	65.03 (23.66)	1374	4.58 (0.39)	1413	64.52 (22.56)	1363	2.49 (0.39)	2.09 (1.00, 3.18)	0.0002	0.14 (0.07, 0.22)	

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Physical Limitation	LVEF at enrolment 2												0.1594
	<= 49	987	66.64 (22.83)	944	4.50 (0.47)	973	65.56 (22.61)	939	3.56 (0.47)	0.94 (-0.35, 2.23)	0.1530	0.07 (-0.02, 0.16)	
	>= 50	1872	63.24 (24.01)	1806	4.65 (0.35)	1877	65.42 (23.20)	1819	2.55 (0.35)	2.10 (1.13, 3.07)	<.0001	0.14 (0.08, 0.21)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.2979
	Yes	290	59.40 (23.85)	270	6.46 (0.96)	287	59.78 (23.33)	272	6.05 (0.95)	0.42 (-2.24, 3.07)	0.7578	0.03 (-0.14, 0.19)	
	No	2569	64.98 (23.58)	2480	4.42 (0.29)	2563	66.11 (22.88)	2486	2.54 (0.29)	1.89 (1.08, 2.70)	<.0001	0.13 (0.07, 0.19)	
	MRAs at baseline												0.6444
	Yes	1225	65.12 (23.83)	1191	4.11 (0.41)	1224	65.76 (22.67)	1193	2.59 (0.41)	1.52 (0.37, 2.66)	0.0094	0.11 (0.03, 0.19)	
	No	1634	63.88 (23.53)	1559	5.00 (0.38)	1626	65.25 (23.24)	1565	3.12 (0.38)	1.88 (0.83, 2.94)	0.0005	0.13 (0.06, 0.20)	
	ACEi+ARB at baseline												0.0982
	Yes	2069	63.90 (23.63)	1999	4.94 (0.33)	2083	65.11 (23.04)	2028	2.82 (0.33)	2.12 (1.21, 3.03)	<.0001	0.14 (0.08, 0.21)	
	No	790	65.77 (23.70)	751	3.74 (0.53)	767	66.45 (22.87)	730	3.08 (0.53)	0.66 (-0.81, 2.13)	0.3775	0.05 (-0.06, 0.15)	
	ARNI at baseline												0.6941
	Yes	155	71.62 (23.91)	147	4.02 (1.07)	123	71.83 (21.75)	122	1.70 (1.17)	2.31 (-0.81, 5.44)	0.1465	0.18 (-0.06, 0.42)	
	No	2704	64.00 (23.58)	2603	4.63 (0.29)	2727	65.18 (23.01)	2636	2.96 (0.29)	1.67 (0.87, 2.47)	<.0001	0.11 (0.06, 0.17)	
	Beta Blocker at baseline												0.8922
	Yes	2378	63.98 (23.49)	2289	4.63 (0.31)	2368	65.35 (22.90)	2293	2.92 (0.31)	1.71 (0.86, 2.56)	<.0001	0.12 (0.06, 0.17)	
	No	481	66.58 (24.40)	461	4.52 (0.68)	482	66.07 (23.47)	465	2.67 (0.68)	1.85 (-0.03, 3.74)	0.0540	0.13 (-0.00, 0.26)	
	Diuretics at baseline												0.7805
	Yes	2555	63.70 (23.56)	2458	4.73 (0.30)	2545	64.78 (23.16)	2463	2.96 (0.30)	1.77 (0.93, 2.61)	<.0001	0.12 (0.06, 0.17)	
	No	304	70.38 (23.70)	292	3.68 (0.72)	305	71.19 (20.73)	295	2.21 (0.72)	1.46 (-0.54, 3.46)	0.1518	0.12 (-0.04, 0.28)	

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p-Value for interaction from test for heterogeneity of the differences of LSMeans in the subgroups using Cochrane`s Q statistic.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Quality of Life	Age												0.2147
	<= median	1443	59.74 (23.31)	1394	7.16 (0.39)	1507	60.20 (22.63)	1471	6.31 (0.38)	0.85 (-0.23, 1.92)	0.1230	0.06 (-0.02, 0.13)	
	> median	1458	61.45 (23.91)	1407	6.20 (0.38)	1379	63.54 (22.20)	1334	4.39 (0.39)	1.81 (0.73, 2.89)	0.0010	0.13 (0.05, 0.20)	
	Gender												0.5967
	Male	1691	62.93 (22.79)	1630	6.46 (0.36)	1648	64.07 (22.04)	1608	5.34 (0.37)	1.12 (0.11, 2.13)	0.0301	0.08 (0.01, 0.15)	
	Female	1210	57.35 (24.39)	1171	7.01 (0.42)	1238	58.77 (22.73)	1197	5.48 (0.41)	1.53 (0.38, 2.69)	0.0093	0.11 (0.03, 0.19)	
	Race												0.4885
	White	2087	60.10 (23.20)	2006	7.09 (0.33)	2094	61.51 (22.20)	2032	5.54 (0.32)	1.54 (0.64, 2.45)	0.0008	0.11 (0.04, 0.17)	
	Black or African	69	54.11 (27.92)	64	9.35 (2.01)	71	56.81 (26.10)	70	5.56 (1.95)	3.78 (-1.76, 9.33)	0.1794	0.23 (-0.11, 0.57)	
	Asian	563	66.80 (23.23)	555	3.77 (0.61)	562	67.26 (21.65)	551	3.33 (0.62)	0.44 (-1.27, 2.14)	0.6138	0.03 (-0.09, 0.15)	
	Other	182	49.68 (22.66)	176	12.07 (1.00)	159	48.48 (20.94)	152	11.68 (1.09)	0.39 (-2.54, 3.31)	0.7953	0.03 (-0.19, 0.25)	
	Geographic region												0.3276
	Asia	544	66.80 (23.08)	536	3.66 (0.62)	544	67.52 (21.65)	536	3.26 (0.62)	0.40 (-1.32, 2.12)	0.6510	0.03 (-0.09, 0.15)	
	Europe and Saudi Arabia	1395	60.23 (21.51)	1341	6.54 (0.38)	1420	61.49 (21.50)	1381	5.50 (0.38)	1.04 (-0.01, 2.10)	0.0522	0.07 (-0.00, 0.15)	
	North America	408	60.76 (27.27)	393	7.16 (0.81)	395	61.98 (24.71)	376	4.41 (0.82)	2.74 (0.48, 5.01)	0.0175	0.17 (0.03, 0.31)	
	Latin America	554	55.32 (24.99)	531	10.39 (0.65)	527	56.58 (22.88)	512	8.37 (0.66)	2.01 (0.19, 3.84)	0.0305	0.13 (0.01, 0.26)	
	NYHA class at enrolment												0.0973
	II	2155	64.54 (22.58)	2083	5.85 (0.30)	2218	65.06 (21.56)	2165	4.84 (0.30)	1.01 (0.17, 1.84)	0.0178	0.07 (0.01, 0.13)	
	III or IV	746	49.22 (22.90)	718	9.60 (0.60)	667	50.90 (22.05)	639	6.98 (0.64)	2.63 (0.91, 4.35)	0.0028	0.16 (0.06, 0.27)	
	LVEF at enrolment												0.0940
	<= 49	1002	59.71 (22.95)	959	6.69 (0.47)	981	59.71 (22.62)	950	6.50 (0.47)	0.18 (-1.13, 1.49)	0.7856	0.01 (-0.08, 0.10)	
	50-59	1051	60.39 (24.48)	1017	6.93 (0.46)	1033	62.04 (22.20)	1009	4.77 (0.46)	2.16 (0.88, 3.44)	0.0009	0.15 (0.06, 0.23)	
	>= 60	848	61.92 (23.31)	825	6.44 (0.50)	872	63.86 (22.50)	846	4.83 (0.50)	1.61 (0.23, 3.00)	0.0222	0.11 (0.02, 0.21)	
	NT-proBNP at enrolment												0.7276
	<= median	1443	61.71 (23.06)	1396	6.49 (0.38)	1442	63.01 (21.65)	1409	5.30 (0.38)	1.19 (0.14, 2.25)	0.0269	0.08 (0.01, 0.16)	
	> median	1458	59.51 (24.14)	1405	6.92 (0.40)	1443	60.61 (23.23)	1395	5.45 (0.40)	1.46 (0.36, 2.57)	0.0094	0.10 (0.02, 0.17)	
	Type 2 Diabetes Medical History												<.0001
	Yes	1276	59.67 (23.42)	1231	7.42 (0.42)	1281	61.03 (22.21)	1243	4.30 (0.42)	3.12 (1.96, 4.28)	<.0001	0.21 (0.13, 0.29)	
	No	1625	61.33 (23.77)	1570	6.14 (0.36)	1605	62.41 (22.69)	1562	6.22 (0.36)	-0.08 (-1.09, 0.93)	0.8734	-0.01 (-0.08, 0.06)	
	Atrial fibrillation or flutter at enrolment ECG												0.3580
	Yes	1234	60.75 (23.88)	1185	6.72 (0.43)	1222	62.19 (22.49)	1188	4.98 (0.43)	1.74 (0.56, 2.93)	0.0040	0.12 (0.04, 0.20)	
	No	1667	60.49 (23.45)	1616	6.70 (0.36)	1664	61.51 (22.49)	1617	5.68 (0.36)	1.02 (0.02, 2.01)	0.0459	0.07 (0.00, 0.14)	
	BMI (kg/m2) at enrolment												0.0532
	< 30	1595	62.23 (23.25)	1547	5.98 (0.36)	1592	63.75 (22.26)	1541	5.32 (0.36)	0.65 (-0.34, 1.65)	0.1981	0.05 (-0.02, 0.12)	
	>= 30	1305	58.61 (23.94)	1253	7.62 (0.43)	1291	59.43 (22.55)	1261	5.44 (0.42)	2.18 (1.00, 3.36)	0.0003	0.14 (0.07, 0.22)	
	Baseline eGFR (mL/min/1.73m^2)												0.7512
	< 60	1391	60.60 (23.61)	1338	6.46 (0.41)	1416	61.29 (23.12)	1377	5.04 (0.40)	1.42 (0.31, 2.54)	0.0125	0.10 (0.02, 0.17)	
	>= 60	1510	60.61 (23.65)	1463	6.92 (0.37)	1469	62.29 (21.86)	1427	5.74 (0.38)	1.18 (0.13, 2.22)	0.0270	0.08 (0.01, 0.16)	
	SBP at randomisation												0.3450
	<= median	1457	59.88 (23.92)	1405	7.04 (0.40)	1459	61.67 (22.80)	1420	6.08 (0.39)	0.96 (-0.14, 2.06)	0.0864	0.06 (-0.01, 0.14)	
	> median	1444	61.33 (23.31)	1396	6.36 (0.38)	1427	61.92 (22.17)	1385	4.67 (0.38)	1.70 (0.64, 2.75)	0.0017	0.12 (0.04, 0.19)	

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AstraZeneca
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Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Quality of Life	LVEF at enrolment 2												0.0347
	<= 49	1002	59.71 (22.95)	959	6.69 (0.47)	981	59.71 (22.62)	950	6.50 (0.47)	0.18 (-1.13, 1.49)	0.7856	0.01 (-0.08, 0.10)	
	>= 50	1899	61.07 (23.97)	1842	6.72 (0.34)	1905	62.87 (22.35)	1855	4.80 (0.34)	1.92 (0.98, 2.86)	<.0001	0.13 (0.07, 0.20)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.9603
	Yes	300	50.33 (21.89)	280	12.08 (0.94)	294	51.90 (22.16)	281	10.70 (0.93)	1.38 (-1.22, 3.97)	0.2973	0.09 (-0.08, 0.25)	
	No	2601	61.79 (23.54)	2521	6.12 (0.29)	2592	62.92 (22.25)	2524	4.81 (0.29)	1.31 (0.51, 2.11)	0.0013	0.09 (0.04, 0.15)	
	MRAs at baseline												0.8222
	Yes	1246	59.47 (23.16)	1216	6.37 (0.42)	1239	60.39 (22.52)	1210	5.14 (0.42)	1.23 (0.06, 2.40)	0.0396	0.08 (0.00, 0.16)	
	No	1655	61.46 (23.95)	1585	6.96 (0.36)	1647	62.86 (22.41)	1595	5.55 (0.36)	1.41 (0.40, 2.41)	0.0060	0.10 (0.03, 0.17)	
	ACEi+ARB at baseline												0.0358
	Yes	2102	60.63 (23.48)	2037	7.02 (0.32)	2105	61.69 (22.27)	2059	5.18 (0.31)	1.84 (0.96, 2.71)	<.0001	0.13 (0.07, 0.19)	
	No	799	60.53 (24.02)	764	5.88 (0.55)	781	62.10 (23.08)	746	5.94 (0.56)	-0.06 (-1.60, 1.48)	0.9400	-0.00 (-0.10, 0.10)	
	ARNI at baseline												0.4266
	Yes	156	60.47 (22.93)	149	4.25 (1.30)	126	65.34 (19.79)	125	4.40 (1.42)	-0.15 (-3.94, 3.64)	0.9378	-0.01 (-0.25, 0.23)	
	No	2745	60.61 (23.67)	2652	6.84 (0.28)	2760	61.64 (22.59)	2680	5.43 (0.28)	1.41 (0.63, 2.19)	0.0004	0.10 (0.04, 0.15)	
	Beta Blocker at baseline												0.0611
	Yes	2410	60.42 (23.50)	2327	6.40 (0.30)	2397	61.89 (22.27)	2330	5.41 (0.30)	0.99 (0.16, 1.83)	0.0201	0.07 (0.01, 0.13)	
	No	491	61.49 (24.24)	474	8.16 (0.66)	489	61.33 (23.55)	475	5.24 (0.66)	2.92 (1.09, 4.75)	0.0018	0.20 (0.08, 0.33)	
	Diuretics at baseline												0.2776
	Yes	2592	60.58 (23.62)	2500	6.79 (0.29)	2577	61.62 (22.59)	2504	5.32 (0.29)	1.46 (0.65, 2.28)	0.0004	0.10 (0.04, 0.16)	
	No	309	60.76 (23.74)	301	6.02 (0.79)	309	63.32 (21.54)	301	5.86 (0.79)	0.16 (-2.04, 2.37)	0.8847	0.01 (-0.15, 0.17)	

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Symptom Burden	Age												0.6898
	<= median	1443	71.09 (23.82)	1394	8.51 (0.37)	1507	70.99 (22.55)	1471	6.32 (0.36)	2.19 (1.19, 3.19)	<.0001	0.16 (0.09, 0.23)	
	> median	1458	70.70 (22.90)	1407	6.64 (0.37)	1379	72.17 (22.31)	1334	4.75 (0.38)	1.89 (0.84, 2.94)	0.0004	0.14 (0.06, 0.21)	
	Gender												0.7668
	Male	1691	73.62 (22.69)	1630	7.30 (0.33)	1648	74.49 (22.01)	1608	5.23 (0.33)	2.07 (1.15, 2.99)	<.0001	0.15 (0.09, 0.22)	
	Female	1210	67.09 (23.75)	1171	7.93 (0.42)	1238	67.64 (22.42)	1197	6.09 (0.42)	1.84 (0.68, 3.00)	0.0018	0.13 (0.05, 0.21)	
	Race												0.5222
	White	2087	68.68 (22.83)	2006	8.14 (0.32)	2094	69.52 (22.19)	2032	6.04 (0.32)	2.10 (1.22, 2.98)	<.0001	0.15 (0.09, 0.21)	
	Black or African	69	62.44 (28.89)	64	10.11 (2.05)	71	64.20 (23.63)	70	8.94 (1.98)	1.17 (-4.47, 6.82)	0.6810	0.07 (-0.27, 0.41)	
	Asian	563	82.42 (20.35)	555	3.84 (0.49)	562	82.30 (19.09)	551	2.68 (0.50)	1.16 (-0.21, 2.54)	0.0972	0.10 (-0.02, 0.22)	
	Other	182	63.92 (24.29)	176	13.89 (1.04)	159	63.68 (24.04)	152	10.54 (1.14)	3.35 (0.32, 6.38)	0.0303	0.24 (0.02, 0.46)	
	Geographic region												0.2802
	Asia	544	82.58 (20.34)	536	3.85 (0.50)	544	82.90 (18.70)	536	2.65 (0.50)	1.20 (-0.18, 2.59)	0.0892	0.10 (-0.02, 0.22)	
	Europe and Saudi Arabia	1395	68.95 (21.91)	1341	7.86 (0.37)	1420	69.86 (21.70)	1381	6.22 (0.36)	1.64 (0.63, 2.65)	0.0014	0.12 (0.05, 0.20)	
	North America	408	66.56 (24.92)	393	6.46 (0.79)	395	67.51 (22.93)	376	3.44 (0.80)	3.02 (0.82, 5.23)	0.0072	0.19 (0.05, 0.34)	
	Latin America	554	67.52 (24.87)	531	12.17 (0.65)	527	67.44 (23.82)	512	9.09 (0.66)	3.08 (1.26, 4.91)	0.0010	0.21 (0.08, 0.33)	
	NYHA class at enrolment												0.0750
	II	2155	75.00 (21.70)	2083	6.54 (0.29)	2218	75.07 (21.05)	2165	4.83 (0.28)	1.71 (0.92, 2.50)	<.0001	0.13 (0.07, 0.19)	
	III or IV	746	59.04 (23.94)	718	11.14 (0.58)	667	59.88 (23.01)	639	7.76 (0.61)	3.37 (1.72, 5.03)	<.0001	0.22 (0.11, 0.32)	
	LVEF at enrolment												0.6217
	<= 49	1002	71.84 (23.45)	959	8.12 (0.43)	981	71.48 (22.64)	950	6.17 (0.43)	1.95 (0.75, 3.15)	0.0014	0.15 (0.06, 0.24)	
	50-59	1051	70.32 (23.90)	1017	7.38 (0.44)	1033	71.04 (22.23)	1009	5.71 (0.44)	1.67 (0.44, 2.89)	0.0076	0.12 (0.03, 0.21)	
	>= 60	848	70.50 (22.54)	825	7.24 (0.49)	872	72.26 (22.48)	846	4.68 (0.49)	2.57 (1.21, 3.93)	0.0002	0.18 (0.08, 0.28)	
	NT-proBNP at enrolment												0.3245
	<= median	1443	72.72 (22.34)	1396	6.62 (0.36)	1442	72.80 (21.40)	1409	4.98 (0.36)	1.63 (0.63, 2.64)	0.0015	0.12 (0.05, 0.19)	
	> median	1458	69.10 (24.19)	1405	8.53 (0.38)	1443	70.35 (23.33)	1395	6.16 (0.38)	2.36 (1.32, 3.41)	<.0001	0.17 (0.09, 0.24)	
	Type 2 Diabetes Medical History												0.0170
	Yes	1276	69.63 (23.61)	1231	8.36 (0.41)	1281	69.94 (22.87)	1243	5.36 (0.41)	3.00 (1.87, 4.14)	<.0001	0.21 (0.13, 0.29)	
	No	1625	71.89 (23.12)	1570	6.96 (0.34)	1605	72.85 (22.02)	1562	5.75 (0.34)	1.21 (0.27, 2.15)	0.0116	0.09 (0.02, 0.16)	
	Atrial fibrillation or flutter at enrolment ECG												0.7716
	Yes	1234	70.35 (23.40)	1185	7.87 (0.40)	1222	70.96 (22.74)	1188	5.73 (0.40)	2.13 (1.01, 3.25)	0.0002	0.15 (0.07, 0.23)	
	No	1667	71.30 (23.32)	1616	7.37 (0.34)	1664	71.99 (22.22)	1617	5.46 (0.34)	1.91 (0.96, 2.87)	<.0001	0.14 (0.07, 0.21)	
	BMI (kg/m2) at enrolment												0.9692
	< 30	1595	74.46 (22.56)	1547	6.82 (0.33)	1592	75.07 (21.51)	1541	4.81 (0.33)	2.01 (1.09, 2.92)	<.0001	0.16 (0.08, 0.23)	
	>= 30	1305	66.58 (23.57)	1253	8.53 (0.42)	1291	67.23 (22.84)	1261	6.55 (0.42)	1.98 (0.82, 3.14)	0.0008	0.13 (0.06, 0.21)	
	Baseline eGFR (mL/min/1.73m^2)												0.7462
	< 60	1391	69.82 (23.27)	1338	7.29 (0.39)	1416	70.44 (22.98)	1377	5.19 (0.39)	2.10 (1.02, 3.17)	0.0001	0.15 (0.07, 0.22)	
	>= 60	1510	71.89 (23.40)	1463	7.82 (0.35)	1469	72.65 (21.86)	1427	5.96 (0.36)	1.86 (0.88, 2.84)	0.0002	0.14 (0.07, 0.21)	
	SBP at randomisation												0.1195
	<= median	1457	70.77 (23.20)	1405	6.99 (0.37)	1459	72.61 (22.64)	1420	5.56 (0.37)	1.43 (0.40, 2.46)	0.0065	0.10 (0.03, 0.18)	
	> median	1444	71.03 (23.53)	1396	8.16 (0.37)	1427	70.48 (22.19)	1385	5.58 (0.37)	2.58 (1.56, 3.61)	<.0001	0.19 (0.11, 0.26)	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Symptom Burden	LVEF at enrolment 2												0.8885
	<= 49	1002	71.84 (23.45)	959	8.12 (0.43)	981	71.48 (22.64)	950	6.17 (0.43)	1.95 (0.75, 3.15)	0.0014	0.15 (0.06, 0.24)	
	>= 50	1899	70.40 (23.30)	1842	7.31 (0.33)	1905	71.59 (22.35)	1855	5.25 (0.33)	2.06 (1.15, 2.97)	<.0001	0.15 (0.08, 0.21)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.5034
	Yes	300	61.83 (23.80)	280	13.33 (0.90)	294	60.76 (23.20)	281	12.09 (0.89)	1.24 (-1.25, 3.73)	0.3291	0.08 (-0.08, 0.25)	
	No	2601	71.94 (23.08)	2521	6.98 (0.27)	2592	72.78 (22.03)	2524	4.85 (0.27)	2.12 (1.37, 2.88)	<.0001	0.15 (0.10, 0.21)	
	MRAs at baseline												0.7883
	Yes	1246	70.68 (23.57)	1216	7.39 (0.39)	1239	71.75 (22.70)	1210	5.27 (0.39)	2.12 (1.03, 3.21)	0.0001	0.15 (0.07, 0.23)	
	No	1655	71.06 (23.20)	1585	7.73 (0.35)	1647	71.41 (22.25)	1595	5.81 (0.35)	1.92 (0.95, 2.89)	0.0001	0.14 (0.07, 0.21)	
	ACEi+ARB at baseline												0.0443
	Yes	2102	70.16 (23.29)	2037	8.20 (0.30)	2105	71.20 (22.39)	2059	5.74 (0.30)	2.47 (1.63, 3.30)	<.0001	0.18 (0.12, 0.24)	
	No	799	72.83 (23.44)	764	5.90 (0.52)	781	72.52 (22.57)	746	5.15 (0.53)	0.75 (-0.70, 2.20)	0.3112	0.05 (-0.05, 0.15)	
	ARNI at baseline												0.3077
	Yes	156	80.66 (19.28)	149	2.97 (1.05)	126	79.17 (19.17)	125	2.53 (1.15)	0.44 (-2.63, 3.51)	0.7775	0.03 (-0.20, 0.27)	
	No	2745	70.34 (23.45)	2652	7.81 (0.27)	2760	71.21 (22.52)	2680	5.74 (0.27)	2.07 (1.33, 2.82)	<.0001	0.15 (0.10, 0.20)	
	Beta Blocker at baseline												0.1358
	Yes	2410	70.53 (23.21)	2327	7.41 (0.29)	2397	71.70 (22.11)	2330	5.66 (0.29)	1.76 (0.96, 2.55)	<.0001	0.13 (0.07, 0.18)	
	No	491	72.70 (24.00)	474	8.37 (0.63)	489	70.84 (24.02)	475	5.14 (0.64)	3.23 (1.46, 4.99)	0.0004	0.23 (0.11, 0.36)	
	Diuretics at baseline												0.8039
	Yes	2592	70.61 (23.33)	2500	7.73 (0.28)	2577	70.94 (22.55)	2504	5.74 (0.28)	1.99 (1.21, 2.76)	<.0001	0.14 (0.09, 0.20)	
	No	309	73.30 (23.48)	301	6.39 (0.71)	309	76.65 (20.82)	301	4.14 (0.71)	2.26 (0.28, 4.24)	0.0256	0.18 (0.02, 0.34)	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Self Efficacy	Age												0.1818
	<= median	1443	73.59 (22.97)	1394	6.35 (0.36)	1507	73.33 (23.31)	1471	6.63 (0.36)	-0.28 (-1.28, 0.72)	0.5830	-0.02 (-0.09, 0.05)	
	> median	1458	72.59 (23.31)	1407	5.21 (0.38)	1379	72.73 (23.69)	1334	4.49 (0.39)	0.72 (-0.36, 1.80)	0.1898	0.05 (-0.02, 0.13)	
	Gender												0.2649
	Male	1691	73.24 (23.09)	1630	6.09 (0.35)	1648	72.85 (23.47)	1608	5.59 (0.35)	0.50 (-0.47, 1.47)	0.3119	0.04 (-0.03, 0.10)	
	Female	1210	72.87 (23.22)	1171	5.34 (0.41)	1238	73.31 (23.52)	1197	5.68 (0.40)	-0.34 (-1.46, 0.78)	0.5493	-0.02 (-0.11, 0.06)	
	Race												0.9818
	White	2087	73.95 (22.84)	2006	5.88 (0.31)	2094	74.13 (23.28)	2032	5.75 (0.31)	0.13 (-0.73, 0.99)	0.7722	0.01 (-0.05, 0.07)	
	Black or African	69	73.91 (28.18)	64	6.67 (1.70)	71	72.54 (23.87)	70	5.71 (1.66)	0.96 (-3.76, 5.68)	0.6872	0.07 (-0.27, 0.41)	
	Asian	563	72.25 (23.31)	555	4.42 (0.61)	562	71.20 (24.11)	551	4.12 (0.61)	0.30 (-1.39, 1.99)	0.7253	0.02 (-0.10, 0.14)	
	Other	182	65.52 (22.71)	176	9.42 (0.98)	159	65.49 (22.30)	152	9.50 (1.07)	-0.08 (-2.94, 2.78)	0.9560	-0.01 (-0.22, 0.21)	
	Geographic region												0.5927
	Asia	544	72.31 (23.20)	536	4.35 (0.62)	544	70.96 (24.22)	536	3.95 (0.62)	0.40 (-1.31, 2.12)	0.6444	0.03 (-0.09, 0.15)	
	Europe and Saudi Arabia	1395	72.43 (22.40)	1341	6.11 (0.37)	1420	72.32 (22.85)	1381	5.60 (0.37)	0.51 (-0.51, 1.54)	0.3254	0.04 (-0.04, 0.11)	
	North America	408	81.31 (21.96)	393	4.78 (0.66)	395	81.04 (21.12)	376	5.17 (0.67)	-0.39 (-2.23, 1.45)	0.6765	-0.03 (-0.17, 0.11)	
	Latin America	554	69.45 (24.40)	531	7.01 (0.64)	527	71.16 (24.92)	512	7.77 (0.65)	-0.76 (-2.54, 1.03)	0.4039	-0.05 (-0.17, 0.07)	
	NYHA class at enrolment												0.1609
	II	2155	73.81 (22.62)	2083	5.55 (0.30)	2218	73.87 (23.21)	2165	5.68 (0.30)	-0.13 (-0.96, 0.71)	0.7689	-0.01 (-0.07, 0.05)	
	III or IV	746	71.00 (24.48)	718	6.55 (0.54)	667	70.30 (24.22)	639	5.42 (0.57)	1.13 (-0.41, 2.67)	0.1514	0.08 (-0.03, 0.18)	
	LVEF at enrolment												0.4956
	<= 49	1002	73.35 (23.29)	959	5.38 (0.44)	981	72.31 (23.13)	950	5.85 (0.44)	-0.48 (-1.71, 0.75)	0.4459	-0.03 (-0.12, 0.05)	
	50-59	1051	73.12 (22.97)	1017	5.70 (0.44)	1033	73.31 (23.40)	1009	5.30 (0.44)	0.40 (-0.82, 1.62)	0.5200	0.03 (-0.06, 0.12)	
	>= 60	848	72.73 (23.20)	825	6.30 (0.50)	872	73.57 (24.00)	846	5.80 (0.50)	0.50 (-0.88, 1.88)	0.4778	0.03 (-0.06, 0.13)	
	NT-proBNP at enrolment												0.7942
	<= median	1443	72.96 (23.19)	1396	5.70 (0.38)	1442	73.29 (23.32)	1409	5.45 (0.38)	0.25 (-0.81, 1.30)	0.6428	0.02 (-0.06, 0.09)	
	> median	1458	73.22 (23.10)	1405	5.86 (0.37)	1443	72.82 (23.66)	1395	5.81 (0.37)	0.05 (-0.97, 1.08)	0.9174	0.00 (-0.07, 0.08)	
	Type 2 Diabetes Medical History												0.0428
	Yes	1276	72.93 (23.29)	1231	6.29 (0.40)	1281	73.49 (23.65)	1243	5.28 (0.40)	1.01 (-0.11, 2.13)	0.0764	0.07 (-0.01, 0.15)	
	No	1625	73.21 (23.03)	1570	5.38 (0.35)	1605	72.69 (23.37)	1562	5.90 (0.35)	-0.52 (-1.50, 0.45)	0.2942	-0.04 (-0.11, 0.03)	
	Atrial fibrillation or flutter at enrolment ECG												0.4528
	Yes	1234	72.39 (23.05)	1185	5.51 (0.41)	1222	73.06 (23.45)	1188	5.04 (0.41)	0.47 (-0.67, 1.61)	0.4206	0.03 (-0.05, 0.11)	
	No	1667	73.61 (23.20)	1616	5.97 (0.34)	1664	73.04 (23.53)	1617	6.07 (0.35)	-0.10 (-1.06, 0.86)	0.8359	-0.01 (-0.08, 0.06)	
	BMI (kg/m2) at enrolment												0.6408
	< 30	1595	72.51 (23.38)	1547	5.27 (0.36)	1592	73.06 (23.95)	1541	5.27 (0.36)	0.00 (-1.00, 1.00)	0.9981	0.00 (-0.07, 0.07)	
	>= 30	1305	73.79 (22.85)	1253	6.38 (0.39)	1291	73.10 (22.87)	1261	6.03 (0.39)	0.35 (-0.73, 1.43)	0.5242	0.03 (-0.05, 0.10)	
	Baseline eGFR (mL/min/1.73m^2)												0.3730
	< 60	1391	73.61 (22.42)	1338	5.41 (0.39)	1416	72.69 (23.65)	1377	5.63 (0.38)	-0.22 (-1.29, 0.85)	0.6890	-0.02 (-0.09, 0.06)	
	>= 60	1510	72.61 (23.79)	1463	6.09 (0.36)	1469	73.39 (23.35)	1427	5.64 (0.37)	0.45 (-0.56, 1.46)	0.3815	0.03 (-0.04, 0.11)	
	SBP at randomisation												0.1562
	<= median	1457	73.57 (23.19)	1405	5.44 (0.37)	1459	73.45 (23.66)	1420	5.82 (0.37)	-0.38 (-1.41, 0.65)	0.4705	-0.03 (-0.10, 0.05)	
	> median	1444	72.60 (23.10)	1396	6.11 (0.38)	1427	72.63 (23.31)	1385	5.43 (0.38)	0.68 (-0.36, 1.73)	0.2012	0.05 (-0.03, 0.12)	

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Self Efficacy	LVEF at enrolment 2												0.2380
	<= 49	1002	73.35 (23.29)	959	5.38 (0.44)	981	72.31 (23.13)	950	5.85 (0.44)	-0.48 (-1.71, 0.75)	0.4459	-0.03 (-0.12, 0.05)	
	>= 50	1899	72.95 (23.07)	1842	5.97 (0.33)	1905	73.43 (23.67)	1855	5.53 (0.33)	0.44 (-0.47, 1.36)	0.3413	0.03 (-0.03, 0.10)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.6286
	Yes	300	68.88 (23.57)	280	6.81 (0.85)	294	67.18 (24.19)	281	7.22 (0.85)	-0.41 (-2.77, 1.95)	0.7338	-0.03 (-0.19, 0.14)	
	No	2601	73.57 (23.05)	2521	5.66 (0.28)	2592	73.71 (23.32)	2524	5.46 (0.28)	0.20 (-0.57, 0.97)	0.6062	0.01 (-0.04, 0.07)	
	MRAs at baseline												0.7373
	Yes	1246	72.78 (23.40)	1216	5.08 (0.40)	1239	72.38 (23.62)	1210	5.07 (0.41)	0.02 (-1.11, 1.14)	0.9761	0.00 (-0.08, 0.08)	
	No	1655	73.32 (22.95)	1585	6.33 (0.35)	1647	73.55 (23.39)	1595	6.05 (0.35)	0.27 (-0.70, 1.24)	0.5831	0.02 (-0.05, 0.09)	
	ACEi+ARB at baseline												0.0574
	Yes	2102	72.62 (23.14)	2037	6.07 (0.31)	2105	72.60 (23.50)	2059	5.48 (0.31)	0.58 (-0.27, 1.43)	0.1796	0.04 (-0.02, 0.10)	
	No	799	74.31 (23.13)	764	5.01 (0.52)	781	74.25 (23.45)	746	6.05 (0.52)	-1.04 (-2.48, 0.40)	0.1574	-0.07 (-0.17, 0.03)	
	ARNI at baseline												0.0883
	Yes	156	80.21 (22.00)	149	2.47 (1.05)	126	78.67 (20.68)	125	4.93 (1.14)	-2.46 (-5.52, 0.60)	0.1140	-0.19 (-0.43, 0.05)	
	No	2745	72.68 (23.14)	2652	5.95 (0.27)	2760	72.79 (23.58)	2680	5.68 (0.27)	0.26 (-0.49, 1.02)	0.4923	0.02 (-0.03, 0.07)	
	Beta Blocker at baseline												0.8630
	Yes	2410	73.42 (23.04)	2327	5.58 (0.29)	2397	73.28 (23.36)	2330	5.47 (0.29)	0.12 (-0.69, 0.92)	0.7745	0.01 (-0.05, 0.07)	
	No	491	71.44 (23.57)	474	6.75 (0.65)	489	71.91 (24.09)	475	6.46 (0.66)	0.29 (-1.53, 2.11)	0.7526	0.02 (-0.11, 0.15)	
	Diuretics at baseline												0.1153
	Yes	2592	73.30 (22.96)	2500	5.70 (0.28)	2577	73.13 (23.47)	2504	5.75 (0.28)	-0.04 (-0.82, 0.73)	0.9106	-0.00 (-0.06, 0.05)	
	No	309	71.32 (24.61)	301	6.44 (0.82)	309	72.37 (23.70)	301	4.54 (0.82)	1.89 (-0.40, 4.18)	0.1047	0.13 (-0.03, 0.29)	

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Symptom Frequency	Age												0.6600
	<= median	1443	69.82 (24.35)	1394	7.93 (0.38)	1507	69.18 (23.67)	1471	6.03 (0.37)	1.91 (0.86, 2.95)	0.0003	0.13 (0.06, 0.21)	
	> median	1458	67.61 (23.36)	1407	6.92 (0.38)	1379	68.72 (22.65)	1334	4.68 (0.39)	2.24 (1.18, 3.31)	<.0001	0.16 (0.08, 0.23)	
	Gender												0.4872
	Male	1691	71.59 (23.30)	1630	6.92 (0.34)	1648	71.64 (23.06)	1608	5.15 (0.35)	1.77 (0.82, 2.73)	0.0003	0.13 (0.06, 0.20)	
	Female	1210	64.68 (24.11)	1171	8.08 (0.43)	1238	65.39 (22.88)	1197	5.77 (0.42)	2.31 (1.13, 3.49)	0.0001	0.16 (0.08, 0.24)	
	Race												0.5940
	White	2087	66.45 (23.31)	2006	7.99 (0.32)	2094	67.26 (22.67)	2032	5.78 (0.32)	2.22 (1.33, 3.10)	<.0001	0.16 (0.09, 0.22)	
	Black or African	69	60.39 (26.41)	64	10.34 (2.33)	71	58.89 (25.26)	70	9.81 (2.25)	0.53 (-5.88, 6.94)	0.8702	0.03 (-0.31, 0.37)	
	Asian	563	79.65 (22.40)	555	3.64 (0.58)	562	78.54 (21.85)	551	2.60 (0.58)	1.04 (-0.56, 2.65)	0.2036	0.08 (-0.04, 0.19)	
	Other	182	63.90 (24.01)	176	13.41 (0.96)	159	61.95 (24.01)	152	10.97 (1.05)	2.45 (-0.36, 5.26)	0.0876	0.19 (-0.03, 0.41)	
	Geographic region												0.3301
	Asia	544	79.86 (22.47)	536	3.66 (0.58)	544	79.32 (21.41)	536	2.57 (0.58)	1.10 (-0.52, 2.71)	0.1845	0.08 (-0.04, 0.20)	
	Europe and Saudi Arabia	1395	67.64 (22.52)	1341	7.32 (0.37)	1420	68.61 (21.68)	1381	5.58 (0.36)	1.73 (0.72, 2.75)	0.0008	0.13 (0.05, 0.20)	
	North America	408	62.10 (24.41)	393	6.51 (0.77)	395	61.31 (24.34)	376	4.03 (0.79)	2.48 (0.32, 4.64)	0.0243	0.16 (0.02, 0.30)	
	Latin America	554	65.32 (24.68)	531	12.91 (0.65)	527	64.92 (24.35)	512	9.67 (0.66)	3.24 (1.43, 5.05)	0.0005	0.22 (0.10, 0.34)	
	NYHA class at enrolment												0.0581
	II	2155	72.75 (22.28)	2083	6.32 (0.30)	2218	72.32 (21.92)	2165	4.64 (0.29)	1.68 (0.86, 2.50)	<.0001	0.12 (0.06, 0.18)	
	III or IV	746	57.02 (24.50)	718	11.15 (0.59)	667	57.76 (23.81)	639	7.65 (0.63)	3.49 (1.80, 5.18)	<.0001	0.22 (0.11, 0.33)	
	LVEF at enrolment												0.9755
	<= 49	1002	70.48 (23.82)	959	7.63 (0.44)	981	69.50 (23.46)	950	5.70 (0.44)	1.92 (0.69, 3.15)	0.0023	0.14 (0.05, 0.23)	
	50-59	1051	68.08 (23.85)	1017	7.29 (0.44)	1033	68.55 (22.57)	1009	5.23 (0.44)	2.05 (0.83, 3.27)	0.0010	0.15 (0.06, 0.23)	
	>= 60	848	67.40 (23.89)	825	7.35 (0.52)	872	68.84 (23.62)	846	5.22 (0.52)	2.13 (0.68, 3.58)	0.0040	0.14 (0.05, 0.24)	
	NT-proBNP at enrolment												0.4874
	<= median	1443	70.64 (22.57)	1396	6.46 (0.37)	1442	70.50 (22.67)	1409	4.71 (0.37)	1.75 (0.71, 2.78)	0.0010	0.12 (0.05, 0.20)	
	> median	1458	66.79 (24.97)	1405	8.37 (0.39)	1443	67.45 (23.58)	1395	6.09 (0.39)	2.28 (1.20, 3.35)	<.0001	0.16 (0.08, 0.23)	
	Type 2 Diabetes Medical History												0.0100
	Yes	1276	67.16 (24.16)	1231	8.49 (0.42)	1281	66.68 (24.35)	1243	5.38 (0.42)	3.12 (1.95, 4.29)	<.0001	0.21 (0.13, 0.29)	
	No	1625	69.93 (23.60)	1570	6.56 (0.35)	1605	70.78 (22.06)	1562	5.43 (0.35)	1.13 (0.16, 2.09)	0.0219	0.08 (0.01, 0.15)	
	Atrial fibrillation or flutter at enrolment ECG												0.2918
	Yes	1234	67.98 (24.42)	1185	8.03 (0.42)	1222	68.03 (22.86)	1188	5.55 (0.41)	2.49 (1.34, 3.64)	<.0001	0.17 (0.09, 0.25)	
	No	1667	69.25 (23.47)	1616	6.96 (0.35)	1664	69.64 (23.41)	1617	5.29 (0.35)	1.67 (0.69, 2.65)	0.0008	0.12 (0.05, 0.19)	
	BMI (kg/m2) at enrolment												0.2815
	< 30	1595	72.95 (22.84)	1547	6.23 (0.34)	1592	72.93 (22.01)	1541	4.59 (0.34)	1.64 (0.70, 2.58)	0.0007	0.12 (0.05, 0.19)	
	>= 30	1305	63.55 (24.11)	1253	8.92 (0.43)	1291	64.05 (23.69)	1261	6.45 (0.43)	2.47 (1.28, 3.66)	<.0001	0.16 (0.08, 0.24)	
	Baseline eGFR (mL/min/1.73m^2)												0.8127
	< 60	1391	67.29 (23.89)	1338	7.15 (0.40)	1416	67.54 (23.43)	1377	5.27 (0.40)	1.88 (0.77, 2.99)	0.0009	0.13 (0.05, 0.20)	
	>= 60	1510	70.02 (23.81)	1463	7.63 (0.36)	1469	70.36 (22.85)	1427	5.57 (0.36)	2.06 (1.06, 3.06)	<.0001	0.15 (0.08, 0.22)	
	SBP at randomisation												0.0243
	<= median	1457	68.73 (23.97)	1405	6.63 (0.39)	1459	69.90 (22.94)	1420	5.47 (0.38)	1.15 (0.09, 2.22)	0.0343	0.08 (0.01, 0.15)	
	> median	1444	68.69 (23.80)	1396	8.19 (0.37)	1427	67.99 (23.41)	1385	5.32 (0.38)	2.87 (1.83, 3.91)	<.0001	0.20 (0.13, 0.28)	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

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Symptom Frequency	LVEF at enrolment 2												0.8363
	<= 49	1002	70.48 (23.82)	959	7.63 (0.44)	981	69.50 (23.46)	950	5.70 (0.44)	1.92 (0.69, 3.15)	0.0023	0.14 (0.05, 0.23)	
	>= 50	1899	67.77 (23.86)	1842	7.32 (0.34)	1905	68.68 (23.05)	1855	5.23 (0.34)	2.08 (1.15, 3.02)	<.0001	0.14 (0.08, 0.21)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.9040
	Yes	300	60.22 (24.68)	280	14.32 (0.92)	294	57.37 (23.00)	281	12.11 (0.92)	2.21 (-0.35, 4.77)	0.0899	0.14 (-0.02, 0.31)	
	No	2601	69.69 (23.60)	2521	6.70 (0.28)	2592	70.27 (22.85)	2524	4.65 (0.28)	2.05 (1.27, 2.83)	<.0001	0.15 (0.09, 0.20)	
	MRAs at baseline												0.8116
	Yes	1246	68.87 (24.24)	1216	7.08 (0.40)	1239	69.19 (23.37)	1210	5.16 (0.40)	1.92 (0.81, 3.03)	0.0007	0.14 (0.06, 0.22)	
	No	1655	68.59 (23.61)	1585	7.69 (0.36)	1647	68.78 (23.06)	1595	5.59 (0.36)	2.10 (1.09, 3.11)	<.0001	0.14 (0.08, 0.21)	
	ACEi+ARB at baseline												0.1177
	Yes	2102	67.88 (24.09)	2037	8.10 (0.31)	2105	68.63 (23.31)	2059	5.72 (0.31)	2.38 (1.52, 3.24)	<.0001	0.17 (0.11, 0.23)	
	No	799	70.90 (23.18)	764	5.60 (0.53)	781	69.84 (22.85)	746	4.59 (0.54)	1.01 (-0.48, 2.50)	0.1843	0.07 (-0.03, 0.17)	
	ARNI at baseline												0.3042
	Yes	156	78.58 (20.44)	149	3.37 (1.07)	126	74.92 (22.15)	125	2.99 (1.18)	0.39 (-2.76, 3.54)	0.8087	0.03 (-0.21, 0.27)	
	No	2745	68.15 (23.94)	2652	7.62 (0.28)	2760	68.69 (23.20)	2680	5.54 (0.28)	2.08 (1.31, 2.85)	<.0001	0.15 (0.09, 0.20)	
	Beta Blocker at baseline												0.7379
	Yes	2410	68.35 (23.75)	2327	7.39 (0.30)	2397	69.21 (22.79)	2330	5.42 (0.29)	1.96 (1.15, 2.78)	<.0001	0.14 (0.08, 0.20)	
	No	491	70.48 (24.47)	474	7.60 (0.66)	489	67.71 (25.06)	475	5.29 (0.66)	2.31 (0.47, 4.14)	0.0137	0.16 (0.03, 0.29)	
	Diuretics at baseline												0.8599
	Yes	2592	68.51 (23.92)	2500	7.49 (0.29)	2577	68.36 (23.30)	2504	5.49 (0.29)	2.00 (1.21, 2.80)	<.0001	0.14 (0.08, 0.19)	
	No	309	70.41 (23.55)	301	6.89 (0.76)	309	73.97 (21.62)	301	4.69 (0.76)	2.20 (0.10, 4.31)	0.0403	0.17 (0.01, 0.33)	

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Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Social Limitation	Age												0.7333
	<= median	1386	67.32 (26.55)	1331	6.82 (0.45)	1449	66.85 (25.77)	1409	5.78 (0.44)	1.04 (-0.20, 2.28)	0.1000	0.06 (-0.01, 0.14)	
	> median	1357	66.00 (27.31)	1294	5.14 (0.47)	1283	67.01 (26.15)	1216	3.79 (0.49)	1.36 (0.03, 2.69)	0.0452	0.08 (0.00, 0.16)	
	Gender												0.1590
	Male	1613	69.07 (26.25)	1538	5.56 (0.42)	1550	69.10 (25.67)	1500	5.03 (0.43)	0.53 (-0.66, 1.71)	0.3830	0.03 (-0.04, 0.10)	
	Female	1130	63.23 (27.52)	1087	6.57 (0.51)	1182	64.07 (26.05)	1125	4.72 (0.50)	1.85 (0.44, 3.26)	0.0101	0.11 (0.03, 0.19)	
	Race												0.2618
	White	1985	65.00 (26.20)	1890	6.41 (0.39)	1999	66.02 (25.42)	1921	4.82 (0.38)	1.60 (0.53, 2.67)	0.0035	0.09 (0.03, 0.16)	
	Black or African	63	60.48 (32.42)	58	4.60 (2.82)	67	59.98 (27.79)	66	8.23 (2.70)	-3.63 (-11.4, 4.11)	0.3553	-0.17 (-0.52, 0.19)	
	Asian	516	75.90 (27.25)	506	3.81 (0.69)	514	74.27 (26.72)	494	3.85 (0.70)	-0.04 (-1.96, 1.89)	0.9709	-0.00 (-0.13, 0.12)	
	Other	179	60.65 (26.05)	171	9.23 (1.27)	152	56.99 (23.39)	144	9.28 (1.40)	-0.05 (-3.78, 3.67)	0.9779	-0.00 (-0.22, 0.22)	
	Geographic region												0.6591
	Asia	502	76.00 (27.27)	492	3.98 (0.69)	498	74.73 (26.47)	482	3.86 (0.70)	0.12 (-1.81, 2.05)	0.9043	0.01 (-0.12, 0.13)	
	Europe and Saudi Arabia	1335	65.61 (24.61)	1273	5.54 (0.43)	1353	66.99 (23.97)	1309	4.43 (0.43)	1.11 (-0.09, 2.30)	0.0688	0.07 (-0.01, 0.15)	
	North America	384	63.76 (29.26)	367	5.31 (0.96)	374	62.49 (27.89)	347	4.52 (0.98)	0.79 (-1.91, 3.48)	0.5652	0.04 (-0.10, 0.19)	
	Latin America	522	62.52 (28.49)	493	10.06 (0.87)	507	62.34 (27.23)	487	8.00 (0.88)	2.07 (-0.36, 4.49)	0.0951	0.11 (-0.02, 0.23)	
	NYHA class at enrolment												0.0928
	II	2039	70.88 (25.24)	1953	5.29 (0.36)	2103	70.59 (24.46)	2031	4.50 (0.36)	0.79 (-0.20, 1.79)	0.1188	0.05 (-0.01, 0.11)	
	III or IV	704	54.47 (27.95)	672	8.54 (0.71)	628	54.61 (26.98)	593	5.81 (0.75)	2.73 (0.70, 4.76)	0.0085	0.15 (0.04, 0.26)	
	LVEF at enrolment												0.4056
	<= 49	952	66.59 (26.57)	907	6.58 (0.55)	936	64.85 (25.77)	896	6.28 (0.55)	0.30 (-1.22, 1.82)	0.7010	0.02 (-0.07, 0.11)	
	50-59	1000	65.80 (27.41)	955	5.81 (0.55)	975	67.76 (25.47)	946	4.11 (0.55)	1.70 (0.18, 3.22)	0.0284	0.10 (0.01, 0.19)	
	>= 60	791	67.85 (26.74)	763	5.53 (0.62)	821	68.29 (26.59)	783	4.12 (0.61)	1.41 (-0.29, 3.12)	0.1031	0.08 (-0.02, 0.18)	
	NT-proBNP at enrolment												0.5323
	<= median	1369	68.43 (25.76)	1312	5.25 (0.45)	1373	68.33 (24.98)	1336	4.42 (0.44)	0.83 (-0.40, 2.07)	0.1863	0.05 (-0.02, 0.13)	
	> median	1374	64.91 (27.95)	1313	6.73 (0.48)	1358	65.54 (26.80)	1288	5.32 (0.48)	1.41 (0.08, 2.75)	0.0384	0.08 (0.00, 0.16)	
	Type 2 Diabetes Medical History												0.1093
	Yes	1201	65.43 (27.31)	1150	6.46 (0.50)	1212	65.08 (26.52)	1169	4.52 (0.50)	1.94 (0.55, 3.32)	0.0061	0.11 (0.03, 0.20)	
	No	1542	67.63 (26.60)	1475	5.61 (0.43)	1520	68.39 (25.39)	1456	5.17 (0.43)	0.44 (-0.76, 1.64)	0.4695	0.03 (-0.05, 0.10)	
	Atrial fibrillation or flutter at enrolment ECG												0.1621
	Yes	1152	66.09 (27.62)	1097	6.39 (0.51)	1156	66.79 (25.72)	1109	4.51 (0.51)	1.88 (0.47, 3.30)	0.0090	0.11 (0.03, 0.19)	
	No	1591	67.08 (26.42)	1528	5.71 (0.43)	1576	67.02 (26.12)	1516	5.14 (0.43)	0.57 (-0.61, 1.75)	0.3451	0.03 (-0.04, 0.11)	
	BMI (kg/m2) at enrolment												0.4095
	< 30	1512	69.10 (26.72)	1452	5.58 (0.42)	1493	69.42 (25.74)	1428	4.84 (0.43)	0.75 (-0.43, 1.92)	0.2150	0.05 (-0.03, 0.12)	
	>= 30	1230	63.66 (26.90)	1172	6.48 (0.51)	1237	63.94 (25.89)	1195	4.97 (0.50)	1.52 (0.11, 2.93)	0.0346	0.09 (0.01, 0.17)	
	Baseline eGFR (mL/min/1.73m^2)												0.5127
	< 60	1300	65.17 (27.29)	1240	5.85 (0.49)	1329	65.16 (26.94)	1270	4.45 (0.49)	1.40 (0.04, 2.76)	0.0441	0.08 (0.00, 0.16)	
	>= 60	1443	68.01 (26.55)	1385	6.09 (0.43)	1402	68.62 (24.84)	1354	5.31 (0.44)	0.79 (-0.42, 2.00)	0.2028	0.05 (-0.03, 0.12)	
	SBP at randomisation												0.0704
	<= median	1387	65.44 (27.42)	1320	5.75 (0.47)	1376	66.81 (25.94)	1323	5.46 (0.47)	0.29 (-1.02, 1.60)	0.6675	0.02 (-0.06, 0.09)	
	> median	1356	67.92 (26.37)	1305	6.23 (0.45)	1356	67.04 (25.96)	1302	4.26 (0.45)	1.96 (0.70, 3.22)	0.0022	0.12 (0.04, 0.20)	

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Social Limitation	LVEF at enrolment 2												0.1875
	<= 49	952	66.59 (26.57)	907	6.58 (0.55)	936	64.85 (25.77)	896	6.28 (0.55)	0.30 (-1.22, 1.82)	0.7010	0.02 (-0.07, 0.11)	
	>= 50	1791	66.70 (27.13)	1718	5.70 (0.41)	1796	68.01 (25.98)	1729	4.13 (0.41)	1.57 (0.44, 2.70)	0.0066	0.09 (0.03, 0.16)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.3792
	Yes	275	58.37 (28.35)	252	9.81 (1.19)	270	58.22 (26.85)	256	10.08 (1.18)	-0.27 (-3.56, 3.02)	0.8731	-0.01 (-0.19, 0.16)	
	No	2468	67.59 (26.62)	2373	5.60 (0.34)	2462	67.88 (25.67)	2369	4.33 (0.34)	1.26 (0.32, 2.20)	0.0084	0.08 (0.02, 0.13)	
	MRAs at baseline												0.3367
	Yes	1183	66.12 (26.70)	1144	5.78 (0.50)	1170	65.71 (25.93)	1131	5.17 (0.51)	0.60 (-0.80, 2.01)	0.3978	0.04 (-0.05, 0.12)	
	No	1560	67.08 (27.11)	1481	6.15 (0.43)	1562	67.83 (25.93)	1494	4.64 (0.43)	1.51 (0.31, 2.70)	0.0133	0.09 (0.02, 0.16)	
	ACEi+ARB at baseline												0.3021
	Yes	1984	66.40 (26.73)	1909	6.46 (0.38)	2000	66.82 (25.75)	1934	5.04 (0.38)	1.42 (0.37, 2.47)	0.0082	0.09 (0.02, 0.15)	
	No	759	67.36 (27.45)	716	4.72 (0.64)	732	67.21 (26.50)	691	4.40 (0.65)	0.33 (-1.47, 2.12)	0.7218	0.02 (-0.09, 0.12)	
	ARNI at baseline												0.7498
	Yes	153	70.60 (25.41)	146	3.35 (1.24)	119	70.13 (24.14)	115	2.82 (1.40)	0.53 (-3.16, 4.22)	0.7784	0.04 (-0.21, 0.28)	
	No	2590	66.43 (27.01)	2479	6.14 (0.34)	2613	66.78 (26.02)	2510	4.99 (0.34)	1.14 (0.21, 2.08)	0.0166	0.07 (0.01, 0.12)	
	Beta Blocker at baseline												0.3516
	Yes	2293	66.40 (26.89)	2195	5.83 (0.36)	2272	67.21 (25.77)	2187	4.91 (0.36)	0.92 (-0.08, 1.92)	0.0720	0.05 (-0.00, 0.11)	
	No	450	68.04 (27.15)	430	6.79 (0.79)	460	65.51 (26.78)	438	4.73 (0.78)	2.05 (-0.12, 4.23)	0.0645	0.13 (-0.01, 0.26)	
	Diuretics at baseline												0.5143
	Yes	2457	66.46 (26.97)	2350	6.00 (0.35)	2441	66.43 (26.08)	2345	4.76 (0.35)	1.23 (0.26, 2.20)	0.0130	0.07 (0.02, 0.13)	
	No	286	68.41 (26.54)	275	6.07 (0.88)	291	71.04 (24.44)	280	5.71 (0.88)	0.36 (-2.09, 2.80)	0.7742	0.02 (-0.14, 0.19)	

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Symptom Stability	Age												0.0734
	<= median	1443	54.89 (18.93)	1394	4.38 (0.38)	1507	54.99 (18.75)	1471	3.74 (0.38)	0.65 (-0.41, 1.70)	0.2292	0.04 (-0.03, 0.12)	
	> median	1458	53.72 (17.39)	1407	4.72 (0.38)	1379	54.10 (18.03)	1334	2.71 (0.39)	2.02 (0.95, 3.08)	0.0002	0.14 (0.07, 0.22)	
	Gender												0.7231
	Male	1691	55.29 (18.23)	1630	3.64 (0.35)	1648	55.69 (18.54)	1608	2.49 (0.36)	1.15 (0.17, 2.13)	0.0219	0.08 (0.01, 0.15)	
	Female	1210	52.91 (18.03)	1171	5.76 (0.42)	1238	53.07 (18.14)	1197	4.33 (0.42)	1.43 (0.26, 2.59)	0.0163	0.10 (0.02, 0.18)	
	Race												0.6813
	White	2087	53.89 (17.31)	2006	4.55 (0.31)	2094	54.37 (18.17)	2032	3.58 (0.31)	0.97 (0.11, 1.83)	0.0279	0.07 (0.01, 0.13)	
	Black or African	69	51.09 (19.85)	64	8.86 (2.21)	71	52.11 (22.66)	70	6.87 (2.14)	1.99 (-4.10, 8.07)	0.5193	0.11 (-0.23, 0.45)	
	Asian	563	57.10 (20.63)	555	1.15 (0.59)	562	56.76 (18.31)	551	-0.47 (0.60)	1.62 (-0.04, 3.27)	0.0558	0.12 (-0.00, 0.23)	
	Other	182	51.51 (18.24)	176	15.49 (1.18)	159	50.47 (18.97)	152	12.60 (1.30)	2.89 (-0.57, 6.34)	0.1014	0.18 (-0.04, 0.40)	
	Geographic region												0.8709
	Asia	544	57.12 (20.49)	536	1.05 (0.60)	544	56.94 (18.30)	536	-0.58 (0.60)	1.63 (-0.03, 3.29)	0.0550	0.12 (-0.00, 0.24)	
	Europe and Saudi Arabia	1395	54.12 (16.65)	1341	4.20 (0.36)	1420	54.14 (17.36)	1381	3.26 (0.36)	0.94 (-0.06, 1.94)	0.0659	0.07 (-0.00, 0.15)	
	North America	408	51.90 (19.06)	393	3.07 (0.78)	395	53.99 (20.73)	376	1.78 (0.79)	1.29 (-0.89, 3.47)	0.2464	0.08 (-0.06, 0.23)	
	Latin America	554	53.75 (18.49)	531	10.56 (0.67)	527	53.70 (19.27)	512	8.93 (0.69)	1.62 (-0.27, 3.52)	0.0920	0.10 (-0.02, 0.23)	
	NYHA class at enrolment												0.0246
	II	2155	54.80 (17.69)	2083	4.21 (0.31)	2218	54.76 (17.72)	2165	3.41 (0.31)	0.80 (-0.06, 1.66)	0.0686	0.06 (-0.00, 0.12)	
	III or IV	746	52.85 (19.46)	718	5.59 (0.54)	667	53.94 (20.56)	639	2.77 (0.57)	2.81 (1.28, 4.35)	0.0003	0.20 (0.09, 0.30)	
	LVEF at enrolment												0.0342
	<= 49	1002	55.39 (19.05)	959	3.66 (0.46)	981	55.48 (18.49)	950	3.06 (0.46)	0.60 (-0.69, 1.88)	0.3622	0.04 (-0.05, 0.13)	
	50-59	1051	53.95 (17.49)	1017	4.88 (0.44)	1033	54.50 (18.75)	1009	2.28 (0.45)	2.59 (1.36, 3.83)	<.0001	0.18 (0.10, 0.27)	
	>= 60	848	53.45 (17.91)	825	5.16 (0.51)	872	53.61 (17.89)	846	4.69 (0.50)	0.47 (-0.93, 1.87)	0.5132	0.03 (-0.06, 0.13)	
	NT-proBNP at enrolment												0.2514
	<= median	1443	54.37 (17.74)	1396	4.53 (0.38)	1442	54.16 (17.65)	1409	3.70 (0.38)	0.84 (-0.23, 1.90)	0.1229	0.06 (-0.02, 0.13)	
	> median	1458	54.24 (18.61)	1405	4.55 (0.38)	1443	54.99 (19.13)	1395	2.83 (0.38)	1.71 (0.65, 2.78)	0.0016	0.12 (0.05, 0.19)	
	Type 2 Diabetes Medical History												0.8085
	Yes	1276	54.55 (18.39)	1231	4.25 (0.41)	1281	53.98 (18.27)	1243	3.07 (0.41)	1.18 (0.05, 2.32)	0.0413	0.08 (0.00, 0.16)	
	No	1625	54.11 (18.01)	1570	4.78 (0.36)	1605	55.03 (18.52)	1562	3.42 (0.36)	1.37 (0.37, 2.37)	0.0074	0.10 (0.03, 0.17)	
	Atrial fibrillation or flutter at enrolment ECG												0.4660
	Yes	1234	54.29 (17.84)	1185	4.28 (0.40)	1222	54.48 (18.63)	1188	2.69 (0.40)	1.60 (0.48, 2.71)	0.0049	0.12 (0.03, 0.20)	
	No	1667	54.30 (18.43)	1616	4.74 (0.37)	1664	54.63 (18.26)	1617	3.70 (0.37)	1.04 (0.02, 2.05)	0.0448	0.07 (0.00, 0.14)	
	BMI (kg/m2) at enrolment												0.2519
	< 30	1595	55.11 (18.55)	1547	3.96 (0.37)	1592	55.54 (18.37)	1541	2.28 (0.37)	1.68 (0.66, 2.71)	0.0013	0.12 (0.05, 0.19)	
	>= 30	1305	53.31 (17.68)	1253	5.29 (0.40)	1291	53.39 (18.41)	1261	4.48 (0.40)	0.80 (-0.30, 1.90)	0.1550	0.06 (-0.02, 0.13)	
	Baseline eGFR (mL/min/1.73m^2)												0.2437
	< 60	1391	54.49 (18.30)	1338	3.40 (0.40)	1416	54.52 (18.77)	1377	2.61 (0.39)	0.79 (-0.30, 1.88)	0.1578	0.05 (-0.02, 0.13)	
	>= 60	1510	54.12 (18.07)	1463	5.55 (0.37)	1469	54.65 (18.01)	1427	3.87 (0.38)	1.68 (0.65, 2.71)	0.0014	0.12 (0.05, 0.19)	
	SBP at randomisation												0.1507
	<= median	1457	54.84 (19.07)	1405	3.39 (0.39)	1459	55.53 (18.90)	1420	2.65 (0.38)	0.74 (-0.33, 1.80)	0.1759	0.05 (-0.02, 0.12)	
	> median	1444	53.76 (17.22)	1396	5.71 (0.38)	1427	53.57 (17.85)	1385	3.88 (0.38)	1.84 (0.78, 2.90)	0.0007	0.13 (0.05, 0.20)	

Repeated measures analysis displays overall results.
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LSMeans and difference of LSMeans estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.
p-Value for interaction from test for heterogeneity of the differences of LSMeans in the subgroups using Cochrane`s Q statistic.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Symptom Stability	LVEF at enrolment 2												0.1986
	<= 49	1002	55.39 (19.05)	959	3.66 (0.46)	981	55.48 (18.49)	950	3.06 (0.46)	0.60 (-0.69, 1.88)	0.3622	0.04 (-0.05, 0.13)	
	>= 50	1899	53.73 (17.68)	1842	5.00 (0.33)	1905	54.09 (18.36)	1855	3.37 (0.33)	1.63 (0.70, 2.56)	0.0006	0.11 (0.05, 0.18)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.2134
	Yes	300	62.50 (23.89)	280	-1.56 (0.91)	294	61.82 (25.01)	281	-1.35 (0.90)	-0.21 (-2.73, 2.30)	0.8680	-0.01 (-0.18, 0.15)	
	No	2601	53.35 (17.15)	2521	5.21 (0.28)	2592	53.74 (17.32)	2524	3.76 (0.28)	1.46 (0.67, 2.24)	0.0003	0.10 (0.05, 0.16)	
	MRAs at baseline												0.2093
	Yes	1246	55.82 (18.97)	1216	3.78 (0.41)	1239	55.21 (19.12)	1210	3.06 (0.42)	0.71 (-0.44, 1.87)	0.2262	0.05 (-0.03, 0.13)	
	No	1655	53.16 (17.48)	1585	5.13 (0.36)	1647	54.08 (17.85)	1595	3.44 (0.36)	1.69 (0.70, 2.67)	0.0008	0.12 (0.05, 0.19)	
	ACEi+ARB at baseline												0.4181
	Yes	2102	54.14 (17.94)	2037	4.91 (0.31)	2105	54.18 (18.00)	2059	3.43 (0.31)	1.48 (0.61, 2.35)	0.0009	0.10 (0.04, 0.17)	
	No	799	54.72 (18.78)	764	3.56 (0.53)	781	55.60 (19.44)	746	2.79 (0.54)	0.77 (-0.72, 2.25)	0.3116	0.05 (-0.05, 0.15)	
	ARNI at baseline												0.5765
	Yes	156	59.94 (20.22)	149	1.59 (1.21)	126	58.93 (19.10)	125	-0.65 (1.32)	2.24 (-1.29, 5.77)	0.2126	0.15 (-0.09, 0.39)	
	No	2745	53.98 (18.01)	2652	4.68 (0.28)	2760	54.37 (18.36)	2680	3.47 (0.28)	1.21 (0.45, 1.98)	0.0020	0.08 (0.03, 0.14)	
	Beta Blocker at baseline												0.1370
	Yes	2410	54.12 (18.09)	2327	4.31 (0.30)	2397	54.83 (18.34)	2330	3.26 (0.30)	1.05 (0.23, 1.87)	0.0118	0.07 (0.02, 0.13)	
	No	491	55.19 (18.59)	474	5.78 (0.67)	489	53.27 (18.72)	475	3.17 (0.68)	2.60 (0.73, 4.48)	0.0065	0.18 (0.05, 0.30)	
	Diuretics at baseline												0.7713
	Yes	2592	54.35 (18.13)	2500	4.45 (0.29)	2577	54.60 (18.36)	2504	3.20 (0.29)	1.25 (0.45, 2.05)	0.0021	0.09 (0.03, 0.14)	
	No	309	53.88 (18.60)	301	5.33 (0.80)	309	54.29 (18.89)	301	3.73 (0.81)	1.60 (-0.64, 3.84)	0.1603	0.11 (-0.05, 0.27)	

Repeated measures analysis displays overall results.
N* displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
LSMeans and difference of LSMeans estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Total Symptom Score	Age												0.9338
	<= median	1443	70.46 (23.14)	1394	8.22 (0.35)	1507	70.08 (22.07)	1471	6.18 (0.35)	2.04 (1.08, 3.01)	<.0001	0.15 (0.08, 0.23)	
	> median	1458	69.16 (22.08)	1407	6.80 (0.35)	1379	70.45 (21.31)	1334	4.70 (0.36)	2.10 (1.11, 3.10)	<.0001	0.16 (0.08, 0.23)	
	Gender												0.8142
	Male	1691	72.60 (22.00)	1630	7.11 (0.32)	1648	73.07 (21.47)	1608	5.18 (0.32)	1.93 (1.05, 2.82)	<.0001	0.15 (0.08, 0.22)	
	Female	1210	65.89 (22.90)	1171	8.02 (0.40)	1238	66.52 (21.48)	1197	5.92 (0.39)	2.10 (1.00, 3.20)	0.0002	0.15 (0.07, 0.23)	
	Race												0.4931
	White	2087	67.57 (22.03)	2006	8.07 (0.30)	2094	68.39 (21.33)	2032	5.89 (0.30)	2.18 (1.35, 3.01)	<.0001	0.16 (0.10, 0.22)	
	Black or African	69	61.41 (26.38)	64	10.19 (2.03)	71	61.55 (22.76)	70	9.36 (1.97)	0.83 (-4.78, 6.43)	0.7710	0.05 (-0.29, 0.39)	
	Asian	563	81.04 (20.48)	555	3.74 (0.50)	562	80.42 (19.25)	551	2.66 (0.51)	1.08 (-0.32, 2.48)	0.1307	0.09 (-0.03, 0.21)	
	Other	182	63.91 (22.95)	176	13.66 (0.95)	159	62.81 (23.12)	152	10.75 (1.03)	2.90 (0.15, 5.66)	0.0392	0.23 (0.01, 0.45)	
	Geographic region												0.2638
	Asia	544	81.22 (20.50)	536	3.76 (0.51)	544	81.11 (18.87)	536	2.62 (0.51)	1.14 (-0.27, 2.55)	0.1133	0.10 (-0.02, 0.22)	
	Europe and Saudi Arabia	1395	68.30 (21.25)	1341	7.60 (0.35)	1420	69.23 (20.64)	1381	5.88 (0.34)	1.71 (0.76, 2.67)	0.0004	0.13 (0.06, 0.21)	
	North America	408	64.33 (23.47)	393	6.50 (0.72)	395	64.41 (22.41)	376	3.72 (0.74)	2.78 (0.75, 4.81)	0.0074	0.19 (0.05, 0.34)	
	Latin America	554	66.42 (23.63)	531	12.54 (0.62)	527	66.18 (22.92)	512	9.39 (0.63)	3.15 (1.42, 4.88)	0.0004	0.22 (0.10, 0.34)	
	NYHA class at enrolment												0.0478
	II	2155	73.88 (20.95)	2083	6.43 (0.28)	2218	73.69 (20.36)	2165	4.73 (0.27)	1.69 (0.93, 2.45)	<.0001	0.13 (0.07, 0.19)	
	III or IV	746	58.03 (23.14)	718	11.16 (0.56)	667	58.82 (22.17)	639	7.69 (0.59)	3.47 (1.88, 5.06)	<.0001	0.23 (0.13, 0.34)	
	LVEF at enrolment												0.8132
	<= 49	1002	71.16 (22.71)	959	7.87 (0.41)	981	70.49 (22.14)	950	5.95 (0.41)	1.92 (0.77, 3.07)	0.0010	0.15 (0.06, 0.24)	
	50-59	1051	69.20 (22.88)	1017	7.35 (0.42)	1033	69.79 (21.13)	1009	5.47 (0.42)	1.88 (0.72, 3.04)	0.0015	0.14 (0.05, 0.23)	
	>= 60	848	68.95 (22.13)	825	7.32 (0.48)	872	70.55 (21.91)	846	4.92 (0.47)	2.41 (1.09, 3.73)	0.0004	0.17 (0.08, 0.27)	
	NT-proBNP at enrolment												0.3515
	<= median	1443	71.68 (21.45)	1396	6.54 (0.35)	1442	71.65 (20.96)	1409	4.85 (0.35)	1.69 (0.73, 2.65)	0.0006	0.13 (0.06, 0.20)	
	> median	1458	67.95 (23.58)	1405	8.46 (0.36)	1443	68.90 (22.32)	1395	6.11 (0.36)	2.35 (1.35, 3.35)	<.0001	0.17 (0.10, 0.25)	
	Type 2 Diabetes Medical History												0.0088
	Yes	1276	68.39 (22.83)	1231	8.43 (0.39)	1281	68.31 (22.46)	1243	5.36 (0.39)	3.07 (1.99, 4.16)	<.0001	0.22 (0.14, 0.30)	
	No	1625	70.91 (22.40)	1570	6.77 (0.32)	1605	71.81 (20.97)	1562	5.58 (0.32)	1.19 (0.29, 2.09)	0.0097	0.09 (0.02, 0.16)	
	Atrial fibrillation or flutter at enrolment ECG												0.4747
	Yes	1234	69.17 (22.85)	1185	7.96 (0.39)	1222	69.50 (21.63)	1188	5.64 (0.39)	2.32 (1.25, 3.40)	<.0001	0.17 (0.09, 0.25)	
	No	1667	70.27 (22.44)	1616	7.18 (0.33)	1664	70.81 (21.76)	1617	5.37 (0.33)	1.81 (0.90, 2.72)	0.0001	0.14 (0.07, 0.21)	
	BMI (kg/m2) at enrolment												0.5697
	< 30	1595	73.70 (21.81)	1547	6.53 (0.32)	1592	74.00 (20.70)	1541	4.69 (0.32)	1.84 (0.96, 2.71)	<.0001	0.15 (0.08, 0.22)	
	>= 30	1305	65.06 (22.68)	1253	8.73 (0.40)	1291	65.64 (22.07)	1261	6.49 (0.40)	2.25 (1.14, 3.35)	<.0001	0.16 (0.08, 0.24)	
	Baseline eGFR (mL/min/1.73m^2)												0.9736
	< 60	1391	68.55 (22.48)	1338	7.23 (0.37)	1416	68.99 (22.07)	1377	5.23 (0.37)	2.00 (0.97, 3.03)	0.0001	0.15 (0.07, 0.22)	
	>= 60	1510	70.96 (22.69)	1463	7.73 (0.34)	1469	71.51 (21.28)	1427	5.76 (0.34)	1.98 (1.04, 2.91)	<.0001	0.15 (0.08, 0.23)	
	SBP at randomisation												0.0528
	<= median	1457	69.75 (22.58)	1405	6.83 (0.36)	1459	71.26 (21.68)	1420	5.50 (0.35)	1.34 (0.35, 2.32)	0.0081	0.10 (0.03, 0.17)	
	> median	1444	69.86 (22.66)	1396	8.17 (0.35)	1427	69.23 (21.70)	1385	5.46 (0.35)	2.71 (1.73, 3.69)	<.0001	0.21 (0.13, 0.28)	

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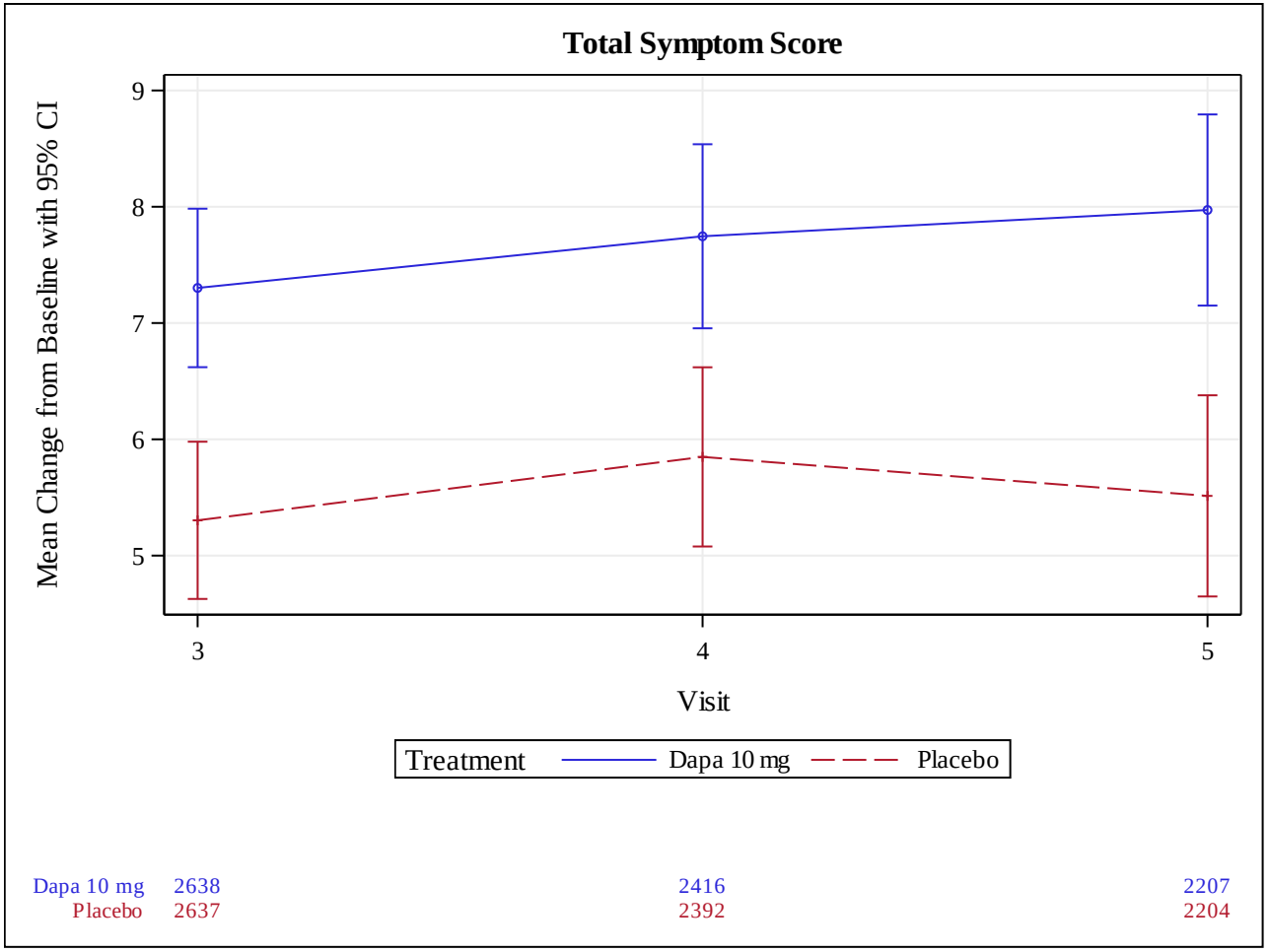
Analysis of change from baseline of KCCQ scores - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
Total Symptom Score	LVEF at enrolment 2												0.7987
	<= 49	1002	71.16 (22.71)	959	7.87 (0.41)	981	70.49 (22.14)	950	5.95 (0.41)	1.92 (0.77, 3.07)	0.0010	0.15 (0.06, 0.24)	
	>= 50	1899	69.09 (22.54)	1842	7.33 (0.31)	1905	70.14 (21.49)	1855	5.23 (0.31)	2.11 (1.24, 2.98)	<.0001	0.16 (0.09, 0.22)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.7344
	Yes	300	61.02 (23.27)	280	13.80 (0.87)	294	59.06 (21.78)	281	12.12 (0.86)	1.68 (-0.72, 4.08)	0.1696	0.12 (-0.05, 0.28)	
	No	2601	70.82 (22.33)	2521	6.85 (0.26)	2592	71.53 (21.34)	2524	4.74 (0.26)	2.11 (1.39, 2.83)	<.0001	0.16 (0.11, 0.22)	
	MRAs at baseline												0.9737
	Yes	1246	69.78 (22.90)	1216	7.25 (0.37)	1239	70.47 (21.93)	1210	5.21 (0.38)	2.04 (1.00, 3.08)	0.0001	0.16 (0.08, 0.24)	
	No	1655	69.82 (22.41)	1585	7.71 (0.34)	1647	70.09 (21.55)	1595	5.69 (0.34)	2.02 (1.08, 2.95)	<.0001	0.15 (0.08, 0.22)	
	ACEi+ARB at baseline												0.0559
	Yes	2102	69.02 (22.71)	2037	8.16 (0.29)	2105	69.91 (21.77)	2059	5.72 (0.29)	2.45 (1.65, 3.25)	<.0001	0.19 (0.13, 0.25)	
	No	799	71.87 (22.25)	764	5.75 (0.50)	781	71.18 (21.53)	746	4.87 (0.51)	0.88 (-0.52, 2.27)	0.2174	0.06 (-0.04, 0.16)	
	ARNI at baseline												0.2649
	Yes	156	79.62 (18.96)	149	3.16 (1.01)	126	77.04 (19.68)	125	2.79 (1.11)	0.37 (-2.60, 3.34)	0.8076	0.03 (-0.21, 0.27)	
	No	2745	69.25 (22.68)	2652	7.73 (0.26)	2760	69.95 (21.75)	2680	5.63 (0.26)	2.10 (1.38, 2.81)	<.0001	0.16 (0.10, 0.21)	
	Beta Blocker at baseline												0.3867
	Yes	2410	69.44 (22.47)	2327	7.42 (0.28)	2397	70.46 (21.35)	2330	5.53 (0.27)	1.89 (1.13, 2.65)	<.0001	0.14 (0.08, 0.20)	
	No	491	71.59 (23.25)	474	7.96 (0.61)	489	69.28 (23.39)	475	5.24 (0.62)	2.71 (1.01, 4.41)	0.0018	0.20 (0.08, 0.33)	
	Diuretics at baseline												0.7475
	Yes	2592	69.56 (22.60)	2500	7.61 (0.27)	2577	69.65 (21.80)	2504	5.61 (0.27)	2.00 (1.26, 2.74)	<.0001	0.15 (0.09, 0.20)	
	No	309	71.86 (22.67)	301	6.70 (0.69)	309	75.31 (20.31)	301	4.36 (0.69)	2.34 (0.41, 4.27)	0.0176	0.19 (0.03, 0.35)	

Repeated measures analysis displays overall results.
N* displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
LSMeans and difference of LSMeans estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.
p-Value for interaction from test for heterogeneity of the differences of LSMeans in the subgroups using Cochrane`s Q statistic.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



AstraZeneca
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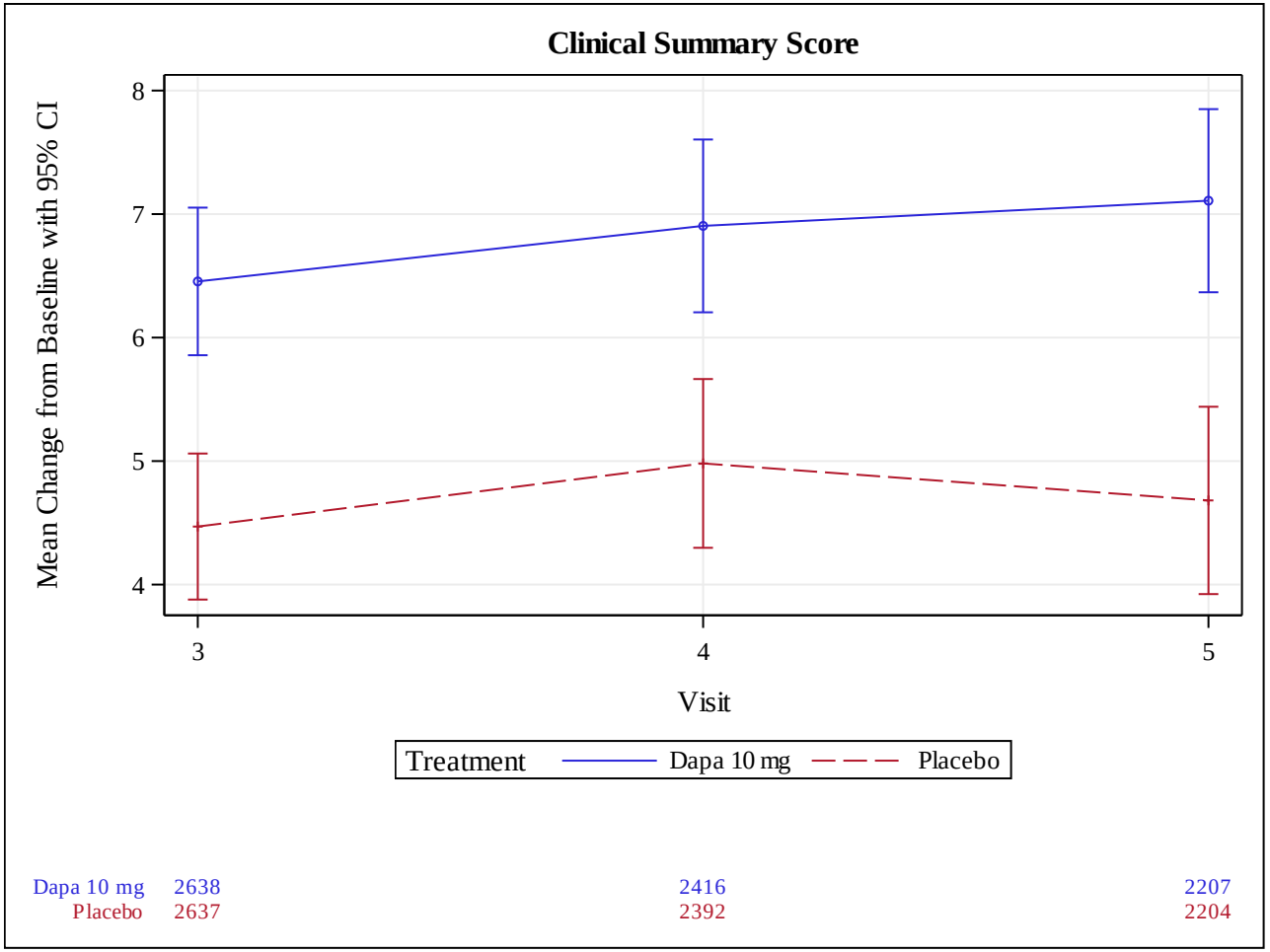
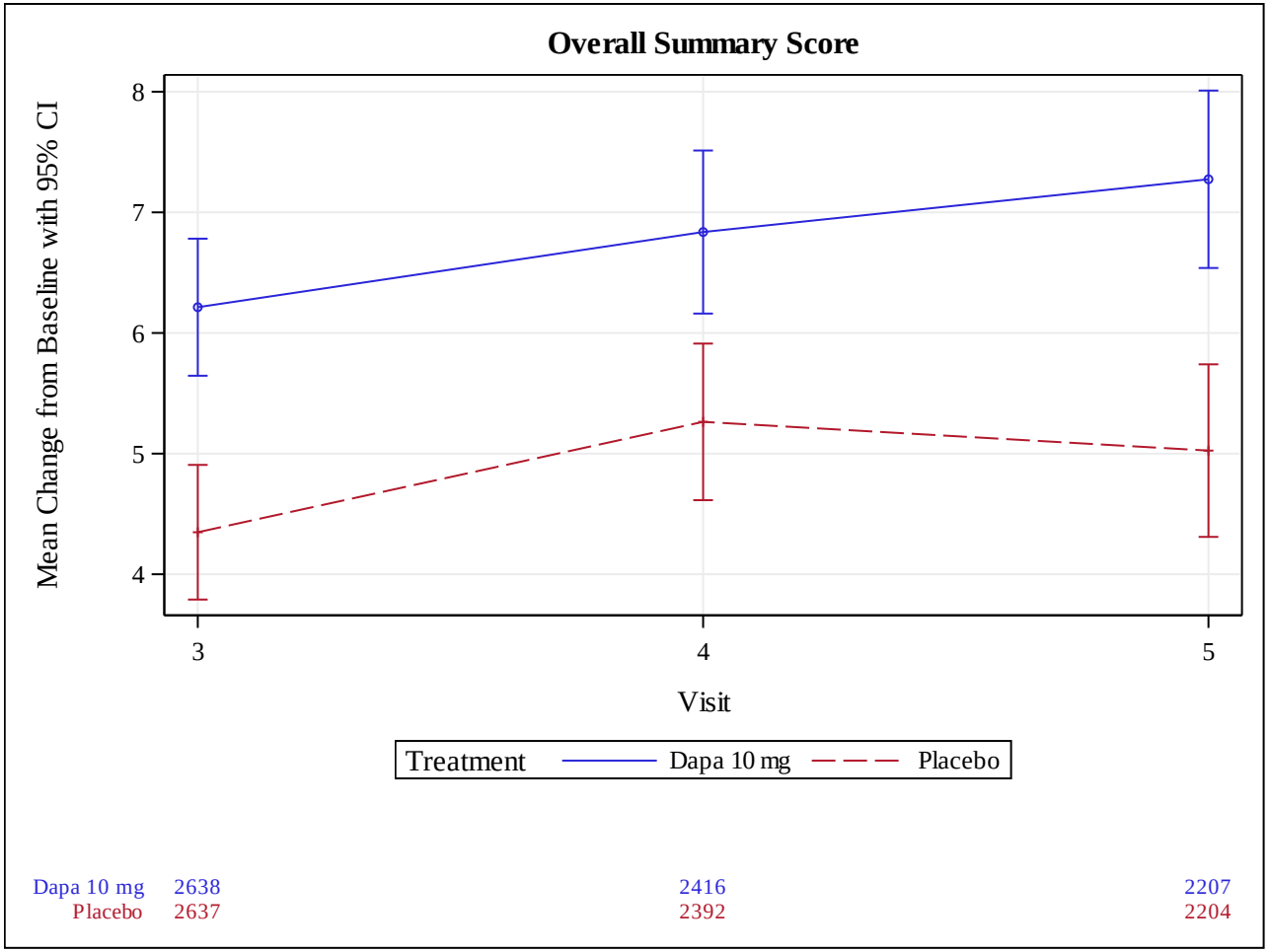
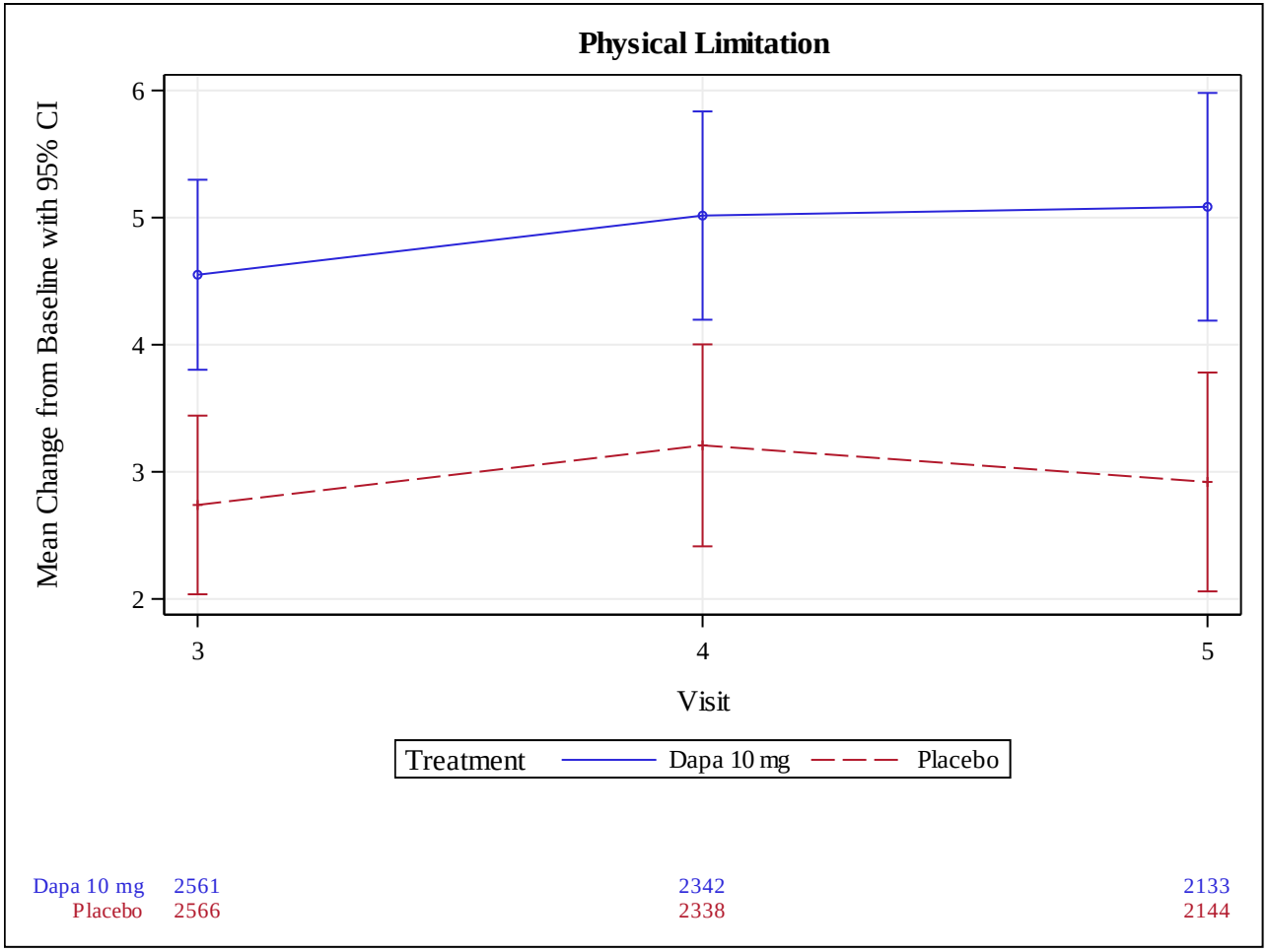
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



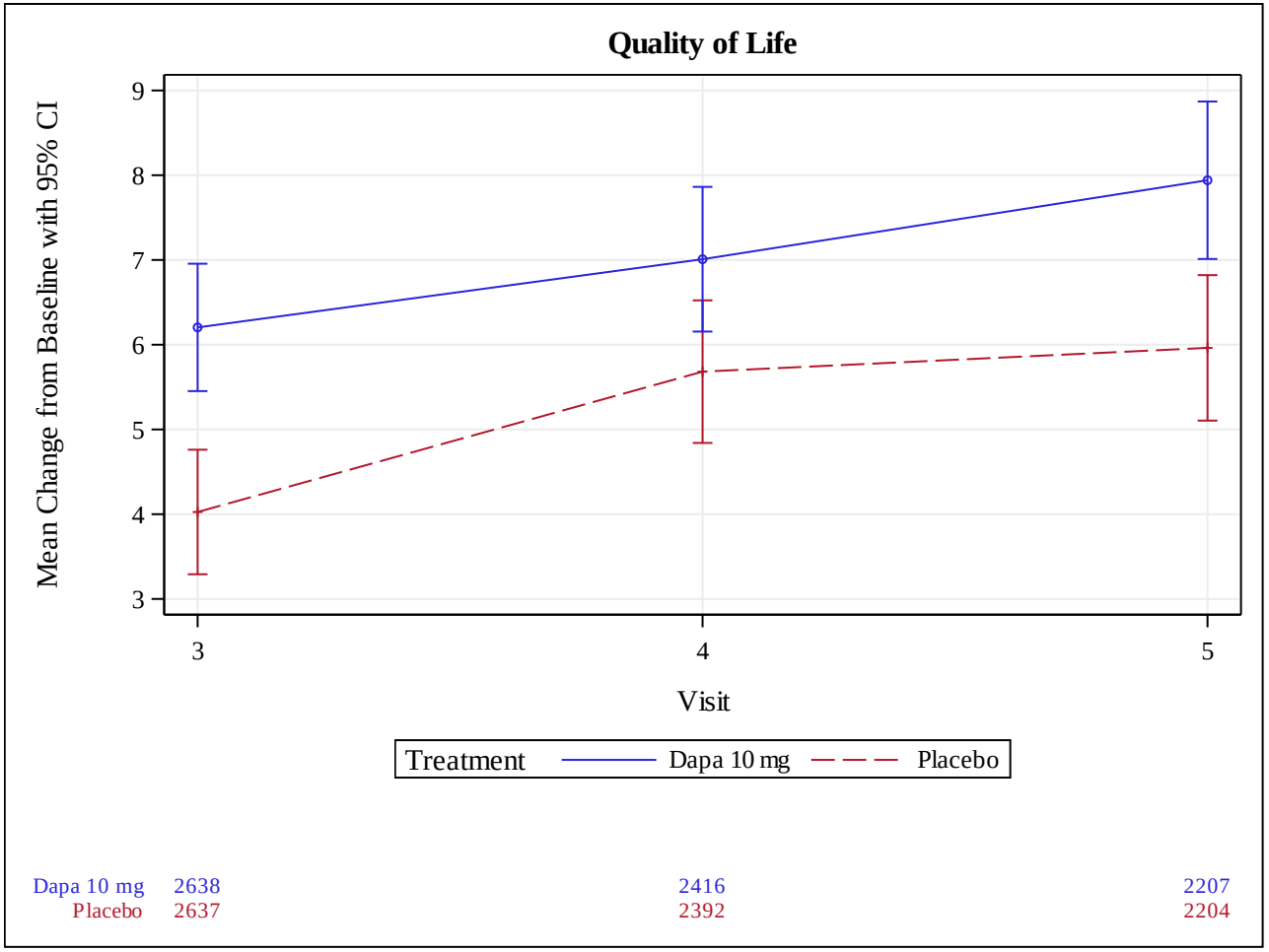
AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



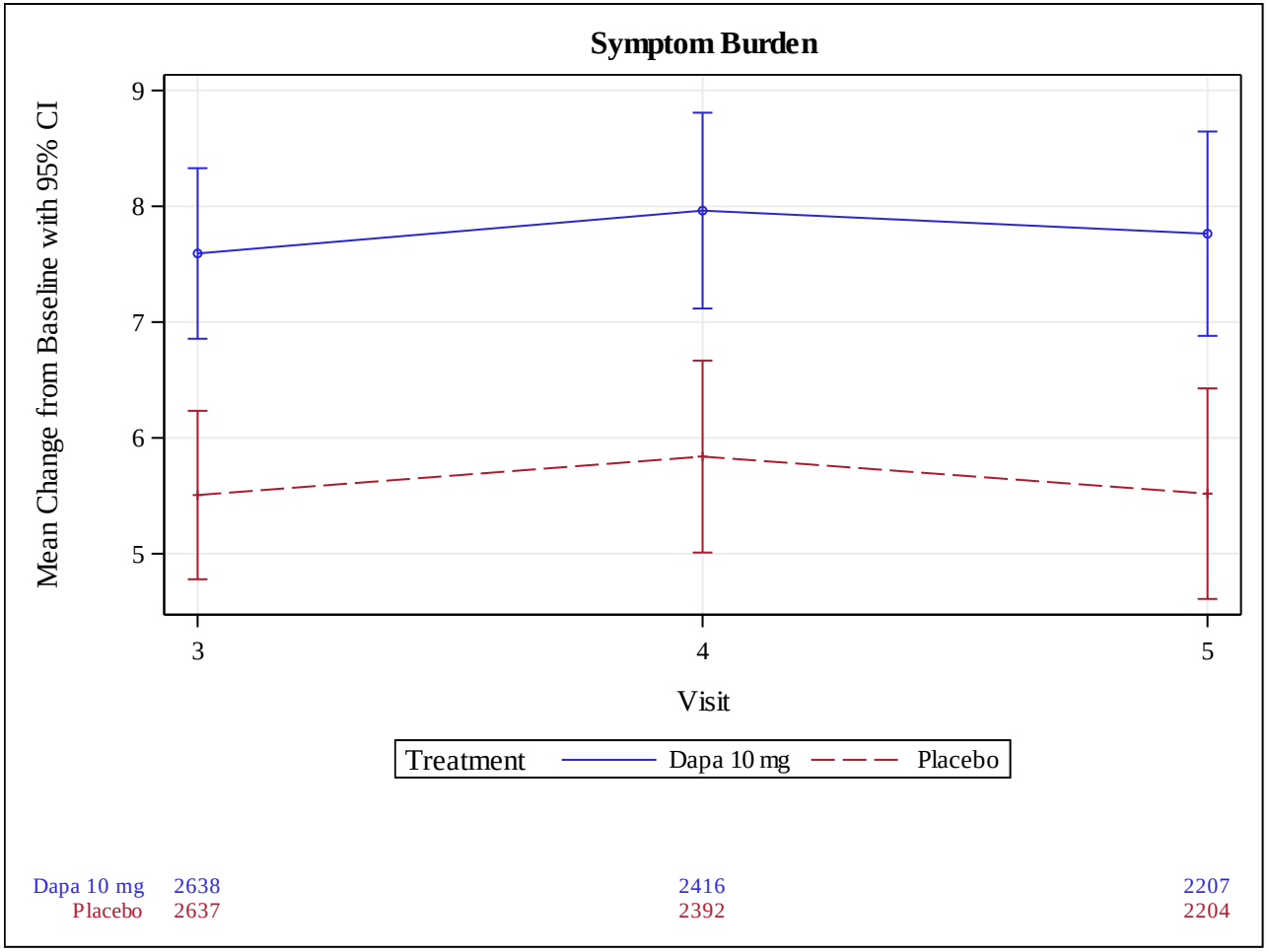
AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



AstraZeneca
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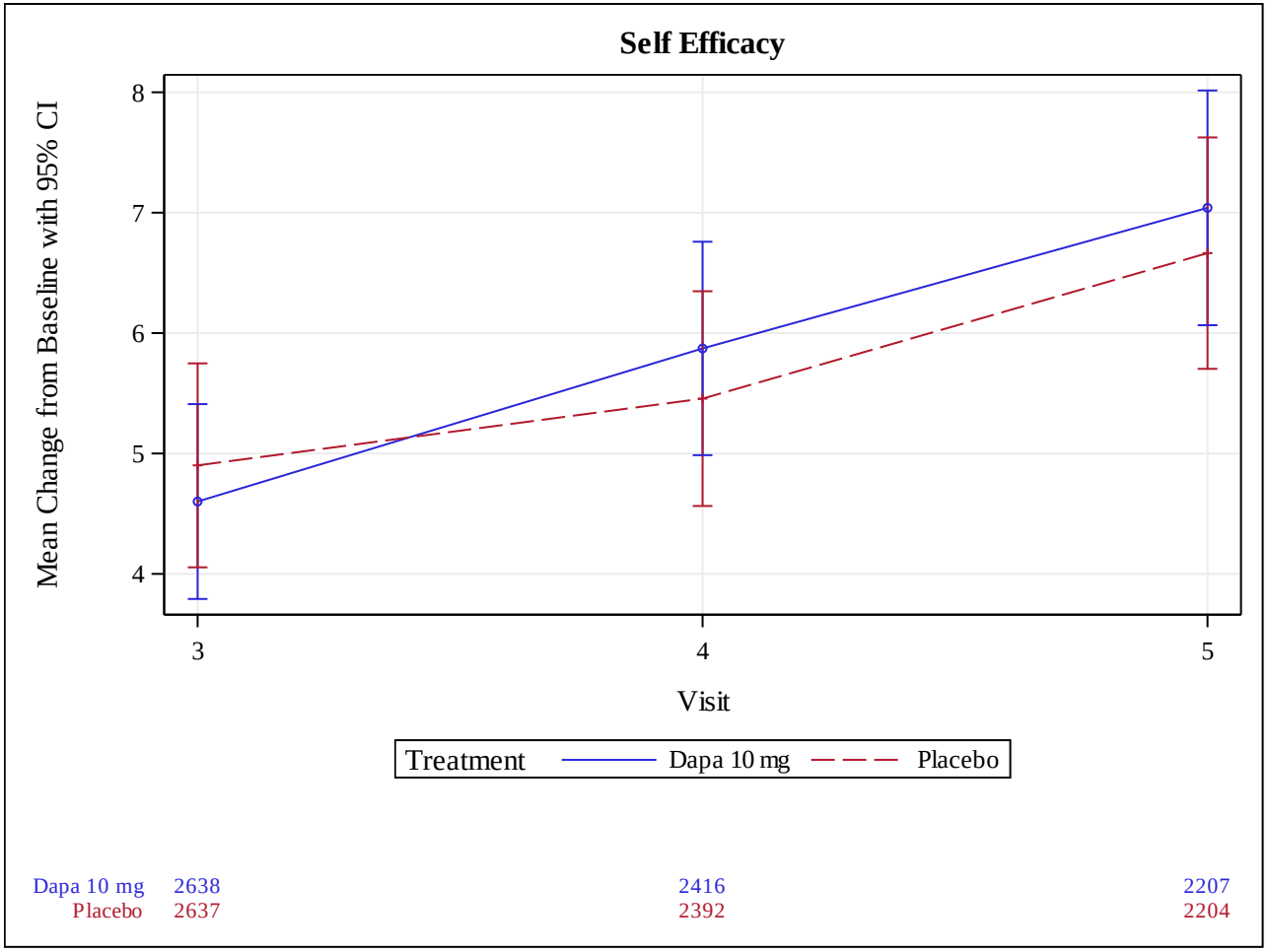
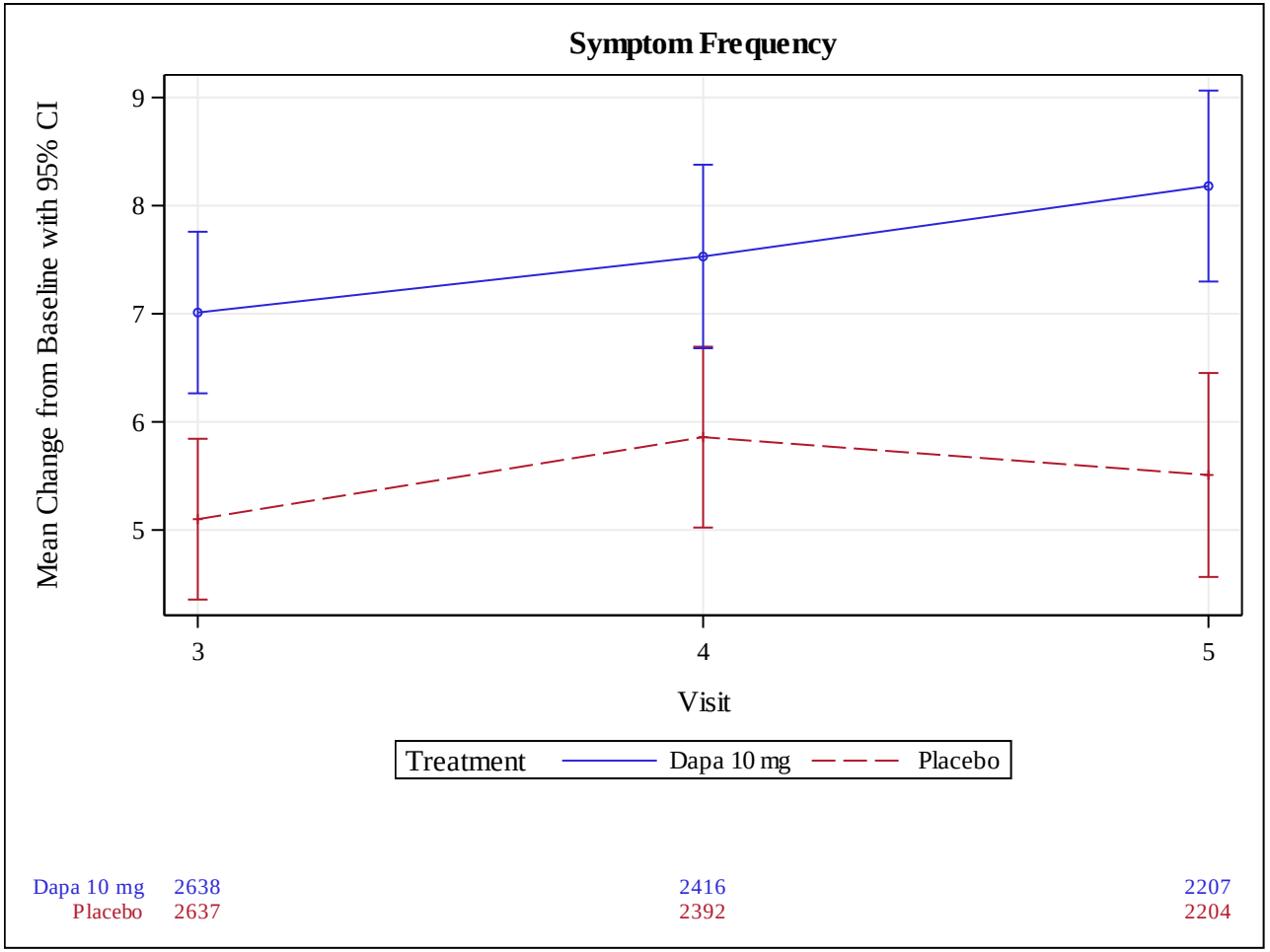
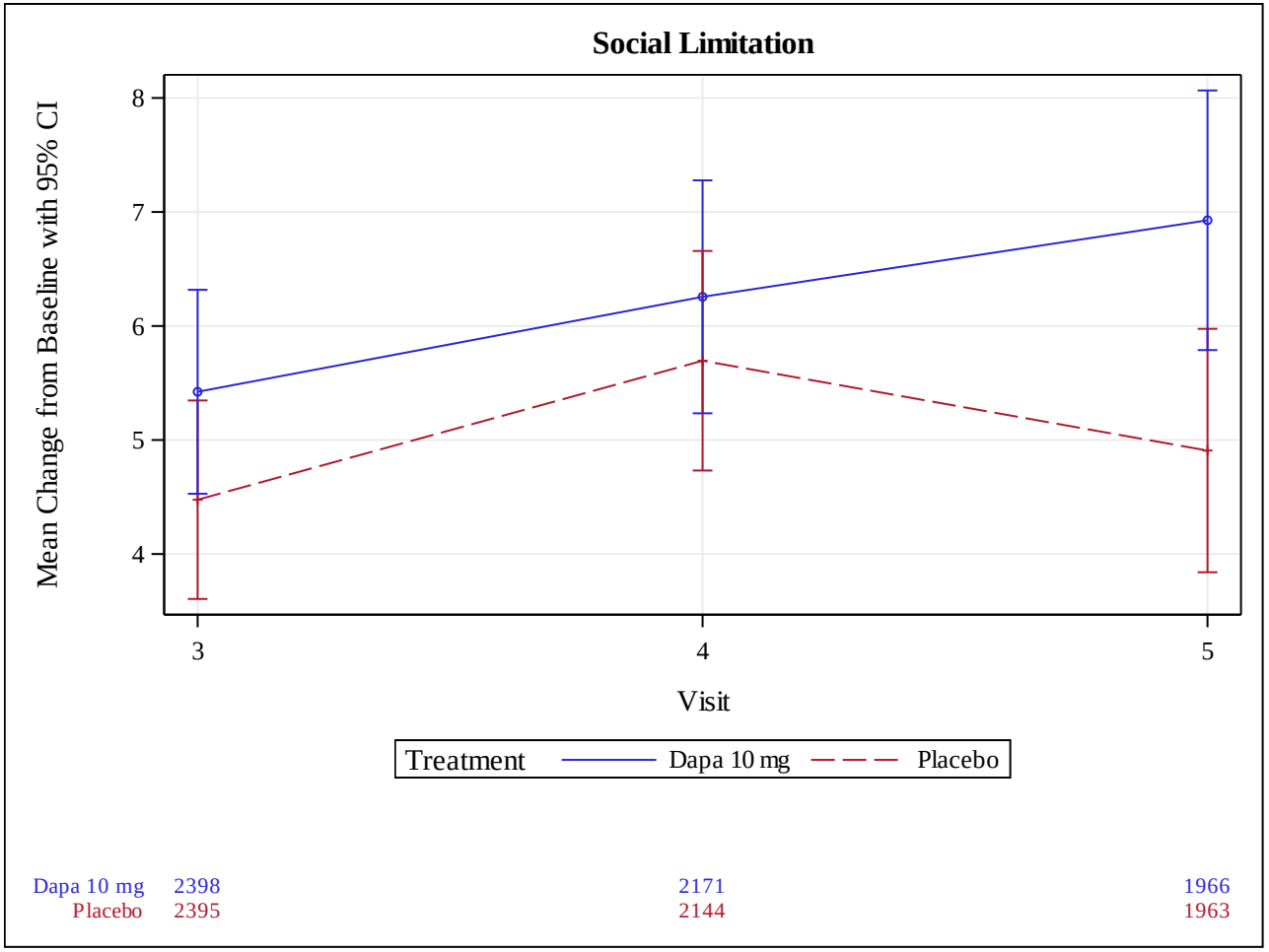
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



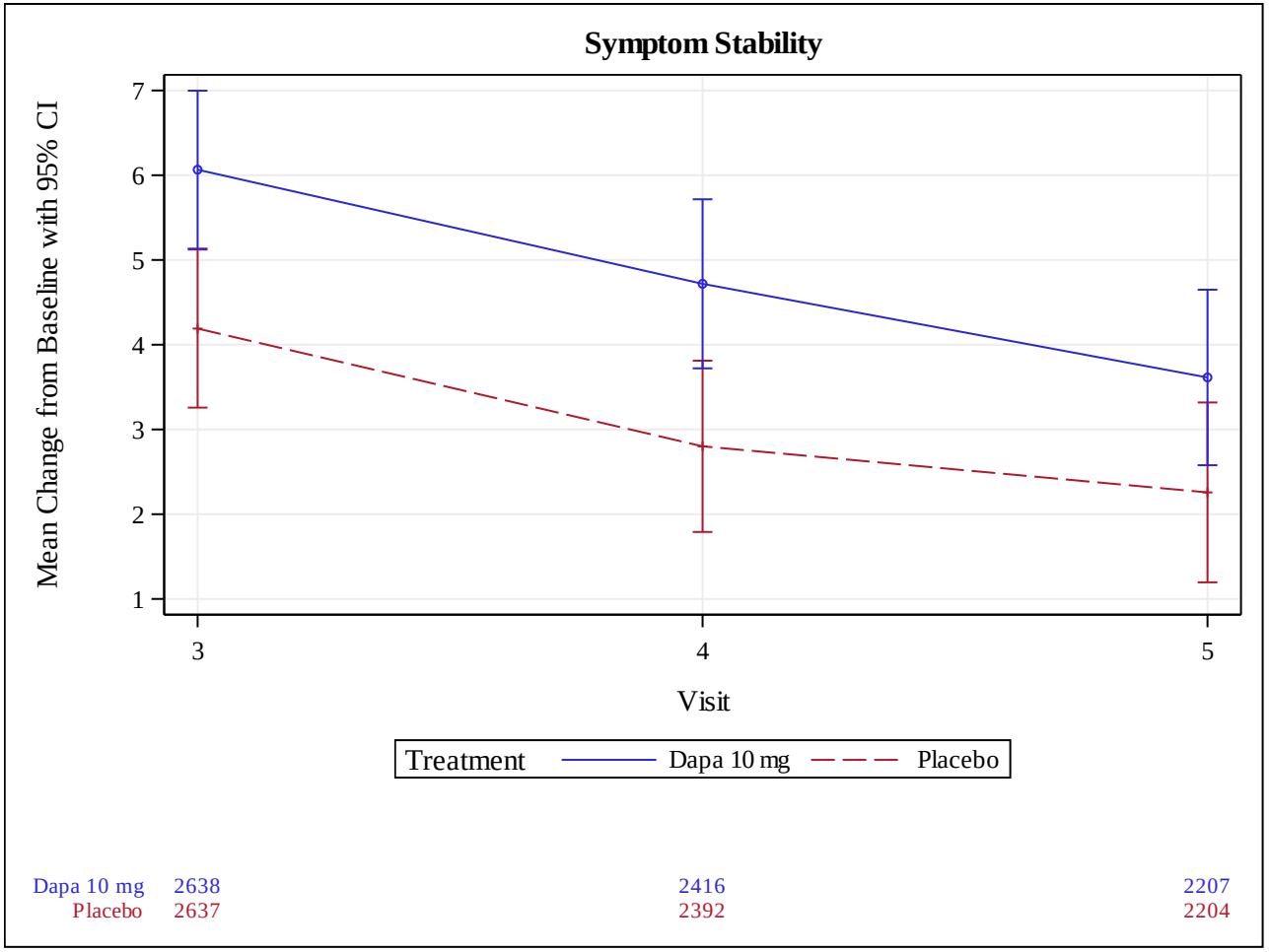
AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of KCCQ scores
Full Analysis Set



AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	1567/2801 (55.9)	1420/2805 (50.6)	1.11 (1.05, 1.16)*<.0001	1.24 (1.11, 1.39) 0.0001	0.05 (0.03, 0.08)*<.0001	
	Age						0.3754*
	<= median	806/1394 (57.8)	784/1471 (53.3)	1.08 (1.02, 1.16)*0.0149	1.23 (1.06, 1.44) 0.0079	0.05 (0.01, 0.08)*0.0148	
	> median	761/1407 (54.1)	636/1334 (47.7)	1.13 (1.05, 1.22)*0.0008	1.26 (1.08, 1.48) 0.0039	0.06 (0.03, 0.10)*0.0008	
	Gender						0.2304*
	Male	904/1630 (55.5)	828/1608 (51.5)	1.08 (1.01, 1.15)*0.0238	1.17 (1.01, 1.36) 0.0311	0.04 (0.01, 0.07)*0.0235	
	Female	663/1171 (56.6)	592/1197 (49.5)	1.14 (1.06, 1.24)*0.0005	1.33 (1.12, 1.58) 0.0012	0.07 (0.03, 0.11)*0.0005	
	Race						0.7544*
	White	1110/2006 (55.3)	1015/2032 (50.0)	1.11 (1.04, 1.17)*0.0006	1.23 (1.07, 1.40) 0.0026	0.05 (0.02, 0.08)*0.0006	
	Black or African	38/ 64 (59.4)	39/ 70 (55.7)	1.14 (0.86, 1.52) 0.3576	1.20 (0.60, 2.42) 0.6034	0.05 (-0.11, 0.22) 0.5298	
	Asian	298/ 555 (53.7)	278/ 551 (50.5)	1.06 (0.95, 1.19)*0.2812	1.15 (0.90, 1.47) 0.2562	0.03 (-0.03, 0.09)*0.2806	
	Other	121/ 176 (68.8)	88/ 152 (57.9)	1.19 (1.00, 1.41)*0.0453	1.64 (1.00, 2.68) 0.0489	0.11 (0.00, 0.21)*0.0411	
	Geographic region						0.3275*
	Asia	287/ 536 (53.5)	270/ 536 (50.4)	1.06 (0.95, 1.19)*0.2990	1.14 (0.89, 1.46) 0.2888	0.03 (-0.03, 0.09)*0.2985	
	Europe and Saudi Arabia	741/1341 (55.3)	676/1381 (49.0)	1.13 (1.05, 1.21)*0.0010	1.28 (1.08, 1.50) 0.0033	0.06 (0.03, 0.10)*0.0010	
	North America	193/ 393 (49.1)	185/ 376 (49.2)	1.02 (0.89, 1.17) 0.7522	0.98 (0.73, 1.31) 0.8998	-0.00 (-0.07, 0.07) 0.9683	
	Latin America	346/ 531 (65.2)	289/ 512 (56.4)	1.15 (1.05, 1.27)*0.0042	1.52 (1.16, 1.99) 0.0022	0.09 (0.03, 0.15)*0.0038	
	NYHA class at enrolment						0.6225*
	II	1146/2083 (55.0)	1073/2165 (49.6)	1.11 (1.05, 1.18)*0.0004	1.28 (1.13, 1.45) 0.0001	0.05 (0.02, 0.08)*0.0004	
	III or IV	421/ 718 (58.6)	347/ 639 (54.3)	1.08 (0.98, 1.19)*0.1095	1.15 (0.92, 1.45) 0.2264	0.04 (-0.01, 0.10)*0.1080	
	LVEF at enrolment						0.2922*
	<= 49	525/ 959 (54.7)	479/ 950 (50.4)	1.09 (1.00, 1.18)*0.0589	1.25 (1.03, 1.51) 0.0239	0.04 (-0.00, 0.09)*0.0583	
	50-59	564/1017 (55.5)	523/1009 (51.8)	1.07 (0.99, 1.16)*0.1023	1.14 (0.95, 1.38) 0.1563	0.04 (-0.01, 0.08)*0.1017	
	>= 60	478/ 825 (57.9)	418/ 846 (49.4)	1.17 (1.07, 1.28)*0.0005	1.36 (1.12, 1.67) 0.0025	0.07 (0.03, 0.12) 0.0017	
	NT-proBNP at enrolment						0.8786*
	<= median	774/1396 (55.4)	704/1409 (50.0)	1.11 (1.03, 1.19)*0.0037	1.27 (1.09, 1.48) 0.0026	0.05 (0.02, 0.09)*0.0036	
	> median	793/1405 (56.4)	715/1395 (51.3)	1.10 (1.03, 1.18)*0.0060	1.21 (1.03, 1.42) 0.0175	0.05 (0.01, 0.09)*0.0058	
	Type 2 Diabetes Medical History						0.0550*
	Yes	706/1231 (57.4)	611/1243 (49.2)	1.17 (1.08, 1.26)*<.0001	1.39 (1.19, 1.63)*<.0001	0.08 (0.04, 0.12)*<.0001	
	No	861/1570 (54.8)	809/1562 (51.8)	1.06 (0.99, 1.13)*0.0875	1.13 (0.98, 1.30)*0.0874	0.03 (-0.00, 0.07)*0.0872	
	Atrial fibrillation or flutter at enrolment ECG						0.9012*
	Yes	666/1185 (56.2)	602/1188 (50.7)	1.11 (1.03, 1.20)*0.0070	1.27 (1.07, 1.50) 0.0068	0.06 (0.02, 0.10)*0.0069	
	No	901/1616 (55.8)	818/1617 (50.6)	1.10 (1.03, 1.18)*0.0033	1.22 (1.06, 1.42) 0.0066	0.05 (0.02, 0.09)*0.0032	
	BMI (kg/m2) at enrolment						0.7611*
	< 30	852/1547 (55.1)	762/1541 (49.4)	1.11 (1.04, 1.19)*0.0018	1.26 (1.09, 1.46) 0.0023	0.06 (0.02, 0.09)*0.0017	
	>= 30	715/1253 (57.1)	656/1261 (52.0)	1.10 (1.02, 1.18)*0.0113	1.22 (1.03, 1.44) 0.0212	0.05 (0.01, 0.09)*0.0110	
	Baseline eGFR (mL/min/1.73m^2)						0.4366*
	< 60	726/1338 (54.3)	663/1377 (48.1)	1.13 (1.05, 1.21)*0.0015	1.29 (1.10, 1.51) 0.0019	0.06 (0.02, 0.10)*0.0014	
	>= 60	841/1463 (57.5)	757/1427 (53.0)	1.08 (1.01, 1.16)*0.0167	1.19 (1.02, 1.39) 0.0268	0.04 (0.01, 0.08)*0.0164	

N displays number of patients in the analysis, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.6182*
	<= median	775/1405 (55.2)	700/1420 (49.3)	1.12 (1.04, 1.20)*0.0018	1.22 (1.04, 1.42) 0.0137	0.06 (0.02, 0.10)*0.0018	
	> median	792/1396 (56.7)	720/1385 (52.0)	1.09 (1.02, 1.17)*0.0121	1.27 (1.08, 1.48) 0.0035	0.05 (0.01, 0.08)*0.0119	
	LVEF at enrolment 2						0.6160*
	<= 49	525/ 959 (54.7)	479/ 950 (50.4)	1.09 (1.00, 1.18)*0.0589	1.25 (1.03, 1.51) 0.0239	0.04 (-0.00, 0.09)*0.0583	
	>= 50	1042/1842 (56.6)	941/1855 (50.7)	1.12 (1.05, 1.18)*0.0004	1.24 (1.08, 1.42) 0.0022	0.06 (0.03, 0.09)*0.0004	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6845*
	Yes	177/ 280 (63.2)	165/ 281 (58.7)	1.08 (0.94, 1.23)*0.2757	1.32 (0.92, 1.91) 0.1359	0.04 (-0.04, 0.13)*0.2746	
	No	1390/2521 (55.1)	1255/2524 (49.7)	1.11 (1.05, 1.17)*0.0001	1.23 (1.10, 1.39) 0.0004	0.05 (0.03, 0.08)*0.0001	
	MRAs at baseline						0.2122*
	Yes	683/1216 (56.2)	593/1210 (49.0)	1.15 (1.06, 1.24)*0.0004	1.35 (1.14, 1.60) 0.0005	0.07 (0.03, 0.11)*0.0004	
	No	884/1585 (55.8)	827/1595 (51.8)	1.08 (1.01, 1.15)*0.0266	1.17 (1.01, 1.35) 0.0398	0.04 (0.00, 0.07)*0.0264	
	ACEi+ARB at baseline						0.0128*
	Yes	1156/2037 (56.8)	1018/2059 (49.4)	1.15 (1.08, 1.22)*<.0001	1.35 (1.18, 1.54) <.0001	0.07 (0.04, 0.10)*<.0001	
	No	411/ 764 (53.8)	402/ 746 (53.9)	1.01 (0.93, 1.10) 0.7584	1.00 (0.81, 1.23) 0.9944	0.00 (-0.05, 0.05) 0.9031	
	ARNI at baseline						0.4289*
	Yes	77/ 149 (51.7)	64/ 125 (51.2)	1.04 (0.84, 1.29) 0.7200	1.10 (0.67, 1.81) 0.7172	0.02 (-0.10, 0.13) 0.7499	
	No	1490/2652 (56.2)	1356/2680 (50.6)	1.11 (1.06, 1.17)*<.0001	1.24 (1.11, 1.39) 0.0002	0.06 (0.03, 0.08)*<.0001	
	Beta Blocker at baseline						0.4830*
	Yes	1292/2327 (55.5)	1180/2330 (50.6)	1.10 (1.04, 1.16)*0.0009	1.20 (1.06, 1.35) 0.0039	0.05 (0.02, 0.08)*0.0008	
	No	275/ 474 (58.0)	240/ 475 (50.5)	1.15 (1.02, 1.29)*0.0210	1.45 (1.11, 1.90) 0.0065	0.09 (0.03, 0.15) 0.0030	
	Diuretics at baseline						0.3918*
	Yes	1393/2500 (55.7)	1272/2504 (50.8)	1.10 (1.04, 1.16)*0.0005	1.23 (1.09, 1.38) 0.0005	0.05 (0.02, 0.08)*0.0005	
	No	174/ 301 (57.8)	148/ 301 (49.2)	1.18 (1.01, 1.37)*0.0345	1.32 (0.94, 1.86) 0.1098	0.09 (0.01, 0.17)*0.0330	

N displays number of patients in the analysis, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	1545/2801 (55.2)	1423/2805 (50.7)	1.09 (1.03, 1.14)*0.0009	1.19 (1.07, 1.33) 0.0021	0.04 (0.02, 0.07)*0.0009	
	Age						0.3941*
	<= median	800/1394 (57.4)	790/1471 (53.7)	1.07 (1.00, 1.14)*0.0473	1.19 (1.02, 1.39) 0.0313	0.04 (0.00, 0.07)*0.0472	
	> median	745/1407 (52.9)	633/1334 (47.5)	1.12 (1.04, 1.20)*0.0041	1.21 (1.03, 1.42) 0.0184	0.05 (0.02, 0.09)*0.0040	
	Gender						0.2402*
	Male	893/1630 (54.8)	831/1608 (51.7)	1.06 (0.99, 1.13)*0.0768	1.13 (0.97, 1.31) 0.1094	0.03 (-0.00, 0.07)*0.0764	
	Female	652/1171 (55.7)	592/1197 (49.5)	1.13 (1.04, 1.22)*0.0025	1.27 (1.07, 1.51) 0.0058	0.06 (0.02, 0.10)*0.0024	
	Race						0.5846*
	White	1115/2006 (55.6)	1019/2032 (50.1)	1.11 (1.05, 1.18)*0.0006	1.22 (1.07, 1.40) 0.0030	0.05 (0.02, 0.09)*0.0005	
	Black or African	38/ 64 (59.4)	38/ 70 (54.3)	1.18 (0.89, 1.58) 0.2569	1.27 (0.63, 2.57) 0.5066	0.07 (-0.09, 0.23) 0.4061	
	Asian	280/ 555 (50.5)	271/ 551 (49.2)	1.03 (0.91, 1.15)*0.6735	1.08 (0.84, 1.37) 0.5615	0.01 (-0.05, 0.07)*0.6734	
	Other	112/ 176 (63.6)	95/ 152 (62.5)	1.02 (0.86, 1.20)*0.8318	1.09 (0.67, 1.78) 0.7370	0.01 (-0.09, 0.12)*0.8316	
	Geographic region						0.4782*
	Asia	272/ 536 (50.7)	264/ 536 (49.3)	1.03 (0.91, 1.16)*0.6251	1.08 (0.84, 1.38) 0.5508	0.01 (-0.04, 0.07)*0.6250	
	Europe and Saudi Arabia	746/1341 (55.6)	682/1381 (49.4)	1.13 (1.05, 1.21)*0.0011	1.26 (1.07, 1.49) 0.0054	0.06 (0.03, 0.10)*0.0011	
	North America	195/ 393 (49.6)	183/ 376 (48.7)	1.03 (0.90, 1.18) 0.6762	1.04 (0.78, 1.39) 0.8098	0.01 (-0.06, 0.08) 0.7771	
	Latin America	332/ 531 (62.5)	294/ 512 (57.4)	1.09 (0.99, 1.20)*0.0936	1.27 (0.97, 1.66) 0.0780	0.05 (-0.01, 0.11)*0.0924	
	NYHA class at enrolment						0.4643*
	II	1119/2083 (53.7)	1084/2165 (50.1)	1.07 (1.01, 1.14)*0.0173	1.18 (1.04, 1.35) 0.0096	0.04 (0.01, 0.07)*0.0172	
	III or IV	426/ 718 (59.3)	339/ 639 (53.1)	1.12 (1.02, 1.23)*0.0207	1.26 (1.00, 1.59) 0.0522	0.06 (0.01, 0.12)*0.0198	
	LVEF at enrolment						0.0321*
	<= 49	528/ 959 (55.1)	497/ 950 (52.3)	1.05 (0.97, 1.14)*0.2300	1.16 (0.96, 1.41) 0.1189	0.03 (-0.02, 0.07)*0.2295	
	50-59	547/1017 (53.8)	526/1009 (52.1)	1.03 (0.95, 1.12)*0.4557	1.03 (0.86, 1.25) 0.7327	0.02 (-0.03, 0.06)*0.4555	
	>= 60	470/ 825 (57.0)	400/ 846 (47.3)	1.20 (1.10, 1.32)*<.0001	1.44 (1.18, 1.77) 0.0004	0.10 (0.05, 0.14)*<.0001	
	NT-proBNP at enrolment						0.8587*
	<= median	754/1396 (54.0)	703/1409 (49.9)	1.08 (1.01, 1.16)*0.0292	1.19 (1.02, 1.39) 0.0270	0.04 (0.00, 0.08)*0.0289	
	> median	791/1405 (56.3)	719/1395 (51.5)	1.09 (1.02, 1.17)*0.0117	1.19 (1.01, 1.39) 0.0338	0.05 (0.01, 0.08)*0.0115	
	Type 2 Diabetes Medical History						0.0618*
	Yes	695/1231 (56.5)	612/1243 (49.2)	1.15 (1.06, 1.24)*0.0003	1.34 (1.14, 1.57)*0.0003	0.07 (0.03, 0.11)*0.0003	
	No	850/1570 (54.1)	811/1562 (51.9)	1.04 (0.98, 1.11)*0.2135	1.09 (0.95, 1.26)*0.2134	0.02 (-0.01, 0.06)*0.2132	
	Atrial fibrillation or flutter at enrolment ECG						0.5382*
	Yes	668/1185 (56.4)	605/1188 (50.9)	1.11 (1.03, 1.19)*0.0079	1.26 (1.06, 1.49) 0.0096	0.05 (0.01, 0.09)*0.0077	
	No	877/1616 (54.3)	818/1617 (50.6)	1.07 (1.00, 1.15)*0.0362	1.15 (0.99, 1.33) 0.0648	0.04 (0.00, 0.07)*0.0359	
	BMI (kg/m2) at enrolment						0.1842*
	< 30	829/1547 (53.6)	782/1541 (50.7)	1.06 (0.99, 1.13)*0.1142	1.11 (0.95, 1.28) 0.1906	0.03 (-0.01, 0.06)*0.1139	
	>= 30	716/1253 (57.1)	638/1261 (50.6)	1.13 (1.05, 1.21)*0.0010	1.31 (1.11, 1.55) 0.0014	0.07 (0.03, 0.10)*0.0010	
	Baseline eGFR (mL/min/1.73m^2)						0.4427*
	< 60	725/1338 (54.2)	673/1377 (48.9)	1.11 (1.03, 1.19)*0.0057	1.24 (1.06, 1.46) 0.0076	0.05 (0.02, 0.09)*0.0056	
	>= 60	820/1463 (56.0)	750/1427 (52.6)	1.07 (1.00, 1.14)*0.0599	1.14 (0.97, 1.33) 0.1059	0.03 (-0.00, 0.07)*0.0594	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.5123*
	<= median	783/1405 (55.7)	716/1420 (50.4)	1.11 (1.03, 1.18)*0.0048	1.19 (1.02, 1.39) 0.0315	0.05 (0.02, 0.09)*0.0047	
	> median	762/1396 (54.6)	707/1385 (51.0)	1.07 (1.00, 1.15)*0.0619	1.20 (1.02, 1.40) 0.0276	0.04 (-0.00, 0.07)*0.0615	
	LVEF at enrolment 2						0.3470*
	<= 49	528/ 959 (55.1)	497/ 950 (52.3)	1.05 (0.97, 1.14)*0.2300	1.16 (0.96, 1.41) 0.1189	0.03 (-0.02, 0.07)*0.2295	
	>= 50	1017/1842 (55.2)	926/1855 (49.9)	1.11 (1.04, 1.18)*0.0013	1.20 (1.05, 1.38) 0.0079	0.05 (0.02, 0.09)*0.0013	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5768*
	Yes	180/ 280 (64.3)	172/ 281 (61.2)	1.05 (0.92, 1.19)*0.4515	1.19 (0.82, 1.72) 0.3589	0.03 (-0.05, 0.11)*0.4510	
	No	1365/2521 (54.1)	1251/2524 (49.6)	1.09 (1.04, 1.15)*0.0011	1.19 (1.06, 1.34) 0.0033	0.05 (0.02, 0.07)*0.0011	
	MRAs at baseline						0.5477*
	Yes	676/1216 (55.6)	608/1210 (50.2)	1.11 (1.03, 1.19)*0.0085	1.25 (1.05, 1.48) 0.0106	0.05 (0.01, 0.09)*0.0083	
	No	869/1585 (54.8)	815/1595 (51.1)	1.07 (1.00, 1.15)*0.0353	1.15 (0.99, 1.33) 0.0629	0.04 (0.00, 0.07)*0.0350	
	ACEi+ARB at baseline						0.2400*
	Yes	1128/2037 (55.4)	1030/2059 (50.0)	1.11 (1.04, 1.17)*0.0006	1.24 (1.08, 1.41) 0.0016	0.05 (0.02, 0.08)*0.0006	
	No	417/ 764 (54.6)	393/ 746 (52.7)	1.04 (0.94, 1.14)*0.4593	1.08 (0.87, 1.33) 0.4850	0.02 (-0.03, 0.07) 0.3722	
	ARNI at baseline						0.0340*
	Yes	70/ 149 (47.0)	69/ 125 (55.2)	0.89 (0.71, 1.10) 0.2788	0.70 (0.42, 1.15) 0.1590	-0.08 (-0.19, 0.04) 0.1902	
	No	1475/2652 (55.6)	1354/2680 (50.5)	1.10 (1.05, 1.16)*0.0002	1.22 (1.09, 1.37) 0.0006	0.05 (0.02, 0.08)*0.0002	
	Beta Blocker at baseline						0.9904*
	Yes	1279/2327 (55.0)	1178/2330 (50.6)	1.09 (1.03, 1.15)*0.0026	1.17 (1.03, 1.32) 0.0126	0.04 (0.02, 0.07)*0.0026	
	No	266/ 474 (56.1)	245/ 475 (51.6)	1.09 (0.97, 1.22)*0.1613	1.30 (0.99, 1.70) 0.0603	0.05 (-0.02, 0.11)*0.1603	
	Diuretics at baseline						0.6802*
	Yes	1376/2500 (55.0)	1263/2504 (50.4)	1.09 (1.04, 1.15)*0.0011	1.21 (1.08, 1.37) 0.0012	0.05 (0.02, 0.07)*0.0011	
	No	169/ 301 (56.1)	160/ 301 (53.2)	1.06 (0.91, 1.22)*0.4615	1.02 (0.72, 1.43) 0.9267	0.03 (-0.05, 0.11)*0.4610	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	1426/2750 (51.9)	1281/2758 (46.4)	1.09 (1.04, 1.15) 0.0005	1.23 (1.10, 1.37) 0.0002	0.05 (0.02, 0.07) 0.0002	
	Age						0.1297
	<= median	733/1382 (53.0)	714/1456 (49.0)	1.07 (1.00, 1.14) 0.0498	1.19 (1.02, 1.38) 0.0281	0.04 (0.00, 0.08) 0.0258	
	> median	693/1368 (50.7)	567/1302 (43.5)	1.12 (1.04, 1.21) 0.0018	1.30 (1.11, 1.52) 0.0012	0.06 (0.02, 0.10) 0.0012	
	Gender						0.4235
	Male	818/1611 (50.8)	738/1583 (46.6)	1.07 (1.01, 1.14) 0.0309	1.18 (1.02, 1.36) 0.0260	0.04 (0.01, 0.07) 0.0190	
	Female	608/1139 (53.4)	543/1175 (46.2)	1.11 (1.03, 1.20) 0.0048	1.30 (1.10, 1.54) 0.0025	0.06 (0.02, 0.10) 0.0038	
	Race						0.9028*
	White	993/1970 (50.4)	897/1998 (44.9)	1.07 (1.01, 1.13) 0.0169	1.23 (1.08, 1.40) 0.0020	0.04 (0.02, 0.07) 0.0027	
	Black or African	31/ 63 (49.2)	33/ 66 (50.0)	1.02 (0.72, 1.47) 0.8929	0.98 (0.49, 1.97) 0.9611	-0.00 (-0.18, 0.17) 0.9686	
	Asian	300/ 548 (54.7)	271/ 546 (49.6)	1.09 (0.98, 1.22) 0.1221	1.21 (0.95, 1.54) 0.1163	0.05 (-0.01, 0.11) 0.1113	
	Other	102/ 169 (60.4)	80/ 148 (54.1)	1.12 (0.92, 1.35)*0.2612	1.38 (0.87, 2.22) 0.1751	0.08 (-0.03, 0.18) 0.1397	
	Geographic region						0.9441*
	Asia	292/ 530 (55.1)	265/ 531 (49.9)	1.09 (0.98, 1.22) 0.1199	1.21 (0.95, 1.55) 0.1171	0.05 (-0.01, 0.11) 0.1120	
	Europe and Saudi Arabia	660/1323 (49.9)	602/1360 (44.3)	1.07 (1.00, 1.14) 0.0572	1.25 (1.06, 1.46) 0.0074	0.05 (0.01, 0.08) 0.0094	
	North America	175/ 386 (45.3)	153/ 362 (42.3)	1.05 (0.90, 1.23) 0.5121	1.10 (0.82, 1.48) 0.5352	0.02 (-0.05, 0.09) 0.4942	
	Latin America	299/ 511 (58.5)	261/ 505 (51.7)	1.13 (1.01, 1.27)*0.0292	1.37 (1.05, 1.78) 0.0202	0.07 (0.01, 0.13) 0.0151	
	NYHA class at enrolment						0.1635
	II	1044/2046 (51.0)	991/2136 (46.4)	1.07 (1.01, 1.13) 0.0181	1.21 (1.07, 1.37) 0.0030	0.04 (0.01, 0.07) 0.0034	
	III or IV	382/ 704 (54.3)	290/ 621 (46.7)	1.14 (1.04, 1.26) 0.0064	1.34 (1.06, 1.68) 0.0133	0.07 (0.02, 0.12) 0.0071	
	LVEF at enrolment						0.1055
	<= 49	482/ 944 (51.1)	457/ 939 (48.7)	1.05 (0.96, 1.14) 0.2781	1.13 (0.94, 1.36) 0.1895	0.03 (-0.01, 0.07) 0.1814	
	50-59	507/1001 (50.6)	454/ 988 (46.0)	1.07 (0.98, 1.16) 0.1121	1.17 (0.98, 1.41) 0.0847	0.04 (-0.00, 0.08) 0.0811	
	>= 60	437/ 805 (54.3)	370/ 831 (44.5)	1.22 (1.10, 1.35)*<.0001	1.43 (1.17, 1.75) 0.0006	0.08 (0.04, 0.13) 0.0005	
	NT-proBNP at enrolment						0.4858
	<= median	720/1371 (52.5)	653/1389 (47.0)	1.09 (1.01, 1.17) 0.0199	1.25 (1.07, 1.46) 0.0047	0.05 (0.01, 0.09) 0.0068	
	> median	706/1379 (51.2)	627/1368 (45.8)	1.12 (1.03, 1.21)*0.0050	1.21 (1.04, 1.42) 0.0154	0.05 (0.01, 0.09) 0.0062	
	Type 2 Diabetes Medical History						0.2316
	Yes	622/1213 (51.3)	551/1219 (45.2)	1.13 (1.04, 1.21) 0.0019	1.28 (1.09, 1.50)*0.0027	0.06 (0.02, 0.10) 0.0020	
	No	804/1537 (52.3)	730/1539 (47.4)	1.07 (1.00, 1.14) 0.0511	1.22 (1.06, 1.40)*0.0069	0.04 (0.01, 0.07) 0.0244	
	Atrial fibrillation or flutter at enrolment ECG						0.6342
	Yes	602/1164 (51.7)	530/1164 (45.5)	1.10 (1.02, 1.18) 0.0135	1.29 (1.09, 1.52) 0.0036	0.06 (0.02, 0.10) 0.0021	
	No	824/1586 (52.0)	751/1594 (47.1)	1.08 (1.02, 1.16) 0.0152	1.20 (1.04, 1.38) 0.0149	0.04 (0.01, 0.07) 0.0159	
	BMI (kg/m2) at enrolment						0.3076
	< 30	798/1520 (52.5)	700/1517 (46.1)	1.13 (1.05, 1.20) 0.0005	1.29 (1.11, 1.49) 0.0007	0.06 (0.03, 0.10) 0.0006	
	>= 30	628/1229 (51.1)	580/1238 (46.8)	1.05 (0.98, 1.13) 0.1694	1.16 (0.98, 1.36) 0.0883	0.03 (-0.00, 0.07) 0.0805	
	Baseline eGFR (mL/min/1.73m^2)						0.3595
	< 60	663/1307 (50.7)	609/1345 (45.3)	1.11 (1.03, 1.19) 0.0052	1.24 (1.06, 1.46) 0.0067	0.05 (0.02, 0.09) 0.0043	
	>= 60	763/1443 (52.9)	672/1412 (47.6)	1.07 (1.00, 1.15) 0.0447	1.21 (1.04, 1.41) 0.0141	0.04 (0.01, 0.08) 0.0182	

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Score	Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.7891
	<= median	711/1376 (51.7)	643/1395 (46.1)	1.08 (1.01, 1.16) 0.0246	1.19 (1.02, 1.39) 0.0240	0.04 (0.01, 0.08) 0.0255	
	> median	715/1374 (52.0)	638/1363 (46.8)	1.09 (1.02, 1.17) 0.0106	1.27 (1.09, 1.48) 0.0028	0.06 (0.02, 0.09) 0.0018	
	LVEF at enrolment 2						0.1571
	<= 49	482/ 944 (51.1)	457/ 939 (48.7)	1.05 (0.96, 1.14) 0.2781	1.13 (0.94, 1.36) 0.1895	0.03 (-0.01, 0.07) 0.1814	
	>= 50	944/1806 (52.3)	824/1819 (45.3)	1.11 (1.04, 1.18) 0.0008	1.28 (1.12, 1.47) 0.0003	0.06 (0.03, 0.09) 0.0003	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5711*
	Yes	154/ 270 (57.0)	133/ 272 (48.9)	1.17 (0.99, 1.37)*0.0586	1.52 (1.05, 2.21) 0.0265	0.08 (-0.00, 0.17)*0.0568	
	No	1272/2480 (51.3)	1148/2486 (46.2)	1.09 (1.03, 1.15) 0.0017	1.21 (1.08, 1.36) 0.0011	0.05 (0.02, 0.07) 0.0009	
	MRAs at baseline						0.9365
	Yes	613/1191 (51.5)	541/1193 (45.3)	1.09 (1.01, 1.18) 0.0225	1.28 (1.09, 1.52) 0.0033	0.06 (0.02, 0.10) 0.0037	
	No	813/1559 (52.1)	740/1565 (47.3)	1.09 (1.03, 1.17) 0.0058	1.19 (1.03, 1.38) 0.0170	0.04 (0.01, 0.08) 0.0132	
	ACEi+ARB at baseline						0.1483
	Yes	1038/1999 (51.9)	925/2028 (45.6)	1.11 (1.05, 1.17) 0.0003	1.27 (1.12, 1.45) 0.0002	0.06 (0.03, 0.09) 0.0002	
	No	388/ 751 (51.7)	356/ 730 (48.8)	1.04 (0.95, 1.15) 0.4136	1.12 (0.91, 1.38) 0.2919	0.03 (-0.02, 0.08) 0.2914	
	ARNI at baseline						0.7280
	Yes	77/ 147 (52.4)	62/ 122 (50.8)	1.09 (0.87, 1.37) 0.4428	1.14 (0.70, 1.87) 0.6035	0.04 (-0.08, 0.16) 0.5427	
	No	1349/2603 (51.8)	1219/2636 (46.2)	1.09 (1.03, 1.14) 0.0010	1.23 (1.10, 1.38) 0.0003	0.05 (0.02, 0.07) 0.0002	
	Beta Blocker at baseline						0.2681
	Yes	1176/2289 (51.4)	1069/2293 (46.6)	1.08 (1.02, 1.13) 0.0079	1.19 (1.06, 1.34) 0.0046	0.04 (0.01, 0.07) 0.0037	
	No	250/ 461 (54.2)	212/ 465 (45.6)	1.17 (1.04, 1.32) 0.0094	1.46 (1.11, 1.90) 0.0059	0.09 (0.03, 0.15) 0.0057	
	Diuretics at baseline						0.9123
	Yes	1275/2458 (51.9)	1144/2463 (46.4)	1.09 (1.03, 1.15) 0.0012	1.23 (1.10, 1.38) 0.0004	0.05 (0.02, 0.08) 0.0004	
	No	151/ 292 (51.7)	137/ 295 (46.4)	1.11 (0.95, 1.30) 0.1957	1.22 (0.87, 1.70) 0.2475	0.05 (-0.03, 0.13) 0.2097	

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Quality of Life (LOCF)							
	Overall	1600/2801 (57.1)	1522/2805 (54.3)	1.03 (1.00, 1.06) 0.0762	1.10 (0.98, 1.23) 0.1083	0.02 (0.00, 0.04) 0.0453	
	Age						0.1346*
	<= median	815/1394 (58.5)	843/1471 (57.3)	1.03 (0.98, 1.08) 0.2199	1.03 (0.88, 1.21) 0.6755	0.02 (-0.02, 0.05) 0.3583	
	> median	785/1407 (55.8)	679/1334 (50.9)	1.10 (1.02, 1.18)*0.0105	1.17 (1.00, 1.38) 0.0550	0.05 (0.01, 0.09)*0.0102	
	Gender						0.0738*
	Male	921/1630 (56.5)	895/1608 (55.7)	1.02 (0.96, 1.08)*0.6286	1.00 (0.86, 1.16) 0.9985	0.01 (-0.03, 0.04)*0.6285	
	Female	679/1171 (58.0)	627/1197 (52.4)	1.04 (0.99, 1.11) 0.1396	1.24 (1.04, 1.48) 0.0158	0.04 (0.00, 0.07) 0.0327	
	Race						0.1128*
	White	1153/2006 (57.5)	1100/2032 (54.1)	1.06 (1.01, 1.12)*0.0325	1.11 (0.97, 1.26) 0.1296	0.03 (0.00, 0.05) 0.0416	
	Black or African	47/ 64 (73.4)	37/ 70 (52.9)	1.39 (1.07, 1.81)*0.0153	2.52 (1.19, 5.36) 0.0162	0.21 (0.06, 0.36) 0.0057	
	Asian	278/ 555 (50.1)	279/ 551 (50.6)	0.99 (0.88, 1.11)*0.8561	0.97 (0.76, 1.25) 0.8303	-0.00 (-0.06, 0.05) 0.8809	
	Other	122/ 176 (69.3)	106/ 152 (69.7)	0.99 (0.86, 1.15)*0.9345	1.00 (0.60, 1.66) 0.9935	-0.00 (-0.10, 0.10)*0.9345	
	Geographic region						0.5219*
	Asia	270/ 536 (50.4)	273/ 536 (50.9)	0.99 (0.88, 1.11)*0.8546	0.97 (0.75, 1.25) 0.7992	-0.01 (-0.06, 0.05) 0.8508	
	Europe and Saudi Arabia	755/1341 (56.3)	744/1381 (53.9)	1.05 (0.98, 1.12)*0.2031	1.06 (0.90, 1.24) 0.5037	0.02 (-0.01, 0.06)*0.2029	
	North America	238/ 393 (60.6)	204/ 376 (54.3)	1.14 (1.03, 1.26) 0.0122	1.29 (0.96, 1.74) 0.0930	0.07 (0.00, 0.13) 0.0416	
	Latin America	337/ 531 (63.5)	301/ 512 (58.8)	1.01 (0.94, 1.10) 0.7155	1.21 (0.92, 1.58) 0.1716	0.02 (-0.03, 0.07) 0.4239	
	NYHA class at enrolment						0.0339*
	II	1157/2083 (55.5)	1178/2165 (54.4)	1.02 (0.97, 1.08)*0.4577	1.04 (0.92, 1.18) 0.5379	0.01 (-0.01, 0.04) 0.3247	
	III or IV	443/ 718 (61.7)	344/ 639 (53.8)	1.15 (1.05, 1.26)*0.0037	1.34 (1.06, 1.69) 0.0132	0.07 (0.02, 0.11) 0.0053	
	LVEF at enrolment						0.5669*
	<= 49	545/ 959 (56.8)	529/ 950 (55.7)	1.02 (0.94, 1.10)*0.6139	1.05 (0.86, 1.27) 0.6416	0.01 (-0.03, 0.05) 0.5484	
	50-59	583/1017 (57.3)	548/1009 (54.3)	1.06 (0.98, 1.14)*0.1722	1.10 (0.91, 1.33) 0.3157	0.03 (-0.01, 0.07)*0.1717	
	>= 60	472/ 825 (57.2)	445/ 846 (52.6)	1.09 (1.00, 1.19)*0.0584	1.15 (0.94, 1.41) 0.1773	0.05 (-0.00, 0.09)*0.0579	
	NT-proBNP at enrolment						<.0001
	<= median	781/1396 (55.9)	778/1409 (55.2)	1.01 (0.95, 1.08)*0.6976	0.99 (0.85, 1.16) 0.9393	0.00 (-0.03, 0.04) 0.7878	
	> median	819/1405 (58.3)	743/1395 (53.3)	1.09 (1.02, 1.17)*0.0075	1.21 (1.03, 1.42) 0.0174	0.04 (0.01, 0.07) 0.0121	
	Type 2 Diabetes Medical History						0.0011
	Yes	729/1231 (59.2)	632/1243 (50.8)	1.12 (1.05, 1.19) 0.0006	1.40 (1.20, 1.65)*<.0001	0.08 (0.04, 0.11) <.0001	
	No	871/1570 (55.5)	890/1562 (57.0)	1.00 (0.97, 1.03) 0.9425	0.94 (0.82, 1.08)*0.3974	-0.01 (-0.04, 0.02) 0.5211	
	Atrial fibrillation or flutter at enrolment ECG						<.0001
	Yes	691/1185 (58.3)	618/1188 (52.0)	1.12 (1.04, 1.21)*0.0021	1.28 (1.08, 1.52) 0.0053	0.05 (0.01, 0.08) 0.0075	
	No	909/1616 (56.3)	904/1617 (55.9)	1.01 (0.95, 1.07)*0.8438	0.98 (0.85, 1.14) 0.7974	0.01 (-0.02, 0.04) 0.5629	
	BMI (kg/m2) at enrolment						0.0506*
	< 30	857/1547 (55.4)	845/1541 (54.8)	1.01 (0.95, 1.08)*0.7531	0.97 (0.83, 1.13) 0.6769	-0.00 (-0.03, 0.03) 0.8726	
	>= 30	743/1253 (59.3)	674/1261 (53.4)	1.11 (1.04, 1.19)*0.0032	1.28 (1.08, 1.52) 0.0038	0.06 (0.02, 0.09) 0.0012	
	Baseline eGFR (mL/min/1.73m^2)						0.7316
	< 60	753/1338 (56.3)	735/1377 (53.4)	1.05 (0.98, 1.13)*0.1289	1.11 (0.95, 1.30) 0.2029	0.02 (-0.01, 0.05) 0.2698	
	>= 60	847/1463 (57.9)	787/1427 (55.2)	1.05 (0.98, 1.12)*0.1371	1.08 (0.92, 1.26) 0.3438	0.03 (-0.00, 0.06) 0.0862	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.5318
	<= median	824/1405 (58.6)	785/1420 (55.3)	1.06 (0.99, 1.13)*0.0710	1.09 (0.93, 1.28) 0.2615	0.02 (-0.01, 0.05) 0.1919	
	> median	776/1396 (55.6)	737/1385 (53.2)	1.04 (0.98, 1.12)*0.2090	1.10 (0.94, 1.29) 0.2470	0.02 (-0.01, 0.06) 0.1250	
	LVEF at enrolment 2						0.3451*
	<= 49	545/ 959 (56.8)	529/ 950 (55.7)	1.02 (0.94, 1.10)*0.6139	1.05 (0.86, 1.27) 0.6416	0.01 (-0.03, 0.05) 0.5484	
	>= 50	1055/1842 (57.3)	993/1855 (53.5)	1.07 (1.01, 1.13)*0.0221	1.12 (0.98, 1.29) 0.1015	0.04 (0.01, 0.07)*0.0219	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2550*
	Yes	174/ 280 (62.1)	178/ 281 (63.3)	0.98 (0.86, 1.11)*0.7684	0.84 (0.57, 1.22) 0.3585	-0.01 (-0.09, 0.07)*0.7684	
	No	1426/2521 (56.6)	1344/2524 (53.2)	1.04 (1.00, 1.07) 0.0459	1.12 (1.00, 1.26) 0.0552	0.03 (0.00, 0.05) 0.0261	
	MRAs at baseline						0.3466*
	Yes	695/1216 (57.2)	640/1210 (52.9)	1.08 (1.01, 1.16)*0.0351	1.18 (0.99, 1.39) 0.0624	0.03 (-0.00, 0.07) 0.0651	
	No	905/1585 (57.1)	882/1595 (55.3)	1.03 (0.97, 1.10)*0.3064	1.04 (0.89, 1.21) 0.6173	0.02 (-0.01, 0.05) 0.1509	
	ACEi+ARB at baseline						0.2658*
	Yes	1162/2037 (57.0)	1098/2059 (53.3)	1.07 (1.01, 1.13)*0.0168	1.15 (1.01, 1.31) 0.0393	0.04 (0.01, 0.07)*0.0167	
	No	438/ 764 (57.3)	424/ 746 (56.8)	1.02 (0.94, 1.09) 0.6658	0.98 (0.79, 1.21) 0.8202	0.00 (-0.05, 0.05) 0.9656	
	ARNI at baseline						0.2535
	Yes	75/ 149 (50.3)	69/ 125 (55.2)	0.91 (0.75, 1.12) 0.3863	0.71 (0.42, 1.17) 0.1766	-0.07 (-0.19, 0.04) 0.2182	
	No	1525/2652 (57.5)	1453/2680 (54.2)	1.03 (1.00, 1.06) 0.0603	1.12 (1.00, 1.26) 0.0470	0.03 (0.00, 0.05) 0.0221	
	Beta Blocker at baseline						0.1806*
	Yes	1327/2327 (57.0)	1244/2330 (53.4)	1.07 (1.01, 1.12)*0.0127	1.13 (1.00, 1.27) 0.0586	0.03 (0.00, 0.05) 0.0210	
	No	273/ 474 (57.6)	278/ 475 (58.5)	1.02 (0.95, 1.10) 0.6000	0.96 (0.73, 1.26) 0.7493	0.00 (-0.05, 0.06) 0.9303	
	Diuretics at baseline						0.2518*
	Yes	1442/2500 (57.7)	1359/2504 (54.3)	1.04 (1.00, 1.07) 0.0433	1.14 (1.01, 1.28) 0.0366	0.03 (0.01, 0.05) 0.0164	
	No	158/ 301 (52.5)	163/ 301 (54.2)	0.97 (0.83, 1.13)*0.6830	0.81 (0.57, 1.15) 0.2342	-0.02 (-0.10, 0.06)*0.6829	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	1796/2801 (64.1)	1642/2805 (58.5)	1.10 (1.05, 1.14)*<.0001	1.26 (1.13, 1.41) <.0001	0.05 (0.03, 0.08) <.0001	
	Age						0.9909*
	<= median	928/1394 (66.6)	892/1471 (60.6)	1.10 (1.04, 1.16)*0.0010	1.31 (1.12, 1.54) 0.0006	0.06 (0.02, 0.09)*0.0009	
	> median	868/1407 (61.7)	750/1334 (56.2)	1.10 (1.03, 1.17)*0.0037	1.23 (1.05, 1.44) 0.0097	0.05 (0.01, 0.08) 0.0072	
	Gender						0.7879*
	Male	1076/1630 (66.0)	965/1608 (60.0)	1.10 (1.04, 1.16)*0.0004	1.29 (1.11, 1.49) 0.0006	0.06 (0.03, 0.09)*0.0004	
	Female	720/1171 (61.5)	677/1197 (56.6)	1.09 (1.02, 1.16)*0.0149	1.23 (1.03, 1.45) 0.0190	0.05 (0.01, 0.08) 0.0179	
	Race						0.6664*
	White	1276/2006 (63.6)	1173/2032 (57.7)	1.10 (1.05, 1.16)*0.0001	1.27 (1.11, 1.45) 0.0003	0.06 (0.03, 0.09)*0.0001	
	Black or African	44/ 64 (68.8)	45/ 70 (64.3)	1.09 (0.87, 1.37) 0.4328	1.26 (0.61, 2.63) 0.5330	0.06 (-0.10, 0.21) 0.4669	
	Asian	350/ 555 (63.1)	331/ 551 (60.1)	1.05 (0.96, 1.15)*0.3070	1.14 (0.89, 1.46) 0.2903	0.03 (-0.02, 0.09) 0.2541	
	Other	126/ 176 (71.6)	93/ 152 (61.2)	1.17 (1.00, 1.37)*0.0501	1.53 (0.95, 2.47) 0.0796	0.09 (-0.00, 0.19) 0.0548	
	Geographic region						0.6611*
	Asia	338/ 536 (63.1)	323/ 536 (60.3)	1.05 (0.95, 1.15)*0.3463	1.13 (0.88, 1.45) 0.3354	0.03 (-0.03, 0.09) 0.3032	
	Europe and Saudi Arabia	854/1341 (63.7)	804/1381 (58.2)	1.09 (1.03, 1.16)*0.0035	1.24 (1.06, 1.46) 0.0086	0.05 (0.02, 0.09)*0.0034	
	North America	229/ 393 (58.3)	196/ 376 (52.1)	1.12 (0.99, 1.26) 0.0691	1.28 (0.96, 1.71) 0.0957	0.06 (-0.01, 0.13) 0.0777	
	Latin America	375/ 531 (70.6)	319/ 512 (62.3)	1.13 (1.04, 1.24)*0.0047	1.47 (1.13, 1.92) 0.0045	0.08 (0.03, 0.14)*0.0043	
	NYHA class at enrolment						0.4453*
	II	1332/2083 (63.9)	1275/2165 (58.9)	1.09 (1.04, 1.14)*0.0007	1.25 (1.10, 1.42) 0.0005	0.05 (0.02, 0.08) 0.0006	
	III or IV	464/ 718 (64.6)	366/ 639 (57.3)	1.13 (1.04, 1.23)*0.0060	1.36 (1.07, 1.71) 0.0103	0.07 (0.02, 0.13)*0.0055	
	LVEF at enrolment						0.2955*
	<= 49	611/ 959 (63.7)	574/ 950 (60.4)	1.05 (0.98, 1.13)*0.1387	1.17 (0.96, 1.41) 0.1145	0.03 (-0.01, 0.08) 0.1018	
	50-59	656/1017 (64.5)	595/1009 (59.0)	1.09 (1.02, 1.17)*0.0106	1.27 (1.06, 1.53) 0.0105	0.06 (0.01, 0.10)*0.0103	
	>= 60	529/ 825 (64.1)	473/ 846 (55.9)	1.15 (1.06, 1.24)*0.0006	1.38 (1.13, 1.68) 0.0017	0.08 (0.03, 0.12) 0.0013	
	NT-proBNP at enrolment						0.7863*
	<= median	886/1396 (63.5)	821/1409 (58.3)	1.09 (1.03, 1.16)*0.0049	1.26 (1.08, 1.47) 0.0039	0.05 (0.01, 0.08) 0.0057	
	> median	910/1405 (64.8)	820/1395 (58.8)	1.10 (1.04, 1.17)*0.0011	1.27 (1.09, 1.49) 0.0028	0.06 (0.02, 0.10)*0.0011	
	Type 2 Diabetes Medical History						0.2069*
	Yes	794/1231 (64.5)	710/1243 (57.1)	1.13 (1.06, 1.20)*0.0002	1.36 (1.16, 1.60)*0.0002	0.07 (0.03, 0.11) 0.0002	
	No	1002/1570 (63.8)	932/1562 (59.7)	1.07 (1.01, 1.13)*0.0169	1.19 (1.03, 1.38)*0.0168	0.04 (0.01, 0.08)*0.0167	
	Atrial fibrillation or flutter at enrolment ECG						0.5148*
	Yes	776/1185 (65.5)	699/1188 (58.8)	1.11 (1.04, 1.19)*0.0009	1.33 (1.12, 1.58) 0.0010	0.07 (0.03, 0.11)*0.0008	
	No	1020/1616 (63.1)	943/1617 (58.3)	1.08 (1.02, 1.14)*0.0053	1.22 (1.05, 1.41) 0.0076	0.05 (0.01, 0.08) 0.0052	
	BMI (kg/m2) at enrolment						0.6768*
	< 30	997/1547 (64.4)	914/1541 (59.3)	1.09 (1.03, 1.15)*0.0034	1.24 (1.07, 1.44) 0.0047	0.05 (0.02, 0.09)*0.0033	
	>= 30	798/1253 (63.7)	726/1261 (57.6)	1.11 (1.04, 1.18)*0.0017	1.30 (1.10, 1.53) 0.0022	0.06 (0.02, 0.10)*0.0017	
	Baseline eGFR (mL/min/1.73m^2)						0.5640*
	< 60	826/1338 (61.7)	767/1377 (55.7)	1.11 (1.04, 1.18)*0.0014	1.28 (1.10, 1.50) 0.0019	0.06 (0.02, 0.09) 0.0023	
	>= 60	970/1463 (66.3)	875/1427 (61.3)	1.08 (1.02, 1.14)*0.0054	1.24 (1.06, 1.45) 0.0069	0.05 (0.01, 0.08)*0.0053	

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Symptom Burden (LOCF)	SBP at randomisation						0.7806*
	<= median	895/1405 (63.7)	821/1420 (57.8)	1.10 (1.04, 1.17)*0.0014	1.25 (1.07, 1.45) 0.0055	0.05 (0.02, 0.08) 0.0045	
	> median	901/1396 (64.5)	821/1385 (59.3)	1.09 (1.03, 1.15)*0.0043	1.29 (1.10, 1.51) 0.0017	0.05 (0.02, 0.09)*0.0042	
	LVEF at enrolment 2						0.1930*
	<= 49	611/ 959 (63.7)	574/ 950 (60.4)	1.05 (0.98, 1.13)*0.1387	1.17 (0.96, 1.41) 0.1145	0.03 (-0.01, 0.08) 0.1018	
	>= 50	1185/1842 (64.3)	1068/1855 (57.6)	1.12 (1.06, 1.18)*<.0001	1.32 (1.15, 1.51) <.0001	0.06 (0.03, 0.09) <.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2366*
	Yes	191/ 280 (68.2)	187/ 281 (66.5)	1.03 (0.91, 1.15)*0.6739	1.13 (0.77, 1.64) 0.5345	0.02 (-0.06, 0.09)*0.6738	
	No	1605/2521 (63.7)	1455/2524 (57.6)	1.10 (1.06, 1.15)*<.0001	1.28 (1.14, 1.44) <.0001	0.06 (0.03, 0.08) <.0001	
	MRAs at baseline						0.6055*
	Yes	776/1216 (63.8)	696/1210 (57.5)	1.11 (1.04, 1.18)*0.0015	1.29 (1.09, 1.53) 0.0029	0.06 (0.02, 0.10)*0.0015	
	No	1020/1585 (64.4)	946/1595 (59.3)	1.09 (1.03, 1.15)*0.0035	1.24 (1.07, 1.44) 0.0035	0.05 (0.02, 0.08) 0.0016	
	ACEi+ARB at baseline						0.7756*
	Yes	1314/2037 (64.5)	1208/2059 (58.7)	1.10 (1.05, 1.15)*0.0001	1.27 (1.12, 1.45) 0.0003	0.06 (0.03, 0.09)*0.0001	
	No	482/ 764 (63.1)	434/ 746 (58.2)	1.08 (1.00, 1.18)*0.0513	1.24 (1.01, 1.53) 0.0436	0.05 (0.01, 0.10) 0.0283	
	ARNI at baseline						0.7775*
	Yes	94/ 149 (63.1)	70/ 125 (56.0)	1.12 (0.92, 1.37) 0.2419	1.33 (0.81, 2.18) 0.2564	0.07 (-0.05, 0.19) 0.2466	
	No	1702/2652 (64.2)	1572/2680 (58.7)	1.09 (1.05, 1.14)*<.0001	1.25 (1.12, 1.41) <.0001	0.06 (0.03, 0.08)*<.0001	
	Beta Blocker at baseline						0.1740*
	Yes	1476/2327 (63.4)	1367/2330 (58.7)	1.08 (1.03, 1.13)*0.0009	1.21 (1.07, 1.36) 0.0024	0.04 (0.01, 0.07) 0.0036	
	No	320/ 474 (67.5)	275/ 475 (57.9)	1.17 (1.06, 1.29)*0.0023	1.59 (1.21, 2.09) 0.0008	0.10 (0.03, 0.16)*0.0021	
	Diuretics at baseline						0.7620*
	Yes	1604/2500 (64.2)	1470/2504 (58.7)	1.09 (1.05, 1.14)*<.0001	1.27 (1.13, 1.43) <.0001	0.05 (0.03, 0.08)*<.0001	
	No	192/ 301 (63.8)	172/ 301 (57.1)	1.09 (0.96, 1.22) 0.1813	1.24 (0.88, 1.73) 0.2155	0.05 (-0.02, 0.13) 0.1824	

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Self Efficacy (LOCF)							
	Overall	1667/2801 (59.5)	1643/2805 (58.6)	1.01 (0.97, 1.04) 0.7149	1.04 (0.93, 1.16) 0.4945	0.01 (-0.02, 0.03) 0.5919	
	Age						0.4903*
	<= median	860/1394 (61.7)	904/1471 (61.5)	1.00 (0.95, 1.06)*0.8958	1.01 (0.87, 1.18) 0.8778	-0.01 (-0.04, 0.03) 0.7550	
	> median	807/1407 (57.4)	739/1334 (55.4)	1.04 (0.97, 1.11)*0.3017	1.08 (0.93, 1.26) 0.3279	0.02 (-0.02, 0.06) 0.2750	
	Gender						0.2330*
	Male	989/1630 (60.7)	939/1608 (58.4)	1.03 (0.98, 1.08) 0.2784	1.11 (0.96, 1.28) 0.1613	0.02 (-0.01, 0.05) 0.2023	
	Female	678/1171 (57.9)	704/1197 (58.8)	0.98 (0.92, 1.05)*0.6518	0.95 (0.81, 1.12) 0.5564	-0.01 (-0.05, 0.03) 0.5078	
	Race						0.9942*
	White	1225/2006 (61.1)	1218/2032 (59.9)	1.00 (0.96, 1.05) 0.9738	1.04 (0.92, 1.18) 0.5252	0.01 (-0.02, 0.04) 0.5932	
	Black or African	36/ 64 (56.3)	39/ 70 (55.7)	0.96 (0.71, 1.28) 0.7608	1.04 (0.51, 2.09) 0.9186	-0.00 (-0.16, 0.16) 0.9926	
	Asian	299/ 555 (53.9)	293/ 551 (53.2)	1.01 (0.91, 1.13)*0.8160	1.07 (0.83, 1.37) 0.6045	0.01 (-0.04, 0.07) 0.6460	
	Other	107/ 176 (60.8)	93/ 152 (61.2)	0.99 (0.84, 1.18)*0.9426	0.98 (0.61, 1.59) 0.9455	-0.00 (-0.11, 0.10)*0.9426	
	Geographic region						0.6287*
	Asia	287/ 536 (53.5)	285/ 536 (53.2)	1.01 (0.90, 1.13)*0.9025	1.06 (0.82, 1.37) 0.6414	0.02 (-0.04, 0.07) 0.5056	
	Europe and Saudi Arabia	807/1341 (60.2)	797/1381 (57.7)	1.04 (0.98, 1.11)*0.1908	1.11 (0.95, 1.29) 0.2075	0.02 (-0.01, 0.06) 0.2012	
	North America	252/ 393 (64.1)	249/ 376 (66.2)	0.97 (0.87, 1.07) 0.5174	0.92 (0.68, 1.24) 0.5704	-0.02 (-0.09, 0.05) 0.5517	
	Latin America	321/ 531 (60.5)	312/ 512 (60.9)	0.99 (0.90, 1.09)*0.8725	0.95 (0.74, 1.23) 0.7202	-0.02 (-0.07, 0.04) 0.5773	
	NYHA class at enrolment						0.0378*
	II	1220/2083 (58.6)	1282/2165 (59.2)	0.99 (0.95, 1.03) 0.6950	0.97 (0.86, 1.10) 0.6247	-0.01 (-0.04, 0.02) 0.5638	
	III or IV	447/ 718 (62.3)	361/ 639 (56.5)	1.10 (1.01, 1.20)*0.0319	1.29 (1.03, 1.60) 0.0251	0.06 (0.00, 0.11) 0.0323	
	LVEF at enrolment						0.0991*
	<= 49	567/ 959 (59.1)	576/ 950 (60.6)	0.98 (0.91, 1.05)*0.5017	0.95 (0.79, 1.14) 0.5946	-0.01 (-0.05, 0.03) 0.6602	
	50-59	590/1017 (58.0)	588/1009 (58.3)	0.98 (0.92, 1.05) 0.5944	0.98 (0.82, 1.18) 0.8590	-0.01 (-0.05, 0.04) 0.7971	
	>= 60	510/ 825 (61.8)	479/ 846 (56.6)	1.09 (1.01, 1.18)*0.0308	1.22 (1.00, 1.49) 0.0492	0.03 (-0.01, 0.08) 0.1367	
	NT-proBNP at enrolment						0.4425*
	<= median	818/1396 (58.6)	827/1409 (58.7)	1.00 (0.94, 1.06)*0.9579	0.99 (0.85, 1.15) 0.8885	-0.01 (-0.04, 0.03) 0.7111	
	> median	849/1405 (60.4)	816/1395 (58.5)	1.03 (0.97, 1.10)*0.2979	1.09 (0.93, 1.27) 0.2803	0.02 (-0.01, 0.06) 0.2474	
	Type 2 Diabetes Medical History						0.5769
	Yes	748/1231 (60.8)	720/1243 (57.9)	1.01 (0.95, 1.08) 0.7286	1.12 (0.96, 1.32)*0.1506	0.02 (-0.02, 0.06) 0.2943	
	No	919/1570 (58.5)	923/1562 (59.1)	0.99 (0.93, 1.05)*0.7520	0.98 (0.85, 1.13)*0.7520	-0.00 (-0.03, 0.03) 0.9913	
	Atrial fibrillation or flutter at enrolment ECG						0.0073*
	Yes	707/1185 (59.7)	649/1188 (54.6)	1.09 (1.02, 1.17)*0.0134	1.22 (1.03, 1.44) 0.0212	0.04 (0.00, 0.08) 0.0273	
	No	960/1616 (59.4)	994/1617 (61.5)	0.97 (0.91, 1.02)*0.2298	0.92 (0.80, 1.06) 0.2697	-0.02 (-0.05, 0.01) 0.2087	
	BMI (kg/m2) at enrolment						0.0537*
	< 30	888/1547 (57.4)	905/1541 (58.7)	0.99 (0.94, 1.04) 0.6549	0.93 (0.80, 1.08) 0.3355	-0.02 (-0.05, 0.02) 0.3566	
	>= 30	778/1253 (62.1)	735/1261 (58.3)	1.05 (0.99, 1.11) 0.1364	1.18 (1.01, 1.39) 0.0410	0.04 (-0.00, 0.08) 0.0512	
	Baseline eGFR (mL/min/1.73m^2)						0.1531*
	< 60	771/1338 (57.6)	808/1377 (58.7)	0.98 (0.93, 1.04) 0.6150	0.97 (0.83, 1.13) 0.6820	-0.01 (-0.05, 0.03) 0.6374	
	>= 60	896/1463 (61.2)	835/1427 (58.5)	1.05 (0.99, 1.11)*0.1348	1.10 (0.95, 1.29) 0.2007	0.02 (-0.02, 0.05) 0.3515	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.8507*
	<= median	837/1405 (59.6)	836/1420 (58.9)	1.01 (0.95, 1.08)*0.7051	1.03 (0.88, 1.20) 0.7054	-0.00 (-0.03, 0.03) 0.9934	
	> median	830/1396 (59.5)	807/1385 (58.3)	1.02 (0.96, 1.08) 0.5536	1.05 (0.90, 1.23) 0.5197	0.01 (-0.02, 0.05) 0.5130	
	LVEF at enrolment 2						0.1784*
	<= 49	567/ 959 (59.1)	576/ 950 (60.6)	0.98 (0.91, 1.05)*0.5017	0.95 (0.79, 1.14) 0.5946	-0.01 (-0.05, 0.03) 0.6602	
	>= 50	1100/1842 (59.7)	1067/1855 (57.5)	1.01 (0.96, 1.06) 0.6685	1.09 (0.95, 1.24) 0.2303	0.01 (-0.02, 0.04) 0.3725	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9467
	Yes	166/ 280 (59.3)	167/ 281 (59.4)	1.00 (0.87, 1.14)*0.9721	1.00 (0.70, 1.41) 0.9853	-0.00 (-0.08, 0.08) 0.9779	
	No	1501/2521 (59.5)	1476/2524 (58.5)	1.01 (0.97, 1.05) 0.6572	1.04 (0.93, 1.17) 0.4803	0.01 (-0.02, 0.03) 0.5669	
	MRAs at baseline						0.2844*
	Yes	690/1216 (56.7)	695/1210 (57.4)	0.99 (0.93, 1.05) 0.7095	0.98 (0.83, 1.15) 0.7782	-0.01 (-0.04, 0.03) 0.7493	
	No	977/1585 (61.6)	948/1595 (59.4)	1.04 (0.98, 1.10)*0.2036	1.09 (0.94, 1.26) 0.2427	0.02 (-0.02, 0.05) 0.3270	
	ACEi+ARB at baseline						0.5792*
	Yes	1200/2037 (58.9)	1203/2059 (58.4)	1.00 (0.95, 1.04) 0.8688	1.02 (0.90, 1.16) 0.7774	0.00 (-0.03, 0.03) 0.9176	
	No	467/ 764 (61.1)	440/ 746 (59.0)	1.04 (0.95, 1.13)*0.3953	1.09 (0.89, 1.35) 0.4057	0.02 (-0.03, 0.07) 0.3665	
	ARNI at baseline						0.7651
	Yes	85/ 149 (57.0)	74/ 125 (59.2)	0.97 (0.80, 1.18) 0.7787	1.00 (0.61, 1.63) 0.9885	-0.00 (-0.12, 0.11) 0.9354	
	No	1582/2652 (59.7)	1569/2680 (58.5)	1.00 (0.97, 1.04) 0.7973	1.04 (0.93, 1.17) 0.4619	0.01 (-0.02, 0.03) 0.5779	
	Beta Blocker at baseline						0.3080*
	Yes	1383/2327 (59.4)	1349/2330 (57.9)	1.02 (0.97, 1.06) 0.4568	1.07 (0.95, 1.20) 0.2815	0.01 (-0.01, 0.04) 0.3369	
	No	284/ 474 (59.9)	294/ 475 (61.9)	0.97 (0.87, 1.07)*0.5323	0.90 (0.69, 1.18) 0.4477	-0.02 (-0.08, 0.04) 0.4350	
	Diuretics at baseline						0.7214*
	Yes	1476/2500 (59.0)	1459/2504 (58.3)	1.01 (0.97, 1.05) 0.5601	1.03 (0.92, 1.16) 0.5676	0.01 (-0.02, 0.03) 0.6249	
	No	191/ 301 (63.5)	184/ 301 (61.1)	1.01 (0.90, 1.14) 0.8429	1.08 (0.78, 1.51) 0.6418	0.02 (-0.06, 0.09) 0.6921	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	1645/2801 (58.7)	1537/2805 (54.8)	1.05 (1.01, 1.10) 0.0077	1.18 (1.06, 1.32) 0.0033	0.04 (0.02, 0.06) 0.0012	
	Age						0.0481
	<= median	841/1394 (60.3)	853/1471 (58.0)	1.05 (1.00, 1.11) 0.0707	1.12 (0.96, 1.31) 0.1430	0.03 (-0.00, 0.06) 0.0808	
	> median	804/1407 (57.1)	684/1334 (51.3)	1.11 (1.04, 1.19)*0.0021	1.26 (1.07, 1.47) 0.0045	0.06 (0.02, 0.10)*0.0020	
	Gender						0.8089*
	Male	976/1630 (59.9)	903/1608 (56.2)	1.07 (1.01, 1.13)*0.0322	1.18 (1.02, 1.36) 0.0264	0.04 (0.00, 0.07)*0.0319	
	Female	669/1171 (57.1)	634/1197 (53.0)	1.08 (1.00, 1.16)*0.0418	1.17 (0.99, 1.39) 0.0670	0.04 (0.00, 0.08) 0.0442	
	Race						0.8630*
	White	1141/2006 (56.9)	1076/2032 (53.0)	1.07 (1.02, 1.14)*0.0122	1.15 (1.01, 1.32) 0.0309	0.03 (0.01, 0.06) 0.0168	
	Black or African	41/ 64 (64.1)	42/ 70 (60.0)	1.12 (0.87, 1.44) 0.3876	1.24 (0.61, 2.52) 0.5559	0.06 (-0.11, 0.22) 0.4897	
	Asian	337/ 555 (60.7)	322/ 551 (58.4)	1.04 (0.94, 1.15)*0.4397	1.12 (0.88, 1.44) 0.3449	0.03 (-0.03, 0.08) 0.3314	
	Other	126/ 176 (71.6)	97/ 152 (63.8)	1.12 (0.96, 1.31)*0.1373	1.50 (0.91, 2.47) 0.1094	0.08 (-0.02, 0.18)*0.1327	
	Geographic region						0.3206*
	Asia	326/ 536 (60.8)	314/ 536 (58.6)	1.04 (0.94, 1.15)*0.4551	1.12 (0.87, 1.43) 0.3808	0.03 (-0.03, 0.08) 0.3714	
	Europe and Saudi Arabia	749/1341 (55.9)	712/1381 (51.6)	1.08 (1.01, 1.16)*0.0247	1.17 (0.99, 1.37) 0.0581	0.04 (0.01, 0.08)*0.0244	
	North America	203/ 393 (51.7)	198/ 376 (52.7)	1.01 (0.89, 1.14) 0.8889	0.98 (0.73, 1.31) 0.8901	0.00 (-0.07, 0.07) 0.9921	
	Latin America	367/ 531 (69.1)	313/ 512 (61.1)	1.13 (1.03, 1.24)*0.0072	1.47 (1.12, 1.92) 0.0052	0.08 (0.02, 0.14)*0.0067	
	NYHA class at enrolment						0.2689*
	II	1207/2083 (57.9)	1189/2165 (54.9)	1.06 (1.00, 1.11)*0.0468	1.16 (1.02, 1.31) 0.0230	0.03 (0.00, 0.06)*0.0466	
	III or IV	438/ 718 (61.0)	348/ 639 (54.5)	1.10 (1.01, 1.19) 0.0203	1.29 (1.03, 1.62) 0.0290	0.06 (0.01, 0.11) 0.0100	
	LVEF at enrolment						0.7734*
	<= 49	571/ 959 (59.5)	529/ 950 (55.7)	1.07 (0.99, 1.15)*0.0885	1.21 (1.00, 1.46) 0.0480	0.04 (-0.01, 0.08)*0.0880	
	50-59	588/1017 (57.8)	554/1009 (54.9)	1.05 (0.98, 1.14)*0.1868	1.13 (0.94, 1.35) 0.1961	0.03 (-0.01, 0.07) 0.2120	
	>= 60	486/ 825 (58.9)	454/ 846 (53.7)	1.10 (1.01, 1.19)*0.0309	1.21 (0.99, 1.47) 0.0688	0.05 (0.01, 0.10) 0.0292	
	NT-proBNP at enrolment						0.2015*
	<= median	788/1396 (56.4)	765/1409 (54.3)	1.04 (0.98, 1.10) 0.1804	1.10 (0.94, 1.28) 0.2247	0.03 (-0.01, 0.06) 0.1586	
	> median	857/1405 (61.0)	771/1395 (55.3)	1.10 (1.04, 1.18)*0.0022	1.27 (1.08, 1.48) 0.0031	0.06 (0.02, 0.09)*0.0021	
	Type 2 Diabetes Medical History						0.0369*
	Yes	737/1231 (59.9)	657/1243 (52.9)	1.13 (1.06, 1.21)*0.0005	1.33 (1.13, 1.56)*0.0004	0.08 (0.04, 0.11) <.0001	
	No	908/1570 (57.8)	880/1562 (56.3)	1.01 (0.97, 1.05) 0.6381	1.06 (0.92, 1.22)*0.3976	0.01 (-0.02, 0.04) 0.4963	
	Atrial fibrillation or flutter at enrolment ECG						0.6023*
	Yes	708/1185 (59.7)	653/1188 (55.0)	1.09 (1.01, 1.17)*0.0187	1.24 (1.05, 1.47) 0.0130	0.05 (0.01, 0.08) 0.0137	
	No	937/1616 (58.0)	884/1617 (54.7)	1.05 (1.00, 1.10) 0.0612	1.14 (0.99, 1.32) 0.0769	0.03 (0.00, 0.07) 0.0343	
	BMI (kg/m2) at enrolment						0.7055*
	< 30	910/1547 (58.8)	852/1541 (55.3)	1.06 (1.00, 1.13)*0.0474	1.17 (1.01, 1.35) 0.0420	0.04 (0.00, 0.07)*0.0471	
	>= 30	735/1253 (58.7)	683/1261 (54.2)	1.06 (1.00, 1.13) 0.0350	1.20 (1.02, 1.42) 0.0306	0.04 (0.01, 0.08) 0.0153	
	Baseline eGFR (mL/min/1.73m^2)						0.0029
	< 60	777/1338 (58.1)	720/1377 (52.3)	1.11 (1.04, 1.19)*0.0025	1.28 (1.09, 1.50) 0.0023	0.06 (0.02, 0.09) 0.0021	
	>= 60	868/1463 (59.3)	817/1427 (57.3)	1.04 (0.97, 1.10)*0.2578	1.09 (0.93, 1.27) 0.2821	0.03 (-0.01, 0.06) 0.1114	

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AstraZeneca
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)	SBP at randomisation						0.9623*
	<= median	822/1405 (58.5)	776/1420 (54.6)	1.04 (0.98, 1.10) 0.1926	1.15 (0.98, 1.34) 0.0781	0.03 (-0.00, 0.07) 0.0809	
	> median	823/1396 (59.0)	761/1385 (54.9)	1.07 (1.01, 1.14)*0.0330	1.21 (1.04, 1.42) 0.0164	0.04 (0.00, 0.08)*0.0327	
	LVEF at enrolment 2						0.9432*
	<= 49	571/ 959 (59.5)	529/ 950 (55.7)	1.07 (0.99, 1.15)*0.0885	1.21 (1.00, 1.46) 0.0480	0.04 (-0.01, 0.08)*0.0880	
	>= 50	1074/1842 (58.3)	1008/1855 (54.3)	1.05 (1.00, 1.10) 0.0355	1.16 (1.02, 1.33) 0.0294	0.04 (0.01, 0.07) 0.0158	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5254*
	Yes	183/ 280 (65.4)	178/ 281 (63.3)	1.03 (0.91, 1.17)*0.6189	1.27 (0.87, 1.84) 0.2094	0.02 (-0.06, 0.10)*0.6188	
	No	1462/2521 (58.0)	1359/2524 (53.8)	1.07 (1.02, 1.11) 0.0033	1.18 (1.05, 1.32) 0.0055	0.04 (0.02, 0.07) 0.0013	
	MRAs at baseline						0.2731*
	Yes	720/1216 (59.2)	649/1210 (53.6)	1.10 (1.03, 1.18)*0.0057	1.27 (1.07, 1.50) 0.0052	0.06 (0.02, 0.10)*0.0056	
	No	925/1585 (58.4)	888/1595 (55.7)	1.04 (0.99, 1.10) 0.1017	1.12 (0.96, 1.29) 0.1411	0.03 (-0.00, 0.06) 0.0803	
	ACEi+ARB at baseline						0.1440*
	Yes	1207/2037 (59.3)	1115/2059 (54.2)	1.09 (1.04, 1.15)*0.0010	1.23 (1.08, 1.40) 0.0018	0.05 (0.02, 0.07) 0.0014	
	No	438/ 764 (57.3)	422/ 746 (56.6)	1.04 (0.96, 1.13) 0.3150	1.05 (0.85, 1.29) 0.6489	0.02 (-0.03, 0.06) 0.5243	
	ARNI at baseline						0.0541*
	Yes	85/ 149 (57.0)	80/ 125 (64.0)	0.92 (0.76, 1.11) 0.3930	0.78 (0.47, 1.28) 0.3217	-0.05 (-0.17, 0.06) 0.3654	
	No	1560/2652 (58.8)	1457/2680 (54.4)	1.06 (1.02, 1.10) 0.0061	1.20 (1.07, 1.34) 0.0018	0.04 (0.02, 0.07) 0.0007	
	Beta Blocker at baseline						0.9683*
	Yes	1361/2327 (58.5)	1272/2330 (54.6)	1.05 (1.00, 1.09) 0.0458	1.16 (1.03, 1.31) 0.0157	0.03 (0.01, 0.06) 0.0107	
	No	284/ 474 (59.9)	265/ 475 (55.8)	1.07 (0.96, 1.20)*0.1985	1.28 (0.98, 1.68) 0.0723	0.04 (-0.02, 0.10)*0.1977	
	Diuretics at baseline						0.1756*
	Yes	1450/2500 (58.0)	1370/2504 (54.7)	1.04 (1.00, 1.09) 0.0371	1.16 (1.03, 1.30) 0.0126	0.04 (0.01, 0.06) 0.0065	
	No	195/ 301 (64.8)	167/ 301 (55.5)	1.17 (1.02, 1.33)*0.0205	1.38 (0.98, 1.93) 0.0640	0.09 (0.02, 0.17)*0.0192	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)							
	Overall	1528/2625 (58.2)	1490/2625 (56.8)	1.02 (0.98, 1.07) 0.3186	1.06 (0.95, 1.19) 0.2925	0.01 (-0.01, 0.04) 0.2794	
	Age						0.5648
	<= median	812/1331 (61.0)	827/1409 (58.7)	1.04 (0.98, 1.10) 0.1758	1.12 (0.96, 1.31) 0.1618	0.03 (-0.01, 0.06) 0.1478	
	> median	716/1294 (55.3)	663/1216 (54.5)	1.01 (0.94, 1.08) 0.8189	1.02 (0.87, 1.20) 0.8185	0.00 (-0.03, 0.04) 0.8312	
	Gender						0.5852
	Male	910/1538 (59.2)	874/1500 (58.3)	1.01 (0.96, 1.07) 0.6818	1.04 (0.90, 1.21) 0.5680	0.01 (-0.02, 0.04) 0.5815	
	Female	618/1087 (56.9)	616/1125 (54.8)	1.03 (0.96, 1.10) 0.3590	1.08 (0.91, 1.28) 0.3947	0.02 (-0.02, 0.06) 0.3899	
	Race						0.1527
	White	1074/1890 (56.8)	1040/1921 (54.1)	1.03 (0.98, 1.08) 0.1988	1.10 (0.96, 1.26) 0.1610	0.02 (-0.01, 0.05) 0.1275	
	Black or African	29/ 58 (50.0)	43/ 66 (65.2)	0.82 (0.60, 1.11) 0.1895	0.54 (0.25, 1.13) 0.1034	-0.13 (-0.30, 0.04) 0.1229	
	Asian	313/ 506 (61.9)	316/ 494 (64.0)	0.97 (0.88, 1.06) 0.4945	0.92 (0.71, 1.19) 0.5084	-0.02 (-0.08, 0.04) 0.5030	
	Other	112/ 171 (65.5)	91/ 144 (63.2)	1.06 (0.90, 1.24) 0.4903	1.18 (0.73, 1.90) 0.4944	0.04 (-0.07, 0.14) 0.4651	
	Geographic region						0.2563
	Asia	306/ 492 (62.2)	312/ 482 (64.7)	0.96 (0.87, 1.06) 0.4116	0.90 (0.69, 1.17) 0.4190	-0.03 (-0.09, 0.04) 0.4159	
	Europe and Saudi Arabia	718/1273 (56.4)	701/1309 (53.6)	1.00 (0.94, 1.07) 0.9167	1.09 (0.93, 1.28) 0.2973	0.02 (-0.02, 0.05) 0.3203	
	North America	200/ 367 (54.5)	192/ 347 (55.3)	0.99 (0.87, 1.12) 0.8559	1.00 (0.74, 1.35) 0.9754	-0.00 (-0.07, 0.07) 0.9381	
	Latin America	304/ 493 (61.7)	285/ 487 (58.5)	1.07 (0.98, 1.18) 0.1226	1.15 (0.89, 1.51) 0.2871	0.04 (-0.02, 0.10) 0.1719	
	NYHA class at enrolment						0.7166
	II	1156/1953 (59.2)	1166/2031 (57.4)	1.03 (0.99, 1.09) 0.1717	1.09 (0.96, 1.24) 0.1934	0.02 (-0.01, 0.05) 0.1758	
	III or IV	372/ 672 (55.4)	324/ 593 (54.6)	1.00 (0.92, 1.09) 0.9446	1.03 (0.81, 1.30) 0.8058	0.01 (-0.04, 0.06) 0.8087	
	LVEF at enrolment						0.7074
	<= 49	537/ 907 (59.2)	529/ 896 (59.0)	1.00 (0.93, 1.08) 0.9261	1.04 (0.86, 1.26) 0.7131	0.01 (-0.04, 0.05) 0.7599	
	50-59	538/ 955 (56.3)	517/ 946 (54.7)	1.02 (0.95, 1.10) 0.5721	1.04 (0.86, 1.25) 0.6972	0.01 (-0.03, 0.05) 0.6301	
	>= 60	453/ 763 (59.4)	444/ 783 (56.7)	1.05 (0.97, 1.14) 0.2023	1.12 (0.91, 1.37) 0.2971	0.03 (-0.02, 0.08) 0.2605	
	NT-proBNP at enrolment						0.9597
	<= median	763/1312 (58.2)	757/1336 (56.7)	1.02 (0.96, 1.09) 0.4257	1.07 (0.92, 1.26) 0.3714	0.02 (-0.02, 0.05) 0.3647	
	> median	765/1313 (58.3)	732/1288 (56.8)	1.02 (0.96, 1.08) 0.5183	1.05 (0.89, 1.23) 0.5528	0.01 (-0.02, 0.05) 0.5157	
	Type 2 Diabetes Medical History						0.1557
	Yes	678/1150 (59.0)	652/1169 (55.8)	1.06 (0.99, 1.13) 0.0832	1.14 (0.97, 1.34)*0.1214	0.03 (-0.01, 0.07) 0.0926	
	No	850/1475 (57.6)	838/1456 (57.6)	0.99 (0.94, 1.05) 0.8218	1.00 (0.87, 1.16)*0.9685	-0.00 (-0.04, 0.03) 0.9300	
	Atrial fibrillation or flutter at enrolment ECG						0.5750
	Yes	647/1097 (59.0)	618/1109 (55.7)	1.04 (0.97, 1.11) 0.2882	1.14 (0.96, 1.36) 0.1309	0.03 (-0.01, 0.07) 0.1651	
	No	881/1528 (57.7)	872/1516 (57.5)	1.01 (0.96, 1.07) 0.6819	1.01 (0.87, 1.17) 0.9246	0.00 (-0.03, 0.04) 0.8080	
	BMI (kg/m2) at enrolment						0.4438
	< 30	857/1452 (59.0)	834/1428 (58.4)	1.01 (0.95, 1.07) 0.7844	1.02 (0.88, 1.19) 0.7739	0.01 (-0.03, 0.04) 0.7662	
	>= 30	671/1172 (57.3)	654/1195 (54.7)	1.04 (0.97, 1.11) 0.2463	1.11 (0.94, 1.31) 0.2117	0.03 (-0.01, 0.06) 0.2005	
	Baseline eGFR (mL/min/1.73m^2)						0.1554
	< 60	687/1240 (55.4)	714/1270 (56.2)	0.99 (0.93, 1.05) 0.6601	0.97 (0.82, 1.14) 0.6856	-0.01 (-0.05, 0.03) 0.6710	
	>= 60	841/1385 (60.7)	776/1354 (57.3)	1.05 (1.00, 1.12) 0.0716	1.15 (0.99, 1.35) 0.0748	0.03 (-0.00, 0.07) 0.0648	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)	SBP at randomisation						0.0320
	<= median	748/1320 (56.7)	765/1323 (57.8)	0.98 (0.92, 1.04) 0.4496	0.93 (0.79, 1.08) 0.3373	-0.02 (-0.05, 0.02) 0.3810	
	> median	780/1305 (59.8)	725/1302 (55.7)	1.07 (1.01, 1.14) 0.0253	1.21 (1.03, 1.42) 0.0189	0.04 (0.01, 0.08) 0.0176	
	LVEF at enrolment 2						0.5040
	<= 49	537/ 907 (59.2)	529/ 896 (59.0)	1.00 (0.93, 1.08) 0.9261	1.04 (0.86, 1.26) 0.7131	0.01 (-0.04, 0.05) 0.7599	
	>= 50	991/1718 (57.7)	961/1729 (55.6)	1.03 (0.98, 1.09) 0.2476	1.07 (0.93, 1.23) 0.3230	0.02 (-0.01, 0.05) 0.2798	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2344
	Yes	153/ 252 (60.7)	156/ 256 (60.9)	1.00 (0.87, 1.15)*0.9589	1.01 (0.69, 1.48) 0.9491	-0.02 (-0.10, 0.06) 0.5479	
	No	1375/2373 (57.9)	1334/2369 (56.3)	1.03 (0.99, 1.08) 0.1881	1.07 (0.95, 1.20) 0.2627	0.02 (-0.01, 0.04) 0.2186	
	MRAs at baseline						0.4329
	Yes	668/1144 (58.4)	657/1131 (58.1)	1.00 (0.94, 1.07) 0.8865	1.02 (0.86, 1.21) 0.8346	0.00 (-0.03, 0.04) 0.8300	
	No	860/1481 (58.1)	833/1494 (55.8)	1.04 (0.98, 1.10) 0.2043	1.09 (0.94, 1.27) 0.2399	0.02 (-0.01, 0.06) 0.2168	
	ACEi+ARB at baseline						0.5477
	Yes	1122/1909 (58.8)	1096/1934 (56.7)	1.03 (0.98, 1.08) 0.2623	1.09 (0.96, 1.24) 0.2025	0.02 (-0.01, 0.05) 0.2029	
	No	406/ 716 (56.7)	394/ 691 (57.0)	1.00 (0.92, 1.09) 0.9986	0.99 (0.80, 1.23) 0.9362	-0.00 (-0.05, 0.05) 0.9695	
	ARNI at baseline						0.7240
	Yes	85/ 146 (58.2)	65/ 115 (56.5)	1.01 (0.82, 1.26) 0.8943	1.04 (0.63, 1.72) 0.8712	0.01 (-0.11, 0.13) 0.8747	
	No	1443/2479 (58.2)	1425/2510 (56.8)	1.02 (0.98, 1.06) 0.3867	1.06 (0.94, 1.19) 0.3245	0.01 (-0.01, 0.04) 0.3235	
	Beta Blocker at baseline						0.4531
	Yes	1267/2195 (57.7)	1237/2187 (56.6)	1.01 (0.97, 1.06) 0.5712	1.04 (0.92, 1.17) 0.5361	0.01 (-0.02, 0.04) 0.5236	
	No	261/ 430 (60.7)	253/ 438 (57.8)	1.07 (0.96, 1.18) 0.2204	1.18 (0.89, 1.55) 0.2436	0.04 (-0.02, 0.10) 0.2239	
	Diuretics at baseline						0.3963
	Yes	1365/2350 (58.1)	1320/2345 (56.3)	1.03 (0.98, 1.08) 0.2373	1.09 (0.96, 1.22) 0.1746	0.02 (-0.01, 0.05) 0.1740	
	No	163/ 275 (59.3)	170/ 280 (60.7)	0.97 (0.85, 1.10) 0.6043	0.91 (0.64, 1.28) 0.5764	-0.02 (-0.10, 0.06) 0.5893	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)							
	Overall	893/2801 (31.9)	831/2805 (29.6)	1.08 (0.99, 1.16)*0.0674	1.11 (0.99, 1.25) 0.0853	0.02 (-0.00, 0.04) 0.1056	
	Age						0.7737*
	<= median	466/1394 (33.4)	451/1471 (30.7)	1.09 (0.98, 1.21)*0.1123	1.13 (0.96, 1.33) 0.1456	0.02 (-0.01, 0.05) 0.2220	
	> median	427/1407 (30.3)	380/1334 (28.5)	1.07 (0.95, 1.20)*0.2853	1.10 (0.93, 1.31) 0.2647	0.02 (-0.01, 0.05) 0.1670	
	Gender						0.0547*
	Male	482/1630 (29.6)	473/1608 (29.4)	1.01 (0.90, 1.12)*0.9229	1.00 (0.85, 1.16) 0.9562	-0.00 (-0.03, 0.03) 0.9620	
	Female	411/1171 (35.1)	358/1197 (29.9)	1.17 (1.04, 1.32)*0.0071	1.30 (1.08, 1.56) 0.0060	0.05 (0.01, 0.09)*0.0069	
	Race						0.8113*
	White	632/2006 (31.5)	601/2032 (29.6)	1.07 (0.97, 1.17)*0.1835	1.09 (0.95, 1.25) 0.2383	0.01 (-0.01, 0.04) 0.3965	
	Black or African	30/ 64 (46.9)	26/ 70 (37.1)	1.08 (0.72, 1.62) 0.7260	1.50 (0.71, 3.17) 0.2827	0.05 (-0.11, 0.21) 0.5137	
	Asian	142/ 555 (25.6)	136/ 551 (24.7)	1.04 (0.86, 1.26) 0.7078	1.05 (0.80, 1.39) 0.7282	0.02 (-0.03, 0.06) 0.5369	
	Other	89/ 176 (50.6)	68/ 152 (44.7)	1.13 (0.90, 1.42)*0.2949	1.42 (0.86, 2.32) 0.1672	0.06 (-0.05, 0.17)*0.2908	
	Geographic region						0.3658*
	Asia	134/ 536 (25.0)	129/ 536 (24.1)	1.04 (0.85, 1.26) 0.7296	1.05 (0.79, 1.40) 0.7298	0.02 (-0.03, 0.07) 0.5111	
	Europe and Saudi Arabia	409/1341 (30.5)	403/1381 (29.2)	1.05 (0.93, 1.17)*0.4525	1.08 (0.91, 1.29) 0.3897	0.01 (-0.02, 0.05)*0.4525	
	North America	107/ 393 (27.2)	104/ 376 (27.7)	0.98 (0.78, 1.24)*0.8930	0.90 (0.65, 1.26) 0.5538	-0.01 (-0.07, 0.04) 0.6177	
	Latin America	243/ 531 (45.8)	195/ 512 (38.1)	1.20 (1.04, 1.39)*0.0125	1.45 (1.11, 1.90) 0.0062	0.06 (0.00, 0.11) 0.0399	
	NYHA class at enrolment						0.1320*
	II	639/2083 (30.7)	641/2165 (29.6)	1.04 (0.95, 1.14)*0.4476	1.06 (0.92, 1.21) 0.4176	0.01 (-0.01, 0.04) 0.2821	
	III or IV	254/ 718 (35.4)	190/ 639 (29.7)	1.19 (1.02, 1.39)*0.0279	1.28 (1.00, 1.65) 0.0520	0.06 (0.01, 0.11)*0.0264	
	LVEF at enrolment						0.4517*
	<= 49	294/ 959 (30.7)	282/ 950 (29.7)	1.03 (0.90, 1.18)*0.6434	1.06 (0.86, 1.29) 0.6037	0.00 (-0.04, 0.04) 0.9454	
	50-59	331/1017 (32.5)	285/1009 (28.2)	1.15 (1.01, 1.32)*0.0357	1.23 (1.01, 1.50) 0.0424	0.04 (0.00, 0.07) 0.0492	
	>= 60	268/ 825 (32.5)	264/ 846 (31.2)	1.04 (0.90, 1.20)*0.5747	1.05 (0.85, 1.31) 0.6397	0.02 (-0.02, 0.05) 0.4338	
	NT-proBNP at enrolment						0.1007*
	<= median	429/1396 (30.7)	430/1409 (30.5)	1.01 (0.90, 1.13)*0.9028	1.01 (0.86, 1.20) 0.8706	0.01 (-0.02, 0.04) 0.7127	
	> median	464/1405 (33.0)	401/1395 (28.7)	1.15 (1.03, 1.28)*0.0145	1.22 (1.03, 1.44) 0.0242	0.03 (-0.00, 0.06) 0.0717	
	Type 2 Diabetes Medical History						0.5679*
	Yes	366/1231 (29.7)	353/1243 (28.4)	1.04 (0.96, 1.13) 0.3465	1.07 (0.90, 1.27)*0.4654	0.01 (-0.02, 0.04) 0.4147	
	No	527/1570 (33.6)	478/1562 (30.6)	1.10 (0.99, 1.21)*0.0758	1.15 (0.99, 1.33)*0.0756	0.02 (-0.01, 0.05) 0.1350	
	Atrial fibrillation or flutter at enrolment ECG						0.8291*
	Yes	359/1185 (30.3)	338/1188 (28.5)	1.06 (0.94, 1.21)*0.3242	1.10 (0.91, 1.32) 0.3320	0.01 (-0.02, 0.05) 0.3899	
	No	534/1616 (33.0)	493/1617 (30.5)	1.08 (0.98, 1.20)*0.1188	1.12 (0.96, 1.31) 0.1601	0.02 (-0.01, 0.05) 0.1614	
	BMI (kg/m2) at enrolment						0.2835*
	< 30	483/1547 (31.2)	429/1541 (27.8)	1.12 (1.01, 1.25)*0.0396	1.17 (0.99, 1.37) 0.0582	0.03 (-0.00, 0.06) 0.0793	
	>= 30	410/1253 (32.7)	401/1261 (31.8)	1.03 (0.92, 1.15)*0.6213	1.05 (0.88, 1.26) 0.5939	0.01 (-0.03, 0.05)*0.6212	
	Baseline eGFR (mL/min/1.73m^2)						0.3045*
	< 60	399/1338 (29.8)	399/1377 (29.0)	1.03 (0.92, 1.16)*0.6291	1.05 (0.88, 1.25) 0.5687	0.01 (-0.02, 0.04) 0.5762	
	>= 60	494/1463 (33.8)	431/1427 (30.2)	1.12 (1.00, 1.24)*0.0404	1.16 (0.99, 1.37) 0.0688	0.03 (-0.00, 0.06) 0.0773	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)	SBP at randomisation						0.3038*
	<= median	432/1405 (30.7)	423/1420 (29.8)	1.03 (0.92, 1.15)*0.5793	1.03 (0.87, 1.22) 0.7261	0.00 (-0.03, 0.03) 0.7870	
	> median	461/1396 (33.0)	408/1385 (29.5)	1.12 (1.00, 1.25)*0.0429	1.20 (1.02, 1.43) 0.0322	0.03 (0.00, 0.06) 0.0319	
	LVEF at enrolment 2						0.4672*
	<= 49	294/ 959 (30.7)	282/ 950 (29.7)	1.03 (0.90, 1.18)*0.6434	1.06 (0.86, 1.29) 0.6037	0.00 (-0.04, 0.04) 0.9454	
	>= 50	599/1842 (32.5)	549/1855 (29.6)	1.10 (1.00, 1.21)*0.0550	1.15 (0.99, 1.33) 0.0708	0.03 (0.00, 0.05) 0.0400	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3304*
	Yes	86/ 280 (30.7)	90/ 281 (32.0)	0.96 (0.75, 1.23)*0.7374	0.97 (0.66, 1.42) 0.8591	-0.02 (-0.08, 0.05) 0.5934	
	No	807/2521 (32.0)	741/2524 (29.4)	1.09 (1.00, 1.18)*0.0412	1.12 (0.99, 1.27) 0.0689	0.02 (0.00, 0.05) 0.0457	
	MRAs at baseline						0.1750*
	Yes	391/1216 (32.2)	384/1210 (31.7)	1.01 (0.90, 1.14)*0.8248	1.04 (0.87, 1.25) 0.6502	0.01 (-0.02, 0.04) 0.5753	
	No	502/1585 (31.7)	447/1595 (28.0)	1.13 (1.02, 1.26)*0.0248	1.17 (0.99, 1.37) 0.0630	0.02 (-0.01, 0.05) 0.1402	
	ACEi+ARB at baseline						0.6218*
	Yes	666/2037 (32.7)	618/2059 (30.0)	1.09 (0.99, 1.19)*0.0646	1.15 (1.00, 1.32) 0.0518	0.02 (-0.00, 0.05) 0.0790	
	No	227/ 764 (29.7)	213/ 746 (28.6)	1.04 (0.89, 1.22)*0.6201	1.02 (0.81, 1.29) 0.8482	0.01 (-0.04, 0.05) 0.7590	
	ARNI at baseline						0.6342*
	Yes	46/ 149 (30.9)	39/ 125 (31.2)	1.05 (0.75, 1.48) 0.7692	1.12 (0.66, 1.91) 0.6755	0.03 (-0.08, 0.13) 0.6160	
	No	847/2652 (31.9)	792/2680 (29.6)	1.08 (1.00, 1.17)*0.0592	1.11 (0.98, 1.26) 0.0887	0.02 (-0.01, 0.04) 0.1316	
	Beta Blocker at baseline						0.9032*
	Yes	740/2327 (31.8)	687/2330 (29.5)	1.08 (0.99, 1.18)*0.0867	1.09 (0.96, 1.25) 0.1785	0.02 (-0.01, 0.04) 0.1555	
	No	153/ 474 (32.3)	144/ 475 (30.3)	1.06 (0.88, 1.29)*0.5146	1.23 (0.92, 1.66) 0.1669	0.02 (-0.04, 0.08)*0.5143	
	Diuretics at baseline						0.7560*
	Yes	784/2500 (31.4)	733/2504 (29.3)	1.07 (0.98, 1.17)*0.1085	1.10 (0.97, 1.25) 0.1282	0.02 (-0.00, 0.04) 0.1077	
	No	109/ 301 (36.2)	98/ 301 (32.6)	1.11 (0.89, 1.39)*0.3458	1.16 (0.82, 1.66) 0.4045	0.03 (-0.04, 0.10) 0.3871	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	1686/2801 (60.2)	1543/2805 (55.0)	1.09 (1.05, 1.14)*<.0001	1.24 (1.11, 1.39) 0.0001	0.05 (0.03, 0.08)*<.0001	
	Age						0.3542*
	<= median	867/1394 (62.2)	851/1471 (57.9)	1.08 (1.01, 1.14)*0.0177	1.23 (1.05, 1.43) 0.0099	0.04 (0.01, 0.08)*0.0175	
	> median	819/1407 (58.2)	692/1334 (51.9)	1.12 (1.05, 1.20)*0.0009	1.28 (1.09, 1.49) 0.0026	0.06 (0.03, 0.10)*0.0008	
	Gender						0.5058*
	Male	995/1630 (61.0)	909/1608 (56.5)	1.08 (1.02, 1.14)*0.0092	1.21 (1.05, 1.40) 0.0097	0.05 (0.01, 0.08)*0.0090	
	Female	691/1171 (59.0)	634/1197 (53.0)	1.11 (1.04, 1.20)*0.0031	1.28 (1.08, 1.52) 0.0043	0.06 (0.02, 0.10)*0.0030	
	Race						0.2675*
	White	1198/2006 (59.7)	1089/2032 (53.6)	1.11 (1.06, 1.18)*<.0001	1.28 (1.12, 1.46) 0.0003	0.06 (0.03, 0.09)*<.0001	
	Black or African	42/ 64 (65.6)	42/ 70 (60.0)	1.12 (0.88, 1.43) 0.3578	1.33 (0.65, 2.72) 0.4371	0.07 (-0.09, 0.23) 0.3952	
	Asian	318/ 555 (57.3)	316/ 551 (57.4)	1.00 (0.90, 1.11)*0.9858	1.02 (0.80, 1.30) 0.8925	0.00 (-0.05, 0.06) 0.8644	
	Other	128/ 176 (72.7)	96/ 152 (63.2)	1.15 (0.99, 1.34)*0.0678	1.52 (0.93, 2.49) 0.0929	0.10 (-0.01, 0.20)*0.0634	
	Geographic region						0.2863*
	Asia	308/ 536 (57.5)	307/ 536 (57.3)	1.00 (0.90, 1.11)*0.9508	1.02 (0.80, 1.31) 0.8624	0.01 (-0.05, 0.06) 0.8357	
	Europe and Saudi Arabia	794/1341 (59.2)	733/1381 (53.1)	1.12 (1.04, 1.19)*0.0013	1.27 (1.08, 1.50) 0.0036	0.06 (0.02, 0.10)*0.0012	
	North America	216/ 393 (55.0)	191/ 376 (50.8)	1.08 (0.95, 1.24)*0.2485	1.20 (0.89, 1.60) 0.2276	0.05 (-0.02, 0.11) 0.1872	
	Latin America	368/ 531 (69.3)	312/ 512 (60.9)	1.14 (1.04, 1.24)*0.0049	1.49 (1.14, 1.95) 0.0036	0.08 (0.03, 0.14)*0.0045	
	NYHA class at enrolment						0.7198*
	II	1246/2083 (59.8)	1190/2165 (55.0)	1.09 (1.03, 1.15)*0.0014	1.25 (1.10, 1.42) 0.0005	0.05 (0.02, 0.08)*0.0014	
	III or IV	440/ 718 (61.3)	353/ 639 (55.2)	1.11 (1.01, 1.21)*0.0252	1.26 (1.00, 1.59) 0.0480	0.06 (0.01, 0.11)*0.0242	
	LVEF at enrolment						0.3301*
	<= 49	570/ 959 (59.4)	521/ 950 (54.8)	1.08 (1.00, 1.17)*0.0429	1.25 (1.03, 1.51) 0.0228	0.05 (0.00, 0.09)*0.0423	
	50-59	613/1017 (60.3)	574/1009 (56.9)	1.06 (0.98, 1.14)*0.1220	1.16 (0.96, 1.39) 0.1228	0.03 (-0.01, 0.08)*0.1215	
	>= 60	503/ 825 (61.0)	448/ 846 (53.0)	1.15 (1.06, 1.25)*0.0010	1.35 (1.11, 1.66) 0.0031	0.07 (0.02, 0.11) 0.0027	
	NT-proBNP at enrolment						0.8462*
	<= median	830/1396 (59.5)	762/1409 (54.1)	1.10 (1.03, 1.17)*0.0041	1.27 (1.08, 1.48) 0.0028	0.05 (0.02, 0.09) 0.0040	
	> median	856/1405 (60.9)	780/1395 (55.9)	1.09 (1.02, 1.16)*0.0072	1.22 (1.04, 1.43) 0.0140	0.05 (0.01, 0.09)*0.0071	
	Type 2 Diabetes Medical History						0.0333*
	Yes	756/1231 (61.4)	660/1243 (53.1)	1.16 (1.08, 1.24)*<.0001	1.41 (1.20, 1.65)*<.0001	0.08 (0.04, 0.12)*<.0001	
	No	930/1570 (59.2)	883/1562 (56.5)	1.05 (0.99, 1.11)*0.1254	1.12 (0.97, 1.29)*0.1252	0.03 (-0.01, 0.06)*0.1251	
	Atrial fibrillation or flutter at enrolment ECG						0.8560*
	Yes	718/1185 (60.6)	661/1188 (55.6)	1.09 (1.02, 1.17)*0.0147	1.24 (1.05, 1.47) 0.0128	0.05 (0.01, 0.09)*0.0144	
	No	968/1616 (59.9)	882/1617 (54.5)	1.10 (1.03, 1.17)*0.0021	1.25 (1.08, 1.44) 0.0030	0.05 (0.02, 0.09)*0.0021	
	BMI (kg/m2) at enrolment						0.4200*
	< 30	922/1547 (59.6)	853/1541 (55.4)	1.08 (1.01, 1.14)*0.0172	1.20 (1.03, 1.39) 0.0181	0.04 (0.01, 0.08)*0.0169	
	>= 30	764/1253 (61.0)	688/1261 (54.6)	1.12 (1.05, 1.20)*0.0012	1.31 (1.11, 1.55) 0.0014	0.06 (0.03, 0.10)*0.0011	
	Baseline eGFR (mL/min/1.73m^2)						0.3210*
	< 60	778/1338 (58.1)	715/1377 (51.9)	1.12 (1.05, 1.20)*0.0011	1.30 (1.11, 1.52) 0.0012	0.06 (0.02, 0.10)*0.0011	
	>= 60	908/1463 (62.1)	828/1427 (58.0)	1.07 (1.01, 1.14)*0.0269	1.19 (1.02, 1.39) 0.0296	0.04 (0.00, 0.08)*0.0265	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.9708*
	<= median	843/1405 (60.0)	778/1420 (54.8)	1.10 (1.03, 1.17)*0.0052	1.21 (1.03, 1.41) 0.0176	0.05 (0.02, 0.09)*0.0050	
	> median	843/1396 (60.4)	765/1385 (55.2)	1.09 (1.03, 1.17)*0.0060	1.28 (1.10, 1.50) 0.0019	0.05 (0.01, 0.09)*0.0059	
	LVEF at enrolment 2						0.7648*
	<= 49	570/ 959 (59.4)	521/ 950 (54.8)	1.08 (1.00, 1.17)*0.0429	1.25 (1.03, 1.51) 0.0228	0.05 (0.00, 0.09)*0.0423	
	>= 50	1116/1842 (60.6)	1022/1855 (55.1)	1.10 (1.04, 1.16)*0.0007	1.24 (1.08, 1.42) 0.0018	0.05 (0.02, 0.09)*0.0007	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1534*
	Yes	179/ 280 (63.9)	179/ 281 (63.7)	1.00 (0.89, 1.14)*0.9553	1.13 (0.78, 1.65) 0.5233	0.00 (-0.08, 0.08)*0.9553	
	No	1507/2521 (59.8)	1364/2524 (54.0)	1.11 (1.05, 1.16)*<.0001	1.26 (1.12, 1.42) <.0001	0.06 (0.03, 0.08)*<.0001	
	MRAs at baseline						0.2736*
	Yes	737/1216 (60.6)	651/1210 (53.8)	1.13 (1.05, 1.21)*0.0007	1.33 (1.12, 1.57) 0.0009	0.07 (0.03, 0.11)*0.0007	
	No	949/1585 (59.9)	892/1595 (55.9)	1.07 (1.01, 1.14)*0.0242	1.18 (1.02, 1.37) 0.0251	0.04 (0.01, 0.07)*0.0240	
	ACEi+ARB at baseline						0.0880*
	Yes	1245/2037 (61.1)	1123/2059 (54.5)	1.12 (1.06, 1.18)*<.0001	1.31 (1.15, 1.50) <.0001	0.07 (0.04, 0.10)*<.0001	
	No	441/ 764 (57.7)	420/ 746 (56.3)	1.03 (0.94, 1.12)*0.5769	1.08 (0.87, 1.33) 0.4909	0.02 (-0.03, 0.07) 0.3769	
	ARNI at baseline						0.0226*
	Yes	77/ 149 (51.7)	75/ 125 (60.0)	0.89 (0.72, 1.09) 0.2547	0.73 (0.45, 1.20) 0.2194	-0.07 (-0.19, 0.05) 0.2342	
	No	1609/2652 (60.7)	1468/2680 (54.8)	1.11 (1.06, 1.16)*<.0001	1.27 (1.14, 1.43) <.0001	0.06 (0.03, 0.09)*<.0001	
	Beta Blocker at baseline						0.2897*
	Yes	1390/2327 (59.7)	1286/2330 (55.2)	1.08 (1.03, 1.14)*0.0018	1.19 (1.05, 1.34) 0.0047	0.05 (0.02, 0.07)*0.0017	
	No	296/ 474 (62.4)	257/ 475 (54.1)	1.15 (1.04, 1.29)*0.0095	1.55 (1.18, 2.03) 0.0018	0.08 (0.02, 0.15)*0.0089	
	Diuretics at baseline						0.4849*
	Yes	1496/2500 (59.8)	1377/2504 (55.0)	1.09 (1.04, 1.14)*0.0005	1.24 (1.10, 1.40) 0.0003	0.05 (0.02, 0.08)*0.0005	
	No	190/ 301 (63.1)	166/ 301 (55.1)	1.14 (1.00, 1.31)*0.0475	1.29 (0.92, 1.81) 0.1365	0.06 (-0.02, 0.13) 0.1263	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	1436/2801 (51.3)	1310/2805 (46.7)	1.10 (1.04, 1.16)*0.0006	1.21 (1.08, 1.36) 0.0012	0.05 (0.02, 0.07)*0.0006	
	Age						0.1912*
	<= median	722/1394 (51.8)	717/1471 (48.7)	1.06 (0.99, 1.14)*0.1025	1.18 (1.00, 1.39) 0.0472	0.03 (-0.01, 0.07)*0.1024	
	> median	714/1407 (50.7)	593/1334 (44.5)	1.14 (1.05, 1.24)*0.0010	1.26 (1.07, 1.49) 0.0060	0.06 (0.03, 0.10)*0.0010	
	Gender						0.2700*
	Male	798/1630 (49.0)	736/1608 (45.8)	1.07 (0.99, 1.15)*0.0697	1.14 (0.98, 1.34) 0.0928	0.03 (-0.00, 0.07)*0.0693	
	Female	638/1171 (54.5)	574/1197 (48.0)	1.14 (1.05, 1.23)*0.0015	1.30 (1.09, 1.55) 0.0036	0.07 (0.03, 0.11)*0.0014	
	Race						0.8160*
	White	1059/2006 (52.8)	971/2032 (47.8)	1.10 (1.04, 1.17)*0.0015	1.21 (1.05, 1.39) 0.0070	0.05 (0.02, 0.08)*0.0014	
	Black or African	37/ 64 (57.8)	37/ 70 (52.9)	1.09 (0.81, 1.48)*0.5641	1.28 (0.63, 2.60) 0.4891	0.07 (-0.10, 0.23) 0.4130	
	Asian	223/ 555 (40.2)	214/ 551 (38.8)	1.03 (0.89, 1.20)*0.6482	1.11 (0.84, 1.46) 0.4632	0.01 (-0.04, 0.07)*0.6481	
	Other	117/ 176 (66.5)	88/ 152 (57.9)	1.15 (0.97, 1.36)*0.1140	1.47 (0.90, 2.43) 0.1264	0.09 (-0.02, 0.19)*0.1091	
	Geographic region						0.3035*
	Asia	213/ 536 (39.7)	206/ 536 (38.4)	1.03 (0.89, 1.20)*0.6613	1.09 (0.82, 1.45) 0.5410	0.01 (-0.05, 0.07)*0.6612	
	Europe and Saudi Arabia	710/1341 (52.9)	652/1381 (47.2)	1.12 (1.04, 1.21)*0.0028	1.25 (1.06, 1.48) 0.0096	0.06 (0.02, 0.09)*0.0027	
	North America	181/ 393 (46.1)	175/ 376 (46.5)	0.99 (0.85, 1.15)*0.8924	0.95 (0.71, 1.29) 0.7540	-0.01 (-0.08, 0.06) 0.7710	
	Latin America	332/ 531 (62.5)	277/ 512 (54.1)	1.16 (1.04, 1.28)*0.0061	1.54 (1.17, 2.03) 0.0023	0.08 (0.02, 0.14)*0.0057	
	NYHA class at enrolment						0.6055*
	II	1022/2083 (49.1)	965/2165 (44.6)	1.10 (1.03, 1.17)*0.0034	1.27 (1.10, 1.45) 0.0007	0.04 (0.01, 0.07)*0.0033	
	III or IV	414/ 718 (57.7)	345/ 639 (54.0)	1.07 (0.97, 1.17)*0.1755	1.12 (0.88, 1.41) 0.3578	0.04 (-0.02, 0.09)*0.1740	
	LVEF at enrolment						0.1017*
	<= 49	474/ 959 (49.4)	442/ 950 (46.5)	1.06 (0.97, 1.17)*0.2051	1.21 (0.99, 1.48) 0.0669	0.03 (-0.02, 0.07)*0.2045	
	50-59	513/1017 (50.4)	484/1009 (48.0)	1.05 (0.96, 1.15)*0.2656	1.08 (0.89, 1.32) 0.4387	0.02 (-0.02, 0.07)*0.2652	
	>= 60	449/ 825 (54.4)	384/ 846 (45.4)	1.20 (1.09, 1.32)*0.0002	1.40 (1.13, 1.73) 0.0017	0.09 (0.04, 0.14)*0.0002	
	NT-proBNP at enrolment						0.9349*
	<= median	700/1396 (50.1)	642/1409 (45.6)	1.10 (1.02, 1.19)*0.0153	1.25 (1.06, 1.47) 0.0085	0.05 (0.01, 0.08)*0.0151	
	> median	736/1405 (52.4)	667/1395 (47.8)	1.10 (1.02, 1.18)*0.0157	1.18 (1.00, 1.39) 0.0513	0.05 (0.01, 0.08)*0.0155	
	Type 2 Diabetes Medical History						0.0542*
	Yes	656/1231 (53.3)	569/1243 (45.8)	1.16 (1.07, 1.26)*0.0002	1.35 (1.15, 1.58)*0.0002	0.08 (0.04, 0.11)*0.0002	
	No	780/1570 (49.7)	741/1562 (47.4)	1.05 (0.97, 1.13)*0.2095	1.09 (0.95, 1.26)*0.2094	0.02 (-0.01, 0.06)*0.2092	
	Atrial fibrillation or flutter at enrolment ECG						0.9667*
	Yes	614/1185 (51.8)	560/1188 (47.1)	1.10 (1.01, 1.19)*0.0229	1.24 (1.04, 1.48) 0.0189	0.05 (0.01, 0.09)*0.0226	
	No	822/1616 (50.9)	750/1617 (46.4)	1.10 (1.02, 1.18)*0.0109	1.19 (1.02, 1.39) 0.0250	0.04 (0.01, 0.08)*0.0107	
	BMI (kg/m2) at enrolment						0.8152*
	< 30	746/1547 (48.2)	672/1541 (43.6)	1.11 (1.02, 1.19)*0.0102	1.23 (1.05, 1.44) 0.0110	0.05 (0.01, 0.08)*0.0100	
	>= 30	690/1253 (55.1)	636/1261 (50.4)	1.09 (1.01, 1.18)*0.0202	1.20 (1.01, 1.43) 0.0392	0.05 (0.01, 0.09)*0.0199	
	Baseline eGFR (mL/min/1.73m^2)						0.5714*
	< 60	677/1338 (50.6)	625/1377 (45.4)	1.11 (1.03, 1.21)*0.0067	1.25 (1.06, 1.47) 0.0089	0.05 (0.01, 0.09)*0.0065	
	>= 60	759/1463 (51.9)	685/1427 (48.0)	1.08 (1.00, 1.16)*0.0374	1.18 (1.00, 1.39) 0.0562	0.04 (0.00, 0.08)*0.0370	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.0949*
	<= median	720/1405 (51.2)	633/1420 (44.6)	1.15 (1.06, 1.24)*0.0004	1.26 (1.07, 1.48) 0.0062	0.07 (0.03, 0.10)*0.0004	
	> median	716/1396 (51.3)	677/1385 (48.9)	1.05 (0.97, 1.13)*0.2043	1.17 (0.99, 1.38) 0.0676	0.02 (-0.01, 0.06)*0.2039	
	LVEF at enrolment 2						0.3961*
	<= 49	474/ 959 (49.4)	442/ 950 (46.5)	1.06 (0.97, 1.17)*0.2051	1.21 (0.99, 1.48) 0.0669	0.03 (-0.02, 0.07)*0.2045	
	>= 50	962/1842 (52.2)	868/1855 (46.8)	1.12 (1.05, 1.19)*0.0010	1.22 (1.05, 1.40) 0.0077	0.05 (0.02, 0.09)*0.0009	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9919*
	Yes	176/ 280 (62.9)	161/ 281 (57.3)	1.10 (0.96, 1.26)*0.1795	1.41 (0.97, 2.05) 0.0687	0.06 (-0.03, 0.14)*0.1779	
	No	1260/2521 (50.0)	1149/2524 (45.5)	1.10 (1.04, 1.16)*0.0016	1.19 (1.05, 1.35) 0.0057	0.04 (0.02, 0.07)*0.0015	
	MRAs at baseline						0.4727*
	Yes	623/1216 (51.2)	552/1210 (45.6)	1.12 (1.03, 1.22)*0.0058	1.28 (1.07, 1.53) 0.0072	0.06 (0.02, 0.10)*0.0056	
	No	813/1585 (51.3)	758/1595 (47.5)	1.08 (1.01, 1.16)*0.0336	1.17 (1.00, 1.36) 0.0503	0.04 (0.00, 0.07)*0.0334	
	ACEi+ARB at baseline						0.0154*
	Yes	1075/2037 (52.8)	951/2059 (46.2)	1.14 (1.07, 1.22)*<.0001	1.32 (1.15, 1.52) <.0001	0.07 (0.04, 0.10)*<.0001	
	No	361/ 764 (47.3)	359/ 746 (48.1)	0.98 (0.88, 1.09)*0.7345	0.97 (0.78, 1.21) 0.7725	-0.01 (-0.06, 0.04)*0.7345	
	ARNI at baseline						0.3229*
	Yes	63/ 149 (42.3)	55/ 125 (44.0)	0.96 (0.73, 1.26)*0.7746	1.11 (0.64, 1.93) 0.7020	-0.02 (-0.13, 0.10)*0.7749	
	No	1373/2652 (51.8)	1255/2680 (46.8)	1.11 (1.05, 1.17)*0.0003	1.22 (1.08, 1.37) 0.0012	0.05 (0.02, 0.08)*0.0003	
	Beta Blocker at baseline						0.7339*
	Yes	1200/2327 (51.6)	1090/2330 (46.8)	1.10 (1.04, 1.17)*0.0011	1.20 (1.05, 1.36) 0.0062	0.05 (0.02, 0.08)*0.0011	
	No	236/ 474 (49.8)	220/ 475 (46.3)	1.07 (0.94, 1.23)*0.2846	1.29 (0.97, 1.71) 0.0832	0.03 (-0.03, 0.10)*0.2840	
	Diuretics at baseline						0.4446*
	Yes	1284/2500 (51.4)	1180/2504 (47.1)	1.09 (1.03, 1.15)*0.0028	1.21 (1.07, 1.37) 0.0024	0.04 (0.01, 0.07)*0.0027	
	No	152/ 301 (50.5)	130/ 301 (43.2)	1.17 (0.99, 1.39)*0.0734	1.21 (0.84, 1.76) 0.3089	0.07 (-0.01, 0.15)*0.0716	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	1462/2801 (52.2)	1363/2805 (48.6)	1.07 (1.02, 1.13)*0.0070	1.15 (1.03, 1.29) 0.0171	0.04 (0.01, 0.06)*0.0069	
	Age						0.1294*
	<= median	749/1394 (53.7)	762/1471 (51.8)	1.04 (0.97, 1.11)*0.3012	1.10 (0.94, 1.30) 0.2276	0.02 (-0.02, 0.06)*0.3012	
	> median	713/1407 (50.7)	601/1334 (45.1)	1.12 (1.04, 1.22)*0.0033	1.22 (1.03, 1.44) 0.0192	0.06 (0.02, 0.09)*0.0032	
	Gender						0.0867*
	Male	823/1630 (50.5)	786/1608 (48.9)	1.03 (0.96, 1.11)*0.3597	1.05 (0.90, 1.22) 0.5393	0.02 (-0.02, 0.05)*0.3595	
	Female	639/1171 (54.6)	577/1197 (48.2)	1.13 (1.05, 1.22)*0.0020	1.29 (1.08, 1.53) 0.0047	0.06 (0.02, 0.10)*0.0019	
	Race						0.2744*
	White	1079/2006 (53.8)	988/2032 (48.6)	1.11 (1.04, 1.18)*0.0010	1.21 (1.05, 1.38) 0.0063	0.05 (0.02, 0.08)*0.0010	
	Black or African	37/ 64 (57.8)	38/ 70 (54.3)	1.18 (0.88, 1.58) 0.2796	1.19 (0.59, 2.42) 0.6245	0.06 (-0.11, 0.22) 0.4995	
	Asian	236/ 555 (42.5)	242/ 551 (43.9)	0.97 (0.85, 1.11)*0.6390	0.97 (0.74, 1.25) 0.7905	-0.01 (-0.07, 0.04)*0.6389	
	Other	110/ 176 (62.5)	95/ 152 (62.5)	1.00 (0.85, 1.18)*1.0000	1.03 (0.62, 1.68) 0.9211	0.00 (-0.11, 0.11)*1.0000	
	Geographic region						0.2065*
	Asia	229/ 536 (42.7)	235/ 536 (43.8)	0.97 (0.85, 1.12)*0.7115	0.97 (0.74, 1.26) 0.8067	-0.01 (-0.07, 0.05)*0.7115	
	Europe and Saudi Arabia	725/1341 (54.1)	666/1381 (48.2)	1.12 (1.04, 1.21)*0.0023	1.24 (1.05, 1.47) 0.0118	0.06 (0.02, 0.10)*0.0023	
	North America	183/ 393 (46.6)	177/ 376 (47.1)	1.01 (0.88, 1.15) 0.9104	0.97 (0.72, 1.30) 0.8329	-0.01 (-0.08, 0.06) 0.7395	
	Latin America	325/ 531 (61.2)	285/ 512 (55.7)	1.10 (0.99, 1.22)*0.0703	1.31 (1.00, 1.72) 0.0521	0.06 (-0.00, 0.12)*0.0691	
	NYHA class at enrolment						0.3377*
	II	1039/2083 (49.9)	1025/2165 (47.3)	1.05 (0.99, 1.12)*0.0983	1.14 (1.00, 1.30) 0.0565	0.03 (-0.00, 0.06)*0.0982	
	III or IV	423/ 718 (58.9)	338/ 639 (52.9)	1.11 (1.01, 1.23)*0.0267	1.24 (0.98, 1.57) 0.0676	0.06 (0.01, 0.11)*0.0256	
	LVEF at enrolment						0.0202*
	<= 49	496/ 959 (51.7)	478/ 950 (50.3)	1.03 (0.94, 1.12)*0.5394	1.11 (0.91, 1.35) 0.2971	0.01 (-0.03, 0.06)*0.5393	
	50-59	519/1017 (51.0)	505/1009 (50.0)	1.02 (0.94, 1.11)*0.6582	0.99 (0.82, 1.20) 0.9296	0.01 (-0.03, 0.05)*0.6582	
	>= 60	447/ 825 (54.2)	380/ 846 (44.9)	1.21 (1.09, 1.33)*0.0002	1.43 (1.16, 1.76) 0.0009	0.09 (0.04, 0.14)*0.0001	
	NT-proBNP at enrolment						0.4552*
	<= median	703/1396 (50.4)	674/1409 (47.8)	1.05 (0.98, 1.14)*0.1816	1.12 (0.95, 1.31) 0.1805	0.03 (-0.01, 0.06)*0.1813	
	> median	759/1405 (54.0)	688/1395 (49.3)	1.10 (1.02, 1.18)*0.0129	1.19 (1.01, 1.40) 0.0416	0.05 (0.01, 0.08)*0.0127	
	Type 2 Diabetes Medical History						0.0947*
	Yes	664/1231 (53.9)	594/1243 (47.8)	1.13 (1.04, 1.22)*0.0023	1.28 (1.09, 1.50)*0.0022	0.06 (0.02, 0.10)*0.0022	
	No	798/1570 (50.8)	769/1562 (49.2)	1.03 (0.96, 1.11)*0.3718	1.07 (0.93, 1.23)*0.3717	0.02 (-0.02, 0.05)*0.3716	
	Atrial fibrillation or flutter at enrolment ECG						0.2561*
	Yes	640/1185 (54.0)	577/1188 (48.6)	1.11 (1.03, 1.20)*0.0082	1.27 (1.06, 1.51) 0.0089	0.05 (0.01, 0.09)*0.0079	
	No	822/1616 (50.9)	786/1617 (48.6)	1.05 (0.98, 1.12)*0.1994	1.07 (0.92, 1.25) 0.3629	0.02 (-0.01, 0.06)*0.1991	
	BMI (kg/m2) at enrolment						0.2022*
	< 30	766/1547 (49.5)	732/1541 (47.5)	1.04 (0.97, 1.12)*0.2631	1.06 (0.91, 1.24) 0.4618	0.02 (-0.02, 0.06)*0.2629	
	>= 30	696/1253 (55.5)	628/1261 (49.8)	1.12 (1.04, 1.20)*0.0040	1.27 (1.07, 1.51) 0.0055	0.06 (0.02, 0.10)*0.0039	
	Baseline eGFR (mL/min/1.73m^2)						0.3669*
	< 60	693/1338 (51.8)	648/1377 (47.1)	1.10 (1.02, 1.19)*0.0137	1.22 (1.03, 1.43) 0.0194	0.05 (0.01, 0.08)*0.0135	
	>= 60	769/1463 (52.6)	715/1427 (50.1)	1.05 (0.98, 1.13)*0.1865	1.08 (0.92, 1.28) 0.3257	0.02 (-0.01, 0.06)*0.1861	

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AstraZeneca
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.1592*
	<= median	751/1405 (53.5)	681/1420 (48.0)	1.11 (1.04, 1.20)*0.0036	1.19 (1.01, 1.40) 0.0342	0.05 (0.02, 0.09)*0.0034	
	> median	711/1396 (50.9)	682/1385 (49.2)	1.03 (0.96, 1.11)*0.3731	1.11 (0.94, 1.31) 0.2024	0.02 (-0.02, 0.05)*0.3729	
	LVEF at enrolment 2						0.2280*
	<= 49	496/ 959 (51.7)	478/ 950 (50.3)	1.03 (0.94, 1.12)*0.5394	1.11 (0.91, 1.35) 0.2971	0.01 (-0.03, 0.06)*0.5393	
	>= 50	966/1842 (52.4)	885/1855 (47.7)	1.10 (1.03, 1.17)*0.0040	1.17 (1.02, 1.35) 0.0283	0.05 (0.02, 0.08)*0.0040	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8675*
	Yes	179/ 280 (63.9)	169/ 281 (60.1)	1.06 (0.93, 1.21)*0.3559	1.24 (0.85, 1.80) 0.2661	0.04 (-0.04, 0.12)*0.3551	
	No	1283/2521 (50.9)	1194/2524 (47.3)	1.08 (1.02, 1.14)*0.0109	1.14 (1.01, 1.29) 0.0324	0.04 (0.01, 0.06)*0.0108	
	MRAs at baseline						0.4739*
	Yes	641/1216 (52.7)	581/1210 (48.0)	1.10 (1.01, 1.19)*0.0209	1.22 (1.02, 1.45) 0.0272	0.05 (0.01, 0.09)*0.0205	
	No	821/1585 (51.8)	782/1595 (49.0)	1.06 (0.99, 1.13)*0.1184	1.10 (0.95, 1.28) 0.2116	0.03 (-0.01, 0.06)*0.1181	
	ACEi+ARB at baseline						0.2037*
	Yes	1076/2037 (52.8)	992/2059 (48.2)	1.10 (1.03, 1.17)*0.0030	1.20 (1.05, 1.38) 0.0079	0.05 (0.02, 0.08)*0.0029	
	No	386/ 764 (50.5)	371/ 746 (49.7)	1.02 (0.92, 1.12)*0.7584	1.03 (0.82, 1.28) 0.8208	0.01 (-0.04, 0.06)*0.7584	
	ARNI at baseline						0.0515*
	Yes	63/ 149 (42.3)	63/ 125 (50.4)	0.84 (0.65, 1.08)*0.1784	0.70 (0.42, 1.18) 0.1812	-0.08 (-0.20, 0.04)*0.1783	
	No	1399/2652 (52.8)	1300/2680 (48.5)	1.09 (1.03, 1.15)*0.0020	1.18 (1.05, 1.33) 0.0065	0.04 (0.02, 0.07)*0.0019	
	Beta Blocker at baseline						0.4897*
	Yes	1218/2327 (52.3)	1126/2330 (48.3)	1.08 (1.02, 1.15)*0.0062	1.15 (1.01, 1.30) 0.0339	0.04 (0.01, 0.07)*0.0061	
	No	244/ 474 (51.5)	237/ 475 (49.9)	1.03 (0.91, 1.17)*0.6260	1.16 (0.88, 1.54) 0.2861	0.02 (-0.05, 0.08)*0.6259	
	Diuretics at baseline						0.8044*
	Yes	1306/2500 (52.2)	1215/2504 (48.5)	1.08 (1.02, 1.14)*0.0086	1.17 (1.04, 1.33) 0.0096	0.04 (0.01, 0.06)*0.0085	
	No	156/ 301 (51.8)	148/ 301 (49.2)	1.05 (0.90, 1.23)*0.5145	0.96 (0.67, 1.37) 0.8076	0.03 (-0.05, 0.11)*0.5142	

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AstraZeneca
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Physical Limitation (LOCF)							
	Overall	1275/2750 (46.4)	1150/2758 (41.7)	1.06 (1.01, 1.11) 0.0147	1.20 (1.07, 1.35) 0.0024	0.03 (0.01, 0.06) 0.0039	
	Age						0.0650
	<= median	634/1382 (45.9)	631/1456 (43.3)	1.05 (0.99, 1.11) 0.0800	1.13 (0.96, 1.33) 0.1447	0.02 (-0.01, 0.05) 0.1253	
	> median	641/1368 (46.9)	519/1302 (39.9)	1.09 (1.02, 1.18) 0.0179	1.30 (1.10, 1.53) 0.0022	0.05 (0.02, 0.08) 0.0043	
	Gender						0.1843*
	Male	695/1611 (43.1)	636/1583 (40.2)	1.07 (0.99, 1.17)*0.0896	1.12 (0.96, 1.31) 0.1468	0.03 (-0.00, 0.06)*0.0892	
	Female	580/1139 (50.9)	514/1175 (43.7)	1.10 (1.02, 1.18) 0.0145	1.30 (1.09, 1.55) 0.0033	0.05 (0.01, 0.09) 0.0106	
	Race						0.7096*
	White	948/1970 (48.1)	851/1998 (42.6)	1.06 (1.00, 1.12) 0.0349	1.24 (1.08, 1.42) 0.0023	0.04 (0.01, 0.07) 0.0053	
	Black or African	27/ 63 (42.9)	29/ 66 (43.9)	1.03 (0.70, 1.52) 0.8828	0.97 (0.47, 2.00) 0.9243	-0.00 (-0.17, 0.16) 0.9830	
	Asian	201/ 548 (36.7)	193/ 546 (35.3)	1.04 (0.89, 1.22)*0.6467	0.98 (0.75, 1.30) 0.9100	0.01 (-0.04, 0.07)*0.6466	
	Other	99/ 169 (58.6)	77/ 148 (52.0)	1.13 (0.92, 1.38)*0.2451	1.44 (0.89, 2.33) 0.1365	0.07 (-0.04, 0.18)*0.2409	
	Geographic region						0.6864*
	Asia	194/ 530 (36.6)	187/ 531 (35.2)	1.04 (0.88, 1.22)*0.6377	0.99 (0.75, 1.31) 0.9377	0.01 (-0.04, 0.07)*0.6377	
	Europe and Saudi Arabia	631/1323 (47.7)	570/1360 (41.9)	1.05 (0.99, 1.13) 0.1125	1.27 (1.07, 1.50) 0.0057	0.04 (0.01, 0.07) 0.0152	
	North America	160/ 386 (41.5)	142/ 362 (39.2)	1.04 (0.89, 1.22) 0.5848	1.04 (0.76, 1.41) 0.8215	0.01 (-0.05, 0.08) 0.7432	
	Latin America	290/ 511 (56.8)	251/ 505 (49.7)	1.14 (1.02, 1.28)*0.0249	1.40 (1.07, 1.84) 0.0141	0.07 (0.01, 0.13)*0.0240	
	NYHA class at enrolment						0.0426
	II	901/2046 (44.0)	865/2136 (40.5)	1.02 (0.98, 1.06) 0.4283	1.17 (1.02, 1.34) 0.0224	0.02 (-0.01, 0.04) 0.1210	
	III or IV	374/ 704 (53.1)	285/ 621 (45.9)	1.13 (1.03, 1.25) 0.0086	1.32 (1.05, 1.66) 0.0198	0.06 (0.01, 0.11) 0.0116	
	LVEF at enrolment						0.0255*
	<= 49	424/ 944 (44.9)	418/ 939 (44.5)	1.02 (0.95, 1.10) 0.5502	1.06 (0.87, 1.29) 0.5562	0.01 (-0.03, 0.05) 0.5715	
	50-59	454/1001 (45.4)	401/ 988 (40.6)	1.12 (1.01, 1.24)*0.0321	1.17 (0.96, 1.42) 0.1188	0.03 (-0.01, 0.06) 0.1686	
	>= 60	397/ 805 (49.3)	331/ 831 (39.8)	1.24 (1.11, 1.38)*0.0001	1.42 (1.15, 1.77) 0.0014	0.09 (0.05, 0.14)*0.0001	
	NT-proBNP at enrolment						0.7537*
	<= median	633/1371 (46.2)	571/1389 (41.1)	1.12 (1.03, 1.22)*0.0074	1.25 (1.06, 1.47) 0.0082	0.03 (0.00, 0.07) 0.0486	
	> median	642/1379 (46.6)	578/1368 (42.3)	1.10 (1.01, 1.20)*0.0234	1.15 (0.98, 1.36) 0.0949	0.04 (0.01, 0.07) 0.0229	
	Type 2 Diabetes Medical History						0.9645*
	Yes	559/1213 (46.1)	506/1219 (41.5)	1.11 (1.01, 1.22)*0.0232	1.20 (1.03, 1.41)*0.0230	0.04 (0.01, 0.08) 0.0233	
	No	716/1537 (46.6)	644/1539 (41.8)	1.03 (0.97, 1.09) 0.3167	1.21 (1.05, 1.40)*0.0082	0.03 (-0.00, 0.06) 0.0852	
	Atrial fibrillation or flutter at enrolment ECG						0.8378
	Yes	535/1164 (46.0)	488/1164 (41.9)	1.05 (0.98, 1.12) 0.1804	1.18 (0.99, 1.42) 0.0662	0.03 (-0.00, 0.07) 0.0669	
	No	740/1586 (46.7)	662/1594 (41.5)	1.07 (1.00, 1.13) 0.0409	1.21 (1.04, 1.41) 0.0144	0.03 (0.00, 0.06) 0.0256	
	BMI (kg/m2) at enrolment						0.5114*
	< 30	677/1520 (44.5)	596/1517 (39.3)	1.13 (1.04, 1.23)*0.0034	1.25 (1.07, 1.46) 0.0060	0.05 (0.02, 0.09)*0.0033	
	>= 30	598/1229 (48.7)	553/1238 (44.7)	1.03 (0.97, 1.11) 0.3199	1.14 (0.96, 1.35) 0.1383	0.02 (-0.01, 0.06) 0.1657	
	Baseline eGFR (mL/min/1.73m^2)						0.0202
	< 60	604/1307 (46.2)	564/1345 (41.9)	1.09 (1.02, 1.16) 0.0135	1.19 (1.01, 1.41) 0.0382	0.04 (0.00, 0.07) 0.0276	
	>= 60	671/1443 (46.5)	586/1412 (41.5)	1.12 (1.03, 1.22)*0.0073	1.20 (1.02, 1.41) 0.0325	0.02 (-0.01, 0.05) 0.1670	

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Physical Limitation (LOCF)	SBP at randomisation						0.2328
	<= median	640/1376 (46.5)	563/1395 (40.4)	1.15 (1.06, 1.26)*0.0011	1.20 (1.02, 1.42) 0.0285	0.04 (0.01, 0.07) 0.0215	
	> median	635/1374 (46.2)	587/1363 (43.1)	1.04 (0.97, 1.11) 0.2805	1.19 (1.01, 1.40) 0.0393	0.03 (-0.01, 0.06) 0.1073	
	LVEF at enrolment 2						0.1651
	<= 49	424/ 944 (44.9)	418/ 939 (44.5)	1.02 (0.95, 1.10) 0.5502	1.06 (0.87, 1.29) 0.5562	0.01 (-0.03, 0.05) 0.5715	
	>= 50	851/1806 (47.1)	732/1819 (40.2)	1.17 (1.09, 1.26)*<.0001	1.28 (1.10, 1.47) 0.0010	0.04 (0.01, 0.07) 0.0029	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3947*
	Yes	149/ 270 (55.2)	126/ 272 (46.3)	1.19 (1.01, 1.41)*0.0400	1.63 (1.10, 2.40) 0.0139	0.09 (0.00, 0.17)*0.0383	
	No	1126/2480 (45.4)	1024/2486 (41.2)	1.06 (1.01, 1.11) 0.0286	1.16 (1.03, 1.32) 0.0146	0.03 (0.00, 0.05) 0.0212	
	MRAs at baseline						0.8824*
	Yes	549/1191 (46.1)	492/1193 (41.2)	1.05 (0.98, 1.13) 0.1513	1.23 (1.03, 1.47) 0.0208	0.03 (-0.00, 0.07) 0.0541	
	No	726/1559 (46.6)	658/1565 (42.0)	1.11 (1.02, 1.20)*0.0110	1.17 (1.01, 1.37) 0.0427	0.04 (0.01, 0.07) 0.0172	
	ACEi+ARB at baseline						0.2160
	Yes	942/1999 (47.1)	840/2028 (41.4)	1.14 (1.06, 1.22)*0.0003	1.25 (1.09, 1.44) 0.0013	0.04 (0.02, 0.07) 0.0013	
	No	333/ 751 (44.3)	310/ 730 (42.5)	0.98 (0.90, 1.08) 0.7461	1.07 (0.85, 1.33) 0.5782	0.01 (-0.04, 0.05) 0.7694	
	ARNI at baseline						0.4477
	Yes	61/ 147 (41.5)	52/ 122 (42.6)	1.13 (0.89, 1.43) 0.3100	1.02 (0.60, 1.75) 0.9384	0.03 (-0.09, 0.14) 0.6553	
	No	1214/2603 (46.6)	1098/2636 (41.7)	1.05 (1.01, 1.10) 0.0248	1.21 (1.07, 1.36) 0.0020	0.03 (0.01, 0.06) 0.0047	
	Beta Blocker at baseline						0.3068
	Yes	1059/2289 (46.3)	962/2293 (42.0)	1.05 (1.00, 1.10) 0.0735	1.17 (1.03, 1.32) 0.0186	0.03 (0.00, 0.05) 0.0264	
	No	216/ 461 (46.9)	188/ 465 (40.4)	1.12 (1.00, 1.25) 0.0486	1.39 (1.04, 1.85) 0.0263	0.06 (0.01, 0.12) 0.0318	
	Diuretics at baseline						0.6269
	Yes	1153/2458 (46.9)	1028/2463 (41.7)	1.06 (1.01, 1.12) 0.0127	1.23 (1.09, 1.39) 0.0010	0.04 (0.01, 0.06) 0.0015	
	No	122/ 292 (41.8)	122/ 295 (41.4)	1.02 (0.87, 1.19) 0.8060	0.96 (0.67, 1.38) 0.8146	-0.01 (-0.08, 0.06) 0.7753	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	1536/2801 (54.8)	1443/2805 (51.4)	1.02 (0.99, 1.05) 0.1345	1.12 (1.00, 1.26) 0.0533	0.02 (-0.00, 0.03) 0.0762	
	Age						0.0619*
	<= median	781/1394 (56.0)	806/1471 (54.8)	1.02 (0.98, 1.06) 0.2611	1.03 (0.88, 1.22) 0.6763	0.01 (-0.01, 0.04) 0.3320	
	> median	755/1407 (53.7)	637/1334 (47.8)	1.12 (1.04, 1.21)*0.0021	1.23 (1.04, 1.45) 0.0170	0.06 (0.02, 0.10)*0.0019	
	Gender						0.1360*
	Male	878/1630 (53.9)	839/1608 (52.2)	1.03 (0.97, 1.10)*0.3359	1.03 (0.88, 1.20) 0.7157	0.02 (-0.02, 0.05)*0.3357	
	Female	658/1171 (56.2)	604/1197 (50.5)	1.03 (0.98, 1.08) 0.3003	1.25 (1.05, 1.50) 0.0137	0.03 (-0.01, 0.06) 0.1230	
	Race						0.0873*
	White	1113/2006 (55.5)	1042/2032 (51.3)	1.08 (1.02, 1.15)*0.0075	1.15 (1.00, 1.32) 0.0465	0.04 (0.01, 0.07)*0.0074	
	Black or African	45/ 64 (70.3)	35/ 70 (50.0)	1.41 (1.06, 1.87)*0.0183	2.51 (1.17, 5.42) 0.0186	0.20 (0.04, 0.37)*0.0140	
	Asian	258/ 555 (46.5)	262/ 551 (47.5)	0.98 (0.86, 1.11)*0.7231	0.94 (0.73, 1.23) 0.6681	-0.01 (-0.07, 0.05)*0.7231	
	Other	120/ 176 (68.2)	104/ 152 (68.4)	1.00 (0.86, 1.16)*0.9630	1.03 (0.61, 1.71) 0.9235	-0.00 (-0.10, 0.10)*0.9630	
	Geographic region						0.4906*
	Asia	251/ 536 (46.8)	256/ 536 (47.8)	0.98 (0.86, 1.11)*0.7597	0.94 (0.73, 1.23) 0.6720	-0.01 (-0.07, 0.05)*0.7597	
	Europe and Saudi Arabia	736/1341 (54.9)	709/1381 (51.3)	1.07 (1.00, 1.15)*0.0640	1.11 (0.94, 1.31) 0.2306	0.04 (-0.00, 0.07)*0.0637	
	North America	221/ 393 (56.2)	190/ 376 (50.5)	1.11 (0.97, 1.27)*0.1143	1.26 (0.92, 1.71) 0.1452	0.07 (0.01, 0.13) 0.0311	
	Latin America	328/ 531 (61.8)	288/ 512 (56.3)	1.01 (0.94, 1.09) 0.7981	1.28 (0.96, 1.69) 0.0884	0.06 (-0.00, 0.11)*0.0696	
	NYHA class at enrolment						0.0457*
	II	1094/2083 (52.5)	1102/2165 (50.9)	1.03 (0.97, 1.09)*0.2909	1.07 (0.93, 1.22) 0.3384	0.02 (-0.01, 0.05)*0.2909	
	III or IV	442/ 718 (61.6)	341/ 639 (53.4)	1.15 (1.05, 1.27)*0.0025	1.36 (1.08, 1.72) 0.0094	0.07 (0.02, 0.11) 0.0035	
	LVEF at enrolment						0.6670*
	<= 49	526/ 959 (54.8)	502/ 950 (52.8)	1.04 (0.96, 1.13)*0.3794	1.09 (0.90, 1.33) 0.3760	0.02 (-0.02, 0.06)*0.3791	
	50-59	561/1017 (55.2)	522/1009 (51.7)	1.07 (0.98, 1.16)*0.1223	1.12 (0.92, 1.36) 0.2559	0.03 (-0.01, 0.08)*0.1217	
	>= 60	449/ 825 (54.4)	419/ 846 (49.5)	1.10 (1.00, 1.21)*0.0454	1.16 (0.94, 1.44) 0.1746	0.05 (0.00, 0.10)*0.0449	
	NT-proBNP at enrolment						<.0001
	<= median	748/1396 (53.6)	738/1409 (52.4)	1.02 (0.95, 1.10)*0.5229	1.01 (0.85, 1.18) 0.9485	0.01 (-0.02, 0.05)*0.5229	
	> median	788/1405 (56.1)	704/1395 (50.5)	1.11 (1.04, 1.19)*0.0029	1.26 (1.06, 1.48) 0.0069	0.06 (0.02, 0.09)*0.0028	
	Type 2 Diabetes Medical History						0.0058
	Yes	703/1231 (57.1)	600/1243 (48.3)	1.10 (1.03, 1.17) 0.0055	1.43 (1.22, 1.67)*<.0001	0.06 (0.03, 0.10) 0.0003	
	No	833/1570 (53.1)	843/1562 (54.0)	1.00 (0.98, 1.03) 0.7566	0.96 (0.84, 1.11)*0.6089	-0.01 (-0.04, 0.03)*0.6089	
	Atrial fibrillation or flutter at enrolment ECG						<.0001
	Yes	665/1185 (56.1)	582/1188 (49.0)	1.15 (1.06, 1.24)*0.0005	1.34 (1.12, 1.61) 0.0013	0.07 (0.03, 0.11)*0.0005	
	No	871/1616 (53.9)	861/1617 (53.2)	1.01 (0.95, 1.08)*0.7102	0.99 (0.85, 1.15) 0.8484	0.01 (-0.01, 0.04) 0.3403	
	BMI (kg/m2) at enrolment						0.1120*
	< 30	815/1547 (52.7)	789/1541 (51.2)	1.03 (0.96, 1.10)*0.4099	0.99 (0.85, 1.16) 0.9154	0.01 (-0.02, 0.05)*0.4098	
	>= 30	721/1253 (57.5)	651/1261 (51.6)	1.11 (1.04, 1.20)*0.0030	1.30 (1.09, 1.54) 0.0030	0.06 (0.02, 0.10)*0.0028	
	Baseline eGFR (mL/min/1.73m^2)						0.3913
	< 60	723/1338 (54.0)	697/1377 (50.6)	1.07 (0.99, 1.15)*0.0747	1.14 (0.96, 1.34) 0.1266	0.03 (-0.00, 0.07)*0.0744	
	>= 60	813/1463 (55.6)	746/1427 (52.3)	1.06 (0.99, 1.14)*0.0761	1.10 (0.94, 1.30) 0.2471	0.03 (-0.00, 0.07)*0.0756	

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AstraZeneca
Protocol: D169CC00001
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.6435
	<= median	791/1405 (56.3)	740/1420 (52.1)	1.08 (1.01, 1.16)*0.0257	1.13 (0.96, 1.33) 0.1571	0.04 (0.01, 0.08)*0.0254	
	> median	745/1396 (53.4)	703/1385 (50.8)	1.05 (0.98, 1.13)*0.1688	1.12 (0.95, 1.32) 0.1893	0.03 (-0.01, 0.06)*0.1684	
	LVEF at enrolment 2						0.4412*
	<= 49	526/ 959 (54.8)	502/ 950 (52.8)	1.04 (0.96, 1.13)*0.3794	1.09 (0.90, 1.33) 0.3760	0.02 (-0.02, 0.06)*0.3791	
	>= 50	1010/1842 (54.8)	941/1855 (50.7)	1.08 (1.02, 1.15)*0.0125	1.14 (0.98, 1.31) 0.0809	0.04 (0.01, 0.07)*0.0124	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2543*
	Yes	173/ 280 (61.8)	175/ 281 (62.3)	0.99 (0.87, 1.13)*0.9045	0.85 (0.58, 1.26) 0.4191	-0.00 (-0.09, 0.08)*0.9045	
	No	1363/2521 (54.1)	1268/2524 (50.2)	1.03 (1.00, 1.06) 0.0980	1.15 (1.02, 1.30) 0.0248	0.02 (0.00, 0.04) 0.0480	
	MRAs at baseline						0.4835*
	Yes	668/1216 (54.9)	611/1210 (50.5)	1.09 (1.01, 1.17)*0.0288	1.19 (1.00, 1.42) 0.0552	0.03 (-0.01, 0.06) 0.1173	
	No	868/1585 (54.8)	832/1595 (52.2)	1.05 (0.98, 1.12)*0.1417	1.07 (0.92, 1.25) 0.3754	0.03 (-0.01, 0.06)*0.1414	
	ACEi+ARB at baseline						0.2554*
	Yes	1118/2037 (54.9)	1042/2059 (50.6)	1.08 (1.02, 1.15)*0.0062	1.19 (1.03, 1.36) 0.0146	0.04 (0.01, 0.07)*0.0061	
	No	418/ 764 (54.7)	401/ 746 (53.8)	1.02 (0.93, 1.12)*0.7086	0.98 (0.79, 1.22) 0.8496	0.00 (-0.04, 0.05) 0.8662	
	ARNI at baseline						0.4480
	Yes	72/ 149 (48.3)	63/ 125 (50.4)	0.96 (0.75, 1.22)*0.7315	0.74 (0.43, 1.25) 0.2555	-0.05 (-0.15, 0.06) 0.3749	
	No	1464/2652 (55.2)	1380/2680 (51.5)	1.02 (0.99, 1.05) 0.1184	1.15 (1.02, 1.29) 0.0236	0.04 (0.01, 0.06)*0.0066	
	Beta Blocker at baseline						0.1948*
	Yes	1276/2327 (54.8)	1181/2330 (50.7)	1.08 (1.02, 1.14)*0.0046	1.15 (1.01, 1.31) 0.0311	0.04 (0.01, 0.07)*0.0045	
	No	260/ 474 (54.9)	262/ 475 (55.2)	1.03 (0.95, 1.11) 0.4723	0.99 (0.74, 1.31) 0.9238	0.01 (-0.04, 0.05) 0.7502	
	Diuretics at baseline						0.3989*
	Yes	1383/2500 (55.3)	1290/2504 (51.5)	1.03 (1.00, 1.06) 0.0972	1.16 (1.03, 1.31) 0.0186	0.02 (0.00, 0.04) 0.0407	
	No	153/ 301 (50.8)	153/ 301 (50.8)	1.00 (0.85, 1.17)*1.0000	0.84 (0.58, 1.20) 0.3319	0.00 (-0.08, 0.08)*1.0000	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	1461/2801 (52.2)	1351/2805 (48.2)	1.08 (1.03, 1.14)*0.0028	1.20 (1.06, 1.35) 0.0036	0.04 (0.01, 0.07)*0.0028	
	Age						0.3748*
	<= median	744/1394 (53.4)	740/1471 (50.3)	1.06 (0.99, 1.14)*0.1006	1.20 (1.01, 1.43) 0.0333	0.03 (-0.01, 0.07)*0.1005	
	> median	717/1407 (51.0)	611/1334 (45.8)	1.11 (1.03, 1.20)*0.0071	1.20 (1.01, 1.43) 0.0352	0.05 (0.01, 0.09)*0.0068	
	Gender						0.4789*
	Male	831/1630 (51.0)	744/1608 (46.3)	1.10 (1.03, 1.18)*0.0074	1.25 (1.06, 1.47) 0.0089	0.05 (0.01, 0.08)*0.0072	
	Female	630/1171 (53.8)	607/1197 (50.7)	1.06 (0.98, 1.15)*0.1324	1.13 (0.95, 1.36) 0.1761	0.03 (-0.01, 0.07)*0.1321	
	Race						0.9299*
	White	1089/2006 (54.3)	1019/2032 (50.1)	1.08 (1.02, 1.15)*0.0085	1.17 (1.02, 1.35) 0.0276	0.04 (0.01, 0.07)*0.0084	
	Black or African	38/ 64 (59.4)	38/ 70 (54.3)	1.09 (0.81, 1.47)*0.5522	1.31 (0.62, 2.77) 0.4831	0.05 (-0.12, 0.22)*0.5518	
	Asian	223/ 555 (40.2)	210/ 551 (38.1)	1.05 (0.91, 1.22)*0.4814	1.22 (0.91, 1.63) 0.1879	0.02 (-0.04, 0.08)*0.4811	
	Other	111/ 176 (63.1)	84/ 152 (55.3)	1.14 (0.95, 1.37)*0.1555	1.37 (0.84, 2.26) 0.2109	0.08 (-0.03, 0.18)*0.1507	
	Geographic region						0.8805*
	Asia	213/ 536 (39.7)	202/ 536 (37.7)	1.05 (0.91, 1.23)*0.4905	1.20 (0.89, 1.62) 0.2375	0.02 (-0.04, 0.08)*0.4903	
	Europe and Saudi Arabia	742/1341 (55.3)	704/1381 (51.0)	1.09 (1.01, 1.16)*0.0229	1.18 (0.99, 1.40) 0.0686	0.04 (0.01, 0.08)*0.0227	
	North America	191/ 393 (48.6)	174/ 376 (46.3)	1.05 (0.90, 1.22)*0.5192	1.07 (0.79, 1.46) 0.6569	0.02 (-0.05, 0.09)*0.5187	
	Latin America	315/ 531 (59.3)	271/ 512 (52.9)	1.12 (1.01, 1.25)*0.0383	1.43 (1.07, 1.90) 0.0150	0.06 (0.00, 0.12)*0.0372	
	NYHA class at enrolment						0.7656*
	II	1025/2083 (49.2)	994/2165 (45.9)	1.07 (1.01, 1.14)*0.0316	1.21 (1.05, 1.40) 0.0077	0.03 (0.00, 0.06)*0.0315	
	III or IV	436/ 718 (60.7)	356/ 639 (55.7)	1.09 (1.00, 1.19)*0.0629	1.22 (0.96, 1.55) 0.1120	0.05 (-0.00, 0.10)*0.0615	
	LVEF at enrolment						0.0620*
	<= 49	489/ 959 (51.0)	473/ 950 (49.8)	1.02 (0.94, 1.12)*0.5998	1.10 (0.89, 1.35) 0.3973	0.01 (-0.03, 0.06)*0.5997	
	50-59	529/1017 (52.0)	497/1009 (49.3)	1.06 (0.97, 1.15)*0.2145	1.14 (0.93, 1.40) 0.2176	0.03 (-0.02, 0.07)*0.2141	
	>= 60	443/ 825 (53.7)	381/ 846 (45.0)	1.19 (1.08, 1.31)*0.0004	1.41 (1.13, 1.74) 0.0020	0.09 (0.04, 0.13)*0.0004	
	NT-proBNP at enrolment						0.2813*
	<= median	710/1396 (50.9)	681/1409 (48.3)	1.05 (0.98, 1.13)*0.1808	1.15 (0.97, 1.36) 0.1093	0.03 (-0.01, 0.06)*0.1806	
	> median	751/1405 (53.5)	669/1395 (48.0)	1.11 (1.04, 1.20)*0.0037	1.25 (1.05, 1.49) 0.0119	0.05 (0.02, 0.09)*0.0036	
	Type 2 Diabetes Medical History						0.1967*
	Yes	662/1231 (53.8)	594/1243 (47.8)	1.13 (1.04, 1.22)*0.0029	1.27 (1.09, 1.49)*0.0029	0.06 (0.02, 0.10)*0.0028	
	No	799/1570 (50.9)	757/1562 (48.5)	1.05 (0.98, 1.13)*0.1744	1.10 (0.96, 1.27)*0.1742	0.02 (-0.01, 0.06)*0.1740	
	Atrial fibrillation or flutter at enrolment ECG						0.5488*
	Yes	637/1185 (53.8)	579/1188 (48.7)	1.10 (1.02, 1.19)*0.0146	1.28 (1.06, 1.55) 0.0101	0.05 (0.01, 0.09)*0.0144	
	No	824/1616 (51.0)	772/1617 (47.7)	1.07 (1.00, 1.15)*0.0650	1.14 (0.97, 1.34) 0.1027	0.03 (-0.00, 0.07)*0.0647	
	BMI (kg/m2) at enrolment						0.8808*
	< 30	766/1547 (49.5)	707/1541 (45.9)	1.08 (1.00, 1.16)*0.0433	1.18 (1.00, 1.39) 0.0548	0.04 (0.00, 0.07)*0.0430	
	>= 30	694/1253 (55.4)	642/1261 (50.9)	1.09 (1.01, 1.17)*0.0247	1.22 (1.02, 1.46) 0.0276	0.04 (0.01, 0.08)*0.0244	
	Baseline eGFR (mL/min/1.73m^2)						0.5629*
	< 60	686/1338 (51.3)	642/1377 (46.6)	1.10 (1.02, 1.19)*0.0155	1.22 (1.03, 1.45) 0.0225	0.05 (0.01, 0.08)*0.0153	
	>= 60	775/1463 (53.0)	709/1427 (49.7)	1.07 (0.99, 1.14)*0.0773	1.17 (0.99, 1.39) 0.0712	0.03 (-0.00, 0.07)*0.0768	

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Symptom Burden (LOCF)	SBP at randomisation						0.1653*
	<= median	734/1405 (52.2)	660/1420 (46.5)	1.12 (1.04, 1.21)*0.0022	1.21 (1.02, 1.43) 0.0316	0.06 (0.02, 0.09)*0.0022	
	> median	727/1396 (52.1)	691/1385 (49.9)	1.04 (0.97, 1.12)*0.2492	1.19 (1.00, 1.42) 0.0484	0.02 (-0.02, 0.06)*0.2489	
	LVEF at enrolment 2						0.1303*
	<= 49	489/ 959 (51.0)	473/ 950 (49.8)	1.02 (0.94, 1.12)*0.5998	1.10 (0.89, 1.35) 0.3973	0.01 (-0.03, 0.06)*0.5997	
	>= 50	972/1842 (52.8)	878/1855 (47.3)	1.11 (1.05, 1.19)*0.0010	1.25 (1.08, 1.45) 0.0031	0.05 (0.02, 0.09)*0.0009	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1143*
	Yes	173/ 280 (61.8)	177/ 281 (63.0)	0.98 (0.86, 1.12)*0.7686	0.99 (0.67, 1.46) 0.9418	-0.01 (-0.09, 0.07)*0.7685	
	No	1288/2521 (51.1)	1174/2524 (46.5)	1.10 (1.04, 1.16)*0.0012	1.22 (1.08, 1.39) 0.0020	0.05 (0.02, 0.07)*0.0011	
	MRAs at baseline						0.8159*
	Yes	626/1216 (51.5)	571/1210 (47.2)	1.09 (1.01, 1.18)*0.0348	1.18 (0.98, 1.42) 0.0840	0.04 (0.00, 0.08)*0.0344	
	No	835/1585 (52.7)	780/1595 (48.9)	1.08 (1.01, 1.15)*0.0332	1.21 (1.03, 1.42) 0.0195	0.04 (0.00, 0.07)*0.0330	
	ACEi+ARB at baseline						0.7099*
	Yes	1088/2037 (53.4)	1009/2059 (49.0)	1.09 (1.03, 1.16)*0.0048	1.20 (1.04, 1.38) 0.0123	0.04 (0.01, 0.07)*0.0047	
	No	373/ 764 (48.8)	342/ 746 (45.8)	1.06 (0.96, 1.18)*0.2471	1.20 (0.95, 1.51) 0.1342	0.03 (-0.02, 0.08)*0.2464	
	ARNI at baseline						0.4580*
	Yes	58/ 149 (38.9)	50/ 125 (40.0)	0.97 (0.73, 1.31)*0.8561	1.04 (0.58, 1.86) 0.8969	-0.01 (-0.13, 0.11)*0.8563	
	No	1403/2652 (52.9)	1301/2680 (48.5)	1.09 (1.03, 1.15)*0.0015	1.20 (1.06, 1.36) 0.0035	0.04 (0.02, 0.07)*0.0014	
	Beta Blocker at baseline						0.9458*
	Yes	1221/2327 (52.5)	1128/2330 (48.4)	1.08 (1.02, 1.15)*0.0057	1.17 (1.02, 1.33) 0.0212	0.04 (0.01, 0.07)*0.0056	
	No	240/ 474 (50.6)	223/ 475 (46.9)	1.08 (0.95, 1.23)*0.2565	1.37 (1.01, 1.85) 0.0445	0.04 (-0.03, 0.10)*0.2558	
	Diuretics at baseline						0.1931*
	Yes	1311/2500 (52.4)	1227/2504 (49.0)	1.07 (1.01, 1.13)*0.0151	1.19 (1.05, 1.35) 0.0082	0.03 (0.01, 0.06)*0.0149	
	No	150/ 301 (49.8)	124/ 301 (41.2)	1.21 (1.01, 1.44)*0.0343	1.25 (0.85, 1.84) 0.2558	0.09 (0.01, 0.17)*0.0327	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	1216/2801 (43.4)	1194/2805 (42.6)	1.02 (0.96, 1.08)*0.5222	1.04 (0.91, 1.18) 0.5705	0.01 (-0.02, 0.03)*0.5222	
	Age						0.4958*
	<= median	625/1394 (44.8)	658/1471 (44.7)	1.00 (0.92, 1.09)*0.9556	1.01 (0.84, 1.21) 0.9106	0.00 (-0.04, 0.04)*0.9556	
	> median	591/1407 (42.0)	536/1334 (40.2)	1.05 (0.96, 1.14)*0.3323	1.08 (0.90, 1.31) 0.3904	0.02 (-0.02, 0.06)*0.3318	
	Gender						0.6342*
	Male	723/1630 (44.4)	691/1608 (43.0)	1.03 (0.95, 1.12)*0.4276	1.11 (0.93, 1.31) 0.2417	0.01 (-0.02, 0.05)*0.4275	
	Female	493/1171 (42.1)	503/1197 (42.0)	1.00 (0.91, 1.10)*0.9689	0.95 (0.78, 1.16) 0.5992	0.00 (-0.04, 0.04)*0.9689	
	Race						0.9052*
	White	863/2006 (43.0)	855/2032 (42.1)	1.02 (0.95, 1.10)*0.5440	1.01 (0.87, 1.18) 0.8496	0.01 (-0.02, 0.04)*0.5440	
	Black or African	23/ 64 (35.9)	29/ 70 (41.4)	0.87 (0.56, 1.33)*0.5166	0.84 (0.36, 1.95) 0.6795	-0.05 (-0.22, 0.11)*0.5135	
	Asian	237/ 555 (42.7)	232/ 551 (42.1)	1.01 (0.88, 1.16)*0.8407	1.13 (0.84, 1.51) 0.4173	0.01 (-0.05, 0.06)*0.8407	
	Other	93/ 176 (52.8)	78/ 152 (51.3)	1.03 (0.84, 1.27)*0.7830	1.12 (0.64, 1.96) 0.6886	0.02 (-0.09, 0.12)*0.7828	
	Geographic region						0.6729*
	Asia	228/ 536 (42.5)	227/ 536 (42.4)	1.00 (0.87, 1.15)*0.9507	1.13 (0.83, 1.52) 0.4374	0.00 (-0.06, 0.06)*0.9507	
	Europe and Saudi Arabia	603/1341 (45.0)	595/1381 (43.1)	1.04 (0.96, 1.14)*0.3228	1.09 (0.90, 1.30) 0.3819	0.02 (-0.02, 0.06)*0.3227	
	North America	142/ 393 (36.1)	147/ 376 (39.1)	0.92 (0.77, 1.11)*0.3964	0.89 (0.62, 1.27) 0.5109	-0.03 (-0.10, 0.04)*0.3963	
	Latin America	243/ 531 (45.8)	225/ 512 (43.9)	1.04 (0.91, 1.19)*0.5554	0.96 (0.71, 1.31) 0.8130	0.02 (-0.04, 0.08)*0.5551	
	NYHA class at enrolment						0.4190*
	II	892/2083 (42.8)	923/2165 (42.6)	1.00 (0.94, 1.08)*0.9004	1.00 (0.86, 1.16) 0.9749	0.00 (-0.03, 0.03)*0.9004	
	III or IV	324/ 718 (45.1)	271/ 639 (42.4)	1.06 (0.94, 1.20)*0.3153	1.18 (0.91, 1.53) 0.2018	0.03 (-0.03, 0.08)*0.3139	
	LVEF at enrolment						0.1043*
	<= 49	402/ 959 (41.9)	410/ 950 (43.2)	0.97 (0.88, 1.08)*0.5840	1.02 (0.81, 1.27) 0.8782	-0.01 (-0.06, 0.03)*0.5840	
	50-59	440/1017 (43.3)	444/1009 (44.0)	0.98 (0.89, 1.09)*0.7372	0.93 (0.75, 1.15) 0.4887	-0.01 (-0.05, 0.04)*0.7372	
	>= 60	374/ 825 (45.3)	340/ 846 (40.2)	1.13 (1.01, 1.26)*0.0338	1.23 (0.96, 1.57) 0.1011	0.05 (0.00, 0.10)*0.0334	
	NT-proBNP at enrolment						0.3585*
	<= median	595/1396 (42.6)	606/1409 (43.0)	0.99 (0.91, 1.08)*0.8357	0.94 (0.79, 1.13) 0.5308	-0.00 (-0.04, 0.03)*0.8357	
	> median	621/1405 (44.2)	588/1395 (42.2)	1.05 (0.96, 1.14)*0.2740	1.14 (0.95, 1.37) 0.1635	0.02 (-0.02, 0.06)*0.2737	
	Type 2 Diabetes Medical History						0.3597*
	Yes	533/1231 (43.3)	511/1243 (41.1)	1.05 (0.96, 1.16)*0.2707	1.09 (0.93, 1.28)*0.2706	0.02 (-0.02, 0.06)*0.2705	
	No	683/1570 (43.5)	683/1562 (43.7)	0.99 (0.92, 1.08)*0.9000	0.99 (0.86, 1.14)*0.9000	-0.00 (-0.04, 0.03)*0.9000	
	Atrial fibrillation or flutter at enrolment ECG						0.0008*
	Yes	537/1185 (45.3)	467/1188 (39.3)	1.15 (1.05, 1.27)*0.0031	1.33 (1.09, 1.62) 0.0055	0.06 (0.02, 0.10)*0.0030	
	No	679/1616 (42.0)	727/1617 (45.0)	0.93 (0.86, 1.01)*0.0917	0.87 (0.73, 1.03) 0.1043	-0.03 (-0.06, 0.00)*0.0914	
	BMI (kg/m2) at enrolment						0.4068*
	< 30	664/1547 (42.9)	663/1541 (43.0)	1.00 (0.92, 1.08)*0.9542	0.94 (0.79, 1.12) 0.4831	-0.00 (-0.04, 0.03)*0.9542	
	>= 30	551/1253 (44.0)	528/1261 (41.9)	1.05 (0.96, 1.15)*0.2869	1.17 (0.96, 1.41) 0.1139	0.02 (-0.02, 0.06)*0.2867	
	Baseline eGFR (mL/min/1.73m^2)						0.1275*
	< 60	549/1338 (41.0)	583/1377 (42.3)	0.97 (0.89, 1.06)*0.4900	0.98 (0.82, 1.18) 0.8338	-0.01 (-0.05, 0.02)*0.4898	
	>= 60	667/1463 (45.6)	611/1427 (42.8)	1.06 (0.98, 1.16)*0.1336	1.09 (0.91, 1.31) 0.3430	0.03 (-0.01, 0.06)*0.1331	

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Self Efficacy (LOCF)	SBP at randomisation						0.7681*
	<= median	605/1405 (43.1)	605/1420 (42.6)	1.01 (0.93, 1.10)*0.8070	1.02 (0.85, 1.23) 0.8204	0.00 (-0.03, 0.04)*0.8070	
	> median	611/1396 (43.8)	589/1385 (42.5)	1.03 (0.94, 1.12)*0.5089	1.06 (0.88, 1.26) 0.5470	0.01 (-0.02, 0.05)*0.5088	
	LVEF at enrolment 2						0.2583*
	<= 49	402/ 959 (41.9)	410/ 950 (43.2)	0.97 (0.88, 1.08)*0.5840	1.02 (0.81, 1.27) 0.8782	-0.01 (-0.06, 0.03)*0.5840	
	>= 50	814/1842 (44.2)	784/1855 (42.3)	1.05 (0.97, 1.13)*0.2371	1.05 (0.90, 1.23) 0.5490	0.02 (-0.01, 0.05)*0.2369	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4654*
	Yes	133/ 280 (47.5)	139/ 281 (49.5)	0.96 (0.81, 1.14)*0.6414	0.92 (0.62, 1.37) 0.6856	-0.02 (-0.10, 0.06)*0.6412	
	No	1083/2521 (43.0)	1055/2524 (41.8)	1.03 (0.96, 1.10)*0.4043	1.05 (0.92, 1.21) 0.4734	0.01 (-0.02, 0.04)*0.4043	
	MRAs at baseline						0.3379*
	Yes	506/1216 (41.6)	511/1210 (42.2)	0.99 (0.90, 1.08)*0.7572	1.00 (0.82, 1.22) 0.9995	-0.01 (-0.05, 0.03)*0.7571	
	No	710/1585 (44.8)	683/1595 (42.8)	1.05 (0.97, 1.13)*0.2621	1.07 (0.90, 1.27) 0.4724	0.02 (-0.01, 0.05)*0.2619	
	ACEi+ARB at baseline						0.7652*
	Yes	883/2037 (43.3)	880/2059 (42.7)	1.01 (0.95, 1.09)*0.6940	1.03 (0.88, 1.19) 0.7351	0.01 (-0.02, 0.04)*0.6939	
	No	333/ 764 (43.6)	314/ 746 (42.1)	1.04 (0.92, 1.16)*0.5573	1.07 (0.83, 1.37) 0.6182	0.01 (-0.03, 0.06)*0.5571	
	ARNI at baseline						0.2681*
	Yes	49/ 149 (32.9)	48/ 125 (38.4)	0.86 (0.62, 1.18)*0.3412	0.95 (0.52, 1.75) 0.8741	-0.06 (-0.17, 0.06)*0.3424	
	No	1167/2652 (44.0)	1146/2680 (42.8)	1.03 (0.97, 1.09)*0.3597	1.05 (0.92, 1.20) 0.4910	0.01 (-0.01, 0.04)*0.3597	
	Beta Blocker at baseline						0.4830*
	Yes	1003/2327 (43.1)	975/2330 (41.8)	1.03 (0.96, 1.10)*0.3855	1.07 (0.93, 1.24) 0.3173	0.01 (-0.02, 0.04)*0.3854	
	No	213/ 474 (44.9)	219/ 475 (46.1)	0.97 (0.85, 1.12)*0.7178	0.87 (0.63, 1.19) 0.3817	-0.01 (-0.08, 0.05)*0.7178	
	Diuretics at baseline						0.8410*
	Yes	1077/2500 (43.1)	1060/2504 (42.3)	1.02 (0.95, 1.09)*0.5929	1.04 (0.91, 1.20) 0.5475	0.01 (-0.02, 0.03)*0.5929	
	No	139/ 301 (46.2)	134/ 301 (44.5)	1.04 (0.87, 1.24)*0.6823	1.01 (0.68, 1.48) 0.9713	0.02 (-0.06, 0.10)*0.6822	

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Symptom Frequency (LOCF)							
	Overall	1371/2801 (48.9)	1313/2805 (46.8)	1.05 (0.99, 1.10)*0.1093	1.10 (0.97, 1.24) 0.1246	0.02 (-0.00, 0.05)*0.1091	
	Age						0.0226*
	<= median	681/1394 (48.9)	729/1471 (49.6)	0.99 (0.92, 1.06)*0.7057	0.99 (0.84, 1.17) 0.9224	-0.01 (-0.04, 0.03)*0.7056	
	> median	690/1407 (49.0)	584/1334 (43.8)	1.12 (1.03, 1.21)*0.0059	1.25 (1.04, 1.48) 0.0143	0.05 (0.02, 0.09)*0.0057	
	Gender						0.4741*
	Male	767/1630 (47.1)	736/1608 (45.8)	1.03 (0.95, 1.11)*0.4639	1.06 (0.90, 1.25) 0.4538	0.01 (-0.02, 0.05)*0.4638	
	Female	604/1171 (51.6)	577/1197 (48.2)	1.07 (0.99, 1.16)*0.1006	1.14 (0.95, 1.36) 0.1639	0.03 (-0.01, 0.07)*0.1002	
	Race						0.4347*
	White	1013/2006 (50.5)	963/2032 (47.4)	1.07 (1.00, 1.13)*0.0484	1.11 (0.96, 1.27) 0.1571	0.03 (0.00, 0.06)*0.0482	
	Black or African	36/ 64 (56.3)	38/ 70 (54.3)	1.04 (0.76, 1.41)*0.8192	1.16 (0.56, 2.40) 0.6842	0.02 (-0.15, 0.19)*0.8193	
	Asian	209/ 555 (37.7)	222/ 551 (40.3)	0.93 (0.81, 1.08)*0.3696	0.96 (0.72, 1.29) 0.8041	-0.03 (-0.08, 0.03)*0.3692	
	Other	113/ 176 (64.2)	90/ 152 (59.2)	1.08 (0.91, 1.29)*0.3561	1.38 (0.81, 2.35) 0.2341	0.05 (-0.06, 0.16)*0.3533	
	Geographic region						0.1460*
	Asia	200/ 536 (37.3)	214/ 536 (39.9)	0.93 (0.80, 1.09)*0.3801	0.94 (0.70, 1.27) 0.6966	-0.03 (-0.08, 0.03)*0.3796	
	Europe and Saudi Arabia	665/1341 (49.6)	637/1381 (46.1)	1.08 (0.99, 1.16)*0.0706	1.12 (0.94, 1.34) 0.1898	0.03 (-0.00, 0.07)*0.0703	
	North America	180/ 393 (45.8)	180/ 376 (47.9)	1.01 (0.90, 1.14) 0.8270	0.93 (0.69, 1.27) 0.6678	-0.01 (-0.07, 0.06) 0.8371	
	Latin America	326/ 531 (61.4)	282/ 512 (55.1)	1.11 (1.01, 1.24)*0.0394	1.41 (1.06, 1.87) 0.0188	0.06 (0.00, 0.12)*0.0383	
	NYHA class at enrolment						0.4169*
	II	961/2083 (46.1)	974/2165 (45.0)	1.03 (0.96, 1.10)*0.4530	1.10 (0.96, 1.27) 0.1761	0.01 (-0.02, 0.04)*0.4530	
	III or IV	410/ 718 (57.1)	339/ 639 (53.1)	1.08 (0.98, 1.19)*0.1356	1.15 (0.90, 1.45) 0.2590	0.03 (-0.01, 0.07) 0.1457	
	LVEF at enrolment						0.2940*
	<= 49	466/ 959 (48.6)	448/ 950 (47.2)	1.03 (0.94, 1.13)*0.5306	1.13 (0.92, 1.40) 0.2451	0.01 (-0.03, 0.06)*0.5304	
	50-59	482/1017 (47.4)	476/1009 (47.2)	1.00 (0.92, 1.10)*0.9214	0.99 (0.81, 1.21) 0.9227	0.00 (-0.04, 0.05)*0.9214	
	>= 60	423/ 825 (51.3)	389/ 846 (46.0)	1.12 (1.01, 1.23)*0.0307	1.21 (0.97, 1.50) 0.0917	0.05 (0.01, 0.10)*0.0303	
	NT-proBNP at enrolment						0.1358*
	<= median	643/1396 (46.1)	648/1409 (46.0)	1.00 (0.92, 1.09)*0.9703	1.01 (0.85, 1.19) 0.9447	0.00 (-0.04, 0.04)*0.9703	
	> median	728/1405 (51.8)	664/1395 (47.6)	1.09 (1.01, 1.17)*0.0259	1.21 (1.01, 1.43) 0.0334	0.04 (0.01, 0.08)*0.0255	
	Type 2 Diabetes Medical History						0.0842*
	Yes	624/1231 (50.7)	571/1243 (45.9)	1.10 (1.02, 1.20)*0.0182	1.21 (1.03, 1.42)*0.0180	0.05 (0.01, 0.09)*0.0179	
	No	747/1570 (47.6)	742/1562 (47.5)	1.00 (0.98, 1.02) 0.9721	1.00 (0.87, 1.15)*0.9658	0.00 (-0.03, 0.04)*0.9658	
	Atrial fibrillation or flutter at enrolment ECG						0.5717*
	Yes	600/1185 (50.6)	565/1188 (47.6)	1.06 (0.98, 1.16)*0.1344	1.19 (0.98, 1.43) 0.0727	0.03 (-0.01, 0.07)*0.1340	
	No	771/1616 (47.7)	748/1617 (46.3)	1.03 (0.96, 1.11)*0.4083	1.04 (0.89, 1.22) 0.6222	0.01 (-0.02, 0.05)*0.4082	
	BMI (kg/m2) at enrolment						0.3756*
	< 30	703/1547 (45.4)	685/1541 (44.5)	1.02 (0.95, 1.11)*0.5799	1.06 (0.89, 1.25) 0.5207	0.01 (-0.03, 0.04)*0.5798	
	>= 30	668/1253 (53.3)	626/1261 (49.6)	1.07 (1.00, 1.16)*0.0659	1.16 (0.98, 1.39) 0.0893	0.04 (-0.00, 0.08)*0.0655	
	Baseline eGFR (mL/min/1.73m^2)						0.0758*
	< 60	664/1338 (49.6)	621/1377 (45.1)	1.10 (1.02, 1.19)*0.0182	1.24 (1.04, 1.48) 0.0141	0.05 (0.01, 0.08)*0.0180	
	>= 60	707/1463 (48.3)	692/1427 (48.5)	1.00 (0.92, 1.07)*0.9280	0.97 (0.82, 1.16) 0.7601	-0.00 (-0.04, 0.03)*0.9280	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)	SBP at randomisation						0.5174*
	<= median	691/1405 (49.2)	656/1420 (46.2)	1.06 (0.99, 1.15)*0.1125	1.09 (0.92, 1.29) 0.3048	0.03 (-0.01, 0.07)*0.1122	
	> median	680/1396 (48.7)	657/1385 (47.4)	1.03 (0.95, 1.11)*0.5015	1.11 (0.93, 1.32) 0.2482	0.01 (-0.02, 0.05)*0.5014	
	LVEF at enrolment 2						0.7050*
	<= 49	466/ 959 (48.6)	448/ 950 (47.2)	1.03 (0.94, 1.13)*0.5306	1.13 (0.92, 1.40) 0.2451	0.01 (-0.03, 0.06)*0.5304	
	>= 50	905/1842 (49.1)	865/1855 (46.6)	1.05 (0.99, 1.13)*0.1282	1.08 (0.93, 1.26) 0.2915	0.03 (-0.01, 0.06)*0.1279	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7834*
	Yes	173/ 280 (61.8)	169/ 281 (60.1)	1.03 (0.90, 1.17)*0.6900	1.31 (0.89, 1.92) 0.1728	0.02 (-0.06, 0.10)*0.6899	
	No	1198/2521 (47.5)	1144/2524 (45.3)	1.05 (0.99, 1.11)*0.1180	1.08 (0.95, 1.22) 0.2536	0.02 (-0.01, 0.05)*0.1178	
	MRAs at baseline						0.2450*
	Yes	598/1216 (49.2)	548/1210 (45.3)	1.09 (1.00, 1.18)*0.0554	1.21 (1.00, 1.46) 0.0446	0.04 (-0.00, 0.08)*0.0549	
	No	773/1585 (48.8)	765/1595 (48.0)	1.02 (0.95, 1.09)*0.6487	1.02 (0.87, 1.20) 0.7655	0.01 (-0.03, 0.04)*0.6487	
	ACEi+ARB at baseline						0.1149*
	Yes	1021/2037 (50.1)	961/2059 (46.7)	1.07 (1.01, 1.14)*0.0273	1.15 (0.99, 1.32) 0.0587	0.03 (0.00, 0.07)*0.0271	
	No	350/ 764 (45.8)	352/ 746 (47.2)	0.97 (0.87, 1.08)*0.5926	0.98 (0.78, 1.23) 0.8620	-0.01 (-0.06, 0.04)*0.5926	
	ARNI at baseline						0.0969*
	Yes	60/ 149 (40.3)	60/ 125 (48.0)	0.84 (0.64, 1.10)*0.1981	0.90 (0.51, 1.57) 0.7103	-0.08 (-0.20, 0.04)*0.1982	
	No	1311/2652 (49.4)	1253/2680 (46.8)	1.06 (1.00, 1.12)*0.0502	1.11 (0.98, 1.26) 0.0998	0.03 (-0.00, 0.05)*0.0501	
	Beta Blocker at baseline						0.1840*
	Yes	1149/2327 (49.4)	1082/2330 (46.4)	1.06 (1.00, 1.13)*0.0448	1.11 (0.97, 1.27) 0.1185	0.03 (0.00, 0.06)*0.0446	
	No	222/ 474 (46.8)	231/ 475 (48.6)	0.96 (0.84, 1.10)*0.5797	1.05 (0.77, 1.42) 0.7638	-0.02 (-0.08, 0.05)*0.5796	
	Diuretics at baseline						0.1076*
	Yes	1217/2500 (48.7)	1184/2504 (47.3)	1.03 (0.97, 1.09)*0.3232	1.08 (0.95, 1.23) 0.2129	0.01 (-0.01, 0.04)*0.3231	
	No	154/ 301 (51.2)	129/ 301 (42.9)	1.19 (1.01, 1.42)*0.0422	1.21 (0.82, 1.78) 0.3330	0.08 (0.00, 0.16)*0.0405	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)							
	Overall	1230/2625 (46.9)	1224/2625 (46.6)	1.00 (0.96, 1.03) 0.8769	1.01 (0.89, 1.14) 0.9056	-0.00 (-0.02, 0.02) 0.7990	
	Age						0.9600
	<= median	638/1331 (47.9)	688/1409 (48.8)	1.00 (0.96, 1.04) 0.9928	0.99 (0.83, 1.17) 0.8656	-0.00 (-0.03, 0.02) 0.8129	
	> median	592/1294 (45.7)	536/1216 (44.1)	1.00 (0.95, 1.05) 0.9756	1.05 (0.87, 1.25) 0.6239	0.00 (-0.03, 0.03) 0.9381	
	Gender						0.5400
	Male	697/1538 (45.3)	699/1500 (46.6)	0.99 (0.95, 1.03) 0.5941	0.94 (0.80, 1.11) 0.4857	-0.01 (-0.05, 0.02)*0.4786	
	Female	533/1087 (49.0)	525/1125 (46.7)	1.01 (0.96, 1.07) 0.6807	1.09 (0.91, 1.32) 0.3565	0.01 (-0.03, 0.04) 0.6723	
	Race						0.6292
	White	923/1890 (48.8)	905/1921 (47.1)	0.99 (0.96, 1.03) 0.7820	1.05 (0.90, 1.21) 0.5489	-0.00 (-0.03, 0.02) 0.8783	
	Black or African	26/ 58 (44.8)	37/ 66 (56.1)	0.82 (0.60, 1.14) 0.2387	0.62 (0.28, 1.36) 0.2307	-0.09 (-0.25, 0.06) 0.2363	
	Asian	185/ 506 (36.6)	198/ 494 (40.1)	0.95 (0.85, 1.06) 0.3304	0.90 (0.67, 1.21) 0.4915	-0.02 (-0.07, 0.03) 0.4650	
	Other	96/ 171 (56.1)	84/ 144 (58.3)	0.96 (0.81, 1.15) 0.6888	1.02 (0.62, 1.69) 0.9244	-0.02 (-0.12, 0.08) 0.6670	
	Geographic region						0.3672*
	Asia	179/ 492 (36.4)	194/ 482 (40.2)	0.94 (0.84, 1.05) 0.2831	0.88 (0.65, 1.18) 0.3845	-0.02 (-0.07, 0.03) 0.3883	
	Europe and Saudi Arabia	622/1273 (48.9)	616/1309 (47.1)	1.04 (0.96, 1.13)*0.3594	1.02 (0.85, 1.22) 0.8425	0.02 (-0.02, 0.06)*0.3594	
	North America	168/ 367 (45.8)	167/ 347 (48.1)	0.96 (0.85, 1.09) 0.5670	0.96 (0.69, 1.32) 0.7901	-0.01 (-0.08, 0.05) 0.6775	
	Latin America	261/ 493 (52.9)	247/ 487 (50.7)	1.05 (0.96, 1.15) 0.3275	1.13 (0.85, 1.50) 0.4038	0.02 (-0.03, 0.08) 0.3405	
	NYHA class at enrolment						0.5817
	II	884/1953 (45.3)	919/2031 (45.2)	1.01 (0.98, 1.04) 0.5258	1.03 (0.89, 1.19) 0.6748	0.00 (-0.03, 0.03)*0.9924	
	III or IV	346/ 672 (51.5)	305/ 593 (51.4)	0.99 (0.91, 1.07) 0.7635	1.00 (0.78, 1.28) 0.9933	-0.01 (-0.05, 0.04) 0.8087	
	LVEF at enrolment						0.3997
	<= 49	421/ 907 (46.4)	448/ 896 (50.0)	0.97 (0.92, 1.03) 0.3597	0.91 (0.74, 1.12) 0.3735	-0.02 (-0.06, 0.01) 0.2083	
	50-59	448/ 955 (46.9)	431/ 946 (45.6)	1.00 (0.94, 1.07) 0.9184	0.98 (0.80, 1.21) 0.8598	-0.00 (-0.04, 0.03) 0.9076	
	>= 60	361/ 763 (47.3)	345/ 783 (44.1)	1.07 (0.96, 1.20)*0.1995	1.18 (0.94, 1.48) 0.1649	0.03 (-0.02, 0.08)*0.1992	
	NT-proBNP at enrolment						0.9491
	<= median	599/1312 (45.7)	616/1336 (46.1)	1.00 (0.95, 1.04) 0.9085	1.00 (0.84, 1.19) 0.9776	-0.00 (-0.03, 0.02) 0.8844	
	> median	631/1313 (48.1)	607/1288 (47.1)	1.00 (0.95, 1.05) 0.9761	1.02 (0.85, 1.21) 0.8670	-0.00 (-0.03, 0.03) 0.9239	
	Type 2 Diabetes Medical History						0.6229
	Yes	555/1150 (48.3)	543/1169 (46.4)	1.01 (0.95, 1.07) 0.6777	1.08 (0.91, 1.27)*0.3825	0.01 (-0.03, 0.04) 0.7001	
	No	675/1475 (45.8)	681/1456 (46.8)	0.99 (0.95, 1.03) 0.7331	0.96 (0.83, 1.11)*0.5838	-0.01 (-0.03, 0.02) 0.6554	
	Atrial fibrillation or flutter at enrolment ECG						0.2374
	Yes	519/1097 (47.3)	505/1109 (45.5)	0.96 (0.91, 1.02) 0.1809	1.08 (0.89, 1.31) 0.4269	-0.01 (-0.04, 0.02) 0.4685	
	No	711/1528 (46.5)	719/1516 (47.4)	1.01 (0.97, 1.06) 0.5707	0.96 (0.81, 1.13) 0.5959	0.00 (-0.02, 0.03) 0.8708	
	BMI (kg/m2) at enrolment						0.8375
	< 30	659/1452 (45.4)	658/1428 (46.1)	1.00 (0.96, 1.04) 0.8889	0.94 (0.80, 1.12) 0.5147	-0.01 (-0.04, 0.03)*0.7091	
	>= 30	571/1172 (48.7)	564/1195 (47.2)	1.01 (0.95, 1.07) 0.7999	1.08 (0.90, 1.29) 0.4093	0.01 (-0.03, 0.04) 0.6489	
	Baseline eGFR (mL/min/1.73m^2)						0.2998
	< 60	576/1240 (46.5)	594/1270 (46.8)	0.98 (0.93, 1.03) 0.4871	0.99 (0.83, 1.18) 0.8882	-0.01 (-0.04, 0.02) 0.5362	
	>= 60	654/1385 (47.2)	630/1354 (46.5)	1.02 (0.97, 1.06) 0.4614	1.02 (0.86, 1.21) 0.8149	0.01 (-0.02, 0.03) 0.6464	

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Social Limitation (LOCF)	SBP at randomisation						0.5107
	<= median	623/1320 (47.2)	630/1323 (47.6)	0.99 (0.94, 1.03) 0.5534	0.91 (0.77, 1.09) 0.3096	-0.01 (-0.04, 0.02) 0.4743	
	> median	607/1305 (46.5)	594/1302 (45.6)	1.01 (0.96, 1.06) 0.7117	1.11 (0.93, 1.32) 0.2510	0.00 (-0.02, 0.03) 0.7514	
	LVEF at enrolment 2						0.2764
	<= 49	421/ 907 (46.4)	448/ 896 (50.0)	0.97 (0.92, 1.03) 0.3597	0.91 (0.74, 1.12) 0.3735	-0.02 (-0.06, 0.01) 0.2083	
	>= 50	809/1718 (47.1)	776/1729 (44.9)	1.01 (0.97, 1.06) 0.6121	1.06 (0.91, 1.24) 0.4298	0.01 (-0.02, 0.03) 0.5359	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8875*
	Yes	140/ 252 (55.6)	143/ 256 (55.9)	0.99 (0.85, 1.16)*0.9451	1.02 (0.68, 1.52) 0.9362	-0.00 (-0.09, 0.08)*0.9450	
	No	1090/2373 (45.9)	1081/2369 (45.6)	1.01 (0.97, 1.05) 0.6224	1.01 (0.89, 1.15) 0.9009	0.00 (-0.02, 0.02) 0.8356	
	MRAs at baseline						0.2591
	Yes	543/1144 (47.5)	545/1131 (48.2)	0.98 (0.93, 1.03) 0.4283	0.98 (0.81, 1.18) 0.8357	-0.01 (-0.04, 0.02) 0.4784	
	No	687/1481 (46.4)	679/1494 (45.4)	1.02 (0.97, 1.07) 0.4797	1.03 (0.87, 1.21) 0.7545	0.00 (-0.02, 0.03) 0.7445	
	ACEi+ARB at baseline						0.8470
	Yes	914/1909 (47.9)	906/1934 (46.8)	1.00 (0.96, 1.03) 0.8930	1.04 (0.90, 1.20) 0.5852	-0.00 (-0.02, 0.02) 0.9784	
	No	316/ 716 (44.1)	318/ 691 (46.0)	0.98 (0.90, 1.06) 0.5552	0.92 (0.73, 1.17) 0.5081	-0.02 (-0.06, 0.03) 0.4591	
	ARNI at baseline						0.4362
	Yes	62/ 146 (42.5)	51/ 115 (44.3)	0.96 (0.72, 1.27)*0.7602	0.92 (0.53, 1.59) 0.7674	0.01 (-0.10, 0.12) 0.8895	
	No	1168/2479 (47.1)	1173/2510 (46.7)	0.99 (0.96, 1.03) 0.7298	1.01 (0.89, 1.15) 0.8705	-0.00 (-0.02, 0.02) 0.6930	
	Beta Blocker at baseline						0.7561
	Yes	1035/2195 (47.2)	1019/2187 (46.6)	1.00 (0.96, 1.03) 0.8370	1.00 (0.87, 1.15) 0.9881	-0.00 (-0.03, 0.02) 0.7582	
	No	195/ 430 (45.3)	205/ 438 (46.8)	0.97 (0.84, 1.12)*0.6673	1.05 (0.77, 1.43) 0.7578	-0.01 (-0.08, 0.05)*0.6672	
	Diuretics at baseline						0.5861
	Yes	1105/2350 (47.0)	1098/2345 (46.8)	1.00 (0.96, 1.03) 0.8416	1.03 (0.90, 1.17) 0.7076	-0.00 (-0.02, 0.02) 0.8543	
	No	125/ 275 (45.5)	126/ 280 (45.0)	1.01 (0.84, 1.21)*0.9143	0.87 (0.59, 1.28) 0.4781	0.00 (-0.08, 0.09)*0.9143	

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AstraZeneca
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Full Analysis Set

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Symptom Stability (LOCF)							
	Overall	849/2801 (30.3)	790/2805 (28.2)	1.08 (0.99, 1.17)*0.0774	1.12 (0.98, 1.27) 0.0873	0.02 (-0.00, 0.05)*0.0772	
	Age						0.6510*
	<= median	441/1394 (31.6)	424/1471 (28.8)	1.10 (0.98, 1.23)*0.1014	1.14 (0.96, 1.36) 0.1377	0.03 (-0.01, 0.06)*0.1014	
	> median	408/1407 (29.0)	366/1334 (27.4)	1.06 (0.94, 1.19)*0.3643	1.10 (0.92, 1.32) 0.2964	0.02 (-0.02, 0.05)*0.3637	
	Gender						0.0711*
	Male	453/1630 (27.8)	444/1608 (27.6)	1.01 (0.90, 1.12)*0.9092	0.99 (0.84, 1.17) 0.9315	0.00 (-0.03, 0.03)*0.9092	
	Female	396/1171 (33.8)	346/1197 (28.9)	1.17 (1.04, 1.32)*0.0101	1.31 (1.08, 1.59) 0.0063	0.05 (0.01, 0.09)*0.0099	
	Race						0.6633*
	White	606/2006 (30.2)	574/2032 (28.2)	1.07 (0.97, 1.18)*0.1708	1.10 (0.95, 1.28) 0.1977	0.02 (-0.01, 0.05)*0.1706	
	Black or African	29/ 64 (45.3)	24/ 70 (34.3)	1.32 (0.87, 2.01)*0.1947	1.75 (0.78, 3.91) 0.1760	0.11 (-0.05, 0.28)*0.1904	
	Asian	127/ 555 (22.9)	126/ 551 (22.9)	1.00 (0.81, 1.24)*0.9951	0.98 (0.73, 1.32) 0.8790	0.00 (-0.05, 0.05)*0.9951	
	Other	87/ 176 (49.4)	66/ 152 (43.4)	1.14 (0.90, 1.44)*0.2797	1.50 (0.89, 2.53) 0.1253	0.06 (-0.05, 0.17)*0.2754	
	Geographic region						0.2740*
	Asia	120/ 536 (22.4)	120/ 536 (22.4)	1.00 (0.80, 1.25)*1.0000	0.98 (0.72, 1.33) 0.8848	0.00 (-0.05, 0.05)*1.0000	
	Europe and Saudi Arabia	395/1341 (29.5)	390/1381 (28.2)	1.04 (0.93, 1.17)*0.4841	1.08 (0.90, 1.30) 0.3892	0.01 (-0.02, 0.05)*0.4842	
	North America	98/ 393 (24.9)	94/ 376 (25.0)	1.00 (0.78, 1.27)*0.9837	0.89 (0.61, 1.29) 0.5416	-0.00 (-0.06, 0.06)*0.9837	
	Latin America	236/ 531 (44.4)	186/ 512 (36.3)	1.22 (1.05, 1.42)*0.0080	1.55 (1.17, 2.05) 0.0023	0.08 (0.02, 0.14)*0.0073	
	NYHA class at enrolment						0.0677*
	II	601/2083 (28.9)	609/2165 (28.1)	1.03 (0.93, 1.13)*0.6016	1.05 (0.91, 1.21) 0.5290	0.01 (-0.02, 0.03)*0.6016	
	III or IV	248/ 718 (34.5)	181/ 639 (28.3)	1.22 (1.04, 1.43)*0.0146	1.36 (1.05, 1.78) 0.0223	0.06 (0.01, 0.11)*0.0135	
	LVEF at enrolment						0.5319*
	<= 49	277/ 959 (28.9)	261/ 950 (27.5)	1.05 (0.91, 1.21)*0.4935	1.08 (0.87, 1.35) 0.4725	0.01 (-0.03, 0.05)*0.4933	
	50-59	314/1017 (30.9)	272/1009 (27.0)	1.15 (1.00, 1.31)*0.0522	1.23 (1.00, 1.53) 0.0539	0.04 (-0.00, 0.08)*0.0516	
	>= 60	258/ 825 (31.3)	257/ 846 (30.4)	1.03 (0.89, 1.19)*0.6922	1.04 (0.83, 1.30) 0.7486	0.01 (-0.04, 0.05)*0.6922	
	NT-proBNP at enrolment						0.0670*
	<= median	408/1396 (29.2)	413/1409 (29.3)	1.00 (0.89, 1.12)*0.9604	1.00 (0.84, 1.19) 0.9730	-0.00 (-0.03, 0.03)*0.9604	
	> median	441/1405 (31.4)	377/1395 (27.0)	1.16 (1.03, 1.30)*0.0113	1.25 (1.05, 1.50) 0.0144	0.04 (0.01, 0.08)*0.0110	
	Type 2 Diabetes Medical History						0.6022*
	Yes	350/1231 (28.4)	337/1243 (27.1)	1.03 (0.96, 1.10) 0.3944	1.07 (0.90, 1.27)*0.4635	0.01 (-0.02, 0.05)*0.4634	
	No	499/1570 (31.8)	453/1562 (29.0)	1.10 (0.99, 1.22)*0.0908	1.14 (0.98, 1.33)*0.0906	0.03 (-0.00, 0.06)*0.0904	
	Atrial fibrillation or flutter at enrolment ECG						0.8819*
	Yes	342/1185 (28.9)	321/1188 (27.0)	1.07 (0.94, 1.22)*0.3179	1.12 (0.92, 1.37) 0.2468	0.02 (-0.02, 0.05)*0.3177	
	No	507/1616 (31.4)	469/1617 (29.0)	1.08 (0.97, 1.20)*0.1425	1.11 (0.94, 1.31) 0.2185	0.02 (-0.01, 0.06)*0.1422	
	BMI (kg/m2) at enrolment						0.2243*
	< 30	454/1547 (29.3)	400/1541 (26.0)	1.13 (1.01, 1.27)*0.0355	1.18 (1.00, 1.40) 0.0537	0.03 (0.00, 0.07)*0.0351	
	>= 30	395/1253 (31.5)	389/1261 (30.8)	1.02 (0.91, 1.15)*0.7146	1.04 (0.86, 1.26) 0.6579	0.01 (-0.03, 0.04)*0.7146	
	Baseline eGFR (mL/min/1.73m^2)						0.3211*
	< 60	379/1338 (28.3)	379/1377 (27.5)	1.03 (0.91, 1.16)*0.6413	1.06 (0.88, 1.28) 0.5334	0.01 (-0.03, 0.04)*0.6413	
	>= 60	470/1463 (32.1)	410/1427 (28.7)	1.12 (1.00, 1.25)*0.0478	1.17 (0.98, 1.39) 0.0809	0.03 (0.00, 0.07)*0.0472	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)	SBP at randomisation						0.4740*
	<= median	409/1405 (29.1)	396/1420 (27.9)	1.04 (0.93, 1.17)*0.4716	1.04 (0.87, 1.25) 0.6559	0.01 (-0.02, 0.05)*0.4715	
	> median	440/1396 (31.5)	394/1385 (28.4)	1.11 (0.99, 1.24)*0.0775	1.20 (1.00, 1.44) 0.0450	0.03 (-0.00, 0.06)*0.0770	
	LVEF at enrolment 2						0.6928*
	<= 49	277/ 959 (28.9)	261/ 950 (27.5)	1.05 (0.91, 1.21)*0.4935	1.08 (0.87, 1.35) 0.4725	0.01 (-0.03, 0.05)*0.4933	
	>= 50	572/1842 (31.1)	529/1855 (28.5)	1.09 (0.99, 1.20)*0.0920	1.14 (0.97, 1.33) 0.1012	0.03 (-0.00, 0.05)*0.0917	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5889*
	Yes	78/ 280 (27.9)	78/ 281 (27.8)	1.00 (0.77, 1.31)*0.9791	1.09 (0.70, 1.69) 0.6975	0.00 (-0.07, 0.08)*0.9791	
	No	771/2521 (30.6)	712/2524 (28.2)	1.08 (1.00, 1.18)*0.0644	1.12 (0.98, 1.27) 0.1069	0.02 (-0.00, 0.05)*0.0641	
	MRAs at baseline						0.1322*
	Yes	365/1216 (30.0)	362/1210 (29.9)	1.00 (0.89, 1.13)*0.9575	1.03 (0.85, 1.25) 0.7340	0.00 (-0.04, 0.04)*0.9575	
	No	484/1585 (30.5)	428/1595 (26.8)	1.14 (1.02, 1.27)*0.0212	1.18 (1.00, 1.40) 0.0501	0.04 (0.01, 0.07)*0.0209	
	ACEi+ARB at baseline						0.6876*
	Yes	638/2037 (31.3)	593/2059 (28.8)	1.09 (0.99, 1.19)*0.0788	1.16 (1.00, 1.34) 0.0519	0.03 (-0.00, 0.05)*0.0785	
	No	211/ 764 (27.6)	197/ 746 (26.4)	1.05 (0.89, 1.23)*0.5966	1.02 (0.79, 1.30) 0.9075	0.01 (-0.03, 0.06)*0.5964	
	ARNI at baseline						0.4490*
	Yes	40/ 149 (26.8)	36/ 125 (28.8)	0.93 (0.64, 1.37)*0.7187	1.04 (0.58, 1.85) 0.8978	-0.02 (-0.13, 0.09)*0.7194	
	No	809/2652 (30.5)	754/2680 (28.1)	1.08 (1.00, 1.18)*0.0573	1.12 (0.99, 1.28) 0.0782	0.02 (-0.00, 0.05)*0.0572	
	Beta Blocker at baseline						0.9833*
	Yes	700/2327 (30.1)	651/2330 (27.9)	1.08 (0.98, 1.18)*0.1075	1.08 (0.94, 1.25) 0.2517	0.02 (-0.00, 0.05)*0.1072	
	No	149/ 474 (31.4)	139/ 475 (29.3)	1.07 (0.89, 1.30)*0.4671	1.30 (0.96, 1.78) 0.0933	0.02 (-0.04, 0.08)*0.4668	
	Diuretics at baseline						0.5890*
	Yes	745/2500 (29.8)	699/2504 (27.9)	1.07 (0.98, 1.16)*0.1414	1.10 (0.96, 1.26) 0.1523	0.02 (-0.01, 0.04)*0.1412	
	No	104/ 301 (34.6)	91/ 301 (30.2)	1.14 (0.91, 1.44)*0.2584	1.22 (0.84, 1.79) 0.2962	0.04 (-0.03, 0.12)*0.2570	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	1450/2801 (51.8)	1333/2805 (47.5)	1.09 (1.03, 1.15)*0.0015	1.22 (1.08, 1.38) 0.0012	0.04 (0.02, 0.07)*0.0015	
	Age						0.1414*
	<= median	731/1394 (52.4)	734/1471 (49.9)	1.05 (0.98, 1.13)*0.1737	1.17 (0.99, 1.39) 0.0650	0.03 (-0.01, 0.06)*0.1737	
	> median	719/1407 (51.1)	599/1334 (44.9)	1.14 (1.05, 1.23)*0.0012	1.29 (1.08, 1.53) 0.0040	0.06 (0.02, 0.10)*0.0011	
	Gender						0.5567*
	Male	815/1630 (50.0)	748/1608 (46.5)	1.07 (1.00, 1.15)*0.0476	1.18 (1.00, 1.39) 0.0443	0.03 (0.00, 0.07)*0.0472	
	Female	635/1171 (54.2)	585/1197 (48.9)	1.11 (1.03, 1.20)*0.0092	1.26 (1.05, 1.51) 0.0114	0.05 (0.01, 0.09)*0.0090	
	Race						0.4386*
	White	1080/2006 (53.8)	986/2032 (48.5)	1.11 (1.04, 1.18)*0.0007	1.24 (1.08, 1.43) 0.0025	0.05 (0.02, 0.08)*0.0007	
	Black or African	38/ 64 (59.4)	38/ 70 (54.3)	1.09 (0.81, 1.47)*0.5522	1.31 (0.64, 2.71) 0.4589	0.06 (-0.10, 0.21) 0.4816	
	Asian	216/ 555 (38.9)	220/ 551 (39.9)	0.97 (0.84, 1.13)*0.7315	1.05 (0.79, 1.39) 0.7373	-0.01 (-0.07, 0.05)*0.7315	
	Other	116/ 176 (65.9)	89/ 152 (58.6)	1.13 (0.95, 1.34)*0.1745	1.39 (0.83, 2.31) 0.2057	0.07 (-0.03, 0.18)*0.1699	
	Geographic region						0.4197*
	Asia	207/ 536 (38.6)	211/ 536 (39.4)	0.98 (0.84, 1.14)*0.8022	1.04 (0.78, 1.40) 0.7681	-0.01 (-0.07, 0.05)*0.8022	
	Europe and Saudi Arabia	718/1341 (53.5)	671/1381 (48.6)	1.10 (1.02, 1.19)*0.0098	1.21 (1.02, 1.45) 0.0288	0.05 (0.01, 0.09)*0.0096	
	North America	194/ 393 (49.4)	172/ 376 (45.7)	1.08 (0.93, 1.25)*0.3159	1.18 (0.87, 1.60) 0.2925	0.04 (-0.03, 0.11)*0.3148	
	Latin America	331/ 531 (62.3)	279/ 512 (54.5)	1.14 (1.03, 1.27)*0.0106	1.52 (1.15, 2.02) 0.0036	0.08 (0.02, 0.14)*0.0100	
	NYHA class at enrolment						0.9629*
	II	1028/2083 (49.4)	987/2165 (45.6)	1.08 (1.02, 1.15)*0.0141	1.26 (1.09, 1.45) 0.0013	0.04 (0.01, 0.07)*0.0140	
	III or IV	422/ 718 (58.8)	346/ 639 (54.1)	1.09 (0.99, 1.19)*0.0874	1.18 (0.93, 1.50) 0.1676	0.05 (-0.01, 0.10)*0.0859	
	LVEF at enrolment						0.1196*
	<= 49	484/ 959 (50.5)	444/ 950 (46.7)	1.08 (0.98, 1.18)*0.1032	1.27 (1.03, 1.56) 0.0265	0.04 (-0.01, 0.08)*0.1026	
	50-59	521/1017 (51.2)	502/1009 (49.8)	1.03 (0.94, 1.12)*0.5063	1.07 (0.87, 1.31) 0.5301	0.01 (-0.03, 0.06)*0.5061	
	>= 60	445/ 825 (53.9)	387/ 846 (45.7)	1.18 (1.07, 1.30)*0.0008	1.38 (1.11, 1.71) 0.0035	0.08 (0.03, 0.13)*0.0008	
	NT-proBNP at enrolment						0.7104*
	<= median	702/1396 (50.3)	657/1409 (46.6)	1.08 (1.00, 1.16)*0.0528	1.21 (1.02, 1.43) 0.0247	0.04 (-0.00, 0.07)*0.0525	
	> median	748/1405 (53.2)	675/1395 (48.4)	1.10 (1.02, 1.18)*0.0104	1.23 (1.03, 1.46) 0.0194	0.05 (0.01, 0.09)*0.0102	
	Type 2 Diabetes Medical History						0.0121*
	Yes	670/1231 (54.4)	576/1243 (46.3)	1.17 (1.09, 1.27)*<.0001	1.38 (1.18, 1.62)*<.0001	0.08 (0.04, 0.12)*<.0001	
	No	780/1570 (49.7)	757/1562 (48.5)	1.03 (0.95, 1.10)*0.4954	1.05 (0.91, 1.21)*0.4954	0.01 (-0.02, 0.05)*0.4954	
	Atrial fibrillation or flutter at enrolment ECG						0.9608*
	Yes	629/1185 (53.1)	578/1188 (48.7)	1.09 (1.01, 1.18)*0.0312	1.25 (1.04, 1.51) 0.0162	0.04 (0.00, 0.08)*0.0309	
	No	821/1616 (50.8)	755/1617 (46.7)	1.09 (1.01, 1.17)*0.0195	1.20 (1.02, 1.40) 0.0270	0.04 (0.01, 0.08)*0.0192	
	BMI (kg/m2) at enrolment						0.5030*
	< 30	750/1547 (48.5)	697/1541 (45.2)	1.07 (0.99, 1.16)*0.0705	1.18 (1.00, 1.39) 0.0518	0.03 (-0.00, 0.07)*0.0702	
	>= 30	700/1253 (55.9)	634/1261 (50.3)	1.11 (1.03, 1.20)*0.0051	1.28 (1.08, 1.53) 0.0055	0.06 (0.02, 0.09)*0.0049	
	Baseline eGFR (mL/min/1.73m^2)						0.2954*
	< 60	682/1338 (51.0)	626/1377 (45.5)	1.12 (1.04, 1.21)*0.0041	1.29 (1.08, 1.53) 0.0040	0.06 (0.02, 0.09)*0.0040	
	>= 60	768/1463 (52.5)	707/1427 (49.5)	1.06 (0.99, 1.14)*0.1130	1.16 (0.98, 1.37) 0.0939	0.03 (-0.01, 0.07)*0.1125	

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AstraZeneca
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Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.1704*
	<= median	738/1405 (52.5)	660/1420 (46.5)	1.13 (1.05, 1.22)*0.0013	1.25 (1.06, 1.48) 0.0091	0.06 (0.02, 0.10)*0.0013	
	> median	712/1396 (51.0)	673/1385 (48.6)	1.05 (0.97, 1.13)*0.2038	1.19 (1.00, 1.42) 0.0457	0.02 (-0.01, 0.06)*0.2035	
	LVEF at enrolment 2						0.8174*
	<= 49	484/ 959 (50.5)	444/ 950 (46.7)	1.08 (0.98, 1.18)*0.1032	1.27 (1.03, 1.56) 0.0265	0.04 (-0.01, 0.08)*0.1026	
	>= 50	966/1842 (52.4)	889/1855 (47.9)	1.09 (1.03, 1.17)*0.0061	1.20 (1.03, 1.39) 0.0158	0.05 (0.01, 0.08)*0.0060	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1973*
	Yes	173/ 280 (61.8)	173/ 281 (61.6)	1.00 (0.88, 1.14)*0.9573	1.15 (0.78, 1.69) 0.4709	0.00 (-0.08, 0.08)*0.9573	
	No	1277/2521 (50.7)	1160/2524 (46.0)	1.10 (1.04, 1.17)*0.0009	1.23 (1.08, 1.39) 0.0015	0.05 (0.02, 0.07)*0.0008	
	MRAs at baseline						0.3325*
	Yes	633/1216 (52.1)	561/1210 (46.4)	1.12 (1.04, 1.22)*0.0051	1.30 (1.08, 1.56) 0.0050	0.06 (0.02, 0.10)*0.0050	
	No	817/1585 (51.5)	772/1595 (48.4)	1.06 (0.99, 1.14)*0.0764	1.16 (0.99, 1.37) 0.0617	0.03 (-0.00, 0.07)*0.0760	
	ACEi+ARB at baseline						0.2181*
	Yes	1081/2037 (53.1)	983/2059 (47.7)	1.11 (1.05, 1.18)*0.0007	1.26 (1.10, 1.45) 0.0013	0.05 (0.02, 0.08)*0.0006	
	No	369/ 764 (48.3)	350/ 746 (46.9)	1.03 (0.93, 1.14)*0.5911	1.11 (0.89, 1.40) 0.3509	0.01 (-0.04, 0.06)*0.5909	
	ARNI at baseline						0.0374*
	Yes	54/ 149 (36.2)	56/ 125 (44.8)	0.81 (0.61, 1.08)*0.1498	0.77 (0.44, 1.36) 0.3709	-0.09 (-0.20, 0.03)*0.1497	
	No	1396/2652 (52.6)	1277/2680 (47.6)	1.10 (1.05, 1.17)*0.0003	1.25 (1.10, 1.41) 0.0004	0.05 (0.02, 0.08)*0.0003	
	Beta Blocker at baseline						0.5090*
	Yes	1214/2327 (52.2)	1107/2330 (47.5)	1.10 (1.04, 1.16)*0.0015	1.21 (1.06, 1.38) 0.0044	0.05 (0.02, 0.08)*0.0015	
	No	236/ 474 (49.8)	226/ 475 (47.6)	1.05 (0.92, 1.19)*0.4960	1.28 (0.95, 1.73) 0.1055	0.02 (-0.04, 0.09)*0.4957	
	Diuretics at baseline						0.0893*
	Yes	1291/2500 (51.6)	1206/2504 (48.2)	1.07 (1.01, 1.13)*0.0140	1.20 (1.06, 1.36) 0.0048	0.03 (0.01, 0.06)*0.0139	
	No	159/ 301 (52.8)	127/ 301 (42.2)	1.25 (1.06, 1.48)*0.0096	1.39 (0.95, 2.02) 0.0874	0.11 (0.03, 0.19)*0.0086	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	1432/2842 (50.4)	1357/2837 (47.8)	1.05 (1.00, 1.11)*0.0543	1.10 (0.98, 1.24) 0.0980	0.03 (-0.00, 0.05)*0.0541	
	Age						0.4222*
	<= median	741/1415 (52.4)	750/1482 (50.6)	1.03 (0.96, 1.11)*0.3432	1.12 (0.95, 1.32) 0.1835	0.02 (-0.02, 0.05)*0.3433	
	> median	691/1427 (48.4)	607/1355 (44.8)	1.08 (1.00, 1.17)*0.0558	1.11 (0.94, 1.31) 0.2162	0.04 (-0.00, 0.07)*0.0551	
	Gender						0.5957*
	Male	782/1656 (47.2)	737/1625 (45.4)	1.04 (0.97, 1.12)*0.2834	1.08 (0.92, 1.26) 0.3601	0.02 (-0.02, 0.05)*0.2831	
	Female	650/1186 (54.8)	620/1212 (51.2)	1.07 (0.99, 1.16)*0.0734	1.14 (0.95, 1.36) 0.1488	0.04 (-0.00, 0.08)*0.0731	
	Race						0.7264*
	White	1053/2039 (51.6)	1018/2058 (49.5)	1.04 (0.98, 1.11)*0.1635	1.06 (0.92, 1.21) 0.4142	0.02 (-0.01, 0.05)*0.1633	
	Black or African	36/ 67 (53.7)	37/ 71 (52.1)	1.03 (0.75, 1.41)*0.8490	1.11 (0.54, 2.27) 0.7784	0.02 (-0.15, 0.18)*0.8490	
	Asian	222/ 558 (39.8)	212/ 555 (38.2)	1.04 (0.90, 1.21)*0.5874	1.12 (0.86, 1.47) 0.3978	0.02 (-0.04, 0.07)*0.5873	
	Other	121/ 178 (68.0)	90/ 153 (58.8)	1.16 (0.98, 1.37)*0.0888	1.83 (1.06, 3.16) 0.0294	0.09 (-0.01, 0.20)*0.0840	
	Geographic region						0.9491*
	Asia	213/ 539 (39.5)	207/ 538 (38.5)	1.03 (0.88, 1.19)*0.7260	1.07 (0.81, 1.41) 0.6285	0.01 (-0.05, 0.07)*0.7260	
	Europe and Saudi Arabia	704/1365 (51.6)	685/1394 (49.1)	1.05 (0.97, 1.13)*0.2008	1.07 (0.91, 1.26) 0.4271	0.02 (-0.01, 0.06)*0.2006	
	North America	188/ 398 (47.2)	167/ 387 (43.2)	1.09 (0.94, 1.28)*0.2512	1.18 (0.87, 1.59) 0.2846	0.03 (-0.03, 0.10) 0.3259	
	Latin America	327/ 540 (60.6)	298/ 518 (57.5)	1.05 (0.95, 1.16)*0.3175	1.20 (0.91, 1.58) 0.2046	0.03 (-0.03, 0.09)*0.3168	
	NYHA class at enrolment						0.5799*
	II	998/2113 (47.2)	996/2187 (45.5)	1.04 (0.97, 1.11)*0.2667	1.10 (0.96, 1.26) 0.1667	0.02 (-0.01, 0.05)*0.2666	
	III or IV	434/ 729 (59.5)	361/ 649 (55.6)	1.07 (0.98, 1.17)*0.1440	1.14 (0.91, 1.44) 0.2518	0.04 (-0.01, 0.09)*0.1425	
	LVEF at enrolment						0.1694*
	<= 49	473/ 980 (48.3)	469/ 963 (48.7)	0.99 (0.90, 1.09)*0.8473	1.04 (0.85, 1.27) 0.7302	-0.00 (-0.05, 0.04)*0.8473	
	50-59	515/1029 (50.0)	482/1017 (47.4)	1.06 (0.97, 1.15)*0.2301	1.09 (0.90, 1.32) 0.3971	0.03 (-0.02, 0.07)*0.2296	
	>= 60	444/ 833 (53.3)	406/ 857 (47.4)	1.13 (1.02, 1.24)*0.0150	1.21 (0.98, 1.49) 0.0718	0.06 (0.01, 0.11)*0.0147	
	NT-proBNP at enrolment						0.1354*
	<= median	683/1418 (48.2)	677/1421 (47.6)	1.01 (0.94, 1.09)*0.7799	1.02 (0.87, 1.20) 0.7985	0.01 (-0.03, 0.04)*0.7799	
	> median	749/1424 (52.6)	679/1415 (48.0)	1.10 (1.02, 1.18)*0.0141	1.20 (1.01, 1.41) 0.0344	0.05 (0.01, 0.08)*0.0139	
	Type 2 Diabetes Medical History						0.8615*
	Yes	643/1250 (51.4)	612/1260 (48.6)	1.06 (0.98, 1.15)*0.1509	1.12 (0.96, 1.31)*0.1507	0.03 (-0.01, 0.07)*0.1505	
	No	789/1592 (49.6)	745/1577 (47.2)	1.05 (0.98, 1.13)*0.1918	1.10 (0.95, 1.26)*0.1916	0.02 (-0.01, 0.06)*0.1915	
	Atrial fibrillation or flutter at enrolment ECG						0.5405*
	Yes	613/1199 (51.1)	593/1199 (49.5)	1.03 (0.95, 1.12)*0.4141	1.07 (0.90, 1.28) 0.4514	0.02 (-0.02, 0.06)*0.4139	
	No	819/1643 (49.8)	764/1638 (46.6)	1.07 (1.00, 1.15)*0.0664	1.13 (0.97, 1.31) 0.1234	0.03 (-0.00, 0.07)*0.0660	
	BMI (kg/m2) at enrolment						0.2093*
	< 30	757/1571 (48.2)	690/1559 (44.3)	1.09 (1.01, 1.17)*0.0278	1.20 (1.02, 1.40) 0.0241	0.04 (0.00, 0.07)*0.0275	
	>= 30	675/1270 (53.1)	666/1275 (52.2)	1.02 (0.95, 1.10)*0.6441	1.00 (0.84, 1.19) 0.9960	0.01 (-0.03, 0.05)*0.6441	
	Baseline eGFR (mL/min/1.73m^2)						0.9816*
	< 60	671/1359 (49.4)	654/1396 (46.8)	1.05 (0.98, 1.14)*0.1846	1.11 (0.94, 1.31) 0.2273	0.03 (-0.01, 0.06)*0.1844	
	>= 60	761/1483 (51.3)	702/1440 (48.8)	1.05 (0.98, 1.13)*0.1659	1.09 (0.93, 1.29) 0.2771	0.03 (-0.01, 0.06)*0.1654	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.0061*
	<= median	727/1424 (51.1)	647/1439 (45.0)	1.14 (1.05, 1.23)*0.0011	1.23 (1.05, 1.45) 0.0118	0.06 (0.02, 0.10)*0.0011	
	> median	705/1418 (49.7)	710/1398 (50.8)	0.98 (0.91, 1.05)*0.5706	0.98 (0.83, 1.16) 0.8469	-0.01 (-0.05, 0.03)*0.5705	
	LVEF at enrolment 2						0.1072*
	<= 49	473/ 980 (48.3)	469/ 963 (48.7)	0.99 (0.90, 1.09)*0.8473	1.04 (0.85, 1.27) 0.7302	-0.00 (-0.05, 0.04)*0.8473	
	>= 50	959/1862 (51.5)	888/1874 (47.4)	1.09 (1.02, 1.16)*0.0119	1.14 (0.99, 1.31) 0.0705	0.04 (0.01, 0.07)*0.0117	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8930*
	Yes	184/ 283 (65.0)	175/ 286 (61.2)	1.06 (0.94, 1.21)*0.3443	1.40 (0.95, 2.05) 0.0858	0.04 (-0.04, 0.12)*0.3435	
	No	1248/2559 (48.8)	1182/2551 (46.3)	1.05 (0.99, 1.11)*0.0816	1.08 (0.96, 1.22) 0.2182	0.02 (-0.00, 0.05)*0.0814	
	MRAs at baseline						0.8340*
	Yes	607/1227 (49.5)	571/1224 (46.7)	1.06 (0.98, 1.15)*0.1626	1.12 (0.94, 1.34) 0.2203	0.03 (-0.01, 0.07)*0.1622	
	No	825/1615 (51.1)	786/1613 (48.7)	1.05 (0.98, 1.12)*0.1812	1.09 (0.94, 1.27) 0.2581	0.02 (-0.01, 0.06)*0.1809	
	ACEi+ARB at baseline						0.1736*
	Yes	1071/2065 (51.9)	1000/2077 (48.1)	1.08 (1.01, 1.14)*0.0168	1.15 (1.00, 1.32) 0.0464	0.04 (0.01, 0.07)*0.0166	
	No	361/ 777 (46.5)	357/ 760 (47.0)	0.99 (0.89, 1.10)*0.8403	0.99 (0.80, 1.23) 0.9214	-0.01 (-0.06, 0.04)*0.8403	
	ARNI at baseline						0.0927*
	Yes	59/ 153 (38.6)	58/ 126 (46.0)	0.84 (0.64, 1.10)*0.2073	0.83 (0.49, 1.41) 0.4887	-0.07 (-0.19, 0.04)*0.2080	
	No	1373/2689 (51.1)	1299/2711 (47.9)	1.07 (1.01, 1.12)*0.0209	1.12 (0.99, 1.26) 0.0611	0.03 (0.00, 0.06)*0.0208	
	Beta Blocker at baseline						0.5276*
	Yes	1191/2360 (50.5)	1120/2356 (47.5)	1.06 (1.00, 1.13)*0.0444	1.10 (0.97, 1.24) 0.1565	0.03 (0.00, 0.06)*0.0442	
	No	241/ 482 (50.0)	237/ 481 (49.3)	1.01 (0.89, 1.15)*0.8214	1.14 (0.86, 1.51) 0.3710	0.01 (-0.06, 0.07)*0.8213	
	Diuretics at baseline						0.8878*
	Yes	1282/2536 (50.6)	1213/2531 (47.9)	1.05 (1.00, 1.12)*0.0617	1.12 (0.99, 1.27) 0.0646	0.03 (-0.00, 0.05)*0.0614	
	No	150/ 306 (49.0)	144/ 306 (47.1)	1.04 (0.88, 1.23)*0.6275	0.92 (0.63, 1.34) 0.6462	0.02 (-0.06, 0.10)*0.6273	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	1450/2842 (51.0)	1399/2837 (49.3)	1.03 (0.98, 1.09)*0.1982	1.05 (0.94, 1.18) 0.3656	0.02 (-0.01, 0.04)*0.1980	
	Age						0.8403*
	<= median	762/1415 (53.9)	773/1482 (52.2)	1.03 (0.96, 1.11)*0.3615	1.10 (0.94, 1.29) 0.2379	0.02 (-0.02, 0.05)*0.3615	
	> median	688/1427 (48.2)	626/1355 (46.2)	1.04 (0.96, 1.13)*0.2880	1.02 (0.87, 1.21) 0.7776	0.02 (-0.02, 0.06)*0.2875	
	Gender						0.2905*
	Male	805/1656 (48.6)	782/1625 (48.1)	1.01 (0.94, 1.08)*0.7797	1.00 (0.86, 1.16) 0.9871	0.00 (-0.03, 0.04)*0.7797	
	Female	645/1186 (54.4)	617/1212 (50.9)	1.07 (0.99, 1.15)*0.0883	1.13 (0.95, 1.34) 0.1806	0.03 (-0.01, 0.07)*0.0880	
	Race						0.5359*
	White	1061/2039 (52.0)	1025/2058 (49.8)	1.04 (0.98, 1.11)*0.1536	1.05 (0.92, 1.21) 0.4423	0.02 (-0.01, 0.05)*0.1534	
	Black or African	33/ 67 (49.3)	40/ 71 (56.3)	0.87 (0.64, 1.20)*0.4072	0.73 (0.36, 1.50) 0.3959	-0.05 (-0.21, 0.11) 0.5519	
	Asian	230/ 558 (41.2)	234/ 555 (42.2)	0.98 (0.85, 1.12)*0.7496	1.00 (0.77, 1.29) 0.9740	-0.01 (-0.07, 0.05)*0.7496	
	Other	126/ 178 (70.8)	100/ 153 (65.4)	1.08 (0.93, 1.26)*0.2942	1.46 (0.87, 2.47) 0.1537	0.05 (-0.05, 0.16)*0.2910	
	Geographic region						0.7843*
	Asia	223/ 539 (41.4)	229/ 538 (42.6)	0.97 (0.84, 1.12)*0.6919	0.96 (0.74, 1.26) 0.7925	-0.01 (-0.07, 0.05)*0.6918	
	Europe and Saudi Arabia	707/1365 (51.8)	687/1394 (49.3)	1.05 (0.98, 1.13)*0.1870	1.06 (0.90, 1.25) 0.4692	0.03 (-0.01, 0.06)*0.1868	
	North America	193/ 398 (48.5)	177/ 387 (45.7)	1.06 (0.91, 1.23)*0.4397	1.12 (0.83, 1.51) 0.4574	0.03 (-0.04, 0.09) 0.3795	
	Latin America	327/ 540 (60.6)	306/ 518 (59.1)	1.03 (0.93, 1.13)*0.6232	1.08 (0.83, 1.42) 0.5632	0.01 (-0.04, 0.07)*0.6230	
	NYHA class at enrolment						0.0491*
	II	1019/2113 (48.2)	1056/2187 (48.3)	1.00 (0.94, 1.06)*0.9686	1.00 (0.88, 1.15) 0.9540	-0.00 (-0.03, 0.03)*0.9686	
	III or IV	431/ 729 (59.1)	343/ 649 (52.9)	1.12 (1.02, 1.23)*0.0200	1.27 (1.01, 1.61) 0.0406	0.06 (0.01, 0.12)*0.0190	
	LVEF at enrolment						0.0572*
	<= 49	491/ 980 (50.1)	505/ 963 (52.4)	0.96 (0.88, 1.04)*0.3026	0.94 (0.77, 1.14) 0.5180	-0.02 (-0.07, 0.02)*0.3024	
	50-59	522/1029 (50.7)	491/1017 (48.3)	1.05 (0.96, 1.15)*0.2681	1.06 (0.88, 1.29) 0.5398	0.02 (-0.02, 0.07)*0.2677	
	>= 60	437/ 833 (52.5)	403/ 857 (47.0)	1.12 (1.01, 1.23)*0.0256	1.20 (0.97, 1.47) 0.0938	0.05 (0.01, 0.10)*0.0252	
	NT-proBNP at enrolment						0.8135*
	<= median	706/1418 (49.8)	688/1421 (48.4)	1.03 (0.95, 1.11)*0.4648	1.06 (0.90, 1.24) 0.5027	0.01 (-0.02, 0.05)*0.4647	
	> median	744/1424 (52.2)	710/1415 (50.2)	1.04 (0.97, 1.12)*0.2700	1.05 (0.89, 1.24) 0.5463	0.02 (-0.02, 0.06)*0.2697	
	Type 2 Diabetes Medical History						0.1771*
	Yes	660/1250 (52.8)	618/1260 (49.0)	1.08 (1.00, 1.16)*0.0603	1.16 (0.99, 1.36)*0.0601	0.04 (-0.00, 0.08)*0.0599	
	No	790/1592 (49.6)	781/1577 (49.5)	1.00 (0.93, 1.07)*0.9557	1.00 (0.87, 1.15)*0.9557	0.00 (-0.03, 0.04)*0.9557	
	Atrial fibrillation or flutter at enrolment ECG						0.8664*
	Yes	629/1199 (52.5)	611/1199 (51.0)	1.03 (0.95, 1.11)*0.4621	1.05 (0.88, 1.25) 0.5961	0.02 (-0.02, 0.06)*0.4619	
	No	821/1643 (50.0)	788/1638 (48.1)	1.04 (0.97, 1.11)*0.2862	1.06 (0.91, 1.23) 0.4584	0.02 (-0.02, 0.05)*0.2860	
	BMI (kg/m2) at enrolment						0.8879*
	< 30	763/1571 (48.6)	729/1559 (46.8)	1.04 (0.97, 1.12)*0.3116	1.06 (0.91, 1.24) 0.4633	0.02 (-0.02, 0.05)*0.3114	
	>= 30	687/1270 (54.1)	669/1275 (52.5)	1.03 (0.96, 1.11)*0.4117	1.05 (0.88, 1.24) 0.5979	0.02 (-0.02, 0.06)*0.4116	
	Baseline eGFR (mL/min/1.73m^2)						0.8403*
	< 60	663/1359 (48.8)	663/1396 (47.5)	1.03 (0.95, 1.11)*0.4970	1.04 (0.89, 1.23) 0.6134	0.01 (-0.02, 0.05)*0.4970	
	>= 60	787/1483 (53.1)	736/1440 (51.1)	1.04 (0.97, 1.11)*0.2899	1.06 (0.90, 1.24) 0.5003	0.02 (-0.02, 0.06)*0.2896	

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Overall Summary Score (LOCF)	SBP at randomisation						0.0537*
	<= median	737/1424 (51.8)	684/1439 (47.5)	1.09 (1.01, 1.17)*0.0240	1.13 (0.96, 1.32) 0.1402	0.04 (0.01, 0.08)*0.0237	
	> median	713/1418 (50.3)	715/1398 (51.1)	0.98 (0.91, 1.06)*0.6472	0.98 (0.84, 1.16) 0.8559	-0.01 (-0.05, 0.03)*0.6472	
	LVEF at enrolment 2						0.0269*
	<= 49	491/ 980 (50.1)	505/ 963 (52.4)	0.96 (0.88, 1.04)*0.3026	0.94 (0.77, 1.14) 0.5180	-0.02 (-0.07, 0.02)*0.3024	
	>= 50	959/1862 (51.5)	894/1874 (47.7)	1.08 (1.01, 1.15)*0.0204	1.12 (0.97, 1.29) 0.1169	0.04 (0.01, 0.07)*0.0202	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4811*
	Yes	182/ 283 (64.3)	170/ 286 (59.4)	1.08 (0.95, 1.23)*0.2323	1.39 (0.95, 2.02) 0.0910	0.05 (-0.03, 0.13)*0.2311	
	No	1268/2559 (49.6)	1229/2551 (48.2)	1.03 (0.97, 1.09)*0.3262	1.03 (0.91, 1.16) 0.6517	0.01 (-0.01, 0.04)*0.3260	
	MRAs at baseline						0.6538*
	Yes	620/1227 (50.5)	606/1224 (49.5)	1.02 (0.94, 1.10)*0.6136	1.03 (0.86, 1.22) 0.7709	0.01 (-0.03, 0.05)*0.6136	
	No	830/1615 (51.4)	793/1613 (49.2)	1.05 (0.98, 1.12)*0.2053	1.08 (0.93, 1.25) 0.3347	0.02 (-0.01, 0.06)*0.2050	
	ACEi+ARB at baseline						0.1362*
	Yes	1081/2065 (52.3)	1026/2077 (49.4)	1.06 (1.00, 1.13)*0.0577	1.11 (0.97, 1.27) 0.1273	0.03 (-0.00, 0.06)*0.0574	
	No	369/ 777 (47.5)	373/ 760 (49.1)	0.97 (0.87, 1.07)*0.5332	0.92 (0.74, 1.14) 0.4568	-0.02 (-0.07, 0.03)*0.5331	
	ARNI at baseline						0.0340*
	Yes	60/ 153 (39.2)	63/ 126 (50.0)	0.78 (0.60, 1.02)*0.0707	0.64 (0.38, 1.08) 0.0934	-0.11 (-0.22, 0.01)*0.0700	
	No	1390/2689 (51.7)	1336/2711 (49.3)	1.05 (0.99, 1.11)*0.0765	1.08 (0.96, 1.22) 0.1845	0.02 (-0.00, 0.05)*0.0763	
	Beta Blocker at baseline						0.1376*
	Yes	1207/2360 (51.1)	1144/2356 (48.6)	1.05 (0.99, 1.12)*0.0758	1.07 (0.95, 1.22) 0.2623	0.03 (-0.00, 0.05)*0.0755	
	No	243/ 482 (50.4)	255/ 481 (53.0)	0.95 (0.84, 1.07)*0.4197	0.97 (0.73, 1.28) 0.8099	-0.03 (-0.09, 0.04)*0.4194	
	Diuretics at baseline						0.3734*
	Yes	1294/2536 (51.0)	1238/2531 (48.9)	1.04 (0.99, 1.10)*0.1329	1.09 (0.97, 1.23) 0.1610	0.02 (-0.01, 0.05)*0.1327	
	No	156/ 306 (51.0)	161/ 306 (52.6)	0.97 (0.83, 1.13)*0.6859	0.78 (0.55, 1.12) 0.1783	-0.02 (-0.10, 0.06)*0.6858	

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Physical Limitation (LOCF)							
	Overall	1298/2792 (46.5)	1171/2792 (41.9)	1.04 (1.00, 1.09) 0.0761	1.19 (1.06, 1.34) 0.0028	0.03 (0.01, 0.05) 0.0121	
	Age						0.6001*
	<= median	663/1403 (47.3)	635/1469 (43.2)	1.09 (1.01, 1.18)*0.0302	1.22 (1.04, 1.44) 0.0159	0.04 (0.00, 0.08)*0.0300	
	> median	635/1389 (45.7)	536/1323 (40.5)	1.06 (0.99, 1.14) 0.0877	1.19 (1.01, 1.40) 0.0397	0.03 (-0.00, 0.07) 0.0608	
	Gender						0.2944*
	Male	715/1638 (43.7)	648/1602 (40.4)	1.08 (1.00, 1.17)*0.0653	1.14 (0.98, 1.33) 0.0949	0.03 (-0.00, 0.07)*0.0648	
	Female	583/1154 (50.5)	523/1190 (43.9)	1.06 (0.98, 1.14) 0.1429	1.26 (1.06, 1.50) 0.0091	0.04 (0.00, 0.08) 0.0319	
	Race						0.7397*
	White	974/2004 (48.6)	877/2025 (43.3)	1.05 (1.00, 1.11) 0.0599	1.22 (1.07, 1.40) 0.0032	0.04 (0.01, 0.06) 0.0104	
	Black or African	27/ 66 (40.9)	24/ 68 (35.3)	0.98 (0.66, 1.47) 0.9363	1.27 (0.59, 2.77) 0.5400	0.06 (-0.11, 0.22)*0.5028	
	Asian	193/ 551 (35.0)	181/ 550 (32.9)	1.06 (0.90, 1.26)*0.4583	1.04 (0.79, 1.37) 0.7946	0.02 (-0.03, 0.08)*0.4580	
	Other	104/ 171 (60.8)	89/ 149 (59.7)	1.02 (0.85, 1.22)*0.8430	1.12 (0.69, 1.82) 0.6366	0.03 (-0.06, 0.13) 0.4793	
	Geographic region						0.3387*
	Asia	186/ 533 (34.9)	177/ 533 (33.2)	1.05 (0.89, 1.24)*0.5609	1.01 (0.76, 1.34) 0.9580	0.02 (-0.04, 0.07)*0.5607	
	Europe and Saudi Arabia	658/1347 (48.8)	586/1373 (42.7)	1.06 (0.99, 1.13) 0.1102	1.29 (1.10, 1.52) 0.0023	0.04 (0.01, 0.07) 0.0156	
	North America	161/ 391 (41.2)	129/ 375 (34.4)	1.20 (1.00, 1.44)*0.0544	1.28 (0.93, 1.76) 0.1258	0.05 (-0.01, 0.11) 0.1365	
	Latin America	293/ 521 (56.2)	279/ 511 (54.6)	1.03 (0.92, 1.15)*0.5965	1.08 (0.83, 1.41) 0.5483	0.02 (-0.04, 0.07) 0.4969	
	NYHA class at enrolment						0.0360
	II	922/2077 (44.4)	886/2159 (41.0)	1.08 (1.01, 1.16)*0.0274	1.16 (1.01, 1.32) 0.0309	0.01 (-0.02, 0.04) 0.4195	
	III or IV	376/ 715 (52.6)	285/ 632 (45.1)	1.13 (1.02, 1.24) 0.0133	1.34 (1.06, 1.68) 0.0133	0.06 (0.02, 0.11) 0.0099	
	LVEF at enrolment						0.6331*
	<= 49	457/ 967 (47.3)	418/ 952 (43.9)	1.04 (0.96, 1.12) 0.3670	1.23 (1.01, 1.50) 0.0384	0.03 (-0.01, 0.07) 0.1763	
	50-59	464/1013 (45.8)	397/ 998 (39.8)	1.15 (1.04, 1.27)*0.0065	1.24 (1.02, 1.50) 0.0300	0.04 (0.01, 0.08) 0.0236	
	>= 60	377/ 812 (46.4)	356/ 842 (42.3)	1.10 (0.99, 1.22)*0.0897	1.10 (0.89, 1.36) 0.3921	0.01 (-0.03, 0.06) 0.5352	
	NT-proBNP at enrolment						0.6312*
	<= median	650/1394 (46.6)	581/1402 (41.4)	1.03 (0.96, 1.10) 0.3924	1.25 (1.06, 1.47) 0.0076	0.03 (-0.01, 0.06) 0.1014	
	> median	648/1398 (46.4)	589/1389 (42.4)	1.09 (1.01, 1.19)*0.0362	1.14 (0.97, 1.34) 0.1160	0.03 (-0.00, 0.06) 0.0536	
	Type 2 Diabetes Medical History						0.5698*
	Yes	573/1232 (46.5)	529/1237 (42.8)	1.09 (1.00, 1.19)*0.0615	1.16 (0.99, 1.36)*0.0613	0.03 (-0.01, 0.06) 0.0978	
	No	725/1560 (46.5)	642/1555 (41.3)	1.03 (0.97, 1.10) 0.3191	1.23 (1.07, 1.42)*0.0035	0.03 (-0.00, 0.06) 0.0556	
	Atrial fibrillation or flutter at enrolment ECG						0.1402*
	Yes	536/1178 (45.5)	508/1175 (43.2)	1.05 (0.96, 1.15)*0.2686	1.08 (0.91, 1.29) 0.3807	0.02 (-0.02, 0.05) 0.3773	
	No	762/1614 (47.2)	663/1617 (41.0)	1.15 (1.07, 1.24)*0.0004	1.28 (1.10, 1.49) 0.0015	0.04 (0.01, 0.07) 0.0098	
	BMI (kg/m2) at enrolment						0.6145*
	< 30	685/1547 (44.3)	604/1535 (39.3)	1.13 (1.04, 1.22)*0.0056	1.23 (1.05, 1.44) 0.0090	0.05 (0.01, 0.08)*0.0055	
	>= 30	613/1244 (49.3)	566/1254 (45.1)	1.02 (0.95, 1.09) 0.5715	1.14 (0.97, 1.36) 0.1178	0.02 (-0.01, 0.06) 0.2070	
	Baseline eGFR (mL/min/1.73m^2)						0.9981*
	< 60	609/1328 (45.9)	566/1367 (41.4)	1.07 (1.00, 1.14) 0.0539	1.21 (1.03, 1.43) 0.0237	0.04 (0.00, 0.07) 0.0357	
	>= 60	689/1464 (47.1)	605/1424 (42.5)	1.11 (1.02, 1.20)*0.0136	1.17 (0.99, 1.37) 0.0615	0.05 (0.01, 0.08)*0.0133	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.1945
	<= median	653/1396 (46.8)	570/1414 (40.3)	1.16 (1.07, 1.26)*0.0006	1.23 (1.05, 1.45) 0.0116	0.04 (0.01, 0.07) 0.0212	
	> median	645/1396 (46.2)	601/1378 (43.6)	1.03 (0.97, 1.09) 0.3691	1.15 (0.98, 1.36) 0.0923	0.02 (-0.01, 0.05) 0.2649	
	LVEF at enrolment 2						0.1552
	<= 49	457/ 967 (47.3)	418/ 952 (43.9)	1.04 (0.96, 1.12) 0.3670	1.23 (1.01, 1.50) 0.0384	0.03 (-0.01, 0.07) 0.1763	
	>= 50	841/1825 (46.1)	753/1840 (40.9)	1.13 (1.05, 1.21)*0.0017	1.17 (1.02, 1.35) 0.0304	0.03 (0.00, 0.06) 0.0386	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2989*
	Yes	152/ 273 (55.7)	128/ 277 (46.2)	1.20 (1.02, 1.42)*0.0272	1.64 (1.13, 2.39) 0.0101	0.09 (0.01, 0.18)*0.0257	
	No	1146/2519 (45.5)	1043/2515 (41.5)	1.04 (0.99, 1.09) 0.1257	1.15 (1.02, 1.30) 0.0200	0.02 (-0.00, 0.05) 0.0571	
	MRAs at baseline						0.8963*
	Yes	548/1200 (45.7)	500/1208 (41.4)	1.04 (0.97, 1.11) 0.2660	1.21 (1.01, 1.44) 0.0388	0.03 (-0.01, 0.06) 0.1197	
	No	750/1592 (47.1)	671/1584 (42.4)	1.11 (1.03, 1.20)*0.0072	1.18 (1.02, 1.38) 0.0303	0.03 (0.00, 0.06) 0.0463	
	ACEi+ARB at baseline						0.2464*
	Yes	973/2029 (48.0)	867/2047 (42.4)	1.13 (1.06, 1.21)*0.0003	1.25 (1.09, 1.43) 0.0014	0.06 (0.03, 0.09)*0.0003	
	No	325/ 763 (42.6)	304/ 745 (40.8)	1.01 (0.91, 1.11) 0.9164	1.06 (0.85, 1.32) 0.5978	0.01 (-0.04, 0.05) 0.8024	
	ARNI at baseline						0.3373
	Yes	57/ 150 (38.0)	48/ 123 (39.0)	0.97 (0.72, 1.32)*0.8625	1.04 (0.61, 1.78) 0.8850	0.01 (-0.10, 0.12) 0.8032	
	No	1241/2642 (47.0)	1123/2669 (42.1)	1.03 (0.99, 1.08) 0.1837	1.20 (1.07, 1.35) 0.0023	0.03 (0.01, 0.05) 0.0153	
	Beta Blocker at baseline						0.3526
	Yes	1088/2323 (46.8)	979/2321 (42.2)	1.03 (0.98, 1.08) 0.2839	1.19 (1.04, 1.34) 0.0084	0.03 (0.00, 0.05) 0.0476	
	No	210/ 469 (44.8)	192/ 471 (40.8)	1.09 (0.97, 1.23) 0.1318	1.23 (0.93, 1.64) 0.1465	0.04 (-0.01, 0.10) 0.1366	
	Diuretics at baseline						0.2061
	Yes	1168/2493 (46.9)	1037/2492 (41.6)	1.05 (1.00, 1.11) 0.0344	1.23 (1.09, 1.39) 0.0007	0.04 (0.01, 0.06) 0.0040	
	No	130/ 299 (43.5)	134/ 300 (44.7)	0.94 (0.81, 1.09) 0.4298	0.89 (0.62, 1.28) 0.5230	-0.02 (-0.08, 0.05) 0.5694	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	1583/2842 (55.7)	1496/2837 (52.7)	1.01 (0.99, 1.03) 0.2169	1.11 (0.99, 1.25) 0.0861	0.03 (0.00, 0.06)*0.0247	
	Age						0.9824*
	<= median	834/1415 (58.9)	825/1482 (55.7)	1.03 (0.99, 1.07) 0.1246	1.16 (0.98, 1.37) 0.0770	0.03 (-0.00, 0.07)*0.0749	
	> median	749/1427 (52.5)	671/1355 (49.5)	1.06 (0.99, 1.14)*0.1181	1.06 (0.90, 1.26) 0.4877	0.03 (-0.01, 0.07)*0.1174	
	Gender						0.1414*
	Male	904/1656 (54.6)	866/1625 (53.3)	1.02 (0.96, 1.09)*0.4562	1.02 (0.87, 1.19) 0.8461	0.01 (-0.02, 0.05)*0.4561	
	Female	679/1186 (57.3)	630/1212 (52.0)	1.01 (0.97, 1.06) 0.5750	1.24 (1.04, 1.49) 0.0198	0.05 (0.01, 0.09)*0.0094	
	Race						0.5636*
	White	1135/2039 (55.7)	1071/2058 (52.0)	1.07 (1.01, 1.13)*0.0201	1.13 (0.98, 1.30) 0.0874	0.04 (0.01, 0.07)*0.0199	
	Black or African	44/ 67 (65.7)	41/ 71 (57.7)	1.14 (0.87, 1.48)*0.3392	1.38 (0.64, 3.00) 0.4117	0.08 (-0.08, 0.24)*0.3366	
	Asian	277/ 558 (49.6)	281/ 555 (50.6)	0.98 (0.87, 1.10)*0.7414	0.96 (0.74, 1.24) 0.7423	-0.01 (-0.07, 0.05)*0.7414	
	Other	127/ 178 (71.3)	103/ 153 (67.3)	1.06 (0.92, 1.22)*0.4303	1.32 (0.78, 2.22) 0.2977	0.04 (-0.06, 0.14)*0.4283	
	Geographic region						0.4208*
	Asia	269/ 539 (49.9)	274/ 538 (50.9)	0.98 (0.87, 1.10)*0.7373	0.94 (0.72, 1.23) 0.6647	-0.01 (-0.07, 0.05)*0.7373	
	Europe and Saudi Arabia	746/1365 (54.7)	718/1394 (51.5)	1.06 (0.99, 1.14)*0.0980	1.10 (0.93, 1.30) 0.2760	0.03 (-0.01, 0.07)*0.0977	
	North America	239/ 398 (60.1)	205/ 387 (53.0)	1.13 (1.00, 1.28)*0.0464	1.39 (1.01, 1.92) 0.0435	0.07 (0.00, 0.14)*0.0450	
	Latin America	329/ 540 (60.9)	299/ 518 (57.7)	1.06 (0.96, 1.17)*0.2896	1.14 (0.86, 1.51) 0.3463	0.03 (-0.03, 0.09)*0.2887	
	NYHA class at enrolment						0.2010*
	II	1127/2113 (53.3)	1129/2187 (51.6)	1.03 (0.98, 1.09)*0.2607	1.08 (0.94, 1.24) 0.2619	0.02 (-0.01, 0.05)*0.2606	
	III or IV	456/ 729 (62.6)	367/ 649 (56.5)	1.04 (0.98, 1.10) 0.1994	1.26 (0.99, 1.60) 0.0622	0.03 (-0.01, 0.07) 0.1106	
	LVEF at enrolment						0.6142*
	<= 49	564/ 980 (57.6)	540/ 963 (56.1)	0.99 (0.95, 1.04) 0.7515	1.09 (0.89, 1.33) 0.4213	0.01 (-0.03, 0.06)*0.5113	
	50-59	565/1029 (54.9)	514/1017 (50.5)	1.09 (1.00, 1.18)*0.0482	1.17 (0.96, 1.43) 0.1095	0.04 (0.00, 0.09)*0.0477	
	>= 60	454/ 833 (54.5)	442/ 857 (51.6)	1.06 (0.97, 1.16)*0.2282	1.06 (0.85, 1.31) 0.6040	0.03 (-0.02, 0.08)*0.2279	
	NT-proBNP at enrolment						0.4775*
	<= median	795/1418 (56.1)	741/1421 (52.1)	1.08 (1.00, 1.15)*0.0364	1.15 (0.98, 1.36) 0.0926	0.04 (0.00, 0.08)*0.0360	
	> median	788/1424 (55.3)	754/1415 (53.3)	1.00 (0.97, 1.03) 0.9151	1.07 (0.90, 1.26) 0.4488	0.02 (-0.02, 0.06)*0.2726	
	Type 2 Diabetes Medical History						0.5593
	Yes	721/1250 (57.7)	654/1260 (51.9)	1.03 (0.98, 1.07) 0.2568	1.26 (1.08, 1.48)*0.0037	0.06 (0.02, 0.10)*0.0036	
	No	862/1592 (54.1)	842/1577 (53.4)	1.01 (0.99, 1.03) 0.4366	1.03 (0.90, 1.19)*0.6707	0.01 (-0.03, 0.04)*0.6707	
	Atrial fibrillation or flutter at enrolment ECG						0.8878*
	Yes	667/1199 (55.6)	634/1199 (52.9)	1.05 (0.98, 1.13)*0.1764	1.09 (0.91, 1.31) 0.3597	0.03 (-0.01, 0.07)*0.1760	
	No	916/1643 (55.8)	862/1638 (52.6)	1.06 (0.99, 1.13)*0.0725	1.12 (0.96, 1.31) 0.1377	0.03 (-0.00, 0.07)*0.0722	
	BMI (kg/m2) at enrolment						0.3458*
	< 30	832/1571 (53.0)	798/1559 (51.2)	1.00 (0.97, 1.02) 0.7603	1.02 (0.87, 1.19) 0.8270	0.02 (-0.02, 0.05)*0.3207	
	>= 30	751/1270 (59.1)	696/1275 (54.6)	1.08 (1.01, 1.16)*0.0208	1.24 (1.04, 1.48) 0.0189	0.05 (0.01, 0.08)*0.0205	
	Baseline eGFR (mL/min/1.73m^2)						0.2300*
	< 60	726/1359 (53.4)	729/1396 (52.2)	1.02 (0.95, 1.10)*0.5278	1.03 (0.87, 1.22) 0.7075	0.01 (-0.03, 0.05)*0.5278	
	>= 60	857/1483 (57.8)	767/1440 (53.3)	1.03 (0.99, 1.06) 0.1342	1.18 (1.00, 1.40) 0.0485	0.05 (0.01, 0.08)*0.0138	

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Quality of Life (LOCF)	SBP at randomisation						0.2308*
	<= median	807/1424 (56.7)	750/1439 (52.1)	1.00 (0.97, 1.03) 0.8913	1.16 (0.98, 1.37) 0.0857	0.05 (0.01, 0.08)*0.0144	
	> median	776/1418 (54.7)	746/1398 (53.4)	1.03 (0.96, 1.10)*0.4681	1.06 (0.90, 1.25) 0.4827	0.01 (-0.02, 0.05)*0.4680	
	LVEF at enrolment 2						0.3782*
	<= 49	564/ 980 (57.6)	540/ 963 (56.1)	0.99 (0.95, 1.04) 0.7515	1.09 (0.89, 1.33) 0.4213	0.01 (-0.03, 0.06)*0.5113	
	>= 50	1019/1862 (54.7)	956/1874 (51.0)	1.07 (1.01, 1.14)*0.0231	1.12 (0.97, 1.30) 0.1288	0.04 (0.01, 0.07)*0.0229	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9130*
	Yes	180/ 283 (63.6)	171/ 286 (59.8)	1.06 (0.93, 1.21)*0.3498	1.13 (0.76, 1.67) 0.5483	0.04 (-0.04, 0.12)*0.3490	
	No	1403/2559 (54.8)	1325/2551 (51.9)	1.01 (0.99, 1.04) 0.2154	1.11 (0.98, 1.25) 0.1071	0.03 (0.00, 0.06)*0.0386	
	MRAs at baseline						0.4492*
	Yes	689/1227 (56.2)	637/1224 (52.0)	1.00 (0.97, 1.05) 0.8254	1.18 (0.99, 1.41) 0.0710	0.04 (0.00, 0.08)*0.0410	
	No	894/1615 (55.4)	859/1613 (53.3)	1.04 (0.98, 1.11)*0.2309	1.06 (0.90, 1.24) 0.4716	0.02 (-0.01, 0.06)*0.2307	
	ACEi+ARB at baseline						0.0723*
	Yes	1166/2065 (56.5)	1081/2077 (52.0)	1.08 (1.03, 1.15)*0.0044	1.21 (1.05, 1.39) 0.0072	0.04 (0.01, 0.07)*0.0043	
	No	417/ 777 (53.7)	415/ 760 (54.6)	0.98 (0.90, 1.08)*0.7123	0.89 (0.71, 1.11) 0.3112	-0.02 (-0.05, 0.02) 0.3814	
	ARNI at baseline						0.4789*
	Yes	82/ 153 (53.6)	69/ 126 (54.8)	0.96 (0.77, 1.19) 0.6960	0.82 (0.49, 1.37) 0.4403	-0.04 (-0.16, 0.08) 0.4968	
	No	1501/2689 (55.8)	1427/2711 (52.6)	1.06 (1.01, 1.11)*0.0190	1.13 (1.00, 1.28) 0.0461	0.03 (0.01, 0.06)*0.0189	
	Beta Blocker at baseline						0.1939*
	Yes	1316/2360 (55.8)	1226/2356 (52.0)	1.07 (1.02, 1.13)*0.0104	1.14 (1.00, 1.29) 0.0530	0.04 (0.01, 0.07)*0.0102	
	No	267/ 482 (55.4)	270/ 481 (56.1)	0.99 (0.88, 1.10)*0.8175	0.98 (0.74, 1.31) 0.8998	-0.01 (-0.07, 0.06)*0.8174	
	Diuretics at baseline						0.2191*
	Yes	1416/2536 (55.8)	1324/2531 (52.3)	1.02 (0.99, 1.04) 0.1895	1.16 (1.02, 1.31) 0.0235	0.04 (0.01, 0.06)*0.0118	
	No	167/ 306 (54.6)	172/ 306 (56.2)	0.97 (0.84, 1.12)*0.6844	0.82 (0.58, 1.16) 0.2603	-0.02 (-0.10, 0.06)*0.6843	

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AstraZeneca
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Full Analysis Set

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Symptom Burden (LOCF)							
	Overall	1467/2842 (51.6)	1401/2837 (49.4)	1.05 (0.99, 1.10)*0.0922	1.10 (0.97, 1.24) 0.1337	0.02 (-0.00, 0.05)*0.0920	
	Age						0.3188*
	<= median	766/1415 (54.1)	784/1482 (52.9)	1.02 (0.96, 1.10)*0.5060	1.10 (0.93, 1.31) 0.2643	0.01 (-0.02, 0.05)*0.5060	
	> median	701/1427 (49.1)	617/1355 (45.5)	1.08 (1.00, 1.17)*0.0585	1.11 (0.94, 1.32) 0.2133	0.04 (-0.00, 0.07)*0.0579	
	Gender						0.8019*
	Male	811/1656 (49.0)	765/1625 (47.1)	1.04 (0.97, 1.12)*0.2772	1.07 (0.91, 1.25) 0.4338	0.02 (-0.02, 0.05)*0.2769	
	Female	656/1186 (55.3)	636/1212 (52.5)	1.05 (0.98, 1.14)*0.1636	1.13 (0.94, 1.35) 0.1891	0.03 (-0.01, 0.07)*0.1634	
	Race						0.3378*
	White	1081/2039 (53.0)	1040/2058 (50.5)	1.05 (0.99, 1.11)*0.1121	1.08 (0.94, 1.25) 0.2758	0.02 (-0.01, 0.06)*0.1118	
	Black or African	35/ 67 (52.2)	45/ 71 (63.4)	0.82 (0.62, 1.10)*0.1902	0.58 (0.28, 1.23) 0.1577	-0.11 (-0.28, 0.05)*0.1827	
	Asian	231/ 558 (41.4)	224/ 555 (40.4)	1.03 (0.89, 1.18)*0.7248	1.15 (0.87, 1.53) 0.3290	0.01 (-0.05, 0.07)*0.7248	
	Other	120/ 178 (67.4)	92/ 153 (60.1)	1.12 (0.95, 1.32)*0.1732	1.46 (0.87, 2.43) 0.1502	0.07 (-0.03, 0.18)*0.1687	
	Geographic region						0.6592*
	Asia	220/ 539 (40.8)	216/ 538 (40.1)	1.02 (0.88, 1.18)*0.8234	1.10 (0.82, 1.47) 0.5378	0.01 (-0.05, 0.07)*0.8234	
	Europe and Saudi Arabia	731/1365 (53.6)	703/1394 (50.4)	1.06 (0.99, 1.14)*0.1008	1.11 (0.93, 1.32) 0.2305	0.03 (-0.01, 0.07)*0.1005	
	North America	207/ 398 (52.0)	184/ 387 (47.5)	1.09 (0.95, 1.26)*0.2119	1.20 (0.88, 1.63) 0.2539	0.04 (-0.03, 0.11)*0.2105	
	Latin America	309/ 540 (57.2)	298/ 518 (57.5)	0.99 (0.90, 1.10)*0.9197	1.00 (0.76, 1.33) 0.9721	-0.00 (-0.06, 0.06)*0.9197	
	NYHA class at enrolment						0.6182*
	II	1023/2113 (48.4)	1027/2187 (47.0)	1.03 (0.97, 1.10)*0.3394	1.10 (0.95, 1.26) 0.1935	0.01 (-0.02, 0.04)*0.3394	
	III or IV	444/ 729 (60.9)	373/ 649 (57.5)	1.06 (0.97, 1.16)*0.1969	1.14 (0.89, 1.45) 0.2926	0.03 (-0.02, 0.09)*0.1956	
	LVEF at enrolment						0.0526*
	<= 49	490/ 980 (50.0)	501/ 963 (52.0)	0.96 (0.88, 1.05)*0.3720	0.94 (0.76, 1.16) 0.5492	-0.02 (-0.06, 0.02)*0.3719	
	50-59	523/1029 (50.8)	482/1017 (47.4)	1.07 (0.98, 1.17)*0.1209	1.17 (0.95, 1.43) 0.1361	0.03 (-0.01, 0.08)*0.1203	
	>= 60	454/ 833 (54.5)	418/ 857 (48.8)	1.12 (1.02, 1.23)*0.0187	1.22 (0.98, 1.52) 0.0730	0.06 (0.01, 0.10)*0.0183	
	NT-proBNP at enrolment						0.1704*
	<= median	705/1418 (49.7)	701/1421 (49.3)	1.01 (0.94, 1.09)*0.8369	1.03 (0.87, 1.21) 0.7537	0.00 (-0.03, 0.04)*0.8369	
	> median	762/1424 (53.5)	699/1415 (49.4)	1.08 (1.01, 1.16)*0.0286	1.18 (0.99, 1.40) 0.0694	0.04 (0.00, 0.08)*0.0283	
	Type 2 Diabetes Medical History						0.4343*
	Yes	661/1250 (52.9)	623/1260 (49.4)	1.07 (0.99, 1.15)*0.0853	1.15 (0.98, 1.34)*0.0852	0.03 (-0.00, 0.07)*0.0849	
	No	806/1592 (50.6)	778/1577 (49.3)	1.03 (0.96, 1.10)*0.4664	1.05 (0.92, 1.21)*0.4664	0.01 (-0.02, 0.05)*0.4663	
	Atrial fibrillation or flutter at enrolment ECG						0.9772*
	Yes	635/1199 (53.0)	608/1199 (50.7)	1.04 (0.97, 1.13)*0.2700	1.11 (0.92, 1.34) 0.2815	0.02 (-0.02, 0.06)*0.2697	
	No	832/1643 (50.6)	793/1638 (48.4)	1.05 (0.98, 1.12)*0.2024	1.09 (0.93, 1.27) 0.2896	0.02 (-0.01, 0.06)*0.2021	
	BMI (kg/m2) at enrolment						0.4885*
	< 30	761/1571 (48.4)	710/1559 (45.5)	1.06 (0.99, 1.15)*0.1045	1.14 (0.97, 1.35) 0.1135	0.03 (-0.01, 0.06)*0.1041	
	>= 30	705/1270 (55.5)	690/1275 (54.1)	1.03 (0.96, 1.10)*0.4799	1.04 (0.87, 1.25) 0.6433	0.01 (-0.02, 0.05)*0.4798	
	Baseline eGFR (mL/min/1.73m^2)						0.8498*
	< 60	682/1359 (50.2)	667/1396 (47.8)	1.05 (0.97, 1.13)*0.2069	1.10 (0.93, 1.31) 0.2780	0.02 (-0.01, 0.06)*0.2067	
	>= 60	785/1483 (52.9)	733/1440 (50.9)	1.04 (0.97, 1.12)*0.2723	1.09 (0.92, 1.29) 0.3292	0.02 (-0.02, 0.06)*0.2719	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)	SBP at randomisation						0.0389*
	<= median	747/1424 (52.5)	684/1439 (47.5)	1.10 (1.03, 1.19)*0.0085	1.16 (0.98, 1.37) 0.0821	0.05 (0.01, 0.09)*0.0083	
	> median	720/1418 (50.8)	717/1398 (51.3)	0.99 (0.92, 1.06)*0.7859	1.03 (0.87, 1.23) 0.7274	-0.01 (-0.04, 0.03)*0.7859	
	LVEF at enrolment 2						0.0201*
	<= 49	490/ 980 (50.0)	501/ 963 (52.0)	0.96 (0.88, 1.05)*0.3720	0.94 (0.76, 1.16) 0.5492	-0.02 (-0.06, 0.02)*0.3719	
	>= 50	977/1862 (52.5)	900/1874 (48.0)	1.09 (1.02, 1.16)*0.0067	1.19 (1.03, 1.38) 0.0217	0.04 (0.01, 0.08)*0.0065	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1432*
	Yes	175/ 283 (61.8)	185/ 286 (64.7)	0.96 (0.84, 1.08)*0.4814	0.95 (0.64, 1.40) 0.7798	-0.03 (-0.11, 0.05)*0.4809	
	No	1292/2559 (50.5)	1216/2551 (47.7)	1.06 (1.00, 1.12)*0.0438	1.12 (0.98, 1.27) 0.0872	0.03 (0.00, 0.06)*0.0436	
	MRAs at baseline						0.6072*
	Yes	627/1227 (51.1)	589/1224 (48.1)	1.06 (0.98, 1.15)*0.1405	1.11 (0.92, 1.33) 0.2759	0.03 (-0.01, 0.07)*0.1400	
	No	840/1615 (52.0)	812/1613 (50.3)	1.03 (0.97, 1.11)*0.3423	1.09 (0.93, 1.28) 0.2864	0.02 (-0.02, 0.05)*0.3421	
	ACEi+ARB at baseline						0.1439*
	Yes	1101/2065 (53.3)	1035/2077 (49.8)	1.07 (1.01, 1.14)*0.0249	1.15 (1.00, 1.32) 0.0585	0.03 (0.00, 0.07)*0.0247	
	No	366/ 777 (47.1)	366/ 760 (48.2)	0.98 (0.88, 1.09)*0.6792	0.98 (0.77, 1.23) 0.8341	-0.01 (-0.06, 0.04)*0.6792	
	ARNI at baseline						0.0555*
	Yes	54/ 153 (35.3)	56/ 126 (44.4)	0.79 (0.59, 1.06)*0.1193	0.70 (0.39, 1.24) 0.2175	-0.09 (-0.21, 0.02)*0.1194	
	No	1413/2689 (52.5)	1345/2711 (49.6)	1.06 (1.01, 1.12)*0.0311	1.12 (0.99, 1.27) 0.0660	0.03 (0.00, 0.06)*0.0309	
	Beta Blocker at baseline						0.4629*
	Yes	1221/2360 (51.7)	1156/2356 (49.1)	1.05 (1.00, 1.12)*0.0667	1.09 (0.96, 1.25) 0.1916	0.03 (-0.00, 0.06)*0.0665	
	No	246/ 482 (51.0)	245/ 481 (50.9)	1.00 (0.89, 1.13)*0.9748	1.12 (0.83, 1.51) 0.4511	0.00 (-0.06, 0.06)*0.9748	
	Diuretics at baseline						0.2585*
	Yes	1304/2536 (51.4)	1258/2531 (49.7)	1.03 (0.98, 1.09)*0.2220	1.09 (0.96, 1.24) 0.1838	0.02 (-0.01, 0.04)*0.2218	
	No	163/ 306 (53.3)	143/ 306 (46.7)	1.14 (0.97, 1.34)*0.1069	1.14 (0.78, 1.68) 0.4934	0.07 (-0.01, 0.14)*0.1052	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	1248/2842 (43.9)	1209/2837 (42.6)	1.03 (0.97, 1.09)*0.3239	1.07 (0.94, 1.22) 0.3007	0.01 (-0.01, 0.04)*0.3238	
	Age						0.0580*
	<= median	621/1415 (43.9)	666/1482 (44.9)	0.98 (0.90, 1.06)*0.5689	0.95 (0.79, 1.14) 0.5534	-0.01 (-0.05, 0.03)*0.5688	
	> median	627/1427 (43.9)	543/1355 (40.1)	1.10 (1.00, 1.20)*0.0394	1.22 (1.02, 1.47) 0.0307	0.04 (0.00, 0.08)*0.0388	
	Gender						0.6980*
	Male	742/1656 (44.8)	714/1625 (43.9)	1.02 (0.94, 1.10)*0.6168	1.08 (0.91, 1.28) 0.3821	0.01 (-0.03, 0.04)*0.6167	
	Female	506/1186 (42.7)	495/1212 (40.8)	1.04 (0.95, 1.15)*0.3655	1.06 (0.87, 1.29) 0.5859	0.02 (-0.02, 0.06)*0.3654	
	Race						0.9306*
	White	878/2039 (43.1)	861/2058 (41.8)	1.03 (0.96, 1.11)*0.4282	1.04 (0.89, 1.21) 0.6077	0.01 (-0.02, 0.04)*0.4282	
	Black or African	29/ 67 (43.3)	33/ 71 (46.5)	0.93 (0.64, 1.35)*0.7065	1.01 (0.41, 2.52) 0.9797	-0.03 (-0.20, 0.13)*0.7059	
	Asian	246/ 558 (44.1)	239/ 555 (43.1)	1.02 (0.90, 1.17)*0.7308	1.15 (0.86, 1.54) 0.3400	0.01 (-0.05, 0.07)*0.7307	
	Other	95/ 178 (53.4)	76/ 153 (49.7)	1.07 (0.87, 1.33)*0.5037	1.35 (0.77, 2.37) 0.3022	0.04 (-0.07, 0.14)*0.5019	
	Geographic region						0.4896*
	Asia	237/ 539 (44.0)	232/ 538 (43.1)	1.02 (0.89, 1.17)*0.7791	1.17 (0.87, 1.57) 0.3105	0.01 (-0.05, 0.07)*0.7791	
	Europe and Saudi Arabia	597/1365 (43.7)	593/1394 (42.5)	1.03 (0.94, 1.12)*0.5257	1.06 (0.89, 1.27) 0.5253	0.01 (-0.02, 0.05)*0.5257	
	North America	146/ 398 (36.7)	152/ 387 (39.3)	0.93 (0.78, 1.12)*0.4543	0.88 (0.60, 1.29) 0.5059	-0.03 (-0.09, 0.04)*0.4541	
	Latin America	268/ 540 (49.6)	232/ 518 (44.8)	1.11 (0.98, 1.26)*0.1157	1.17 (0.86, 1.59) 0.3046	0.05 (-0.01, 0.11)*0.1143	
	NYHA class at enrolment						0.2429*
	II	901/2113 (42.6)	926/2187 (42.3)	1.01 (0.94, 1.08)*0.8425	1.01 (0.87, 1.17) 0.9383	0.00 (-0.03, 0.03)*0.8425	
	III or IV	347/ 729 (47.6)	283/ 649 (43.6)	1.09 (0.97, 1.23)*0.1387	1.30 (1.00, 1.68) 0.0501	0.04 (-0.01, 0.09)*0.1369	
	LVEF at enrolment						0.4727*
	<= 49	425/ 980 (43.4)	423/ 963 (43.9)	0.99 (0.89, 1.09)*0.8042	1.07 (0.86, 1.34) 0.5278	-0.01 (-0.05, 0.04)*0.8042	
	50-59	437/1029 (42.5)	419/1017 (41.2)	1.03 (0.93, 1.14)*0.5608	1.05 (0.85, 1.30) 0.6650	0.01 (-0.03, 0.06)*0.5607	
	>= 60	386/ 833 (46.3)	367/ 857 (42.8)	1.08 (0.97, 1.20)*0.1463	1.10 (0.87, 1.40) 0.4271	0.04 (-0.01, 0.08)*0.1459	
	NT-proBNP at enrolment						0.8222*
	<= median	614/1418 (43.3)	601/1421 (42.3)	1.02 (0.94, 1.11)*0.5880	1.02 (0.86, 1.23) 0.7950	0.01 (-0.03, 0.05)*0.5879	
	> median	634/1424 (44.5)	607/1415 (42.9)	1.04 (0.95, 1.13)*0.3829	1.12 (0.93, 1.35) 0.2221	0.02 (-0.02, 0.05)*0.3827	
	Type 2 Diabetes Medical History						0.4498*
	Yes	557/1250 (44.6)	531/1260 (42.1)	1.06 (0.97, 1.16)*0.2219	1.10 (0.94, 1.29)*0.2218	0.02 (-0.01, 0.06)*0.2216	
	No	691/1592 (43.4)	678/1577 (43.0)	1.01 (0.93, 1.09)*0.8151	1.02 (0.88, 1.17)*0.8151	0.00 (-0.03, 0.04)*0.8151	
	Atrial fibrillation or flutter at enrolment ECG						0.0547*
	Yes	544/1199 (45.4)	493/1199 (41.1)	1.10 (1.01, 1.21)*0.0358	1.20 (0.99, 1.46) 0.0698	0.04 (0.00, 0.08)*0.0354	
	No	704/1643 (42.8)	716/1638 (43.7)	0.98 (0.91, 1.06)*0.6177	0.99 (0.83, 1.17) 0.8697	-0.01 (-0.04, 0.03)*0.6177	
	BMI (kg/m2) at enrolment						0.5866*
	< 30	669/1571 (42.6)	654/1559 (41.9)	1.02 (0.94, 1.10)*0.7194	0.99 (0.83, 1.17) 0.8798	0.01 (-0.03, 0.04)*0.7194	
	>= 30	578/1270 (45.5)	553/1275 (43.4)	1.05 (0.96, 1.14)*0.2776	1.18 (0.97, 1.43) 0.0910	0.02 (-0.02, 0.06)*0.2774	
	Baseline eGFR (mL/min/1.73m^2)						0.7575*
	< 60	581/1359 (42.8)	585/1396 (41.9)	1.02 (0.94, 1.11)*0.6530	1.12 (0.93, 1.35) 0.2178	0.01 (-0.03, 0.05)*0.6530	
	>= 60	667/1483 (45.0)	623/1440 (43.3)	1.04 (0.96, 1.13)*0.3514	1.02 (0.86, 1.22) 0.7984	0.02 (-0.02, 0.05)*0.3511	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.9969*
	<= median	625/1424 (43.9)	613/1439 (42.6)	1.03 (0.95, 1.12)*0.4856	1.08 (0.89, 1.30) 0.4379	0.01 (-0.02, 0.05)*0.4855	
	> median	623/1418 (43.9)	596/1398 (42.6)	1.03 (0.95, 1.12)*0.4855	1.07 (0.89, 1.28) 0.4679	0.01 (-0.02, 0.05)*0.4854	
	LVEF at enrolment 2						0.3070*
	<= 49	425/ 980 (43.4)	423/ 963 (43.9)	0.99 (0.89, 1.09)*0.8042	1.07 (0.86, 1.34) 0.5278	-0.01 (-0.05, 0.04)*0.8042	
	>= 50	823/1862 (44.2)	786/1874 (41.9)	1.05 (0.98, 1.13)*0.1637	1.07 (0.91, 1.26) 0.3913	0.02 (-0.01, 0.05)*0.1634	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9785*
	Yes	139/ 283 (49.1)	136/ 286 (47.6)	1.03 (0.87, 1.22)*0.7089	1.15 (0.77, 1.73) 0.4891	0.02 (-0.07, 0.10)*0.7089	
	No	1109/2559 (43.3)	1073/2551 (42.1)	1.03 (0.97, 1.10)*0.3568	1.06 (0.93, 1.21) 0.3988	0.01 (-0.01, 0.04)*0.3567	
	MRAs at baseline						0.8334*
	Yes	538/1227 (43.8)	517/1224 (42.2)	1.04 (0.95, 1.14)*0.4215	1.15 (0.94, 1.40) 0.1735	0.02 (-0.02, 0.06)*0.4213	
	No	710/1615 (44.0)	692/1613 (42.9)	1.02 (0.95, 1.11)*0.5430	1.02 (0.86, 1.21) 0.8211	0.01 (-0.02, 0.04)*0.5429	
	ACEi+ARB at baseline						0.2843*
	Yes	930/2065 (45.0)	890/2077 (42.9)	1.05 (0.98, 1.13)*0.1565	1.13 (0.97, 1.31) 0.1113	0.02 (-0.01, 0.05)*0.1563	
	No	318/ 777 (40.9)	319/ 760 (42.0)	0.98 (0.87, 1.10)*0.6770	0.92 (0.72, 1.18) 0.5292	-0.01 (-0.06, 0.04)*0.6770	
	ARNI at baseline						0.4431*
	Yes	51/ 153 (33.3)	46/ 126 (36.5)	0.91 (0.66, 1.26)*0.5789	0.96 (0.51, 1.80) 0.8883	-0.03 (-0.14, 0.08)*0.5801	
	No	1197/2689 (44.5)	1163/2711 (42.9)	1.04 (0.98, 1.10)*0.2315	1.08 (0.94, 1.23) 0.2667	0.02 (-0.01, 0.04)*0.2314	
	Beta Blocker at baseline						0.6088*
	Yes	1023/2360 (43.3)	984/2356 (41.8)	1.04 (0.97, 1.11)*0.2721	1.10 (0.95, 1.27) 0.1914	0.02 (-0.01, 0.04)*0.2719	
	No	225/ 482 (46.7)	225/ 481 (46.8)	1.00 (0.87, 1.14)*0.9759	0.95 (0.70, 1.28) 0.7249	-0.00 (-0.06, 0.06)*0.9759	
	Diuretics at baseline						0.4273*
	Yes	1109/2536 (43.7)	1065/2531 (42.1)	1.04 (0.98, 1.11)*0.2349	1.10 (0.96, 1.26) 0.1668	0.02 (-0.01, 0.04)*0.2348	
	No	139/ 306 (45.4)	144/ 306 (47.1)	0.97 (0.81, 1.15)*0.6853	0.83 (0.55, 1.26) 0.3900	-0.02 (-0.10, 0.06)*0.6852	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	1383/2842 (48.7)	1335/2837 (47.1)	1.03 (0.98, 1.09)*0.2258	1.08 (0.96, 1.22) 0.2178	0.02 (-0.01, 0.04)*0.2256	
	Age						0.2628*
	<= median	701/1415 (49.5)	730/1482 (49.3)	1.01 (0.93, 1.08)*0.8790	1.06 (0.89, 1.25) 0.5128	0.00 (-0.03, 0.04)*0.8790	
	> median	682/1427 (47.8)	605/1355 (44.6)	1.07 (0.99, 1.16)*0.0970	1.12 (0.94, 1.32) 0.2116	0.03 (-0.01, 0.07)*0.0963	
	Gender						0.3851*
	Male	763/1656 (46.1)	739/1625 (45.5)	1.01 (0.94, 1.09)*0.7311	1.03 (0.88, 1.21) 0.7039	0.01 (-0.03, 0.04)*0.7310	
	Female	620/1186 (52.3)	596/1212 (49.2)	1.06 (0.98, 1.15)*0.1289	1.13 (0.95, 1.36) 0.1698	0.03 (-0.01, 0.07)*0.1286	
	Race						0.6766*
	White	1029/2039 (50.5)	991/2058 (48.2)	1.05 (0.98, 1.12)*0.1389	1.07 (0.93, 1.23) 0.3175	0.02 (-0.01, 0.05)*0.1387	
	Black or African	35/ 67 (52.2)	40/ 71 (56.3)	0.93 (0.68, 1.26)*0.6298	0.90 (0.43, 1.88) 0.7823	-0.04 (-0.21, 0.13)*0.6287	
	Asian	209/ 558 (37.5)	215/ 555 (38.7)	0.97 (0.83, 1.12)*0.6593	1.05 (0.79, 1.40) 0.7385	-0.01 (-0.07, 0.04)*0.6593	
	Other	110/ 178 (61.8)	89/ 153 (58.2)	1.06 (0.89, 1.27)*0.5034	1.44 (0.84, 2.49) 0.1849	0.04 (-0.07, 0.14)*0.5017	
	Geographic region						0.6892*
	Asia	201/ 539 (37.3)	206/ 538 (38.3)	0.97 (0.84, 1.14)*0.7354	1.04 (0.77, 1.39) 0.8100	-0.01 (-0.07, 0.05)*0.7354	
	Europe and Saudi Arabia	682/1365 (50.0)	659/1394 (47.3)	1.06 (0.98, 1.14)*0.1577	1.09 (0.92, 1.29) 0.3245	0.03 (-0.01, 0.06)*0.1575	
	North America	187/ 398 (47.0)	185/ 387 (47.8)	1.06 (0.95, 1.19) 0.3082	1.00 (0.74, 1.36) 0.9980	0.01 (-0.05, 0.07) 0.7085	
	Latin America	313/ 540 (58.0)	285/ 518 (55.0)	1.05 (0.95, 1.17)*0.3349	1.20 (0.91, 1.60) 0.1999	0.03 (-0.03, 0.09)*0.3341	
	NYHA class at enrolment						0.5148*
	II	961/2113 (45.5)	979/2187 (44.8)	1.02 (0.95, 1.09)*0.6372	1.08 (0.94, 1.24) 0.2854	0.01 (-0.02, 0.04)*0.6372	
	III or IV	422/ 729 (57.9)	356/ 649 (54.9)	1.06 (0.96, 1.16)*0.2581	1.12 (0.88, 1.41) 0.3572	0.03 (-0.02, 0.08)*0.2569	
	LVEF at enrolment						0.4317*
	<= 49	472/ 980 (48.2)	454/ 963 (47.1)	1.02 (0.93, 1.12)*0.6530	1.13 (0.92, 1.39) 0.2542	0.01 (-0.03, 0.05)*0.6530	
	50-59	483/1029 (46.9)	477/1017 (46.9)	1.00 (0.91, 1.10)*0.9869	0.98 (0.81, 1.20) 0.8652	0.00 (-0.04, 0.04)*0.9869	
	>= 60	428/ 833 (51.4)	404/ 857 (47.1)	1.09 (0.99, 1.20)*0.0816	1.15 (0.93, 1.43) 0.1991	0.04 (-0.01, 0.09)*0.0811	
	NT-proBNP at enrolment						0.1003*
	<= median	655/1418 (46.2)	665/1421 (46.8)	0.99 (0.91, 1.07)*0.7461	0.98 (0.83, 1.15) 0.7769	-0.01 (-0.04, 0.03)*0.7461	
	> median	728/1424 (51.1)	669/1415 (47.3)	1.08 (1.00, 1.17)*0.0407	1.20 (1.01, 1.42) 0.0385	0.04 (0.00, 0.08)*0.0403	
	Type 2 Diabetes Medical History						0.3080*
	Yes	635/1250 (50.8)	600/1260 (47.6)	1.07 (0.99, 1.16)*0.1112	1.14 (0.97, 1.33)*0.1110	0.03 (-0.01, 0.07)*0.1108	
	No	748/1592 (47.0)	735/1577 (46.6)	1.01 (0.94, 1.09)*0.8314	1.02 (0.88, 1.17)*0.8314	0.00 (-0.03, 0.04)*0.8314	
	Atrial fibrillation or flutter at enrolment ECG						0.9112*
	Yes	604/1199 (50.4)	582/1199 (48.5)	1.04 (0.96, 1.13)*0.3690	1.11 (0.93, 1.34) 0.2474	0.02 (-0.02, 0.06)*0.3688	
	No	779/1643 (47.4)	753/1638 (46.0)	1.03 (0.96, 1.11)*0.4077	1.05 (0.90, 1.23) 0.5216	0.01 (-0.02, 0.05)*0.4076	
	BMI (kg/m2) at enrolment						0.9979*
	< 30	708/1571 (45.1)	679/1559 (43.6)	1.03 (0.96, 1.12)*0.3942	1.10 (0.93, 1.30) 0.2496	0.02 (-0.02, 0.05)*0.3941	
	>= 30	675/1270 (53.1)	655/1275 (51.4)	1.03 (0.96, 1.11)*0.3696	1.06 (0.89, 1.26) 0.4996	0.02 (-0.02, 0.06)*0.3694	
	Baseline eGFR (mL/min/1.73m^2)						0.4132*
	< 60	667/1359 (49.1)	647/1396 (46.3)	1.06 (0.98, 1.15)*0.1510	1.14 (0.96, 1.35) 0.1236	0.03 (-0.01, 0.06)*0.1508	
	>= 60	716/1483 (48.3)	687/1440 (47.7)	1.01 (0.94, 1.09)*0.7569	1.02 (0.86, 1.20) 0.8534	0.01 (-0.03, 0.04)*0.7569	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
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Full Analysis Set

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Symptom Frequency (LOCF)	SBP at randomisation						0.1687*
	<= median	685/1424 (48.1)	644/1439 (44.8)	1.07 (0.99, 1.16)*0.0724	1.12 (0.95, 1.33) 0.1801	0.03 (-0.00, 0.07)*0.0721	
	> median	698/1418 (49.2)	691/1398 (49.4)	1.00 (0.92, 1.07)*0.9140	1.03 (0.87, 1.22) 0.7338	-0.00 (-0.04, 0.03)*0.9140	
	LVEF at enrolment 2						0.7516*
	<= 49	472/ 980 (48.2)	454/ 963 (47.1)	1.02 (0.93, 1.12)*0.6530	1.13 (0.92, 1.39) 0.2542	0.01 (-0.03, 0.05)*0.6530	
	>= 50	911/1862 (48.9)	881/1874 (47.0)	1.04 (0.97, 1.11)*0.2417	1.06 (0.91, 1.22) 0.4687	0.02 (-0.01, 0.05)*0.2415	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6008*
	Yes	185/ 283 (65.4)	175/ 286 (61.2)	1.07 (0.94, 1.21)*0.3012	1.63 (1.10, 2.44) 0.0161	0.04 (-0.04, 0.12)*0.3003	
	No	1198/2559 (46.8)	1160/2551 (45.5)	1.03 (0.97, 1.09)*0.3357	1.04 (0.91, 1.18) 0.5694	0.01 (-0.01, 0.04)*0.3356	
	MRAs at baseline						0.8172*
	Yes	587/1227 (47.8)	562/1224 (45.9)	1.04 (0.96, 1.13)*0.3397	1.10 (0.91, 1.32) 0.3301	0.02 (-0.02, 0.06)*0.3395	
	No	796/1615 (49.3)	773/1613 (47.9)	1.03 (0.96, 1.10)*0.4380	1.07 (0.91, 1.25) 0.4217	0.01 (-0.02, 0.05)*0.4379	
	ACEi+ARB at baseline						0.0523*
	Yes	1044/2065 (50.6)	983/2077 (47.3)	1.07 (1.00, 1.14)*0.0378	1.14 (0.99, 1.32) 0.0654	0.03 (0.00, 0.06)*0.0376	
	No	339/ 777 (43.6)	352/ 760 (46.3)	0.94 (0.84, 1.05)*0.2899	0.92 (0.74, 1.16) 0.4944	-0.03 (-0.08, 0.02)*0.2897	
	ARNI at baseline						0.1282*
	Yes	58/ 153 (37.9)	57/ 126 (45.2)	0.84 (0.63, 1.11)*0.2149	0.96 (0.54, 1.70) 0.8785	-0.07 (-0.19, 0.04)*0.2157	
	No	1325/2689 (49.3)	1278/2711 (47.1)	1.05 (0.99, 1.10)*0.1168	1.09 (0.96, 1.23) 0.1780	0.02 (-0.01, 0.05)*0.1166	
	Beta Blocker at baseline						0.3533*
	Yes	1158/2360 (49.1)	1105/2356 (46.9)	1.05 (0.99, 1.11)*0.1367	1.08 (0.95, 1.23) 0.2655	0.02 (-0.01, 0.05)*0.1364	
	No	225/ 482 (46.7)	230/ 481 (47.8)	0.98 (0.85, 1.12)*0.7239	1.09 (0.81, 1.46) 0.5849	-0.01 (-0.07, 0.05)*0.7239	
	Diuretics at baseline						0.5472*
	Yes	1229/2536 (48.5)	1193/2531 (47.1)	1.03 (0.97, 1.09)*0.3446	1.09 (0.96, 1.23) 0.1921	0.01 (-0.01, 0.04)*0.3445	
	No	154/ 306 (50.3)	142/ 306 (46.4)	1.08 (0.92, 1.28)*0.3322	0.95 (0.64, 1.40) 0.7966	0.04 (-0.04, 0.12)*0.3313	

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Social Limitation (LOCF)							
	Overall	1282/2669 (48.0)	1249/2664 (46.9)	1.01 (0.98, 1.04) 0.6148	1.06 (0.94, 1.20) 0.3503	0.00 (-0.02, 0.02) 0.6468	
	Age						0.6668
	<= median	683/1352 (50.5)	698/1422 (49.1)	1.02 (0.98, 1.06) 0.2993	1.11 (0.94, 1.32) 0.2100	0.01 (-0.02, 0.05)*0.4508	
	> median	599/1317 (45.5)	551/1242 (44.4)	1.00 (0.94, 1.05) 0.9107	1.02 (0.86, 1.22) 0.8143	-0.00 (-0.03, 0.03) 0.9781	
	Gender						0.7109
	Male	740/1568 (47.2)	715/1518 (47.1)	1.00 (0.96, 1.04) 0.9088	1.02 (0.87, 1.20) 0.7999	-0.00 (-0.02, 0.02) 0.9290	
	Female	542/1101 (49.2)	534/1146 (46.6)	1.01 (0.96, 1.07) 0.6106	1.10 (0.92, 1.33) 0.2997	0.01 (-0.02, 0.05) 0.4460	
	Race						0.6662
	White	958/1925 (49.8)	925/1952 (47.4)	1.00 (0.96, 1.04) 0.9633	1.08 (0.94, 1.24) 0.2839	0.00 (-0.02, 0.03) 0.7719	
	Black or African	27/ 61 (44.3)	34/ 67 (50.7)	0.87 (0.60, 1.26)*0.4658	0.79 (0.35, 1.77) 0.5598	-0.02 (-0.17, 0.14) 0.8123	
	Asian	186/ 510 (36.5)	203/ 500 (40.6)	0.95 (0.86, 1.06) 0.3505	0.89 (0.67, 1.20) 0.4460	-0.02 (-0.07, 0.03) 0.3622	
	Other	111/ 173 (64.2)	87/ 145 (60.0)	1.08 (0.91, 1.28) 0.4012	1.46 (0.87, 2.43) 0.1487	0.04 (-0.07, 0.15)*0.4462	
	Geographic region						0.2208*
	Asia	182/ 496 (36.7)	198/ 486 (40.7)	0.95 (0.85, 1.06) 0.3665	0.88 (0.66, 1.19) 0.4082	-0.02 (-0.07, 0.03) 0.3462	
	Europe and Saudi Arabia	641/1299 (49.3)	628/1323 (47.5)	1.04 (0.96, 1.13)*0.3361	1.03 (0.87, 1.22) 0.7283	0.02 (-0.02, 0.06)*0.3360	
	North America	175/ 372 (47.0)	169/ 359 (47.1)	1.03 (0.91, 1.17) 0.6395	1.06 (0.77, 1.46) 0.7065	0.01 (-0.06, 0.07) 0.8314	
	Latin America	284/ 502 (56.6)	254/ 496 (51.2)	1.10 (0.98, 1.24)*0.0899	1.34 (1.01, 1.79) 0.0419	0.05 (-0.01, 0.12)*0.0887	
	NYHA class at enrolment						0.1885*
	II	917/1986 (46.2)	952/2059 (46.2)	1.00 (0.93, 1.07)*0.9680	1.03 (0.89, 1.18) 0.7286	-0.00 (-0.03, 0.03)*0.9680	
	III or IV	365/ 683 (53.4)	297/ 604 (49.2)	1.03 (0.95, 1.11) 0.4913	1.24 (0.97, 1.59) 0.0828	0.03 (-0.02, 0.08) 0.2066	
	LVEF at enrolment						0.4212
	<= 49	451/ 928 (48.6)	467/ 912 (51.2)	0.99 (0.93, 1.04) 0.6389	0.97 (0.79, 1.19) 0.7422	-0.01 (-0.05, 0.02) 0.5117	
	50-59	457/ 970 (47.1)	417/ 956 (43.6)	1.03 (0.97, 1.10) 0.2961	1.09 (0.89, 1.34) 0.3930	0.02 (-0.02, 0.05) 0.3989	
	>= 60	374/ 771 (48.5)	365/ 796 (45.9)	1.06 (0.95, 1.17)*0.2927	1.15 (0.91, 1.44) 0.2346	0.03 (-0.02, 0.08)*0.2925	
	NT-proBNP at enrolment						0.6358
	<= median	628/1334 (47.1)	632/1350 (46.8)	1.00 (0.95, 1.05) 0.9811	1.03 (0.87, 1.22) 0.7210	0.00 (-0.03, 0.03) 0.9547	
	> median	654/1335 (49.0)	616/1313 (46.9)	1.02 (0.97, 1.07) 0.5109	1.09 (0.92, 1.30) 0.3240	0.01 (-0.02, 0.04) 0.5527	
	Type 2 Diabetes Medical History						0.7728
	Yes	583/1169 (49.9)	563/1186 (47.5)	1.02 (0.96, 1.08) 0.4976	1.10 (0.94, 1.29)*0.2438	0.01 (-0.02, 0.05) 0.4539	
	No	699/1500 (46.6)	686/1478 (46.4)	1.00 (0.97, 1.04) 0.8351	1.01 (0.87, 1.16)*0.9190	0.00 (-0.02, 0.03) 0.9096	
	Atrial fibrillation or flutter at enrolment ECG						0.1848
	Yes	547/1113 (49.1)	539/1123 (48.0)	0.98 (0.93, 1.03) 0.3874	1.05 (0.87, 1.27) 0.5951	-0.01 (-0.04, 0.02) 0.4819	
	No	735/1556 (47.2)	710/1541 (46.1)	1.02 (0.98, 1.07) 0.3163	1.07 (0.91, 1.25) 0.4306	0.01 (-0.01, 0.04) 0.3334	
	BMI (kg/m2) at enrolment						0.6917
	< 30	676/1478 (45.7)	641/1451 (44.2)	1.02 (0.97, 1.07) 0.4690	1.08 (0.91, 1.27) 0.3799	0.01 (-0.02, 0.03) 0.5297	
	>= 30	606/1190 (50.9)	606/1211 (50.0)	1.02 (0.96, 1.07) 0.5990	1.04 (0.87, 1.25) 0.6412	0.00 (-0.03, 0.04) 0.8156	
	Baseline eGFR (mL/min/1.73m^2)						0.8036
	< 60	591/1266 (46.7)	591/1297 (45.6)	1.01 (0.96, 1.06) 0.7456	1.07 (0.90, 1.28) 0.4431	0.01 (-0.03, 0.04) 0.6999	
	>= 60	691/1403 (49.3)	658/1366 (48.2)	1.01 (0.97, 1.05) 0.6725	1.04 (0.88, 1.23) 0.6443	0.01 (-0.03, 0.05)*0.5691	

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Social Limitation (LOCF)	SBP at randomisation						0.6085
	<= median	653/1344 (48.6)	645/1344 (48.0)	1.00 (0.95, 1.05) 0.9834	0.98 (0.82, 1.16) 0.7728	-0.00 (-0.03, 0.03) 0.9554	
	> median	629/1325 (47.5)	604/1320 (45.8)	1.01 (0.97, 1.06) 0.5581	1.16 (0.97, 1.38) 0.1004	0.01 (-0.02, 0.04) 0.5332	
	LVEF at enrolment 2						0.2427
	<= 49	451/ 928 (48.6)	467/ 912 (51.2)	0.99 (0.93, 1.04) 0.6389	0.97 (0.79, 1.19) 0.7422	-0.01 (-0.05, 0.02) 0.5117	
	>= 50	831/1741 (47.7)	782/1752 (44.6)	1.02 (0.98, 1.07) 0.3348	1.11 (0.96, 1.29) 0.1624	0.01 (-0.01, 0.04) 0.2820	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8709*
	Yes	140/ 257 (54.5)	137/ 261 (52.5)	1.04 (0.88, 1.22)*0.6508	1.15 (0.78, 1.71) 0.4703	-0.01 (-0.09, 0.06) 0.7127	
	No	1142/2412 (47.3)	1112/2403 (46.3)	1.02 (0.98, 1.05) 0.3424	1.05 (0.92, 1.19) 0.4464	0.01 (-0.01, 0.03) 0.4949	
	MRAs at baseline						0.2057
	Yes	552/1155 (47.8)	556/1146 (48.5)	0.98 (0.93, 1.04) 0.5677	0.99 (0.82, 1.19) 0.9108	-0.01 (-0.04, 0.02) 0.6049	
	No	730/1514 (48.2)	693/1518 (45.7)	1.03 (0.98, 1.08) 0.2284	1.12 (0.95, 1.31) 0.1788	0.01 (-0.01, 0.04) 0.3362	
	ACEi+ARB at baseline						0.5003
	Yes	956/1940 (49.3)	918/1959 (46.9)	1.01 (0.97, 1.05) 0.5249	1.12 (0.97, 1.29) 0.1151	0.01 (-0.01, 0.03) 0.4166	
	No	326/ 729 (44.7)	331/ 705 (47.0)	0.97 (0.90, 1.05) 0.4355	0.91 (0.72, 1.15) 0.4276	-0.02 (-0.06, 0.02) 0.3705	
	ARNI at baseline						0.6612
	Yes	63/ 149 (42.3)	50/ 116 (43.1)	1.06 (0.82, 1.38) 0.6428	1.01 (0.59, 1.73) 0.9611	0.02 (-0.09, 0.13) 0.7186	
	No	1219/2520 (48.4)	1199/2548 (47.1)	1.01 (0.97, 1.04) 0.7469	1.06 (0.94, 1.20) 0.3378	0.00 (-0.02, 0.02) 0.7572	
	Beta Blocker at baseline						0.7562
	Yes	1075/2232 (48.2)	1041/2218 (46.9)	1.01 (0.97, 1.04) 0.7267	1.04 (0.91, 1.19) 0.5781	0.00 (-0.02, 0.02) 0.8160	
	No	207/ 437 (47.4)	208/ 446 (46.6)	1.02 (0.88, 1.17)*0.8276	1.18 (0.87, 1.60) 0.2793	0.01 (-0.06, 0.07)*0.8276	
	Diuretics at baseline						0.6903
	Yes	1153/2391 (48.2)	1116/2379 (46.9)	1.01 (0.97, 1.04) 0.6595	1.09 (0.96, 1.24) 0.2000	0.01 (-0.02, 0.03) 0.5879	
	No	129/ 278 (46.4)	133/ 285 (46.7)	0.99 (0.83, 1.19)*0.9500	0.84 (0.57, 1.23) 0.3642	-0.00 (-0.09, 0.08)*0.9500	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)							
	Overall	767/2842 (27.0)	750/2837 (26.4)	1.02 (0.94, 1.11)*0.6385	1.02 (0.90, 1.16) 0.7506	0.01 (-0.02, 0.03)*0.6385	
	Age						0.0285*
	<= median	417/1415 (29.5)	390/1482 (26.3)	1.12 (1.00, 1.26)*0.0585	1.18 (0.99, 1.41) 0.0694	0.03 (-0.00, 0.06)*0.0584	
	> median	350/1427 (24.5)	360/1355 (26.6)	0.92 (0.81, 1.05)*0.2172	0.88 (0.73, 1.06) 0.1831	-0.02 (-0.05, 0.01)*0.2173	
	Gender						0.9887*
	Male	415/1656 (25.1)	398/1625 (24.5)	1.02 (0.91, 1.15)*0.7063	1.02 (0.86, 1.21) 0.8196	0.01 (-0.02, 0.04)*0.7063	
	Female	352/1186 (29.7)	352/1212 (29.0)	1.02 (0.90, 1.16)*0.7321	1.03 (0.84, 1.25) 0.7901	0.01 (-0.03, 0.04)*0.7321	
	Race						0.7176*
	White	558/2039 (27.4)	541/2058 (26.3)	1.04 (0.94, 1.15)*0.4359	1.05 (0.90, 1.23) 0.5072	0.01 (-0.02, 0.04)*0.4359	
	Black or African	26/ 67 (38.8)	31/ 71 (43.7)	0.89 (0.60, 1.33)*0.5637	0.74 (0.35, 1.57) 0.4370	-0.05 (-0.21, 0.12)*0.5619	
	Asian	116/ 558 (20.8)	124/ 555 (22.3)	0.93 (0.74, 1.16)*0.5287	0.87 (0.64, 1.19) 0.3887	-0.02 (-0.06, 0.03)*0.5285	
	Other	67/ 178 (37.6)	54/ 153 (35.3)	1.07 (0.80, 1.42)*0.6591	1.27 (0.74, 2.18) 0.3796	0.02 (-0.08, 0.13)*0.6581	
	Geographic region						0.5818*
	Asia	111/ 539 (20.6)	120/ 538 (22.3)	0.92 (0.73, 1.16)*0.4941	0.87 (0.63, 1.18) 0.3653	-0.02 (-0.07, 0.03)*0.4939	
	Europe and Saudi Arabia	378/1365 (27.7)	366/1394 (26.3)	1.05 (0.93, 1.19)*0.3952	1.10 (0.91, 1.32) 0.3185	0.01 (-0.02, 0.05)*0.3952	
	North America	96/ 398 (24.1)	101/ 387 (26.1)	0.92 (0.73, 1.18)*0.5230	0.79 (0.55, 1.14) 0.2051	-0.02 (-0.08, 0.04)*0.5229	
	Latin America	182/ 540 (33.7)	163/ 518 (31.5)	1.07 (0.90, 1.27)*0.4383	1.18 (0.88, 1.58) 0.2731	0.02 (-0.03, 0.08)*0.4376	
	NYHA class at enrolment						0.7711*
	II	542/2113 (25.7)	556/2187 (25.4)	1.01 (0.91, 1.12)*0.8640	1.02 (0.88, 1.19) 0.7798	0.00 (-0.02, 0.03)*0.8640	
	III or IV	225/ 729 (30.9)	193/ 649 (29.7)	1.04 (0.88, 1.22)*0.6501	1.00 (0.77, 1.31) 0.9884	0.01 (-0.04, 0.06)*0.6497	
	LVEF at enrolment						0.3159*
	<= 49	270/ 980 (27.6)	247/ 963 (25.6)	1.07 (0.93, 1.25)*0.3431	1.11 (0.89, 1.38) 0.3640	0.02 (-0.02, 0.06)*0.3426	
	50-59	272/1029 (26.4)	253/1017 (24.9)	1.06 (0.92, 1.23)*0.4205	1.09 (0.87, 1.35) 0.4637	0.02 (-0.02, 0.05)*0.4202	
	>= 60	225/ 833 (27.0)	250/ 857 (29.2)	0.93 (0.79, 1.08)*0.3236	0.87 (0.69, 1.10) 0.2563	-0.02 (-0.06, 0.02)*0.3229	
	NT-proBNP at enrolment						0.9263*
	<= median	388/1418 (27.4)	382/1421 (26.9)	1.02 (0.90, 1.15)*0.7736	1.03 (0.86, 1.24) 0.7137	0.00 (-0.03, 0.04)*0.7736	
	> median	379/1424 (26.6)	367/1415 (25.9)	1.03 (0.91, 1.16)*0.6812	1.01 (0.84, 1.21) 0.9237	0.01 (-0.03, 0.04)*0.6812	
	Type 2 Diabetes Medical History						0.3286*
	Yes	325/1250 (26.0)	337/1260 (26.7)	1.01 (0.96, 1.07) 0.6104	0.96 (0.81, 1.15)*0.6715	-0.01 (-0.04, 0.03)*0.6715	
	No	442/1592 (27.8)	413/1577 (26.2)	1.06 (0.95, 1.19)*0.3181	1.08 (0.93, 1.27)*0.3180	0.02 (-0.02, 0.05)*0.3178	
	Atrial fibrillation or flutter at enrolment ECG						0.1951*
	Yes	295/1199 (24.6)	310/1199 (25.9)	0.95 (0.83, 1.09)*0.4807	0.93 (0.76, 1.15) 0.5153	-0.01 (-0.05, 0.02)*0.4806	
	No	472/1643 (28.7)	440/1638 (26.9)	1.00 (0.95, 1.05) 0.8823	1.08 (0.91, 1.28) 0.3650	0.02 (-0.01, 0.05)*0.2328	
	BMI (kg/m2) at enrolment						0.5674*
	< 30	402/1571 (25.6)	381/1559 (24.4)	1.05 (0.93, 1.18)*0.4577	1.04 (0.87, 1.24) 0.6421	0.01 (-0.02, 0.04)*0.4575	
	>= 30	365/1270 (28.7)	368/1275 (28.9)	1.00 (0.88, 1.13)*0.9456	1.00 (0.83, 1.21) 0.9922	-0.00 (-0.04, 0.03)*0.9456	
	Baseline eGFR (mL/min/1.73m^2)						0.0061*
	< 60	324/1359 (23.8)	372/1396 (26.6)	0.89 (0.79, 1.02)*0.0905	0.84 (0.70, 1.02) 0.0808	-0.03 (-0.06, 0.00)*0.0898	
	>= 60	443/1483 (29.9)	377/1440 (26.2)	1.14 (1.02, 1.28)*0.0267	1.20 (1.00, 1.44) 0.0439	0.04 (0.00, 0.07)*0.0261	

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AstraZeneca
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Full Analysis Set

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Symptom Stability (LOCF)	SBP at randomisation						0.1462*
	<= median	391/1424 (27.5)	363/1439 (25.2)	1.09 (0.96, 1.23)*0.1754	1.11 (0.92, 1.33) 0.2747	0.02 (-0.01, 0.05)*0.1751	
	> median	376/1418 (26.5)	387/1398 (27.7)	0.96 (0.85, 1.08)*0.4864	0.95 (0.79, 1.14) 0.5725	-0.01 (-0.04, 0.02)*0.4863	
	LVEF at enrolment 2						0.4063*
	<= 49	270/ 980 (27.6)	247/ 963 (25.6)	1.07 (0.93, 1.25)*0.3431	1.11 (0.89, 1.38) 0.3640	0.02 (-0.02, 0.06)*0.3426	
	>= 50	497/1862 (26.7)	503/1874 (26.8)	0.99 (0.89, 1.11)*0.9179	0.98 (0.84, 1.15) 0.8090	-0.00 (-0.03, 0.03)*0.9179	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4467*
	Yes	83/ 283 (29.3)	90/ 286 (31.5)	0.93 (0.73, 1.20)*0.5792	0.97 (0.62, 1.51) 0.8830	-0.02 (-0.10, 0.05)*0.5789	
	No	684/2559 (26.7)	660/2551 (25.9)	0.98 (0.93, 1.04) 0.5806	1.03 (0.90, 1.18) 0.6925	0.01 (-0.02, 0.03)*0.4866	
	MRAs at baseline						0.5709*
	Yes	339/1227 (27.6)	322/1224 (26.3)	1.05 (0.92, 1.20)*0.4613	1.11 (0.91, 1.36) 0.2846	0.01 (-0.02, 0.05)*0.4611	
	No	428/1615 (26.5)	428/1613 (26.5)	1.00 (0.89, 1.12)*0.9831	0.96 (0.80, 1.14) 0.6072	-0.00 (-0.03, 0.03)*0.9831	
	ACEi+ARB at baseline						0.5233*
	Yes	558/2065 (27.0)	559/2077 (26.9)	1.00 (0.91, 1.11)*0.9376	1.01 (0.87, 1.17) 0.9380	0.00 (-0.03, 0.03)*0.9376	
	No	209/ 777 (26.9)	191/ 760 (25.1)	1.07 (0.90, 1.27)*0.4302	1.07 (0.83, 1.38) 0.6185	0.02 (-0.03, 0.06)*0.4298	
	ARNI at baseline						0.7882*
	Yes	40/ 153 (26.1)	34/ 126 (27.0)	0.97 (0.65, 1.43)*0.8742	1.04 (0.58, 1.86) 0.8890	-0.01 (-0.11, 0.10)*0.8744	
	No	727/2689 (27.0)	716/2711 (26.4)	1.02 (0.94, 1.12)*0.6037	1.02 (0.89, 1.17) 0.7672	0.01 (-0.02, 0.03)*0.6037	
	Beta Blocker at baseline						0.6360*
	Yes	640/2360 (27.1)	620/2356 (26.3)	1.03 (0.94, 1.13)*0.5333	1.01 (0.87, 1.16) 0.9374	0.01 (-0.02, 0.03)*0.5333	
	No	127/ 482 (26.3)	130/ 481 (27.0)	0.97 (0.79, 1.20)*0.8119	1.11 (0.80, 1.52) 0.5354	-0.01 (-0.06, 0.05)*0.8119	
	Diuretics at baseline						0.3650*
	Yes	681/2536 (26.9)	675/2531 (26.7)	0.97 (0.92, 1.03) 0.3935	1.00 (0.87, 1.15) 0.9994	0.00 (-0.02, 0.03)*0.8824	
	No	86/ 306 (28.1)	75/ 306 (24.5)	1.15 (0.88, 1.50)*0.3133	1.23 (0.82, 1.86) 0.3136	0.04 (-0.03, 0.11)*0.3122	

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Total Symptom Score (LOCF)							
	Overall	1458/2842 (51.3)	1393/2837 (49.1)	1.04 (0.99, 1.10)*0.0973	1.10 (0.98, 1.24) 0.1032	0.02 (-0.00, 0.05)*0.0971	
	Age						0.1194*
	<= median	754/1415 (53.3)	783/1482 (52.8)	1.01 (0.94, 1.08)*0.8074	1.06 (0.90, 1.25) 0.4831	0.00 (-0.03, 0.04)*0.8074	
	> median	704/1427 (49.3)	610/1355 (45.0)	1.10 (1.01, 1.19)*0.0230	1.17 (0.99, 1.39) 0.0677	0.04 (0.01, 0.08)*0.0225	
	Gender						0.3263*
	Male	805/1656 (48.6)	773/1625 (47.6)	1.02 (0.95, 1.10)*0.5504	1.04 (0.89, 1.22) 0.6388	0.01 (-0.02, 0.04)*0.5504	
	Female	653/1186 (55.1)	620/1212 (51.2)	1.08 (1.00, 1.16)*0.0556	1.18 (0.99, 1.41) 0.0635	0.04 (-0.00, 0.08)*0.0553	
	Race						0.6119*
	White	1069/2039 (52.4)	1029/2058 (50.0)	1.05 (0.99, 1.11)*0.1202	1.08 (0.94, 1.24) 0.2843	0.02 (-0.01, 0.05)*0.1200	
	Black or African	37/ 67 (55.2)	43/ 71 (60.6)	0.91 (0.69, 1.21)*0.5269	0.81 (0.39, 1.71) 0.5839	-0.05 (-0.22, 0.11)*0.5250	
	Asian	231/ 558 (41.4)	228/ 555 (41.1)	1.01 (0.88, 1.16)*0.9145	1.13 (0.86, 1.49) 0.3804	0.00 (-0.05, 0.06)*0.9145	
	Other	121/ 178 (68.0)	93/ 153 (60.8)	1.12 (0.95, 1.32)*0.1770	1.57 (0.92, 2.68) 0.1002	0.07 (-0.03, 0.18)*0.1726	
	Geographic region						0.7662*
	Asia	221/ 539 (41.0)	221/ 538 (41.1)	1.00 (0.87, 1.15)*0.9797	1.08 (0.81, 1.43) 0.6007	-0.00 (-0.06, 0.06)*0.9797	
	Europe and Saudi Arabia	710/1365 (52.0)	689/1394 (49.4)	1.05 (0.98, 1.13)*0.1740	1.08 (0.91, 1.28) 0.3667	0.03 (-0.01, 0.06)*0.1738	
	North America	203/ 398 (51.0)	179/ 387 (46.3)	1.10 (0.95, 1.27)*0.1839	1.26 (0.92, 1.71) 0.1458	0.05 (-0.02, 0.12)*0.1824	
	Latin America	324/ 540 (60.0)	304/ 518 (58.7)	1.02 (0.93, 1.13)*0.6640	1.10 (0.83, 1.45) 0.5130	0.01 (-0.05, 0.07)*0.6639	
	NYHA class at enrolment						0.2630*
	II	1016/2113 (48.1)	1030/2187 (47.1)	1.02 (0.96, 1.09)*0.5171	1.08 (0.94, 1.24) 0.2615	0.01 (-0.02, 0.04)*0.5171	
	III or IV	442/ 729 (60.6)	362/ 649 (55.8)	1.09 (0.99, 1.19)*0.0695	1.22 (0.96, 1.55) 0.0972	0.05 (-0.00, 0.10)*0.0681	
	LVEF at enrolment						0.2630*
	<= 49	496/ 980 (50.6)	480/ 963 (49.8)	1.02 (0.93, 1.11)*0.7350	1.10 (0.90, 1.35) 0.3667	0.01 (-0.04, 0.05)*0.7350	
	50-59	510/1029 (49.6)	496/1017 (48.8)	1.02 (0.93, 1.11)*0.7202	1.02 (0.84, 1.25) 0.8268	0.01 (-0.04, 0.05)*0.7202	
	>= 60	452/ 833 (54.3)	417/ 857 (48.7)	1.12 (1.02, 1.22)*0.0214	1.22 (0.99, 1.51) 0.0681	0.06 (0.01, 0.10)*0.0210	
	NT-proBNP at enrolment						0.0547*
	<= median	692/1418 (48.8)	699/1421 (49.2)	0.99 (0.92, 1.07)*0.8355	0.99 (0.84, 1.17) 0.8923	-0.00 (-0.04, 0.03)*0.8355	
	> median	766/1424 (53.8)	693/1415 (49.0)	1.10 (1.02, 1.18)*0.0104	1.24 (1.05, 1.48) 0.0128	0.05 (0.01, 0.08)*0.0102	
	Type 2 Diabetes Medical History						0.1854*
	Yes	668/1250 (53.4)	620/1260 (49.2)	1.09 (1.01, 1.17)*0.0340	1.18 (1.01, 1.39)*0.0339	0.04 (0.00, 0.08)*0.0337	
	No	790/1592 (49.6)	773/1577 (49.0)	1.01 (0.94, 1.09)*0.7330	1.02 (0.89, 1.18)*0.7330	0.01 (-0.03, 0.04)*0.7330	
	Atrial fibrillation or flutter at enrolment ECG						0.7361*
	Yes	632/1199 (52.7)	611/1199 (51.0)	1.03 (0.96, 1.12)*0.3908	1.10 (0.91, 1.32) 0.3266	0.02 (-0.02, 0.06)*0.3907	
	No	826/1643 (50.3)	782/1638 (47.7)	1.05 (0.98, 1.13)*0.1470	1.11 (0.95, 1.30) 0.1914	0.03 (-0.01, 0.06)*0.1466	
	BMI (kg/m2) at enrolment						0.4206*
	< 30	756/1571 (48.1)	703/1559 (45.1)	1.07 (0.99, 1.15)*0.0896	1.18 (1.00, 1.38) 0.0514	0.03 (-0.00, 0.07)*0.0892	
	>= 30	702/1270 (55.3)	689/1275 (54.0)	1.02 (0.95, 1.10)*0.5311	1.03 (0.87, 1.23) 0.7164	0.01 (-0.03, 0.05)*0.5310	
	Baseline eGFR (mL/min/1.73m^2)						0.7499*
	< 60	677/1359 (49.8)	660/1396 (47.3)	1.05 (0.98, 1.14)*0.1827	1.12 (0.94, 1.32) 0.2068	0.03 (-0.01, 0.06)*0.1825	
	>= 60	781/1483 (52.7)	732/1440 (50.8)	1.04 (0.97, 1.11)*0.3224	1.09 (0.92, 1.28) 0.3322	0.02 (-0.02, 0.05)*0.3221	

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Total Symptom Score (LOCF)	SBP at randomisation						0.0318*
	<= median	741/1424 (52.0)	677/1439 (47.0)	1.11 (1.03, 1.19)*0.0077	1.19 (1.01, 1.41) 0.0379	0.05 (0.01, 0.09)*0.0075	
	> median	717/1418 (50.6)	716/1398 (51.2)	0.99 (0.92, 1.06)*0.7294	1.02 (0.86, 1.20) 0.8494	-0.01 (-0.04, 0.03)*0.7294	
	LVEF at enrolment 2						0.4359*
	<= 49	496/ 980 (50.6)	480/ 963 (49.8)	1.02 (0.93, 1.11)*0.7350	1.10 (0.90, 1.35) 0.3667	0.01 (-0.04, 0.05)*0.7350	
	>= 50	962/1862 (51.7)	913/1874 (48.7)	1.06 (0.99, 1.13)*0.0719	1.11 (0.96, 1.28) 0.1696	0.03 (-0.00, 0.06)*0.0717	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8624*
	Yes	185/ 283 (65.4)	177/ 286 (61.9)	1.06 (0.93, 1.20)*0.3881	1.47 (0.99, 2.17) 0.0568	0.03 (-0.04, 0.11)*0.3875	
	No	1273/2559 (49.7)	1216/2551 (47.7)	1.04 (0.99, 1.10)*0.1373	1.08 (0.95, 1.22) 0.2503	0.02 (-0.01, 0.05)*0.1371	
	MRAs at baseline						0.9221*
	Yes	614/1227 (50.0)	588/1224 (48.0)	1.04 (0.96, 1.13)*0.3218	1.08 (0.90, 1.29) 0.4113	0.02 (-0.02, 0.06)*0.3215	
	No	844/1615 (52.3)	805/1613 (49.9)	1.05 (0.98, 1.12)*0.1813	1.12 (0.96, 1.32) 0.1411	0.02 (-0.01, 0.06)*0.1810	
	ACEi+ARB at baseline						0.0188*
	Yes	1099/2065 (53.2)	1019/2077 (49.1)	1.08 (1.02, 1.15)*0.0075	1.19 (1.04, 1.37) 0.0138	0.04 (0.01, 0.07)*0.0074	
	No	359/ 777 (46.2)	374/ 760 (49.2)	0.94 (0.85, 1.04)*0.2381	0.90 (0.72, 1.12) 0.3534	-0.03 (-0.08, 0.02)*0.2377	
	ARNI at baseline						0.1218*
	Yes	56/ 153 (36.6)	55/ 126 (43.7)	0.84 (0.63, 1.12)*0.2304	0.87 (0.49, 1.54) 0.6411	-0.07 (-0.19, 0.04)*0.2313	
	No	1402/2689 (52.1)	1338/2711 (49.4)	1.06 (1.00, 1.11)*0.0408	1.12 (0.99, 1.26) 0.0691	0.03 (0.00, 0.05)*0.0407	
	Beta Blocker at baseline						0.3520*
	Yes	1216/2360 (51.5)	1149/2356 (48.8)	1.06 (1.00, 1.12)*0.0585	1.10 (0.97, 1.26) 0.1345	0.03 (-0.00, 0.06)*0.0583	
	No	242/ 482 (50.2)	244/ 481 (50.7)	0.99 (0.87, 1.12)*0.8718	1.10 (0.82, 1.48) 0.5111	-0.01 (-0.07, 0.06)*0.8718	
	Diuretics at baseline						0.3840*
	Yes	1294/2536 (51.0)	1246/2531 (49.2)	1.04 (0.98, 1.10)*0.2013	1.10 (0.97, 1.25) 0.1210	0.02 (-0.01, 0.05)*0.2011	
	No	164/ 306 (53.6)	147/ 306 (48.0)	1.12 (0.95, 1.30)*0.1701	1.07 (0.73, 1.57) 0.7444	0.06 (-0.02, 0.13)*0.1686	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	1563/2842 (55.0)	1447/2837 (51.0)	1.08 (1.03, 1.13)*0.0026	1.17 (1.05, 1.31) 0.0045	0.04 (0.01, 0.07)*0.0026	
	Age						0.4713*
	<= median	825/1415 (58.3)	812/1482 (54.8)	1.06 (1.00, 1.13)*0.0565	1.19 (1.02, 1.39) 0.0292	0.04 (-0.00, 0.07)*0.0564	
	> median	738/1427 (51.7)	635/1355 (46.9)	1.10 (1.02, 1.19)*0.0107	1.18 (1.01, 1.38) 0.0415	0.05 (0.01, 0.09)*0.0104	
	Gender						0.5715*
	Male	885/1656 (53.4)	815/1625 (50.2)	1.07 (1.00, 1.14)*0.0597	1.14 (0.99, 1.32) 0.0708	0.03 (-0.00, 0.07)*0.0593	
	Female	678/1186 (57.2)	632/1212 (52.1)	1.10 (1.02, 1.18)*0.0136	1.21 (1.02, 1.44) 0.0280	0.05 (0.01, 0.09)*0.0134	
	Race						0.4779*
	White	1102/2039 (54.0)	1050/2058 (51.0)	1.06 (1.00, 1.12)*0.0526	1.10 (0.97, 1.26) 0.1372	0.03 (-0.00, 0.06)*0.0524	
	Black or African	36/ 67 (53.7)	39/ 71 (54.9)	0.98 (0.72, 1.33)*0.8877	0.98 (0.48, 1.99) 0.9525	-0.01 (-0.18, 0.15)*0.8877	
	Asian	299/ 558 (53.6)	267/ 555 (48.1)	1.11 (0.99, 1.25)*0.0683	1.27 (1.00, 1.61) 0.0549	0.06 (0.00, 0.12) 0.0475	
	Other	126/ 178 (70.8)	91/ 153 (59.5)	1.19 (1.01, 1.40)*0.0344	1.98 (1.16, 3.36) 0.0117	0.11 (0.01, 0.22)*0.0306	
	Geographic region						0.9518*
	Asia	289/ 539 (53.6)	262/ 538 (48.7)	1.10 (0.98, 1.24)*0.1069	1.23 (0.96, 1.57) 0.0990	0.05 (-0.01, 0.11) 0.0960	
	Europe and Saudi Arabia	734/1365 (53.8)	706/1394 (50.6)	1.06 (0.99, 1.14)*0.1003	1.11 (0.94, 1.30) 0.2132	0.03 (-0.01, 0.07)*0.1000	
	North America	199/ 398 (50.0)	177/ 387 (45.7)	1.09 (0.94, 1.27)*0.2327	1.18 (0.89, 1.58) 0.2540	0.04 (-0.03, 0.11) 0.2545	
	Latin America	341/ 540 (63.1)	302/ 518 (58.3)	1.08 (0.98, 1.19)*0.1075	1.29 (0.99, 1.70) 0.0631	0.05 (-0.01, 0.11)*0.1062	
	NYHA class at enrolment						0.8308*
	II	1119/2113 (53.0)	1082/2187 (49.5)	1.07 (1.01, 1.13)*0.0224	1.18 (1.04, 1.33) 0.0123	0.03 (0.00, 0.06)*0.0222	
	III or IV	444/ 729 (60.9)	365/ 649 (56.2)	1.08 (0.99, 1.18)*0.0806	1.19 (0.94, 1.49) 0.1420	0.05 (-0.01, 0.10)*0.0791	
	LVEF at enrolment						0.3801*
	<= 49	529/ 980 (54.0)	503/ 963 (52.2)	1.03 (0.95, 1.12)*0.4406	1.12 (0.93, 1.35) 0.2369	0.02 (-0.03, 0.06)*0.4403	
	50-59	563/1029 (54.7)	514/1017 (50.5)	1.08 (1.00, 1.18)*0.0591	1.17 (0.97, 1.41) 0.0964	0.04 (-0.00, 0.08)*0.0586	
	>= 60	471/ 833 (56.5)	430/ 857 (50.2)	1.13 (1.03, 1.23)*0.0088	1.24 (1.02, 1.52) 0.0342	0.06 (0.02, 0.11)*0.0086	
	NT-proBNP at enrolment						0.3818*
	<= median	760/1418 (53.6)	722/1421 (50.8)	1.05 (0.98, 1.13)*0.1373	1.13 (0.97, 1.32) 0.1277	0.03 (-0.01, 0.06)*0.1370	
	> median	803/1424 (56.4)	724/1415 (51.2)	1.10 (1.03, 1.18)*0.0053	1.22 (1.04, 1.43) 0.0127	0.05 (0.02, 0.09)*0.0052	
	Type 2 Diabetes Medical History						0.7146*
	Yes	696/1250 (55.7)	644/1260 (51.1)	1.09 (1.01, 1.17)*0.0219	1.20 (1.03, 1.41)*0.0218	0.05 (0.01, 0.08)*0.0216	
	No	867/1592 (54.5)	803/1577 (50.9)	1.07 (1.00, 1.14)*0.0462	1.15 (1.00, 1.33)*0.0460	0.04 (0.00, 0.07)*0.0458	
	Atrial fibrillation or flutter at enrolment ECG						0.5954*
	Yes	668/1199 (55.7)	629/1199 (52.5)	1.06 (0.99, 1.14)*0.1102	1.15 (0.97, 1.36) 0.1187	0.03 (-0.01, 0.07)*0.1098	
	No	895/1643 (54.5)	818/1638 (49.9)	1.09 (1.02, 1.16)*0.0094	1.19 (1.03, 1.38) 0.0162	0.05 (0.01, 0.08)*0.0093	
	BMI (kg/m2) at enrolment						0.1438*
	< 30	862/1571 (54.9)	767/1559 (49.2)	1.12 (1.04, 1.19)*0.0015	1.27 (1.10, 1.47) 0.0015	0.06 (0.02, 0.09)*0.0015	
	>= 30	701/1270 (55.2)	679/1275 (53.3)	1.04 (0.97, 1.11)*0.3256	1.06 (0.89, 1.25) 0.5296	0.02 (-0.02, 0.06)*0.3254	
	Baseline eGFR (mL/min/1.73m^2)						0.5443*
	< 60	711/1359 (52.3)	689/1396 (49.4)	1.06 (0.98, 1.14)*0.1200	1.13 (0.96, 1.32) 0.1432	0.03 (-0.01, 0.07)*0.1198	
	>= 60	852/1483 (57.5)	757/1440 (52.6)	1.09 (1.02, 1.17)*0.0081	1.21 (1.04, 1.42) 0.0138	0.05 (0.01, 0.08)*0.0079	

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Clinical Summary Score (LOCF)	SBP at randomisation						0.0185*
	<= median	785/1424 (55.1)	693/1439 (48.2)	1.14 (1.07, 1.23)*0.0002	1.28 (1.10, 1.50) 0.0016	0.07 (0.03, 0.11)*0.0002	
	> median	778/1418 (54.9)	754/1398 (53.9)	1.02 (0.95, 1.09)*0.6197	1.07 (0.91, 1.25) 0.4172	0.01 (-0.03, 0.05)*0.6196	
	LVEF at enrolment 2						0.2202*
	<= 49	529/ 980 (54.0)	503/ 963 (52.2)	1.03 (0.95, 1.12)*0.4406	1.12 (0.93, 1.35) 0.2369	0.02 (-0.03, 0.06)*0.4403	
	>= 50	1034/1862 (55.5)	944/1874 (50.4)	1.10 (1.04, 1.17)*0.0016	1.20 (1.05, 1.38) 0.0086	0.05 (0.02, 0.08)*0.0016	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9362*
	Yes	188/ 283 (66.4)	177/ 286 (61.9)	1.07 (0.95, 1.21)*0.2590	1.43 (0.98, 2.08) 0.0648	0.05 (-0.03, 0.12)*0.2579	
	No	1375/2559 (53.7)	1270/2551 (49.8)	1.08 (1.02, 1.14)*0.0048	1.16 (1.03, 1.30) 0.0127	0.04 (0.01, 0.07)*0.0047	
	MRAs at baseline						0.3282*
	Yes	674/1227 (54.9)	606/1224 (49.5)	1.11 (1.03, 1.20)*0.0073	1.25 (1.06, 1.48) 0.0086	0.05 (0.01, 0.09)*0.0071	
	No	889/1615 (55.0)	841/1613 (52.1)	1.06 (0.99, 1.13)*0.0979	1.12 (0.97, 1.29) 0.1350	0.03 (-0.01, 0.06)*0.0975	
	ACEi+ARB at baseline						0.0797*
	Yes	1155/2065 (55.9)	1049/2077 (50.5)	1.11 (1.05, 1.17)*0.0005	1.24 (1.09, 1.41) 0.0012	0.05 (0.02, 0.08)*0.0005	
	No	408/ 777 (52.5)	398/ 760 (52.4)	0.99 (0.91, 1.08) 0.8766	1.01 (0.82, 1.24) 0.9116	0.00 (-0.05, 0.05) 0.9367	
	ARNI at baseline						0.1051*
	Yes	74/ 153 (48.4)	68/ 126 (54.0)	0.98 (0.78, 1.24) 0.8750	0.85 (0.52, 1.39) 0.5248	-0.03 (-0.15, 0.09) 0.5857	
	No	1489/2689 (55.4)	1379/2711 (50.9)	1.09 (1.04, 1.14)*0.0009	1.19 (1.06, 1.33) 0.0026	0.05 (0.02, 0.07)*0.0009	
	Beta Blocker at baseline						0.6894*
	Yes	1289/2360 (54.6)	1188/2356 (50.4)	1.08 (1.03, 1.14)*0.0040	1.16 (1.03, 1.31) 0.0141	0.04 (0.01, 0.07)*0.0039	
	No	274/ 482 (56.8)	259/ 481 (53.8)	1.06 (0.94, 1.18)*0.3493	1.21 (0.92, 1.58) 0.1669	0.03 (-0.03, 0.09)*0.3488	
	Diuretics at baseline						0.9655*
	Yes	1391/2536 (54.9)	1287/2531 (50.8)	1.08 (1.02, 1.14)*0.0044	1.18 (1.05, 1.33) 0.0044	0.04 (0.01, 0.07)*0.0043	
	No	172/ 306 (56.2)	160/ 306 (52.3)	1.08 (0.93, 1.24)*0.3307	1.07 (0.76, 1.51) 0.6995	0.04 (-0.04, 0.12)*0.3298	

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AstraZeneca
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Overall Summary Score (LOCF)							
	Overall	1533/2842 (53.9)	1457/2837 (51.4)	1.05 (1.00, 1.10)*0.0513	1.10 (0.98, 1.23) 0.0949	0.03 (-0.00, 0.05)*0.0511	
	Age						0.8047*
	<= median	807/1415 (57.0)	807/1482 (54.5)	1.05 (0.98, 1.12)*0.1624	1.14 (0.97, 1.33) 0.1056	0.03 (-0.01, 0.06)*0.1624	
	> median	726/1427 (50.9)	650/1355 (48.0)	1.06 (0.98, 1.14)*0.1260	1.08 (0.92, 1.26) 0.3542	0.03 (-0.01, 0.07)*0.1253	
	Gender						0.4148*
	Male	873/1656 (52.7)	830/1625 (51.1)	1.03 (0.97, 1.10)*0.3472	1.06 (0.92, 1.23) 0.4383	0.02 (-0.02, 0.05)*0.3470	
	Female	660/1186 (55.6)	627/1212 (51.7)	1.08 (1.00, 1.16)*0.0546	1.15 (0.97, 1.36) 0.1108	0.04 (-0.00, 0.08)*0.0543	
	Race						0.4884*
	White	1097/2039 (53.8)	1048/2058 (50.9)	1.06 (1.00, 1.12)*0.0653	1.09 (0.96, 1.24) 0.1966	0.03 (-0.00, 0.06)*0.0651	
	Black or African	33/ 67 (49.3)	40/ 71 (56.3)	0.87 (0.64, 1.20)*0.4072	0.73 (0.36, 1.50) 0.3959	-0.05 (-0.21, 0.11) 0.5519	
	Asian	273/ 558 (48.9)	269/ 555 (48.5)	1.01 (0.89, 1.14)*0.8790	1.04 (0.82, 1.33) 0.7467	0.01 (-0.05, 0.07) 0.7403	
	Other	130/ 178 (73.0)	100/ 153 (65.4)	1.12 (0.97, 1.29)*0.1358	1.63 (0.97, 2.75) 0.0637	0.08 (-0.02, 0.18)*0.1313	
	Geographic region						0.8050*
	Asia	265/ 539 (49.2)	264/ 538 (49.1)	1.00 (0.89, 1.13)*0.9753	1.01 (0.79, 1.30) 0.9062	0.00 (-0.05, 0.06) 0.9101	
	Europe and Saudi Arabia	730/1365 (53.5)	699/1394 (50.1)	1.07 (0.99, 1.15)*0.0796	1.11 (0.94, 1.30) 0.2112	0.03 (-0.00, 0.07)*0.0793	
	North America	204/ 398 (51.3)	184/ 387 (47.5)	1.08 (0.94, 1.24)*0.2992	1.17 (0.87, 1.56) 0.3005	0.04 (-0.03, 0.11) 0.2427	
	Latin America	334/ 540 (61.9)	310/ 518 (59.8)	1.03 (0.94, 1.14)*0.5042	1.11 (0.85, 1.45) 0.4535	0.02 (-0.04, 0.08)*0.5039	
	NYHA class at enrolment						0.1209*
	II	1100/2113 (52.1)	1112/2187 (50.8)	1.02 (0.97, 1.09)*0.4263	1.06 (0.94, 1.21) 0.3548	0.01 (-0.02, 0.04)*0.4263	
	III or IV	433/ 729 (59.4)	345/ 649 (53.2)	1.12 (1.02, 1.23)*0.0206	1.27 (1.01, 1.60) 0.0416	0.06 (0.01, 0.11)*0.0196	
	LVEF at enrolment						0.0462*
	<= 49	517/ 980 (52.8)	526/ 963 (54.6)	0.97 (0.89, 1.05)*0.4096	0.95 (0.79, 1.15) 0.6269	-0.02 (-0.06, 0.03)*0.4095	
	50-59	556/1029 (54.0)	506/1017 (49.8)	1.09 (1.00, 1.18)*0.0531	1.16 (0.97, 1.40) 0.1122	0.04 (-0.00, 0.09)*0.0526	
	>= 60	460/ 833 (55.2)	425/ 857 (49.6)	1.11 (1.02, 1.22)*0.0207	1.21 (0.99, 1.48) 0.0634	0.06 (0.01, 0.10)*0.0203	
	NT-proBNP at enrolment						0.8699*
	<= median	758/1418 (53.5)	720/1421 (50.7)	1.06 (0.98, 1.13)*0.1374	1.12 (0.96, 1.31) 0.1435	0.03 (-0.01, 0.06)*0.1371	
	> median	775/1424 (54.4)	736/1415 (52.0)	1.05 (0.98, 1.12)*0.1984	1.07 (0.91, 1.26) 0.3858	0.02 (-0.01, 0.06)*0.1980	
	Type 2 Diabetes Medical History						0.1263*
	Yes	694/1250 (55.5)	638/1260 (50.6)	1.10 (1.02, 1.18)*0.0143	1.22 (1.04, 1.42)*0.0142	0.05 (0.01, 0.09)*0.0141	
	No	839/1592 (52.7)	819/1577 (51.9)	1.01 (0.95, 1.08)*0.6656	1.03 (0.90, 1.19)*0.6656	0.01 (-0.03, 0.04)*0.6656	
	Atrial fibrillation or flutter at enrolment ECG						0.8412*
	Yes	660/1199 (55.0)	632/1199 (52.7)	1.04 (0.97, 1.12)*0.2515	1.09 (0.92, 1.29) 0.3227	0.02 (-0.02, 0.06)*0.2512	
	No	873/1643 (53.1)	825/1638 (50.4)	1.05 (0.99, 1.13)*0.1128	1.11 (0.96, 1.28) 0.1750	0.03 (-0.01, 0.06)*0.1125	
	BMI (kg/m2) at enrolment						0.9743*
	< 30	824/1571 (52.5)	779/1559 (50.0)	1.05 (0.98, 1.12)*0.1649	1.09 (0.94, 1.27) 0.2339	0.02 (-0.01, 0.06)*0.1646	
	>= 30	709/1270 (55.8)	677/1275 (53.1)	1.05 (0.98, 1.13)*0.1671	1.10 (0.93, 1.31) 0.2476	0.03 (-0.01, 0.07)*0.1668	
	Baseline eGFR (mL/min/1.73m^2)						0.7407*
	< 60	695/1359 (51.1)	687/1396 (49.2)	1.04 (0.96, 1.12)*0.3115	1.08 (0.92, 1.26) 0.3676	0.02 (-0.02, 0.06)*0.3114	
	>= 60	838/1483 (56.5)	770/1440 (53.5)	1.06 (0.99, 1.13)*0.0995	1.11 (0.95, 1.30) 0.1756	0.03 (-0.01, 0.07)*0.0990	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.1924*
	<= median	768/1424 (53.9)	715/1439 (49.7)	1.09 (1.01, 1.17)*0.0232	1.14 (0.97, 1.33) 0.1066	0.04 (0.01, 0.08)*0.0229	
	> median	765/1418 (53.9)	742/1398 (53.1)	1.02 (0.95, 1.09)*0.6422	1.06 (0.91, 1.24) 0.4611	0.01 (-0.03, 0.05)*0.6422	
	LVEF at enrolment 2						0.0145*
	<= 49	517/ 980 (52.8)	526/ 963 (54.6)	0.97 (0.89, 1.05)*0.4096	0.95 (0.79, 1.15) 0.6269	-0.02 (-0.06, 0.03)*0.4095	
	>= 50	1016/1862 (54.6)	931/1874 (49.7)	1.10 (1.03, 1.17)*0.0028	1.18 (1.03, 1.35) 0.0164	0.05 (0.02, 0.08)*0.0028	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6442*
	Yes	184/ 283 (65.0)	172/ 286 (60.1)	1.08 (0.95, 1.23)*0.2299	1.38 (0.95, 2.01) 0.0908	0.05 (-0.03, 0.13)*0.2287	
	No	1349/2559 (52.7)	1285/2551 (50.4)	1.05 (0.99, 1.10)*0.0939	1.08 (0.96, 1.21) 0.1972	0.02 (-0.00, 0.05)*0.0936	
	MRAs at baseline						0.8623*
	Yes	660/1227 (53.8)	630/1224 (51.5)	1.05 (0.97, 1.13)*0.2504	1.09 (0.92, 1.29) 0.3023	0.02 (-0.02, 0.06)*0.2501	
	No	873/1615 (54.1)	827/1613 (51.3)	1.05 (0.99, 1.13)*0.1133	1.11 (0.95, 1.28) 0.1809	0.03 (-0.01, 0.06)*0.1130	
	ACEi+ARB at baseline						0.0598*
	Yes	1135/2065 (55.0)	1056/2077 (50.8)	1.08 (1.02, 1.15)*0.0080	1.17 (1.03, 1.34) 0.0175	0.04 (0.01, 0.07)*0.0078	
	No	398/ 777 (51.2)	401/ 760 (52.8)	1.00 (0.92, 1.08) 0.9783	0.93 (0.76, 1.15) 0.5034	-0.01 (-0.06, 0.03) 0.5777	
	ARNI at baseline						0.0039*
	Yes	64/ 153 (41.8)	71/ 126 (56.3)	0.81 (0.63, 1.03) 0.0819	0.55 (0.33, 0.90) 0.0178	-0.14 (-0.25, -0.02) 0.0174	
	No	1469/2689 (54.6)	1386/2711 (51.1)	1.07 (1.02, 1.12)*0.0099	1.14 (1.02, 1.28) 0.0245	0.04 (0.01, 0.06)*0.0098	
	Beta Blocker at baseline						0.2967*
	Yes	1266/2360 (53.6)	1189/2356 (50.5)	1.06 (1.01, 1.12)*0.0291	1.11 (0.98, 1.25) 0.0980	0.03 (0.00, 0.06)*0.0289	
	No	267/ 482 (55.4)	268/ 481 (55.7)	0.99 (0.89, 1.11)*0.9196	1.05 (0.80, 1.38) 0.7096	-0.00 (-0.07, 0.06)*0.9196	
	Diuretics at baseline						0.4171*
	Yes	1362/2536 (53.7)	1285/2531 (50.8)	1.06 (1.00, 1.12)*0.0365	1.13 (1.00, 1.27) 0.0428	0.03 (0.00, 0.06)*0.0363	
	No	171/ 306 (55.9)	172/ 306 (56.2)	0.99 (0.86, 1.14)*0.9351	0.88 (0.63, 1.24) 0.4764	-0.03 (-0.10, 0.04) 0.3827	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	1433/2792 (51.3)	1295/2792 (46.4)	1.08 (1.03, 1.13) 0.0026	1.21 (1.08, 1.35) 0.0007	0.04 (0.02, 0.07) 0.0009	
	Age						0.6992*
	<= median	751/1403 (53.5)	716/1469 (48.7)	1.10 (1.02, 1.18)*0.0103	1.23 (1.06, 1.43) 0.0072	0.05 (0.01, 0.08) 0.0104	
	> median	682/1389 (49.1)	579/1323 (43.8)	1.09 (1.01, 1.17) 0.0229	1.20 (1.03, 1.41) 0.0223	0.04 (0.01, 0.08) 0.0215	
	Gender						0.6146
	Male	816/1638 (49.8)	745/1602 (46.5)	1.07 (1.00, 1.14) 0.0387	1.14 (0.99, 1.31) 0.0772	0.03 (-0.00, 0.06) 0.0654	
	Female	617/1154 (53.5)	550/1190 (46.2)	1.09 (1.01, 1.18) 0.0225	1.30 (1.10, 1.54) 0.0022	0.06 (0.02, 0.10) 0.0032	
	Race						0.6479*
	White	1012/2004 (50.5)	921/2025 (45.5)	1.06 (1.01, 1.13) 0.0271	1.20 (1.06, 1.37) 0.0050	0.04 (0.01, 0.07) 0.0103	
	Black or African	30/ 66 (45.5)	27/ 68 (39.7)	1.09 (0.75, 1.59) 0.6465	1.29 (0.63, 2.65) 0.4839	0.05 (-0.11, 0.21) 0.5681	
	Asian	284/ 551 (51.5)	253/ 550 (46.0)	1.11 (0.99, 1.25) 0.0843	1.24 (0.97, 1.57) 0.0830	0.05 (-0.00, 0.11) 0.0711	
	Other	107/ 171 (62.6)	94/ 149 (63.1)	1.04 (0.89, 1.21) 0.6418	1.01 (0.63, 1.63) 0.9611	0.01 (-0.09, 0.11) 0.8214	
	Geographic region						0.3616*
	Asia	276/ 533 (51.8)	248/ 533 (46.5)	1.10 (0.98, 1.24) 0.1136	1.22 (0.96, 1.55) 0.1105	0.05 (-0.01, 0.11) 0.0953	
	Europe and Saudi Arabia	681/1347 (50.6)	618/1373 (45.0)	1.07 (1.00, 1.14) 0.0601	1.24 (1.06, 1.46) 0.0069	0.04 (0.01, 0.08) 0.0199	
	North America	174/ 391 (44.5)	139/ 375 (37.1)	1.14 (0.98, 1.34) 0.0968	1.32 (0.98, 1.79) 0.0685	0.06 (-0.00, 0.13) 0.0595	
	Latin America	302/ 521 (58.0)	290/ 511 (56.8)	1.03 (0.95, 1.13) 0.4685	1.06 (0.82, 1.37) 0.6650	0.02 (-0.04, 0.07) 0.6000	
	NYHA class at enrolment						0.1306
	II	1048/2077 (50.5)	1004/2159 (46.5)	1.05 (1.00, 1.12) 0.0693	1.17 (1.04, 1.33) 0.0112	0.04 (0.01, 0.06) 0.0153	
	III or IV	385/ 715 (53.8)	291/ 632 (46.0)	1.13 (1.03, 1.25) 0.0104	1.35 (1.08, 1.70) 0.0090	0.07 (0.02, 0.12) 0.0068	
	LVEF at enrolment						0.4793
	<= 49	512/ 967 (52.9)	461/ 952 (48.4)	1.08 (1.00, 1.17) 0.0608	1.25 (1.04, 1.50) 0.0193	0.05 (0.01, 0.09) 0.0256	
	50-59	515/1013 (50.8)	442/ 998 (44.3)	1.11 (1.03, 1.21) 0.0109	1.27 (1.06, 1.52) 0.0104	0.06 (0.01, 0.10) 0.0082	
	>= 60	406/ 812 (50.0)	392/ 842 (46.6)	1.04 (0.95, 1.13) 0.4341	1.08 (0.89, 1.33) 0.4331	0.02 (-0.03, 0.06) 0.4899	
	NT-proBNP at enrolment						0.9719
	<= median	732/1394 (52.5)	651/1402 (46.4)	1.09 (1.02, 1.17) 0.0145	1.28 (1.10, 1.49) 0.0018	0.05 (0.02, 0.09) 0.0032	
	> median	701/1398 (50.1)	643/1389 (46.3)	1.07 (1.00, 1.15) 0.0396	1.14 (0.98, 1.33) 0.0967	0.03 (-0.00, 0.07) 0.0723	
	Type 2 Diabetes Medical History						0.5288
	Yes	630/1232 (51.1)	569/1237 (46.0)	1.09 (1.02, 1.17) 0.0170	1.23 (1.05, 1.44)*0.0107	0.05 (0.01, 0.09) 0.0103	
	No	803/1560 (51.5)	726/1555 (46.7)	1.07 (1.00, 1.14) 0.0470	1.21 (1.05, 1.39)*0.0076	0.04 (0.00, 0.07) 0.0292	
	Atrial fibrillation or flutter at enrolment ECG						0.5175
	Yes	600/1178 (50.9)	555/1175 (47.2)	1.06 (0.98, 1.14) 0.1436	1.15 (0.97, 1.36) 0.0963	0.04 (-0.00, 0.07) 0.0740	
	No	833/1614 (51.6)	740/1617 (45.8)	1.09 (1.02, 1.17) 0.0075	1.25 (1.08, 1.44) 0.0024	0.05 (0.02, 0.08) 0.0042	
	BMI (kg/m2) at enrolment						0.3238
	< 30	793/1547 (51.3)	704/1535 (45.9)	1.11 (1.04, 1.19) 0.0021	1.24 (1.07, 1.43) 0.0041	0.05 (0.02, 0.08) 0.0037	
	>= 30	640/1244 (51.4)	590/1254 (47.0)	1.04 (0.97, 1.11) 0.2770	1.16 (0.99, 1.37) 0.0746	0.03 (-0.01, 0.07) 0.0949	
	Baseline eGFR (mL/min/1.73m^2)						0.5472
	< 60	659/1328 (49.6)	614/1367 (44.9)	1.08 (1.01, 1.16) 0.0316	1.21 (1.03, 1.42) 0.0172	0.04 (0.01, 0.08) 0.0178	
	>= 60	774/1464 (52.9)	681/1424 (47.8)	1.07 (1.00, 1.14) 0.0614	1.20 (1.03, 1.39) 0.0208	0.04 (0.01, 0.08) 0.0252	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.4518
	<= median	721/1396 (51.6)	638/1414 (45.1)	1.10 (1.03, 1.18) 0.0082	1.25 (1.07, 1.46) 0.0044	0.05 (0.02, 0.09) 0.0047	
	> median	712/1396 (51.0)	657/1378 (47.7)	1.06 (0.99, 1.13) 0.1097	1.17 (1.00, 1.36) 0.0526	0.03 (-0.00, 0.07) 0.0593	
	LVEF at enrolment 2						0.6476
	<= 49	512/ 967 (52.9)	461/ 952 (48.4)	1.08 (1.00, 1.17) 0.0608	1.25 (1.04, 1.50) 0.0193	0.05 (0.01, 0.09) 0.0256	
	>= 50	921/1825 (50.5)	834/1840 (45.3)	1.08 (1.01, 1.14) 0.0156	1.18 (1.03, 1.35) 0.0153	0.04 (0.01, 0.07) 0.0150	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3561*
	Yes	158/ 273 (57.9)	135/ 277 (48.7)	1.19 (1.01, 1.39)*0.0325	1.57 (1.09, 2.26) 0.0146	0.09 (0.01, 0.17)*0.0310	
	No	1275/2519 (50.6)	1160/2515 (46.1)	1.07 (1.02, 1.13) 0.0103	1.18 (1.05, 1.32) 0.0047	0.04 (0.01, 0.06) 0.0054	
	MRAs at baseline						0.9060
	Yes	611/1200 (50.9)	548/1208 (45.4)	1.08 (1.00, 1.16) 0.0485	1.26 (1.06, 1.48) 0.0072	0.05 (0.01, 0.09) 0.0085	
	No	822/1592 (51.6)	747/1584 (47.2)	1.08 (1.01, 1.15) 0.0227	1.17 (1.01, 1.35) 0.0322	0.04 (0.00, 0.07) 0.0343	
	ACEi+ARB at baseline						0.2696
	Yes	1058/2029 (52.1)	946/2047 (46.2)	1.09 (1.03, 1.15) 0.0022	1.25 (1.10, 1.43) 0.0005	0.05 (0.02, 0.08) 0.0006	
	No	375/ 763 (49.1)	349/ 745 (46.8)	1.04 (0.94, 1.15) 0.4464	1.09 (0.89, 1.34) 0.4100	0.02 (-0.03, 0.07) 0.4270	
	ARNI at baseline						0.4941
	Yes	72/ 150 (48.0)	58/ 123 (47.2)	1.12 (0.87, 1.44) 0.3856	1.12 (0.69, 1.83) 0.6483	0.03 (-0.09, 0.15) 0.6175	
	No	1361/2642 (51.5)	1237/2669 (46.3)	1.07 (1.02, 1.13) 0.0070	1.21 (1.08, 1.36) 0.0008	0.04 (0.02, 0.07) 0.0011	
	Beta Blocker at baseline						0.5515
	Yes	1190/2323 (51.2)	1077/2321 (46.4)	1.07 (1.01, 1.12) 0.0189	1.19 (1.06, 1.34) 0.0039	0.04 (0.01, 0.07) 0.0051	
	No	243/ 469 (51.8)	218/ 471 (46.3)	1.12 (1.00, 1.27) 0.0586	1.27 (0.98, 1.66) 0.0721	0.06 (-0.00, 0.12) 0.0658	
	Diuretics at baseline						0.2423
	Yes	1277/2493 (51.2)	1145/2492 (45.9)	1.09 (1.03, 1.14) 0.0018	1.22 (1.09, 1.37) 0.0006	0.05 (0.02, 0.07) 0.0008	
	No	156/ 299 (52.2)	150/ 300 (50.0)	1.00 (0.87, 1.15) 0.9558	1.07 (0.77, 1.50) 0.6890	0.01 (-0.06, 0.09) 0.7352	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	1644/2842 (57.8)	1558/2837 (54.9)	1.02 (0.99, 1.04) 0.1438	1.11 (0.99, 1.24) 0.0810	0.02 (-0.00, 0.04) 0.0635	
	Age						0.8966*
	<= median	866/1415 (61.2)	861/1482 (58.1)	1.04 (1.00, 1.08) 0.0735	1.14 (0.97, 1.34) 0.1003	0.03 (0.00, 0.06) 0.0434	
	> median	778/1427 (54.5)	697/1355 (51.4)	1.06 (0.99, 1.14)*0.1042	1.08 (0.91, 1.27) 0.3791	0.03 (-0.01, 0.07)*0.1035	
	Gender						0.0955*
	Male	948/1656 (57.2)	913/1625 (56.2)	1.02 (0.96, 1.08)*0.5395	1.01 (0.87, 1.18) 0.8633	0.01 (-0.02, 0.04)*0.5394	
	Female	696/1186 (58.7)	645/1212 (53.2)	1.02 (0.97, 1.07) 0.3808	1.25 (1.04, 1.49) 0.0150	0.02 (-0.01, 0.06) 0.1358	
	Race						0.6520*
	White	1173/2039 (57.5)	1113/2058 (54.1)	1.06 (1.01, 1.12)*0.0264	1.12 (0.98, 1.28) 0.0992	0.03 (0.00, 0.06)*0.0263	
	Black or African	45/ 67 (67.2)	42/ 71 (59.2)	1.14 (0.88, 1.47)*0.3304	1.39 (0.65, 2.97) 0.3965	0.08 (-0.08, 0.24)*0.3276	
	Asian	297/ 558 (53.2)	298/ 555 (53.7)	0.99 (0.89, 1.11)*0.8757	0.98 (0.76, 1.26) 0.8872	-0.00 (-0.06, 0.05)*0.8757	
	Other	129/ 178 (72.5)	105/ 153 (68.6)	0.97 (0.84, 1.14) 0.7446	1.28 (0.77, 2.13) 0.3487	-0.00 (-0.10, 0.10) 0.9756	
	Geographic region						0.2805*
	Asia	289/ 539 (53.6)	291/ 538 (54.1)	0.99 (0.89, 1.11)*0.8767	0.97 (0.75, 1.25) 0.8319	-0.00 (-0.06, 0.05)*0.8767	
	Europe and Saudi Arabia	765/1365 (56.0)	744/1394 (53.4)	1.05 (0.98, 1.12)*0.1586	1.08 (0.91, 1.27) 0.3838	0.03 (-0.01, 0.06)*0.1584	
	North America	255/ 398 (64.1)	214/ 387 (55.3)	1.16 (1.03, 1.30)*0.0128	1.49 (1.10, 2.04) 0.0113	0.09 (0.02, 0.16)*0.0119	
	Latin America	335/ 540 (62.0)	309/ 518 (59.7)	1.04 (0.94, 1.15)*0.4274	1.09 (0.83, 1.43) 0.5269	0.02 (-0.03, 0.07) 0.3960	
	NYHA class at enrolment						0.1939*
	II	1186/2113 (56.1)	1189/2187 (54.4)	1.03 (0.98, 1.09)*0.2453	1.08 (0.95, 1.23) 0.2599	0.02 (-0.01, 0.05)*0.2453	
	III or IV	458/ 729 (62.8)	369/ 649 (56.9)	1.04 (0.98, 1.10) 0.1881	1.26 (0.99, 1.60) 0.0632	0.03 (-0.01, 0.07) 0.0958	
	LVEF at enrolment						0.2355*
	<= 49	578/ 980 (59.0)	566/ 963 (58.8)	0.99 (0.95, 1.04) 0.7901	1.02 (0.84, 1.23) 0.8771	-0.00 (-0.03, 0.03) 0.9677	
	50-59	592/1029 (57.5)	531/1017 (52.2)	1.10 (1.02, 1.19)*0.0159	1.23 (1.02, 1.49) 0.0344	0.05 (0.01, 0.10)*0.0155	
	>= 60	474/ 833 (56.9)	461/ 857 (53.8)	1.06 (0.97, 1.15)*0.1985	1.08 (0.88, 1.33) 0.4765	0.03 (-0.02, 0.08)*0.1982	
	NT-proBNP at enrolment						0.4625*
	<= median	830/1418 (58.5)	776/1421 (54.6)	1.07 (1.00, 1.14)*0.0351	1.15 (0.98, 1.35) 0.0814	0.04 (0.00, 0.08)*0.0348	
	> median	814/1424 (57.2)	781/1415 (55.2)	1.00 (0.97, 1.04) 0.8581	1.06 (0.90, 1.25) 0.4601	0.01 (-0.02, 0.03) 0.6005	
	Type 2 Diabetes Medical History						0.3709
	Yes	745/1250 (59.6)	680/1260 (54.0)	1.04 (0.99, 1.09) 0.1322	1.26 (1.07, 1.47)*0.0044	0.04 (0.00, 0.07) 0.0267	
	No	899/1592 (56.5)	878/1577 (55.7)	1.01 (0.99, 1.04) 0.4075	1.03 (0.90, 1.19)*0.6523	0.01 (-0.01, 0.03) 0.4648	
	Atrial fibrillation or flutter at enrolment ECG						0.9981*
	Yes	692/1199 (57.7)	657/1199 (54.8)	1.05 (0.98, 1.13)*0.1499	1.10 (0.92, 1.31) 0.2854	0.03 (-0.01, 0.07)*0.1495	
	No	952/1643 (57.9)	901/1638 (55.0)	1.05 (0.99, 1.12)*0.0900	1.11 (0.96, 1.29) 0.1623	0.03 (-0.00, 0.06)*0.0897	
	BMI (kg/m2) at enrolment						0.3377*
	< 30	875/1571 (55.7)	841/1559 (53.9)	1.00 (0.97, 1.03) 0.9523	1.03 (0.88, 1.20) 0.7084	0.00 (-0.02, 0.03) 0.8566	
	>= 30	769/1270 (60.6)	715/1275 (56.1)	1.08 (1.01, 1.15)*0.0223	1.22 (1.03, 1.45) 0.0234	0.04 (0.01, 0.08)*0.0220	
	Baseline eGFR (mL/min/1.73m^2)						0.2805*
	< 60	755/1359 (55.6)	757/1396 (54.2)	1.02 (0.96, 1.10)*0.4833	1.04 (0.88, 1.23) 0.6294	0.01 (-0.02, 0.05)*0.4833	
	>= 60	889/1483 (59.9)	801/1440 (55.6)	1.04 (1.00, 1.08) 0.0851	1.17 (1.00, 1.37) 0.0570	0.03 (0.00, 0.05) 0.0475	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.2129*
	<= median	840/1424 (59.0)	783/1439 (54.4)	1.01 (0.97, 1.05) 0.6295	1.16 (0.99, 1.37) 0.0660	0.01 (-0.01, 0.04) 0.3040	
	> median	804/1418 (56.7)	775/1398 (55.4)	1.02 (0.96, 1.09)*0.4996	1.05 (0.90, 1.24) 0.5329	0.01 (-0.02, 0.05)*0.4994	
	LVEF at enrolment 2						0.1195*
	<= 49	578/ 980 (59.0)	566/ 963 (58.8)	0.99 (0.95, 1.04) 0.7901	1.02 (0.84, 1.23) 0.8771	-0.00 (-0.03, 0.03) 0.9677	
	>= 50	1066/1862 (57.3)	992/1874 (52.9)	1.08 (1.02, 1.15)*0.0081	1.16 (1.00, 1.33) 0.0430	0.04 (0.01, 0.08)*0.0080	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8103*
	Yes	182/ 283 (64.3)	172/ 286 (60.1)	1.07 (0.94, 1.22)*0.3053	1.16 (0.79, 1.70) 0.4602	0.04 (-0.04, 0.12)*0.3044	
	No	1462/2559 (57.1)	1386/2551 (54.3)	1.02 (0.99, 1.05) 0.1412	1.10 (0.98, 1.24) 0.1126	0.02 (-0.00, 0.04) 0.0696	
	MRAs at baseline						0.4936*
	Yes	711/1227 (57.9)	661/1224 (54.0)	1.01 (0.97, 1.06) 0.6403	1.17 (0.98, 1.39) 0.0823	0.02 (-0.01, 0.05) 0.2443	
	No	933/1615 (57.8)	897/1613 (55.6)	1.04 (0.98, 1.10)*0.2157	1.07 (0.91, 1.24) 0.4145	0.02 (-0.01, 0.06)*0.2154	
	ACEi+ARB at baseline						0.1143*
	Yes	1206/2065 (58.4)	1126/2077 (54.2)	1.08 (1.02, 1.14)*0.0066	1.19 (1.04, 1.36) 0.0126	0.04 (0.01, 0.07)*0.0065	
	No	438/ 777 (56.4)	432/ 760 (56.8)	0.98 (0.93, 1.05) 0.6122	0.93 (0.75, 1.15) 0.5043	-0.01 (-0.05, 0.03) 0.6064	
	ARNI at baseline						0.2174*
	Yes	86/ 153 (56.2)	76/ 126 (60.3)	0.94 (0.76, 1.15) 0.5240	0.77 (0.47, 1.27) 0.3027	-0.05 (-0.17, 0.06) 0.3594	
	No	1558/2689 (57.9)	1482/2711 (54.7)	1.06 (1.01, 1.11)*0.0154	1.13 (1.01, 1.27) 0.0367	0.03 (0.01, 0.06)*0.0153	
	Beta Blocker at baseline						0.1476*
	Yes	1365/2360 (57.8)	1274/2356 (54.1)	1.07 (1.02, 1.13)*0.0093	1.14 (1.01, 1.29) 0.0414	0.04 (0.01, 0.07)*0.0092	
	No	279/ 482 (57.9)	284/ 481 (59.0)	0.98 (0.88, 1.09)*0.7150	0.96 (0.73, 1.27) 0.7678	0.00 (-0.05, 0.05) 0.9453	
	Diuretics at baseline						0.0648*
	Yes	1471/2536 (58.0)	1373/2531 (54.2)	1.02 (0.99, 1.05) 0.1116	1.16 (1.03, 1.31) 0.0144	0.02 (0.00, 0.04) 0.0274	
	No	173/ 306 (56.5)	185/ 306 (60.5)	0.94 (0.82, 1.07)*0.3254	0.77 (0.55, 1.08) 0.1289	-0.04 (-0.12, 0.04)*0.3245	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	1795/2842 (63.2)	1668/2837 (58.8)	1.07 (1.03, 1.12)*0.0008	1.20 (1.08, 1.34) 0.0011	0.04 (0.02, 0.07)*0.0007	
	Age						0.5572*
	<= median	947/1415 (66.9)	931/1482 (62.8)	1.07 (1.01, 1.12)*0.0207	1.22 (1.04, 1.43) 0.0135	0.04 (0.01, 0.08)*0.0205	
	> median	848/1427 (59.4)	737/1355 (54.4)	1.09 (1.02, 1.17)*0.0075	1.21 (1.03, 1.41) 0.0183	0.04 (0.01, 0.08) 0.0236	
	Gender						0.6203*
	Male	1049/1656 (63.3)	967/1625 (59.5)	1.06 (1.01, 1.12)*0.0241	1.17 (1.01, 1.35) 0.0332	0.04 (0.01, 0.07)*0.0239	
	Female	746/1186 (62.9)	701/1212 (57.8)	1.09 (1.02, 1.16)*0.0114	1.24 (1.05, 1.47) 0.0129	0.05 (0.01, 0.09)*0.0112	
	Race						0.3474*
	White	1258/2039 (61.7)	1185/2058 (57.6)	1.07 (1.02, 1.13)*0.0073	1.18 (1.03, 1.34) 0.0150	0.04 (0.01, 0.07)*0.0072	
	Black or African	41/ 67 (61.2)	49/ 71 (69.0)	0.89 (0.69, 1.13)*0.3385	0.70 (0.34, 1.45) 0.3401	-0.05 (-0.21, 0.11) 0.5149	
	Asian	363/ 558 (65.1)	335/ 555 (60.4)	1.07 (0.98, 1.17) 0.1410	1.24 (0.97, 1.58) 0.0872	0.05 (-0.01, 0.10) 0.1024	
	Other	133/ 178 (74.7)	99/ 153 (64.7)	1.15 (1.01, 1.30) 0.0283	1.63 (0.99, 2.69) 0.0528	0.10 (0.01, 0.19) 0.0325	
	Geographic region						0.3054*
	Asia	350/ 539 (64.9)	327/ 538 (60.8)	1.05 (0.96, 1.15) 0.2414	1.20 (0.94, 1.55) 0.1449	0.04 (-0.02, 0.10) 0.1764	
	Europe and Saudi Arabia	830/1365 (60.8)	800/1394 (57.4)	1.06 (1.00, 1.13)*0.0681	1.13 (0.97, 1.33) 0.1247	0.03 (-0.00, 0.07)*0.0678	
	North America	249/ 398 (62.6)	203/ 387 (52.5)	1.19 (1.06, 1.35)*0.0045	1.53 (1.14, 2.05) 0.0044	0.10 (0.03, 0.16) 0.0044	
	Latin America	366/ 540 (67.8)	338/ 518 (65.3)	1.04 (0.95, 1.13)*0.3845	1.14 (0.87, 1.48) 0.3458	0.03 (-0.03, 0.08)*0.3839	
	NYHA class at enrolment						0.9917*
	II	1326/2113 (62.8)	1278/2187 (58.4)	1.07 (1.02, 1.13)*0.0038	1.21 (1.07, 1.38) 0.0025	0.04 (0.01, 0.07)*0.0037	
	III or IV	469/ 729 (64.3)	389/ 649 (59.9)	1.07 (0.99, 1.17)*0.0944	1.19 (0.94, 1.50) 0.1393	0.04 (-0.01, 0.10)*0.0929	
	LVEF at enrolment						0.1003*
	<= 49	610/ 980 (62.2)	593/ 963 (61.6)	1.01 (0.94, 1.08)*0.7623	1.05 (0.87, 1.27) 0.6271	0.01 (-0.04, 0.05)*0.7623	
	50-59	646/1029 (62.8)	569/1017 (55.9)	1.12 (1.04, 1.21)*0.0017	1.34 (1.11, 1.61) 0.0018	0.07 (0.03, 0.11)*0.0016	
	>= 60	539/ 833 (64.7)	506/ 857 (59.0)	1.10 (1.02, 1.18)*0.0167	1.24 (1.01, 1.51) 0.0385	0.05 (0.00, 0.09) 0.0395	
	NT-proBNP at enrolment						0.5292*
	<= median	879/1418 (62.0)	831/1421 (58.5)	1.06 (1.00, 1.13)*0.0563	1.17 (1.00, 1.36) 0.0491	0.03 (-0.00, 0.07) 0.0701	
	> median	916/1424 (64.3)	836/1415 (59.1)	1.09 (1.03, 1.15)*0.0041	1.24 (1.06, 1.45) 0.0086	0.05 (0.02, 0.09)*0.0040	
	Type 2 Diabetes Medical History						0.3257*
	Yes	789/1250 (63.1)	723/1260 (57.4)	1.10 (1.03, 1.17)*0.0034	1.27 (1.08, 1.49)*0.0033	0.06 (0.02, 0.10)*0.0033	
	No	1006/1592 (63.2)	945/1577 (59.9)	1.05 (1.00, 1.11)*0.0589	1.15 (0.99, 1.32)*0.0588	0.03 (-0.01, 0.06) 0.1027	
	Atrial fibrillation or flutter at enrolment ECG						0.9310*
	Yes	774/1199 (64.6)	722/1199 (60.2)	1.07 (1.01, 1.14)*0.0286	1.21 (1.02, 1.43) 0.0326	0.04 (0.00, 0.08)*0.0282	
	No	1021/1643 (62.1)	946/1638 (57.8)	1.08 (1.02, 1.14)*0.0104	1.20 (1.04, 1.38) 0.0135	0.04 (0.01, 0.08)*0.0102	
	BMI (kg/m2) at enrolment						0.5656*
	< 30	990/1571 (63.0)	905/1559 (58.1)	1.09 (1.03, 1.15)*0.0045	1.23 (1.06, 1.43) 0.0054	0.05 (0.01, 0.08) 0.0052	
	>= 30	804/1270 (63.3)	762/1275 (59.8)	1.06 (1.00, 1.13)*0.0665	1.16 (0.98, 1.37) 0.0860	0.04 (-0.00, 0.07)*0.0661	
	Baseline eGFR (mL/min/1.73m^2)						0.6663*
	< 60	813/1359 (59.8)	786/1396 (56.3)	1.06 (1.00, 1.13)*0.0613	1.15 (0.99, 1.35) 0.0726	0.04 (-0.00, 0.07)*0.0611	
	>= 60	982/1483 (66.2)	881/1440 (61.2)	1.08 (1.02, 1.14)*0.0047	1.24 (1.06, 1.45) 0.0063	0.05 (0.02, 0.09)*0.0046	

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Symptom Burden (LOCF)	SBP at randomisation						0.1147*
	<= median	909/1424 (63.8)	827/1439 (57.5)	1.11 (1.05, 1.18)*0.0005	1.27 (1.09, 1.49) 0.0022	0.05 (0.02, 0.08) 0.0041	
	> median	886/1418 (62.5)	841/1398 (60.2)	1.04 (0.98, 1.10)*0.2055	1.13 (0.97, 1.32) 0.1269	0.02 (-0.01, 0.06)*0.2052	
	LVEF at enrolment 2						0.0360*
	<= 49	610/ 980 (62.2)	593/ 963 (61.6)	1.01 (0.94, 1.08)*0.7623	1.05 (0.87, 1.27) 0.6271	0.01 (-0.04, 0.05)*0.7623	
	>= 50	1185/1862 (63.6)	1075/1874 (57.4)	1.11 (1.05, 1.17)*<.0001	1.29 (1.13, 1.47) 0.0002	0.06 (0.03, 0.09)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2301*
	Yes	192/ 283 (67.8)	193/ 286 (67.5)	1.01 (0.90, 1.13)*0.9265	1.11 (0.76, 1.61) 0.6014	0.00 (-0.07, 0.08)*0.9265	
	No	1603/2559 (62.6)	1475/2551 (57.8)	1.08 (1.04, 1.13)*0.0004	1.22 (1.08, 1.36) 0.0009	0.04 (0.02, 0.07) 0.0010	
	MRAs at baseline						0.5042*
	Yes	774/1227 (63.1)	707/1224 (57.8)	1.09 (1.02, 1.16)*0.0072	1.24 (1.05, 1.47) 0.0110	0.05 (0.01, 0.09)*0.0070	
	No	1021/1615 (63.2)	961/1613 (59.6)	1.06 (1.00, 1.12)*0.0338	1.17 (1.01, 1.36) 0.0325	0.04 (0.00, 0.07)*0.0335	
	ACEi+ARB at baseline						0.1524*
	Yes	1322/2065 (64.0)	1215/2077 (58.5)	1.09 (1.04, 1.15)*0.0003	1.26 (1.10, 1.43) 0.0006	0.06 (0.03, 0.08)*0.0003	
	No	473/ 777 (60.9)	453/ 760 (59.6)	1.02 (0.94, 1.11)*0.6111	1.06 (0.86, 1.31) 0.5568	0.01 (-0.03, 0.06) 0.5876	
	ARNI at baseline						0.1130*
	Yes	86/ 153 (56.2)	77/ 126 (61.1)	0.96 (0.78, 1.17) 0.6824	0.87 (0.53, 1.42) 0.5760	-0.03 (-0.15, 0.09) 0.6137	
	No	1709/2689 (63.6)	1591/2711 (58.7)	1.08 (1.04, 1.13)*0.0002	1.22 (1.09, 1.37) 0.0005	0.05 (0.02, 0.07)*0.0002	
	Beta Blocker at baseline						0.8394*
	Yes	1476/2360 (62.5)	1369/2356 (58.1)	1.08 (1.03, 1.13)*0.0019	1.19 (1.06, 1.34) 0.0046	0.04 (0.02, 0.07)*0.0018	
	No	319/ 482 (66.2)	299/ 481 (62.2)	1.06 (0.97, 1.17)*0.1937	1.24 (0.95, 1.63) 0.1129	0.05 (-0.01, 0.11) 0.0918	
	Diuretics at baseline						0.9925*
	Yes	1591/2536 (62.7)	1478/2531 (58.4)	1.07 (1.03, 1.12)*0.0016	1.21 (1.08, 1.36) 0.0014	0.04 (0.02, 0.07)*0.0016	
	No	204/ 306 (66.7)	190/ 306 (62.1)	1.07 (0.95, 1.21)*0.2379	1.14 (0.81, 1.60) 0.4503	0.05 (-0.03, 0.12)*0.2368	

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Self Efficacy (LOCF)							
	Overall	1678/2842 (59.0)	1658/2837 (58.4)	1.01 (0.97, 1.06)*0.6456	1.02 (0.92, 1.14) 0.6618	0.01 (-0.01, 0.03) 0.4383	
	Age						0.0116*
	<= median	847/1415 (59.9)	924/1482 (62.3)	0.96 (0.91, 1.02)*0.1699	0.90 (0.77, 1.05) 0.1744	-0.02 (-0.06, 0.01) 0.2165	
	> median	831/1427 (58.2)	734/1355 (54.2)	1.08 (1.01, 1.15)*0.0312	1.18 (1.01, 1.37) 0.0370	0.04 (0.01, 0.08) 0.0183	
	Gender						0.6174*
	Male	992/1656 (59.9)	973/1625 (59.9)	1.00 (0.95, 1.06)*0.9877	1.01 (0.87, 1.16) 0.9231	0.01 (-0.03, 0.04) 0.7367	
	Female	686/1186 (57.8)	685/1212 (56.5)	1.02 (0.95, 1.10)*0.5126	1.05 (0.89, 1.23) 0.5931	0.01 (-0.02, 0.05) 0.4483	
	Race						0.8960*
	White	1222/2039 (59.9)	1225/2058 (59.5)	1.03 (0.98, 1.08) 0.1881	1.01 (0.89, 1.15) 0.8619	0.01 (-0.02, 0.04) 0.6235	
	Black or African	42/ 67 (62.7)	44/ 71 (62.0)	1.01 (0.78, 1.31)*0.9310	1.08 (0.52, 2.23) 0.8354	0.01 (-0.15, 0.17)*0.9310	
	Asian	301/ 558 (53.9)	299/ 555 (53.9)	1.00 (0.90, 1.12)*0.9816	1.04 (0.81, 1.33) 0.7670	0.00 (-0.06, 0.06)*0.9816	
	Other	113/ 178 (63.5)	90/ 153 (58.8)	1.08 (0.91, 1.28)*0.3883	1.26 (0.78, 2.02) 0.3468	0.05 (-0.06, 0.15)*0.3857	
	Geographic region						0.5059*
	Asia	291/ 539 (54.0)	288/ 538 (53.5)	1.01 (0.90, 1.13)*0.8804	1.07 (0.83, 1.37) 0.6174	0.00 (-0.05, 0.06)*0.8804	
	Europe and Saudi Arabia	784/1365 (57.4)	798/1394 (57.2)	1.00 (0.94, 1.07)*0.9194	1.01 (0.86, 1.17) 0.9356	0.01 (-0.03, 0.04) 0.7792	
	North America	250/ 398 (62.8)	254/ 387 (65.6)	0.96 (0.86, 1.06)*0.4101	0.89 (0.66, 1.19) 0.4208	-0.02 (-0.08, 0.05) 0.6280	
	Latin America	353/ 540 (65.4)	318/ 518 (61.4)	1.06 (0.97, 1.17)*0.1800	1.18 (0.91, 1.52) 0.2155	0.05 (-0.01, 0.11) 0.0803	
	NYHA class at enrolment						0.0080*
	II	1217/2113 (57.6)	1291/2187 (59.0)	0.98 (0.93, 1.03)*0.3403	0.94 (0.83, 1.06) 0.3070	-0.01 (-0.04, 0.02) 0.4768	
	III or IV	461/ 729 (63.2)	367/ 649 (56.5)	1.12 (1.02, 1.22)*0.0120	1.36 (1.09, 1.70) 0.0067	0.07 (0.02, 0.12)*0.0113	
	LVEF at enrolment						0.4632*
	<= 49	582/ 980 (59.4)	587/ 963 (61.0)	0.97 (0.91, 1.05)*0.4804	0.95 (0.79, 1.15) 0.6017	-0.01 (-0.05, 0.04) 0.7620	
	50-59	585/1029 (56.9)	564/1017 (55.5)	1.03 (0.95, 1.11)*0.5253	1.06 (0.88, 1.26) 0.5455	0.01 (-0.03, 0.06) 0.5182	
	>= 60	511/ 833 (61.3)	507/ 857 (59.2)	1.04 (0.96, 1.12)*0.3589	1.08 (0.88, 1.32) 0.4654	0.03 (-0.02, 0.07) 0.2416	
	NT-proBNP at enrolment						0.9972*
	<= median	834/1418 (58.8)	827/1421 (58.2)	1.03 (0.97, 1.09) 0.3059	1.02 (0.88, 1.19) 0.8043	0.01 (-0.03, 0.04) 0.6554	
	> median	844/1424 (59.3)	830/1415 (58.7)	1.01 (0.95, 1.07)*0.7401	1.03 (0.88, 1.20) 0.6961	0.01 (-0.02, 0.05) 0.5646	
	Type 2 Diabetes Medical History						0.2296*
	Yes	771/1250 (61.7)	747/1260 (59.3)	1.05 (0.99, 1.11) 0.1079	1.11 (0.94, 1.30)*0.2200	0.02 (-0.01, 0.06) 0.2015	
	No	907/1592 (57.0)	911/1577 (57.8)	0.99 (0.93, 1.05)*0.6507	0.97 (0.84, 1.11)*0.6507	-0.00 (-0.03, 0.03) 0.9426	
	Atrial fibrillation or flutter at enrolment ECG						0.4139*
	Yes	698/1199 (58.2)	676/1199 (56.4)	1.03 (0.96, 1.11)*0.3639	1.06 (0.90, 1.26) 0.4700	0.02 (-0.02, 0.05) 0.4268	
	No	980/1643 (59.6)	982/1638 (60.0)	0.99 (0.94, 1.05)*0.8590	1.00 (0.86, 1.15) 0.9583	0.00 (-0.03, 0.04) 0.8004	
	BMI (kg/m2) at enrolment						0.1939*
	< 30	878/1571 (55.9)	886/1559 (56.8)	0.98 (0.92, 1.05)*0.5947	0.95 (0.82, 1.09) 0.4552	-0.00 (-0.04, 0.03) 0.8228	
	>= 30	799/1270 (62.9)	770/1275 (60.4)	1.04 (0.98, 1.11)*0.1911	1.12 (0.96, 1.32) 0.1557	0.03 (-0.01, 0.06) 0.1480	
	Baseline eGFR (mL/min/1.73m^2)						0.4288*
	< 60	788/1359 (58.0)	816/1396 (58.5)	0.99 (0.93, 1.06)*0.8030	0.99 (0.85, 1.16) 0.9241	-0.00 (-0.04, 0.04) 0.9923	
	>= 60	890/1483 (60.0)	841/1440 (58.4)	1.03 (0.97, 1.09)*0.3759	1.05 (0.90, 1.22) 0.5141	0.02 (-0.02, 0.05) 0.2945	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.4911*
	<= median	833/1424 (58.5)	846/1439 (58.8)	1.00 (0.94, 1.06)*0.8733	0.98 (0.84, 1.15) 0.8274	-0.00 (-0.04, 0.03)*0.8733	
	> median	845/1418 (59.6)	812/1398 (58.1)	1.05 (0.99, 1.12) 0.0772	1.07 (0.92, 1.25) 0.3911	0.02 (-0.02, 0.06) 0.2626	
	LVEF at enrolment 2						0.2296*
	<= 49	582/ 980 (59.4)	587/ 963 (61.0)	0.97 (0.91, 1.05)*0.4804	0.95 (0.79, 1.15) 0.6017	-0.01 (-0.05, 0.04) 0.7620	
	>= 50	1096/1862 (58.9)	1071/1874 (57.2)	1.03 (0.98, 1.09)*0.2895	1.06 (0.93, 1.22) 0.3658	0.02 (-0.01, 0.05) 0.2372	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5855*
	Yes	174/ 283 (61.5)	168/ 286 (58.7)	1.05 (0.92, 1.20)*0.5042	1.15 (0.81, 1.62) 0.4433	0.03 (-0.05, 0.11) 0.4687	
	No	1504/2559 (58.8)	1490/2551 (58.4)	1.01 (0.96, 1.05)*0.7914	1.01 (0.90, 1.13) 0.8335	0.01 (-0.02, 0.03) 0.6037	
	MRAs at baseline						0.7413*
	Yes	711/1227 (57.9)	696/1224 (56.9)	1.02 (0.95, 1.09)*0.5876	1.06 (0.90, 1.25) 0.5188	0.01 (-0.02, 0.05) 0.4591	
	No	967/1615 (59.9)	962/1613 (59.6)	1.00 (0.95, 1.06)*0.8914	1.01 (0.87, 1.16) 0.9347	0.01 (-0.03, 0.04) 0.7232	
	ACEi+ARB at baseline						0.8342*
	Yes	1227/2065 (59.4)	1218/2077 (58.6)	1.01 (0.96, 1.07)*0.6113	1.03 (0.91, 1.17) 0.6229	0.01 (-0.01, 0.04) 0.3233	
	No	451/ 777 (58.0)	440/ 760 (57.9)	1.00 (0.92, 1.09)*0.9528	1.01 (0.82, 1.24) 0.9594	-0.00 (-0.05, 0.05) 0.9847	
	ARNI at baseline						0.7118*
	Yes	88/ 153 (57.5)	69/ 126 (54.8)	1.05 (0.85, 1.29)*0.6456	1.17 (0.72, 1.90) 0.5339	0.03 (-0.09, 0.15) 0.6022	
	No	1590/2689 (59.1)	1589/2711 (58.6)	1.01 (0.96, 1.05)*0.6996	1.02 (0.91, 1.14) 0.7474	0.01 (-0.02, 0.03) 0.4778	
	Beta Blocker at baseline						0.7902*
	Yes	1380/2360 (58.5)	1360/2356 (57.7)	1.01 (0.97, 1.06)*0.6019	1.03 (0.92, 1.16) 0.5960	0.01 (-0.02, 0.04) 0.3913	
	No	298/ 482 (61.8)	298/ 481 (62.0)	1.01 (0.92, 1.11) 0.8468	0.99 (0.76, 1.28) 0.9128	-0.00 (-0.06, 0.06) 0.9865	
	Diuretics at baseline						0.1865*
	Yes	1492/2536 (58.8)	1459/2531 (57.6)	1.02 (0.97, 1.07)*0.3914	1.05 (0.94, 1.18) 0.3767	0.02 (-0.01, 0.04) 0.2414	
	No	186/ 306 (60.8)	199/ 306 (65.0)	0.93 (0.83, 1.06)*0.2772	0.80 (0.57, 1.13) 0.2049	-0.04 (-0.12, 0.03)*0.2762	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	1633/2842 (57.5)	1544/2837 (54.4)	1.06 (1.01, 1.11)*0.0213	1.14 (1.02, 1.27) 0.0199	0.03 (0.01, 0.06) 0.0099	
	Age						0.3324*
	<= median	849/1415 (60.0)	858/1482 (57.9)	1.04 (0.98, 1.10)*0.2495	1.12 (0.96, 1.30) 0.1554	0.03 (-0.00, 0.07) 0.0665	
	> median	784/1427 (54.9)	686/1355 (50.6)	1.09 (1.01, 1.16)*0.0231	1.18 (1.01, 1.38) 0.0429	0.04 (0.01, 0.08)*0.0226	
	Gender						0.4967*
	Male	954/1656 (57.6)	899/1625 (55.3)	1.04 (0.98, 1.11)*0.1870	1.11 (0.96, 1.28) 0.1584	0.03 (-0.00, 0.06) 0.0667	
	Female	679/1186 (57.3)	645/1212 (53.2)	1.08 (1.00, 1.16)*0.0472	1.18 (0.99, 1.39) 0.0635	0.03 (-0.00, 0.07) 0.0718	
	Race						0.6966*
	White	1139/2039 (55.9)	1096/2058 (53.3)	1.05 (0.99, 1.11)*0.0941	1.09 (0.96, 1.25) 0.1744	0.03 (-0.00, 0.05) 0.0652	
	Black or African	38/ 67 (56.7)	44/ 71 (62.0)	0.92 (0.69, 1.21)*0.5313	0.84 (0.41, 1.71) 0.6363	-0.01 (-0.17, 0.15) 0.8792	
	Asian	335/ 558 (60.0)	309/ 555 (55.7)	1.07 (0.97, 1.18) 0.1491	1.23 (0.96, 1.56) 0.0959	0.05 (-0.01, 0.10) 0.1015	
	Other	121/ 178 (68.0)	95/ 153 (62.1)	1.09 (0.93, 1.28)*0.2663	1.50 (0.91, 2.48) 0.1152	0.06 (-0.04, 0.16)*0.2627	
	Geographic region						0.7679*
	Asia	325/ 539 (60.3)	300/ 538 (55.8)	1.07 (0.97, 1.18) 0.2011	1.23 (0.96, 1.57) 0.0995	0.05 (-0.01, 0.10) 0.1175	
	Europe and Saudi Arabia	758/1365 (55.5)	734/1394 (52.7)	1.05 (0.98, 1.13)*0.1296	1.10 (0.94, 1.29) 0.2315	0.03 (-0.01, 0.07)*0.1293	
	North America	206/ 398 (51.8)	202/ 387 (52.2)	1.03 (0.92, 1.17) 0.5827	1.01 (0.76, 1.35) 0.9505	0.01 (-0.06, 0.08) 0.8134	
	Latin America	344/ 540 (63.7)	308/ 518 (59.5)	1.07 (0.97, 1.18)*0.1568	1.25 (0.95, 1.63) 0.1065	0.04 (-0.02, 0.10)*0.1556	
	NYHA class at enrolment						0.5480*
	II	1186/2113 (56.1)	1175/2187 (53.7)	1.04 (0.99, 1.10)*0.1135	1.13 (1.00, 1.28) 0.0566	0.03 (-0.00, 0.05) 0.0711	
	III or IV	447/ 729 (61.3)	369/ 649 (56.9)	1.08 (0.99, 1.18)*0.0941	1.19 (0.95, 1.50) 0.1260	0.05 (0.00, 0.10) 0.0395	
	LVEF at enrolment						0.8716*
	<= 49	574/ 980 (58.6)	536/ 963 (55.7)	1.05 (0.97, 1.14)*0.1951	1.17 (0.97, 1.41) 0.0993	0.03 (-0.01, 0.07)*0.1945	
	50-59	571/1029 (55.5)	541/1017 (53.2)	1.04 (0.96, 1.13)*0.2976	1.10 (0.92, 1.32) 0.3140	0.02 (-0.02, 0.06) 0.2553	
	>= 60	488/ 833 (58.6)	467/ 857 (54.5)	1.08 (0.99, 1.17)*0.0900	1.15 (0.94, 1.41) 0.1699	0.03 (-0.01, 0.08) 0.1287	
	NT-proBNP at enrolment						0.1821*
	<= median	790/1418 (55.7)	774/1421 (54.5)	1.03 (0.97, 1.09) 0.2864	1.06 (0.91, 1.24) 0.4541	0.02 (-0.02, 0.05) 0.3789	
	> median	843/1424 (59.2)	769/1415 (54.3)	1.09 (1.02, 1.16)*0.0092	1.23 (1.05, 1.44) 0.0103	0.05 (0.01, 0.08)*0.0090	
	Type 2 Diabetes Medical History						0.1720*
	Yes	733/1250 (58.6)	675/1260 (53.6)	1.09 (1.02, 1.17)*0.0106	1.23 (1.05, 1.44)*0.0106	0.05 (0.02, 0.09) 0.0038	
	No	900/1592 (56.5)	869/1577 (55.1)	1.03 (0.96, 1.09)*0.4184	1.06 (0.92, 1.22)*0.4183	0.01 (-0.02, 0.05) 0.3546	
	Atrial fibrillation or flutter at enrolment ECG						0.5964*
	Yes	709/1199 (59.1)	662/1199 (55.2)	1.07 (1.00, 1.15)*0.0527	1.20 (1.01, 1.42) 0.0370	0.03 (-0.00, 0.07) 0.0627	
	No	924/1643 (56.2)	882/1638 (53.8)	1.04 (0.98, 1.11)*0.1686	1.10 (0.95, 1.27) 0.1973	0.03 (-0.00, 0.06) 0.0860	
	BMI (kg/m2) at enrolment						0.6466*
	< 30	894/1571 (56.9)	832/1559 (53.4)	1.07 (1.00, 1.14)*0.0468	1.17 (1.01, 1.36) 0.0338	0.04 (0.00, 0.07)*0.0464	
	>= 30	739/1270 (58.2)	711/1275 (55.8)	1.04 (0.98, 1.12)*0.2170	1.10 (0.93, 1.29) 0.2730	0.03 (-0.01, 0.06) 0.1557	
	Baseline eGFR (mL/min/1.73m^2)						0.9043*
	< 60	759/1359 (55.8)	741/1396 (53.1)	1.05 (0.98, 1.13)*0.1445	1.13 (0.96, 1.32) 0.1346	0.02 (-0.01, 0.06) 0.2425	
	>= 60	874/1483 (58.9)	802/1440 (55.7)	1.06 (0.99, 1.13)*0.0770	1.15 (0.98, 1.34) 0.0795	0.04 (0.01, 0.08) 0.0133	

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Symptom Frequency (LOCF)	SBP at randomisation						0.2389*
	<= median	809/1424 (56.8)	753/1439 (52.3)	1.09 (1.02, 1.16)*0.0161	1.18 (1.01, 1.38) 0.0319	0.03 (-0.00, 0.07) 0.0547	
	> median	824/1418 (58.1)	791/1398 (56.6)	1.03 (0.96, 1.09)*0.4121	1.09 (0.93, 1.27) 0.2784	0.03 (-0.01, 0.06) 0.1284	
	LVEF at enrolment 2						0.9224*
	<= 49	574/ 980 (58.6)	536/ 963 (55.7)	1.05 (0.97, 1.14)*0.1951	1.17 (0.97, 1.41) 0.0993	0.03 (-0.01, 0.07)*0.1945	
	>= 50	1059/1862 (56.9)	1008/1874 (53.8)	1.06 (1.00, 1.12)*0.0580	1.12 (0.98, 1.28) 0.0998	0.03 (-0.00, 0.06) 0.0659	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8697*
	Yes	192/ 283 (67.8)	182/ 286 (63.6)	1.07 (0.95, 1.20)*0.2907	1.54 (1.05, 2.27) 0.0284	0.04 (-0.04, 0.12)*0.2897	
	No	1441/2559 (56.3)	1362/2551 (53.4)	1.05 (1.00, 1.11)*0.0361	1.12 (1.00, 1.25) 0.0539	0.03 (0.00, 0.05) 0.0275	
	MRAs at baseline						0.4902*
	Yes	699/1227 (57.0)	648/1224 (52.9)	1.08 (1.00, 1.16)*0.0454	1.19 (1.01, 1.41) 0.0395	0.04 (0.00, 0.08)*0.0449	
	No	934/1615 (57.8)	896/1613 (55.5)	1.04 (0.99, 1.09) 0.1074	1.10 (0.95, 1.27) 0.1877	0.02 (-0.01, 0.05) 0.1559	
	ACEi+ARB at baseline						0.0381*
	Yes	1209/2065 (58.5)	1118/2077 (53.8)	1.09 (1.03, 1.15)*0.0022	1.21 (1.07, 1.38) 0.0034	0.05 (0.02, 0.08)*0.0022	
	No	424/ 777 (54.6)	426/ 760 (56.1)	0.99 (0.91, 1.08) 0.8149	0.96 (0.78, 1.17) 0.6708	-0.01 (-0.06, 0.04) 0.7117	
	ARNI at baseline						0.1232*
	Yes	86/ 153 (56.2)	78/ 126 (61.9)	0.91 (0.75, 1.10)*0.3339	0.85 (0.52, 1.39) 0.5224	-0.03 (-0.15, 0.08) 0.5579	
	No	1547/2689 (57.5)	1466/2711 (54.1)	1.06 (1.01, 1.12)*0.0106	1.15 (1.03, 1.29) 0.0148	0.03 (0.01, 0.06) 0.0074	
	Beta Blocker at baseline						0.9606*
	Yes	1347/2360 (57.1)	1273/2356 (54.0)	1.06 (1.00, 1.11)*0.0355	1.12 (1.00, 1.27) 0.0601	0.03 (-0.00, 0.05) 0.0587	
	No	286/ 482 (59.3)	271/ 481 (56.3)	1.05 (0.95, 1.17)*0.3469	1.21 (0.93, 1.58) 0.1581	0.06 (-0.00, 0.12) 0.0592	
	Diuretics at baseline						0.3351*
	Yes	1440/2536 (56.8)	1372/2531 (54.2)	1.05 (1.00, 1.10)*0.0653	1.13 (1.01, 1.27) 0.0406	0.03 (0.00, 0.06) 0.0222	
	No	193/ 306 (63.1)	172/ 306 (56.2)	1.12 (0.98, 1.28)*0.0845	1.23 (0.87, 1.72) 0.2392	0.07 (-0.01, 0.15)*0.0828	

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Social Limitation (LOCF)							
	Overall	1569/2669 (58.8)	1486/2664 (55.8)	1.04 (1.00, 1.09) 0.0482	1.14 (1.02, 1.27) 0.0234	0.03 (0.00, 0.05) 0.0265	
	Age						0.2369
	<= median	851/1352 (62.9)	823/1422 (57.9)	1.07 (1.02, 1.13) 0.0106	1.27 (1.08, 1.48) 0.0031	0.05 (0.02, 0.09) 0.0040	
	> median	718/1317 (54.5)	663/1242 (53.4)	1.01 (0.95, 1.08) 0.7267	1.03 (0.88, 1.21) 0.6821	0.01 (-0.03, 0.04) 0.6929	
	Gender						0.8910
	Male	939/1568 (59.9)	864/1518 (56.9)	1.05 (0.99, 1.11) 0.0923	1.14 (0.99, 1.33) 0.0705	0.03 (-0.00, 0.06) 0.0678	
	Female	630/1101 (57.2)	622/1146 (54.3)	1.03 (0.97, 1.11) 0.3223	1.12 (0.94, 1.33) 0.2083	0.02 (-0.02, 0.06) 0.2373	
	Race						0.6476
	White	1092/1925 (56.7)	1045/1952 (53.5)	1.04 (0.99, 1.09) 0.1346	1.12 (0.99, 1.28) 0.0816	0.03 (-0.00, 0.06) 0.0783	
	Black or African	33/ 61 (54.1)	38/ 67 (56.7)	0.95 (0.70, 1.30)*0.7664	0.96 (0.46, 2.03) 0.9239	0.02 (-0.15, 0.19) 0.7987	
	Asian	323/ 510 (63.3)	309/ 500 (61.8)	1.02 (0.93, 1.12) 0.6603	1.08 (0.83, 1.39) 0.5700	0.02 (-0.04, 0.08) 0.6041	
	Other	121/ 173 (69.9)	94/ 145 (64.8)	1.12 (0.96, 1.30) 0.1562	1.40 (0.86, 2.29) 0.1783	0.07 (-0.03, 0.17) 0.1513	
	Geographic region						0.3258
	Asia	318/ 496 (64.1)	304/ 486 (62.6)	1.02 (0.93, 1.12) 0.6449	1.08 (0.83, 1.40) 0.5804	0.02 (-0.04, 0.08) 0.6060	
	Europe and Saudi Arabia	721/1299 (55.5)	709/1323 (53.6)	1.01 (0.95, 1.07) 0.6794	1.05 (0.89, 1.23) 0.5492	0.01 (-0.02, 0.05) 0.5205	
	North America	208/ 372 (55.9)	191/ 359 (53.2)	1.05 (0.93, 1.19) 0.4092	1.16 (0.86, 1.56) 0.3347	0.03 (-0.04, 0.10) 0.3485	
	Latin America	322/ 502 (64.1)	282/ 496 (56.9)	1.11 (1.02, 1.21) 0.0214	1.41 (1.08, 1.84) 0.0124	0.07 (0.02, 0.13) 0.0097	
	NYHA class at enrolment						0.5779
	II	1178/1986 (59.3)	1166/2059 (56.6)	1.04 (0.99, 1.09) 0.0849	1.13 (1.00, 1.29) 0.0549	0.03 (-0.00, 0.06) 0.0616	
	III or IV	391/ 683 (57.2)	320/ 604 (53.0)	1.05 (0.96, 1.14) 0.2850	1.21 (0.96, 1.53) 0.1050	0.04 (-0.01, 0.09) 0.1386	
	LVEF at enrolment						0.2660
	<= 49	553/ 928 (59.6)	539/ 912 (59.1)	1.01 (0.95, 1.08) 0.7220	1.06 (0.88, 1.29) 0.5367	0.01 (-0.03, 0.06) 0.5952	
	50-59	555/ 970 (57.2)	491/ 956 (51.4)	1.09 (1.01, 1.17) 0.0230	1.24 (1.03, 1.49) 0.0233	0.05 (0.01, 0.09) 0.0177	
	>= 60	461/ 771 (59.8)	456/ 796 (57.3)	1.03 (0.96, 1.12) 0.4020	1.11 (0.91, 1.37) 0.3089	0.02 (-0.02, 0.07) 0.3455	
	NT-proBNP at enrolment						0.5271
	<= median	780/1334 (58.5)	757/1350 (56.1)	1.03 (0.97, 1.10) 0.3268	1.11 (0.95, 1.30) 0.1730	0.02 (-0.01, 0.06) 0.2116	
	> median	789/1335 (59.1)	728/1313 (55.4)	1.06 (0.99, 1.12) 0.0742	1.16 (0.99, 1.36) 0.0643	0.03 (-0.00, 0.07) 0.0581	
	Type 2 Diabetes Medical History						0.3082
	Yes	698/1169 (59.7)	652/1186 (55.0)	1.07 (1.01, 1.15) 0.0336	1.21 (1.03, 1.43)*0.0203	0.05 (0.01, 0.09) 0.0192	
	No	871/1500 (58.1)	834/1478 (56.4)	1.02 (0.97, 1.08) 0.4297	1.07 (0.92, 1.24)*0.3660	0.02 (-0.02, 0.05) 0.3791	
	Atrial fibrillation or flutter at enrolment ECG						0.6812
	Yes	666/1113 (59.8)	644/1123 (57.3)	1.03 (0.97, 1.10) 0.3006	1.11 (0.93, 1.32) 0.2387	0.02 (-0.02, 0.06) 0.2453	
	No	903/1556 (58.0)	842/1541 (54.6)	1.05 (0.99, 1.11) 0.0886	1.16 (1.00, 1.34) 0.0474	0.03 (-0.00, 0.07) 0.0517	
	BMI (kg/m2) at enrolment						0.4626
	< 30	878/1478 (59.4)	801/1451 (55.2)	1.06 (1.00, 1.13) 0.0350	1.19 (1.03, 1.39) 0.0197	0.04 (0.01, 0.08) 0.0218	
	>= 30	691/1190 (58.1)	683/1211 (56.4)	1.02 (0.96, 1.09) 0.4376	1.07 (0.91, 1.27) 0.4040	0.02 (-0.02, 0.05) 0.4076	
	Baseline eGFR (mL/min/1.73m^2)						0.9602
	< 60	708/1266 (55.9)	702/1297 (54.1)	1.04 (0.97, 1.10) 0.2679	1.09 (0.92, 1.27) 0.3157	0.02 (-0.02, 0.06) 0.2893	
	>= 60	861/1403 (61.4)	784/1366 (57.4)	1.05 (0.99, 1.11) 0.1254	1.18 (1.01, 1.38) 0.0363	0.03 (-0.00, 0.07) 0.0583	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)	SBP at randomisation						0.1599
	<= median	785/1344 (58.4)	763/1344 (56.8)	1.01 (0.96, 1.08) 0.6531	1.05 (0.90, 1.23) 0.5403	0.01 (-0.03, 0.05) 0.5553	
	> median	784/1325 (59.2)	723/1320 (54.8)	1.08 (1.01, 1.14) 0.0184	1.23 (1.05, 1.44) 0.0099	0.05 (0.01, 0.08) 0.0106	
	LVEF at enrolment 2						0.2564
	<= 49	553/ 928 (59.6)	539/ 912 (59.1)	1.01 (0.95, 1.08) 0.7220	1.06 (0.88, 1.29) 0.5367	0.01 (-0.03, 0.06) 0.5952	
	>= 50	1016/1741 (58.4)	947/1752 (54.1)	1.06 (1.01, 1.12) 0.0300	1.18 (1.03, 1.35) 0.0197	0.04 (0.01, 0.07) 0.0197	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4131
	Yes	151/ 257 (58.8)	149/ 261 (57.1)	0.96 (0.84, 1.08) 0.4660	1.11 (0.77, 1.61) 0.5691	0.00 (-0.08, 0.08) 0.9545	
	No	1418/2412 (58.8)	1337/2403 (55.6)	1.05 (1.01, 1.10) 0.0285	1.14 (1.02, 1.28) 0.0261	0.03 (0.00, 0.06) 0.0233	
	MRAs at baseline						0.3382
	Yes	676/1155 (58.5)	650/1146 (56.7)	1.02 (0.96, 1.09) 0.5291	1.09 (0.92, 1.29) 0.3090	0.02 (-0.02, 0.06) 0.3559	
	No	893/1514 (59.0)	836/1518 (55.1)	1.06 (1.01, 1.12) 0.0327	1.17 (1.01, 1.36) 0.0366	0.04 (0.00, 0.07) 0.0333	
	ACEi+ARB at baseline						0.3169
	Yes	1146/1940 (59.1)	1082/1959 (55.2)	1.05 (1.00, 1.11) 0.0362	1.18 (1.03, 1.34) 0.0152	0.04 (0.01, 0.07) 0.0182	
	No	423/ 729 (58.0)	404/ 705 (57.3)	1.01 (0.93, 1.10) 0.8407	1.04 (0.84, 1.28) 0.7426	0.01 (-0.04, 0.06) 0.7543	
	ARNI at baseline						0.9160
	Yes	84/ 149 (56.4)	65/ 116 (56.0)	1.00 (0.81, 1.24) 0.9969	0.99 (0.61, 1.63) 0.9819	-0.00 (-0.12, 0.12) 0.9859	
	No	1485/2520 (58.9)	1421/2548 (55.8)	1.04 (1.00, 1.09) 0.0554	1.14 (1.02, 1.28) 0.0225	0.03 (0.00, 0.06) 0.0271	
	Beta Blocker at baseline						0.2754
	Yes	1295/2232 (58.0)	1237/2218 (55.8)	1.03 (0.98, 1.08) 0.2047	1.09 (0.96, 1.23) 0.1659	0.02 (-0.01, 0.05) 0.1669	
	No	274/ 437 (62.7)	249/ 446 (55.8)	1.11 (1.00, 1.23) 0.0441	1.40 (1.07, 1.85) 0.0160	0.07 (0.01, 0.14) 0.0209	
	Diuretics at baseline						0.3370
	Yes	1400/2391 (58.6)	1309/2379 (55.0)	1.05 (1.00, 1.10) 0.0317	1.17 (1.04, 1.32) 0.0082	0.04 (0.01, 0.06) 0.0111	
	No	169/ 278 (60.8)	177/ 285 (62.1)	0.97 (0.85, 1.10) 0.6159	0.91 (0.64, 1.28) 0.5878	-0.02 (-0.10, 0.06) 0.6027	

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AstraZeneca
Protocol: D169CC00001
Overall study population
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)							
	Overall	797/2842 (28.0)	793/2837 (28.0)	1.00 (0.92, 1.09)*0.9387	0.99 (0.88, 1.12) 0.9015	-0.01 (-0.03, 0.01) 0.2982	
	Age						0.0369*
	<= median	435/1415 (30.7)	417/1482 (28.1)	1.09 (0.98, 1.22)*0.1242	1.13 (0.95, 1.34) 0.1566	0.01 (-0.02, 0.04) 0.6209	
	> median	362/1427 (25.4)	376/1355 (27.7)	0.91 (0.81, 1.03)*0.1552	0.87 (0.73, 1.04) 0.1224	-0.02 (-0.06, 0.01)*0.1552	
	Gender						0.8035*
	Male	435/1656 (26.3)	429/1625 (26.4)	0.97 (0.89, 1.06) 0.5168	0.98 (0.83, 1.15) 0.7985	-0.01 (-0.04, 0.01) 0.3062	
	Female	362/1186 (30.5)	364/1212 (30.0)	1.02 (0.90, 1.15)*0.7941	1.01 (0.84, 1.22) 0.8772	0.00 (-0.03, 0.04)*0.7941	
	Race						0.6340*
	White	576/2039 (28.2)	565/2058 (27.5)	1.00 (0.93, 1.08) 0.9664	1.03 (0.89, 1.19) 0.7034	-0.01 (-0.03, 0.02) 0.6372	
	Black or African	26/ 67 (38.8)	33/ 71 (46.5)	0.83 (0.56, 1.23)*0.3655	0.67 (0.32, 1.38) 0.2725	-0.08 (-0.24, 0.09)*0.3607	
	Asian	128/ 558 (22.9)	138/ 555 (24.9)	0.93 (0.77, 1.13) 0.4586	0.89 (0.67, 1.18) 0.4240	-0.02 (-0.07, 0.03) 0.3901	
	Other	67/ 178 (37.6)	57/ 153 (37.3)	1.01 (0.76, 1.34)*0.9424	1.10 (0.66, 1.84) 0.7109	0.00 (-0.10, 0.11)*0.9424	
	Geographic region						0.5857*
	Asia	122/ 539 (22.6)	133/ 538 (24.7)	0.92 (0.75, 1.12) 0.3909	0.88 (0.66, 1.17) 0.3880	-0.02 (-0.07, 0.03) 0.3786	
	Europe and Saudi Arabia	388/1365 (28.4)	380/1394 (27.3)	1.04 (0.92, 1.18)*0.4948	1.07 (0.90, 1.28) 0.4487	0.01 (-0.02, 0.05)*0.4948	
	North America	103/ 398 (25.9)	110/ 387 (28.4)	0.91 (0.72, 1.15)*0.4231	0.80 (0.58, 1.12) 0.1971	-0.04 (-0.09, 0.02) 0.1857	
	Latin America	184/ 540 (34.1)	170/ 518 (32.8)	1.04 (0.88, 1.23)*0.6654	1.09 (0.83, 1.45) 0.5330	0.01 (-0.04, 0.07)*0.6652	
	NYHA class at enrolment						0.7827*
	II	568/2113 (26.9)	592/2187 (27.1)	0.96 (0.90, 1.02) 0.2145	0.99 (0.86, 1.14) 0.9022	-0.01 (-0.03, 0.02) 0.5278	
	III or IV	229/ 729 (31.4)	200/ 649 (30.8)	1.02 (0.87, 1.19)*0.8115	0.97 (0.75, 1.25) 0.8267	0.01 (-0.04, 0.05)*0.8114	
	LVEF at enrolment						0.2399*
	<= 49	286/ 980 (29.2)	263/ 963 (27.3)	0.99 (0.88, 1.11) 0.8884	1.10 (0.89, 1.35) 0.3759	0.01 (-0.03, 0.04) 0.6729	
	50-59	280/1029 (27.2)	267/1017 (26.3)	1.04 (0.90, 1.20)*0.6248	1.04 (0.84, 1.28) 0.7137	-0.01 (-0.04, 0.02) 0.6360	
	>= 60	231/ 833 (27.7)	263/ 857 (30.7)	0.90 (0.78, 1.05)*0.1820	0.84 (0.67, 1.05) 0.1298	-0.04 (-0.07, -0.00) 0.0435	
	NT-proBNP at enrolment						0.8520*
	<= median	403/1418 (28.4)	399/1421 (28.1)	1.00 (0.91, 1.10) 0.9578	1.02 (0.86, 1.22) 0.7954	-0.00 (-0.03, 0.03) 0.8265	
	> median	394/1424 (27.7)	393/1415 (27.8)	1.00 (0.88, 1.12)*0.9500	0.96 (0.81, 1.15) 0.6811	-0.02 (-0.05, 0.01) 0.2360	
	Type 2 Diabetes Medical History						0.2038*
	Yes	332/1250 (26.6)	355/1260 (28.2)	1.01 (0.95, 1.08) 0.7735	0.92 (0.77, 1.10)*0.3644	-0.03 (-0.06, -0.00) 0.0426	
	No	465/1592 (29.2)	438/1577 (27.8)	1.05 (0.94, 1.17)*0.3713	1.07 (0.92, 1.25)*0.3712	0.01 (-0.02, 0.03) 0.6749	
	Atrial fibrillation or flutter at enrolment ECG						0.1853*
	Yes	303/1199 (25.3)	324/1199 (27.0)	0.94 (0.82, 1.07)*0.3293	0.90 (0.74, 1.10) 0.3050	-0.02 (-0.05, 0.02)*0.3290	
	No	494/1643 (30.1)	469/1638 (28.6)	1.00 (0.93, 1.07) 0.9771	1.06 (0.90, 1.24) 0.4980	-0.00 (-0.03, 0.03) 0.9573	
	BMI (kg/m2) at enrolment						0.5502*
	< 30	425/1571 (27.1)	410/1559 (26.3)	0.99 (0.91, 1.07) 0.7421	1.02 (0.86, 1.20) 0.8198	-0.00 (-0.03, 0.02) 0.8223	
	>= 30	372/1270 (29.3)	382/1275 (30.0)	0.98 (0.87, 1.10)*0.7115	0.97 (0.80, 1.16) 0.7212	-0.01 (-0.04, 0.03)*0.7115	
	Baseline eGFR (mL/min/1.73m^2)						0.0030*
	< 60	336/1359 (24.7)	395/1396 (28.3)	0.87 (0.77, 0.99)*0.0341	0.82 (0.68, 0.98) 0.0283	-0.04 (-0.07, -0.01) 0.0051	
	>= 60	461/1483 (31.1)	397/1440 (27.6)	1.13 (1.01, 1.26)*0.0372	1.17 (0.99, 1.39) 0.0658	0.02 (-0.01, 0.05) 0.2305	

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Symptom Stability (LOCF)	SBP at randomisation						0.2896*
	<= median	403/1424 (28.3)	388/1439 (27.0)	1.05 (0.93, 1.18)*0.4237	1.05 (0.88, 1.25) 0.5932	-0.01 (-0.04, 0.02) 0.3966	
	> median	394/1418 (27.8)	405/1398 (29.0)	0.98 (0.91, 1.06) 0.6253	0.95 (0.80, 1.12) 0.5223	-0.01 (-0.04, 0.02) 0.4792	
	LVEF at enrolment 2						0.2814*
	<= 49	286/ 980 (29.2)	263/ 963 (27.3)	0.99 (0.88, 1.11) 0.8884	1.10 (0.89, 1.35) 0.3759	0.01 (-0.03, 0.04) 0.6729	
	>= 50	511/1862 (27.4)	530/1874 (28.3)	0.97 (0.88, 1.08)*0.5678	0.94 (0.81, 1.10) 0.4409	-0.02 (-0.05, 0.00) 0.0812	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1516*
	Yes	89/ 283 (31.4)	105/ 286 (36.7)	0.86 (0.68, 1.08)*0.1865	0.80 (0.54, 1.18) 0.2538	-0.07 (-0.13, -0.01) 0.0253	
	No	708/2559 (27.7)	688/2551 (27.0)	0.98 (0.92, 1.05) 0.5827	1.02 (0.89, 1.16) 0.7851	-0.00 (-0.02, 0.02) 0.8304	
	MRAs at baseline						0.5929*
	Yes	360/1227 (29.3)	349/1224 (28.5)	0.99 (0.89, 1.09) 0.8140	1.06 (0.89, 1.28) 0.5090	0.00 (-0.03, 0.03) 0.9634	
	No	437/1615 (27.1)	444/1613 (27.5)	0.98 (0.88, 1.10)*0.7656	0.94 (0.79, 1.10) 0.4283	-0.00 (-0.04, 0.03)*0.7656	
	ACEi+ARB at baseline						0.6624*
	Yes	577/2065 (27.9)	585/2077 (28.2)	0.96 (0.89, 1.03) 0.2304	0.99 (0.85, 1.14) 0.8420	-0.01 (-0.03, 0.01) 0.4428	
	No	220/ 777 (28.3)	208/ 760 (27.4)	1.03 (0.88, 1.22)*0.6793	1.01 (0.80, 1.28) 0.9204	-0.01 (-0.05, 0.03) 0.5264	
	ARNI at baseline						0.9077*
	Yes	46/ 153 (30.1)	37/ 126 (29.4)	1.02 (0.71, 1.47)*0.8987	1.15 (0.67, 1.97) 0.6045	0.03 (-0.08, 0.13) 0.6045	
	No	751/2689 (27.9)	756/2711 (27.9)	1.00 (0.92, 1.09)*0.9724	0.99 (0.87, 1.12) 0.8184	-0.01 (-0.03, 0.01) 0.1927	
	Beta Blocker at baseline						0.6517*
	Yes	667/2360 (28.3)	658/2356 (27.9)	1.01 (0.92, 1.11)*0.7986	0.99 (0.86, 1.13) 0.8315	-0.01 (-0.03, 0.01) 0.3640	
	No	130/ 482 (27.0)	135/ 481 (28.1)	0.96 (0.78, 1.18)*0.7035	1.05 (0.77, 1.42) 0.7706	-0.01 (-0.05, 0.03) 0.6192	
	Diuretics at baseline						0.4658*
	Yes	705/2536 (27.8)	709/2531 (28.0)	0.97 (0.91, 1.03) 0.3030	0.98 (0.86, 1.11) 0.7246	-0.01 (-0.03, 0.01) 0.2453	
	No	92/ 306 (30.1)	84/ 306 (27.5)	1.10 (0.85, 1.41)*0.4753	1.13 (0.78, 1.62) 0.5271	0.01 (-0.06, 0.08) 0.8104	

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Total Symptom Score (LOCF)							
	Overall	1684/2842 (59.3)	1580/2837 (55.7)	1.06 (1.02, 1.11)*0.0067	1.16 (1.04, 1.30) 0.0074	0.04 (0.01, 0.06)*0.0066	
	Age						0.1288*
	<= median	888/1415 (62.8)	899/1482 (60.7)	1.03 (0.98, 1.10)*0.2461	1.12 (0.96, 1.30) 0.1648	0.02 (-0.01, 0.06)*0.2461	
	> median	796/1427 (55.8)	681/1355 (50.3)	1.11 (1.03, 1.19)*0.0036	1.23 (1.05, 1.44) 0.0092	0.06 (0.02, 0.09)*0.0035	
	Gender						0.3405*
	Male	978/1656 (59.1)	919/1625 (56.6)	1.04 (0.98, 1.11)*0.1467	1.11 (0.96, 1.28) 0.1556	0.03 (-0.01, 0.06)*0.1464	
	Female	706/1186 (59.5)	661/1212 (54.5)	1.09 (1.02, 1.17)*0.0137	1.23 (1.04, 1.46) 0.0164	0.05 (0.01, 0.09)*0.0135	
	Race						0.5909*
	White	1171/2039 (57.4)	1118/2058 (54.3)	1.06 (1.00, 1.12)*0.0454	1.12 (0.98, 1.27) 0.0935	0.03 (0.00, 0.06)*0.0452	
	Black or African	41/ 67 (61.2)	47/ 71 (66.2)	0.92 (0.72, 1.19)*0.5426	0.82 (0.40, 1.69) 0.5968	-0.01 (-0.17, 0.15) 0.9069	
	Asian	342/ 558 (61.3)	316/ 555 (56.9)	1.08 (0.98, 1.19)*0.1402	1.23 (0.96, 1.56) 0.0990	0.05 (-0.01, 0.10) 0.1081	
	Other	130/ 178 (73.0)	99/ 153 (64.7)	1.13 (0.97, 1.31)*0.1069	1.58 (0.95, 2.63) 0.0809	0.08 (-0.02, 0.18)*0.1024	
	Geographic region						0.9369*
	Asia	331/ 539 (61.4)	309/ 538 (57.4)	1.07 (0.97, 1.18)*0.1845	1.20 (0.94, 1.53) 0.1488	0.04 (-0.02, 0.10) 0.1760	
	Europe and Saudi Arabia	780/1365 (57.1)	749/1394 (53.7)	1.06 (0.99, 1.14)*0.0715	1.13 (0.96, 1.33) 0.1385	0.03 (-0.00, 0.07)*0.0712	
	North America	220/ 398 (55.3)	196/ 387 (50.6)	1.09 (0.96, 1.25)*0.1947	1.23 (0.92, 1.64) 0.1677	0.05 (-0.02, 0.11) 0.1737	
	Latin America	353/ 540 (65.4)	326/ 518 (62.9)	1.04 (0.95, 1.14)*0.4093	1.14 (0.87, 1.49) 0.3397	0.02 (-0.03, 0.08)*0.4087	
	NYHA class at enrolment						0.3556*
	II	1224/2113 (57.9)	1207/2187 (55.2)	1.05 (1.00, 1.11)*0.0702	1.14 (1.01, 1.29) 0.0391	0.03 (-0.00, 0.06)*0.0701	
	III or IV	460/ 729 (63.1)	372/ 649 (57.3)	1.10 (1.01, 1.20)*0.0295	1.27 (1.01, 1.60) 0.0418	0.06 (0.01, 0.11)*0.0285	
	LVEF at enrolment						0.6630*
	<= 49	586/ 980 (59.8)	554/ 963 (57.5)	1.04 (0.96, 1.12)*0.3105	1.13 (0.94, 1.37) 0.1896	0.02 (-0.02, 0.07)*0.3101	
	50-59	594/1029 (57.7)	552/1017 (54.3)	1.06 (0.98, 1.15)*0.1165	1.16 (0.96, 1.39) 0.1222	0.03 (-0.01, 0.08)*0.1159	
	>= 60	504/ 833 (60.5)	474/ 857 (55.3)	1.09 (1.01, 1.19)*0.0307	1.20 (0.98, 1.47) 0.0711	0.05 (0.00, 0.10)*0.0303	
	NT-proBNP at enrolment						0.3487*
	<= median	822/1418 (58.0)	791/1421 (55.7)	1.04 (0.98, 1.11)*0.2154	1.11 (0.95, 1.29) 0.1854	0.02 (-0.01, 0.06) 0.2399	
	> median	862/1424 (60.5)	788/1415 (55.7)	1.09 (1.02, 1.16)*0.0090	1.22 (1.04, 1.43) 0.0139	0.05 (0.01, 0.08)*0.0088	
	Type 2 Diabetes Medical History						0.1291*
	Yes	754/1250 (60.3)	687/1260 (54.5)	1.11 (1.03, 1.18)*0.0034	1.27 (1.08, 1.49)*0.0033	0.06 (0.02, 0.10)*0.0033	
	No	930/1592 (58.4)	893/1577 (56.6)	1.03 (0.97, 1.10)*0.3081	1.08 (0.93, 1.24)*0.3080	0.02 (-0.02, 0.05)*0.3079	
	Atrial fibrillation or flutter at enrolment ECG						0.7589*
	Yes	723/1199 (60.3)	685/1199 (57.1)	1.06 (0.99, 1.13)*0.1152	1.15 (0.97, 1.37) 0.1053	0.03 (-0.01, 0.07)*0.1148	
	No	961/1643 (58.5)	895/1638 (54.6)	1.07 (1.01, 1.14)*0.0262	1.17 (1.01, 1.35) 0.0328	0.04 (0.00, 0.07)*0.0260	
	BMI (kg/m2) at enrolment						0.2951*
	< 30	925/1571 (58.9)	844/1559 (54.1)	1.09 (1.02, 1.16)*0.0075	1.23 (1.06, 1.42) 0.0062	0.05 (0.01, 0.08)*0.0074	
	>= 30	759/1270 (59.8)	735/1275 (57.6)	1.04 (0.97, 1.11)*0.2783	1.08 (0.92, 1.28) 0.3593	0.02 (-0.02, 0.06)*0.2781	
	Baseline eGFR (mL/min/1.73m^2)						0.8927*
	< 60	762/1359 (56.1)	739/1396 (52.9)	1.06 (0.99, 1.13)*0.0987	1.14 (0.97, 1.33) 0.1062	0.03 (-0.01, 0.07)*0.0985	
	>= 60	922/1483 (62.2)	840/1440 (58.3)	1.07 (1.00, 1.13)*0.0343	1.18 (1.01, 1.37) 0.0385	0.04 (0.00, 0.07)*0.0339	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.2463*
	<= median	839/1424 (58.9)	776/1439 (53.9)	1.09 (1.02, 1.17)*0.0071	1.20 (1.03, 1.40) 0.0220	0.05 (0.01, 0.09)*0.0070	
	> median	845/1418 (59.6)	804/1398 (57.5)	1.04 (0.97, 1.10)*0.2628	1.12 (0.96, 1.31) 0.1509	0.02 (-0.02, 0.06)*0.2625	
	LVEF at enrolment 2						0.4548*
	<= 49	586/ 980 (59.8)	554/ 963 (57.5)	1.04 (0.96, 1.12)*0.3105	1.13 (0.94, 1.37) 0.1896	0.02 (-0.02, 0.07)*0.3101	
	>= 50	1098/1862 (59.0)	1026/1874 (54.7)	1.08 (1.02, 1.14)*0.0093	1.17 (1.03, 1.34) 0.0203	0.04 (0.01, 0.07)*0.0092	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8992*
	Yes	192/ 283 (67.8)	181/ 286 (63.3)	1.07 (0.95, 1.21)*0.2531	1.51 (1.03, 2.22) 0.0367	0.05 (-0.03, 0.12)*0.2520	
	No	1492/2559 (58.3)	1399/2551 (54.8)	1.06 (1.01, 1.12)*0.0126	1.14 (1.02, 1.28) 0.0218	0.03 (0.01, 0.06)*0.0125	
	MRAs at baseline						0.6955*
	Yes	721/1227 (58.8)	669/1224 (54.7)	1.08 (1.00, 1.15)*0.0405	1.19 (1.00, 1.40) 0.0461	0.04 (0.00, 0.08)*0.0401	
	No	963/1615 (59.6)	911/1613 (56.5)	1.06 (1.00, 1.12)*0.0700	1.15 (0.99, 1.33) 0.0642	0.03 (-0.00, 0.07)*0.0696	
	ACEi+ARB at baseline						0.0143*
	Yes	1251/2065 (60.6)	1143/2077 (55.0)	1.10 (1.04, 1.16)*0.0003	1.26 (1.10, 1.43) 0.0006	0.06 (0.03, 0.09)*0.0003	
	No	433/ 777 (55.7)	437/ 760 (57.5)	0.98 (0.90, 1.06) 0.5646	0.94 (0.77, 1.16) 0.5640	-0.01 (-0.06, 0.03) 0.5611	
	ARNI at baseline						0.1785*
	Yes	82/ 153 (53.6)	73/ 126 (57.9)	0.93 (0.75, 1.14)*0.4661	0.91 (0.56, 1.49) 0.7145	-0.02 (-0.14, 0.10) 0.7400	
	No	1602/2689 (59.6)	1507/2711 (55.6)	1.07 (1.02, 1.12)*0.0031	1.18 (1.05, 1.32) 0.0051	0.04 (0.01, 0.07)*0.0030	
	Beta Blocker at baseline						0.9180*
	Yes	1384/2360 (58.6)	1300/2356 (55.2)	1.06 (1.01, 1.12)*0.0163	1.14 (1.01, 1.29) 0.0339	0.03 (0.01, 0.06)*0.0162	
	No	300/ 482 (62.2)	280/ 481 (58.2)	1.07 (0.96, 1.18)*0.2020	1.27 (0.97, 1.66) 0.0839	0.04 (-0.02, 0.10)*0.2012	
	Diuretics at baseline						0.5814*
	Yes	1486/2536 (58.6)	1400/2531 (55.3)	1.06 (1.01, 1.11)*0.0184	1.16 (1.03, 1.30) 0.0121	0.03 (0.01, 0.06)*0.0182	
	No	198/ 306 (64.7)	180/ 306 (58.8)	1.10 (0.97, 1.25)*0.1352	1.18 (0.84, 1.66) 0.3480	0.06 (-0.02, 0.14)*0.1336	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	590/2801 (21.1)	735/2805 (26.2)	0.82 (0.74, 0.89) <.0001	0.75 (0.66, 0.85) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Age						0.3135
	<= median	262/1394 (18.8)	354/1471 (24.1)	0.77 (0.67, 0.89) 0.0003	0.71 (0.59, 0.86) 0.0003	-0.05 (-0.08, -0.02)*0.0006	
	> median	328/1407 (23.3)	381/1334 (28.6)	0.85 (0.75, 0.96) 0.0085	0.78 (0.65, 0.92) 0.0046	-0.05 (-0.09, -0.02)*0.0017	
	Gender						0.2886
	Male	329/1630 (20.2)	417/1608 (25.9)	0.78 (0.69, 0.89) 0.0001	0.72 (0.61, 0.85) 0.0001	-0.06 (-0.09, -0.03)*<.0001	
	Female	261/1171 (22.3)	318/1197 (26.6)	0.87 (0.76, 0.99) 0.0421	0.80 (0.66, 0.97) 0.0238	-0.04 (-0.08, -0.01)*0.0153	
	Race						0.5456
	White	431/2006 (21.5)	551/2032 (27.1)	0.81 (0.73, 0.90) <.0001	0.74 (0.64, 0.86) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Black or African	16/ 64 (25.0)	21/ 70 (30.0)	0.83 (0.48, 1.44) 0.5000	0.76 (0.36, 1.65) 0.4929	-0.06 (-0.21, 0.09) 0.4638	
	Asian	122/ 555 (22.0)	134/ 551 (24.3)	0.91 (0.73, 1.13) 0.3817	0.88 (0.66, 1.16) 0.3539	-0.03 (-0.07, 0.02) 0.2993	
	Other	21/ 176 (11.9)	29/ 152 (19.1)	0.61 (0.37, 1.02) 0.0578	0.55 (0.29, 1.03) 0.0616	-0.06 (-0.14, 0.01) 0.0829	
	Geographic region						0.3763
	Asia	117/ 536 (21.8)	130/ 536 (24.3)	0.91 (0.73, 1.13) 0.3786	0.87 (0.66, 1.16) 0.3497	-0.03 (-0.08, 0.02) 0.3039	
	Europe and Saudi Arabia	288/1341 (21.5)	376/1381 (27.2)	0.82 (0.72, 0.93) 0.0019	0.74 (0.61, 0.89) 0.0012	-0.06 (-0.09, -0.03)*0.0005	
	North America	99/ 393 (25.2)	109/ 376 (29.0)	0.87 (0.69, 1.09) 0.2154	0.82 (0.60, 1.14) 0.2388	-0.04 (-0.10, 0.02) 0.2067	
	Latin America	86/ 531 (16.2)	120/ 512 (23.4)	0.69 (0.54, 0.88) 0.0025	0.61 (0.44, 0.83) 0.0020	-0.07 (-0.12, -0.02)*0.0033	
	NYHA class at enrolment						0.3466
	II	448/2083 (21.5)	561/2165 (25.9)	0.83 (0.75, 0.92) 0.0005	0.77 (0.67, 0.89) 0.0004	-0.04 (-0.07, -0.02)*0.0007	
	III or IV	142/ 718 (19.8)	174/ 639 (27.2)	0.75 (0.63, 0.91) 0.0025	0.66 (0.51, 0.86) 0.0022	-0.07 (-0.12, -0.03)*0.0012	
	LVEF at enrolment						0.8537
	<= 49	194/ 959 (20.2)	242/ 950 (25.5)	0.79 (0.67, 0.93) 0.0041	0.72 (0.58, 0.89) 0.0030	-0.05 (-0.09, -0.01)*0.0063	
	50-59	220/1017 (21.6)	264/1009 (26.2)	0.84 (0.72, 0.97) 0.0195	0.78 (0.63, 0.96) 0.0196	-0.05 (-0.08, -0.01)*0.0166	
	>= 60	176/ 825 (21.3)	229/ 846 (27.1)	0.82 (0.70, 0.97) 0.0233	0.76 (0.60, 0.96) 0.0188	-0.06 (-0.10, -0.02)*0.0061	
	NT-proBNP at enrolment						0.3373
	<= median	305/1396 (21.8)	362/1409 (25.7)	0.85 (0.75, 0.97) 0.0155	0.80 (0.67, 0.96) 0.0149	-0.04 (-0.07, -0.01)*0.0167	
	> median	285/1405 (20.3)	373/1395 (26.7)	0.78 (0.69, 0.89) 0.0002	0.70 (0.59, 0.84) 0.0001	-0.06 (-0.10, -0.03)*<.0001	
	Type 2 Diabetes Medical History						0.0176
	Yes	243/1231 (19.7)	347/1243 (27.9)	0.72 (0.62, 0.83) <.0001	0.64 (0.53, 0.77)*<.0001	-0.08 (-0.12, -0.05)*<.0001	
	No	347/1570 (22.1)	388/1562 (24.8)	0.90 (0.80, 1.02) 0.0994	0.86 (0.73, 1.01)*0.0708	-0.03 (-0.06, 0.00)*0.0705	
	Atrial fibrillation or flutter at enrolment ECG						0.9621
	Yes	252/1185 (21.3)	312/1188 (26.3)	0.81 (0.71, 0.94) 0.0038	0.75 (0.62, 0.91) 0.0039	-0.05 (-0.08, -0.02)*0.0042	
	No	338/1616 (20.9)	423/1617 (26.2)	0.81 (0.72, 0.92) 0.0010	0.75 (0.64, 0.89) 0.0007	-0.05 (-0.08, -0.02)*0.0004	
	BMI (kg/m2) at enrolment						0.2874
	< 30	332/1547 (21.5)	392/1541 (25.4)	0.85 (0.75, 0.97) 0.0134	0.80 (0.68, 0.95) 0.0107	-0.04 (-0.07, -0.01)*0.0090	
	>= 30	258/1253 (20.6)	342/1261 (27.1)	0.77 (0.68, 0.89) 0.0002	0.70 (0.58, 0.84) 0.0002	-0.07 (-0.10, -0.03)*0.0001	
	Baseline eGFR (mL/min/1.73m^2)						0.9441
	< 60	301/1338 (22.5)	385/1377 (28.0)	0.81 (0.72, 0.92) 0.0013	0.75 (0.62, 0.89) 0.0013	-0.05 (-0.09, -0.02)*0.0010	
	>= 60	289/1463 (19.8)	349/1427 (24.5)	0.82 (0.72, 0.94) 0.0043	0.76 (0.64, 0.91) 0.0030	-0.05 (-0.08, -0.02)*0.0023	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.3082
	<= median	306/1405 (21.8)	376/1420 (26.5)	0.85 (0.75, 0.97) 0.0141	0.80 (0.67, 0.95) 0.0120	-0.05 (-0.08, -0.02)*0.0035	
	> median	284/1396 (20.3)	359/1385 (25.9)	0.78 (0.68, 0.89) 0.0002	0.70 (0.58, 0.84) 0.0001	-0.06 (-0.09, -0.02)*0.0005	
	LVEF at enrolment 2						0.5807
	<= 49	194/ 959 (20.2)	242/ 950 (25.5)	0.79 (0.67, 0.93) 0.0041	0.72 (0.58, 0.89) 0.0030	-0.05 (-0.09, -0.01)*0.0063	
	>= 50	396/1842 (21.5)	493/1855 (26.6)	0.83 (0.74, 0.93) 0.0012	0.77 (0.66, 0.90) 0.0010	-0.05 (-0.08, -0.02)*0.0003	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2245
	Yes	54/ 280 (19.3)	53/ 281 (18.9)	0.98 (0.70, 1.35) 0.8813	0.95 (0.61, 1.47) 0.8141	0.00 (-0.06, 0.07)*0.8982	
	No	536/2521 (21.3)	682/2524 (27.0)	0.80 (0.73, 0.88) <.0001	0.73 (0.64, 0.84) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	MRAs at baseline						0.7497
	Yes	253/1216 (20.8)	315/1210 (26.0)	0.80 (0.70, 0.92) 0.0023	0.75 (0.62, 0.91) 0.0030	-0.05 (-0.09, -0.02)*0.0023	
	No	337/1585 (21.3)	420/1595 (26.3)	0.83 (0.73, 0.93) 0.0022	0.75 (0.64, 0.89) 0.0010	-0.05 (-0.08, -0.02)*0.0008	
	ACEi+ARB at baseline						0.0088
	Yes	411/2037 (20.2)	560/2059 (27.2)	0.76 (0.68, 0.84) <.0001	0.68 (0.58, 0.78) <.0001	-0.07 (-0.10, -0.04)*<.0001	
	No	179/ 764 (23.4)	175/ 746 (23.5)	1.00 (0.84, 1.20) 0.9820	1.00 (0.78, 1.27) 0.9764	-0.01 (-0.05, 0.04) 0.7833	
	ARNI at baseline						0.1374
	Yes	32/ 149 (21.5)	22/ 125 (17.6)	1.23 (0.75, 2.01) 0.4201	1.25 (0.67, 2.32) 0.4786	0.04 (-0.06, 0.13)*0.4181	
	No	558/2652 (21.0)	713/2680 (26.6)	0.81 (0.73, 0.89) <.0001	0.74 (0.65, 0.84) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Beta Blocker at baseline						0.0268
	Yes	505/2327 (21.7)	607/2330 (26.1)	0.85 (0.77, 0.94) 0.0021	0.80 (0.69, 0.92) 0.0013	-0.04 (-0.07, -0.02)*0.0005	
	No	85/ 474 (17.9)	128/ 475 (26.9)	0.64 (0.50, 0.81) 0.0002	0.55 (0.40, 0.75) 0.0002	-0.09 (-0.14, -0.04)*0.0008	
	Diuretics at baseline						0.4826
	Yes	528/2500 (21.1)	662/2504 (26.4)	0.81 (0.73, 0.89) <.0001	0.74 (0.65, 0.84) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	No	62/ 301 (20.6)	73/ 301 (24.3)	0.89 (0.66, 1.20) 0.4438	0.85 (0.58, 1.25) 0.4093	-0.04 (-0.10, 0.03) 0.2721	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	590/2801 (21.1)	717/2805 (25.6)	0.83 (0.76, 0.91) 0.0001	0.78 (0.69, 0.88) 0.0001	-0.04 (-0.07, -0.02)*<.0001	
	Age						0.4562
	<= median	266/1394 (19.1)	345/1471 (23.5)	0.80 (0.70, 0.92) 0.0018	0.76 (0.63, 0.91) 0.0028	-0.04 (-0.07, -0.01)*0.0042	
	> median	324/1407 (23.0)	372/1334 (27.9)	0.86 (0.76, 0.97) 0.0157	0.79 (0.66, 0.94) 0.0087	-0.05 (-0.08, -0.02)*0.0035	
	Gender						0.9655
	Male	339/1630 (20.8)	403/1608 (25.1)	0.84 (0.74, 0.95) 0.0046	0.79 (0.66, 0.93) 0.0048	-0.04 (-0.07, -0.01)*0.0039	
	Female	251/1171 (21.4)	314/1197 (26.2)	0.83 (0.73, 0.96) 0.0109	0.77 (0.63, 0.94) 0.0093	-0.05 (-0.08, -0.01)*0.0061	
	Race						0.2532
	White	426/2006 (21.2)	548/2032 (27.0)	0.81 (0.72, 0.90) <.0001	0.74 (0.63, 0.86) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Black or African	16/ 64 (25.0)	16/ 70 (22.9)	1.10 (0.60, 1.99) 0.7663	1.11 (0.50, 2.48) 0.7969	0.00 (-0.14, 0.15) 0.9471	
	Asian	124/ 555 (22.3)	125/ 551 (22.7)	0.99 (0.80, 1.23) 0.9269	0.98 (0.74, 1.30) 0.8810	-0.01 (-0.06, 0.04) 0.7709	
	Other	24/ 176 (13.6)	28/ 152 (18.4)	0.67 (0.42, 1.09) 0.1043	0.65 (0.35, 1.21) 0.1780	-0.05 (-0.13, 0.03)*0.2399	
	Geographic region						0.1071
	Asia	119/ 536 (22.2)	120/ 536 (22.4)	1.00 (0.80, 1.25) 0.9804	0.99 (0.74, 1.32) 0.9372	-0.01 (-0.05, 0.04) 0.8419	
	Europe and Saudi Arabia	296/1341 (22.1)	373/1381 (27.0)	0.84 (0.74, 0.95) 0.0072	0.78 (0.65, 0.94) 0.0084	-0.05 (-0.08, -0.02)*0.0027	
	North America	93/ 393 (23.7)	105/ 376 (27.9)	0.85 (0.67, 1.08) 0.1873	0.80 (0.57, 1.10) 0.1702	-0.05 (-0.11, 0.01) 0.1255	
	Latin America	82/ 531 (15.4)	119/ 512 (23.2)	0.66 (0.52, 0.84) 0.0008	0.58 (0.42, 0.80) 0.0010	-0.08 (-0.13, -0.03)*0.0014	
	NYHA class at enrolment						0.5564
	II	444/2083 (21.3)	548/2165 (25.3)	0.84 (0.76, 0.94) 0.0016	0.79 (0.68, 0.91) 0.0013	-0.04 (-0.07, -0.01)*0.0020	
	III or IV	146/ 718 (20.3)	168/ 639 (26.3)	0.79 (0.66, 0.95) 0.0104	0.72 (0.55, 0.95) 0.0181	-0.06 (-0.10, -0.01)*0.0096	
	LVEF at enrolment						0.6613
	<= 49	192/ 959 (20.0)	212/ 950 (22.3)	0.89 (0.75, 1.05) 0.1631	0.85 (0.68, 1.06) 0.1551	-0.02 (-0.06, 0.01)*0.2196	
	50-59	224/1017 (22.0)	271/1009 (26.9)	0.83 (0.72, 0.97) 0.0162	0.77 (0.63, 0.95) 0.0155	-0.05 (-0.09, -0.01)*0.0113	
	>= 60	174/ 825 (21.1)	234/ 846 (27.7)	0.79 (0.67, 0.93) 0.0052	0.72 (0.57, 0.91) 0.0050	-0.07 (-0.11, -0.02)*0.0017	
	NT-proBNP at enrolment						0.7822
	<= median	299/1396 (21.4)	356/1409 (25.3)	0.84 (0.74, 0.96) 0.0124	0.80 (0.67, 0.96) 0.0153	-0.04 (-0.07, -0.01)*0.0159	
	> median	291/1405 (20.7)	361/1395 (25.9)	0.83 (0.73, 0.94) 0.0042	0.76 (0.63, 0.91) 0.0025	-0.05 (-0.08, -0.02)*0.0012	
	Type 2 Diabetes Medical History						0.0232
	Yes	243/1231 (19.7)	337/1243 (27.1)	0.74 (0.64, 0.85) <.0001	0.66 (0.55, 0.80)*<.0001	-0.07 (-0.11, -0.04)*<.0001	
	No	347/1570 (22.1)	380/1562 (24.3)	0.92 (0.81, 1.04) 0.1766	0.88 (0.75, 1.04)*0.1403	-0.02 (-0.05, 0.01)*0.1400	
	Atrial fibrillation or flutter at enrolment ECG						0.3148
	Yes	245/1185 (20.7)	313/1188 (26.3)	0.79 (0.69, 0.91) 0.0011	0.72 (0.59, 0.88) 0.0011	-0.06 (-0.09, -0.02)*0.0011	
	No	345/1616 (21.3)	404/1617 (25.0)	0.87 (0.77, 0.98) 0.0231	0.82 (0.69, 0.97) 0.0201	-0.04 (-0.07, -0.01)*0.0142	
	BMI (kg/m2) at enrolment						0.1133
	< 30	334/1547 (21.6)	380/1541 (24.7)	0.89 (0.78, 1.01) 0.0713	0.85 (0.71, 1.01) 0.0576	-0.03 (-0.06, -0.00)*0.0430	
	>= 30	256/1253 (20.4)	337/1261 (26.7)	0.77 (0.67, 0.88) 0.0001	0.70 (0.58, 0.85) 0.0002	-0.06 (-0.10, -0.03)*0.0002	
	Baseline eGFR (mL/min/1.73m^2)						0.4707
	< 60	303/1338 (22.6)	365/1377 (26.5)	0.86 (0.76, 0.98) 0.0248	0.81 (0.68, 0.97) 0.0239	-0.04 (-0.07, -0.01)*0.0193	
	>= 60	287/1463 (19.6)	351/1427 (24.6)	0.81 (0.71, 0.93) 0.0020	0.75 (0.63, 0.90) 0.0017	-0.05 (-0.08, -0.02)*0.0012	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.1824
	<= median	310/1405 (22.1)	365/1420 (25.7)	0.89 (0.78, 1.01) 0.0695	0.85 (0.71, 1.01) 0.0665	-0.04 (-0.07, -0.00)*0.0231	
	> median	280/1396 (20.1)	352/1385 (25.4)	0.78 (0.68, 0.89) 0.0003	0.71 (0.59, 0.85) 0.0003	-0.05 (-0.08, -0.02)*0.0007	
	LVEF at enrolment 2						0.4299
	<= 49	192/ 959 (20.0)	212/ 950 (22.3)	0.89 (0.75, 1.05) 0.1631	0.85 (0.68, 1.06) 0.1551	-0.02 (-0.06, 0.01)*0.2196	
	>= 50	398/1842 (21.6)	505/1855 (27.2)	0.81 (0.73, 0.91) 0.0003	0.75 (0.64, 0.87) 0.0002	-0.06 (-0.08, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6161
	Yes	48/ 280 (17.1)	52/ 281 (18.5)	0.88 (0.63, 1.24) 0.4743	0.85 (0.54, 1.33) 0.4690	-0.01 (-0.08, 0.05)*0.6733	
	No	542/2521 (21.5)	665/2524 (26.3)	0.83 (0.75, 0.91) 0.0001	0.77 (0.67, 0.88) 0.0001	-0.05 (-0.07, -0.02)*<.0001	
	MRAs at baseline						0.9916
	Yes	260/1216 (21.4)	310/1210 (25.6)	0.83 (0.72, 0.96) 0.0111	0.79 (0.65, 0.96) 0.0163	-0.04 (-0.08, -0.01)*0.0137	
	No	330/1585 (20.8)	407/1595 (25.5)	0.83 (0.74, 0.94) 0.0042	0.77 (0.65, 0.91) 0.0024	-0.05 (-0.08, -0.02)*0.0017	
	ACEi+ARB at baseline						0.1172
	Yes	419/2037 (20.6)	538/2059 (26.1)	0.80 (0.72, 0.89) <.0001	0.73 (0.63, 0.85) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	No	171/ 764 (22.4)	179/ 746 (24.0)	0.94 (0.78, 1.13) 0.5040	0.91 (0.72, 1.16) 0.4697	-0.02 (-0.06, 0.02) 0.3729	
	ARNI at baseline						0.1004
	Yes	33/ 149 (22.1)	22/ 125 (17.6)	1.27 (0.78, 2.08) 0.3357	1.34 (0.73, 2.47) 0.3498	0.04 (-0.05, 0.14) 0.3539	
	No	557/2652 (21.0)	695/2680 (25.9)	0.82 (0.75, 0.90) <.0001	0.76 (0.67, 0.87) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Beta Blocker at baseline						0.2377
	Yes	497/2327 (21.4)	595/2330 (25.5)	0.86 (0.77, 0.95) 0.0028	0.80 (0.70, 0.92) 0.0021	-0.04 (-0.07, -0.02)*0.0008	
	No	93/ 474 (19.6)	122/ 475 (25.7)	0.74 (0.58, 0.93) 0.0101	0.67 (0.49, 0.92) 0.0134	-0.06 (-0.11, -0.01) 0.0170	
	Diuretics at baseline						0.5053
	Yes	526/2500 (21.0)	643/2504 (25.7)	0.82 (0.75, 0.91) 0.0001	0.77 (0.67, 0.88) 0.0001	-0.05 (-0.07, -0.02)*0.0001	
	No	64/ 301 (21.3)	74/ 301 (24.6)	0.91 (0.68, 1.22) 0.5310	0.88 (0.60, 1.29) 0.5109	-0.01 (-0.08, 0.05) 0.6571	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	727/2750 (26.4)	796/2758 (28.9)	0.93 (0.85, 1.00) 0.0643	0.90 (0.80, 1.01) 0.0812	-0.02 (-0.04, -0.00) 0.0223	
	Age						0.2375
	<= median	340/1382 (24.6)	368/1456 (25.3)	0.97 (0.86, 1.10) 0.6266	0.96 (0.80, 1.14) 0.6250	-0.01 (-0.04, 0.03)*0.6788	
	> median	387/1368 (28.3)	428/1302 (32.9)	0.88 (0.79, 0.98) 0.0199	0.83 (0.70, 0.98) 0.0325	-0.05 (-0.08, -0.01)*0.0101	
	Gender						0.5932
	Male	433/1611 (26.9)	450/1583 (28.4)	0.95 (0.85, 1.05) 0.3147	0.93 (0.80, 1.09) 0.3837	-0.01 (-0.04, 0.01) 0.2771	
	Female	294/1139 (25.8)	346/1175 (29.4)	0.91 (0.80, 1.03) 0.1201	0.86 (0.71, 1.04) 0.1224	-0.04 (-0.07, 0.00)*0.0503	
	Race						0.6391
	White	541/1970 (27.5)	599/1998 (30.0)	0.94 (0.85, 1.03) 0.1655	0.90 (0.78, 1.04) 0.1691	-0.03 (-0.05, 0.00)*0.0795	
	Black or African	20/ 63 (31.7)	18/ 66 (27.3)	1.18 (0.69, 2.00) 0.5512	1.23 (0.57, 2.63) 0.6029	0.03 (-0.14, 0.19) 0.7583	
	Asian	128/ 548 (23.4)	150/ 546 (27.5)	0.86 (0.70, 1.05) 0.1323	0.81 (0.62, 1.07) 0.1414	-0.03 (-0.09, 0.02) 0.1869	
	Other	38/ 169 (22.5)	29/ 148 (19.6)	1.06 (0.71, 1.59) 0.7731	1.12 (0.63, 1.97) 0.6976	0.03 (-0.06, 0.12)*0.5278	
	Geographic region						0.5106
	Asia	121/ 530 (22.8)	143/ 531 (26.9)	0.86 (0.70, 1.06) 0.1465	0.81 (0.61, 1.08) 0.1490	-0.03 (-0.08, 0.02) 0.2051	
	Europe and Saudi Arabia	367/1323 (27.7)	390/1360 (28.7)	0.99 (0.88, 1.11) 0.8485	0.98 (0.83, 1.17) 0.8570	-0.01 (-0.04, 0.02)*0.5899	
	North America	118/ 386 (30.6)	127/ 362 (35.1)	0.88 (0.72, 1.07) 0.1951	0.83 (0.61, 1.13) 0.2339	-0.04 (-0.11, 0.02) 0.2102	
	Latin America	121/ 511 (23.7)	136/ 505 (26.9)	0.88 (0.73, 1.07) 0.2081	0.81 (0.60, 1.10) 0.1800	-0.03 (-0.09, 0.02)*0.2330	
	NYHA class at enrolment						0.8801
	II	536/2046 (26.2)	602/2136 (28.2)	0.92 (0.84, 1.02) 0.1066	0.90 (0.79, 1.04) 0.1567	-0.02 (-0.05, 0.01)*0.1488	
	III or IV	191/ 704 (27.1)	193/ 621 (31.1)	0.91 (0.78, 1.07) 0.2638	0.84 (0.66, 1.08) 0.1801	-0.04 (-0.09, 0.01)*0.1145	
	LVEF at enrolment						0.1082
	<= 49	258/ 944 (27.3)	253/ 939 (26.9)	1.00 (0.87, 1.16) 0.9858	1.00 (0.81, 1.22) 0.9633	-0.01 (-0.05, 0.02) 0.4728	
	50-59	280/1001 (28.0)	289/ 988 (29.3)	0.96 (0.84, 1.10) 0.5851	0.97 (0.80, 1.19) 0.7814	0.00 (-0.03, 0.04) 0.9777	
	>= 60	189/ 805 (23.5)	254/ 831 (30.6)	0.81 (0.69, 0.94) 0.0072	0.73 (0.58, 0.91) 0.0061	-0.07 (-0.11, -0.03)*0.0012	
	NT-proBNP at enrolment						0.5295
	<= median	353/1371 (25.7)	377/1389 (27.1)	0.95 (0.84, 1.07) 0.4025	0.93 (0.79, 1.11) 0.4428	-0.00 (-0.03, 0.03) 0.8837	
	> median	374/1379 (27.1)	419/1368 (30.6)	0.90 (0.81, 1.01) 0.0723	0.86 (0.73, 1.02) 0.0892	-0.04 (-0.07, -0.00)*0.0424	
	Type 2 Diabetes Medical History						0.0386
	Yes	310/1213 (25.6)	368/1219 (30.2)	0.84 (0.74, 0.95) 0.0060	0.79 (0.66, 0.95)*0.0109	-0.05 (-0.08, -0.01)*0.0107	
	No	417/1537 (27.1)	428/1539 (27.8)	1.00 (0.90, 1.12) 0.9754	0.97 (0.82, 1.13)*0.6729	-0.01 (-0.04, 0.02) 0.5520	
	Atrial fibrillation or flutter at enrolment ECG						0.9818
	Yes	314/1164 (27.0)	337/1164 (29.0)	0.92 (0.81, 1.04) 0.1985	0.91 (0.76, 1.10) 0.3334	-0.02 (-0.06, 0.02)*0.2881	
	No	413/1586 (26.0)	459/1594 (28.8)	0.92 (0.83, 1.03) 0.1500	0.89 (0.75, 1.04) 0.1339	-0.03 (-0.05, 0.00) 0.0751	
	BMI (kg/m2) at enrolment						0.1647
	< 30	389/1520 (25.6)	446/1517 (29.4)	0.88 (0.78, 0.98) 0.0257	0.83 (0.71, 0.98) 0.0244	-0.04 (-0.07, -0.01) 0.0109	
	>= 30	338/1229 (27.5)	350/1238 (28.3)	0.99 (0.88, 1.12) 0.8768	1.00 (0.83, 1.20) 0.9943	-0.01 (-0.04, 0.03)*0.6700	
	Baseline eGFR (mL/min/1.73m^2)						0.9416
	< 60	367/1307 (28.1)	407/1345 (30.3)	0.92 (0.82, 1.03) 0.1672	0.91 (0.76, 1.08) 0.2826	-0.02 (-0.05, 0.01) 0.2015	
	>= 60	360/1443 (24.9)	389/1412 (27.5)	0.93 (0.82, 1.05) 0.2210	0.89 (0.75, 1.06) 0.1856	-0.03 (-0.06, 0.01)*0.1141	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.5409
	<= median	352/1376 (25.6)	411/1395 (29.5)	0.90 (0.80, 1.01) 0.0754	0.86 (0.73, 1.02) 0.0868	-0.03 (-0.06, 0.00) 0.0729	
	> median	375/1374 (27.3)	385/1363 (28.2)	0.95 (0.84, 1.06) 0.3484	0.93 (0.78, 1.10) 0.4057	-0.01 (-0.04, 0.02)*0.5774	
	LVEF at enrolment 2						0.2176
	<= 49	258/ 944 (27.3)	253/ 939 (26.9)	1.00 (0.87, 1.16) 0.9858	1.00 (0.81, 1.22) 0.9633	-0.01 (-0.05, 0.02) 0.4728	
	>= 50	469/1806 (26.0)	543/1819 (29.9)	0.89 (0.81, 0.99) 0.0275	0.86 (0.74, 0.99) 0.0414	-0.04 (-0.07, -0.01)*0.0091	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7541
	Yes	69/ 270 (25.6)	72/ 272 (26.5)	0.98 (0.75, 1.28) 0.8663	0.94 (0.63, 1.41) 0.7743	-0.01 (-0.08, 0.06)*0.8082	
	No	658/2480 (26.5)	724/2486 (29.1)	0.92 (0.84, 1.00) 0.0630	0.89 (0.79, 1.01) 0.0815	-0.02 (-0.05, -0.00) 0.0299	
	MRAs at baseline						0.2723
	Yes	304/1191 (25.5)	346/1193 (29.0)	0.88 (0.77, 1.00) 0.0451	0.84 (0.70, 1.01) 0.0609	-0.03 (-0.06, 0.00) 0.0571	
	No	423/1559 (27.1)	450/1565 (28.8)	0.96 (0.86, 1.07) 0.4924	0.95 (0.81, 1.11) 0.4973	-0.02 (-0.05, 0.01) 0.1690	
	ACEi+ARB at baseline						0.1492
	Yes	523/1999 (26.2)	605/2028 (29.8)	0.89 (0.81, 0.98) 0.0218	0.85 (0.73, 0.98) 0.0213	-0.04 (-0.06, -0.01)*0.0094	
	No	204/ 751 (27.2)	191/ 730 (26.2)	1.03 (0.87, 1.22) 0.7026	1.06 (0.84, 1.34) 0.6190	0.01 (-0.03, 0.05) 0.6696	
	ARNI at baseline						0.9846
	Yes	34/ 147 (23.1)	29/ 122 (23.8)	0.93 (0.60, 1.44) 0.7408	0.92 (0.51, 1.63) 0.7673	-0.02 (-0.12, 0.08) 0.7197	
	No	693/2603 (26.6)	767/2636 (29.1)	0.93 (0.85, 1.01) 0.0850	0.90 (0.80, 1.02) 0.1013	-0.02 (-0.05, -0.00)*0.0457	
	Beta Blocker at baseline						0.9228
	Yes	600/2289 (26.2)	659/2293 (28.7)	0.93 (0.85, 1.01) 0.0990	0.90 (0.79, 1.03) 0.1146	-0.03 (-0.05, 0.00)*0.0552	
	No	127/ 461 (27.5)	137/ 465 (29.5)	0.92 (0.76, 1.12) 0.4219	0.90 (0.67, 1.20) 0.4679	-0.02 (-0.08, 0.03) 0.3970	
	Diuretics at baseline						0.0722
	Yes	646/2458 (26.3)	726/2463 (29.5)	0.90 (0.83, 0.98) 0.0181	0.86 (0.76, 0.98) 0.0243	-0.03 (-0.06, -0.01)*0.0124	
	No	81/ 292 (27.7)	70/ 295 (23.7)	1.17 (0.89, 1.53) 0.2514	1.26 (0.86, 1.84) 0.2299	0.04 (-0.03, 0.11)*0.2659	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	739/2801 (26.4)	819/2805 (29.2)	0.94 (0.87, 1.02) 0.1391	0.88 (0.78, 1.00) 0.0475	-0.02 (-0.03, 0.00) 0.0672	
	Age						0.3803
	<= median	355/1394 (25.5)	390/1471 (26.5)	0.98 (0.87, 1.10) 0.7006	0.96 (0.80, 1.14) 0.6271	-0.01 (-0.03, 0.01) 0.3214	
	> median	384/1407 (27.3)	429/1334 (32.2)	0.91 (0.82, 1.01) 0.0857	0.81 (0.68, 0.96) 0.0181	-0.05 (-0.08, -0.01)*0.0053	
	Gender						0.2461
	Male	435/1630 (26.7)	449/1608 (27.9)	0.98 (0.89, 1.09) 0.7534	0.96 (0.82, 1.13) 0.6639	-0.01 (-0.04, 0.02)*0.4300	
	Female	304/1171 (26.0)	370/1197 (30.9)	0.90 (0.80, 1.01) 0.0671	0.78 (0.65, 0.95) 0.0127	-0.02 (-0.05, 0.01) 0.2036	
	Race						0.5233
	White	524/2006 (26.1)	597/2032 (29.4)	0.93 (0.85, 1.02) 0.1251	0.87 (0.75, 1.01) 0.0659	-0.03 (-0.06, -0.00)*0.0207	
	Black or African	11/ 64 (17.2)	21/ 70 (30.0)	0.60 (0.31, 1.14) 0.1195	0.48 (0.21, 1.12) 0.0890	-0.13 (-0.27, 0.01)*0.0763	
	Asian	174/ 555 (31.4)	175/ 551 (31.8)	1.02 (0.86, 1.20) 0.8421	0.97 (0.75, 1.27) 0.8472	-0.00 (-0.06, 0.05)*0.8836	
	Other	30/ 176 (17.0)	26/ 152 (17.1)	0.91 (0.60, 1.37) 0.6485	0.90 (0.48, 1.70) 0.7521	-0.00 (-0.08, 0.08)*0.9885	
	Geographic region						0.2077
	Asia	168/ 536 (31.3)	169/ 536 (31.5)	1.03 (0.87, 1.21) 0.7506	0.99 (0.76, 1.30) 0.9471	-0.00 (-0.06, 0.05)*0.9475	
	Europe and Saudi Arabia	362/1341 (27.0)	399/1381 (28.9)	0.99 (0.89, 1.10) 0.8568	0.95 (0.80, 1.14) 0.6060	-0.02 (-0.05, 0.01)*0.2699	
	North America	102/ 393 (26.0)	125/ 376 (33.2)	0.80 (0.65, 0.99) 0.0411	0.70 (0.51, 0.96) 0.0290	-0.09 (-0.15, -0.03) 0.0044	
	Latin America	107/ 531 (20.2)	126/ 512 (24.6)	0.87 (0.71, 1.07) 0.1794	0.77 (0.56, 1.05) 0.0961	-0.04 (-0.10, 0.01)*0.0839	
	NYHA class at enrolment						0.2036
	II	565/2083 (27.1)	625/2165 (28.9)	0.96 (0.88, 1.05) 0.4316	0.91 (0.79, 1.05) 0.2043	-0.02 (-0.04, 0.01)*0.2055	
	III or IV	174/ 718 (24.2)	193/ 639 (30.2)	0.87 (0.76, 1.01) 0.0745	0.76 (0.59, 0.99) 0.0390	-0.06 (-0.11, -0.01)*0.0136	
	LVEF at enrolment						0.7532
	<= 49	236/ 959 (24.6)	253/ 950 (26.6)	0.94 (0.82, 1.08) 0.4089	0.89 (0.72, 1.11) 0.3025	-0.02 (-0.06, 0.02)*0.3113	
	50-59	285/1017 (28.0)	303/1009 (30.0)	0.98 (0.86, 1.11) 0.7165	0.92 (0.75, 1.13) 0.4281	-0.02 (-0.06, 0.02)*0.3198	
	>= 60	218/ 825 (26.4)	263/ 846 (31.1)	0.90 (0.78, 1.04) 0.1615	0.83 (0.66, 1.04) 0.1032	-0.05 (-0.09, -0.00)*0.0349	
	NT-proBNP at enrolment						0.8961
	<= median	370/1396 (26.5)	411/1409 (29.2)	0.95 (0.85, 1.06) 0.3262	0.89 (0.75, 1.06) 0.1865	-0.03 (-0.06, 0.01)*0.1151	
	> median	369/1405 (26.3)	408/1395 (29.2)	0.94 (0.85, 1.05) 0.2930	0.87 (0.73, 1.04) 0.1346	-0.03 (-0.06, 0.00)*0.0777	
	Type 2 Diabetes Medical History						0.0311
	Yes	314/1231 (25.5)	390/1243 (31.4)	0.85 (0.76, 0.96) 0.0084	0.75 (0.63, 0.89)*0.0012	-0.03 (-0.07, -0.00) 0.0304	
	No	425/1570 (27.1)	429/1562 (27.5)	1.02 (0.92, 1.14) 0.6633	0.98 (0.84, 1.15)*0.8041	-0.01 (-0.02, 0.01) 0.3993	
	Atrial fibrillation or flutter at enrolment ECG						0.9011
	Yes	321/1185 (27.1)	355/1188 (29.9)	0.95 (0.84, 1.07) 0.3912	0.89 (0.73, 1.07) 0.2101	-0.03 (-0.06, 0.01)*0.1315	
	No	418/1616 (25.9)	464/1617 (28.7)	0.94 (0.84, 1.04) 0.2033	0.88 (0.74, 1.03) 0.1131	-0.03 (-0.06, 0.00)*0.0708	
	BMI (kg/m2) at enrolment						0.3294
	< 30	420/1547 (27.1)	454/1541 (29.5)	0.98 (0.88, 1.08) 0.6423	0.93 (0.78, 1.09) 0.3629	-0.02 (-0.05, 0.01)*0.1537	
	>= 30	318/1253 (25.4)	365/1261 (28.9)	0.90 (0.80, 1.01) 0.0804	0.83 (0.69, 1.00) 0.0470	-0.04 (-0.07, -0.00)*0.0442	
	Baseline eGFR (mL/min/1.73m^2)						0.6884
	< 60	367/1338 (27.4)	420/1377 (30.5)	0.93 (0.83, 1.03) 0.1736	0.87 (0.73, 1.03) 0.1132	-0.03 (-0.06, 0.00)*0.0774	
	>= 60	372/1463 (25.4)	398/1427 (27.9)	0.96 (0.86, 1.08) 0.4951	0.90 (0.76, 1.07) 0.2502	-0.02 (-0.06, 0.01)*0.1342	

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AstraZeneca
Protocol: D169CC00001
Overall study population
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.2599
	<= median	366/1405 (26.0)	404/1420 (28.5)	0.99 (0.89, 1.11) 0.8849	0.93 (0.78, 1.10) 0.3989	-0.02 (-0.06, 0.01)*0.1517	
	> median	373/1396 (26.7)	415/1385 (30.0)	0.90 (0.81, 1.01) 0.0669	0.84 (0.71, 1.00) 0.0567	-0.03 (-0.07, 0.00)*0.0575	
	LVEF at enrolment 2						0.9534
	<= 49	236/ 959 (24.6)	253/ 950 (26.6)	0.94 (0.82, 1.08) 0.4089	0.89 (0.72, 1.11) 0.3025	-0.02 (-0.06, 0.02)*0.3113	
	>= 50	503/1842 (27.3)	566/1855 (30.5)	0.94 (0.86, 1.04) 0.2248	0.88 (0.76, 1.02) 0.0927	-0.03 (-0.06, -0.00)*0.0315	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2602
	Yes	61/ 280 (21.8)	59/ 281 (21.0)	1.14 (0.86, 1.50) 0.3591	1.17 (0.75, 1.81) 0.4870	0.01 (-0.06, 0.08)*0.8197	
	No	678/2521 (26.9)	760/2524 (30.1)	0.93 (0.86, 1.01) 0.0818	0.86 (0.76, 0.98) 0.0251	-0.02 (-0.04, -0.00) 0.0379	
	MRAs at baseline						0.6710
	Yes	327/1216 (26.9)	353/1210 (29.2)	0.96 (0.85, 1.08) 0.4723	0.90 (0.75, 1.09) 0.2949	-0.01 (-0.04, 0.02) 0.5970	
	No	412/1585 (26.0)	466/1595 (29.2)	0.93 (0.84, 1.03) 0.1790	0.86 (0.73, 1.02) 0.0798	-0.03 (-0.06, -0.00)*0.0420	
	ACEi+ARB at baseline						0.2404
	Yes	535/2037 (26.3)	616/2059 (29.9)	0.92 (0.84, 1.01) 0.0656	0.84 (0.72, 0.97) 0.0155	-0.04 (-0.06, -0.01)*0.0092	
	No	204/ 764 (26.7)	203/ 746 (27.2)	1.02 (0.87, 1.20) 0.7922	1.02 (0.80, 1.29) 0.8997	-0.01 (-0.05, 0.03) 0.6559	
	ARNI at baseline						0.2914
	Yes	44/ 149 (29.5)	36/ 125 (28.8)	1.15 (0.81, 1.62) 0.4470	1.20 (0.69, 2.11) 0.5169	0.01 (-0.10, 0.12)*0.8946	
	No	695/2652 (26.2)	783/2680 (29.2)	0.93 (0.86, 1.01) 0.0927	0.87 (0.77, 0.99) 0.0298	-0.02 (-0.03, 0.00) 0.0584	
	Beta Blocker at baseline						0.8771
	Yes	615/2327 (26.4)	688/2330 (29.5)	0.94 (0.86, 1.02) 0.1633	0.88 (0.77, 1.00) 0.0548	-0.03 (-0.06, -0.01)*0.0184	
	No	124/ 474 (26.2)	131/ 475 (27.6)	0.96 (0.79, 1.16) 0.6425	0.92 (0.68, 1.25) 0.5949	-0.01 (-0.05, 0.03) 0.5482	
	Diuretics at baseline						0.0476
	Yes	650/2500 (26.0)	735/2504 (29.4)	0.92 (0.85, 1.00) 0.0431	0.85 (0.74, 0.97) 0.0143	-0.02 (-0.04, -0.00) 0.0385	
	No	89/ 301 (29.6)	84/ 301 (27.9)	1.17 (0.94, 1.47) 0.1671	1.22 (0.84, 1.78) 0.2963	0.02 (-0.06, 0.09)*0.6524	

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Symptom Burden (LOCF)							
	Overall	655/2801 (23.4)	782/2805 (27.9)	0.85 (0.78, 0.92) 0.0002	0.79 (0.70, 0.89) 0.0002	-0.04 (-0.07, -0.02)*0.0001	
	Age						0.3561
	<= median	289/1394 (20.7)	376/1471 (25.6)	0.81 (0.71, 0.92) 0.0014	0.74 (0.62, 0.89) 0.0012	-0.05 (-0.08, -0.02)*0.0021	
	> median	366/1407 (26.0)	406/1334 (30.4)	0.88 (0.78, 0.98) 0.0256	0.82 (0.69, 0.97) 0.0246	-0.04 (-0.08, -0.01)*0.0101	
	Gender						0.2338
	Male	350/1630 (21.5)	429/1608 (26.7)	0.81 (0.72, 0.91) 0.0006	0.75 (0.64, 0.89) 0.0008	-0.05 (-0.08, -0.02)*0.0005	
	Female	305/1171 (26.0)	353/1197 (29.5)	0.90 (0.80, 1.02) 0.0981	0.84 (0.70, 1.01) 0.0664	-0.03 (-0.07, 0.00)*0.0611	
	Race						0.1672
	White	471/2006 (23.5)	582/2032 (28.6)	0.83 (0.75, 0.92) 0.0002	0.77 (0.66, 0.89) 0.0004	-0.05 (-0.08, -0.02)*0.0002	
	Black or African	13/ 64 (20.3)	19/ 70 (27.1)	0.73 (0.40, 1.34) 0.3098	0.66 (0.29, 1.49) 0.3118	-0.08 (-0.22, 0.06) 0.2373	
	Asian	144/ 555 (25.9)	142/ 551 (25.8)	1.00 (0.82, 1.22) 0.9803	1.00 (0.76, 1.31) 0.9937	0.00 (-0.05, 0.05)*0.9471	
	Other	27/ 176 (15.3)	39/ 152 (25.7)	0.62 (0.40, 0.95) 0.0294	0.53 (0.30, 0.93) 0.0259	-0.10 (-0.19, -0.02)*0.0208	
	Geographic region						0.2220
	Asia	138/ 536 (25.7)	138/ 536 (25.7)	1.00 (0.82, 1.22) 0.9931	0.99 (0.75, 1.31) 0.9634	0.00 (-0.05, 0.05)*1.0000	
	Europe and Saudi Arabia	316/1341 (23.6)	393/1381 (28.5)	0.84 (0.75, 0.95) 0.0047	0.78 (0.65, 0.94) 0.0083	-0.05 (-0.08, -0.02)*0.0036	
	North America	106/ 393 (27.0)	123/ 376 (32.7)	0.84 (0.68, 1.04) 0.1018	0.76 (0.55, 1.04) 0.0838	-0.06 (-0.12, 0.00) 0.0589	
	Latin America	95/ 531 (17.9)	128/ 512 (25.0)	0.72 (0.58, 0.91) 0.0050	0.64 (0.47, 0.87) 0.0043	-0.07 (-0.12, -0.02)*0.0050	
	NYHA class at enrolment						0.3893
	II	489/2083 (23.5)	596/2165 (27.5)	0.86 (0.77, 0.95) 0.0022	0.79 (0.69, 0.91) 0.0013	-0.04 (-0.07, -0.01)*0.0024	
	III or IV	166/ 718 (23.1)	186/ 639 (29.1)	0.78 (0.66, 0.93) 0.0043	0.73 (0.57, 0.95) 0.0179	-0.06 (-0.11, -0.01)*0.0122	
	LVEF at enrolment						0.7044
	<= 49	219/ 959 (22.8)	252/ 950 (26.5)	0.85 (0.73, 0.99) 0.0333	0.80 (0.64, 0.99) 0.0414	-0.04 (-0.08, 0.00)*0.0613	
	50-59	246/1017 (24.2)	277/1009 (27.5)	0.89 (0.77, 1.02) 0.0907	0.83 (0.68, 1.02) 0.0823	-0.03 (-0.07, 0.01)*0.0930	
	>= 60	190/ 825 (23.0)	253/ 846 (29.9)	0.80 (0.68, 0.94) 0.0055	0.72 (0.58, 0.91) 0.0049	-0.07 (-0.11, -0.03)*0.0014	
	NT-proBNP at enrolment						0.4943
	<= median	338/1396 (24.2)	389/1409 (27.6)	0.87 (0.77, 0.99) 0.0283	0.82 (0.69, 0.98) 0.0297	-0.03 (-0.07, -0.00)*0.0399	
	> median	317/1405 (22.6)	393/1395 (28.2)	0.82 (0.73, 0.93) 0.0021	0.75 (0.63, 0.90) 0.0015	-0.06 (-0.09, -0.02)*0.0006	
	Type 2 Diabetes Medical History						0.2600
	Yes	290/1231 (23.6)	372/1243 (29.9)	0.80 (0.71, 0.91) 0.0007	0.72 (0.60, 0.86)*0.0004	-0.06 (-0.10, -0.03)*0.0003	
	No	365/1570 (23.2)	410/1562 (26.2)	0.89 (0.79, 1.00) 0.0520	0.85 (0.72, 1.00)*0.0518	-0.03 (-0.06, 0.00)*0.0516	
	Atrial fibrillation or flutter at enrolment ECG						0.9167
	Yes	267/1185 (22.5)	318/1188 (26.8)	0.84 (0.74, 0.97) 0.0141	0.79 (0.65, 0.96) 0.0185	-0.04 (-0.08, -0.01)*0.0165	
	No	388/1616 (24.0)	464/1617 (28.7)	0.85 (0.76, 0.95) 0.0044	0.78 (0.67, 0.92) 0.0030	-0.05 (-0.08, -0.02)*0.0025	
	BMI (kg/m2) at enrolment						0.1711
	< 30	369/1547 (23.9)	414/1541 (26.9)	0.90 (0.80, 1.01) 0.0682	0.86 (0.72, 1.01) 0.0678	-0.03 (-0.06, 0.00)*0.0542	
	>= 30	286/1253 (22.8)	368/1261 (29.2)	0.79 (0.70, 0.90) 0.0003	0.71 (0.59, 0.85) 0.0003	-0.06 (-0.10, -0.03)*0.0003	
	Baseline eGFR (mL/min/1.73m^2)						0.9412
	< 60	343/1338 (25.6)	420/1377 (30.5)	0.85 (0.75, 0.95) 0.0049	0.78 (0.66, 0.93) 0.0061	-0.05 (-0.08, -0.01)*0.0047	
	>= 60	312/1463 (21.3)	361/1427 (25.3)	0.86 (0.75, 0.97) 0.0169	0.80 (0.67, 0.95) 0.0126	-0.04 (-0.07, -0.01)*0.0115	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Symptom Burden (LOCF)	SBP at randomisation						0.9981
	<= median	323/1405 (23.0)	400/1420 (28.2)	0.85 (0.75, 0.96) 0.0072	0.78 (0.66, 0.93) 0.0062	-0.05 (-0.08, -0.02)*0.0016	
	> median	332/1396 (23.8)	382/1385 (27.6)	0.85 (0.75, 0.96) 0.0072	0.78 (0.66, 0.94) 0.0071	-0.04 (-0.07, -0.01)*0.0217	
	LVEF at enrolment 2						0.9677
	<= 49	219/ 959 (22.8)	252/ 950 (26.5)	0.85 (0.73, 0.99) 0.0333	0.80 (0.64, 0.99) 0.0414	-0.04 (-0.08, 0.00)*0.0613	
	>= 50	436/1842 (23.7)	530/1855 (28.6)	0.85 (0.76, 0.94) 0.0023	0.78 (0.67, 0.91) 0.0016	-0.05 (-0.08, -0.02)*0.0007	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9222
	Yes	57/ 280 (20.4)	64/ 281 (22.8)	0.86 (0.64, 1.16) 0.3161	0.82 (0.53, 1.25) 0.3536	-0.02 (-0.09, 0.04)*0.4859	
	No	598/2521 (23.7)	718/2524 (28.4)	0.85 (0.77, 0.93) 0.0003	0.78 (0.69, 0.89) 0.0002	-0.05 (-0.07, -0.02)*0.0001	
	MRAs at baseline						0.9437
	Yes	287/1216 (23.6)	342/1210 (28.3)	0.85 (0.74, 0.96) 0.0124	0.79 (0.66, 0.96) 0.0150	-0.05 (-0.08, -0.01)*0.0087	
	No	368/1585 (23.2)	440/1595 (27.6)	0.85 (0.76, 0.95) 0.0059	0.79 (0.67, 0.93) 0.0042	-0.04 (-0.07, -0.01)*0.0046	
	ACEi+ARB at baseline						0.0848
	Yes	462/2037 (22.7)	587/2059 (28.5)	0.81 (0.73, 0.90) <.0001	0.74 (0.64, 0.85) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	No	193/ 764 (25.3)	195/ 746 (26.1)	0.96 (0.81, 1.14) 0.6673	0.95 (0.75, 1.20) 0.6477	-0.01 (-0.05, 0.04)*0.6964	
	ARNI at baseline						0.6334
	Yes	36/ 149 (24.2)	30/ 125 (24.0)	0.95 (0.62, 1.45) 0.8189	0.95 (0.54, 1.69) 0.8728	0.00 (-0.10, 0.10)*0.9752	
	No	619/2652 (23.3)	752/2680 (28.1)	0.85 (0.78, 0.92) 0.0002	0.78 (0.69, 0.89) 0.0002	-0.05 (-0.07, -0.02)*<.0001	
	Beta Blocker at baseline						0.1131
	Yes	550/2327 (23.6)	642/2330 (27.6)	0.88 (0.80, 0.96) 0.0061	0.82 (0.72, 0.94) 0.0050	-0.04 (-0.06, -0.01)*0.0022	
	No	105/ 474 (22.2)	140/ 475 (29.5)	0.73 (0.59, 0.90) 0.0029	0.63 (0.47, 0.86) 0.0033	-0.07 (-0.13, -0.02)*0.0097	
	Diuretics at baseline						0.9263
	Yes	587/2500 (23.5)	696/2504 (27.8)	0.85 (0.77, 0.93) 0.0003	0.79 (0.69, 0.90) 0.0004	-0.04 (-0.07, -0.02)*0.0005	
	No	68/ 301 (22.6)	86/ 301 (28.6)	0.85 (0.65, 1.12) 0.2496	0.78 (0.54, 1.14) 0.2005	-0.06 (-0.13, 0.01)*0.0919	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	622/2801 (22.2)	645/2805 (23.0)	0.97 (0.89, 1.06) 0.5336	0.96 (0.84, 1.09) 0.5322	-0.01 (-0.03, 0.01)*0.4804	
	Age						0.6478
	<= median	284/1394 (20.4)	318/1471 (21.6)	0.95 (0.83, 1.08) 0.4213	0.92 (0.76, 1.11) 0.3832	-0.01 (-0.04, 0.02)*0.4133	
	> median	338/1407 (24.0)	327/1334 (24.5)	0.98 (0.87, 1.11) 0.8036	0.98 (0.82, 1.18) 0.8696	-0.00 (-0.04, 0.03)*0.7649	
	Gender						0.2039
	Male	353/1630 (21.7)	374/1608 (23.3)	0.92 (0.82, 1.04) 0.1960	0.90 (0.76, 1.07) 0.2285	-0.02 (-0.04, 0.01)*0.2746	
	Female	269/1171 (23.0)	271/1197 (22.6)	1.04 (0.91, 1.19) 0.5824	1.05 (0.86, 1.29) 0.6461	0.00 (-0.03, 0.04)*0.8474	
	Race						0.8360
	White	413/2006 (20.6)	449/2032 (22.1)	0.94 (0.84, 1.05) 0.3004	0.92 (0.79, 1.08) 0.3283	-0.02 (-0.04, 0.01)*0.2421	
	Black or African	17/ 64 (26.6)	17/ 70 (24.3)	0.96 (0.55, 1.68) 0.8910	1.03 (0.46, 2.31) 0.9517	0.02 (-0.12, 0.17)*0.7625	
	Asian	161/ 555 (29.0)	150/ 551 (27.2)	1.04 (0.88, 1.23) 0.6611	1.07 (0.80, 1.41) 0.6608	0.02 (-0.04, 0.07)*0.5088	
	Other	31/ 176 (17.6)	29/ 152 (19.1)	1.00 (0.67, 1.50) 0.9970	0.88 (0.47, 1.64) 0.6899	-0.01 (-0.10, 0.07)*0.7327	
	Geographic region						0.4309
	Asia	156/ 536 (29.1)	147/ 536 (27.4)	1.03 (0.87, 1.22) 0.7359	1.05 (0.78, 1.40) 0.7564	0.02 (-0.04, 0.07)*0.5415	
	Europe and Saudi Arabia	280/1341 (20.9)	313/1381 (22.7)	0.93 (0.81, 1.06) 0.2713	0.90 (0.74, 1.09) 0.2950	-0.02 (-0.05, 0.01)*0.2591	
	North America	89/ 393 (22.6)	72/ 376 (19.1)	1.15 (0.88, 1.51) 0.3120	1.22 (0.85, 1.74) 0.2725	0.03 (-0.02, 0.09)*0.2323	
	Latin America	97/ 531 (18.3)	113/ 512 (22.1)	0.89 (0.71, 1.12) 0.3133	0.83 (0.61, 1.14) 0.2576	-0.04 (-0.09, 0.01)*0.1258	
	NYHA class at enrolment						0.6971
	II	464/2083 (22.3)	500/2165 (23.1)	0.98 (0.89, 1.09) 0.7424	0.96 (0.83, 1.12) 0.6261	-0.01 (-0.03, 0.02)*0.5239	
	III or IV	158/ 718 (22.0)	144/ 639 (22.5)	0.95 (0.78, 1.14) 0.5553	0.95 (0.73, 1.24) 0.7105	-0.01 (-0.05, 0.04)*0.8150	
	LVEF at enrolment						0.2414
	<= 49	208/ 959 (21.7)	207/ 950 (21.8)	0.98 (0.84, 1.16) 0.8349	0.96 (0.76, 1.20) 0.7043	-0.00 (-0.04, 0.04)*0.9577	
	50-59	238/1017 (23.4)	222/1009 (22.0)	1.05 (0.91, 1.22) 0.5158	1.11 (0.89, 1.38) 0.3542	0.01 (-0.02, 0.05)*0.4518	
	>= 60	176/ 825 (21.3)	216/ 846 (25.5)	0.87 (0.74, 1.02) 0.0937	0.81 (0.64, 1.03) 0.0855	-0.04 (-0.08, -0.00)*0.0425	
	NT-proBNP at enrolment						0.7367
	<= median	308/1396 (22.1)	327/1409 (23.2)	0.96 (0.84, 1.09) 0.5164	0.94 (0.78, 1.14) 0.5348	-0.01 (-0.04, 0.02)*0.4687	
	> median	314/1405 (22.3)	317/1395 (22.7)	0.99 (0.87, 1.13) 0.8836	0.98 (0.81, 1.18) 0.8295	-0.00 (-0.03, 0.03)*0.8122	
	Type 2 Diabetes Medical History						0.0748
	Yes	257/1231 (20.9)	298/1243 (24.0)	0.88 (0.77, 1.01) 0.0779	0.84 (0.69, 1.01)*0.0650	-0.03 (-0.06, 0.00)*0.0646	
	No	365/1570 (23.2)	347/1562 (22.2)	1.04 (0.93, 1.18) 0.4779	1.06 (0.90, 1.25)*0.4903	0.01 (-0.02, 0.04)*0.4902	
	Atrial fibrillation or flutter at enrolment ECG						0.4188
	Yes	271/1185 (22.9)	302/1188 (25.4)	0.93 (0.82, 1.07) 0.3152	0.89 (0.73, 1.09) 0.2577	-0.03 (-0.06, 0.01)*0.1462	
	No	351/1616 (21.7)	343/1617 (21.2)	1.01 (0.89, 1.14) 0.9293	1.02 (0.85, 1.21) 0.8506	0.01 (-0.02, 0.03)*0.7249	
	BMI (kg/m2) at enrolment						0.0394
	< 30	373/1547 (24.1)	359/1541 (23.3)	1.06 (0.94, 1.19) 0.3680	1.09 (0.91, 1.30) 0.3366	0.01 (-0.02, 0.04)*0.5945	
	>= 30	249/1253 (19.9)	286/1261 (22.7)	0.87 (0.75, 1.00) 0.0548	0.82 (0.67, 1.00) 0.0485	-0.03 (-0.06, 0.00)*0.0852	
	Baseline eGFR (mL/min/1.73m^2)						0.5924
	< 60	308/1338 (23.0)	314/1377 (22.8)	0.99 (0.87, 1.13) 0.9130	1.00 (0.83, 1.20) 0.9714	0.00 (-0.03, 0.03)*0.8934	
	>= 60	314/1463 (21.5)	330/1427 (23.1)	0.95 (0.84, 1.08) 0.4344	0.92 (0.77, 1.11) 0.3980	-0.02 (-0.05, 0.01)*0.2830	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
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Full Analysis Set

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Self Efficacy (LOCF)	SBP at randomisation						0.6478
	<= median	331/1405 (23.6)	337/1420 (23.7)	0.99 (0.87, 1.12) 0.8544	1.00 (0.83, 1.20) 0.9788	-0.00 (-0.03, 0.03)*0.9135	
	> median	291/1396 (20.8)	308/1385 (22.2)	0.95 (0.83, 1.08) 0.4432	0.92 (0.76, 1.11) 0.3789	-0.01 (-0.04, 0.02)*0.3716	
	LVEF at enrolment 2						0.8081
	<= 49	208/ 959 (21.7)	207/ 950 (21.8)	0.98 (0.84, 1.16) 0.8349	0.96 (0.76, 1.20) 0.7043	-0.00 (-0.04, 0.04)*0.9577	
	>= 50	414/1842 (22.5)	438/1855 (23.6)	0.96 (0.86, 1.08) 0.5234	0.96 (0.82, 1.13) 0.6231	-0.01 (-0.04, 0.02)*0.4120	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8024
	Yes	64/ 280 (22.9)	63/ 281 (22.4)	1.01 (0.76, 1.34) 0.9298	1.01 (0.66, 1.54) 0.9664	0.00 (-0.06, 0.07)*0.9015	
	No	558/2521 (22.1)	582/2524 (23.1)	0.97 (0.88, 1.06) 0.4999	0.95 (0.83, 1.10) 0.5087	-0.01 (-0.03, 0.01)*0.4324	
	MRAs at baseline						0.6915
	Yes	293/1216 (24.1)	292/1210 (24.1)	0.99 (0.87, 1.13) 0.8798	0.99 (0.81, 1.20) 0.9000	-0.00 (-0.03, 0.03)*0.9831	
	No	329/1585 (20.8)	353/1595 (22.1)	0.95 (0.84, 1.08) 0.4602	0.93 (0.78, 1.12) 0.4572	-0.01 (-0.04, 0.01)*0.3449	
	ACEi+ARB at baseline						0.1120
	Yes	437/2037 (21.5)	482/2059 (23.4)	0.93 (0.83, 1.03) 0.1731	0.89 (0.76, 1.04) 0.1393	-0.02 (-0.05, 0.01)*0.1333	
	No	185/ 764 (24.2)	163/ 746 (21.8)	1.10 (0.92, 1.31) 0.2990	1.17 (0.91, 1.51) 0.2227	0.02 (-0.02, 0.07)*0.2749	
	ARNI at baseline						0.1779
	Yes	45/ 149 (30.2)	27/ 125 (21.6)	1.27 (0.85, 1.90) 0.2515	1.49 (0.84, 2.66) 0.1771	0.09 (-0.02, 0.19)*0.1022	
	No	577/2652 (21.8)	618/2680 (23.1)	0.96 (0.87, 1.05) 0.3575	0.93 (0.82, 1.07) 0.3311	-0.01 (-0.04, 0.01)*0.2540	
	Beta Blocker at baseline						0.9407
	Yes	517/2327 (22.2)	534/2330 (22.9)	0.97 (0.88, 1.07) 0.5500	0.96 (0.83, 1.11) 0.5700	-0.01 (-0.03, 0.02)*0.5672	
	No	105/ 474 (22.2)	111/ 475 (23.4)	0.98 (0.79, 1.22) 0.8594	0.96 (0.69, 1.32) 0.7914	-0.01 (-0.07, 0.04)*0.6549	
	Diuretics at baseline						0.7520
	Yes	562/2500 (22.5)	578/2504 (23.1)	0.98 (0.89, 1.07) 0.6236	0.97 (0.84, 1.11) 0.6307	-0.01 (-0.03, 0.02)*0.6111	
	No	60/ 301 (19.9)	67/ 301 (22.3)	0.93 (0.69, 1.24) 0.6078	0.89 (0.59, 1.35) 0.5879	-0.02 (-0.09, 0.04)*0.4842	

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AstraZeneca
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Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	604/2801 (21.6)	753/2805 (26.8)	0.81 (0.74, 0.89) <.0001	0.74 (0.65, 0.84) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	Age						0.9545
	<= median	286/1394 (20.5)	368/1471 (25.0)	0.81 (0.71, 0.92) 0.0015	0.75 (0.63, 0.90) 0.0018	-0.05 (-0.08, -0.01)*0.0040	
	> median	318/1407 (22.6)	385/1334 (28.9)	0.81 (0.72, 0.92) 0.0007	0.72 (0.60, 0.86) 0.0003	-0.06 (-0.10, -0.03)*0.0002	
	Gender						0.7189
	Male	337/1630 (20.7)	413/1608 (25.7)	0.80 (0.71, 0.90) 0.0004	0.74 (0.63, 0.88) 0.0005	-0.05 (-0.08, -0.02)*0.0007	
	Female	267/1171 (22.8)	340/1197 (28.4)	0.83 (0.73, 0.95) 0.0053	0.74 (0.61, 0.90) 0.0022	-0.06 (-0.09, -0.02)*0.0017	
	Race						0.3769
	White	440/2006 (21.9)	555/2032 (27.3)	0.82 (0.74, 0.91) 0.0002	0.75 (0.64, 0.87) 0.0002	-0.05 (-0.08, -0.03)*<.0001	
	Black or African	15/ 64 (23.4)	18/ 70 (25.7)	0.90 (0.50, 1.62) 0.7176	0.87 (0.39, 1.92) 0.7235	-0.04 (-0.19, 0.11) 0.5620	
	Asian	130/ 555 (23.4)	150/ 551 (27.2)	0.85 (0.70, 1.04) 0.1161	0.79 (0.60, 1.04) 0.0991	-0.04 (-0.09, 0.01)*0.1459	
	Other	19/ 176 (10.8)	30/ 152 (19.7)	0.53 (0.32, 0.89) 0.0168	0.46 (0.24, 0.88) 0.0192	-0.09 (-0.17, -0.01)*0.0249	
	Geographic region						0.2040
	Asia	126/ 536 (23.5)	146/ 536 (27.2)	0.86 (0.70, 1.05) 0.1421	0.80 (0.61, 1.06) 0.1209	-0.04 (-0.09, 0.01)*0.1600	
	Europe and Saudi Arabia	303/1341 (22.6)	383/1381 (27.7)	0.83 (0.74, 0.94) 0.0032	0.76 (0.64, 0.92) 0.0036	-0.05 (-0.08, -0.02)*0.0020	
	North America	93/ 393 (23.7)	100/ 376 (26.6)	0.89 (0.70, 1.12) 0.3150	0.84 (0.60, 1.17) 0.3008	-0.04 (-0.09, 0.02) 0.2167	
	Latin America	82/ 531 (15.4)	124/ 512 (24.2)	0.64 (0.51, 0.82) 0.0003	0.55 (0.40, 0.75) 0.0002	-0.09 (-0.14, -0.04)*0.0004	
	NYHA class at enrolment						0.7835
	II	460/2083 (22.1)	586/2165 (27.1)	0.81 (0.73, 0.90) <.0001	0.74 (0.64, 0.85) <.0001	-0.05 (-0.08, -0.02)*0.0002	
	III or IV	144/ 718 (20.1)	167/ 639 (26.1)	0.79 (0.65, 0.95) 0.0111	0.71 (0.55, 0.93) 0.0126	-0.06 (-0.11, -0.02)*0.0080	
	LVEF at enrolment						0.9614
	<= 49	209/ 959 (21.8)	249/ 950 (26.2)	0.82 (0.71, 0.96) 0.0148	0.76 (0.61, 0.94) 0.0124	-0.04 (-0.08, -0.01)*0.0237	
	50-59	214/1017 (21.0)	260/1009 (25.8)	0.81 (0.70, 0.95) 0.0077	0.75 (0.61, 0.93) 0.0086	-0.05 (-0.08, -0.01)*0.0119	
	>= 60	181/ 825 (21.9)	244/ 846 (28.8)	0.80 (0.68, 0.94) 0.0055	0.71 (0.56, 0.89) 0.0032	-0.07 (-0.11, -0.03)*0.0011	
	NT-proBNP at enrolment						0.4189
	<= median	319/1396 (22.9)	382/1409 (27.1)	0.84 (0.74, 0.95) 0.0058	0.78 (0.66, 0.94) 0.0069	-0.04 (-0.07, -0.01) 0.0151	
	> median	285/1405 (20.3)	371/1395 (26.6)	0.78 (0.69, 0.89) 0.0002	0.69 (0.57, 0.83) <.0001	-0.06 (-0.09, -0.03)*<.0001	
	Type 2 Diabetes Medical History						0.1098
	Yes	255/1231 (20.7)	349/1243 (28.1)	0.75 (0.65, 0.85) <.0001	0.67 (0.56, 0.81)*<.0001	-0.07 (-0.11, -0.04)*<.0001	
	No	349/1570 (22.2)	404/1562 (25.9)	0.87 (0.77, 0.98) 0.0181	0.82 (0.70, 0.97)*0.0174	-0.02 (-0.05, 0.00) 0.1080	
	Atrial fibrillation or flutter at enrolment ECG						0.4736
	Yes	254/1185 (21.4)	327/1188 (27.5)	0.78 (0.68, 0.89) 0.0004	0.69 (0.57, 0.84) 0.0002	-0.06 (-0.10, -0.03)*0.0005	
	No	350/1616 (21.7)	426/1617 (26.3)	0.83 (0.74, 0.94) 0.0027	0.77 (0.65, 0.91) 0.0024	-0.05 (-0.08, -0.02)*0.0018	
	BMI (kg/m2) at enrolment						0.3252
	< 30	342/1547 (22.1)	405/1541 (26.3)	0.84 (0.75, 0.95) 0.0058	0.78 (0.66, 0.93) 0.0046	-0.04 (-0.07, -0.01)*0.0067	
	>= 30	262/1253 (20.9)	347/1261 (27.5)	0.77 (0.67, 0.88) 0.0001	0.69 (0.57, 0.83) 0.0001	-0.07 (-0.10, -0.03)*0.0001	
	Baseline eGFR (mL/min/1.73m^2)						0.8597
	< 60	295/1338 (22.0)	383/1377 (27.8)	0.80 (0.71, 0.91) 0.0006	0.72 (0.60, 0.86) 0.0004	-0.06 (-0.09, -0.03)*0.0005	
	>= 60	309/1463 (21.1)	369/1427 (25.9)	0.82 (0.72, 0.93) 0.0023	0.76 (0.64, 0.91) 0.0023	-0.05 (-0.08, -0.02)*0.0026	

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Symptom Frequency (LOCF)	SBP at randomisation						0.3870
	<= median	314/1405 (22.3)	389/1420 (27.4)	0.84 (0.74, 0.95) 0.0066	0.77 (0.65, 0.92) 0.0037	-0.05 (-0.08, -0.02)*0.0019	
	> median	290/1396 (20.8)	364/1385 (26.3)	0.78 (0.68, 0.89) 0.0001	0.71 (0.59, 0.85) 0.0002	-0.06 (-0.09, -0.02)*0.0006	
	LVEF at enrolment 2						0.8263
	<= 49	209/ 959 (21.8)	249/ 950 (26.2)	0.82 (0.71, 0.96) 0.0148	0.76 (0.61, 0.94) 0.0124	-0.04 (-0.08, -0.01)*0.0237	
	>= 50	395/1842 (21.4)	504/1855 (27.2)	0.81 (0.72, 0.90) 0.0001	0.73 (0.62, 0.85) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5007
	Yes	48/ 280 (17.1)	62/ 281 (22.1)	0.69 (0.50, 0.95) 0.0217	0.58 (0.37, 0.91) 0.0191	-0.05 (-0.11, 0.02)*0.1413	
	No	556/2521 (22.1)	691/2524 (27.4)	0.82 (0.74, 0.90) <.0001	0.75 (0.66, 0.85) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	MRAs at baseline						0.6232
	Yes	270/1216 (22.2)	330/1210 (27.3)	0.83 (0.73, 0.95) 0.0067	0.75 (0.62, 0.91) 0.0031	-0.05 (-0.08, -0.02)*0.0038	
	No	334/1585 (21.1)	423/1595 (26.5)	0.79 (0.70, 0.90) 0.0002	0.73 (0.62, 0.86) 0.0003	-0.05 (-0.08, -0.02)*0.0003	
	ACEi+ARB at baseline						0.0111
	Yes	415/2037 (20.4)	565/2059 (27.4)	0.75 (0.68, 0.84) <.0001	0.67 (0.57, 0.78) <.0001	-0.07 (-0.10, -0.04)*<.0001	
	No	189/ 764 (24.7)	188/ 746 (25.2)	0.98 (0.82, 1.16) 0.7819	0.96 (0.75, 1.21) 0.7087	-0.00 (-0.05, 0.04)*0.8354	
	ARNI at baseline						0.0606
	Yes	38/ 149 (25.5)	24/ 125 (19.2)	1.25 (0.80, 1.96) 0.3297	1.35 (0.74, 2.45) 0.3282	0.06 (-0.04, 0.16)*0.2089	
	No	566/2652 (21.3)	729/2680 (27.2)	0.80 (0.73, 0.87) <.0001	0.72 (0.63, 0.82) <.0001	-0.06 (-0.08, -0.04)*<.0001	
	Beta Blocker at baseline						0.2397
	Yes	502/2327 (21.6)	619/2330 (26.6)	0.83 (0.75, 0.92) 0.0002	0.76 (0.66, 0.87) 0.0001	-0.05 (-0.07, -0.03)*<.0001	
	No	102/ 474 (21.5)	134/ 475 (28.2)	0.71 (0.58, 0.88) 0.0018	0.63 (0.46, 0.86) 0.0036	-0.07 (-0.12, -0.01)*0.0168	
	Diuretics at baseline						0.3793
	Yes	546/2500 (21.8)	664/2504 (26.5)	0.82 (0.75, 0.90) <.0001	0.75 (0.66, 0.86) <.0001	-0.05 (-0.07, -0.02)*0.0001	
	No	58/ 301 (19.3)	89/ 301 (29.6)	0.71 (0.54, 0.95) 0.0189	0.60 (0.41, 0.89) 0.0110	-0.10 (-0.17, -0.03)*0.0031	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)							
	Overall	784/2625 (29.9)	808/2625 (30.8)	0.97 (0.90, 1.05) 0.4448	0.95 (0.85, 1.08) 0.4530	-0.01 (-0.03, 0.01) 0.4860	
	Age						0.4786
	<= median	382/1331 (28.7)	422/1409 (30.0)	0.94 (0.84, 1.05) 0.2947	0.93 (0.78, 1.09) 0.3655	-0.01 (-0.05, 0.02) 0.4039	
	> median	402/1294 (31.1)	386/1216 (31.7)	1.00 (0.89, 1.11) 0.9461	0.98 (0.82, 1.17) 0.8171	-0.00 (-0.04, 0.03) 0.7829	
	Gender						0.3993
	Male	466/1538 (30.3)	448/1500 (29.9)	1.00 (0.90, 1.11) 0.9946	1.02 (0.87, 1.19) 0.8539	0.00 (-0.03, 0.03) 0.7640	
	Female	318/1087 (29.3)	360/1125 (32.0)	0.93 (0.83, 1.05) 0.2659	0.88 (0.73, 1.06) 0.1897	-0.02 (-0.06, 0.01) 0.1865	
	Race						0.2835
	White	588/1890 (31.1)	624/1921 (32.5)	0.97 (0.89, 1.06) 0.4676	0.95 (0.83, 1.10) 0.5156	-0.01 (-0.03, 0.02) 0.6179	
	Black or African	26/ 58 (44.8)	20/ 66 (30.3)	1.48 (0.94, 2.33) 0.0866	1.87 (0.87, 4.02) 0.1065	0.13 (-0.04, 0.29) 0.1393	
	Asian	129/ 506 (25.5)	133/ 494 (26.9)	0.94 (0.76, 1.16) 0.5675	0.92 (0.69, 1.22) 0.5482	-0.02 (-0.07, 0.04) 0.5284	
	Other	41/ 171 (24.0)	31/ 144 (21.5)	1.03 (0.69, 1.54) 0.8821	1.05 (0.61, 1.82) 0.8529	0.01 (-0.08, 0.10) 0.8341	
	Geographic region						0.7927
	Asia	123/ 492 (25.0)	128/ 482 (26.6)	0.94 (0.76, 1.16) 0.5497	0.91 (0.68, 1.22) 0.5357	-0.02 (-0.07, 0.04) 0.5211	
	Europe and Saudi Arabia	398/1273 (31.3)	431/1309 (32.9)	0.96 (0.87, 1.07) 0.4844	0.96 (0.80, 1.14) 0.6272	0.00 (-0.03, 0.04) 0.7563	
	North America	131/ 367 (35.7)	115/ 347 (33.1)	1.07 (0.88, 1.31) 0.5025	1.09 (0.80, 1.49) 0.5799	0.02 (-0.05, 0.09) 0.6174	
	Latin America	132/ 493 (26.8)	134/ 487 (27.5)	0.96 (0.79, 1.17) 0.7134	0.96 (0.71, 1.28) 0.7617	-0.01 (-0.06, 0.04) 0.7956	
	NYHA class at enrolment						0.9048
	II	564/1953 (28.9)	608/2031 (29.9)	0.96 (0.87, 1.05) 0.3630	0.93 (0.81, 1.07) 0.3438	-0.01 (-0.04, 0.01) 0.3172	
	III or IV	220/ 672 (32.7)	199/ 593 (33.6)	0.97 (0.84, 1.11) 0.6361	0.96 (0.75, 1.23) 0.7559	-0.00 (-0.05, 0.04) 0.8622	
	LVEF at enrolment						0.2497
	<= 49	270/ 907 (29.8)	249/ 896 (27.8)	1.04 (0.90, 1.20) 0.6040	1.07 (0.87, 1.31) 0.5373	0.01 (-0.03, 0.05) 0.5017	
	50-59	303/ 955 (31.7)	307/ 946 (32.5)	1.00 (0.88, 1.13) 0.9453	1.00 (0.82, 1.22) 0.9850	-0.00 (-0.04, 0.04) 0.9813	
	>= 60	211/ 763 (27.7)	252/ 783 (32.2)	0.88 (0.75, 1.02) 0.0780	0.80 (0.64, 1.00) 0.0527	-0.04 (-0.09, -0.00) 0.0424	
	NT-proBNP at enrolment						0.7603
	<= median	397/1312 (30.3)	416/1336 (31.1)	0.96 (0.86, 1.07) 0.4519	0.95 (0.80, 1.12) 0.5271	-0.01 (-0.04, 0.03) 0.6894	
	> median	387/1313 (29.5)	392/1288 (30.4)	0.98 (0.88, 1.10) 0.7351	0.96 (0.81, 1.14) 0.6678	-0.01 (-0.04, 0.02) 0.5347	
	Type 2 Diabetes Medical History						0.9201
	Yes	342/1150 (29.7)	362/1169 (31.0)	0.97 (0.86, 1.09) 0.5651	0.94 (0.79, 1.13)*0.5204	-0.01 (-0.05, 0.02) 0.4514	
	No	442/1475 (30.0)	446/1456 (30.6)	0.97 (0.88, 1.08) 0.6114	0.97 (0.83, 1.13)*0.6949	-0.00 (-0.03, 0.03) 0.7942	
	Atrial fibrillation or flutter at enrolment ECG						0.4301
	Yes	317/1097 (28.9)	344/1109 (31.0)	0.93 (0.83, 1.05) 0.2686	0.90 (0.75, 1.09) 0.2728	-0.01 (-0.05, 0.02) 0.5191	
	No	467/1528 (30.6)	464/1516 (30.6)	1.00 (0.90, 1.10) 0.9368	0.99 (0.85, 1.16) 0.9490	-0.00 (-0.03, 0.03) 0.7906	
	BMI (kg/m2) at enrolment						0.7677
	< 30	424/1452 (29.2)	426/1428 (29.8)	0.98 (0.88, 1.09) 0.7080	0.97 (0.82, 1.14) 0.7203	-0.01 (-0.04, 0.02) 0.6208	
	>= 30	359/1172 (30.6)	382/1195 (32.0)	0.96 (0.85, 1.07) 0.4567	0.94 (0.78, 1.12) 0.4658	-0.01 (-0.05, 0.02) 0.5540	
	Baseline eGFR (mL/min/1.73m^2)						0.1084
	< 60	401/1240 (32.3)	397/1270 (31.3)	1.04 (0.93, 1.16) 0.5327	1.05 (0.88, 1.25) 0.5819	0.01 (-0.02, 0.04) 0.5803	
	>= 60	383/1385 (27.7)	410/1354 (30.3)	0.91 (0.81, 1.02) 0.1054	0.88 (0.74, 1.04) 0.1281	-0.02 (-0.06, 0.01) 0.1395	

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Social Limitation (LOCF)	SBP at randomisation						0.3907
	<= median	399/1320 (30.2)	405/1323 (30.6)	1.01 (0.90, 1.13) 0.8818	1.01 (0.85, 1.20) 0.9259	0.00 (-0.03, 0.03) 0.9660	
	> median	385/1305 (29.5)	403/1302 (31.0)	0.94 (0.84, 1.05) 0.2911	0.91 (0.77, 1.08) 0.2991	-0.02 (-0.05, 0.02) 0.3069	
	LVEF at enrolment 2						0.2898
	<= 49	270/ 907 (29.8)	249/ 896 (27.8)	1.04 (0.90, 1.20) 0.6040	1.07 (0.87, 1.31) 0.5373	0.01 (-0.03, 0.05) 0.5017	
	>= 50	514/1718 (29.9)	559/1729 (32.3)	0.94 (0.86, 1.04) 0.2294	0.91 (0.78, 1.05) 0.1927	-0.02 (-0.05, 0.01) 0.1956	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3004
	Yes	73/ 252 (29.0)	66/ 256 (25.8)	1.09 (0.84, 1.43) 0.5104	1.16 (0.77, 1.75) 0.4808	0.03 (-0.05, 0.11)*0.4203	
	No	711/2373 (30.0)	742/2369 (31.3)	0.96 (0.88, 1.04) 0.3061	0.94 (0.82, 1.06) 0.3019	-0.01 (-0.04, 0.01) 0.2686	
	MRAs at baseline						0.2143
	Yes	348/1144 (30.4)	332/1131 (29.4)	1.03 (0.91, 1.17) 0.6122	1.05 (0.87, 1.26) 0.6315	0.01 (-0.03, 0.04) 0.6396	
	No	436/1481 (29.4)	476/1494 (31.9)	0.93 (0.84, 1.03) 0.1723	0.89 (0.76, 1.05) 0.1706	-0.02 (-0.05, 0.01) 0.1535	
	ACEi+ARB at baseline						0.7527
	Yes	563/1909 (29.5)	585/1934 (30.2)	0.98 (0.89, 1.07) 0.6171	0.97 (0.84, 1.11) 0.6284	-0.01 (-0.03, 0.02) 0.6415	
	No	221/ 716 (30.9)	223/ 691 (32.3)	0.95 (0.82, 1.11) 0.5204	0.93 (0.74, 1.17) 0.5266	-0.01 (-0.06, 0.03) 0.5826	
	ARNI at baseline						0.2608
	Yes	42/ 146 (28.8)	41/ 115 (35.7)	0.83 (0.58, 1.19) 0.3069	0.76 (0.45, 1.30) 0.3162	-0.06 (-0.17, 0.06) 0.3239	
	No	742/2479 (29.9)	767/2510 (30.6)	0.98 (0.90, 1.06) 0.6318	0.97 (0.86, 1.10) 0.6380	-0.00 (-0.03, 0.02) 0.7037	
	Beta Blocker at baseline						0.7598
	Yes	662/2195 (30.2)	681/2187 (31.1)	0.98 (0.90, 1.06) 0.5689	0.96 (0.84, 1.10) 0.5636	-0.01 (-0.03, 0.02) 0.6390	
	No	122/ 430 (28.4)	127/ 438 (29.0)	0.95 (0.77, 1.17) 0.6304	0.93 (0.69, 1.26) 0.6465	-0.02 (-0.07, 0.04) 0.6024	
	Diuretics at baseline						0.2398
	Yes	709/2350 (30.2)	738/2345 (31.5)	0.95 (0.88, 1.03) 0.2501	0.93 (0.82, 1.06) 0.2625	-0.01 (-0.04, 0.01) 0.3371	
	No	75/ 275 (27.3)	70/ 280 (25.0)	1.13 (0.86, 1.48) 0.3929	1.18 (0.80, 1.74) 0.3937	0.03 (-0.04, 0.10) 0.4280	

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Symptom Stability (LOCF)							
	Overall	556/2801 (19.9)	637/2805 (22.7)	0.95 (0.89, 1.01) 0.1136	0.82 (0.70, 0.95) 0.0108	-0.03 (-0.05, -0.01)*0.0089	
	Age						0.3509
	<= median	279/1394 (20.0)	327/1471 (22.2)	0.98 (0.89, 1.07) 0.6011	0.85 (0.68, 1.05) 0.1302	-0.02 (-0.05, 0.01)*0.1461	
	> median	277/1407 (19.7)	310/1334 (23.2)	0.92 (0.84, 1.00) 0.0523	0.78 (0.62, 0.97) 0.0269	-0.04 (-0.07, -0.00)*0.0236	
	Gender						0.2418
	Male	332/1630 (20.4)	354/1608 (22.0)	0.99 (0.91, 1.07) 0.7217	0.92 (0.74, 1.13) 0.4098	-0.02 (-0.04, 0.01)*0.2515	
	Female	224/1171 (19.1)	283/1197 (23.6)	0.89 (0.80, 1.00) 0.0409	0.71 (0.57, 0.90) 0.0041	-0.05 (-0.08, -0.01)*0.0073	
	Race						0.8258*
	White	383/2006 (19.1)	447/2032 (22.0)	0.96 (0.89, 1.04) 0.3373	0.85 (0.71, 1.02) 0.0807	-0.03 (-0.05, -0.00)*0.0222	
	Black or African	12/ 64 (18.8)	19/ 70 (27.1)	0.85 (0.51, 1.41) 0.5295	0.63 (0.25, 1.61) 0.3357	-0.08 (-0.23, 0.06)*0.2447	
	Asian	132/ 555 (23.8)	146/ 551 (26.5)	0.90 (0.79, 1.02) 0.1034	0.74 (0.53, 1.02) 0.0677	-0.03 (-0.08, 0.02)*0.2981	
	Other	29/ 176 (16.5)	25/ 152 (16.4)	1.00 (0.61, 1.63)*0.9942	0.94 (0.47, 1.91) 0.8745	0.00 (-0.08, 0.08)*0.9942	
	Geographic region						0.8273
	Asia	125/ 536 (23.3)	143/ 536 (26.7)	0.90 (0.79, 1.02) 0.0959	0.70 (0.50, 0.99) 0.0424	-0.03 (-0.09, 0.02)*0.2039	
	Europe and Saudi Arabia	260/1341 (19.4)	297/1381 (21.5)	0.97 (0.90, 1.06) 0.5018	0.85 (0.68, 1.07) 0.1686	-0.02 (-0.05, 0.01)*0.1706	
	North America	78/ 393 (19.8)	95/ 376 (25.3)	0.93 (0.76, 1.13) 0.4534	0.83 (0.56, 1.23) 0.3546	-0.05 (-0.11, 0.00)*0.0720	
	Latin America	93/ 531 (17.5)	102/ 512 (19.9)	1.00 (0.85, 1.18) 0.9804	0.83 (0.57, 1.19) 0.3078	-0.02 (-0.07, 0.02)*0.3189	
	NYHA class at enrolment						0.3773
	II	405/2083 (19.4)	467/2165 (21.6)	0.94 (0.87, 1.02) 0.1175	0.84 (0.70, 1.00) 0.0497	-0.02 (-0.05, 0.00)*0.0858	
	III or IV	151/ 718 (21.0)	170/ 639 (26.6)	0.98 (0.88, 1.10) 0.7916	0.75 (0.55, 1.01) 0.0619	-0.06 (-0.10, -0.01)*0.0162	
	LVEF at enrolment						0.1601
	<= 49	206/ 959 (21.5)	211/ 950 (22.2)	1.03 (0.92, 1.15) 0.5831	0.92 (0.71, 1.19) 0.5135	-0.01 (-0.04, 0.03)*0.6996	
	50-59	200/1017 (19.7)	240/1009 (23.8)	0.92 (0.83, 1.03) 0.1622	0.79 (0.62, 1.02) 0.0674	-0.04 (-0.08, -0.01)*0.0244	
	>= 60	150/ 825 (18.2)	186/ 846 (22.0)	0.83 (0.68, 1.00)*0.0531	0.74 (0.55, 1.00) 0.0469	-0.04 (-0.08, 0.00)*0.0519	
	NT-proBNP at enrolment						0.9629
	<= median	266/1396 (19.1)	290/1409 (20.6)	0.96 (0.87, 1.05) 0.3381	0.87 (0.70, 1.09) 0.2155	-0.02 (-0.04, 0.01)*0.3101	
	> median	290/1405 (20.6)	347/1395 (24.9)	0.95 (0.87, 1.04) 0.3029	0.77 (0.62, 0.96) 0.0181	-0.04 (-0.07, -0.01)*0.0075	
	Type 2 Diabetes Medical History						0.2844
	Yes	259/1231 (21.0)	279/1243 (22.4)	0.98 (0.89, 1.08) 0.6940	0.92 (0.76, 1.11)*0.3967	-0.01 (-0.05, 0.02)*0.3966	
	No	297/1570 (18.9)	358/1562 (22.9)	0.92 (0.84, 1.01) 0.0649	0.78 (0.66, 0.93)*0.0060	-0.04 (-0.07, -0.01)*0.0058	
	Atrial fibrillation or flutter at enrolment ECG						0.9822
	Yes	234/1185 (19.7)	268/1188 (22.6)	0.95 (0.87, 1.05) 0.3213	0.83 (0.65, 1.06) 0.1358	-0.03 (-0.06, 0.00)*0.0933	
	No	322/1616 (19.9)	369/1617 (22.8)	0.95 (0.87, 1.03) 0.2172	0.81 (0.66, 0.99) 0.0368	-0.03 (-0.06, -0.00)*0.0446	
	BMI (kg/m2) at enrolment						0.4781
	< 30	327/1547 (21.1)	361/1541 (23.4)	0.97 (0.89, 1.05) 0.4187	0.86 (0.70, 1.06) 0.1507	-0.02 (-0.05, 0.01)*0.1264	
	>= 30	229/1253 (18.3)	276/1261 (21.9)	0.93 (0.84, 1.03) 0.1551	0.77 (0.61, 0.97) 0.0264	-0.04 (-0.07, -0.00)*0.0237	
	Baseline eGFR (mL/min/1.73m^2)						0.4615
	< 60	296/1338 (22.1)	335/1377 (24.3)	0.96 (0.88, 1.05) 0.3690	0.86 (0.70, 1.07) 0.1759	-0.02 (-0.05, 0.01)*0.1734	
	>= 60	260/1463 (17.8)	302/1427 (21.2)	0.93 (0.84, 1.03) 0.1592	0.78 (0.62, 0.97) 0.0256	-0.03 (-0.06, -0.01)*0.0213	

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Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)	SBP at randomisation						0.3660
	<= median	297/1405 (21.1)	338/1420 (23.8)	0.97 (0.89, 1.06) 0.5101	0.85 (0.68, 1.04) 0.1204	-0.03 (-0.06, 0.00)*0.0897	
	> median	259/1396 (18.6)	299/1385 (21.6)	0.92 (0.84, 1.01) 0.0827	0.79 (0.63, 0.99) 0.0429	-0.03 (-0.06, -0.00)*0.0456	
	LVEF at enrolment 2						0.0603
	<= 49	206/ 959 (21.5)	211/ 950 (22.2)	1.03 (0.92, 1.15) 0.5831	0.92 (0.71, 1.19) 0.5135	-0.01 (-0.04, 0.03)*0.6996	
	>= 50	350/1842 (19.0)	426/1855 (23.0)	0.91 (0.84, 0.98) 0.0159	0.77 (0.64, 0.93) 0.0078	-0.04 (-0.07, -0.01)*0.0030	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0365
	Yes	101/ 280 (36.1)	100/ 281 (35.6)	1.06 (0.92, 1.22) 0.4089	1.08 (0.70, 1.67) 0.7254	0.00 (-0.07, 0.08)*0.9048	
	No	455/2521 (18.0)	537/2524 (21.3)	0.92 (0.86, 0.99) 0.0255	0.79 (0.67, 0.93) 0.0049	-0.03 (-0.05, -0.01)*0.0039	
	MRAs at baseline						0.8852
	Yes	261/1216 (21.5)	285/1210 (23.6)	0.94 (0.85, 1.04) 0.2357	0.82 (0.65, 1.03) 0.0827	-0.02 (-0.05, 0.01)*0.2177	
	No	295/1585 (18.6)	352/1595 (22.1)	0.96 (0.89, 1.05) 0.3756	0.82 (0.67, 1.02) 0.0702	-0.03 (-0.06, -0.01)*0.0154	
	ACEi+ARB at baseline						0.8094
	Yes	397/2037 (19.5)	447/2059 (21.7)	0.96 (0.89, 1.03) 0.2441	0.83 (0.69, 1.00) 0.0508	-0.02 (-0.05, 0.00)*0.0788	
	No	159/ 764 (20.8)	190/ 746 (25.5)	0.93 (0.82, 1.05) 0.2355	0.78 (0.58, 1.04) 0.0858	-0.05 (-0.09, -0.00)*0.0317	
	ARNI at baseline						0.2947
	Yes	32/ 149 (21.5)	36/ 125 (28.8)	0.82 (0.61, 1.10) 0.1798	0.51 (0.26, 1.02) 0.0554	-0.07 (-0.18, 0.03)*0.1643	
	No	524/2652 (19.8)	601/2680 (22.4)	0.96 (0.90, 1.03) 0.2216	0.84 (0.72, 0.99) 0.0369	-0.03 (-0.05, -0.00)*0.0169	
	Beta Blocker at baseline						0.7860
	Yes	449/2327 (19.3)	523/2330 (22.4)	0.94 (0.87, 1.01) 0.0978	0.83 (0.70, 0.98) 0.0271	-0.03 (-0.05, -0.01)*0.0081	
	No	107/ 474 (22.6)	114/ 475 (24.0)	0.94 (0.75, 1.19)*0.6034	0.76 (0.52, 1.11) 0.1492	-0.01 (-0.07, 0.04)*0.6032	
	Diuretics at baseline						0.4562
	Yes	497/2500 (19.9)	570/2504 (22.8)	0.94 (0.88, 1.01) 0.0713	0.81 (0.69, 0.96) 0.0126	-0.03 (-0.05, -0.01)*0.0127	
	No	59/ 301 (19.6)	67/ 301 (22.3)	0.93 (0.76, 1.14) 0.4855	0.87 (0.55, 1.39) 0.5602	-0.03 (-0.09, 0.04)*0.4226	

N displays number of patients in the analysis, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	606/2801 (21.6)	743/2805 (26.5)	0.82 (0.75, 0.90) <.0001	0.76 (0.67, 0.86) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Age						0.6264
	<= median	279/1394 (20.0)	363/1471 (24.7)	0.80 (0.70, 0.92) 0.0012	0.74 (0.62, 0.89) 0.0013	-0.05 (-0.08, -0.02)*0.0027	
	> median	327/1407 (23.2)	380/1334 (28.5)	0.84 (0.74, 0.95) 0.0048	0.77 (0.64, 0.92) 0.0037	-0.05 (-0.09, -0.02)*0.0017	
	Gender						0.2020
	Male	330/1630 (20.2)	414/1608 (25.7)	0.78 (0.69, 0.89) 0.0001	0.72 (0.61, 0.86) 0.0002	-0.06 (-0.08, -0.03)*0.0002	
	Female	276/1171 (23.6)	329/1197 (27.5)	0.88 (0.78, 1.01) 0.0665	0.81 (0.67, 0.98) 0.0323	-0.04 (-0.07, -0.00)*0.0287	
	Race						0.2172
	White	442/2006 (22.0)	553/2032 (27.2)	0.82 (0.74, 0.91) 0.0002	0.76 (0.65, 0.88) 0.0003	-0.05 (-0.08, -0.03)*0.0001	
	Black or African	11/ 64 (17.2)	21/ 70 (30.0)	0.57 (0.30, 1.09) 0.0916	0.47 (0.20, 1.09) 0.0772	-0.13 (-0.27, 0.01)*0.0763	
	Asian	131/ 555 (23.6)	137/ 551 (24.9)	0.94 (0.77, 1.16) 0.5840	0.92 (0.69, 1.21) 0.5384	-0.01 (-0.06, 0.04)*0.6248	
	Other	22/ 176 (12.5)	32/ 152 (21.1)	0.60 (0.37, 0.97) 0.0363	0.53 (0.28, 0.97) 0.0394	-0.09 (-0.17, -0.00)*0.0389	
	Geographic region						0.2550
	Asia	127/ 536 (23.7)	132/ 536 (24.6)	0.96 (0.78, 1.18) 0.6921	0.94 (0.71, 1.24) 0.6526	-0.01 (-0.06, 0.04)*0.7213	
	Europe and Saudi Arabia	302/1341 (22.5)	384/1381 (27.8)	0.82 (0.73, 0.93) 0.0019	0.76 (0.63, 0.91) 0.0030	-0.05 (-0.09, -0.02)*0.0015	
	North America	93/ 393 (23.7)	108/ 376 (28.7)	0.82 (0.65, 1.04) 0.1055	0.76 (0.55, 1.05) 0.1005	-0.06 (-0.11, 0.00) 0.0700	
	Latin America	84/ 531 (15.8)	119/ 512 (23.2)	0.69 (0.54, 0.87) 0.0022	0.60 (0.43, 0.82) 0.0017	-0.07 (-0.12, -0.03)*0.0024	
	NYHA class at enrolment						0.4052
	II	456/2083 (21.9)	567/2165 (26.2)	0.83 (0.75, 0.92) 0.0005	0.77 (0.66, 0.89) 0.0004	-0.04 (-0.07, -0.02)*0.0010	
	III or IV	150/ 718 (20.9)	176/ 639 (27.5)	0.76 (0.64, 0.91) 0.0027	0.70 (0.54, 0.90) 0.0065	-0.07 (-0.11, -0.02)*0.0043	
	LVEF at enrolment						0.8100
	<= 49	211/ 959 (22.0)	242/ 950 (25.5)	0.85 (0.73, 0.99) 0.0427	0.80 (0.64, 1.00) 0.0455	-0.03 (-0.07, 0.00)*0.0745	
	50-59	220/1017 (21.6)	263/1009 (26.1)	0.83 (0.71, 0.97) 0.0155	0.77 (0.62, 0.95) 0.0153	-0.04 (-0.08, -0.01)*0.0191	
	>= 60	175/ 825 (21.2)	238/ 846 (28.1)	0.79 (0.67, 0.93) 0.0047	0.71 (0.56, 0.89) 0.0035	-0.07 (-0.11, -0.03)*0.0010	
	NT-proBNP at enrolment						0.2748
	<= median	320/1396 (22.9)	372/1409 (26.4)	0.86 (0.76, 0.98) 0.0219	0.82 (0.69, 0.98) 0.0255	-0.03 (-0.07, -0.00)*0.0324	
	> median	286/1405 (20.4)	371/1395 (26.6)	0.79 (0.69, 0.89) 0.0003	0.70 (0.59, 0.84) 0.0001	-0.06 (-0.09, -0.03)*<.0001	
	Type 2 Diabetes Medical History						0.0167
	Yes	255/1231 (20.7)	359/1243 (28.9)	0.73 (0.63, 0.83) <.0001	0.64 (0.53, 0.77)*<.0001	-0.08 (-0.12, -0.05)*<.0001	
	No	351/1570 (22.4)	384/1562 (24.6)	0.91 (0.81, 1.03) 0.1304	0.88 (0.75, 1.04)*0.1415	-0.02 (-0.05, 0.01)*0.1413	
	Atrial fibrillation or flutter at enrolment ECG						0.6234
	Yes	244/1185 (20.6)	303/1188 (25.5)	0.80 (0.69, 0.92) 0.0019	0.74 (0.60, 0.90) 0.0028	-0.05 (-0.08, -0.02)*0.0044	
	No	362/1616 (22.4)	440/1617 (27.2)	0.84 (0.74, 0.94) 0.0027	0.77 (0.65, 0.91) 0.0019	-0.05 (-0.08, -0.02)*0.0015	
	BMI (kg/m2) at enrolment						0.2395
	< 30	347/1547 (22.4)	401/1541 (26.0)	0.87 (0.77, 0.98) 0.0201	0.82 (0.69, 0.97) 0.0187	-0.04 (-0.07, -0.01)*0.0198	
	>= 30	259/1253 (20.7)	341/1261 (27.0)	0.78 (0.68, 0.89) 0.0002	0.70 (0.58, 0.84) 0.0002	-0.06 (-0.10, -0.03)*0.0002	
	Baseline eGFR (mL/min/1.73m^2)						0.9027
	< 60	312/1338 (23.3)	390/1377 (28.3)	0.83 (0.73, 0.94) 0.0024	0.76 (0.64, 0.91) 0.0030	-0.05 (-0.08, -0.02)*0.0028	
	>= 60	294/1463 (20.1)	352/1427 (24.7)	0.82 (0.72, 0.94) 0.0036	0.76 (0.64, 0.91) 0.0030	-0.05 (-0.08, -0.02)*0.0032	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.1368
	<= median	316/1405 (22.5)	375/1420 (26.4)	0.88 (0.77, 1.00) 0.0448	0.83 (0.69, 0.99) 0.0364	-0.04 (-0.07, -0.01)*0.0153	
	> median	290/1396 (20.8)	368/1385 (26.6)	0.77 (0.67, 0.87) <.0001	0.69 (0.58, 0.83) <.0001	-0.06 (-0.09, -0.03)*0.0003	
	LVEF at enrolment 2						0.6236
	<= 49	211/ 959 (22.0)	242/ 950 (25.5)	0.85 (0.73, 0.99) 0.0427	0.80 (0.64, 1.00) 0.0455	-0.03 (-0.07, 0.00)*0.0745	
	>= 50	395/1842 (21.4)	501/1855 (27.0)	0.81 (0.72, 0.90) 0.0002	0.74 (0.63, 0.87) 0.0002	-0.06 (-0.08, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8857
	Yes	51/ 280 (18.2)	60/ 281 (21.4)	0.78 (0.57, 1.07) 0.1256	0.71 (0.46, 1.11) 0.1317	-0.03 (-0.10, 0.03)*0.3505	
	No	555/2521 (22.0)	683/2524 (27.1)	0.82 (0.75, 0.91) <.0001	0.76 (0.67, 0.87) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	MRAs at baseline						0.4671
	Yes	275/1216 (22.6)	324/1210 (26.8)	0.85 (0.75, 0.98) 0.0219	0.80 (0.66, 0.97) 0.0204	-0.04 (-0.08, -0.01)*0.0173	
	No	331/1585 (20.9)	419/1595 (26.3)	0.80 (0.71, 0.90) 0.0003	0.73 (0.62, 0.86) 0.0003	-0.05 (-0.08, -0.02)*0.0003	
	ACEi+ARB at baseline						0.0083
	Yes	423/2037 (20.8)	568/2059 (27.6)	0.77 (0.69, 0.85) <.0001	0.68 (0.59, 0.79) <.0001	-0.07 (-0.09, -0.04)*<.0001	
	No	183/ 764 (24.0)	175/ 746 (23.5)	1.01 (0.85, 1.21) 0.8979	1.02 (0.80, 1.29) 0.9032	-0.01 (-0.05, 0.03) 0.7277	
	ARNI at baseline						0.2013
	Yes	33/ 149 (22.1)	23/ 125 (18.4)	1.16 (0.72, 1.88) 0.5383	1.22 (0.66, 2.25) 0.5253	0.02 (-0.07, 0.12) 0.6305	
	No	573/2652 (21.6)	720/2680 (26.9)	0.82 (0.74, 0.89) <.0001	0.75 (0.66, 0.85) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	Beta Blocker at baseline						0.0098
	Yes	513/2327 (22.0)	603/2330 (25.9)	0.87 (0.79, 0.96) 0.0056	0.82 (0.71, 0.94) 0.0042	-0.04 (-0.06, -0.01)*0.0022	
	No	93/ 474 (19.6)	140/ 475 (29.5)	0.63 (0.50, 0.78) <.0001	0.53 (0.38, 0.72) <.0001	-0.10 (-0.15, -0.04)*0.0004	
	Diuretics at baseline						0.8593
	Yes	545/2500 (21.8)	661/2504 (26.4)	0.82 (0.75, 0.91) <.0001	0.76 (0.67, 0.87) <.0001	-0.05 (-0.07, -0.02)*0.0001	
	No	61/ 301 (20.3)	82/ 301 (27.2)	0.80 (0.60, 1.06) 0.1260	0.73 (0.49, 1.07) 0.1076	-0.07 (-0.14, -0.00)*0.0436	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	590/2801 (21.1)	735/2805 (26.2)	0.82 (0.74, 0.89) <.0001	0.75 (0.66, 0.85) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Age						0.3135
	<= median	262/1394 (18.8)	354/1471 (24.1)	0.77 (0.67, 0.89) 0.0003	0.71 (0.59, 0.86) 0.0003	-0.05 (-0.08, -0.02)*0.0006	
	> median	328/1407 (23.3)	381/1334 (28.6)	0.85 (0.75, 0.96) 0.0085	0.78 (0.65, 0.92) 0.0046	-0.05 (-0.09, -0.02)*0.0017	
	Gender						0.2886
	Male	329/1630 (20.2)	417/1608 (25.9)	0.78 (0.69, 0.89) 0.0001	0.72 (0.61, 0.85) 0.0001	-0.06 (-0.09, -0.03)*<.0001	
	Female	261/1171 (22.3)	318/1197 (26.6)	0.87 (0.76, 0.99) 0.0421	0.80 (0.66, 0.97) 0.0238	-0.04 (-0.08, -0.01)*0.0153	
	Race						0.5456
	White	431/2006 (21.5)	551/2032 (27.1)	0.81 (0.73, 0.90) <.0001	0.74 (0.64, 0.86) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Black or African	16/ 64 (25.0)	21/ 70 (30.0)	0.83 (0.48, 1.44) 0.5000	0.76 (0.36, 1.65) 0.4929	-0.06 (-0.21, 0.09) 0.4638	
	Asian	122/ 555 (22.0)	134/ 551 (24.3)	0.91 (0.73, 1.13) 0.3817	0.88 (0.66, 1.16) 0.3539	-0.03 (-0.07, 0.02) 0.2993	
	Other	21/ 176 (11.9)	29/ 152 (19.1)	0.61 (0.37, 1.02) 0.0578	0.55 (0.29, 1.03) 0.0616	-0.06 (-0.14, 0.01) 0.0829	
	Geographic region						0.3763
	Asia	117/ 536 (21.8)	130/ 536 (24.3)	0.91 (0.73, 1.13) 0.3786	0.87 (0.66, 1.16) 0.3497	-0.03 (-0.08, 0.02) 0.3039	
	Europe and Saudi Arabia	288/1341 (21.5)	376/1381 (27.2)	0.82 (0.72, 0.93) 0.0019	0.74 (0.61, 0.89) 0.0012	-0.06 (-0.09, -0.03)*0.0005	
	North America	99/ 393 (25.2)	109/ 376 (29.0)	0.87 (0.69, 1.09) 0.2154	0.82 (0.60, 1.14) 0.2388	-0.04 (-0.10, 0.02) 0.2067	
	Latin America	86/ 531 (16.2)	120/ 512 (23.4)	0.69 (0.54, 0.88) 0.0025	0.61 (0.44, 0.83) 0.0020	-0.07 (-0.12, -0.02)*0.0033	
	NYHA class at enrolment						0.3466
	II	448/2083 (21.5)	561/2165 (25.9)	0.83 (0.75, 0.92) 0.0005	0.77 (0.67, 0.89) 0.0004	-0.04 (-0.07, -0.02)*0.0007	
	III or IV	142/ 718 (19.8)	174/ 639 (27.2)	0.75 (0.63, 0.91) 0.0025	0.66 (0.51, 0.86) 0.0022	-0.07 (-0.12, -0.03)*0.0012	
	LVEF at enrolment						0.8537
	<= 49	194/ 959 (20.2)	242/ 950 (25.5)	0.79 (0.67, 0.93) 0.0041	0.72 (0.58, 0.89) 0.0030	-0.05 (-0.09, -0.01)*0.0063	
	50-59	220/1017 (21.6)	264/1009 (26.2)	0.84 (0.72, 0.97) 0.0195	0.78 (0.63, 0.96) 0.0196	-0.05 (-0.08, -0.01)*0.0166	
	>= 60	176/ 825 (21.3)	229/ 846 (27.1)	0.82 (0.70, 0.97) 0.0233	0.76 (0.60, 0.96) 0.0188	-0.06 (-0.10, -0.02)*0.0061	
	NT-proBNP at enrolment						0.3373
	<= median	305/1396 (21.8)	362/1409 (25.7)	0.85 (0.75, 0.97) 0.0155	0.80 (0.67, 0.96) 0.0149	-0.04 (-0.07, -0.01)*0.0167	
	> median	285/1405 (20.3)	373/1395 (26.7)	0.78 (0.69, 0.89) 0.0002	0.70 (0.59, 0.84) 0.0001	-0.06 (-0.10, -0.03)*<.0001	
	Type 2 Diabetes Medical History						0.0176
	Yes	243/1231 (19.7)	347/1243 (27.9)	0.72 (0.62, 0.83) <.0001	0.64 (0.53, 0.77)*<.0001	-0.08 (-0.12, -0.05)*<.0001	
	No	347/1570 (22.1)	388/1562 (24.8)	0.90 (0.80, 1.02) 0.0994	0.86 (0.73, 1.01)*0.0708	-0.03 (-0.06, 0.00)*0.0705	
	Atrial fibrillation or flutter at enrolment ECG						0.9621
	Yes	252/1185 (21.3)	312/1188 (26.3)	0.81 (0.71, 0.94) 0.0038	0.75 (0.62, 0.91) 0.0039	-0.05 (-0.08, -0.02)*0.0042	
	No	338/1616 (20.9)	423/1617 (26.2)	0.81 (0.72, 0.92) 0.0010	0.75 (0.64, 0.89) 0.0007	-0.05 (-0.08, -0.02)*0.0004	
	BMI (kg/m2) at enrolment						0.2874
	< 30	332/1547 (21.5)	392/1541 (25.4)	0.85 (0.75, 0.97) 0.0134	0.80 (0.68, 0.95) 0.0107	-0.04 (-0.07, -0.01)*0.0090	
	>= 30	258/1253 (20.6)	342/1261 (27.1)	0.77 (0.68, 0.89) 0.0002	0.70 (0.58, 0.84) 0.0002	-0.07 (-0.10, -0.03)*0.0001	
	Baseline eGFR (mL/min/1.73m^2)						0.9441
	< 60	301/1338 (22.5)	385/1377 (28.0)	0.81 (0.72, 0.92) 0.0013	0.75 (0.62, 0.89) 0.0013	-0.05 (-0.09, -0.02)*0.0010	
	>= 60	289/1463 (19.8)	349/1427 (24.5)	0.82 (0.72, 0.94) 0.0043	0.76 (0.64, 0.91) 0.0030	-0.05 (-0.08, -0.02)*0.0023	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.3082
	<= median	306/1405 (21.8)	376/1420 (26.5)	0.85 (0.75, 0.97) 0.0141	0.80 (0.67, 0.95) 0.0120	-0.05 (-0.08, -0.02)*0.0035	
	> median	284/1396 (20.3)	359/1385 (25.9)	0.78 (0.68, 0.89) 0.0002	0.70 (0.58, 0.84) 0.0001	-0.06 (-0.09, -0.02)*0.0005	
	LVEF at enrolment 2						0.5807
	<= 49	194/ 959 (20.2)	242/ 950 (25.5)	0.79 (0.67, 0.93) 0.0041	0.72 (0.58, 0.89) 0.0030	-0.05 (-0.09, -0.01)*0.0063	
	>= 50	396/1842 (21.5)	493/1855 (26.6)	0.83 (0.74, 0.93) 0.0012	0.77 (0.66, 0.90) 0.0010	-0.05 (-0.08, -0.02)*0.0003	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2245
	Yes	54/ 280 (19.3)	53/ 281 (18.9)	0.98 (0.70, 1.35) 0.8813	0.95 (0.61, 1.47) 0.8141	0.00 (-0.06, 0.07)*0.8982	
	No	536/2521 (21.3)	682/2524 (27.0)	0.80 (0.73, 0.88) <.0001	0.73 (0.64, 0.84) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	MRAs at baseline						0.7497
	Yes	253/1216 (20.8)	315/1210 (26.0)	0.80 (0.70, 0.92) 0.0023	0.75 (0.62, 0.91) 0.0030	-0.05 (-0.09, -0.02)*0.0023	
	No	337/1585 (21.3)	420/1595 (26.3)	0.83 (0.73, 0.93) 0.0022	0.75 (0.64, 0.89) 0.0010	-0.05 (-0.08, -0.02)*0.0008	
	ACEi+ARB at baseline						0.0088
	Yes	411/2037 (20.2)	560/2059 (27.2)	0.76 (0.68, 0.84) <.0001	0.68 (0.58, 0.78) <.0001	-0.07 (-0.10, -0.04)*<.0001	
	No	179/ 764 (23.4)	175/ 746 (23.5)	1.00 (0.84, 1.20) 0.9820	1.00 (0.78, 1.27) 0.9764	-0.01 (-0.05, 0.04) 0.7833	
	ARNI at baseline						0.1374
	Yes	32/ 149 (21.5)	22/ 125 (17.6)	1.23 (0.75, 2.01) 0.4201	1.25 (0.67, 2.32) 0.4786	0.04 (-0.06, 0.13)*0.4181	
	No	558/2652 (21.0)	713/2680 (26.6)	0.81 (0.73, 0.89) <.0001	0.74 (0.65, 0.84) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Beta Blocker at baseline						0.0268
	Yes	505/2327 (21.7)	607/2330 (26.1)	0.85 (0.77, 0.94) 0.0021	0.80 (0.69, 0.92) 0.0013	-0.04 (-0.07, -0.02)*0.0005	
	No	85/ 474 (17.9)	128/ 475 (26.9)	0.64 (0.50, 0.81) 0.0002	0.55 (0.40, 0.75) 0.0002	-0.09 (-0.14, -0.04)*0.0008	
	Diuretics at baseline						0.4826
	Yes	528/2500 (21.1)	662/2504 (26.4)	0.81 (0.73, 0.89) <.0001	0.74 (0.65, 0.84) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	No	62/ 301 (20.6)	73/ 301 (24.3)	0.89 (0.66, 1.20) 0.4438	0.85 (0.58, 1.25) 0.4093	-0.04 (-0.10, 0.03) 0.2721	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	590/2801 (21.1)	717/2805 (25.6)	0.83 (0.76, 0.91) 0.0001	0.78 (0.69, 0.88) 0.0001	-0.04 (-0.07, -0.02)*<.0001	
	Age						0.4562
	<= median	266/1394 (19.1)	345/1471 (23.5)	0.80 (0.70, 0.92) 0.0018	0.76 (0.63, 0.91) 0.0028	-0.04 (-0.07, -0.01)*0.0042	
	> median	324/1407 (23.0)	372/1334 (27.9)	0.86 (0.76, 0.97) 0.0157	0.79 (0.66, 0.94) 0.0087	-0.05 (-0.08, -0.02)*0.0035	
	Gender						0.9655
	Male	339/1630 (20.8)	403/1608 (25.1)	0.84 (0.74, 0.95) 0.0046	0.79 (0.66, 0.93) 0.0048	-0.04 (-0.07, -0.01)*0.0039	
	Female	251/1171 (21.4)	314/1197 (26.2)	0.83 (0.73, 0.96) 0.0109	0.77 (0.63, 0.94) 0.0093	-0.05 (-0.08, -0.01)*0.0061	
	Race						0.2532
	White	426/2006 (21.2)	548/2032 (27.0)	0.81 (0.72, 0.90) <.0001	0.74 (0.63, 0.86) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Black or African	16/ 64 (25.0)	16/ 70 (22.9)	1.10 (0.60, 1.99) 0.7663	1.11 (0.50, 2.48) 0.7969	0.00 (-0.14, 0.15) 0.9471	
	Asian	124/ 555 (22.3)	125/ 551 (22.7)	0.99 (0.80, 1.23) 0.9269	0.98 (0.74, 1.30) 0.8810	-0.01 (-0.06, 0.04) 0.7709	
	Other	24/ 176 (13.6)	28/ 152 (18.4)	0.67 (0.42, 1.09) 0.1043	0.65 (0.35, 1.21) 0.1780	-0.05 (-0.13, 0.03)*0.2399	
	Geographic region						0.1071
	Asia	119/ 536 (22.2)	120/ 536 (22.4)	1.00 (0.80, 1.25) 0.9804	0.99 (0.74, 1.32) 0.9372	-0.01 (-0.05, 0.04) 0.8419	
	Europe and Saudi Arabia	296/1341 (22.1)	373/1381 (27.0)	0.84 (0.74, 0.95) 0.0072	0.78 (0.65, 0.94) 0.0084	-0.05 (-0.08, -0.02)*0.0027	
	North America	93/ 393 (23.7)	105/ 376 (27.9)	0.85 (0.67, 1.08) 0.1873	0.80 (0.57, 1.10) 0.1702	-0.05 (-0.11, 0.01) 0.1255	
	Latin America	82/ 531 (15.4)	119/ 512 (23.2)	0.66 (0.52, 0.84) 0.0008	0.58 (0.42, 0.80) 0.0010	-0.08 (-0.13, -0.03)*0.0014	
	NYHA class at enrolment						0.5564
	II	444/2083 (21.3)	548/2165 (25.3)	0.84 (0.76, 0.94) 0.0016	0.79 (0.68, 0.91) 0.0013	-0.04 (-0.07, -0.01)*0.0020	
	III or IV	146/ 718 (20.3)	168/ 639 (26.3)	0.79 (0.66, 0.95) 0.0104	0.72 (0.55, 0.95) 0.0181	-0.06 (-0.10, -0.01)*0.0096	
	LVEF at enrolment						0.6613
	<= 49	192/ 959 (20.0)	212/ 950 (22.3)	0.89 (0.75, 1.05) 0.1631	0.85 (0.68, 1.06) 0.1551	-0.02 (-0.06, 0.01)*0.2196	
	50-59	224/1017 (22.0)	271/1009 (26.9)	0.83 (0.72, 0.97) 0.0162	0.77 (0.63, 0.95) 0.0155	-0.05 (-0.09, -0.01)*0.0113	
	>= 60	174/ 825 (21.1)	234/ 846 (27.7)	0.79 (0.67, 0.93) 0.0052	0.72 (0.57, 0.91) 0.0050	-0.07 (-0.11, -0.02)*0.0017	
	NT-proBNP at enrolment						0.7822
	<= median	299/1396 (21.4)	356/1409 (25.3)	0.84 (0.74, 0.96) 0.0124	0.80 (0.67, 0.96) 0.0153	-0.04 (-0.07, -0.01)*0.0159	
	> median	291/1405 (20.7)	361/1395 (25.9)	0.83 (0.73, 0.94) 0.0042	0.76 (0.63, 0.91) 0.0025	-0.05 (-0.08, -0.02)*0.0012	
	Type 2 Diabetes Medical History						0.0232
	Yes	243/1231 (19.7)	337/1243 (27.1)	0.74 (0.64, 0.85) <.0001	0.66 (0.55, 0.80)*<.0001	-0.07 (-0.11, -0.04)*<.0001	
	No	347/1570 (22.1)	380/1562 (24.3)	0.92 (0.81, 1.04) 0.1766	0.88 (0.75, 1.04)*0.1403	-0.02 (-0.05, 0.01)*0.1400	
	Atrial fibrillation or flutter at enrolment ECG						0.3148
	Yes	245/1185 (20.7)	313/1188 (26.3)	0.79 (0.69, 0.91) 0.0011	0.72 (0.59, 0.88) 0.0011	-0.06 (-0.09, -0.02)*0.0011	
	No	345/1616 (21.3)	404/1617 (25.0)	0.87 (0.77, 0.98) 0.0231	0.82 (0.69, 0.97) 0.0201	-0.04 (-0.07, -0.01)*0.0142	
	BMI (kg/m2) at enrolment						0.1133
	< 30	334/1547 (21.6)	380/1541 (24.7)	0.89 (0.78, 1.01) 0.0713	0.85 (0.71, 1.01) 0.0576	-0.03 (-0.06, -0.00)*0.0430	
	>= 30	256/1253 (20.4)	337/1261 (26.7)	0.77 (0.67, 0.88) 0.0001	0.70 (0.58, 0.85) 0.0002	-0.06 (-0.10, -0.03)*0.0002	
	Baseline eGFR (mL/min/1.73m^2)						0.4707
	< 60	303/1338 (22.6)	365/1377 (26.5)	0.86 (0.76, 0.98) 0.0248	0.81 (0.68, 0.97) 0.0239	-0.04 (-0.07, -0.01)*0.0193	
	>= 60	287/1463 (19.6)	351/1427 (24.6)	0.81 (0.71, 0.93) 0.0020	0.75 (0.63, 0.90) 0.0017	-0.05 (-0.08, -0.02)*0.0012	

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Overall Summary Score (LOCF)	SBP at randomisation						0.1824
	<= median	310/1405 (22.1)	365/1420 (25.7)	0.89 (0.78, 1.01) 0.0695	0.85 (0.71, 1.01) 0.0665	-0.04 (-0.07, -0.00)*0.0231	
	> median	280/1396 (20.1)	352/1385 (25.4)	0.78 (0.68, 0.89) 0.0003	0.71 (0.59, 0.85) 0.0003	-0.05 (-0.08, -0.02)*0.0007	
	LVEF at enrolment 2						0.4299
	<= 49	192/ 959 (20.0)	212/ 950 (22.3)	0.89 (0.75, 1.05) 0.1631	0.85 (0.68, 1.06) 0.1551	-0.02 (-0.06, 0.01)*0.2196	
	>= 50	398/1842 (21.6)	505/1855 (27.2)	0.81 (0.73, 0.91) 0.0003	0.75 (0.64, 0.87) 0.0002	-0.06 (-0.08, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6161
	Yes	48/ 280 (17.1)	52/ 281 (18.5)	0.88 (0.63, 1.24) 0.4743	0.85 (0.54, 1.33) 0.4690	-0.01 (-0.08, 0.05)*0.6733	
	No	542/2521 (21.5)	665/2524 (26.3)	0.83 (0.75, 0.91) 0.0001	0.77 (0.67, 0.88) 0.0001	-0.05 (-0.07, -0.02)*<.0001	
	MRAs at baseline						0.9916
	Yes	260/1216 (21.4)	310/1210 (25.6)	0.83 (0.72, 0.96) 0.0111	0.79 (0.65, 0.96) 0.0163	-0.04 (-0.08, -0.01)*0.0137	
	No	330/1585 (20.8)	407/1595 (25.5)	0.83 (0.74, 0.94) 0.0042	0.77 (0.65, 0.91) 0.0024	-0.05 (-0.08, -0.02)*0.0017	
	ACEi+ARB at baseline						0.1172
	Yes	419/2037 (20.6)	538/2059 (26.1)	0.80 (0.72, 0.89) <.0001	0.73 (0.63, 0.85) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	No	171/ 764 (22.4)	179/ 746 (24.0)	0.94 (0.78, 1.13) 0.5040	0.91 (0.72, 1.16) 0.4697	-0.02 (-0.06, 0.02) 0.3729	
	ARNI at baseline						0.1004
	Yes	33/ 149 (22.1)	22/ 125 (17.6)	1.27 (0.78, 2.08) 0.3357	1.34 (0.73, 2.47) 0.3498	0.04 (-0.05, 0.14) 0.3539	
	No	557/2652 (21.0)	695/2680 (25.9)	0.82 (0.75, 0.90) <.0001	0.76 (0.67, 0.87) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Beta Blocker at baseline						0.2377
	Yes	497/2327 (21.4)	595/2330 (25.5)	0.86 (0.77, 0.95) 0.0028	0.80 (0.70, 0.92) 0.0021	-0.04 (-0.07, -0.02)*0.0008	
	No	93/ 474 (19.6)	122/ 475 (25.7)	0.74 (0.58, 0.93) 0.0101	0.67 (0.49, 0.92) 0.0134	-0.06 (-0.11, -0.01) 0.0170	
	Diuretics at baseline						0.5053
	Yes	526/2500 (21.0)	643/2504 (25.7)	0.82 (0.75, 0.91) 0.0001	0.77 (0.67, 0.88) 0.0001	-0.05 (-0.07, -0.02)*0.0001	
	No	64/ 301 (21.3)	74/ 301 (24.6)	0.91 (0.68, 1.22) 0.5310	0.88 (0.60, 1.29) 0.5109	-0.01 (-0.08, 0.05) 0.6571	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Physical Limitation (LOCF)							
	Overall	726/2750 (26.4)	792/2758 (28.7)	0.93 (0.85, 1.01) 0.0741	0.90 (0.80, 1.02) 0.0990	-0.02 (-0.05, 0.00)*0.0543	
	Age						0.2286
	<= median	340/1382 (24.6)	366/1456 (25.1)	0.97 (0.86, 1.10) 0.6691	0.96 (0.81, 1.15) 0.6842	-0.01 (-0.04, 0.03)*0.7415	
	> median	386/1368 (28.2)	426/1302 (32.7)	0.88 (0.79, 0.98) 0.0218	0.83 (0.70, 0.99) 0.0371	-0.05 (-0.08, -0.01)*0.0115	
	Gender						0.6211
	Male	432/1611 (26.8)	448/1583 (28.3)	0.95 (0.85, 1.06) 0.3263	0.93 (0.80, 1.10) 0.4067	-0.01 (-0.05, 0.02)*0.3476	
	Female	294/1139 (25.8)	344/1175 (29.3)	0.91 (0.80, 1.03) 0.1376	0.87 (0.72, 1.05) 0.1484	-0.03 (-0.07, 0.00)*0.0619	
	Race						0.5706
	White	541/1970 (27.5)	596/1998 (29.8)	0.94 (0.86, 1.03) 0.1901	0.91 (0.79, 1.05) 0.2069	-0.02 (-0.05, 0.00)*0.0989	
	Black or African	20/ 63 (31.7)	17/ 66 (25.8)	1.24 (0.72, 2.12) 0.4413	1.32 (0.61, 2.87) 0.4861	0.03 (-0.13, 0.19) 0.7061	
	Asian	127/ 548 (23.2)	150/ 546 (27.5)	0.85 (0.69, 1.04) 0.1174	0.81 (0.61, 1.06) 0.1238	-0.04 (-0.09, 0.01) 0.1385	
	Other	38/ 169 (22.5)	29/ 148 (19.6)	1.06 (0.71, 1.59) 0.7731	1.12 (0.63, 1.97) 0.6976	0.03 (-0.06, 0.12)*0.5278	
	Geographic region						0.4851
	Asia	120/ 530 (22.6)	143/ 531 (26.9)	0.85 (0.69, 1.05) 0.1304	0.80 (0.61, 1.07) 0.1299	-0.04 (-0.09, 0.01)*0.1053	
	Europe and Saudi Arabia	367/1323 (27.7)	388/1360 (28.5)	0.99 (0.89, 1.11) 0.8981	0.99 (0.83, 1.18) 0.9324	-0.01 (-0.04, 0.03)*0.6493	
	North America	118/ 386 (30.6)	125/ 362 (34.5)	0.89 (0.72, 1.08) 0.2370	0.85 (0.62, 1.16) 0.3071	-0.03 (-0.09, 0.04) 0.3888	
	Latin America	121/ 511 (23.7)	136/ 505 (26.9)	0.88 (0.73, 1.07) 0.2081	0.81 (0.60, 1.10) 0.1800	-0.03 (-0.09, 0.02)*0.2330	
	NYHA class at enrolment						0.9782
	II	535/2046 (26.1)	601/2136 (28.1)	0.92 (0.84, 1.02) 0.1049	0.90 (0.79, 1.04) 0.1555	-0.02 (-0.05, 0.01)*0.1482	
	III or IV	191/ 704 (27.1)	190/ 621 (30.6)	0.93 (0.79, 1.08) 0.3288	0.86 (0.67, 1.11) 0.2553	-0.03 (-0.08, 0.01)*0.1650	
	LVEF at enrolment						0.1104
	<= 49	258/ 944 (27.3)	251/ 939 (26.7)	1.01 (0.87, 1.16) 0.9285	1.01 (0.82, 1.24) 0.9600	0.01 (-0.03, 0.05)*0.7694	
	50-59	279/1001 (27.9)	288/ 988 (29.1)	0.96 (0.84, 1.10) 0.5833	0.97 (0.80, 1.19) 0.7865	-0.01 (-0.05, 0.03)*0.5280	
	>= 60	189/ 805 (23.5)	253/ 831 (30.4)	0.81 (0.70, 0.95) 0.0082	0.73 (0.58, 0.92) 0.0073	-0.07 (-0.11, -0.03)*0.0014	
	NT-proBNP at enrolment						0.6022
	<= median	352/1371 (25.7)	377/1389 (27.1)	0.95 (0.84, 1.07) 0.3830	0.93 (0.78, 1.11) 0.4163	-0.01 (-0.05, 0.02)*0.3819	
	> median	374/1379 (27.1)	415/1368 (30.3)	0.91 (0.81, 1.02) 0.0940	0.88 (0.74, 1.04) 0.1289	-0.03 (-0.07, 0.00)*0.0625	
	Type 2 Diabetes Medical History						0.0404
	Yes	310/1213 (25.6)	366/1219 (30.0)	0.84 (0.75, 0.96) 0.0072	0.80 (0.67, 0.96)*0.0140	-0.04 (-0.08, -0.01)*0.0138	
	No	416/1537 (27.1)	426/1539 (27.7)	1.00 (0.90, 1.12) 0.9453	0.97 (0.83, 1.14)*0.7023	-0.01 (-0.04, 0.03)*0.7023	
	Atrial fibrillation or flutter at enrolment ECG						0.9660
	Yes	314/1164 (27.0)	336/1164 (28.9)	0.92 (0.82, 1.05) 0.2088	0.92 (0.76, 1.10) 0.3577	-0.02 (-0.06, 0.02)*0.3093	
	No	412/1586 (26.0)	456/1594 (28.6)	0.93 (0.83, 1.03) 0.1694	0.89 (0.76, 1.05) 0.1574	-0.03 (-0.06, 0.00)*0.0958	
	BMI (kg/m2) at enrolment						0.1676
	< 30	388/1520 (25.5)	443/1517 (29.2)	0.88 (0.79, 0.99) 0.0301	0.83 (0.71, 0.98) 0.0299	-0.04 (-0.07, -0.01)*0.0230	
	>= 30	338/1229 (27.5)	349/1238 (28.2)	0.99 (0.88, 1.12) 0.9016	1.00 (0.84, 1.21) 0.9664	-0.01 (-0.04, 0.03)*0.7028	
	Baseline eGFR (mL/min/1.73m^2)						0.9487
	< 60	366/1307 (28.0)	404/1345 (30.0)	0.93 (0.83, 1.04) 0.1835	0.92 (0.77, 1.09) 0.3249	-0.02 (-0.05, 0.01)*0.2483	
	>= 60	360/1443 (24.9)	388/1412 (27.5)	0.93 (0.83, 1.05) 0.2339	0.89 (0.75, 1.06) 0.2009	-0.03 (-0.06, 0.01)*0.1241	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.5347
	<= median	351/1376 (25.5)	409/1395 (29.3)	0.90 (0.80, 1.01) 0.0823	0.87 (0.73, 1.03) 0.0979	-0.04 (-0.07, -0.00)*0.0244	
	> median	375/1374 (27.3)	383/1363 (28.1)	0.95 (0.85, 1.07) 0.3760	0.94 (0.79, 1.11) 0.4519	-0.01 (-0.04, 0.03)*0.6370	
	LVEF at enrolment 2						0.2034
	<= 49	258/ 944 (27.3)	251/ 939 (26.7)	1.01 (0.87, 1.16) 0.9285	1.01 (0.82, 1.24) 0.9600	0.01 (-0.03, 0.05)*0.7694	
	>= 50	468/1806 (25.9)	541/1819 (29.7)	0.89 (0.81, 0.99) 0.0296	0.86 (0.74, 1.00) 0.0461	-0.04 (-0.07, -0.01)*0.0101	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7688
	Yes	69/ 270 (25.6)	72/ 272 (26.5)	0.98 (0.75, 1.28) 0.8663	0.94 (0.63, 1.41) 0.7743	-0.01 (-0.08, 0.06)*0.8082	
	No	657/2480 (26.5)	720/2486 (29.0)	0.92 (0.85, 1.01) 0.0732	0.90 (0.79, 1.02) 0.1006	-0.02 (-0.05, 0.00)*0.0518	
	MRAs at baseline						0.2622
	Yes	303/1191 (25.4)	344/1193 (28.8)	0.88 (0.77, 1.00) 0.0473	0.84 (0.70, 1.01) 0.0663	-0.03 (-0.07, 0.00)*0.0622	
	No	423/1559 (27.1)	448/1565 (28.6)	0.97 (0.87, 1.08) 0.5326	0.95 (0.81, 1.12) 0.5537	-0.01 (-0.05, 0.02)*0.3519	
	ACEi+ARB at baseline						0.1472
	Yes	522/1999 (26.1)	602/2028 (29.7)	0.90 (0.82, 0.99) 0.0249	0.85 (0.74, 0.98) 0.0256	-0.04 (-0.06, -0.01)*0.0114	
	No	204/ 751 (27.2)	190/ 730 (26.0)	1.04 (0.88, 1.23) 0.6668	1.07 (0.85, 1.35) 0.5751	0.01 (-0.03, 0.06) 0.4997	
	ARNI at baseline						0.8980
	Yes	34/ 147 (23.1)	28/ 122 (23.0)	0.96 (0.61, 1.49) 0.8415	0.96 (0.54, 1.72) 0.8946	-0.00 (-0.10, 0.10) 0.9911	
	No	692/2603 (26.6)	764/2636 (29.0)	0.93 (0.86, 1.01) 0.0933	0.90 (0.80, 1.02) 0.1158	-0.02 (-0.05, 0.00)*0.0525	
	Beta Blocker at baseline						0.8884
	Yes	600/2289 (26.2)	656/2293 (28.6)	0.93 (0.85, 1.02) 0.1157	0.90 (0.79, 1.03) 0.1410	-0.02 (-0.05, 0.00)*0.0689	
	No	126/ 461 (27.3)	136/ 465 (29.2)	0.92 (0.75, 1.12) 0.4099	0.90 (0.67, 1.20) 0.4608	-0.02 (-0.08, 0.04)*0.5175	
	Diuretics at baseline						0.0762
	Yes	645/2458 (26.2)	722/2463 (29.3)	0.90 (0.83, 0.99) 0.0217	0.87 (0.76, 0.99) 0.0312	-0.03 (-0.06, -0.01)*0.0160	
	No	81/ 292 (27.7)	70/ 295 (23.7)	1.17 (0.89, 1.53) 0.2514	1.26 (0.86, 1.84) 0.2299	0.04 (-0.03, 0.11)*0.2659	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	737/2801 (26.3)	816/2805 (29.1)	0.94 (0.87, 1.02) 0.1473	0.88 (0.78, 1.00) 0.0508	-0.03 (-0.05, -0.00)*0.0200	
	Age						0.3789
	<= median	353/1394 (25.3)	387/1471 (26.3)	0.98 (0.87, 1.10) 0.7218	0.96 (0.81, 1.15) 0.6544	-0.01 (-0.04, 0.02)*0.5466	
	> median	384/1407 (27.3)	429/1334 (32.2)	0.91 (0.82, 1.01) 0.0857	0.81 (0.68, 0.96) 0.0181	-0.05 (-0.08, -0.01)*0.0053	
	Gender						0.2229
	Male	435/1630 (26.7)	447/1608 (27.8)	0.99 (0.89, 1.09) 0.7996	0.97 (0.83, 1.14) 0.7275	-0.01 (-0.04, 0.02)*0.4775	
	Female	302/1171 (25.8)	369/1197 (30.8)	0.90 (0.80, 1.01) 0.0642	0.78 (0.64, 0.94) 0.0107	-0.05 (-0.09, -0.01)*0.0064	
	Race						0.5748
	White	523/2006 (26.1)	595/2032 (29.3)	0.93 (0.85, 1.02) 0.1338	0.87 (0.76, 1.01) 0.0715	-0.03 (-0.06, -0.00)*0.0225	
	Black or African	11/ 64 (17.2)	20/ 70 (28.6)	0.64 (0.33, 1.21) 0.1671	0.52 (0.22, 1.21) 0.1280	-0.11 (-0.25, 0.03)*0.1123	
	Asian	174/ 555 (31.4)	175/ 551 (31.8)	1.02 (0.86, 1.20) 0.8421	0.97 (0.75, 1.27) 0.8472	-0.00 (-0.06, 0.05)*0.8836	
	Other	29/ 176 (16.5)	26/ 152 (17.1)	0.96 (0.59, 1.56)*0.8793	0.85 (0.44, 1.63) 0.6251	-0.01 (-0.09, 0.07)*0.8795	
	Geographic region						0.2185
	Asia	168/ 536 (31.3)	169/ 536 (31.5)	1.03 (0.87, 1.21) 0.7506	0.99 (0.76, 1.30) 0.9471	-0.00 (-0.06, 0.05)*0.9475	
	Europe and Saudi Arabia	362/1341 (27.0)	399/1381 (28.9)	0.99 (0.89, 1.10) 0.8568	0.95 (0.80, 1.14) 0.6060	-0.02 (-0.05, 0.01)*0.2699	
	North America	102/ 393 (26.0)	123/ 376 (32.7)	0.81 (0.65, 1.00) 0.0527	0.72 (0.52, 0.99) 0.0419	-0.07 (-0.13, -0.01) 0.0169	
	Latin America	105/ 531 (19.8)	125/ 512 (24.4)	0.87 (0.71, 1.06) 0.1764	0.75 (0.54, 1.03) 0.0754	-0.05 (-0.10, 0.00)*0.0707	
	NYHA class at enrolment						0.2220
	II	564/2083 (27.1)	624/2165 (28.8)	0.96 (0.88, 1.06) 0.4329	0.91 (0.79, 1.05) 0.2025	-0.02 (-0.04, 0.01)*0.2048	
	III or IV	173/ 718 (24.1)	191/ 639 (29.9)	0.88 (0.76, 1.02) 0.0904	0.77 (0.59, 1.00) 0.0464	-0.06 (-0.11, -0.01)*0.0163	
	LVEF at enrolment						0.7712
	<= 49	235/ 959 (24.5)	252/ 950 (26.5)	0.94 (0.82, 1.08) 0.4091	0.89 (0.72, 1.11) 0.2993	-0.02 (-0.06, 0.02)*0.3109	
	50-59	284/1017 (27.9)	302/1009 (29.9)	0.98 (0.86, 1.11) 0.7200	0.92 (0.75, 1.13) 0.4254	-0.02 (-0.06, 0.02)*0.3195	
	>= 60	218/ 825 (26.4)	262/ 846 (31.0)	0.91 (0.79, 1.04) 0.1751	0.84 (0.67, 1.05) 0.1159	-0.05 (-0.09, -0.00)*0.0397	
	NT-proBNP at enrolment						0.8818
	<= median	369/1396 (26.4)	409/1409 (29.0)	0.95 (0.85, 1.06) 0.3455	0.89 (0.75, 1.06) 0.2008	-0.03 (-0.06, 0.01)*0.1246	
	> median	368/1405 (26.2)	407/1395 (29.2)	0.94 (0.85, 1.05) 0.2944	0.87 (0.73, 1.04) 0.1341	-0.03 (-0.06, 0.00)*0.0776	
	Type 2 Diabetes Medical History						0.0301
	Yes	313/1231 (25.4)	389/1243 (31.3)	0.85 (0.76, 0.96) 0.0086	0.75 (0.63, 0.89)*0.0012	-0.06 (-0.09, -0.02)*0.0012	
	No	424/1570 (27.0)	427/1562 (27.3)	1.03 (0.92, 1.14) 0.6393	0.98 (0.84, 1.15)*0.8354	-0.00 (-0.03, 0.03)*0.8354	
	Atrial fibrillation or flutter at enrolment ECG						0.9124
	Yes	320/1185 (27.0)	354/1188 (29.8)	0.95 (0.85, 1.07) 0.3960	0.89 (0.73, 1.07) 0.2093	-0.03 (-0.06, 0.01)*0.1311	
	No	417/1616 (25.8)	462/1617 (28.6)	0.94 (0.84, 1.04) 0.2141	0.88 (0.75, 1.04) 0.1220	-0.03 (-0.06, 0.00)*0.0769	
	BMI (kg/m2) at enrolment						0.3365
	< 30	419/1547 (27.1)	453/1541 (29.4)	0.98 (0.88, 1.08) 0.6471	0.93 (0.78, 1.09) 0.3642	-0.02 (-0.05, 0.01)*0.1535	
	>= 30	317/1253 (25.3)	363/1261 (28.8)	0.90 (0.80, 1.01) 0.0862	0.83 (0.69, 1.00) 0.0512	-0.03 (-0.07, -0.00)*0.0488	
	Baseline eGFR (mL/min/1.73m^2)						0.6462
	< 60	366/1338 (27.4)	420/1377 (30.5)	0.93 (0.83, 1.03) 0.1655	0.86 (0.73, 1.03) 0.1033	-0.03 (-0.07, 0.00)*0.0704	
	>= 60	371/1463 (25.4)	395/1427 (27.7)	0.97 (0.86, 1.08) 0.5387	0.91 (0.76, 1.08) 0.2882	-0.02 (-0.06, 0.01)*0.1574	

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Quality of Life (LOCF)	SBP at randomisation						0.2649
	<= median	365/1405 (26.0)	403/1420 (28.4)	0.99 (0.89, 1.11) 0.8889	0.93 (0.78, 1.11) 0.3994	-0.02 (-0.06, 0.01)*0.1512	
	> median	372/1396 (26.6)	413/1385 (29.8)	0.91 (0.81, 1.01) 0.0715	0.85 (0.71, 1.01) 0.0610	-0.03 (-0.07, 0.00)*0.0630	
	LVEF at enrolment 2						0.9404
	<= 49	235/ 959 (24.5)	252/ 950 (26.5)	0.94 (0.82, 1.08) 0.4091	0.89 (0.72, 1.11) 0.2993	-0.02 (-0.06, 0.02)*0.3109	
	>= 50	502/1842 (27.3)	564/1855 (30.4)	0.95 (0.86, 1.04) 0.2378	0.88 (0.76, 1.02) 0.1000	-0.03 (-0.06, -0.00)*0.0343	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2587
	Yes	61/ 280 (21.8)	59/ 281 (21.0)	1.14 (0.86, 1.50) 0.3591	1.17 (0.75, 1.81) 0.4870	0.01 (-0.06, 0.08)*0.8197	
	No	676/2521 (26.8)	757/2524 (30.0)	0.93 (0.86, 1.01) 0.0874	0.86 (0.76, 0.98) 0.0270	-0.03 (-0.06, -0.01)*0.0123	
	MRAs at baseline						0.6815
	Yes	326/1216 (26.8)	352/1210 (29.1)	0.96 (0.85, 1.08) 0.4772	0.90 (0.75, 1.09) 0.2952	-0.02 (-0.06, 0.01)*0.2104	
	No	411/1585 (25.9)	464/1595 (29.1)	0.93 (0.84, 1.03) 0.1901	0.87 (0.73, 1.02) 0.0864	-0.03 (-0.06, -0.00)*0.0459	
	ACEi+ARB at baseline						0.2472
	Yes	534/2037 (26.2)	614/2059 (29.8)	0.92 (0.84, 1.01) 0.0705	0.84 (0.72, 0.97) 0.0168	-0.04 (-0.06, -0.01)*0.0101	
	No	203/ 764 (26.6)	202/ 746 (27.1)	1.02 (0.87, 1.20) 0.7896	1.02 (0.80, 1.29) 0.8931	-0.01 (-0.05, 0.04)*0.8240	
	ARNI at baseline						0.2912
	Yes	44/ 149 (29.5)	36/ 125 (28.8)	1.15 (0.81, 1.62) 0.4470	1.20 (0.69, 2.11) 0.5169	0.01 (-0.10, 0.12)*0.8946	
	No	693/2652 (26.1)	780/2680 (29.1)	0.93 (0.86, 1.01) 0.0985	0.87 (0.77, 0.99) 0.0319	-0.03 (-0.05, -0.01)*0.0151	
	Beta Blocker at baseline						0.8906
	Yes	614/2327 (26.4)	686/2330 (29.4)	0.94 (0.87, 1.03) 0.1732	0.88 (0.77, 1.01) 0.0592	-0.03 (-0.06, -0.00)*0.0200	
	No	123/ 474 (25.9)	130/ 475 (27.4)	0.96 (0.79, 1.16) 0.6425	0.92 (0.68, 1.25) 0.5901	-0.01 (-0.07, 0.04)*0.6210	
	Diuretics at baseline						0.0476
	Yes	648/2500 (25.9)	732/2504 (29.2)	0.92 (0.85, 1.00) 0.0463	0.85 (0.75, 0.97) 0.0153	-0.03 (-0.06, -0.01)*0.0087	
	No	89/ 301 (29.6)	84/ 301 (27.9)	1.17 (0.94, 1.47) 0.1671	1.22 (0.84, 1.78) 0.2963	0.02 (-0.06, 0.09)*0.6524	

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Symptom Burden (LOCF)							
	Overall	655/2801 (23.4)	782/2805 (27.9)	0.85 (0.78, 0.92) 0.0002	0.79 (0.70, 0.89) 0.0002	-0.04 (-0.07, -0.02)*0.0001	
	Age						0.3561
	<= median	289/1394 (20.7)	376/1471 (25.6)	0.81 (0.71, 0.92) 0.0014	0.74 (0.62, 0.89) 0.0012	-0.05 (-0.08, -0.02)*0.0021	
	> median	366/1407 (26.0)	406/1334 (30.4)	0.88 (0.78, 0.98) 0.0256	0.82 (0.69, 0.97) 0.0246	-0.04 (-0.08, -0.01)*0.0101	
	Gender						0.2338
	Male	350/1630 (21.5)	429/1608 (26.7)	0.81 (0.72, 0.91) 0.0006	0.75 (0.64, 0.89) 0.0008	-0.05 (-0.08, -0.02)*0.0005	
	Female	305/1171 (26.0)	353/1197 (29.5)	0.90 (0.80, 1.02) 0.0981	0.84 (0.70, 1.01) 0.0664	-0.03 (-0.07, 0.00)*0.0611	
	Race						0.1672
	White	471/2006 (23.5)	582/2032 (28.6)	0.83 (0.75, 0.92) 0.0002	0.77 (0.66, 0.89) 0.0004	-0.05 (-0.08, -0.02)*0.0002	
	Black or African	13/ 64 (20.3)	19/ 70 (27.1)	0.73 (0.40, 1.34) 0.3098	0.66 (0.29, 1.49) 0.3118	-0.08 (-0.22, 0.06) 0.2373	
	Asian	144/ 555 (25.9)	142/ 551 (25.8)	1.00 (0.82, 1.22) 0.9803	1.00 (0.76, 1.31) 0.9937	0.00 (-0.05, 0.05)*0.9471	
	Other	27/ 176 (15.3)	39/ 152 (25.7)	0.62 (0.40, 0.95) 0.0294	0.53 (0.30, 0.93) 0.0259	-0.10 (-0.19, -0.02)*0.0208	
	Geographic region						0.2220
	Asia	138/ 536 (25.7)	138/ 536 (25.7)	1.00 (0.82, 1.22) 0.9931	0.99 (0.75, 1.31) 0.9634	0.00 (-0.05, 0.05)*1.0000	
	Europe and Saudi Arabia	316/1341 (23.6)	393/1381 (28.5)	0.84 (0.75, 0.95) 0.0047	0.78 (0.65, 0.94) 0.0083	-0.05 (-0.08, -0.02)*0.0036	
	North America	106/ 393 (27.0)	123/ 376 (32.7)	0.84 (0.68, 1.04) 0.1018	0.76 (0.55, 1.04) 0.0838	-0.06 (-0.12, 0.00) 0.0589	
	Latin America	95/ 531 (17.9)	128/ 512 (25.0)	0.72 (0.58, 0.91) 0.0050	0.64 (0.47, 0.87) 0.0043	-0.07 (-0.12, -0.02)*0.0050	
	NYHA class at enrolment						0.3893
	II	489/2083 (23.5)	596/2165 (27.5)	0.86 (0.77, 0.95) 0.0022	0.79 (0.69, 0.91) 0.0013	-0.04 (-0.07, -0.01)*0.0024	
	III or IV	166/ 718 (23.1)	186/ 639 (29.1)	0.78 (0.66, 0.93) 0.0043	0.73 (0.57, 0.95) 0.0179	-0.06 (-0.11, -0.01)*0.0122	
	LVEF at enrolment						0.7044
	<= 49	219/ 959 (22.8)	252/ 950 (26.5)	0.85 (0.73, 0.99) 0.0333	0.80 (0.64, 0.99) 0.0414	-0.04 (-0.08, 0.00)*0.0613	
	50-59	246/1017 (24.2)	277/1009 (27.5)	0.89 (0.77, 1.02) 0.0907	0.83 (0.68, 1.02) 0.0823	-0.03 (-0.07, 0.01)*0.0930	
	>= 60	190/ 825 (23.0)	253/ 846 (29.9)	0.80 (0.68, 0.94) 0.0055	0.72 (0.58, 0.91) 0.0049	-0.07 (-0.11, -0.03)*0.0014	
	NT-proBNP at enrolment						0.4943
	<= median	338/1396 (24.2)	389/1409 (27.6)	0.87 (0.77, 0.99) 0.0283	0.82 (0.69, 0.98) 0.0297	-0.03 (-0.07, -0.00)*0.0399	
	> median	317/1405 (22.6)	393/1395 (28.2)	0.82 (0.73, 0.93) 0.0021	0.75 (0.63, 0.90) 0.0015	-0.06 (-0.09, -0.02)*0.0006	
	Type 2 Diabetes Medical History						0.2600
	Yes	290/1231 (23.6)	372/1243 (29.9)	0.80 (0.71, 0.91) 0.0007	0.72 (0.60, 0.86)*0.0004	-0.06 (-0.10, -0.03)*0.0003	
	No	365/1570 (23.2)	410/1562 (26.2)	0.89 (0.79, 1.00) 0.0520	0.85 (0.72, 1.00)*0.0518	-0.03 (-0.06, 0.00)*0.0516	
	Atrial fibrillation or flutter at enrolment ECG						0.9167
	Yes	267/1185 (22.5)	318/1188 (26.8)	0.84 (0.74, 0.97) 0.0141	0.79 (0.65, 0.96) 0.0185	-0.04 (-0.08, -0.01)*0.0165	
	No	388/1616 (24.0)	464/1617 (28.7)	0.85 (0.76, 0.95) 0.0044	0.78 (0.67, 0.92) 0.0030	-0.05 (-0.08, -0.02)*0.0025	
	BMI (kg/m2) at enrolment						0.1711
	< 30	369/1547 (23.9)	414/1541 (26.9)	0.90 (0.80, 1.01) 0.0682	0.86 (0.72, 1.01) 0.0678	-0.03 (-0.06, 0.00)*0.0542	
	>= 30	286/1253 (22.8)	368/1261 (29.2)	0.79 (0.70, 0.90) 0.0003	0.71 (0.59, 0.85) 0.0003	-0.06 (-0.10, -0.03)*0.0003	
	Baseline eGFR (mL/min/1.73m^2)						0.9412
	< 60	343/1338 (25.6)	420/1377 (30.5)	0.85 (0.75, 0.95) 0.0049	0.78 (0.66, 0.93) 0.0061	-0.05 (-0.08, -0.01)*0.0047	
	>= 60	312/1463 (21.3)	361/1427 (25.3)	0.86 (0.75, 0.97) 0.0169	0.80 (0.67, 0.95) 0.0126	-0.04 (-0.07, -0.01)*0.0115	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)	SBP at randomisation						0.9981
	<= median	323/1405 (23.0)	400/1420 (28.2)	0.85 (0.75, 0.96) 0.0072	0.78 (0.66, 0.93) 0.0062	-0.05 (-0.08, -0.02)*0.0016	
	> median	332/1396 (23.8)	382/1385 (27.6)	0.85 (0.75, 0.96) 0.0072	0.78 (0.66, 0.94) 0.0071	-0.04 (-0.07, -0.01)*0.0217	
	LVEF at enrolment 2						0.9677
	<= 49	219/ 959 (22.8)	252/ 950 (26.5)	0.85 (0.73, 0.99) 0.0333	0.80 (0.64, 0.99) 0.0414	-0.04 (-0.08, 0.00)*0.0613	
	>= 50	436/1842 (23.7)	530/1855 (28.6)	0.85 (0.76, 0.94) 0.0023	0.78 (0.67, 0.91) 0.0016	-0.05 (-0.08, -0.02)*0.0007	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9222
	Yes	57/ 280 (20.4)	64/ 281 (22.8)	0.86 (0.64, 1.16) 0.3161	0.82 (0.53, 1.25) 0.3536	-0.02 (-0.09, 0.04)*0.4859	
	No	598/2521 (23.7)	718/2524 (28.4)	0.85 (0.77, 0.93) 0.0003	0.78 (0.69, 0.89) 0.0002	-0.05 (-0.07, -0.02)*0.0001	
	MRAs at baseline						0.9437
	Yes	287/1216 (23.6)	342/1210 (28.3)	0.85 (0.74, 0.96) 0.0124	0.79 (0.66, 0.96) 0.0150	-0.05 (-0.08, -0.01)*0.0087	
	No	368/1585 (23.2)	440/1595 (27.6)	0.85 (0.76, 0.95) 0.0059	0.79 (0.67, 0.93) 0.0042	-0.04 (-0.07, -0.01)*0.0046	
	ACEi+ARB at baseline						0.0848
	Yes	462/2037 (22.7)	587/2059 (28.5)	0.81 (0.73, 0.90) <.0001	0.74 (0.64, 0.85) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	No	193/ 764 (25.3)	195/ 746 (26.1)	0.96 (0.81, 1.14) 0.6673	0.95 (0.75, 1.20) 0.6477	-0.01 (-0.05, 0.04)*0.6964	
	ARNI at baseline						0.6334
	Yes	36/ 149 (24.2)	30/ 125 (24.0)	0.95 (0.62, 1.45) 0.8189	0.95 (0.54, 1.69) 0.8728	0.00 (-0.10, 0.10)*0.9752	
	No	619/2652 (23.3)	752/2680 (28.1)	0.85 (0.78, 0.92) 0.0002	0.78 (0.69, 0.89) 0.0002	-0.05 (-0.07, -0.02)*<.0001	
	Beta Blocker at baseline						0.1131
	Yes	550/2327 (23.6)	642/2330 (27.6)	0.88 (0.80, 0.96) 0.0061	0.82 (0.72, 0.94) 0.0050	-0.04 (-0.06, -0.01)*0.0022	
	No	105/ 474 (22.2)	140/ 475 (29.5)	0.73 (0.59, 0.90) 0.0029	0.63 (0.47, 0.86) 0.0033	-0.07 (-0.13, -0.02)*0.0097	
	Diuretics at baseline						0.9263
	Yes	587/2500 (23.5)	696/2504 (27.8)	0.85 (0.77, 0.93) 0.0003	0.79 (0.69, 0.90) 0.0004	-0.04 (-0.07, -0.02)*0.0005	
	No	68/ 301 (22.6)	86/ 301 (28.6)	0.85 (0.65, 1.12) 0.2496	0.78 (0.54, 1.14) 0.2005	-0.06 (-0.13, 0.01)*0.0919	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	620/2801 (22.1)	644/2805 (23.0)	0.97 (0.89, 1.06) 0.5200	0.96 (0.84, 1.09) 0.5108	-0.01 (-0.03, 0.01)*0.4604	
	Age						0.5939
	<= median	282/1394 (20.2)	318/1471 (21.6)	0.94 (0.82, 1.08) 0.3828	0.91 (0.75, 1.10) 0.3293	-0.01 (-0.04, 0.02)*0.3609	
	> median	338/1407 (24.0)	326/1334 (24.4)	0.99 (0.87, 1.12) 0.8283	0.99 (0.82, 1.19) 0.9084	-0.00 (-0.04, 0.03)*0.7999	
	Gender						0.2120
	Male	352/1630 (21.6)	373/1608 (23.2)	0.92 (0.82, 1.04) 0.1957	0.90 (0.76, 1.07) 0.2273	-0.02 (-0.04, 0.01)*0.2744	
	Female	268/1171 (22.9)	271/1197 (22.6)	1.04 (0.90, 1.19) 0.6036	1.04 (0.85, 1.28) 0.6812	0.00 (-0.03, 0.04)*0.8863	
	Race						0.8294
	White	412/2006 (20.5)	449/2032 (22.1)	0.94 (0.84, 1.05) 0.2879	0.92 (0.79, 1.08) 0.3093	-0.02 (-0.04, 0.01)*0.2266	
	Black or African	17/ 64 (26.6)	17/ 70 (24.3)	0.96 (0.55, 1.68) 0.8910	1.03 (0.46, 2.31) 0.9517	0.02 (-0.12, 0.17)*0.7625	
	Asian	160/ 555 (28.8)	149/ 551 (27.0)	1.04 (0.88, 1.23) 0.6639	1.07 (0.80, 1.42) 0.6633	0.02 (-0.04, 0.07)*0.5077	
	Other	31/ 176 (17.6)	29/ 152 (19.1)	1.00 (0.67, 1.50) 0.9970	0.88 (0.47, 1.64) 0.6899	-0.01 (-0.10, 0.07)*0.7327	
	Geographic region						0.4762
	Asia	156/ 536 (29.1)	146/ 536 (27.2)	1.03 (0.87, 1.22) 0.7056	1.06 (0.79, 1.41) 0.7046	0.02 (-0.04, 0.07)*0.4971	
	Europe and Saudi Arabia	280/1341 (20.9)	313/1381 (22.7)	0.93 (0.81, 1.06) 0.2713	0.90 (0.74, 1.09) 0.2950	-0.02 (-0.05, 0.01)*0.2591	
	North America	87/ 393 (22.1)	72/ 376 (19.1)	1.13 (0.86, 1.47) 0.3906	1.18 (0.83, 1.70) 0.3606	0.03 (-0.03, 0.09)*0.3054	
	Latin America	97/ 531 (18.3)	113/ 512 (22.1)	0.89 (0.71, 1.12) 0.3133	0.83 (0.61, 1.14) 0.2576	-0.04 (-0.09, 0.01)*0.1258	
	NYHA class at enrolment						0.7008
	II	462/2083 (22.2)	499/2165 (23.0)	0.98 (0.89, 1.09) 0.7284	0.96 (0.82, 1.12) 0.6010	-0.01 (-0.03, 0.02)*0.4985	
	III or IV	158/ 718 (22.0)	144/ 639 (22.5)	0.95 (0.78, 1.14) 0.5553	0.95 (0.73, 1.24) 0.7105	-0.01 (-0.05, 0.04)*0.8150	
	LVEF at enrolment						0.2297
	<= 49	208/ 959 (21.7)	207/ 950 (21.8)	0.98 (0.84, 1.16) 0.8349	0.96 (0.76, 1.20) 0.7043	-0.00 (-0.04, 0.04)*0.9577	
	50-59	237/1017 (23.3)	221/1009 (21.9)	1.05 (0.91, 1.22) 0.5190	1.11 (0.89, 1.39) 0.3494	0.01 (-0.02, 0.05)*0.4509	
	>= 60	175/ 825 (21.2)	216/ 846 (25.5)	0.87 (0.74, 1.02) 0.0866	0.80 (0.63, 1.02) 0.0751	-0.04 (-0.08, -0.00)*0.0366	
	NT-proBNP at enrolment						0.6817
	<= median	306/1396 (21.9)	327/1409 (23.2)	0.95 (0.84, 1.08) 0.4743	0.93 (0.77, 1.13) 0.4735	-0.01 (-0.04, 0.02)*0.4144	
	> median	314/1405 (22.3)	316/1395 (22.7)	0.99 (0.87, 1.13) 0.9102	0.98 (0.82, 1.19) 0.8677	-0.00 (-0.03, 0.03)*0.8475	
	Type 2 Diabetes Medical History						0.0634
	Yes	255/1231 (20.7)	298/1243 (24.0)	0.88 (0.76, 1.01) 0.0670	0.83 (0.69, 1.00)*0.0519	-0.03 (-0.07, 0.00)*0.0515	
	No	365/1570 (23.2)	346/1562 (22.2)	1.05 (0.93, 1.18) 0.4585	1.06 (0.90, 1.26)*0.4636	0.01 (-0.02, 0.04)*0.4635	
	Atrial fibrillation or flutter at enrolment ECG						0.4347
	Yes	270/1185 (22.8)	301/1188 (25.3)	0.93 (0.82, 1.07) 0.3200	0.89 (0.73, 1.09) 0.2599	-0.03 (-0.06, 0.01)*0.1457	
	No	350/1616 (21.7)	343/1617 (21.2)	1.00 (0.89, 1.14) 0.9553	1.01 (0.85, 1.21) 0.8864	0.00 (-0.02, 0.03)*0.7572	
	BMI (kg/m2) at enrolment						0.0363
	< 30	372/1547 (24.0)	358/1541 (23.2)	1.06 (0.94, 1.19) 0.3647	1.09 (0.91, 1.30) 0.3303	0.01 (-0.02, 0.04)*0.5941	
	>= 30	248/1253 (19.8)	286/1261 (22.7)	0.87 (0.75, 1.00) 0.0502	0.81 (0.67, 0.99) 0.0423	-0.03 (-0.06, 0.00)*0.0765	
	Baseline eGFR (mL/min/1.73m^2)						0.5776
	< 60	307/1338 (22.9)	313/1377 (22.7)	0.99 (0.87, 1.13) 0.9123	1.00 (0.83, 1.20) 0.9710	0.00 (-0.03, 0.03)*0.8943	
	>= 60	313/1463 (21.4)	330/1427 (23.1)	0.95 (0.84, 1.08) 0.4165	0.92 (0.76, 1.11) 0.3714	-0.02 (-0.05, 0.01)*0.2634	

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Self Efficacy (LOCF)	SBP at randomisation						0.6632
	<= median	330/1405 (23.5)	337/1420 (23.7)	0.99 (0.87, 1.12) 0.8311	0.99 (0.83, 1.19) 0.9434	-0.00 (-0.03, 0.03)*0.8782	
	> median	290/1396 (20.8)	307/1385 (22.2)	0.95 (0.83, 1.08) 0.4450	0.92 (0.76, 1.11) 0.3781	-0.01 (-0.04, 0.02)*0.3712	
	LVEF at enrolment 2						0.7942
	<= 49	208/ 959 (21.7)	207/ 950 (21.8)	0.98 (0.84, 1.16) 0.8349	0.96 (0.76, 1.20) 0.7043	-0.00 (-0.04, 0.04)*0.9577	
	>= 50	412/1842 (22.4)	437/1855 (23.6)	0.96 (0.86, 1.08) 0.5067	0.96 (0.81, 1.13) 0.5990	-0.01 (-0.04, 0.02)*0.3893	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7982
	Yes	64/ 280 (22.9)	63/ 281 (22.4)	1.01 (0.76, 1.34) 0.9298	1.01 (0.66, 1.54) 0.9664	0.00 (-0.06, 0.07)*0.9015	
	No	556/2521 (22.1)	581/2524 (23.0)	0.97 (0.88, 1.06) 0.4865	0.95 (0.83, 1.09) 0.4871	-0.01 (-0.03, 0.01)*0.4124	
	MRAs at baseline						0.6766
	Yes	292/1216 (24.0)	291/1210 (24.0)	0.99 (0.87, 1.13) 0.8801	0.99 (0.81, 1.20) 0.8987	-0.00 (-0.03, 0.03)*0.9832	
	No	328/1585 (20.7)	353/1595 (22.1)	0.95 (0.84, 1.08) 0.4422	0.93 (0.78, 1.11) 0.4303	-0.01 (-0.04, 0.01)*0.3230	
	ACEi+ARB at baseline						0.1096
	Yes	435/2037 (21.4)	481/2059 (23.4)	0.93 (0.83, 1.03) 0.1663	0.89 (0.76, 1.04) 0.1282	-0.02 (-0.05, 0.01)*0.1233	
	No	185/ 764 (24.2)	163/ 746 (21.8)	1.10 (0.92, 1.31) 0.2990	1.17 (0.91, 1.51) 0.2227	0.02 (-0.02, 0.07)*0.2749	
	ARNI at baseline						0.1783
	Yes	45/ 149 (30.2)	27/ 125 (21.6)	1.27 (0.85, 1.90) 0.2515	1.49 (0.84, 2.66) 0.1771	0.09 (-0.02, 0.19)*0.1022	
	No	575/2652 (21.7)	617/2680 (23.0)	0.96 (0.87, 1.05) 0.3473	0.93 (0.81, 1.07) 0.3147	-0.01 (-0.04, 0.01)*0.2400	
	Beta Blocker at baseline						0.9286
	Yes	515/2327 (22.1)	533/2330 (22.9)	0.97 (0.88, 1.07) 0.5338	0.96 (0.83, 1.11) 0.5447	-0.01 (-0.03, 0.02)*0.5432	
	No	105/ 474 (22.2)	111/ 475 (23.4)	0.98 (0.79, 1.22) 0.8594	0.96 (0.69, 1.32) 0.7914	-0.01 (-0.07, 0.04)*0.6549	
	Diuretics at baseline						0.6968
	Yes	561/2500 (22.4)	577/2504 (23.0)	0.98 (0.89, 1.07) 0.6246	0.97 (0.84, 1.11) 0.6310	-0.01 (-0.03, 0.02)*0.6108	
	No	59/ 301 (19.6)	67/ 301 (22.3)	0.92 (0.68, 1.23) 0.5615	0.87 (0.58, 1.32) 0.5204	-0.03 (-0.09, 0.04)*0.4226	

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Symptom Frequency (LOCF)							
	Overall	603/2801 (21.5)	752/2805 (26.8)	0.81 (0.74, 0.89) <.0001	0.74 (0.65, 0.84) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	Age						0.9427
	<= median	285/1394 (20.4)	367/1471 (24.9)	0.81 (0.71, 0.92) 0.0014	0.75 (0.62, 0.90) 0.0017	-0.05 (-0.08, -0.01)*0.0039	
	> median	318/1407 (22.6)	385/1334 (28.9)	0.81 (0.72, 0.92) 0.0007	0.72 (0.60, 0.86) 0.0003	-0.06 (-0.10, -0.03)*0.0002	
	Gender						0.7520
	Male	337/1630 (20.7)	412/1608 (25.6)	0.80 (0.71, 0.91) 0.0004	0.74 (0.63, 0.88) 0.0005	-0.05 (-0.08, -0.02)*0.0008	
	Female	266/1171 (22.7)	340/1197 (28.4)	0.83 (0.73, 0.94) 0.0047	0.73 (0.61, 0.89) 0.0018	-0.06 (-0.09, -0.02)*0.0015	
	Race						0.3767
	White	439/2006 (21.9)	554/2032 (27.3)	0.82 (0.74, 0.91) 0.0002	0.75 (0.64, 0.87) 0.0001	-0.05 (-0.08, -0.03)*<.0001	
	Black or African	15/ 64 (23.4)	18/ 70 (25.7)	0.90 (0.50, 1.62) 0.7176	0.87 (0.39, 1.92) 0.7235	-0.04 (-0.19, 0.11) 0.5620	
	Asian	130/ 555 (23.4)	150/ 551 (27.2)	0.85 (0.70, 1.04) 0.1161	0.79 (0.60, 1.04) 0.0991	-0.04 (-0.09, 0.01)*0.1459	
	Other	19/ 176 (10.8)	30/ 152 (19.7)	0.53 (0.32, 0.89) 0.0168	0.46 (0.24, 0.88) 0.0192	-0.09 (-0.17, -0.01)*0.0249	
	Geographic region						0.2060
	Asia	126/ 536 (23.5)	146/ 536 (27.2)	0.86 (0.70, 1.05) 0.1421	0.80 (0.61, 1.06) 0.1209	-0.04 (-0.09, 0.01)*0.1600	
	Europe and Saudi Arabia	303/1341 (22.6)	383/1381 (27.7)	0.83 (0.74, 0.94) 0.0032	0.76 (0.64, 0.92) 0.0036	-0.05 (-0.08, -0.02)*0.0020	
	North America	92/ 393 (23.4)	99/ 376 (26.3)	0.88 (0.70, 1.12) 0.3098	0.84 (0.60, 1.17) 0.2932	-0.03 (-0.09, 0.03)*0.3490	
	Latin America	82/ 531 (15.4)	124/ 512 (24.2)	0.64 (0.51, 0.82) 0.0003	0.55 (0.40, 0.75) 0.0002	-0.09 (-0.14, -0.04)*0.0004	
	NYHA class at enrolment						0.7765
	II	460/2083 (22.1)	586/2165 (27.1)	0.81 (0.73, 0.90) <.0001	0.74 (0.64, 0.85) <.0001	-0.05 (-0.08, -0.02)*0.0002	
	III or IV	143/ 718 (19.9)	166/ 639 (26.0)	0.79 (0.65, 0.95) 0.0107	0.71 (0.55, 0.93) 0.0127	-0.06 (-0.11, -0.02)*0.0080	
	LVEF at enrolment						0.9639
	<= 49	209/ 959 (21.8)	249/ 950 (26.2)	0.82 (0.71, 0.96) 0.0148	0.76 (0.61, 0.94) 0.0124	-0.04 (-0.08, -0.01)*0.0237	
	50-59	213/1017 (20.9)	259/1009 (25.7)	0.81 (0.70, 0.95) 0.0074	0.75 (0.60, 0.93) 0.0081	-0.05 (-0.08, -0.01)*0.0118	
	>= 60	181/ 825 (21.9)	244/ 846 (28.8)	0.80 (0.68, 0.94) 0.0055	0.71 (0.56, 0.89) 0.0032	-0.07 (-0.11, -0.03)*0.0011	
	NT-proBNP at enrolment						0.4238
	<= median	318/1396 (22.8)	381/1409 (27.0)	0.84 (0.74, 0.95) 0.0057	0.78 (0.66, 0.93) 0.0067	-0.04 (-0.07, -0.01)*0.0090	
	> median	285/1405 (20.3)	371/1395 (26.6)	0.78 (0.69, 0.89) 0.0002	0.69 (0.57, 0.83) <.0001	-0.06 (-0.09, -0.03)*<.0001	
	Type 2 Diabetes Medical History						0.1116
	Yes	255/1231 (20.7)	349/1243 (28.1)	0.75 (0.65, 0.85) <.0001	0.67 (0.56, 0.81)*<.0001	-0.07 (-0.11, -0.04)*<.0001	
	No	348/1570 (22.2)	403/1562 (25.8)	0.86 (0.77, 0.98) 0.0178	0.82 (0.69, 0.97)*0.0173	-0.04 (-0.07, -0.01)*0.0171	
	Atrial fibrillation or flutter at enrolment ECG						0.4772
	Yes	254/1185 (21.4)	327/1188 (27.5)	0.78 (0.68, 0.89) 0.0004	0.69 (0.57, 0.84) 0.0002	-0.06 (-0.10, -0.03)*0.0005	
	No	349/1616 (21.6)	425/1617 (26.3)	0.83 (0.74, 0.94) 0.0026	0.77 (0.65, 0.91) 0.0023	-0.05 (-0.08, -0.02)*0.0018	
	BMI (kg/m2) at enrolment						0.3226
	< 30	342/1547 (22.1)	405/1541 (26.3)	0.84 (0.75, 0.95) 0.0058	0.78 (0.66, 0.93) 0.0046	-0.04 (-0.07, -0.01)*0.0067	
	>= 30	261/1253 (20.8)	346/1261 (27.4)	0.77 (0.67, 0.88) 0.0001	0.69 (0.57, 0.83) 0.0001	-0.07 (-0.10, -0.03)*0.0001	
	Baseline eGFR (mL/min/1.73m^2)						0.8660
	< 60	295/1338 (22.0)	383/1377 (27.8)	0.80 (0.71, 0.91) 0.0006	0.72 (0.60, 0.86) 0.0004	-0.06 (-0.09, -0.03)*0.0005	
	>= 60	308/1463 (21.1)	368/1427 (25.8)	0.82 (0.72, 0.93) 0.0023	0.76 (0.63, 0.91) 0.0022	-0.05 (-0.08, -0.02)*0.0026	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)	SBP at randomisation						0.4120
	<= median	313/1405 (22.3)	389/1420 (27.4)	0.84 (0.74, 0.95) 0.0059	0.77 (0.64, 0.91) 0.0032	-0.05 (-0.08, -0.02)*0.0016	
	> median	290/1396 (20.8)	363/1385 (26.2)	0.78 (0.68, 0.89) 0.0002	0.71 (0.59, 0.85) 0.0002	-0.05 (-0.09, -0.02)*0.0007	
	LVEF at enrolment 2						0.8249
	<= 49	209/ 959 (21.8)	249/ 950 (26.2)	0.82 (0.71, 0.96) 0.0148	0.76 (0.61, 0.94) 0.0124	-0.04 (-0.08, -0.01)*0.0237	
	>= 50	394/1842 (21.4)	503/1855 (27.1)	0.80 (0.72, 0.90) 0.0001	0.73 (0.62, 0.85) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4979
	Yes	48/ 280 (17.1)	62/ 281 (22.1)	0.69 (0.50, 0.95) 0.0217	0.58 (0.37, 0.91) 0.0191	-0.05 (-0.11, 0.02)*0.1413	
	No	555/2521 (22.0)	690/2524 (27.3)	0.82 (0.74, 0.90) <.0001	0.75 (0.65, 0.85) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	MRAs at baseline						0.6175
	Yes	270/1216 (22.2)	330/1210 (27.3)	0.83 (0.73, 0.95) 0.0067	0.75 (0.62, 0.91) 0.0031	-0.05 (-0.08, -0.02)*0.0038	
	No	333/1585 (21.0)	422/1595 (26.5)	0.79 (0.70, 0.90) 0.0002	0.73 (0.61, 0.86) 0.0002	-0.05 (-0.08, -0.02)*0.0003	
	ACEi+ARB at baseline						0.0096
	Yes	414/2037 (20.3)	565/2059 (27.4)	0.75 (0.68, 0.84) <.0001	0.67 (0.57, 0.77) <.0001	-0.07 (-0.10, -0.05)*<.0001	
	No	189/ 764 (24.7)	187/ 746 (25.1)	0.98 (0.83, 1.16) 0.8156	0.96 (0.76, 1.22) 0.7498	-0.00 (-0.05, 0.04)*0.8826	
	ARNI at baseline						0.0611
	Yes	38/ 149 (25.5)	24/ 125 (19.2)	1.25 (0.80, 1.96) 0.3297	1.35 (0.74, 2.45) 0.3282	0.06 (-0.04, 0.16)*0.2089	
	No	565/2652 (21.3)	728/2680 (27.2)	0.80 (0.73, 0.87) <.0001	0.72 (0.63, 0.82) <.0001	-0.06 (-0.08, -0.04)*<.0001	
	Beta Blocker at baseline						0.2603
	Yes	501/2327 (21.5)	619/2330 (26.6)	0.83 (0.75, 0.91) 0.0002	0.76 (0.66, 0.87) 0.0001	-0.05 (-0.07, -0.03)*<.0001	
	No	102/ 474 (21.5)	133/ 475 (28.0)	0.71 (0.58, 0.88) 0.0019	0.64 (0.47, 0.87) 0.0042	-0.06 (-0.12, -0.01)*0.0204	
	Diuretics at baseline						0.3837
	Yes	545/2500 (21.8)	663/2504 (26.5)	0.82 (0.75, 0.90) <.0001	0.75 (0.66, 0.86) <.0001	-0.05 (-0.07, -0.02)*0.0001	
	No	58/ 301 (19.3)	89/ 301 (29.6)	0.71 (0.54, 0.95) 0.0189	0.60 (0.41, 0.89) 0.0110	-0.10 (-0.17, -0.03)*0.0031	

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AstraZeneca
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Full Analysis Set

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Social Limitation (LOCF)							
	Overall	774/2625 (29.5)	801/2625 (30.5)	0.97 (0.89, 1.05) 0.3949	0.95 (0.84, 1.07) 0.3895	-0.01 (-0.03, 0.01) 0.3020	
	Age						0.4631
	<= median	377/1331 (28.3)	418/1409 (29.7)	0.94 (0.84, 1.05) 0.2598	0.92 (0.77, 1.09) 0.3233	-0.02 (-0.05, 0.01) 0.2360	
	> median	397/1294 (30.7)	383/1216 (31.5)	0.99 (0.89, 1.11) 0.9106	0.97 (0.82, 1.16) 0.7602	-0.01 (-0.04, 0.03) 0.6608	
	Gender						0.4166
	Male	461/1538 (30.0)	445/1500 (29.7)	1.00 (0.90, 1.11) 0.9409	1.01 (0.86, 1.18) 0.9227	-0.00 (-0.03, 0.03) 0.8626	
	Female	313/1087 (28.8)	356/1125 (31.6)	0.93 (0.83, 1.05) 0.2534	0.88 (0.73, 1.06) 0.1679	-0.03 (-0.06, 0.01) 0.1601	
	Race						0.2816
	White	584/1890 (30.9)	623/1921 (32.4)	0.96 (0.88, 1.05) 0.4217	0.95 (0.82, 1.09) 0.4489	-0.01 (-0.04, 0.01) 0.2876	
	Black or African	25/ 58 (43.1)	19/ 66 (28.8)	1.48 (0.93, 2.34) 0.0972	1.89 (0.86, 4.17) 0.1118	0.14 (-0.02, 0.31)*0.0946	
	Asian	125/ 506 (24.7)	129/ 494 (26.1)	0.94 (0.76, 1.15) 0.5357	0.91 (0.68, 1.21) 0.5003	-0.02 (-0.07, 0.03) 0.4902	
	Other	40/ 171 (23.4)	30/ 144 (20.8)	1.02 (0.68, 1.53) 0.9346	1.04 (0.60, 1.82) 0.8900	0.03 (-0.07, 0.12)*0.5849	
	Geographic region						0.8078
	Asia	119/ 492 (24.2)	124/ 482 (25.7)	0.93 (0.75, 1.16) 0.5186	0.90 (0.67, 1.21) 0.4904	-0.02 (-0.07, 0.03) 0.4892	
	Europe and Saudi Arabia	396/1273 (31.1)	431/1309 (32.9)	0.96 (0.87, 1.07) 0.4475	0.95 (0.80, 1.13) 0.5676	-0.02 (-0.05, 0.02)*0.3220	
	North America	128/ 367 (34.9)	113/ 347 (32.6)	1.06 (0.87, 1.30) 0.5446	1.08 (0.78, 1.48) 0.6534	0.01 (-0.06, 0.08) 0.7343	
	Latin America	131/ 493 (26.6)	133/ 487 (27.3)	0.96 (0.79, 1.17) 0.7078	0.95 (0.71, 1.28) 0.7567	-0.01 (-0.06, 0.05)*0.7946	
	NYHA class at enrolment						0.9442
	II	562/1953 (28.8)	604/2031 (29.7)	0.96 (0.87, 1.05) 0.3825	0.94 (0.82, 1.08) 0.3696	-0.01 (-0.03, 0.02) 0.5464	
	III or IV	212/ 672 (31.5)	196/ 593 (33.1)	0.95 (0.83, 1.10) 0.4949	0.92 (0.72, 1.19) 0.5406	-0.02 (-0.07, 0.02) 0.2721	
	LVEF at enrolment						0.2823
	<= 49	267/ 907 (29.4)	247/ 896 (27.6)	1.03 (0.90, 1.19) 0.6584	1.06 (0.86, 1.31) 0.5909	0.01 (-0.03, 0.05) 0.6259	
	50-59	297/ 955 (31.1)	303/ 946 (32.0)	0.99 (0.87, 1.12) 0.8889	0.99 (0.81, 1.21) 0.9247	-0.01 (-0.04, 0.03) 0.7905	
	>= 60	210/ 763 (27.5)	251/ 783 (32.1)	0.88 (0.75, 1.02) 0.0785	0.80 (0.64, 1.00) 0.0520	-0.05 (-0.09, 0.00)*0.0510	
	NT-proBNP at enrolment						0.7988
	<= median	394/1312 (30.0)	413/1336 (30.9)	0.96 (0.86, 1.07) 0.4390	0.95 (0.80, 1.12) 0.5152	-0.01 (-0.04, 0.03) 0.7256	
	> median	380/1313 (28.9)	388/1288 (30.1)	0.98 (0.87, 1.09) 0.6622	0.95 (0.80, 1.13) 0.5730	-0.02 (-0.05, 0.01) 0.2466	
	Type 2 Diabetes Medical History						0.8620
	Yes	336/1150 (29.2)	359/1169 (30.7)	0.96 (0.85, 1.08) 0.4916	0.93 (0.78, 1.11)*0.4328	-0.02 (-0.06, 0.01) 0.2313	
	No	438/1475 (29.7)	442/1456 (30.4)	0.97 (0.87, 1.08) 0.6011	0.97 (0.83, 1.13)*0.6957	-0.00 (-0.03, 0.03) 0.7614	
	Atrial fibrillation or flutter at enrolment ECG						0.3114
	Yes	310/1097 (28.3)	343/1109 (30.9)	0.92 (0.81, 1.04) 0.1825	0.87 (0.72, 1.05) 0.1587	-0.03 (-0.06, 0.01)*0.1694	
	No	464/1528 (30.4)	458/1516 (30.2)	1.00 (0.90, 1.11) 0.9978	1.00 (0.86, 1.18) 0.9592	0.00 (-0.03, 0.03) 0.9254	
	BMI (kg/m2) at enrolment						0.7129
	< 30	419/1452 (28.9)	421/1428 (29.5)	0.98 (0.88, 1.09) 0.6965	0.97 (0.82, 1.14) 0.7138	-0.01 (-0.04, 0.03)*0.7122	
	>= 30	354/1172 (30.2)	380/1195 (31.8)	0.95 (0.85, 1.07) 0.3918	0.92 (0.77, 1.10) 0.3795	-0.02 (-0.05, 0.02) 0.3572	
	Baseline eGFR (mL/min/1.73m^2)						0.1318
	< 60	394/1240 (31.8)	394/1270 (31.0)	1.03 (0.92, 1.15) 0.6199	1.03 (0.87, 1.23) 0.7147	0.00 (-0.03, 0.03) 0.9900	
	>= 60	380/1385 (27.4)	406/1354 (30.0)	0.91 (0.81, 1.02) 0.1087	0.88 (0.74, 1.04) 0.1360	-0.02 (-0.05, 0.01) 0.1813	

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Social Limitation (LOCF)	SBP at randomisation						0.3612
	<= median	394/1320 (29.8)	401/1323 (30.3)	1.01 (0.90, 1.13) 0.8967	1.01 (0.85, 1.19) 0.9481	-0.00 (-0.03, 0.03) 0.9814	
	> median	380/1305 (29.1)	400/1302 (30.7)	0.94 (0.84, 1.05) 0.2492	0.90 (0.76, 1.07) 0.2468	-0.02 (-0.06, 0.01) 0.1534	
	LVEF at enrolment 2						0.3099
	<= 49	267/ 907 (29.4)	247/ 896 (27.6)	1.03 (0.90, 1.19) 0.6584	1.06 (0.86, 1.31) 0.5909	0.01 (-0.03, 0.05) 0.6259	
	>= 50	507/1718 (29.5)	554/1729 (32.0)	0.94 (0.86, 1.04) 0.2126	0.90 (0.78, 1.05) 0.1683	-0.02 (-0.05, 0.01) 0.1121	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4190
	Yes	70/ 252 (27.8)	66/ 256 (25.8)	1.06 (0.81, 1.39) 0.6745	1.08 (0.71, 1.65) 0.7049	0.02 (-0.06, 0.10)*0.6113	
	No	704/2373 (29.7)	735/2369 (31.0)	0.96 (0.88, 1.04) 0.2993	0.93 (0.82, 1.06) 0.2952	-0.01 (-0.04, 0.01) 0.2392	
	MRAs at baseline						0.2457
	Yes	343/1144 (30.0)	330/1131 (29.2)	1.02 (0.91, 1.16) 0.6960	1.03 (0.86, 1.24) 0.7416	-0.00 (-0.04, 0.03) 0.9601	
	No	431/1481 (29.1)	471/1494 (31.5)	0.93 (0.84, 1.03) 0.1679	0.89 (0.76, 1.05) 0.1660	-0.02 (-0.05, 0.01) 0.1737	
	ACEi+ARB at baseline						0.7842
	Yes	556/1909 (29.1)	581/1934 (30.0)	0.97 (0.89, 1.07) 0.5531	0.96 (0.83, 1.10) 0.5457	-0.01 (-0.04, 0.01) 0.3039	
	No	218/ 716 (30.4)	220/ 691 (31.8)	0.95 (0.82, 1.11) 0.5120	0.93 (0.74, 1.17) 0.5150	-0.01 (-0.06, 0.03) 0.6106	
	ARNI at baseline						0.3159
	Yes	42/ 146 (28.8)	40/ 115 (34.8)	0.85 (0.59, 1.21) 0.3614	0.79 (0.46, 1.34) 0.3766	-0.05 (-0.17, 0.06) 0.3856	
	No	732/2479 (29.5)	761/2510 (30.3)	0.98 (0.90, 1.06) 0.5556	0.96 (0.85, 1.09) 0.5393	-0.01 (-0.03, 0.01) 0.3929	
	Beta Blocker at baseline						0.7574
	Yes	654/2195 (29.8)	676/2187 (30.9)	0.97 (0.89, 1.06) 0.5184	0.95 (0.84, 1.09) 0.4965	-0.01 (-0.03, 0.02) 0.4551	
	No	120/ 430 (27.9)	125/ 438 (28.5)	0.95 (0.77, 1.16) 0.5945	0.92 (0.68, 1.25) 0.6109	-0.02 (-0.08, 0.03) 0.4267	
	Diuretics at baseline						0.1956
	Yes	699/2350 (29.7)	732/2345 (31.2)	0.95 (0.87, 1.03) 0.2038	0.92 (0.81, 1.05) 0.2004	-0.02 (-0.04, 0.01) 0.1454	
	No	75/ 275 (27.3)	69/ 280 (24.6)	1.14 (0.87, 1.50) 0.3453	1.21 (0.82, 1.78) 0.3332	0.04 (-0.03, 0.11) 0.2576	

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Symptom Stability (LOCF)							
	Overall	553/2801 (19.7)	634/2805 (22.6)	0.95 (0.89, 1.01) 0.1153	0.82 (0.70, 0.95) 0.0105	-0.03 (-0.05, -0.01)*0.0087	
	Age						0.3410
	<= median	278/1394 (19.9)	325/1471 (22.1)	0.98 (0.89, 1.07) 0.6166	0.85 (0.68, 1.06) 0.1411	-0.02 (-0.05, 0.01)*0.1574	
	> median	275/1407 (19.5)	309/1334 (23.2)	0.92 (0.85, 1.00) 0.0516	0.77 (0.62, 0.96) 0.0229	-0.04 (-0.07, -0.01)*0.0208	
	Gender						0.1750*
	Male	331/1630 (20.3)	352/1608 (21.9)	0.99 (0.91, 1.07) 0.7382	0.92 (0.75, 1.14) 0.4445	-0.02 (-0.04, 0.01)*0.2694	
	Female	222/1171 (19.0)	282/1197 (23.6)	0.80 (0.69, 0.94)*0.0064	0.70 (0.56, 0.89) 0.0031	-0.05 (-0.08, -0.01)*0.0061	
	Race						0.7423*
	White	383/2006 (19.1)	445/2032 (21.9)	0.96 (0.89, 1.04) 0.3574	0.86 (0.71, 1.03) 0.0985	-0.03 (-0.05, -0.00)*0.0270	
	Black or African	11/ 64 (17.2)	19/ 70 (27.1)	0.63 (0.33, 1.23)*0.1753	0.55 (0.20, 1.48) 0.2383	-0.10 (-0.24, 0.04)*0.1612	
	Asian	130/ 555 (23.4)	145/ 551 (26.3)	0.90 (0.79, 1.02) 0.0988	0.71 (0.51, 1.00) 0.0498	-0.03 (-0.08, 0.02)*0.2656	
	Other	29/ 176 (16.5)	25/ 152 (16.4)	1.00 (0.61, 1.63)*0.9942	0.94 (0.47, 1.91) 0.8745	0.00 (-0.08, 0.08)*0.9942	
	Geographic region						0.8026*
	Asia	123/ 536 (22.9)	142/ 536 (26.5)	0.90 (0.79, 1.02) 0.0915	0.68 (0.48, 0.96) 0.0299	-0.04 (-0.09, 0.02)*0.1782	
	Europe and Saudi Arabia	260/1341 (19.4)	297/1381 (21.5)	0.97 (0.90, 1.06) 0.5018	0.85 (0.68, 1.07) 0.1686	-0.02 (-0.05, 0.01)*0.1706	
	North America	77/ 393 (19.6)	95/ 376 (25.3)	0.92 (0.75, 1.13) 0.4298	0.82 (0.55, 1.21) 0.3167	-0.06 (-0.12, 0.00)*0.0590	
	Latin America	93/ 531 (17.5)	100/ 512 (19.5)	0.90 (0.69, 1.16)*0.4020	0.85 (0.59, 1.24) 0.3989	-0.02 (-0.07, 0.03)*0.4019	
	NYHA class at enrolment						0.3500
	II	402/2083 (19.3)	465/2165 (21.5)	0.94 (0.87, 1.01) 0.1127	0.83 (0.69, 0.99) 0.0432	-0.02 (-0.05, 0.00)*0.0778	
	III or IV	151/ 718 (21.0)	169/ 639 (26.4)	0.99 (0.88, 1.10) 0.8227	0.76 (0.56, 1.03) 0.0738	-0.05 (-0.10, -0.01)*0.0193	
	LVEF at enrolment						0.1605
	<= 49	205/ 959 (21.4)	210/ 950 (22.1)	1.03 (0.92, 1.15) 0.5835	0.92 (0.70, 1.19) 0.5118	-0.01 (-0.04, 0.03)*0.6995	
	50-59	200/1017 (19.7)	239/1009 (23.7)	0.93 (0.83, 1.03) 0.1705	0.80 (0.62, 1.03) 0.0774	-0.04 (-0.08, -0.00)*0.0279	
	>= 60	148/ 825 (17.9)	185/ 846 (21.9)	0.82 (0.68, 1.00)*0.0451	0.72 (0.53, 0.98) 0.0366	-0.04 (-0.08, -0.00)*0.0440	
	NT-proBNP at enrolment						0.9662
	<= median	265/1396 (19.0)	289/1409 (20.5)	0.96 (0.87, 1.05) 0.3389	0.87 (0.69, 1.09) 0.2139	-0.02 (-0.04, 0.01)*0.3092	
	> median	288/1405 (20.5)	345/1395 (24.7)	0.95 (0.87, 1.04) 0.3081	0.77 (0.62, 0.96) 0.0176	-0.04 (-0.07, -0.01)*0.0074	
	Type 2 Diabetes Medical History						0.2793
	Yes	257/1231 (20.9)	276/1243 (22.2)	0.98 (0.90, 1.08) 0.7164	0.92 (0.76, 1.12)*0.4222	-0.01 (-0.05, 0.02)*0.4220	
	No	296/1570 (18.9)	358/1562 (22.9)	0.92 (0.84, 1.00) 0.0624	0.78 (0.66, 0.93)*0.0052	-0.04 (-0.07, -0.01)*0.0051	
	Atrial fibrillation or flutter at enrolment ECG						0.9718
	Yes	233/1185 (19.7)	267/1188 (22.5)	0.95 (0.87, 1.05) 0.3257	0.83 (0.65, 1.06) 0.1346	-0.03 (-0.06, 0.00)*0.0928	
	No	320/1616 (19.8)	367/1617 (22.7)	0.95 (0.87, 1.03) 0.2177	0.80 (0.66, 0.99) 0.0358	-0.03 (-0.06, -0.00)*0.0441	
	BMI (kg/m2) at enrolment						0.4807
	< 30	325/1547 (21.0)	359/1541 (23.3)	0.97 (0.89, 1.05) 0.4244	0.86 (0.70, 1.06) 0.1504	-0.02 (-0.05, 0.01)*0.1257	
	>= 30	228/1253 (18.2)	275/1261 (21.8)	0.93 (0.84, 1.03) 0.1550	0.76 (0.60, 0.97) 0.0258	-0.04 (-0.07, -0.00)*0.0234	
	Baseline eGFR (mL/min/1.73m^2)						0.4536
	< 60	295/1338 (22.0)	334/1377 (24.3)	0.96 (0.88, 1.05) 0.3730	0.86 (0.69, 1.07) 0.1757	-0.02 (-0.05, 0.01)*0.1725	
	>= 60	258/1463 (17.6)	300/1427 (21.0)	0.93 (0.84, 1.03) 0.1590	0.77 (0.62, 0.97) 0.0244	-0.03 (-0.06, -0.01)*0.0210	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)	SBP at randomisation						0.3756
	<= median	295/1405 (21.0)	337/1420 (23.7)	0.97 (0.89, 1.06) 0.5055	0.84 (0.68, 1.04) 0.1073	-0.03 (-0.06, 0.00)*0.0808	
	> median	258/1396 (18.5)	297/1385 (21.4)	0.86 (0.74, 1.00)*0.0510	0.79 (0.63, 1.00) 0.0482	-0.03 (-0.06, 0.00)*0.0505	
	LVEF at enrolment 2						0.0616
	<= 49	205/ 959 (21.4)	210/ 950 (22.1)	1.03 (0.92, 1.15) 0.5835	0.92 (0.70, 1.19) 0.5118	-0.01 (-0.04, 0.03)*0.6995	
	>= 50	348/1842 (18.9)	424/1855 (22.9)	0.91 (0.84, 0.98) 0.0164	0.77 (0.63, 0.93) 0.0076	-0.04 (-0.07, -0.01)*0.0030	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0418
	Yes	100/ 280 (35.7)	100/ 281 (35.6)	1.06 (0.92, 1.22) 0.4291	1.06 (0.68, 1.65) 0.7900	0.00 (-0.08, 0.08)*0.9749	
	No	453/2521 (18.0)	534/2524 (21.2)	0.92 (0.86, 0.99) 0.0272	0.79 (0.67, 0.93) 0.0053	-0.03 (-0.05, -0.01)*0.0043	
	MRAs at baseline						0.9032
	Yes	260/1216 (21.4)	283/1210 (23.4)	0.94 (0.85, 1.04) 0.2472	0.82 (0.65, 1.03) 0.0916	-0.02 (-0.05, 0.01)*0.2356	
	No	293/1585 (18.5)	351/1595 (22.0)	0.96 (0.89, 1.05) 0.3682	0.82 (0.66, 1.01) 0.0614	-0.04 (-0.06, -0.01)*0.0134	
	ACEi+ARB at baseline						0.8261
	Yes	394/2037 (19.3)	444/2059 (21.6)	0.96 (0.89, 1.03) 0.2436	0.83 (0.69, 1.00) 0.0483	-0.02 (-0.05, 0.00)*0.0778	
	No	159/ 764 (20.8)	190/ 746 (25.5)	0.93 (0.82, 1.05) 0.2355	0.78 (0.58, 1.04) 0.0858	-0.05 (-0.09, -0.00)*0.0317	
	ARNI at baseline						0.2964
	Yes	32/ 149 (21.5)	36/ 125 (28.8)	0.82 (0.61, 1.10) 0.1798	0.51 (0.26, 1.02) 0.0554	-0.07 (-0.18, 0.03)*0.1643	
	No	521/2652 (19.6)	598/2680 (22.3)	0.96 (0.90, 1.03) 0.2246	0.84 (0.72, 0.99) 0.0362	-0.03 (-0.05, -0.00)*0.0167	
	Beta Blocker at baseline						0.7322
	Yes	446/2327 (19.2)	521/2330 (22.4)	0.94 (0.87, 1.01) 0.0945	0.82 (0.69, 0.97) 0.0242	-0.03 (-0.06, -0.01)*0.0072	
	No	107/ 474 (22.6)	113/ 475 (23.8)	0.95 (0.75, 1.20)*0.6573	0.77 (0.52, 1.12) 0.1708	-0.01 (-0.07, 0.04)*0.6572	
	Diuretics at baseline						0.4979
	Yes	495/2500 (19.8)	567/2504 (22.6)	0.94 (0.88, 1.01) 0.0753	0.81 (0.69, 0.96) 0.0137	-0.03 (-0.05, -0.01)*0.0138	
	No	58/ 301 (19.3)	67/ 301 (22.3)	0.93 (0.76, 1.13) 0.4433	0.85 (0.53, 1.36) 0.4883	-0.03 (-0.09, 0.03)*0.3655	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	606/2801 (21.6)	743/2805 (26.5)	0.82 (0.75, 0.90) <.0001	0.76 (0.67, 0.86) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Age						0.6264
	<= median	279/1394 (20.0)	363/1471 (24.7)	0.80 (0.70, 0.92) 0.0012	0.74 (0.62, 0.89) 0.0013	-0.05 (-0.08, -0.02)*0.0027	
	> median	327/1407 (23.2)	380/1334 (28.5)	0.84 (0.74, 0.95) 0.0048	0.77 (0.64, 0.92) 0.0037	-0.05 (-0.09, -0.02)*0.0017	
	Gender						0.2020
	Male	330/1630 (20.2)	414/1608 (25.7)	0.78 (0.69, 0.89) 0.0001	0.72 (0.61, 0.86) 0.0002	-0.06 (-0.08, -0.03)*0.0002	
	Female	276/1171 (23.6)	329/1197 (27.5)	0.88 (0.78, 1.01) 0.0665	0.81 (0.67, 0.98) 0.0323	-0.04 (-0.07, -0.00)*0.0287	
	Race						0.2172
	White	442/2006 (22.0)	553/2032 (27.2)	0.82 (0.74, 0.91) 0.0002	0.76 (0.65, 0.88) 0.0003	-0.05 (-0.08, -0.03)*0.0001	
	Black or African	11/ 64 (17.2)	21/ 70 (30.0)	0.57 (0.30, 1.09) 0.0916	0.47 (0.20, 1.09) 0.0772	-0.13 (-0.27, 0.01)*0.0763	
	Asian	131/ 555 (23.6)	137/ 551 (24.9)	0.94 (0.77, 1.16) 0.5840	0.92 (0.69, 1.21) 0.5384	-0.01 (-0.06, 0.04)*0.6248	
	Other	22/ 176 (12.5)	32/ 152 (21.1)	0.60 (0.37, 0.97) 0.0363	0.53 (0.28, 0.97) 0.0394	-0.09 (-0.17, -0.00)*0.0389	
	Geographic region						0.2550
	Asia	127/ 536 (23.7)	132/ 536 (24.6)	0.96 (0.78, 1.18) 0.6921	0.94 (0.71, 1.24) 0.6526	-0.01 (-0.06, 0.04)*0.7213	
	Europe and Saudi Arabia	302/1341 (22.5)	384/1381 (27.8)	0.82 (0.73, 0.93) 0.0019	0.76 (0.63, 0.91) 0.0030	-0.05 (-0.09, -0.02)*0.0015	
	North America	93/ 393 (23.7)	108/ 376 (28.7)	0.82 (0.65, 1.04) 0.1055	0.76 (0.55, 1.05) 0.1005	-0.06 (-0.11, 0.00) 0.0700	
	Latin America	84/ 531 (15.8)	119/ 512 (23.2)	0.69 (0.54, 0.87) 0.0022	0.60 (0.43, 0.82) 0.0017	-0.07 (-0.12, -0.03)*0.0024	
	NYHA class at enrolment						0.4052
	II	456/2083 (21.9)	567/2165 (26.2)	0.83 (0.75, 0.92) 0.0005	0.77 (0.66, 0.89) 0.0004	-0.04 (-0.07, -0.02)*0.0010	
	III or IV	150/ 718 (20.9)	176/ 639 (27.5)	0.76 (0.64, 0.91) 0.0027	0.70 (0.54, 0.90) 0.0065	-0.07 (-0.11, -0.02)*0.0043	
	LVEF at enrolment						0.8100
	<= 49	211/ 959 (22.0)	242/ 950 (25.5)	0.85 (0.73, 0.99) 0.0427	0.80 (0.64, 1.00) 0.0455	-0.03 (-0.07, 0.00)*0.0745	
	50-59	220/1017 (21.6)	263/1009 (26.1)	0.83 (0.71, 0.97) 0.0155	0.77 (0.62, 0.95) 0.0153	-0.04 (-0.08, -0.01)*0.0191	
	>= 60	175/ 825 (21.2)	238/ 846 (28.1)	0.79 (0.67, 0.93) 0.0047	0.71 (0.56, 0.89) 0.0035	-0.07 (-0.11, -0.03)*0.0010	
	NT-proBNP at enrolment						0.2748
	<= median	320/1396 (22.9)	372/1409 (26.4)	0.86 (0.76, 0.98) 0.0219	0.82 (0.69, 0.98) 0.0255	-0.03 (-0.07, -0.00)*0.0324	
	> median	286/1405 (20.4)	371/1395 (26.6)	0.79 (0.69, 0.89) 0.0003	0.70 (0.59, 0.84) 0.0001	-0.06 (-0.09, -0.03)*<.0001	
	Type 2 Diabetes Medical History						0.0167
	Yes	255/1231 (20.7)	359/1243 (28.9)	0.73 (0.63, 0.83) <.0001	0.64 (0.53, 0.77)*<.0001	-0.08 (-0.12, -0.05)*<.0001	
	No	351/1570 (22.4)	384/1562 (24.6)	0.91 (0.81, 1.03) 0.1304	0.88 (0.75, 1.04)*0.1415	-0.02 (-0.05, 0.01)*0.1413	
	Atrial fibrillation or flutter at enrolment ECG						0.6234
	Yes	244/1185 (20.6)	303/1188 (25.5)	0.80 (0.69, 0.92) 0.0019	0.74 (0.60, 0.90) 0.0028	-0.05 (-0.08, -0.02)*0.0044	
	No	362/1616 (22.4)	440/1617 (27.2)	0.84 (0.74, 0.94) 0.0027	0.77 (0.65, 0.91) 0.0019	-0.05 (-0.08, -0.02)*0.0015	
	BMI (kg/m2) at enrolment						0.2395
	< 30	347/1547 (22.4)	401/1541 (26.0)	0.87 (0.77, 0.98) 0.0201	0.82 (0.69, 0.97) 0.0187	-0.04 (-0.07, -0.01)*0.0198	
	>= 30	259/1253 (20.7)	341/1261 (27.0)	0.78 (0.68, 0.89) 0.0002	0.70 (0.58, 0.84) 0.0002	-0.06 (-0.10, -0.03)*0.0002	
	Baseline eGFR (mL/min/1.73m^2)						0.9027
	< 60	312/1338 (23.3)	390/1377 (28.3)	0.83 (0.73, 0.94) 0.0024	0.76 (0.64, 0.91) 0.0030	-0.05 (-0.08, -0.02)*0.0028	
	>= 60	294/1463 (20.1)	352/1427 (24.7)	0.82 (0.72, 0.94) 0.0036	0.76 (0.64, 0.91) 0.0030	-0.05 (-0.08, -0.02)*0.0032	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Protocol: D169CC00001
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.1368
	<= median	316/1405 (22.5)	375/1420 (26.4)	0.88 (0.77, 1.00) 0.0448	0.83 (0.69, 0.99) 0.0364	-0.04 (-0.07, -0.01)*0.0153	
	> median	290/1396 (20.8)	368/1385 (26.6)	0.77 (0.67, 0.87) <.0001	0.69 (0.58, 0.83) <.0001	-0.06 (-0.09, -0.03)*0.0003	
	LVEF at enrolment 2						0.6236
	<= 49	211/ 959 (22.0)	242/ 950 (25.5)	0.85 (0.73, 0.99) 0.0427	0.80 (0.64, 1.00) 0.0455	-0.03 (-0.07, 0.00)*0.0745	
	>= 50	395/1842 (21.4)	501/1855 (27.0)	0.81 (0.72, 0.90) 0.0002	0.74 (0.63, 0.87) 0.0002	-0.06 (-0.08, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8857
	Yes	51/ 280 (18.2)	60/ 281 (21.4)	0.78 (0.57, 1.07) 0.1256	0.71 (0.46, 1.11) 0.1317	-0.03 (-0.10, 0.03)*0.3505	
	No	555/2521 (22.0)	683/2524 (27.1)	0.82 (0.75, 0.91) <.0001	0.76 (0.67, 0.87) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	MRAs at baseline						0.4671
	Yes	275/1216 (22.6)	324/1210 (26.8)	0.85 (0.75, 0.98) 0.0219	0.80 (0.66, 0.97) 0.0204	-0.04 (-0.08, -0.01)*0.0173	
	No	331/1585 (20.9)	419/1595 (26.3)	0.80 (0.71, 0.90) 0.0003	0.73 (0.62, 0.86) 0.0003	-0.05 (-0.08, -0.02)*0.0003	
	ACEi+ARB at baseline						0.0083
	Yes	423/2037 (20.8)	568/2059 (27.6)	0.77 (0.69, 0.85) <.0001	0.68 (0.59, 0.79) <.0001	-0.07 (-0.09, -0.04)*<.0001	
	No	183/ 764 (24.0)	175/ 746 (23.5)	1.01 (0.85, 1.21) 0.8979	1.02 (0.80, 1.29) 0.9032	-0.01 (-0.05, 0.03) 0.7277	
	ARNI at baseline						0.2013
	Yes	33/ 149 (22.1)	23/ 125 (18.4)	1.16 (0.72, 1.88) 0.5383	1.22 (0.66, 2.25) 0.5253	0.02 (-0.07, 0.12) 0.6305	
	No	573/2652 (21.6)	720/2680 (26.9)	0.82 (0.74, 0.89) <.0001	0.75 (0.66, 0.85) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	Beta Blocker at baseline						0.0098
	Yes	513/2327 (22.0)	603/2330 (25.9)	0.87 (0.79, 0.96) 0.0056	0.82 (0.71, 0.94) 0.0042	-0.04 (-0.06, -0.01)*0.0022	
	No	93/ 474 (19.6)	140/ 475 (29.5)	0.63 (0.50, 0.78) <.0001	0.53 (0.38, 0.72) <.0001	-0.10 (-0.15, -0.04)*0.0004	
	Diuretics at baseline						0.8593
	Yes	545/2500 (21.8)	661/2504 (26.4)	0.82 (0.75, 0.91) <.0001	0.76 (0.67, 0.87) <.0001	-0.05 (-0.07, -0.02)*0.0001	
	No	61/ 301 (20.3)	82/ 301 (27.2)	0.80 (0.60, 1.06) 0.1260	0.73 (0.49, 1.07) 0.1076	-0.07 (-0.14, -0.00)*0.0436	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	685/2842 (24.1)	809/2837 (28.5)	0.85 (0.78, 0.92) 0.0001	0.79 (0.70, 0.90) 0.0002	-0.04 (-0.07, -0.02)*0.0002	
	Age						0.5342
	<= median	299/1415 (21.1)	376/1482 (25.4)	0.82 (0.72, 0.93) 0.0026	0.77 (0.64, 0.92) 0.0034	-0.04 (-0.07, -0.01)*0.0068	
	> median	386/1427 (27.0)	433/1355 (32.0)	0.87 (0.78, 0.97) 0.0102	0.81 (0.68, 0.96) 0.0128	-0.05 (-0.08, -0.02)*0.0045	
	Gender						0.8216
	Male	406/1656 (24.5)	467/1625 (28.7)	0.85 (0.76, 0.95) 0.0052	0.80 (0.68, 0.94) 0.0066	-0.04 (-0.07, -0.01)*0.0062	
	Female	279/1186 (23.5)	342/1212 (28.2)	0.84 (0.74, 0.96) 0.0084	0.79 (0.65, 0.95) 0.0131	-0.05 (-0.08, -0.01)*0.0086	
	Race						0.3068
	White	500/2039 (24.5)	604/2058 (29.3)	0.84 (0.77, 0.93) 0.0005	0.79 (0.68, 0.91) 0.0011	-0.05 (-0.08, -0.02)*0.0005	
	Black or African	23/ 67 (34.3)	20/ 71 (28.2)	1.28 (0.79, 2.07) 0.3180	1.31 (0.63, 2.75) 0.4719	0.02 (-0.14, 0.17) 0.8481	
	Asian	136/ 558 (24.4)	161/ 555 (29.0)	0.84 (0.69, 1.02) 0.0728	0.78 (0.60, 1.02) 0.0747	-0.05 (-0.10, 0.01) 0.0798	
	Other	26/ 178 (14.6)	24/ 153 (15.7)	0.94 (0.59, 1.51) 0.8050	0.90 (0.47, 1.71) 0.7500	-0.01 (-0.09, 0.07)*0.7850	
	Geographic region						0.8277
	Asia	129/ 539 (23.9)	155/ 538 (28.8)	0.83 (0.68, 1.01) 0.0646	0.78 (0.59, 1.02) 0.0678	-0.05 (-0.10, 0.01) 0.0798	
	Europe and Saudi Arabia	332/1365 (24.3)	413/1394 (29.6)	0.83 (0.74, 0.94) 0.0021	0.77 (0.64, 0.92) 0.0035	-0.05 (-0.09, -0.02)*0.0017	
	North America	116/ 398 (29.1)	127/ 387 (32.8)	0.90 (0.73, 1.10) 0.3016	0.84 (0.62, 1.14) 0.2680	-0.04 (-0.10, 0.02) 0.2219	
	Latin America	108/ 540 (20.0)	114/ 518 (22.0)	0.90 (0.72, 1.11) 0.3226	0.86 (0.63, 1.17) 0.3334	-0.02 (-0.07, 0.03)*0.4229	
	NYHA class at enrolment						0.8986
	II	523/2113 (24.8)	636/2187 (29.1)	0.84 (0.77, 0.93) 0.0005	0.79 (0.69, 0.90) 0.0007	-0.04 (-0.07, -0.02)*0.0013	
	III or IV	162/ 729 (22.2)	173/ 649 (26.7)	0.85 (0.72, 1.02) 0.0793	0.80 (0.62, 1.03) 0.0811	-0.04 (-0.09, 0.00)*0.0560	
	LVEF at enrolment						0.8724
	<= 49	232/ 980 (23.7)	261/ 963 (27.1)	0.86 (0.74, 1.00) 0.0447	0.80 (0.65, 0.99) 0.0404	-0.03 (-0.07, 0.00)*0.0823	
	50-59	263/1029 (25.6)	312/1017 (30.7)	0.82 (0.72, 0.94) 0.0035	0.77 (0.63, 0.95) 0.0121	-0.05 (-0.09, -0.01)*0.0099	
	>= 60	190/ 833 (22.8)	236/ 857 (27.5)	0.87 (0.74, 1.02) 0.0778	0.81 (0.64, 1.01) 0.0643	-0.05 (-0.09, -0.01)*0.0249	
	NT-proBNP at enrolment						0.3677
	<= median	351/1418 (24.8)	395/1421 (27.8)	0.88 (0.78, 0.99) 0.0400	0.85 (0.72, 1.01) 0.0594	-0.03 (-0.06, 0.00)*0.0652	
	> median	334/1424 (23.5)	414/1415 (29.3)	0.82 (0.73, 0.92) 0.0009	0.74 (0.62, 0.88) 0.0008	-0.06 (-0.09, -0.03)*0.0004	
	Type 2 Diabetes Medical History						0.2001
	Yes	295/1250 (23.6)	372/1260 (29.5)	0.80 (0.70, 0.91) 0.0005	0.74 (0.62, 0.88)*0.0008	-0.06 (-0.09, -0.02)*0.0008	
	No	390/1592 (24.5)	437/1577 (27.7)	0.89 (0.80, 1.00) 0.0495	0.85 (0.72, 0.99)*0.0395	-0.03 (-0.06, -0.00)*0.0394	
	Atrial fibrillation or flutter at enrolment ECG						0.9689
	Yes	281/1199 (23.4)	330/1199 (27.5)	0.85 (0.74, 0.97) 0.0129	0.80 (0.66, 0.96) 0.0198	-0.04 (-0.08, -0.01)*0.0215	
	No	404/1643 (24.6)	479/1638 (29.2)	0.85 (0.76, 0.95) 0.0033	0.79 (0.67, 0.93) 0.0037	-0.05 (-0.08, -0.02)*0.0026	
	BMI (kg/m2) at enrolment						0.5672
	< 30	375/1571 (23.9)	450/1559 (28.9)	0.83 (0.74, 0.93) 0.0015	0.77 (0.65, 0.90) 0.0015	-0.05 (-0.08, -0.02)*0.0015	
	>= 30	310/1270 (24.4)	357/1275 (28.0)	0.87 (0.77, 0.99) 0.0321	0.84 (0.70, 1.01) 0.0588	-0.04 (-0.07, -0.00)*0.0393	
	Baseline eGFR (mL/min/1.73m^2)						0.7128
	< 60	366/1359 (26.9)	434/1396 (31.1)	0.86 (0.77, 0.97) 0.0104	0.81 (0.69, 0.97) 0.0179	-0.04 (-0.08, -0.01)*0.0161	
	>= 60	319/1483 (21.5)	375/1440 (26.0)	0.84 (0.74, 0.95) 0.0055	0.78 (0.65, 0.93) 0.0053	-0.05 (-0.08, -0.01)*0.0040	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.7677
	<= median	348/1424 (24.4)	420/1439 (29.2)	0.86 (0.76, 0.96) 0.0097	0.81 (0.68, 0.96) 0.0132	-0.05 (-0.08, -0.02)*0.0041	
	> median	337/1418 (23.8)	389/1398 (27.8)	0.84 (0.74, 0.94) 0.0038	0.78 (0.65, 0.93) 0.0047	-0.04 (-0.07, -0.01)*0.0137	
	LVEF at enrolment 2						0.8543
	<= 49	232/ 980 (23.7)	261/ 963 (27.1)	0.86 (0.74, 1.00) 0.0447	0.80 (0.65, 0.99) 0.0404	-0.03 (-0.07, 0.00)*0.0823	
	>= 50	453/1862 (24.3)	548/1874 (29.2)	0.84 (0.76, 0.94) 0.0012	0.79 (0.68, 0.92) 0.0024	-0.05 (-0.08, -0.02)*0.0007	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5655
	Yes	47/ 283 (16.6)	59/ 286 (20.6)	0.76 (0.55, 1.06) 0.1065	0.67 (0.43, 1.06) 0.0862	-0.04 (-0.10, 0.02)*0.2172	
	No	638/2559 (24.9)	750/2551 (29.4)	0.85 (0.78, 0.93) 0.0004	0.80 (0.71, 0.91) 0.0007	-0.04 (-0.07, -0.02)*0.0003	
	MRAs at baseline						0.2291
	Yes	295/1227 (24.0)	365/1224 (29.8)	0.80 (0.70, 0.91) 0.0005	0.74 (0.61, 0.89) 0.0013	-0.06 (-0.09, -0.02)*0.0012	
	No	390/1615 (24.1)	444/1613 (27.5)	0.89 (0.79, 0.99) 0.0400	0.84 (0.71, 0.99) 0.0343	-0.03 (-0.06, -0.00)*0.0283	
	ACEi+ARB at baseline						0.0035
	Yes	466/2065 (22.6)	604/2077 (29.1)	0.78 (0.71, 0.87) <.0001	0.71 (0.61, 0.82) <.0001	-0.07 (-0.09, -0.04)*<.0001	
	No	219/ 777 (28.2)	205/ 760 (27.0)	1.04 (0.89, 1.22) 0.6180	1.06 (0.85, 1.33) 0.6154	0.01 (-0.04, 0.05) 0.7127	
	ARNI at baseline						0.0287
	Yes	42/ 153 (27.5)	24/ 126 (19.0)	1.33 (0.85, 2.08) 0.2186	1.47 (0.82, 2.62) 0.1961	0.07 (-0.03, 0.16) 0.1737	
	No	643/2689 (23.9)	785/2711 (29.0)	0.83 (0.76, 0.91) <.0001	0.77 (0.68, 0.88) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Beta Blocker at baseline						0.7953
	Yes	575/2360 (24.4)	689/2356 (29.2)	0.85 (0.77, 0.93) 0.0003	0.79 (0.69, 0.90) 0.0004	-0.05 (-0.07, -0.02)*0.0002	
	No	110/ 482 (22.8)	120/ 481 (24.9)	0.87 (0.70, 1.08) 0.2060	0.84 (0.62, 1.14) 0.2656	-0.02 (-0.08, 0.03)*0.4389	
	Diuretics at baseline						0.7539
	Yes	621/2536 (24.5)	728/2531 (28.8)	0.85 (0.78, 0.93) 0.0004	0.80 (0.70, 0.91) 0.0005	-0.04 (-0.07, -0.02)*0.0006	
	No	64/ 306 (20.9)	81/ 306 (26.5)	0.81 (0.61, 1.06) 0.1230	0.77 (0.52, 1.13) 0.1792	-0.06 (-0.12, 0.01)*0.1053	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Overall Summary Score (LOCF)							
	Overall	681/2842 (24.0)	795/2837 (28.0)	0.86 (0.79, 0.94) 0.0005	0.81 (0.71, 0.91) 0.0006	-0.04 (-0.06, -0.02)*0.0005	
	Age						0.3318
	<= median	294/1415 (20.8)	371/1482 (25.0)	0.82 (0.72, 0.93) 0.0023	0.76 (0.64, 0.91) 0.0032	-0.04 (-0.07, -0.01)*0.0063	
	> median	387/1427 (27.1)	424/1355 (31.3)	0.89 (0.80, 0.99) 0.0381	0.84 (0.71, 0.99) 0.0391	-0.04 (-0.08, -0.01)*0.0155	
	Gender						0.3834
	Male	408/1656 (24.6)	453/1625 (27.9)	0.89 (0.79, 0.99) 0.0323	0.84 (0.72, 0.99) 0.0384	-0.03 (-0.06, -0.00)*0.0349	
	Female	273/1186 (23.0)	342/1212 (28.2)	0.82 (0.72, 0.94) 0.0035	0.76 (0.63, 0.92) 0.0052	-0.05 (-0.09, -0.02)*0.0035	
	Race						0.6080
	White	499/2039 (24.5)	599/2058 (29.1)	0.85 (0.78, 0.94) 0.0011	0.80 (0.69, 0.92) 0.0022	-0.05 (-0.07, -0.02)*0.0008	
	Black or African	21/ 67 (31.3)	19/ 71 (26.8)	1.18 (0.72, 1.94) 0.5156	1.23 (0.57, 2.63) 0.5996	0.05 (-0.11, 0.20)*0.5532	
	Asian	134/ 558 (24.0)	153/ 555 (27.6)	0.87 (0.71, 1.06) 0.1578	0.82 (0.63, 1.08) 0.1543	-0.04 (-0.09, 0.01) 0.1654	
	Other	27/ 178 (15.2)	24/ 153 (15.7)	0.91 (0.58, 1.45) 0.7037	0.90 (0.48, 1.71) 0.7538	-0.01 (-0.08, 0.07)*0.8966	
	Geographic region						0.9917
	Asia	128/ 539 (23.7)	145/ 538 (27.0)	0.88 (0.72, 1.08) 0.2106	0.84 (0.64, 1.11) 0.2121	-0.03 (-0.08, 0.02) 0.2468	
	Europe and Saudi Arabia	341/1365 (25.0)	408/1394 (29.3)	0.87 (0.78, 0.98) 0.0208	0.82 (0.69, 0.98) 0.0278	-0.04 (-0.08, -0.01)*0.0112	
	North America	104/ 398 (26.1)	121/ 387 (31.3)	0.85 (0.68, 1.05) 0.1233	0.76 (0.55, 1.05) 0.0951	-0.05 (-0.11, 0.01)*0.1113	
	Latin America	108/ 540 (20.0)	121/ 518 (23.4)	0.84 (0.68, 1.04) 0.1036	0.79 (0.58, 1.08) 0.1455	-0.03 (-0.08, 0.02)*0.1849	
	NYHA class at enrolment						0.2538
	II	512/2113 (24.2)	628/2187 (28.7)	0.84 (0.76, 0.92) 0.0003	0.78 (0.68, 0.89) 0.0004	-0.04 (-0.07, -0.02)*0.0008	
	III or IV	169/ 729 (23.2)	166/ 649 (25.6)	0.95 (0.80, 1.12) 0.5342	0.90 (0.69, 1.17) 0.4227	-0.02 (-0.07, 0.02)*0.3016	
	LVEF at enrolment						0.7331
	<= 49	233/ 980 (23.8)	248/ 963 (25.8)	0.90 (0.78, 1.05) 0.1843	0.87 (0.70, 1.07) 0.1828	-0.02 (-0.06, 0.02)*0.3126	
	50-59	256/1029 (24.9)	302/1017 (29.7)	0.84 (0.73, 0.96) 0.0106	0.79 (0.64, 0.96) 0.0199	-0.05 (-0.09, -0.01)*0.0143	
	>= 60	192/ 833 (23.0)	245/ 857 (28.6)	0.84 (0.71, 0.98) 0.0264	0.77 (0.62, 0.97) 0.0238	-0.06 (-0.10, -0.01)*0.0091	
	NT-proBNP at enrolment						0.6342
	<= median	346/1418 (24.4)	389/1421 (27.4)	0.88 (0.78, 0.99) 0.0356	0.85 (0.72, 1.01) 0.0661	-0.03 (-0.06, 0.00)*0.0703	
	> median	335/1424 (23.5)	406/1415 (28.7)	0.85 (0.75, 0.95) 0.0053	0.77 (0.64, 0.91) 0.0028	-0.05 (-0.08, -0.02)*0.0017	
	Type 2 Diabetes Medical History						0.6565
	Yes	302/1250 (24.2)	363/1260 (28.8)	0.84 (0.74, 0.96) 0.0077	0.79 (0.66, 0.94)*0.0084	-0.05 (-0.08, -0.01)*0.0082	
	No	379/1592 (23.8)	432/1577 (27.4)	0.88 (0.78, 0.98) 0.0241	0.83 (0.71, 0.97)*0.0208	-0.04 (-0.07, -0.01)*0.0206	
	Atrial fibrillation or flutter at enrolment ECG						0.5953
	Yes	280/1199 (23.4)	318/1199 (26.5)	0.88 (0.77, 1.01) 0.0693	0.84 (0.69, 1.02) 0.0761	-0.03 (-0.07, 0.00)*0.0727	
	No	401/1643 (24.4)	477/1638 (29.1)	0.84 (0.76, 0.94) 0.0021	0.78 (0.67, 0.92) 0.0029	-0.05 (-0.08, -0.02)*0.0023	
	BMI (kg/m2) at enrolment						0.4707
	< 30	371/1571 (23.6)	443/1559 (28.4)	0.84 (0.75, 0.94) 0.0026	0.78 (0.66, 0.92) 0.0027	-0.05 (-0.08, -0.02)*0.0022	
	>= 30	310/1270 (24.4)	351/1275 (27.5)	0.89 (0.79, 1.01) 0.0653	0.85 (0.71, 1.02) 0.0885	-0.03 (-0.07, 0.00)*0.0725	
	Baseline eGFR (mL/min/1.73m^2)						0.2758
	< 60	367/1359 (27.0)	419/1396 (30.0)	0.90 (0.80, 1.01) 0.0718	0.86 (0.73, 1.02) 0.0883	-0.03 (-0.06, 0.00)*0.0800	
	>= 60	314/1483 (21.2)	376/1440 (26.1)	0.82 (0.72, 0.93) 0.0020	0.76 (0.63, 0.90) 0.0022	-0.05 (-0.08, -0.02)*0.0017	

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Overall Summary Score (LOCF)	SBP at randomisation						0.9982
	<= median	345/1424 (24.2)	414/1439 (28.8)	0.86 (0.76, 0.97) 0.0121	0.81 (0.69, 0.97) 0.0192	-0.05 (-0.08, -0.01)*0.0058	
	> median	336/1418 (23.7)	381/1398 (27.3)	0.86 (0.76, 0.97) 0.0148	0.80 (0.67, 0.95) 0.0129	-0.04 (-0.07, -0.00)*0.0302	
	LVEF at enrolment 2						0.4426
	<= 49	233/ 980 (23.8)	248/ 963 (25.8)	0.90 (0.78, 1.05) 0.1843	0.87 (0.70, 1.07) 0.1828	-0.02 (-0.06, 0.02)*0.3126	
	>= 50	448/1862 (24.1)	547/1874 (29.2)	0.84 (0.76, 0.93) 0.0009	0.78 (0.67, 0.91) 0.0014	-0.05 (-0.08, -0.02)*0.0004	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4502
	Yes	45/ 283 (15.9)	58/ 286 (20.3)	0.74 (0.53, 1.03) 0.0778	0.65 (0.41, 1.03) 0.0690	-0.04 (-0.11, 0.02)*0.1741	
	No	636/2559 (24.9)	737/2551 (28.9)	0.87 (0.80, 0.95) 0.0014	0.82 (0.72, 0.93) 0.0020	-0.04 (-0.06, -0.02)*0.0011	
	MRAs at baseline						0.0929
	Yes	291/1227 (23.7)	363/1224 (29.7)	0.79 (0.70, 0.90) 0.0004	0.73 (0.61, 0.88) 0.0009	-0.06 (-0.09, -0.02)*0.0009	
	No	390/1615 (24.1)	432/1613 (26.8)	0.92 (0.82, 1.03) 0.1307	0.87 (0.74, 1.03) 0.1106	-0.03 (-0.06, 0.00)*0.0858	
	ACEi+ARB at baseline						0.1206
	Yes	477/2065 (23.1)	586/2077 (28.2)	0.82 (0.75, 0.91) 0.0001	0.76 (0.66, 0.88) 0.0002	-0.05 (-0.08, -0.02)*0.0002	
	No	204/ 777 (26.3)	209/ 760 (27.5)	0.96 (0.81, 1.13) 0.6064	0.94 (0.75, 1.18) 0.5888	-0.02 (-0.06, 0.03) 0.4285	
	ARNI at baseline						0.4046
	Yes	35/ 153 (22.9)	27/ 126 (21.4)	1.05 (0.67, 1.65) 0.8188	1.06 (0.60, 1.90) 0.8325	0.01 (-0.09, 0.10) 0.9040	
	No	646/2689 (24.0)	768/2711 (28.3)	0.86 (0.79, 0.93) 0.0004	0.80 (0.71, 0.91) 0.0005	-0.04 (-0.07, -0.02)*0.0003	
	Beta Blocker at baseline						0.8783
	Yes	576/2360 (24.4)	682/2356 (28.9)	0.86 (0.79, 0.94) 0.0011	0.80 (0.70, 0.92) 0.0011	-0.05 (-0.07, -0.02)*0.0004	
	No	105/ 482 (21.8)	113/ 481 (23.5)	0.88 (0.70, 1.11) 0.2760	0.86 (0.63, 1.17) 0.3316	-0.02 (-0.07, 0.04)*0.5264	
	Diuretics at baseline						0.7490
	Yes	617/2536 (24.3)	721/2531 (28.5)	0.86 (0.78, 0.93) 0.0005	0.80 (0.70, 0.91) 0.0007	-0.04 (-0.07, -0.02)*0.0008	
	No	64/ 306 (20.9)	74/ 306 (24.2)	0.89 (0.67, 1.19) 0.4498	0.87 (0.59, 1.28) 0.4795	-0.01 (-0.08, 0.05) 0.6642	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	821/2792 (29.4)	927/2792 (33.2)	0.90 (0.84, 0.97) 0.0052	0.85 (0.75, 0.95) 0.0051	-0.04 (-0.06, -0.01)*0.0022	
	Age						0.9764
	<= median	367/1403 (26.2)	426/1469 (29.0)	0.90 (0.80, 1.00) 0.0608	0.85 (0.72, 1.01) 0.0639	-0.03 (-0.06, 0.00)*0.0883	
	> median	454/1389 (32.7)	501/1323 (37.9)	0.90 (0.81, 0.99) 0.0242	0.82 (0.70, 0.97) 0.0211	-0.05 (-0.09, -0.02)*0.0047	
	Gender						0.0494
	Male	508/1638 (31.0)	526/1602 (32.8)	0.96 (0.87, 1.05) 0.3512	0.92 (0.79, 1.08) 0.3125	-0.02 (-0.05, 0.01)*0.2664	
	Female	313/1154 (27.1)	401/1190 (33.7)	0.82 (0.73, 0.92) 0.0010	0.75 (0.62, 0.90) 0.0022	-0.07 (-0.10, -0.03)*0.0005	
	Race						0.2778
	White	616/2004 (30.7)	679/2025 (33.5)	0.94 (0.87, 1.02) 0.1556	0.90 (0.78, 1.03) 0.1272	-0.03 (-0.06, 0.00)*0.0576	
	Black or African	23/ 66 (34.8)	26/ 68 (38.2)	0.96 (0.63, 1.45) 0.8409	0.85 (0.40, 1.78) 0.6607	-0.03 (-0.20, 0.13)*0.6838	
	Asian	150/ 551 (27.2)	194/ 550 (35.3)	0.78 (0.65, 0.93) 0.0052	0.69 (0.53, 0.90) 0.0053	-0.08 (-0.13, -0.03) 0.0039	
	Other	32/ 171 (18.7)	28/ 149 (18.8)	1.00 (0.65, 1.54) 0.9995	0.92 (0.51, 1.66) 0.7824	-0.00 (-0.09, 0.08)*0.9857	
	Geographic region						0.3254
	Asia	143/ 533 (26.8)	184/ 533 (34.5)	0.78 (0.66, 0.94) 0.0083	0.70 (0.54, 0.91) 0.0088	-0.08 (-0.13, -0.02)*0.0063	
	Europe and Saudi Arabia	408/1347 (30.3)	458/1373 (33.4)	0.94 (0.85, 1.04) 0.2320	0.88 (0.74, 1.05) 0.1478	-0.03 (-0.07, 0.00)*0.0857	
	North America	137/ 391 (35.0)	150/ 375 (40.0)	0.90 (0.76, 1.07) 0.2431	0.83 (0.61, 1.12) 0.2164	-0.04 (-0.11, 0.02) 0.1971	
	Latin America	133/ 521 (25.5)	135/ 511 (26.4)	0.98 (0.81, 1.18) 0.8030	0.94 (0.70, 1.26) 0.6951	-0.01 (-0.06, 0.04)*0.7442	
	NYHA class at enrolment						0.6181
	II	616/2077 (29.7)	711/2159 (32.9)	0.90 (0.83, 0.99) 0.0212	0.86 (0.75, 0.98) 0.0229	-0.03 (-0.06, -0.00)*0.0215	
	III or IV	205/ 715 (28.7)	215/ 632 (34.0)	0.87 (0.75, 1.01) 0.0598	0.79 (0.62, 1.01) 0.0567	-0.05 (-0.10, -0.00)*0.0347	
	LVEF at enrolment						0.5393
	<= 49	287/ 967 (29.7)	291/ 952 (30.6)	0.95 (0.83, 1.08) 0.4479	0.93 (0.76, 1.13) 0.4554	-0.01 (-0.05, 0.03)*0.6717	
	50-59	304/1013 (30.0)	353/ 998 (35.4)	0.86 (0.76, 0.97) 0.0116	0.80 (0.66, 0.98) 0.0275	-0.05 (-0.09, -0.01)*0.0103	
	>= 60	230/ 812 (28.3)	283/ 842 (33.6)	0.90 (0.78, 1.03) 0.1370	0.82 (0.66, 1.01) 0.0670	-0.05 (-0.10, -0.01)*0.0199	
	NT-proBNP at enrolment						0.4166
	<= median	391/1394 (28.0)	455/1402 (32.5)	0.87 (0.78, 0.97) 0.0131	0.81 (0.69, 0.96) 0.0136	-0.04 (-0.08, -0.01)*0.0111	
	> median	430/1398 (30.8)	472/1389 (34.0)	0.93 (0.84, 1.02) 0.1370	0.88 (0.75, 1.04) 0.1361	-0.03 (-0.07, 0.00)*0.0689	
	Type 2 Diabetes Medical History						0.7320
	Yes	373/1232 (30.3)	407/1237 (32.9)	0.91 (0.82, 1.02) 0.0989	0.89 (0.75, 1.05)*0.1606	-0.03 (-0.06, 0.01)*0.1603	
	No	448/1560 (28.7)	520/1555 (33.4)	0.89 (0.80, 0.98) 0.0206	0.80 (0.69, 0.93)*0.0044	-0.05 (-0.08, -0.01)*0.0044	
	Atrial fibrillation or flutter at enrolment ECG						0.5051
	Yes	358/1178 (30.4)	386/1175 (32.9)	0.93 (0.83, 1.04) 0.1816	0.90 (0.75, 1.07) 0.2399	-0.02 (-0.06, 0.01)*0.1992	
	No	463/1614 (28.7)	541/1617 (33.5)	0.88 (0.80, 0.97) 0.0103	0.81 (0.69, 0.94) 0.0069	-0.05 (-0.08, -0.02)*0.0033	
	BMI (kg/m2) at enrolment						0.3577
	< 30	443/1547 (28.6)	513/1535 (33.4)	0.87 (0.79, 0.97) 0.0090	0.80 (0.68, 0.94) 0.0052	-0.05 (-0.08, -0.02)*0.0041	
	>= 30	378/1244 (30.4)	413/1254 (32.9)	0.94 (0.84, 1.04) 0.2423	0.92 (0.77, 1.09) 0.3335	-0.03 (-0.06, 0.01)*0.1707	
	Baseline eGFR (mL/min/1.73m^2)						0.6460
	< 60	419/1328 (31.6)	469/1367 (34.3)	0.92 (0.83, 1.01) 0.0909	0.89 (0.75, 1.05) 0.1651	-0.03 (-0.06, 0.01)*0.1276	
	>= 60	402/1464 (27.5)	458/1424 (32.2)	0.88 (0.79, 0.99) 0.0258	0.81 (0.69, 0.96) 0.0131	-0.05 (-0.08, -0.01)*0.0057	

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Full Analysis Set

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Physical Limitation (LOCF)	SBP at randomisation						0.6249
	<= median	407/1396 (29.2)	468/1414 (33.1)	0.91 (0.82, 1.02) 0.0940	0.87 (0.74, 1.02) 0.0956	-0.04 (-0.07, -0.01)*0.0239	
	> median	414/1396 (29.7)	459/1378 (33.3)	0.88 (0.79, 0.98) 0.0179	0.82 (0.69, 0.97) 0.0178	-0.04 (-0.07, -0.00)*0.0382	
	LVEF at enrolment 2						0.3480
	<= 49	287/ 967 (29.7)	291/ 952 (30.6)	0.95 (0.83, 1.08) 0.4479	0.93 (0.76, 1.13) 0.4554	-0.01 (-0.05, 0.03)*0.6717	
	>= 50	534/1825 (29.3)	636/1840 (34.6)	0.88 (0.80, 0.96) 0.0053	0.81 (0.70, 0.94) 0.0045	-0.05 (-0.08, -0.02)*0.0006	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1823
	Yes	67/ 273 (24.5)	88/ 277 (31.8)	0.77 (0.60, 0.99) 0.0448	0.67 (0.45, 1.00) 0.0479	-0.07 (-0.15, 0.00)*0.0587	
	No	754/2519 (29.9)	839/2515 (33.4)	0.91 (0.84, 0.99) 0.0216	0.87 (0.77, 0.98) 0.0213	-0.03 (-0.06, -0.01)*0.0089	
	MRAs at baseline						0.4514
	Yes	364/1200 (30.3)	419/1208 (34.7)	0.87 (0.78, 0.98) 0.0163	0.82 (0.68, 0.97) 0.0237	-0.04 (-0.08, -0.01)*0.0225	
	No	457/1592 (28.7)	508/1584 (32.1)	0.92 (0.83, 1.02) 0.1187	0.87 (0.75, 1.02) 0.0898	-0.03 (-0.07, -0.00)*0.0391	
	ACEi+ARB at baseline						0.2329
	Yes	577/2029 (28.4)	680/2047 (33.2)	0.88 (0.80, 0.96) 0.0028	0.81 (0.70, 0.93) 0.0025	-0.05 (-0.08, -0.02)*0.0009	
	No	244/ 763 (32.0)	247/ 745 (33.2)	0.97 (0.84, 1.11) 0.6486	0.95 (0.77, 1.19) 0.6747	-0.01 (-0.05, 0.04) 0.6955	
	ARNI at baseline						0.6693
	Yes	47/ 150 (31.3)	39/ 123 (31.7)	0.96 (0.68, 1.37) 0.8224	0.93 (0.55, 1.57) 0.7846	-0.02 (-0.14, 0.09) 0.6582	
	No	774/2642 (29.3)	888/2669 (33.3)	0.90 (0.83, 0.97) 0.0055	0.84 (0.75, 0.95) 0.0057	-0.04 (-0.06, -0.01)*0.0018	
	Beta Blocker at baseline						0.6752
	Yes	675/2323 (29.1)	774/2321 (33.3)	0.89 (0.82, 0.97) 0.0065	0.83 (0.73, 0.95) 0.0048	-0.04 (-0.07, -0.02)*0.0016	
	No	146/ 469 (31.1)	153/ 471 (32.5)	0.93 (0.78, 1.11) 0.4400	0.92 (0.69, 1.22) 0.5755	-0.03 (-0.08, 0.03) 0.3232	
	Diuretics at baseline						0.4136
	Yes	728/2493 (29.2)	835/2492 (33.5)	0.89 (0.82, 0.96) 0.0037	0.83 (0.73, 0.93) 0.0025	-0.04 (-0.07, -0.02)*0.0010	
	No	93/ 299 (31.1)	92/ 300 (30.7)	0.98 (0.78, 1.24) 0.8837	1.03 (0.72, 1.48) 0.8545	0.01 (-0.05, 0.08) 0.6875	

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Quality of Life (LOCF)							
	Overall	785/2842 (27.6)	867/2837 (30.6)	0.93 (0.87, 1.00) 0.0484	0.87 (0.77, 0.99) 0.0314	-0.03 (-0.05, -0.01)*0.0147	
	Age						0.6803
	<= median	350/1415 (24.7)	391/1482 (26.4)	0.94 (0.84, 1.06) 0.3133	0.92 (0.77, 1.09) 0.3340	-0.02 (-0.05, 0.02)*0.3091	
	> median	435/1427 (30.5)	476/1355 (35.1)	0.91 (0.83, 1.00) 0.0610	0.83 (0.70, 0.98) 0.0297	-0.05 (-0.08, -0.01)*0.0090	
	Gender						0.8099
	Male	459/1656 (27.7)	487/1625 (30.0)	0.94 (0.85, 1.03) 0.2012	0.91 (0.77, 1.07) 0.2528	-0.02 (-0.05, 0.01)*0.1545	
	Female	326/1186 (27.5)	380/1212 (31.4)	0.92 (0.83, 1.03) 0.1472	0.83 (0.68, 1.00) 0.0540	-0.04 (-0.08, -0.00)*0.0376	
	Race						0.6248
	White	568/2039 (27.9)	640/2058 (31.1)	0.93 (0.86, 1.01) 0.0815	0.87 (0.75, 1.01) 0.0621	-0.03 (-0.06, -0.00)*0.0228	
	Black or African	19/ 67 (28.4)	18/ 71 (25.4)	1.21 (0.73, 2.00) 0.4597	1.27 (0.57, 2.84) 0.5621	0.03 (-0.12, 0.18)*0.6904	
	Asian	169/ 558 (30.3)	177/ 555 (31.9)	0.95 (0.80, 1.11) 0.4982	0.91 (0.70, 1.19) 0.5062	-0.02 (-0.07, 0.04)*0.5629	
	Other	29/ 178 (16.3)	32/ 153 (20.9)	0.81 (0.54, 1.21) 0.2994	0.66 (0.36, 1.20) 0.1726	-0.05 (-0.13, 0.04)*0.2821	
	Geographic region						0.5261
	Asia	162/ 539 (30.1)	169/ 538 (31.4)	0.95 (0.80, 1.12) 0.5596	0.93 (0.71, 1.22) 0.6170	-0.01 (-0.07, 0.04)*0.6293	
	Europe and Saudi Arabia	386/1365 (28.3)	437/1394 (31.3)	0.94 (0.85, 1.04) 0.2507	0.89 (0.74, 1.06) 0.1892	-0.03 (-0.06, 0.00)*0.0777	
	North America	104/ 398 (26.1)	125/ 387 (32.3)	0.82 (0.67, 1.00) 0.0467	0.72 (0.51, 0.99) 0.0464	-0.06 (-0.13, 0.00)*0.0569	
	Latin America	133/ 540 (24.6)	136/ 518 (26.3)	1.01 (0.85, 1.20) 0.8757	0.92 (0.68, 1.25) 0.5830	-0.02 (-0.07, 0.04)*0.5440	
	NYHA class at enrolment						0.5301
	II	593/2113 (28.1)	678/2187 (31.0)	0.92 (0.85, 1.00) 0.0450	0.85 (0.74, 0.98) 0.0237	-0.03 (-0.06, -0.00)*0.0347	
	III or IV	192/ 729 (26.3)	188/ 649 (29.0)	0.97 (0.84, 1.11) 0.6193	0.92 (0.71, 1.19) 0.5071	-0.03 (-0.07, 0.02)*0.2761	
	LVEF at enrolment						0.3633
	<= 49	264/ 980 (26.9)	265/ 963 (27.5)	1.00 (0.88, 1.14) 0.9989	0.96 (0.77, 1.19) 0.6924	-0.01 (-0.05, 0.03)*0.7742	
	50-59	293/1029 (28.5)	329/1017 (32.4)	0.89 (0.79, 1.00) 0.0522	0.83 (0.68, 1.02) 0.0757	-0.04 (-0.08, 0.00)*0.0565	
	>= 60	228/ 833 (27.4)	273/ 857 (31.9)	0.90 (0.79, 1.03) 0.1176	0.84 (0.67, 1.04) 0.1151	-0.04 (-0.09, -0.00)*0.0432	
	NT-proBNP at enrolment						0.1773
	<= median	378/1418 (26.7)	442/1421 (31.1)	0.88 (0.80, 0.98) 0.0203	0.80 (0.68, 0.96) 0.0148	-0.04 (-0.08, -0.01)*0.0089	
	> median	407/1424 (28.6)	425/1415 (30.0)	0.98 (0.88, 1.08) 0.6505	0.95 (0.79, 1.13) 0.5346	-0.01 (-0.05, 0.02)*0.3948	
	Type 2 Diabetes Medical History						0.5424
	Yes	334/1250 (26.7)	389/1260 (30.9)	0.90 (0.81, 1.01) 0.0764	0.82 (0.69, 0.97)*0.0217	-0.04 (-0.08, -0.01)*0.0214	
	No	451/1592 (28.3)	478/1577 (30.3)	0.95 (0.86, 1.04) 0.2874	0.91 (0.78, 1.06)*0.2205	-0.02 (-0.05, 0.01)*0.2204	
	Atrial fibrillation or flutter at enrolment ECG						0.6055
	Yes	331/1199 (27.6)	355/1199 (29.6)	0.95 (0.85, 1.06) 0.3215	0.92 (0.76, 1.11) 0.3895	-0.02 (-0.06, 0.02)*0.2780	
	No	454/1643 (27.6)	512/1638 (31.3)	0.91 (0.83, 1.00) 0.0448	0.84 (0.71, 0.99) 0.0322	-0.04 (-0.07, -0.01)*0.0226	
	BMI (kg/m2) at enrolment						0.7317
	< 30	449/1571 (28.6)	501/1559 (32.1)	0.92 (0.83, 1.01) 0.0781	0.86 (0.73, 1.02) 0.0765	-0.04 (-0.07, -0.00)*0.0304	
	>= 30	335/1270 (26.4)	365/1275 (28.6)	0.95 (0.85, 1.06) 0.3270	0.88 (0.73, 1.07) 0.2010	-0.02 (-0.06, 0.01)*0.2037	
	Baseline eGFR (mL/min/1.73m^2)						0.1014
	< 60	416/1359 (30.6)	439/1396 (31.4)	0.98 (0.89, 1.09) 0.7601	0.97 (0.82, 1.16) 0.7588	-0.01 (-0.04, 0.03)*0.6352	
	>= 60	369/1483 (24.9)	427/1440 (29.7)	0.88 (0.79, 0.98) 0.0172	0.78 (0.66, 0.94) 0.0070	-0.05 (-0.08, -0.02)*0.0037	

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Quality of Life (LOCF)	SBP at randomisation						0.3095
	<= median	401/1424 (28.2)	439/1439 (30.5)	0.97 (0.88, 1.07) 0.5222	0.93 (0.78, 1.11) 0.4235	-0.02 (-0.06, 0.01)*0.1677	
	> median	384/1418 (27.1)	428/1398 (30.6)	0.90 (0.81, 0.99) 0.0396	0.82 (0.69, 0.98) 0.0283	-0.04 (-0.07, -0.00)*0.0383	
	LVEF at enrolment 2						0.1644
	<= 49	264/ 980 (26.9)	265/ 963 (27.5)	1.00 (0.88, 1.14) 0.9989	0.96 (0.77, 1.19) 0.6924	-0.01 (-0.05, 0.03)*0.7742	
	>= 50	521/1862 (28.0)	602/1874 (32.1)	0.90 (0.82, 0.98) 0.0149	0.83 (0.72, 0.97) 0.0185	-0.04 (-0.07, -0.01)*0.0057	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8632
	Yes	59/ 283 (20.8)	68/ 286 (23.8)	0.92 (0.71, 1.19) 0.5226	0.87 (0.57, 1.34) 0.5347	-0.03 (-0.10, 0.04)*0.4012	
	No	726/2559 (28.4)	799/2551 (31.3)	0.93 (0.86, 1.00) 0.0617	0.87 (0.77, 0.99) 0.0392	-0.03 (-0.05, -0.00)*0.0211	
	MRAs at baseline						0.8094
	Yes	335/1227 (27.3)	373/1224 (30.5)	0.92 (0.82, 1.02) 0.1251	0.86 (0.71, 1.04) 0.1202	-0.03 (-0.07, 0.00)*0.0831	
	No	450/1615 (27.9)	494/1613 (30.6)	0.94 (0.85, 1.03) 0.1818	0.88 (0.75, 1.04) 0.1271	-0.03 (-0.06, 0.00)*0.0844	
	ACEi+ARB at baseline						0.4471
	Yes	568/2065 (27.5)	645/2077 (31.1)	0.92 (0.84, 1.00) 0.0404	0.84 (0.72, 0.97) 0.0161	-0.04 (-0.06, -0.01)*0.0120	
	No	217/ 777 (27.9)	222/ 760 (29.2)	0.98 (0.84, 1.13) 0.7422	0.97 (0.77, 1.23) 0.8098	-0.01 (-0.06, 0.03)*0.5778	
	ARNI at baseline						0.0755
	Yes	40/ 153 (26.1)	28/ 126 (22.2)	1.31 (0.87, 1.97) 0.1939	1.42 (0.80, 2.54) 0.2330	0.04 (-0.06, 0.14)*0.4448	
	No	745/2689 (27.7)	839/2711 (30.9)	0.92 (0.85, 0.99) 0.0206	0.85 (0.75, 0.97) 0.0144	-0.03 (-0.06, -0.01)*0.0088	
	Beta Blocker at baseline						0.6400
	Yes	660/2360 (28.0)	729/2356 (30.9)	0.94 (0.87, 1.01) 0.1034	0.88 (0.77, 1.01) 0.0667	-0.03 (-0.06, -0.00)*0.0249	
	No	125/ 482 (25.9)	138/ 481 (28.7)	0.89 (0.75, 1.07) 0.2285	0.83 (0.61, 1.13) 0.2369	-0.03 (-0.08, 0.03)*0.3369	
	Diuretics at baseline						0.0489
	Yes	702/2536 (27.7)	788/2531 (31.1)	0.91 (0.84, 0.98) 0.0099	0.84 (0.74, 0.96) 0.0098	-0.03 (-0.06, -0.01)*0.0070	
	No	83/ 306 (27.1)	79/ 306 (25.8)	1.16 (0.90, 1.48) 0.2485	1.16 (0.80, 1.69) 0.4385	0.01 (-0.06, 0.08)*0.7140	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	707/2842 (24.9)	848/2837 (29.9)	0.84 (0.77, 0.91) <.0001	0.77 (0.68, 0.87) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Age						0.5924
	<= median	303/1415 (21.4)	388/1482 (26.2)	0.81 (0.71, 0.92) 0.0012	0.75 (0.63, 0.89) 0.0012	-0.05 (-0.08, -0.02)*0.0025	
	> median	404/1427 (28.3)	460/1355 (33.9)	0.85 (0.77, 0.94) 0.0025	0.78 (0.66, 0.92) 0.0035	-0.06 (-0.09, -0.02)*0.0013	
	Gender						0.3322
	Male	396/1656 (23.9)	484/1625 (29.8)	0.81 (0.72, 0.90) 0.0001	0.74 (0.63, 0.86) 0.0002	-0.06 (-0.09, -0.03)*0.0001	
	Female	311/1186 (26.2)	364/1212 (30.0)	0.88 (0.78, 0.99) 0.0364	0.82 (0.68, 0.99) 0.0383	-0.04 (-0.07, -0.00)*0.0378	
	Race						0.3206
	White	530/2039 (26.0)	631/2058 (30.7)	0.86 (0.78, 0.94) 0.0012	0.80 (0.69, 0.92) 0.0017	-0.05 (-0.07, -0.02)*0.0009	
	Black or African	18/ 67 (26.9)	17/ 71 (23.9)	1.08 (0.62, 1.88) 0.7978	1.16 (0.53, 2.54) 0.7177	-0.01 (-0.16, 0.14) 0.9384	
	Asian	135/ 558 (24.2)	164/ 555 (29.5)	0.81 (0.67, 0.98) 0.0324	0.74 (0.57, 0.97) 0.0314	-0.05 (-0.11, -0.00)*0.0435	
	Other	24/ 178 (13.5)	36/ 153 (23.5)	0.59 (0.37, 0.94) 0.0248	0.50 (0.28, 0.91) 0.0220	-0.10 (-0.18, -0.02) 0.0183	
	Geographic region						0.5851
	Asia	129/ 539 (23.9)	155/ 538 (28.8)	0.82 (0.68, 1.00) 0.0558	0.76 (0.58, 1.01) 0.0567	-0.05 (-0.10, 0.00)*0.0689	
	Europe and Saudi Arabia	368/1365 (27.0)	435/1394 (31.2)	0.89 (0.80, 0.99) 0.0302	0.82 (0.69, 0.98) 0.0265	-0.04 (-0.08, -0.01)*0.0140	
	North America	107/ 398 (26.9)	135/ 387 (34.9)	0.77 (0.62, 0.94) 0.0102	0.68 (0.49, 0.93) 0.0147	-0.08 (-0.14, -0.02)*0.0150	
	Latin America	103/ 540 (19.1)	123/ 518 (23.7)	0.80 (0.64, 1.00) 0.0492	0.74 (0.54, 1.00) 0.0480	-0.05 (-0.10, 0.00)*0.0639	
	NYHA class at enrolment						0.5988
	II	526/2113 (24.9)	659/2187 (30.1)	0.82 (0.75, 0.90) <.0001	0.75 (0.65, 0.86) <.0001	-0.05 (-0.08, -0.03)*0.0001	
	III or IV	181/ 729 (24.8)	189/ 649 (29.1)	0.87 (0.74, 1.02) 0.0813	0.80 (0.62, 1.03) 0.0879	-0.04 (-0.09, 0.00)*0.0732	
	LVEF at enrolment						0.8599
	<= 49	238/ 980 (24.3)	266/ 963 (27.6)	0.87 (0.75, 1.00) 0.0520	0.81 (0.66, 1.00) 0.0533	-0.03 (-0.07, 0.01)*0.0933	
	50-59	270/1029 (26.2)	323/1017 (31.8)	0.83 (0.73, 0.94) 0.0038	0.75 (0.62, 0.92) 0.0052	-0.06 (-0.09, -0.02)*0.0058	
	>= 60	199/ 833 (23.9)	259/ 857 (30.2)	0.82 (0.70, 0.95) 0.0104	0.75 (0.60, 0.93) 0.0103	-0.06 (-0.11, -0.02)*0.0033	
	NT-proBNP at enrolment						0.7598
	<= median	352/1418 (24.8)	412/1421 (29.0)	0.85 (0.75, 0.95) 0.0052	0.79 (0.67, 0.94) 0.0080	-0.04 (-0.07, -0.01)*0.0121	
	> median	355/1424 (24.9)	436/1415 (30.8)	0.83 (0.74, 0.93) 0.0012	0.75 (0.63, 0.89) 0.0009	-0.06 (-0.09, -0.03)*0.0005	
	Type 2 Diabetes Medical History						0.1264
	Yes	308/1250 (24.6)	401/1260 (31.8)	0.78 (0.69, 0.88) <.0001	0.70 (0.59, 0.83)*<.0001	-0.07 (-0.11, -0.04)*<.0001	
	No	399/1592 (25.1)	447/1577 (28.3)	0.89 (0.80, 0.99) 0.0383	0.85 (0.72, 0.99)*0.0369	-0.03 (-0.06, -0.00)*0.0367	
	Atrial fibrillation or flutter at enrolment ECG						0.6439
	Yes	284/1199 (23.7)	347/1199 (28.9)	0.82 (0.72, 0.93) 0.0022	0.75 (0.62, 0.91) 0.0034	-0.05 (-0.09, -0.02)*0.0034	
	No	423/1643 (25.7)	501/1638 (30.6)	0.85 (0.76, 0.94) 0.0023	0.78 (0.67, 0.91) 0.0022	-0.05 (-0.08, -0.02)*0.0020	
	BMI (kg/m2) at enrolment						0.6891
	< 30	387/1571 (24.6)	468/1559 (30.0)	0.83 (0.74, 0.92) 0.0008	0.76 (0.64, 0.89) 0.0008	-0.05 (-0.09, -0.02)*0.0007	
	>= 30	320/1270 (25.2)	378/1275 (29.6)	0.85 (0.76, 0.96) 0.0096	0.79 (0.66, 0.95) 0.0135	-0.04 (-0.08, -0.01)*0.0118	
	Baseline eGFR (mL/min/1.73m^2)						0.6596
	< 60	377/1359 (27.7)	457/1396 (32.7)	0.85 (0.77, 0.95) 0.0042	0.78 (0.66, 0.93) 0.0045	-0.05 (-0.08, -0.02)*0.0042	
	>= 60	330/1483 (22.3)	391/1440 (27.2)	0.82 (0.73, 0.93) 0.0021	0.76 (0.64, 0.91) 0.0023	-0.05 (-0.08, -0.02)*0.0021	

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Symptom Burden (LOCF)	SBP at randomisation						0.2220
	<= median	346/1424 (24.3)	451/1439 (31.3)	0.80 (0.71, 0.89) 0.0001	0.72 (0.61, 0.85) 0.0001	-0.07 (-0.10, -0.04)*<.0001	
	> median	361/1418 (25.5)	397/1398 (28.4)	0.88 (0.78, 0.99) 0.0308	0.83 (0.69, 0.98) 0.0317	-0.03 (-0.06, 0.00)*0.0786	
	LVEF at enrolment 2						0.6011
	<= 49	238/ 980 (24.3)	266/ 963 (27.6)	0.87 (0.75, 1.00) 0.0520	0.81 (0.66, 1.00) 0.0533	-0.03 (-0.07, 0.01)*0.0933	
	>= 50	469/1862 (25.2)	582/1874 (31.1)	0.82 (0.75, 0.91) 0.0001	0.75 (0.65, 0.87) 0.0002	-0.06 (-0.09, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7400
	Yes	54/ 283 (19.1)	65/ 286 (22.7)	0.76 (0.56, 1.02) 0.0655	0.70 (0.45, 1.08) 0.1053	-0.04 (-0.10, 0.03)*0.2843	
	No	653/2559 (25.5)	783/2551 (30.7)	0.84 (0.77, 0.91) <.0001	0.77 (0.68, 0.88) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	MRAs at baseline						0.1574
	Yes	290/1227 (23.6)	376/1224 (30.7)	0.78 (0.69, 0.88) 0.0001	0.70 (0.58, 0.84) 0.0001	-0.07 (-0.11, -0.04)*<.0001	
	No	417/1615 (25.8)	472/1613 (29.3)	0.88 (0.79, 0.98) 0.0200	0.83 (0.71, 0.98) 0.0240	-0.03 (-0.07, -0.00)*0.0285	
	ACEi+ARB at baseline						0.0375
	Yes	488/2065 (23.6)	630/2077 (30.3)	0.79 (0.72, 0.87) <.0001	0.71 (0.61, 0.82) <.0001	-0.07 (-0.09, -0.04)*<.0001	
	No	219/ 777 (28.2)	218/ 760 (28.7)	0.97 (0.83, 1.13) 0.6782	0.97 (0.77, 1.21) 0.7611	-0.00 (-0.05, 0.04)*0.8284	
	ARNI at baseline						0.0620
	Yes	47/ 153 (30.7)	31/ 126 (24.6)	1.17 (0.80, 1.72) 0.4117	1.26 (0.73, 2.18) 0.4087	0.04 (-0.06, 0.14) 0.4368	
	No	660/2689 (24.5)	817/2711 (30.1)	0.82 (0.76, 0.90) <.0001	0.75 (0.66, 0.85) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Beta Blocker at baseline						0.6445
	Yes	598/2360 (25.3)	716/2356 (30.4)	0.84 (0.77, 0.92) 0.0002	0.78 (0.68, 0.89) 0.0002	-0.05 (-0.08, -0.02)*0.0001	
	No	109/ 482 (22.6)	132/ 481 (27.4)	0.80 (0.65, 0.99) 0.0408	0.72 (0.54, 0.98) 0.0368	-0.05 (-0.10, 0.01)*0.0832	
	Diuretics at baseline						0.3487
	Yes	648/2536 (25.6)	761/2531 (30.1)	0.85 (0.78, 0.92) 0.0001	0.79 (0.69, 0.89) 0.0002	-0.05 (-0.07, -0.02)*0.0003	
	No	59/ 306 (19.3)	87/ 306 (28.4)	0.74 (0.56, 0.98) 0.0381	0.63 (0.43, 0.93) 0.0215	-0.09 (-0.16, -0.02)*0.0076	

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Self Efficacy (LOCF)							
	Overall	716/2842 (25.2)	710/2837 (25.0)	1.02 (0.94, 1.11) 0.6922	1.02 (0.89, 1.15) 0.8084	0.00 (-0.02, 0.02)*0.8846	
	Age						0.1955
	<= median	343/1415 (24.2)	336/1482 (22.7)	1.07 (0.95, 1.22) 0.2539	1.10 (0.91, 1.31) 0.3236	0.02 (-0.02, 0.05)*0.3194	
	> median	373/1427 (26.1)	374/1355 (27.6)	0.96 (0.86, 1.08) 0.5152	0.94 (0.78, 1.12) 0.4752	-0.01 (-0.05, 0.02)*0.3844	
	Gender						0.6620
	Male	417/1656 (25.2)	394/1625 (24.2)	1.03 (0.92, 1.16) 0.5512	1.05 (0.89, 1.24) 0.5765	0.01 (-0.02, 0.04)*0.5347	
	Female	299/1186 (25.2)	316/1212 (26.1)	1.00 (0.88, 1.13) 0.9786	0.98 (0.80, 1.19) 0.8016	-0.01 (-0.04, 0.03)*0.6289	
	Race						0.9886
	White	497/2039 (24.4)	498/2058 (24.2)	1.02 (0.92, 1.13) 0.6685	1.03 (0.88, 1.19) 0.7285	0.00 (-0.02, 0.03)*0.8952	
	Black or African	16/ 67 (23.9)	17/ 71 (23.9)	0.93 (0.54, 1.58) 0.7795	0.86 (0.36, 2.03) 0.7321	-0.00 (-0.14, 0.14)*0.9931	
	Asian	168/ 558 (30.1)	166/ 555 (29.9)	1.01 (0.86, 1.18) 0.9231	0.97 (0.73, 1.28) 0.8268	0.00 (-0.05, 0.06)*0.9427	
	Other	35/ 178 (19.7)	29/ 153 (19.0)	1.04 (0.67, 1.61)*0.8708	1.04 (0.57, 1.90) 0.9011	0.01 (-0.08, 0.09)*0.8706	
	Geographic region						0.4541
	Asia	162/ 539 (30.1)	161/ 538 (29.9)	0.99 (0.84, 1.17) 0.9197	0.96 (0.72, 1.27) 0.7515	0.00 (-0.05, 0.06)*0.9629	
	Europe and Saudi Arabia	358/1365 (26.2)	353/1394 (25.3)	1.04 (0.93, 1.17) 0.4777	1.06 (0.89, 1.27) 0.5249	0.01 (-0.02, 0.04)*0.5872	
	North America	99/ 398 (24.9)	84/ 387 (21.7)	1.13 (0.88, 1.44) 0.3305	1.18 (0.84, 1.67) 0.3367	0.03 (-0.03, 0.09)*0.2931	
	Latin America	97/ 540 (18.0)	112/ 518 (21.6)	0.87 (0.70, 1.10) 0.2454	0.82 (0.60, 1.14) 0.2367	-0.04 (-0.08, 0.01)*0.1353	
	NYHA class at enrolment						0.2177
	II	541/2113 (25.6)	546/2187 (25.0)	1.04 (0.95, 1.15) 0.3698	1.05 (0.91, 1.21) 0.5133	0.01 (-0.02, 0.03)*0.6305	
	III or IV	175/ 729 (24.0)	164/ 649 (25.3)	0.92 (0.78, 1.09) 0.3599	0.90 (0.70, 1.17) 0.4489	-0.01 (-0.06, 0.03)*0.5869	
	LVEF at enrolment						0.4721
	<= 49	246/ 980 (25.1)	218/ 963 (22.6)	1.09 (0.93, 1.26) 0.2785	1.11 (0.90, 1.39) 0.3328	0.02 (-0.01, 0.06)*0.2024	
	50-59	269/1029 (26.1)	266/1017 (26.2)	1.00 (0.87, 1.14) 0.9969	1.01 (0.82, 1.25) 0.9180	-0.00 (-0.04, 0.04)*0.9945	
	>= 60	201/ 833 (24.1)	226/ 857 (26.4)	0.96 (0.82, 1.12) 0.6004	0.92 (0.73, 1.15) 0.4563	-0.02 (-0.06, 0.02)*0.2887	
	NT-proBNP at enrolment						0.4142
	<= median	353/1418 (24.9)	367/1421 (25.8)	0.98 (0.87, 1.10) 0.7531	0.96 (0.80, 1.15) 0.6447	-0.01 (-0.04, 0.02)*0.5679	
	> median	363/1424 (25.5)	343/1415 (24.2)	1.05 (0.93, 1.18) 0.3984	1.08 (0.90, 1.29) 0.4151	0.01 (-0.02, 0.04)*0.4405	
	Type 2 Diabetes Medical History						0.2679
	Yes	291/1250 (23.3)	311/1260 (24.7)	0.96 (0.84, 1.09) 0.5298	0.93 (0.77, 1.11)*0.4107	-0.01 (-0.05, 0.02)*0.4105	
	No	425/1592 (26.7)	399/1577 (25.3)	1.06 (0.95, 1.18) 0.3139	1.08 (0.92, 1.26)*0.3708	0.01 (-0.02, 0.04)*0.3707	
	Atrial fibrillation or flutter at enrolment ECG						0.5727
	Yes	324/1199 (27.0)	319/1199 (26.6)	1.05 (0.93, 1.18) 0.4740	1.06 (0.88, 1.29) 0.5226	0.00 (-0.03, 0.04)*0.8177	
	No	392/1643 (23.9)	391/1638 (23.9)	1.00 (0.89, 1.12) 0.9332	0.98 (0.83, 1.16) 0.8361	-0.00 (-0.03, 0.03)*0.9937	
	BMI (kg/m2) at enrolment						0.6122
	< 30	429/1571 (27.3)	421/1559 (27.0)	1.04 (0.93, 1.15) 0.5002	1.05 (0.89, 1.24) 0.5568	0.00 (-0.03, 0.03)*0.8489	
	>= 30	287/1270 (22.6)	289/1275 (22.7)	0.99 (0.86, 1.14) 0.8997	0.98 (0.80, 1.18) 0.8045	-0.00 (-0.03, 0.03)*0.9672	
	Baseline eGFR (mL/min/1.73m^2)						0.8155
	< 60	338/1359 (24.9)	342/1396 (24.5)	1.03 (0.91, 1.16) 0.6762	1.00 (0.84, 1.21) 0.9613	0.00 (-0.03, 0.04)*0.8206	
	>= 60	378/1483 (25.5)	368/1440 (25.6)	1.01 (0.90, 1.13) 0.9100	1.02 (0.86, 1.22) 0.7856	-0.00 (-0.03, 0.03)*0.9670	

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Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.1967
	<= median	377/1424 (26.5)	361/1439 (25.1)	1.07 (0.95, 1.20) 0.2515	1.10 (0.92, 1.31) 0.3160	0.01 (-0.02, 0.05)*0.3959	
	> median	339/1418 (23.9)	349/1398 (25.0)	0.96 (0.85, 1.08) 0.4966	0.94 (0.78, 1.12) 0.4844	-0.01 (-0.04, 0.02)*0.5138	
	LVEF at enrolment 2						0.2481
	<= 49	246/ 980 (25.1)	218/ 963 (22.6)	1.09 (0.93, 1.26) 0.2785	1.11 (0.90, 1.39) 0.3328	0.02 (-0.01, 0.06)*0.2024	
	>= 50	470/1862 (25.2)	492/1874 (26.3)	0.98 (0.89, 1.09) 0.7574	0.97 (0.83, 1.13) 0.6982	-0.01 (-0.04, 0.02)*0.4792	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4351
	Yes	61/ 283 (21.6)	68/ 286 (23.8)	0.91 (0.68, 1.20) 0.4964	0.84 (0.55, 1.27) 0.4014	-0.02 (-0.09, 0.05)*0.5267	
	No	655/2559 (25.6)	642/2551 (25.2)	1.03 (0.94, 1.12) 0.5422	1.04 (0.91, 1.18) 0.6102	0.00 (-0.02, 0.03)*0.7244	
	MRAs at baseline						0.5646
	Yes	315/1227 (25.7)	320/1224 (26.1)	0.99 (0.87, 1.12) 0.8252	0.96 (0.79, 1.16) 0.6824	-0.00 (-0.04, 0.03)*0.7900	
	No	401/1615 (24.8)	390/1613 (24.2)	1.04 (0.93, 1.16) 0.5032	1.05 (0.89, 1.25) 0.5431	0.01 (-0.02, 0.04)*0.6671	
	ACEi+ARB at baseline						0.9017
	Yes	500/2065 (24.2)	507/2077 (24.4)	1.01 (0.92, 1.12) 0.7778	0.99 (0.86, 1.16) 0.9434	-0.00 (-0.03, 0.02)*0.8824	
	No	216/ 777 (27.8)	203/ 760 (26.7)	1.03 (0.88, 1.20) 0.7290	1.07 (0.84, 1.35) 0.5931	0.01 (-0.03, 0.06)*0.6317	
	ARNI at baseline						0.6099
	Yes	45/ 153 (29.4)	37/ 126 (29.4)	0.92 (0.64, 1.32) 0.6569	0.94 (0.54, 1.61) 0.8120	0.00 (-0.11, 0.11)*0.9932	
	No	671/2689 (25.0)	673/2711 (24.8)	1.02 (0.94, 1.12) 0.6059	1.02 (0.90, 1.16) 0.7658	0.00 (-0.02, 0.02)*0.9129	
	Beta Blocker at baseline						0.6844
	Yes	610/2360 (25.8)	600/2356 (25.5)	1.02 (0.94, 1.12) 0.6062	1.02 (0.89, 1.18) 0.7349	0.00 (-0.02, 0.03)*0.7648	
	No	106/ 482 (22.0)	110/ 481 (22.9)	0.97 (0.78, 1.21) 0.8051	0.97 (0.70, 1.33) 0.8416	-0.01 (-0.06, 0.04)*0.7442	
	Diuretics at baseline						0.5068
	Yes	645/2536 (25.4)	643/2531 (25.4)	1.01 (0.92, 1.10) 0.8795	1.00 (0.88, 1.15) 0.9474	0.00 (-0.02, 0.02)*0.9812	
	No	71/ 306 (23.2)	67/ 306 (21.9)	1.12 (0.85, 1.47) 0.4151	1.13 (0.75, 1.69) 0.5632	0.01 (-0.05, 0.08)*0.6988	

N displays number of patients in the analysis, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	691/2842 (24.3)	828/2837 (29.2)	0.83 (0.77, 0.90) <.0001	0.76 (0.68, 0.86) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Age						0.8931
	<= median	315/1415 (22.3)	387/1482 (26.1)	0.84 (0.74, 0.95) 0.0053	0.78 (0.66, 0.93) 0.0061	-0.04 (-0.07, -0.01)*0.0153	
	> median	376/1427 (26.3)	441/1355 (32.5)	0.83 (0.74, 0.92) 0.0006	0.74 (0.62, 0.88) 0.0005	-0.06 (-0.10, -0.03)*0.0003	
	Gender						0.4610
	Male	405/1656 (24.5)	462/1625 (28.4)	0.86 (0.77, 0.95) 0.0052	0.80 (0.68, 0.94) 0.0060	-0.04 (-0.07, -0.01)*0.0098	
	Female	286/1186 (24.1)	366/1212 (30.2)	0.81 (0.71, 0.91) 0.0006	0.72 (0.60, 0.87) 0.0008	-0.06 (-0.10, -0.03)*0.0008	
	Race						0.1255
	White	513/2039 (25.2)	611/2058 (29.7)	0.86 (0.78, 0.94) 0.0016	0.79 (0.69, 0.92) 0.0018	-0.05 (-0.07, -0.02)*0.0011	
	Black or African	20/ 67 (29.9)	16/ 71 (22.5)	1.29 (0.76, 2.21) 0.3501	1.40 (0.63, 3.10) 0.4074	0.07 (-0.07, 0.22)*0.3276	
	Asian	133/ 558 (23.8)	168/ 555 (30.3)	0.77 (0.64, 0.94) 0.0094	0.70 (0.53, 0.92) 0.0091	-0.07 (-0.12, -0.02) 0.0078	
	Other	25/ 178 (14.0)	33/ 153 (21.6)	0.60 (0.39, 0.92) 0.0187	0.51 (0.27, 0.94) 0.0313	-0.08 (-0.16, 0.01)*0.0749	
	Geographic region						0.2564
	Asia	127/ 539 (23.6)	161/ 538 (29.9)	0.78 (0.64, 0.95) 0.0121	0.70 (0.54, 0.93) 0.0122	-0.06 (-0.12, -0.01) 0.0140	
	Europe and Saudi Arabia	345/1365 (25.3)	430/1394 (30.8)	0.84 (0.75, 0.94) 0.0020	0.76 (0.63, 0.90) 0.0017	-0.06 (-0.09, -0.02)*0.0011	
	North America	114/ 398 (28.6)	110/ 387 (28.4)	1.00 (0.81, 1.24) 0.9853	0.98 (0.71, 1.35) 0.9198	0.00 (-0.06, 0.07)*0.9457	
	Latin America	105/ 540 (19.4)	127/ 518 (24.5)	0.77 (0.63, 0.95) 0.0144	0.69 (0.51, 0.95) 0.0229	-0.05 (-0.10, -0.00)*0.0462	
	NYHA class at enrolment						0.3412
	II	522/2113 (24.7)	654/2187 (29.9)	0.81 (0.74, 0.89) <.0001	0.74 (0.64, 0.85) <.0001	-0.05 (-0.08, -0.03)*0.0001	
	III or IV	169/ 729 (23.2)	174/ 649 (26.8)	0.90 (0.76, 1.06) 0.2029	0.83 (0.64, 1.07) 0.1436	-0.04 (-0.08, 0.01)*0.1207	
	LVEF at enrolment						0.9151
	<= 49	235/ 980 (24.0)	266/ 963 (27.6)	0.86 (0.74, 0.99) 0.0380	0.79 (0.64, 0.98) 0.0282	-0.04 (-0.08, 0.00)*0.0664	
	50-59	266/1029 (25.9)	312/1017 (30.7)	0.82 (0.72, 0.94) 0.0035	0.77 (0.63, 0.94) 0.0105	-0.05 (-0.09, -0.01)*0.0152	
	>= 60	190/ 833 (22.8)	250/ 857 (29.2)	0.82 (0.70, 0.96) 0.0113	0.73 (0.58, 0.92) 0.0067	-0.06 (-0.11, -0.02)*0.0028	
	NT-proBNP at enrolment						0.1873
	<= median	352/1418 (24.8)	393/1421 (27.7)	0.88 (0.78, 0.99) 0.0363	0.85 (0.72, 1.01) 0.0652	-0.03 (-0.06, 0.00)*0.0861	
	> median	339/1424 (23.8)	435/1415 (30.7)	0.79 (0.71, 0.89) <.0001	0.68 (0.58, 0.81) <.0001	-0.07 (-0.10, -0.04)*<.0001	
	Type 2 Diabetes Medical History						0.4217
	Yes	306/1250 (24.5)	384/1260 (30.5)	0.81 (0.71, 0.91) 0.0005	0.74 (0.62, 0.88)*0.0008	-0.06 (-0.09, -0.03)*0.0007	
	No	385/1592 (24.2)	444/1577 (28.2)	0.86 (0.77, 0.96) 0.0094	0.81 (0.69, 0.95)*0.0110	-0.04 (-0.07, -0.01)*0.0109	
	Atrial fibrillation or flutter at enrolment ECG						0.6966
	Yes	284/1199 (23.7)	344/1199 (28.7)	0.82 (0.72, 0.93) 0.0018	0.74 (0.61, 0.90) 0.0020	-0.05 (-0.09, -0.01)*0.0052	
	No	407/1643 (24.8)	484/1638 (29.5)	0.84 (0.76, 0.94) 0.0020	0.78 (0.66, 0.91) 0.0021	-0.05 (-0.08, -0.02)*0.0021	
	BMI (kg/m2) at enrolment						0.7902
	< 30	392/1571 (25.0)	470/1559 (30.1)	0.83 (0.74, 0.92) 0.0007	0.75 (0.64, 0.88) 0.0005	-0.05 (-0.08, -0.02)*0.0011	
	>= 30	299/1270 (23.5)	356/1275 (27.9)	0.85 (0.75, 0.96) 0.0084	0.79 (0.65, 0.95) 0.0124	-0.04 (-0.08, -0.01)*0.0114	
	Baseline eGFR (mL/min/1.73m^2)						0.8950
	< 60	356/1359 (26.2)	440/1396 (31.5)	0.83 (0.74, 0.93) 0.0010	0.75 (0.63, 0.89) 0.0012	-0.05 (-0.09, -0.02)*0.0020	
	>= 60	335/1483 (22.6)	388/1440 (26.9)	0.84 (0.75, 0.95) 0.0055	0.78 (0.66, 0.93) 0.0051	-0.04 (-0.07, -0.01)*0.0063	

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Symptom Frequency (LOCF)	SBP at randomisation						0.8911
	<= median	358/1424 (25.1)	435/1439 (30.2)	0.84 (0.75, 0.94) 0.0025	0.78 (0.66, 0.92) 0.0037	-0.05 (-0.08, -0.02)*0.0023	
	> median	333/1418 (23.5)	393/1398 (28.1)	0.83 (0.74, 0.93) 0.0021	0.75 (0.63, 0.90) 0.0015	-0.05 (-0.08, -0.01)*0.0050	
	LVEF at enrolment 2						0.7049
	<= 49	235/ 980 (24.0)	266/ 963 (27.6)	0.86 (0.74, 0.99) 0.0380	0.79 (0.64, 0.98) 0.0282	-0.04 (-0.08, 0.00)*0.0664	
	>= 50	456/1862 (24.5)	562/1874 (30.0)	0.82 (0.75, 0.91) 0.0002	0.75 (0.65, 0.88) 0.0002	-0.05 (-0.08, -0.03)*0.0002	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6746
	Yes	57/ 283 (20.1)	61/ 286 (21.3)	0.85 (0.64, 1.13) 0.2641	0.72 (0.46, 1.13) 0.1519	-0.01 (-0.08, 0.05)*0.7268	
	No	634/2559 (24.8)	767/2551 (30.1)	0.83 (0.76, 0.90) <.0001	0.76 (0.67, 0.86) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	MRAs at baseline						0.6680
	Yes	299/1227 (24.4)	364/1224 (29.7)	0.81 (0.72, 0.92) 0.0012	0.74 (0.61, 0.89) 0.0015	-0.05 (-0.09, -0.02)*0.0027	
	No	392/1615 (24.3)	464/1613 (28.8)	0.85 (0.76, 0.95) 0.0032	0.78 (0.66, 0.92) 0.0027	-0.04 (-0.08, -0.01)*0.0038	
	ACEi+ARB at baseline						0.0737
	Yes	487/2065 (23.6)	621/2077 (29.9)	0.80 (0.72, 0.88) <.0001	0.71 (0.61, 0.82) <.0001	-0.06 (-0.09, -0.04)*<.0001	
	No	204/ 777 (26.3)	207/ 760 (27.2)	0.95 (0.81, 1.12) 0.5615	0.93 (0.74, 1.17) 0.5341	-0.01 (-0.05, 0.03)*0.6637	
	ARNI at baseline						0.1684
	Yes	38/ 153 (24.8)	25/ 126 (19.8)	1.17 (0.75, 1.83) 0.4936	1.25 (0.69, 2.24) 0.4616	0.05 (-0.05, 0.15)*0.3161	
	No	653/2689 (24.3)	803/2711 (29.6)	0.83 (0.76, 0.90) <.0001	0.75 (0.66, 0.85) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	Beta Blocker at baseline						0.1516
	Yes	584/2360 (24.7)	689/2356 (29.2)	0.86 (0.78, 0.94) 0.0008	0.79 (0.69, 0.91) 0.0007	-0.04 (-0.07, -0.02)*0.0005	
	No	107/ 482 (22.2)	139/ 481 (28.9)	0.72 (0.59, 0.89) 0.0022	0.63 (0.47, 0.86) 0.0034	-0.07 (-0.12, -0.01)*0.0168	
	Diuretics at baseline						0.1873
	Yes	635/2536 (25.0)	743/2531 (29.4)	0.85 (0.78, 0.92) 0.0002	0.78 (0.69, 0.89) 0.0002	-0.04 (-0.07, -0.02)*0.0005	
	No	56/ 306 (18.3)	85/ 306 (27.8)	0.70 (0.53, 0.93) 0.0129	0.61 (0.41, 0.91) 0.0152	-0.09 (-0.16, -0.03)*0.0051	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Social Limitation (LOCF)							
	Overall	829/2669 (31.1)	855/2664 (32.1)	0.96 (0.89, 1.03) 0.2861	0.95 (0.84, 1.07) 0.3708	-0.01 (-0.03, 0.01) 0.3264	
	Age						0.0640
	<= median	375/1352 (27.7)	435/1422 (30.6)	0.89 (0.79, 0.99) 0.0324	0.84 (0.71, 1.00) 0.0502	-0.03 (-0.06, 0.01)*0.0980	
	> median	454/1317 (34.5)	420/1242 (33.8)	1.03 (0.93, 1.14) 0.6301	1.05 (0.88, 1.24) 0.5976	0.01 (-0.03, 0.04) 0.7035	
	Gender						0.9651
	Male	485/1568 (30.9)	480/1518 (31.6)	0.96 (0.87, 1.06) 0.4212	0.95 (0.82, 1.12) 0.5640	-0.01 (-0.04, 0.03)*0.6796	
	Female	344/1101 (31.2)	375/1146 (32.7)	0.96 (0.86, 1.08) 0.5283	0.94 (0.78, 1.13) 0.5330	-0.01 (-0.05, 0.02) 0.4444	
	Race						0.6451
	White	632/1925 (32.8)	664/1952 (34.0)	0.97 (0.90, 1.06) 0.5351	0.97 (0.84, 1.11) 0.6207	-0.01 (-0.04, 0.02) 0.4259	
	Black or African	25/ 61 (41.0)	23/ 67 (34.3)	1.10 (0.73, 1.67) 0.6517	1.26 (0.59, 2.71) 0.5517	0.07 (-0.10, 0.23)*0.4370	
	Asian	133/ 510 (26.1)	140/ 500 (28.0)	0.90 (0.74, 1.11) 0.3296	0.88 (0.66, 1.16) 0.3656	-0.02 (-0.07, 0.04) 0.5598	
	Other	39/ 173 (22.5)	28/ 145 (19.3)	1.08 (0.72, 1.62) 0.7047	1.06 (0.59, 1.89) 0.8450	0.03 (-0.06, 0.12)*0.4788	
	Geographic region						0.7726
	Asia	125/ 496 (25.2)	132/ 486 (27.2)	0.90 (0.73, 1.11) 0.3420	0.88 (0.66, 1.17) 0.3758	-0.02 (-0.07, 0.04) 0.5523	
	Europe and Saudi Arabia	435/1299 (33.5)	454/1323 (34.3)	1.00 (0.90, 1.10) 0.9613	1.00 (0.84, 1.18) 0.9780	-0.01 (-0.04, 0.03)*0.6540	
	North America	136/ 372 (36.6)	131/ 359 (36.5)	0.98 (0.82, 1.18) 0.8497	0.96 (0.71, 1.32) 0.8175	-0.01 (-0.07, 0.06) 0.8354	
	Latin America	133/ 502 (26.5)	138/ 496 (27.8)	0.93 (0.77, 1.12) 0.4310	0.92 (0.68, 1.23) 0.5581	-0.01 (-0.07, 0.04)*0.6370	
	NYHA class at enrolment						0.6333
	II	605/1986 (30.5)	637/2059 (30.9)	0.96 (0.88, 1.05) 0.4048	0.96 (0.84, 1.10) 0.5564	-0.00 (-0.03, 0.02)*0.7438	
	III or IV	224/ 683 (32.8)	217/ 604 (35.9)	0.93 (0.81, 1.06) 0.2676	0.85 (0.66, 1.08) 0.1867	-0.03 (-0.08, 0.02)*0.2380	
	LVEF at enrolment						0.4525
	<= 49	282/ 928 (30.4)	260/ 912 (28.5)	1.03 (0.90, 1.18) 0.7034	1.04 (0.85, 1.28) 0.6859	0.00 (-0.04, 0.04) 0.9231	
	50-59	321/ 970 (33.1)	347/ 956 (36.3)	0.92 (0.82, 1.03) 0.1508	0.89 (0.73, 1.09) 0.2582	-0.03 (-0.07, 0.01)*0.1395	
	>= 60	226/ 771 (29.3)	248/ 796 (31.2)	0.95 (0.82, 1.09) 0.4651	0.91 (0.73, 1.14) 0.4249	-0.01 (-0.05, 0.03) 0.5535	
	NT-proBNP at enrolment						0.4379
	<= median	425/1334 (31.9)	426/1350 (31.6)	0.99 (0.89, 1.10) 0.8402	1.00 (0.85, 1.19) 0.9718	0.01 (-0.03, 0.04) 0.7539	
	> median	404/1335 (30.3)	429/1313 (32.7)	0.93 (0.84, 1.04) 0.1885	0.89 (0.75, 1.06) 0.1863	-0.02 (-0.06, 0.01) 0.1359	
	Type 2 Diabetes Medical History						0.9550
	Yes	362/1169 (31.0)	380/1186 (32.0)	0.96 (0.86, 1.07) 0.4706	0.95 (0.80, 1.13)*0.5749	-0.01 (-0.04, 0.02) 0.5450	
	No	467/1500 (31.1)	475/1478 (32.1)	0.96 (0.87, 1.06) 0.4565	0.95 (0.82, 1.11)*0.5556	-0.01 (-0.04, 0.02)*0.5555	
	Atrial fibrillation or flutter at enrolment ECG						0.8532
	Yes	329/1113 (29.6)	345/1123 (30.7)	0.97 (0.86, 1.09) 0.5782	0.94 (0.78, 1.14) 0.5287	-0.02 (-0.06, 0.01) 0.2448	
	No	500/1556 (32.1)	510/1541 (33.1)	0.95 (0.86, 1.05) 0.3121	0.95 (0.81, 1.11) 0.5098	-0.00 (-0.03, 0.03) 0.7577	
	BMI (kg/m2) at enrolment						0.1547
	< 30	440/1478 (29.8)	469/1451 (32.3)	0.91 (0.82, 1.01) 0.0856	0.88 (0.75, 1.03) 0.1131	-0.03 (-0.06, 0.01)*0.1354	
	>= 30	388/1190 (32.6)	386/1211 (31.9)	1.02 (0.91, 1.14) 0.7357	1.04 (0.87, 1.24) 0.6989	0.00 (-0.03, 0.04) 0.7940	
	Baseline eGFR (mL/min/1.73m^2)						0.7053
	< 60	424/1266 (33.5)	442/1297 (34.1)	0.98 (0.88, 1.08) 0.6684	0.96 (0.81, 1.14) 0.6799	-0.01 (-0.05, 0.02) 0.4227	
	>= 60	405/1403 (28.9)	412/1366 (30.2)	0.95 (0.85, 1.06) 0.3245	0.94 (0.79, 1.11) 0.4535	-0.01 (-0.05, 0.02)*0.4553	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)	SBP at randomisation						0.6205
	<= median	416/1344 (31.0)	423/1344 (31.5)	0.98 (0.88, 1.09) 0.6951	0.99 (0.84, 1.18) 0.9487	-0.00 (-0.03, 0.03) 0.9907	
	> median	413/1325 (31.2)	432/1320 (32.7)	0.94 (0.85, 1.05) 0.2664	0.90 (0.76, 1.07) 0.2235	-0.02 (-0.05, 0.02)*0.3903	
	LVEF at enrolment 2						0.2384
	<= 49	282/ 928 (30.4)	260/ 912 (28.5)	1.03 (0.90, 1.18) 0.7034	1.04 (0.85, 1.28) 0.6859	0.00 (-0.04, 0.04) 0.9231	
	>= 50	547/1741 (31.4)	595/1752 (34.0)	0.93 (0.85, 1.02) 0.1265	0.90 (0.78, 1.05) 0.1755	-0.02 (-0.05, 0.01) 0.2570	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4392
	Yes	80/ 257 (31.1)	77/ 261 (29.5)	1.06 (0.83, 1.34) 0.6543	1.07 (0.71, 1.59) 0.7529	0.01 (-0.06, 0.09) 0.7038	
	No	749/2412 (31.1)	778/2403 (32.4)	0.95 (0.88, 1.03) 0.2209	0.94 (0.83, 1.06) 0.3043	-0.01 (-0.04, 0.01) 0.2686	
	MRAs at baseline						0.5439
	Yes	354/1155 (30.6)	366/1146 (31.9)	0.94 (0.84, 1.05) 0.2845	0.92 (0.77, 1.11) 0.3912	-0.01 (-0.05, 0.02) 0.3997	
	No	475/1514 (31.4)	489/1518 (32.2)	0.98 (0.89, 1.08) 0.6799	0.97 (0.83, 1.13) 0.6895	-0.01 (-0.04, 0.02)*0.6196	
	ACEi+ARB at baseline						0.6884
	Yes	591/1940 (30.5)	628/1959 (32.1)	0.95 (0.87, 1.04) 0.2526	0.92 (0.80, 1.06) 0.2716	-0.02 (-0.05, 0.01)*0.2832	
	No	238/ 729 (32.6)	227/ 705 (32.2)	0.99 (0.86, 1.15) 0.9259	1.01 (0.81, 1.27) 0.9280	0.00 (-0.04, 0.05) 0.8633	
	ARNI at baseline						0.9029
	Yes	47/ 149 (31.5)	36/ 116 (31.0)	1.04 (0.73, 1.49) 0.8173	1.07 (0.62, 1.82) 0.8148	0.01 (-0.10, 0.12) 0.8784	
	No	782/2520 (31.0)	819/2548 (32.1)	0.96 (0.89, 1.04) 0.2929	0.95 (0.84, 1.07) 0.3779	-0.01 (-0.03, 0.01) 0.3557	
	Beta Blocker at baseline						0.5457
	Yes	701/2232 (31.4)	720/2218 (32.5)	0.97 (0.89, 1.05) 0.4663	0.96 (0.84, 1.09) 0.5206	-0.01 (-0.03, 0.02) 0.4556	
	No	128/ 437 (29.3)	135/ 446 (30.3)	0.92 (0.75, 1.11) 0.3740	0.90 (0.67, 1.21) 0.4756	-0.02 (-0.08, 0.04) 0.5027	
	Diuretics at baseline						0.1500
	Yes	748/2391 (31.3)	781/2379 (32.8)	0.94 (0.87, 1.02) 0.1224	0.91 (0.81, 1.04) 0.1665	-0.02 (-0.04, 0.01)*0.2529	
	No	81/ 278 (29.1)	74/ 285 (26.0)	1.15 (0.89, 1.50) 0.2918	1.24 (0.85, 1.80) 0.2713	0.05 (-0.02, 0.12) 0.1894	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)							
	Overall	647/2842 (22.8)	648/2837 (22.8)	1.05 (1.00, 1.11) 0.0623	1.06 (0.91, 1.24) 0.4515	-0.00 (-0.02, 0.02)*0.9460	
	Age						0.7435
	<= median	311/1415 (22.0)	328/1482 (22.1)	1.06 (0.98, 1.14) 0.1254	1.03 (0.83, 1.29) 0.7609	-0.00 (-0.03, 0.03)*0.9207	
	> median	336/1427 (23.5)	320/1355 (23.6)	1.04 (0.97, 1.11) 0.3154	1.07 (0.86, 1.33) 0.5458	-0.00 (-0.03, 0.03)*0.9652	
	Gender						0.3560
	Male	386/1656 (23.3)	374/1625 (23.0)	1.07 (1.00, 1.15) 0.0375	1.13 (0.92, 1.39) 0.2556	0.00 (-0.03, 0.03)*0.8419	
	Female	261/1186 (22.0)	274/1212 (22.6)	1.01 (0.93, 1.10) 0.7691	0.99 (0.78, 1.25) 0.9200	-0.01 (-0.04, 0.03)*0.7239	
	Race						0.5838*
	White	456/2039 (22.4)	476/2058 (23.1)	1.04 (0.98, 1.10) 0.2304	1.05 (0.87, 1.26) 0.6147	-0.01 (-0.03, 0.02)*0.5590	
	Black or African	17/ 67 (25.4)	15/ 71 (21.1)	1.20 (0.65, 2.21)*0.5554	1.75 (0.66, 4.64) 0.2575	0.04 (-0.10, 0.18)*0.5549	
	Asian	150/ 558 (26.9)	134/ 555 (24.1)	1.06 (0.93, 1.20) 0.4182	1.14 (0.82, 1.58) 0.4495	0.03 (-0.02, 0.08)*0.2946	
	Other	24/ 178 (13.5)	23/ 153 (15.0)	0.90 (0.53, 1.52)*0.6872	0.73 (0.33, 1.62) 0.4455	-0.02 (-0.09, 0.06)*0.6881	
	Geographic region						0.6463
	Asia	143/ 539 (26.5)	130/ 538 (24.2)	1.05 (0.93, 1.20) 0.4225	1.12 (0.80, 1.57) 0.4956	0.02 (-0.03, 0.08)*0.3717	
	Europe and Saudi Arabia	285/1365 (20.9)	312/1394 (22.4)	1.02 (0.94, 1.10) 0.6446	0.91 (0.73, 1.15) 0.4456	-0.02 (-0.05, 0.02)*0.3377	
	North America	95/ 398 (23.9)	96/ 387 (24.8)	1.09 (0.93, 1.26) 0.2914	1.21 (0.82, 1.79) 0.3452	-0.01 (-0.07, 0.05)*0.7598	
	Latin America	124/ 540 (23.0)	110/ 518 (21.2)	1.11 (1.00, 1.24) 0.0556	1.25 (0.86, 1.82) 0.2511	0.02 (-0.03, 0.07)*0.4982	
	NYHA class at enrolment						0.7946
	II	461/2113 (21.8)	470/2187 (21.5)	1.05 (0.99, 1.12) 0.1192	1.06 (0.88, 1.26) 0.5561	0.00 (-0.02, 0.03)*0.7949	
	III or IV	186/ 729 (25.5)	178/ 649 (27.4)	1.04 (0.96, 1.13) 0.3466	1.03 (0.76, 1.40) 0.8279	-0.02 (-0.07, 0.03)*0.4221	
	LVEF at enrolment						0.4233
	<= 49	214/ 980 (21.8)	223/ 963 (23.2)	1.02 (0.92, 1.12) 0.7563	0.90 (0.69, 1.18) 0.4402	-0.01 (-0.05, 0.02)*0.4860	
	50-59	241/1029 (23.4)	244/1017 (24.0)	1.05 (0.97, 1.13) 0.2189	1.08 (0.84, 1.39) 0.5567	-0.01 (-0.04, 0.03)*0.7613	
	>= 60	192/ 833 (23.0)	181/ 857 (21.1)	1.10 (1.00, 1.22) 0.0583	1.25 (0.94, 1.67) 0.1216	0.02 (-0.02, 0.06)*0.3392	
	NT-proBNP at enrolment						0.8143
	<= median	317/1418 (22.4)	303/1421 (21.3)	1.04 (0.97, 1.12) 0.2766	1.11 (0.89, 1.38) 0.3531	0.01 (-0.02, 0.04)*0.5056	
	> median	330/1424 (23.2)	345/1415 (24.4)	1.06 (0.98, 1.14) 0.1354	1.02 (0.82, 1.26) 0.8911	-0.01 (-0.04, 0.02)*0.4498	
	Type 2 Diabetes Medical History						0.0346
	Yes	311/1250 (24.9)	285/1260 (22.6)	1.10 (1.03, 1.19) 0.0085	1.13 (0.94, 1.36)*0.1833	0.02 (-0.01, 0.06)*0.1831	
	No	336/1592 (21.1)	363/1577 (23.0)	0.98 (0.91, 1.06) 0.6748	0.89 (0.76, 1.06)*0.1942	-0.02 (-0.05, 0.01)*0.1941	
	Atrial fibrillation or flutter at enrolment ECG						0.8283
	Yes	274/1199 (22.9)	274/1199 (22.9)	1.04 (0.97, 1.12) 0.2553	1.08 (0.85, 1.38) 0.5380	0.00 (-0.03, 0.03)*1.0000	
	No	373/1643 (22.7)	374/1638 (22.8)	1.06 (0.99, 1.14) 0.0929	1.05 (0.86, 1.28) 0.6658	-0.00 (-0.03, 0.03)*0.9291	
	BMI (kg/m2) at enrolment						0.3336
	< 30	362/1571 (23.0)	366/1559 (23.5)	1.03 (0.96, 1.11) 0.4154	1.03 (0.84, 1.26) 0.7853	-0.00 (-0.03, 0.03)*0.7739	
	>= 30	285/1270 (22.4)	282/1275 (22.1)	1.08 (1.01, 1.16) 0.0296	1.10 (0.87, 1.40) 0.4080	0.00 (-0.03, 0.04)*0.8446	
	Baseline eGFR (mL/min/1.73m^2)						0.1012
	< 60	352/1359 (25.9)	331/1396 (23.7)	1.10 (1.02, 1.18) 0.0141	1.25 (1.01, 1.55) 0.0380	0.02 (-0.01, 0.05)*0.1831	
	>= 60	295/1483 (19.9)	317/1440 (22.0)	1.01 (0.93, 1.09) 0.8560	0.89 (0.71, 1.12) 0.3218	-0.02 (-0.05, 0.01)*0.1587	

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Symptom Stability (LOCF)	SBP at randomisation						0.1353
	<= median	363/1424 (25.5)	350/1439 (24.3)	1.09 (1.02, 1.16) 0.0084	1.18 (0.96, 1.46) 0.1169	0.01 (-0.02, 0.04)*0.4695	
	> median	284/1418 (20.0)	298/1398 (21.3)	1.00 (0.92, 1.09) 0.9619	0.94 (0.75, 1.18) 0.5795	-0.01 (-0.04, 0.02)*0.3987	
	LVEF at enrolment 2						0.3048
	<= 49	214/ 980 (21.8)	223/ 963 (23.2)	1.02 (0.92, 1.12) 0.7563	0.90 (0.69, 1.18) 0.4402	-0.01 (-0.05, 0.02)*0.4860	
	>= 50	433/1862 (23.3)	425/1874 (22.7)	1.07 (1.01, 1.14) 0.0290	1.15 (0.95, 1.39) 0.1442	0.01 (-0.02, 0.03)*0.6757	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0604
	Yes	104/ 283 (36.7)	96/ 286 (33.6)	1.17 (1.03, 1.34) 0.0179	1.32 (0.84, 2.06) 0.2317	0.03 (-0.05, 0.11)*0.4264	
	No	543/2559 (21.2)	552/2551 (21.6)	1.02 (0.97, 1.08) 0.4396	1.03 (0.88, 1.22) 0.6943	-0.00 (-0.03, 0.02)*0.7149	
	MRAs at baseline						0.6425
	Yes	289/1227 (23.6)	288/1224 (23.5)	1.04 (0.95, 1.14) 0.3694	0.99 (0.79, 1.24) 0.9230	0.00 (-0.03, 0.03)*0.9888	
	No	358/1615 (22.2)	360/1613 (22.3)	1.06 (1.01, 1.13) 0.0319	1.13 (0.92, 1.40) 0.2467	-0.00 (-0.03, 0.03)*0.9176	
	ACEi+ARB at baseline						0.6162
	Yes	458/2065 (22.2)	464/2077 (22.3)	1.04 (0.97, 1.10) 0.2631	1.02 (0.85, 1.23) 0.8283	-0.00 (-0.03, 0.02)*0.9010	
	No	189/ 777 (24.3)	184/ 760 (24.2)	1.08 (0.98, 1.19) 0.1030	1.15 (0.87, 1.53) 0.3324	0.00 (-0.04, 0.04)*0.9585	
	ARNI at baseline						0.2182
	Yes	38/ 153 (24.8)	34/ 126 (27.0)	0.92 (0.62, 1.37)*0.6831	0.73 (0.38, 1.43) 0.3611	-0.02 (-0.12, 0.08)*0.6840	
	No	609/2689 (22.6)	614/2711 (22.6)	1.06 (1.01, 1.12) 0.0285	1.08 (0.93, 1.27) 0.3161	-0.00 (-0.02, 0.02)*0.9995	
	Beta Blocker at baseline						0.6504
	Yes	528/2360 (22.4)	529/2356 (22.5)	1.06 (0.99, 1.12) 0.0746	1.11 (0.93, 1.32) 0.2355	-0.00 (-0.02, 0.02)*0.9472	
	No	119/ 482 (24.7)	119/ 481 (24.7)	1.03 (0.93, 1.14) 0.5572	0.86 (0.60, 1.24) 0.4278	-0.00 (-0.06, 0.05)*0.9853	
	Diuretics at baseline						0.9074
	Yes	587/2536 (23.1)	585/2531 (23.1)	1.05 (1.00, 1.10) 0.0727	1.07 (0.91, 1.26) 0.4280	0.00 (-0.02, 0.02)*0.9776	
	No	60/ 306 (19.6)	63/ 306 (20.6)	0.95 (0.69, 1.31)*0.7622	0.99 (0.61, 1.60) 0.9652	-0.01 (-0.07, 0.05)*0.7622	

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Total Symptom Score (LOCF)							
	Overall	705/2842 (24.8)	809/2837 (28.5)	0.87 (0.80, 0.94) 0.0009	0.82 (0.72, 0.92) 0.0013	-0.04 (-0.06, -0.01)*0.0016	
	Age						0.4073
	<= median	304/1415 (21.5)	376/1482 (25.4)	0.83 (0.73, 0.95) 0.0052	0.78 (0.65, 0.93) 0.0062	-0.04 (-0.07, -0.01)*0.0134	
	> median	401/1427 (28.1)	433/1355 (32.0)	0.89 (0.80, 1.00) 0.0402	0.84 (0.71, 1.00) 0.0496	-0.04 (-0.07, -0.00)*0.0266	
	Gender						0.6551
	Male	403/1656 (24.3)	462/1625 (28.4)	0.85 (0.77, 0.95) 0.0054	0.80 (0.68, 0.94) 0.0069	-0.04 (-0.07, -0.01)*0.0077	
	Female	302/1186 (25.5)	347/1212 (28.6)	0.89 (0.79, 1.01) 0.0634	0.85 (0.70, 1.02) 0.0822	-0.03 (-0.07, 0.00)*0.0807	
	Race						0.4497
	White	525/2039 (25.7)	609/2058 (29.6)	0.88 (0.80, 0.96) 0.0065	0.83 (0.72, 0.96) 0.0100	-0.04 (-0.07, -0.01)*0.0059	
	Black or African	19/ 67 (28.4)	15/ 71 (21.1)	1.28 (0.72, 2.26) 0.4004	1.44 (0.65, 3.23) 0.3714	0.07 (-0.07, 0.22)*0.3241	
	Asian	136/ 558 (24.4)	155/ 555 (27.9)	0.86 (0.71, 1.05) 0.1373	0.81 (0.62, 1.07) 0.1355	-0.04 (-0.09, 0.01) 0.1300	
	Other	25/ 178 (14.0)	30/ 153 (19.6)	0.72 (0.46, 1.14) 0.1578	0.63 (0.34, 1.17) 0.1471	-0.06 (-0.14, 0.03)*0.1784	
	Geographic region						0.9785
	Asia	130/ 539 (24.1)	148/ 538 (27.5)	0.87 (0.71, 1.06) 0.1648	0.82 (0.63, 1.09) 0.1698	-0.03 (-0.09, 0.02) 0.1910	
	Europe and Saudi Arabia	356/1365 (26.1)	417/1394 (29.9)	0.89 (0.79, 0.99) 0.0359	0.83 (0.70, 0.99) 0.0413	-0.04 (-0.07, -0.00)*0.0248	
	North America	109/ 398 (27.4)	121/ 387 (31.3)	0.87 (0.71, 1.07) 0.1952	0.81 (0.59, 1.11) 0.1955	-0.04 (-0.10, 0.02)*0.2323	
	Latin America	110/ 540 (20.4)	123/ 518 (23.7)	0.84 (0.68, 1.04) 0.1036	0.79 (0.58, 1.07) 0.1292	-0.03 (-0.08, 0.02)*0.1856	
	NYHA class at enrolment						0.6165
	II	532/2113 (25.2)	636/2187 (29.1)	0.85 (0.78, 0.94) 0.0011	0.80 (0.69, 0.92) 0.0013	-0.04 (-0.07, -0.01)*0.0040	
	III or IV	173/ 729 (23.7)	173/ 649 (26.7)	0.90 (0.76, 1.07) 0.2202	0.86 (0.67, 1.11) 0.2531	-0.03 (-0.08, 0.02)*0.2121	
	LVEF at enrolment						0.5384
	<= 49	239/ 980 (24.4)	253/ 963 (26.3)	0.92 (0.79, 1.06) 0.2454	0.87 (0.71, 1.08) 0.2126	-0.02 (-0.06, 0.02)*0.3396	
	50-59	273/1029 (26.5)	303/1017 (29.8)	0.88 (0.77, 1.00) 0.0470	0.84 (0.69, 1.03) 0.0866	-0.03 (-0.07, 0.01)*0.1007	
	>= 60	193/ 833 (23.2)	253/ 857 (29.5)	0.81 (0.70, 0.95) 0.0087	0.74 (0.59, 0.93) 0.0085	-0.06 (-0.11, -0.02)*0.0029	
	NT-proBNP at enrolment						0.5233
	<= median	360/1418 (25.4)	396/1421 (27.9)	0.89 (0.79, 1.01) 0.0614	0.87 (0.73, 1.03) 0.1083	-0.02 (-0.06, 0.01)*0.1348	
	> median	345/1424 (24.2)	413/1415 (29.2)	0.85 (0.76, 0.95) 0.0056	0.77 (0.65, 0.92) 0.0033	-0.05 (-0.08, -0.02)*0.0028	
	Type 2 Diabetes Medical History						0.2986
	Yes	316/1250 (25.3)	384/1260 (30.5)	0.83 (0.74, 0.94) 0.0026	0.77 (0.65, 0.92)*0.0037	-0.05 (-0.09, -0.02)*0.0036	
	No	389/1592 (24.4)	425/1577 (26.9)	0.91 (0.81, 1.02) 0.0960	0.88 (0.75, 1.03)*0.1053	-0.03 (-0.06, 0.01)*0.1051	
	Atrial fibrillation or flutter at enrolment ECG						0.8413
	Yes	283/1199 (23.6)	319/1199 (26.6)	0.88 (0.77, 1.00) 0.0523	0.84 (0.69, 1.01) 0.0689	-0.03 (-0.06, 0.00)*0.0898	
	No	422/1643 (25.7)	490/1638 (29.9)	0.86 (0.78, 0.96) 0.0064	0.80 (0.69, 0.94) 0.0070	-0.04 (-0.07, -0.01)*0.0068	
	BMI (kg/m2) at enrolment						0.8551
	< 30	391/1571 (24.9)	448/1559 (28.7)	0.87 (0.77, 0.97) 0.0118	0.81 (0.69, 0.95) 0.0117	-0.04 (-0.07, -0.01)*0.0150	
	>= 30	314/1270 (24.7)	359/1275 (28.2)	0.88 (0.78, 0.99) 0.0358	0.84 (0.70, 1.01) 0.0576	-0.03 (-0.07, -0.00)*0.0494	
	Baseline eGFR (mL/min/1.73m^2)						0.3361
	< 60	375/1359 (27.6)	425/1396 (30.4)	0.91 (0.81, 1.01) 0.0778	0.86 (0.73, 1.03) 0.0939	-0.03 (-0.06, 0.01)*0.0991	
	>= 60	330/1483 (22.3)	384/1440 (26.7)	0.84 (0.74, 0.95) 0.0046	0.78 (0.65, 0.93) 0.0051	-0.04 (-0.08, -0.01)*0.0055	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.3922
	<= median	350/1424 (24.6)	428/1439 (29.7)	0.84 (0.75, 0.94) 0.0031	0.78 (0.66, 0.93) 0.0046	-0.05 (-0.08, -0.02)*0.0019	
	> median	355/1418 (25.0)	381/1398 (27.3)	0.90 (0.80, 1.02) 0.0896	0.86 (0.72, 1.02) 0.0919	-0.02 (-0.05, 0.01)*0.1804	
	LVEF at enrolment 2						0.4179
	<= 49	239/ 980 (24.4)	253/ 963 (26.3)	0.92 (0.79, 1.06) 0.2454	0.87 (0.71, 1.08) 0.2126	-0.02 (-0.06, 0.02)*0.3396	
	>= 50	466/1862 (25.0)	556/1874 (29.7)	0.85 (0.77, 0.94) 0.0013	0.80 (0.68, 0.92) 0.0027	-0.05 (-0.07, -0.02)*0.0014	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6123
	Yes	58/ 283 (20.5)	59/ 286 (20.6)	0.90 (0.67, 1.21) 0.4936	0.83 (0.54, 1.30) 0.4180	-0.00 (-0.07, 0.07)*0.9683	
	No	647/2559 (25.3)	750/2551 (29.4)	0.86 (0.79, 0.94) 0.0009	0.81 (0.72, 0.92) 0.0014	-0.04 (-0.07, -0.02)*0.0010	
	MRAs at baseline						0.6206
	Yes	301/1227 (24.5)	354/1224 (28.9)	0.85 (0.75, 0.96) 0.0104	0.79 (0.66, 0.95) 0.0137	-0.04 (-0.08, -0.01)*0.0139	
	No	404/1615 (25.0)	455/1613 (28.2)	0.89 (0.79, 0.99) 0.0293	0.84 (0.71, 0.99) 0.0327	-0.03 (-0.06, -0.00)*0.0400	
	ACEi+ARB at baseline						0.0153
	Yes	486/2065 (23.5)	606/2077 (29.2)	0.82 (0.74, 0.90) <.0001	0.74 (0.64, 0.86) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	No	219/ 777 (28.2)	203/ 760 (26.7)	1.04 (0.89, 1.22) 0.6408	1.06 (0.85, 1.33) 0.6014	0.00 (-0.04, 0.05) 0.8273	
	ARNI at baseline						0.0529
	Yes	42/ 153 (27.5)	24/ 126 (19.0)	1.33 (0.85, 2.09) 0.2086	1.48 (0.83, 2.65) 0.1857	0.08 (-0.01, 0.18)*0.0945	
	No	663/2689 (24.7)	785/2711 (29.0)	0.86 (0.79, 0.93) 0.0003	0.80 (0.71, 0.91) 0.0005	-0.04 (-0.07, -0.02)*0.0004	
	Beta Blocker at baseline						0.4238
	Yes	595/2360 (25.2)	678/2356 (28.8)	0.88 (0.81, 0.97) 0.0071	0.84 (0.73, 0.96) 0.0096	-0.04 (-0.06, -0.01)*0.0058	
	No	110/ 482 (22.8)	131/ 481 (27.2)	0.81 (0.65, 1.00) 0.0452	0.73 (0.54, 0.99) 0.0427	-0.04 (-0.10, 0.01)*0.1135	
	Diuretics at baseline						0.0741
	Yes	651/2536 (25.7)	724/2531 (28.6)	0.89 (0.82, 0.97) 0.0083	0.85 (0.74, 0.96) 0.0110	-0.03 (-0.05, -0.00)*0.0188	
	No	54/ 306 (17.6)	85/ 306 (27.8)	0.69 (0.52, 0.92) 0.0106	0.58 (0.39, 0.87) 0.0087	-0.10 (-0.17, -0.04)*0.0026	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	685/2842 (24.1)	809/2837 (28.5)	0.85 (0.78, 0.92) 0.0001	0.79 (0.70, 0.90) 0.0002	-0.04 (-0.07, -0.02)*0.0002	
	Age						0.5342
	<= median	299/1415 (21.1)	376/1482 (25.4)	0.82 (0.72, 0.93) 0.0026	0.77 (0.64, 0.92) 0.0034	-0.04 (-0.07, -0.01)*0.0068	
	> median	386/1427 (27.0)	433/1355 (32.0)	0.87 (0.78, 0.97) 0.0102	0.81 (0.68, 0.96) 0.0128	-0.05 (-0.08, -0.02)*0.0045	
	Gender						0.8216
	Male	406/1656 (24.5)	467/1625 (28.7)	0.85 (0.76, 0.95) 0.0052	0.80 (0.68, 0.94) 0.0066	-0.04 (-0.07, -0.01)*0.0062	
	Female	279/1186 (23.5)	342/1212 (28.2)	0.84 (0.74, 0.96) 0.0084	0.79 (0.65, 0.95) 0.0131	-0.05 (-0.08, -0.01)*0.0086	
	Race						0.3068
	White	500/2039 (24.5)	604/2058 (29.3)	0.84 (0.77, 0.93) 0.0005	0.79 (0.68, 0.91) 0.0011	-0.05 (-0.08, -0.02)*0.0005	
	Black or African	23/ 67 (34.3)	20/ 71 (28.2)	1.28 (0.79, 2.07) 0.3180	1.31 (0.63, 2.75) 0.4719	0.02 (-0.14, 0.17) 0.8481	
	Asian	136/ 558 (24.4)	161/ 555 (29.0)	0.84 (0.69, 1.02) 0.0728	0.78 (0.60, 1.02) 0.0747	-0.05 (-0.10, 0.01) 0.0798	
	Other	26/ 178 (14.6)	24/ 153 (15.7)	0.94 (0.59, 1.51) 0.8050	0.90 (0.47, 1.71) 0.7500	-0.01 (-0.09, 0.07)*0.7850	
	Geographic region						0.8277
	Asia	129/ 539 (23.9)	155/ 538 (28.8)	0.83 (0.68, 1.01) 0.0646	0.78 (0.59, 1.02) 0.0678	-0.05 (-0.10, 0.01) 0.0798	
	Europe and Saudi Arabia	332/1365 (24.3)	413/1394 (29.6)	0.83 (0.74, 0.94) 0.0021	0.77 (0.64, 0.92) 0.0035	-0.05 (-0.09, -0.02)*0.0017	
	North America	116/ 398 (29.1)	127/ 387 (32.8)	0.90 (0.73, 1.10) 0.3016	0.84 (0.62, 1.14) 0.2680	-0.04 (-0.10, 0.02) 0.2219	
	Latin America	108/ 540 (20.0)	114/ 518 (22.0)	0.90 (0.72, 1.11) 0.3226	0.86 (0.63, 1.17) 0.3334	-0.02 (-0.07, 0.03)*0.4229	
	NYHA class at enrolment						0.8986
	II	523/2113 (24.8)	636/2187 (29.1)	0.84 (0.77, 0.93) 0.0005	0.79 (0.69, 0.90) 0.0007	-0.04 (-0.07, -0.02)*0.0013	
	III or IV	162/ 729 (22.2)	173/ 649 (26.7)	0.85 (0.72, 1.02) 0.0793	0.80 (0.62, 1.03) 0.0811	-0.04 (-0.09, 0.00)*0.0560	
	LVEF at enrolment						0.8724
	<= 49	232/ 980 (23.7)	261/ 963 (27.1)	0.86 (0.74, 1.00) 0.0447	0.80 (0.65, 0.99) 0.0404	-0.03 (-0.07, 0.00)*0.0823	
	50-59	263/1029 (25.6)	312/1017 (30.7)	0.82 (0.72, 0.94) 0.0035	0.77 (0.63, 0.95) 0.0121	-0.05 (-0.09, -0.01)*0.0099	
	>= 60	190/ 833 (22.8)	236/ 857 (27.5)	0.87 (0.74, 1.02) 0.0778	0.81 (0.64, 1.01) 0.0643	-0.05 (-0.09, -0.01)*0.0249	
	NT-proBNP at enrolment						0.3677
	<= median	351/1418 (24.8)	395/1421 (27.8)	0.88 (0.78, 0.99) 0.0400	0.85 (0.72, 1.01) 0.0594	-0.03 (-0.06, 0.00)*0.0652	
	> median	334/1424 (23.5)	414/1415 (29.3)	0.82 (0.73, 0.92) 0.0009	0.74 (0.62, 0.88) 0.0008	-0.06 (-0.09, -0.03)*0.0004	
	Type 2 Diabetes Medical History						0.2001
	Yes	295/1250 (23.6)	372/1260 (29.5)	0.80 (0.70, 0.91) 0.0005	0.74 (0.62, 0.88)*0.0008	-0.06 (-0.09, -0.02)*0.0008	
	No	390/1592 (24.5)	437/1577 (27.7)	0.89 (0.80, 1.00) 0.0495	0.85 (0.72, 0.99)*0.0395	-0.03 (-0.06, -0.00)*0.0394	
	Atrial fibrillation or flutter at enrolment ECG						0.9689
	Yes	281/1199 (23.4)	330/1199 (27.5)	0.85 (0.74, 0.97) 0.0129	0.80 (0.66, 0.96) 0.0198	-0.04 (-0.08, -0.01)*0.0215	
	No	404/1643 (24.6)	479/1638 (29.2)	0.85 (0.76, 0.95) 0.0033	0.79 (0.67, 0.93) 0.0037	-0.05 (-0.08, -0.02)*0.0026	
	BMI (kg/m2) at enrolment						0.5672
	< 30	375/1571 (23.9)	450/1559 (28.9)	0.83 (0.74, 0.93) 0.0015	0.77 (0.65, 0.90) 0.0015	-0.05 (-0.08, -0.02)*0.0015	
	>= 30	310/1270 (24.4)	357/1275 (28.0)	0.87 (0.77, 0.99) 0.0321	0.84 (0.70, 1.01) 0.0588	-0.04 (-0.07, -0.00)*0.0393	
	Baseline eGFR (mL/min/1.73m^2)						0.7128
	< 60	366/1359 (26.9)	434/1396 (31.1)	0.86 (0.77, 0.97) 0.0104	0.81 (0.69, 0.97) 0.0179	-0.04 (-0.08, -0.01)*0.0161	
	>= 60	319/1483 (21.5)	375/1440 (26.0)	0.84 (0.74, 0.95) 0.0055	0.78 (0.65, 0.93) 0.0053	-0.05 (-0.08, -0.01)*0.0040	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.7677
	<= median	348/1424 (24.4)	420/1439 (29.2)	0.86 (0.76, 0.96) 0.0097	0.81 (0.68, 0.96) 0.0132	-0.05 (-0.08, -0.02)*0.0041	
	> median	337/1418 (23.8)	389/1398 (27.8)	0.84 (0.74, 0.94) 0.0038	0.78 (0.65, 0.93) 0.0047	-0.04 (-0.07, -0.01)*0.0137	
	LVEF at enrolment 2						0.8543
	<= 49	232/ 980 (23.7)	261/ 963 (27.1)	0.86 (0.74, 1.00) 0.0447	0.80 (0.65, 0.99) 0.0404	-0.03 (-0.07, 0.00)*0.0823	
	>= 50	453/1862 (24.3)	548/1874 (29.2)	0.84 (0.76, 0.94) 0.0012	0.79 (0.68, 0.92) 0.0024	-0.05 (-0.08, -0.02)*0.0007	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5655
	Yes	47/ 283 (16.6)	59/ 286 (20.6)	0.76 (0.55, 1.06) 0.1065	0.67 (0.43, 1.06) 0.0862	-0.04 (-0.10, 0.02)*0.2172	
	No	638/2559 (24.9)	750/2551 (29.4)	0.85 (0.78, 0.93) 0.0004	0.80 (0.71, 0.91) 0.0007	-0.04 (-0.07, -0.02)*0.0003	
	MRAs at baseline						0.2291
	Yes	295/1227 (24.0)	365/1224 (29.8)	0.80 (0.70, 0.91) 0.0005	0.74 (0.61, 0.89) 0.0013	-0.06 (-0.09, -0.02)*0.0012	
	No	390/1615 (24.1)	444/1613 (27.5)	0.89 (0.79, 0.99) 0.0400	0.84 (0.71, 0.99) 0.0343	-0.03 (-0.06, -0.00)*0.0283	
	ACEi+ARB at baseline						0.0035
	Yes	466/2065 (22.6)	604/2077 (29.1)	0.78 (0.71, 0.87) <.0001	0.71 (0.61, 0.82) <.0001	-0.07 (-0.09, -0.04)*<.0001	
	No	219/ 777 (28.2)	205/ 760 (27.0)	1.04 (0.89, 1.22) 0.6180	1.06 (0.85, 1.33) 0.6154	0.01 (-0.04, 0.05) 0.7127	
	ARNI at baseline						0.0287
	Yes	42/ 153 (27.5)	24/ 126 (19.0)	1.33 (0.85, 2.08) 0.2186	1.47 (0.82, 2.62) 0.1961	0.07 (-0.03, 0.16) 0.1737	
	No	643/2689 (23.9)	785/2711 (29.0)	0.83 (0.76, 0.91) <.0001	0.77 (0.68, 0.88) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Beta Blocker at baseline						0.7953
	Yes	575/2360 (24.4)	689/2356 (29.2)	0.85 (0.77, 0.93) 0.0003	0.79 (0.69, 0.90) 0.0004	-0.05 (-0.07, -0.02)*0.0002	
	No	110/ 482 (22.8)	120/ 481 (24.9)	0.87 (0.70, 1.08) 0.2060	0.84 (0.62, 1.14) 0.2656	-0.02 (-0.08, 0.03)*0.4389	
	Diuretics at baseline						0.7539
	Yes	621/2536 (24.5)	728/2531 (28.8)	0.85 (0.78, 0.93) 0.0004	0.80 (0.70, 0.91) 0.0005	-0.04 (-0.07, -0.02)*0.0006	
	No	64/ 306 (20.9)	81/ 306 (26.5)	0.81 (0.61, 1.06) 0.1230	0.77 (0.52, 1.13) 0.1792	-0.06 (-0.12, 0.01)*0.1053	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	681/2842 (24.0)	795/2837 (28.0)	0.86 (0.79, 0.94) 0.0005	0.81 (0.71, 0.91) 0.0006	-0.04 (-0.06, -0.02)*0.0005	
	Age						0.3318
	<= median	294/1415 (20.8)	371/1482 (25.0)	0.82 (0.72, 0.93) 0.0023	0.76 (0.64, 0.91) 0.0032	-0.04 (-0.07, -0.01)*0.0063	
	> median	387/1427 (27.1)	424/1355 (31.3)	0.89 (0.80, 0.99) 0.0381	0.84 (0.71, 0.99) 0.0391	-0.04 (-0.08, -0.01)*0.0155	
	Gender						0.3834
	Male	408/1656 (24.6)	453/1625 (27.9)	0.89 (0.79, 0.99) 0.0323	0.84 (0.72, 0.99) 0.0384	-0.03 (-0.06, -0.00)*0.0349	
	Female	273/1186 (23.0)	342/1212 (28.2)	0.82 (0.72, 0.94) 0.0035	0.76 (0.63, 0.92) 0.0052	-0.05 (-0.09, -0.02)*0.0035	
	Race						0.6080
	White	499/2039 (24.5)	599/2058 (29.1)	0.85 (0.78, 0.94) 0.0011	0.80 (0.69, 0.92) 0.0022	-0.05 (-0.07, -0.02)*0.0008	
	Black or African	21/ 67 (31.3)	19/ 71 (26.8)	1.18 (0.72, 1.94) 0.5156	1.23 (0.57, 2.63) 0.5996	0.05 (-0.11, 0.20)*0.5532	
	Asian	134/ 558 (24.0)	153/ 555 (27.6)	0.87 (0.71, 1.06) 0.1578	0.82 (0.63, 1.08) 0.1543	-0.04 (-0.09, 0.01) 0.1654	
	Other	27/ 178 (15.2)	24/ 153 (15.7)	0.91 (0.58, 1.45) 0.7037	0.90 (0.48, 1.71) 0.7538	-0.01 (-0.08, 0.07)*0.8966	
	Geographic region						0.9917
	Asia	128/ 539 (23.7)	145/ 538 (27.0)	0.88 (0.72, 1.08) 0.2106	0.84 (0.64, 1.11) 0.2121	-0.03 (-0.08, 0.02) 0.2468	
	Europe and Saudi Arabia	341/1365 (25.0)	408/1394 (29.3)	0.87 (0.78, 0.98) 0.0208	0.82 (0.69, 0.98) 0.0278	-0.04 (-0.08, -0.01)*0.0112	
	North America	104/ 398 (26.1)	121/ 387 (31.3)	0.85 (0.68, 1.05) 0.1233	0.76 (0.55, 1.05) 0.0951	-0.05 (-0.11, 0.01)*0.1113	
	Latin America	108/ 540 (20.0)	121/ 518 (23.4)	0.84 (0.68, 1.04) 0.1036	0.79 (0.58, 1.08) 0.1455	-0.03 (-0.08, 0.02)*0.1849	
	NYHA class at enrolment						0.2538
	II	512/2113 (24.2)	628/2187 (28.7)	0.84 (0.76, 0.92) 0.0003	0.78 (0.68, 0.89) 0.0004	-0.04 (-0.07, -0.02)*0.0008	
	III or IV	169/ 729 (23.2)	166/ 649 (25.6)	0.95 (0.80, 1.12) 0.5342	0.90 (0.69, 1.17) 0.4227	-0.02 (-0.07, 0.02)*0.3016	
	LVEF at enrolment						0.7331
	<= 49	233/ 980 (23.8)	248/ 963 (25.8)	0.90 (0.78, 1.05) 0.1843	0.87 (0.70, 1.07) 0.1828	-0.02 (-0.06, 0.02)*0.3126	
	50-59	256/1029 (24.9)	302/1017 (29.7)	0.84 (0.73, 0.96) 0.0106	0.79 (0.64, 0.96) 0.0199	-0.05 (-0.09, -0.01)*0.0143	
	>= 60	192/ 833 (23.0)	245/ 857 (28.6)	0.84 (0.71, 0.98) 0.0264	0.77 (0.62, 0.97) 0.0238	-0.06 (-0.10, -0.01)*0.0091	
	NT-proBNP at enrolment						0.6342
	<= median	346/1418 (24.4)	389/1421 (27.4)	0.88 (0.78, 0.99) 0.0356	0.85 (0.72, 1.01) 0.0661	-0.03 (-0.06, 0.00)*0.0703	
	> median	335/1424 (23.5)	406/1415 (28.7)	0.85 (0.75, 0.95) 0.0053	0.77 (0.64, 0.91) 0.0028	-0.05 (-0.08, -0.02)*0.0017	
	Type 2 Diabetes Medical History						0.6565
	Yes	302/1250 (24.2)	363/1260 (28.8)	0.84 (0.74, 0.96) 0.0077	0.79 (0.66, 0.94)*0.0084	-0.05 (-0.08, -0.01)*0.0082	
	No	379/1592 (23.8)	432/1577 (27.4)	0.88 (0.78, 0.98) 0.0241	0.83 (0.71, 0.97)*0.0208	-0.04 (-0.07, -0.01)*0.0206	
	Atrial fibrillation or flutter at enrolment ECG						0.5953
	Yes	280/1199 (23.4)	318/1199 (26.5)	0.88 (0.77, 1.01) 0.0693	0.84 (0.69, 1.02) 0.0761	-0.03 (-0.07, 0.00)*0.0727	
	No	401/1643 (24.4)	477/1638 (29.1)	0.84 (0.76, 0.94) 0.0021	0.78 (0.67, 0.92) 0.0029	-0.05 (-0.08, -0.02)*0.0023	
	BMI (kg/m2) at enrolment						0.4707
	< 30	371/1571 (23.6)	443/1559 (28.4)	0.84 (0.75, 0.94) 0.0026	0.78 (0.66, 0.92) 0.0027	-0.05 (-0.08, -0.02)*0.0022	
	>= 30	310/1270 (24.4)	351/1275 (27.5)	0.89 (0.79, 1.01) 0.0653	0.85 (0.71, 1.02) 0.0885	-0.03 (-0.07, 0.00)*0.0725	
	Baseline eGFR (mL/min/1.73m^2)						0.2758
	< 60	367/1359 (27.0)	419/1396 (30.0)	0.90 (0.80, 1.01) 0.0718	0.86 (0.73, 1.02) 0.0883	-0.03 (-0.06, 0.00)*0.0800	
	>= 60	314/1483 (21.2)	376/1440 (26.1)	0.82 (0.72, 0.93) 0.0020	0.76 (0.63, 0.90) 0.0022	-0.05 (-0.08, -0.02)*0.0017	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.9982
	<= median	345/1424 (24.2)	414/1439 (28.8)	0.86 (0.76, 0.97) 0.0121	0.81 (0.69, 0.97) 0.0192	-0.05 (-0.08, -0.01)*0.0058	
	> median	336/1418 (23.7)	381/1398 (27.3)	0.86 (0.76, 0.97) 0.0148	0.80 (0.67, 0.95) 0.0129	-0.04 (-0.07, -0.00)*0.0302	
	LVEF at enrolment 2						0.4426
	<= 49	233/ 980 (23.8)	248/ 963 (25.8)	0.90 (0.78, 1.05) 0.1843	0.87 (0.70, 1.07) 0.1828	-0.02 (-0.06, 0.02)*0.3126	
	>= 50	448/1862 (24.1)	547/1874 (29.2)	0.84 (0.76, 0.93) 0.0009	0.78 (0.67, 0.91) 0.0014	-0.05 (-0.08, -0.02)*0.0004	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4502
	Yes	45/ 283 (15.9)	58/ 286 (20.3)	0.74 (0.53, 1.03) 0.0778	0.65 (0.41, 1.03) 0.0690	-0.04 (-0.11, 0.02)*0.1741	
	No	636/2559 (24.9)	737/2551 (28.9)	0.87 (0.80, 0.95) 0.0014	0.82 (0.72, 0.93) 0.0020	-0.04 (-0.06, -0.02)*0.0011	
	MRAs at baseline						0.0929
	Yes	291/1227 (23.7)	363/1224 (29.7)	0.79 (0.70, 0.90) 0.0004	0.73 (0.61, 0.88) 0.0009	-0.06 (-0.09, -0.02)*0.0009	
	No	390/1615 (24.1)	432/1613 (26.8)	0.92 (0.82, 1.03) 0.1307	0.87 (0.74, 1.03) 0.1106	-0.03 (-0.06, 0.00)*0.0858	
	ACEi+ARB at baseline						0.1206
	Yes	477/2065 (23.1)	586/2077 (28.2)	0.82 (0.75, 0.91) 0.0001	0.76 (0.66, 0.88) 0.0002	-0.05 (-0.08, -0.02)*0.0002	
	No	204/ 777 (26.3)	209/ 760 (27.5)	0.96 (0.81, 1.13) 0.6064	0.94 (0.75, 1.18) 0.5888	-0.02 (-0.06, 0.03) 0.4285	
	ARNI at baseline						0.4046
	Yes	35/ 153 (22.9)	27/ 126 (21.4)	1.05 (0.67, 1.65) 0.8188	1.06 (0.60, 1.90) 0.8325	0.01 (-0.09, 0.10) 0.9040	
	No	646/2689 (24.0)	768/2711 (28.3)	0.86 (0.79, 0.93) 0.0004	0.80 (0.71, 0.91) 0.0005	-0.04 (-0.07, -0.02)*0.0003	
	Beta Blocker at baseline						0.8783
	Yes	576/2360 (24.4)	682/2356 (28.9)	0.86 (0.79, 0.94) 0.0011	0.80 (0.70, 0.92) 0.0011	-0.05 (-0.07, -0.02)*0.0004	
	No	105/ 482 (21.8)	113/ 481 (23.5)	0.88 (0.70, 1.11) 0.2760	0.86 (0.63, 1.17) 0.3316	-0.02 (-0.07, 0.04)*0.5264	
	Diuretics at baseline						0.7490
	Yes	617/2536 (24.3)	721/2531 (28.5)	0.86 (0.78, 0.93) 0.0005	0.80 (0.70, 0.91) 0.0007	-0.04 (-0.07, -0.02)*0.0008	
	No	64/ 306 (20.9)	74/ 306 (24.2)	0.89 (0.67, 1.19) 0.4498	0.87 (0.59, 1.28) 0.4795	-0.01 (-0.08, 0.05) 0.6642	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	823/2792 (29.5)	930/2792 (33.3)	0.90 (0.83, 0.97) 0.0049	0.84 (0.75, 0.95) 0.0047	-0.03 (-0.05, -0.01) 0.0033	
	Age						0.9902
	<= median	367/1403 (26.2)	427/1469 (29.1)	0.90 (0.80, 1.00) 0.0571	0.85 (0.72, 1.01) 0.0585	-0.03 (-0.06, 0.00)*0.0810	
	> median	456/1389 (32.8)	503/1323 (38.0)	0.90 (0.81, 0.99) 0.0236	0.82 (0.70, 0.97) 0.0203	-0.04 (-0.07, -0.01) 0.0147	
	Gender						0.0517
	Male	509/1638 (31.1)	528/1602 (33.0)	0.95 (0.87, 1.05) 0.3378	0.92 (0.79, 1.07) 0.2940	-0.02 (-0.05, 0.01) 0.1588	
	Female	314/1154 (27.2)	402/1190 (33.8)	0.82 (0.73, 0.92) 0.0010	0.75 (0.63, 0.90) 0.0022	-0.05 (-0.08, -0.01) 0.0063	
	Race						0.3085
	White	617/2004 (30.8)	682/2025 (33.7)	0.94 (0.86, 1.02) 0.1415	0.89 (0.78, 1.03) 0.1097	-0.03 (-0.06, -0.00)*0.0495	
	Black or African	23/ 66 (34.8)	26/ 68 (38.2)	0.96 (0.63, 1.45) 0.8409	0.85 (0.40, 1.78) 0.6607	-0.03 (-0.20, 0.13)*0.6838	
	Asian	151/ 551 (27.4)	194/ 550 (35.3)	0.78 (0.66, 0.93) 0.0062	0.70 (0.54, 0.90) 0.0065	-0.07 (-0.13, -0.02) 0.0073	
	Other	32/ 171 (18.7)	28/ 149 (18.8)	1.00 (0.65, 1.54) 0.9995	0.92 (0.51, 1.66) 0.7824	-0.00 (-0.09, 0.08)*0.9857	
	Geographic region						0.3541
	Asia	144/ 533 (27.0)	184/ 533 (34.5)	0.79 (0.66, 0.94) 0.0098	0.71 (0.54, 0.92) 0.0108	-0.07 (-0.12, -0.01) 0.0135	
	Europe and Saudi Arabia	409/1347 (30.4)	460/1373 (33.5)	0.94 (0.85, 1.04) 0.2181	0.88 (0.74, 1.04) 0.1352	-0.03 (-0.07, 0.00)*0.0789	
	North America	137/ 391 (35.0)	151/ 375 (40.3)	0.90 (0.75, 1.07) 0.2222	0.82 (0.60, 1.10) 0.1870	-0.05 (-0.12, 0.02) 0.1324	
	Latin America	133/ 521 (25.5)	135/ 511 (26.4)	0.98 (0.81, 1.18) 0.8030	0.94 (0.70, 1.26) 0.6951	-0.01 (-0.06, 0.04)*0.7442	
	NYHA class at enrolment						0.5601
	II	617/2077 (29.7)	711/2159 (32.9)	0.91 (0.83, 0.99) 0.0227	0.86 (0.75, 0.98) 0.0251	-0.03 (-0.06, -0.00)*0.0235	
	III or IV	206/ 715 (28.8)	218/ 632 (34.5)	0.86 (0.75, 1.00) 0.0482	0.78 (0.61, 0.99) 0.0416	-0.06 (-0.11, -0.01)*0.0252	
	LVEF at enrolment						0.5538
	<= 49	287/ 967 (29.7)	292/ 952 (30.7)	0.95 (0.83, 1.08) 0.4275	0.92 (0.75, 1.13) 0.4273	-0.01 (-0.05, 0.03)*0.6357	
	50-59	305/1013 (30.1)	354/ 998 (35.5)	0.86 (0.76, 0.97) 0.0118	0.80 (0.66, 0.98) 0.0273	-0.05 (-0.09, -0.01)*0.0103	
	>= 60	231/ 812 (28.4)	284/ 842 (33.7)	0.90 (0.78, 1.03) 0.1335	0.82 (0.66, 1.01) 0.0661	-0.04 (-0.08, -0.00) 0.0432	
	NT-proBNP at enrolment						0.4805
	<= median	393/1394 (28.2)	455/1402 (32.5)	0.87 (0.78, 0.97) 0.0156	0.82 (0.69, 0.97) 0.0173	-0.03 (-0.06, 0.01) 0.0997	
	> median	430/1398 (30.8)	475/1389 (34.2)	0.92 (0.83, 1.02) 0.1157	0.87 (0.74, 1.03) 0.1049	-0.03 (-0.07, 0.00)*0.0524	
	Type 2 Diabetes Medical History						0.7738
	Yes	373/1232 (30.3)	409/1237 (33.1)	0.91 (0.82, 1.01) 0.0887	0.88 (0.74, 1.04)*0.1366	-0.03 (-0.06, 0.01)*0.1363	
	No	450/1560 (28.8)	521/1555 (33.5)	0.89 (0.80, 0.98) 0.0218	0.80 (0.69, 0.94)*0.0050	-0.04 (-0.07, -0.01) 0.0155	
	Atrial fibrillation or flutter at enrolment ECG						0.5195
	Yes	358/1178 (30.4)	387/1175 (32.9)	0.92 (0.83, 1.03) 0.1720	0.89 (0.75, 1.07) 0.2221	-0.03 (-0.06, 0.01) 0.1204	
	No	465/1614 (28.8)	543/1617 (33.6)	0.88 (0.80, 0.97) 0.0102	0.81 (0.69, 0.94) 0.0069	-0.04 (-0.07, -0.01) 0.0148	
	BMI (kg/m2) at enrolment						0.3488
	< 30	444/1547 (28.7)	515/1535 (33.6)	0.87 (0.79, 0.97) 0.0082	0.80 (0.68, 0.93) 0.0047	-0.05 (-0.08, -0.02) 0.0015	
	>= 30	379/1244 (30.5)	414/1254 (33.0)	0.94 (0.84, 1.04) 0.2427	0.92 (0.77, 1.09) 0.3314	-0.01 (-0.04, 0.02) 0.4707	
	Baseline eGFR (mL/min/1.73m^2)						0.6501
	< 60	421/1328 (31.7)	472/1367 (34.5)	0.92 (0.83, 1.01) 0.0873	0.89 (0.75, 1.05) 0.1524	-0.02 (-0.05, 0.01) 0.1964	
	>= 60	402/1464 (27.5)	458/1424 (32.2)	0.88 (0.79, 0.99) 0.0258	0.81 (0.69, 0.96) 0.0131	-0.05 (-0.08, -0.01)*0.0057	

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Physical Limitation (LOCF)	SBP at randomisation						0.5891
	<= median	409/1396 (29.3)	469/1414 (33.2)	0.91 (0.82, 1.02) 0.0978	0.87 (0.74, 1.03) 0.1010	-0.03 (-0.06, 0.01) 0.1116	
	> median	414/1396 (29.7)	461/1378 (33.5)	0.88 (0.79, 0.98) 0.0157	0.81 (0.69, 0.96) 0.0145	-0.04 (-0.07, -0.00)*0.0313	
	LVEF at enrolment 2						0.3594
	<= 49	287/ 967 (29.7)	292/ 952 (30.7)	0.95 (0.83, 1.08) 0.4275	0.92 (0.75, 1.13) 0.4273	-0.01 (-0.05, 0.03)*0.6357	
	>= 50	536/1825 (29.4)	638/1840 (34.7)	0.88 (0.80, 0.96) 0.0052	0.81 (0.70, 0.94) 0.0044	-0.04 (-0.07, -0.01) 0.0055	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1841
	Yes	67/ 273 (24.5)	88/ 277 (31.8)	0.77 (0.60, 0.99) 0.0448	0.67 (0.45, 1.00) 0.0479	-0.07 (-0.15, 0.00)*0.0587	
	No	756/2519 (30.0)	842/2515 (33.5)	0.91 (0.84, 0.99) 0.0205	0.86 (0.76, 0.98) 0.0195	-0.03 (-0.05, -0.01) 0.0107	
	MRAs at baseline						0.4443
	Yes	365/1200 (30.4)	421/1208 (34.9)	0.87 (0.78, 0.97) 0.0155	0.81 (0.68, 0.97) 0.0216	-0.04 (-0.07, -0.01) 0.0176	
	No	458/1592 (28.8)	509/1584 (32.1)	0.92 (0.83, 1.02) 0.1182	0.87 (0.75, 1.02) 0.0892	-0.03 (-0.07, -0.00)*0.0392	
	ACEi+ARB at baseline						0.2460
	Yes	579/2029 (28.5)	682/2047 (33.3)	0.88 (0.80, 0.96) 0.0029	0.81 (0.70, 0.93) 0.0025	-0.05 (-0.08, -0.02)*0.0009	
	No	244/ 763 (32.0)	248/ 745 (33.3)	0.96 (0.84, 1.11) 0.6183	0.95 (0.76, 1.18) 0.6327	-0.01 (-0.06, 0.03) 0.5567	
	ARNI at baseline						0.7402
	Yes	47/ 150 (31.3)	40/ 123 (32.5)	0.94 (0.66, 1.33) 0.7208	0.89 (0.53, 1.51) 0.6731	-0.03 (-0.15, 0.08) 0.5449	
	No	776/2642 (29.4)	890/2669 (33.3)	0.90 (0.83, 0.97) 0.0055	0.84 (0.75, 0.95) 0.0057	-0.03 (-0.05, -0.01) 0.0083	
	Beta Blocker at baseline						0.6579
	Yes	676/2323 (29.1)	776/2321 (33.4)	0.89 (0.82, 0.97) 0.0060	0.83 (0.73, 0.94) 0.0043	-0.04 (-0.07, -0.02)*0.0014	
	No	147/ 469 (31.3)	154/ 471 (32.7)	0.93 (0.78, 1.12) 0.4517	0.92 (0.70, 1.23) 0.5827	-0.02 (-0.07, 0.04) 0.4921	
	Diuretics at baseline						0.4044
	Yes	730/2493 (29.3)	838/2492 (33.6)	0.89 (0.82, 0.96) 0.0034	0.82 (0.73, 0.93) 0.0022	-0.04 (-0.06, -0.01) 0.0018	
	No	93/ 299 (31.1)	92/ 300 (30.7)	0.98 (0.78, 1.24) 0.8837	1.03 (0.72, 1.48) 0.8545	0.01 (-0.05, 0.08) 0.6875	

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Quality of Life (LOCF)							
	Overall	787/2842 (27.7)	870/2837 (30.7)	0.93 (0.86, 1.00) 0.0459	0.87 (0.77, 0.99) 0.0295	-0.03 (-0.05, -0.01)*0.0136	
	Age						0.6864
	<= median	352/1415 (24.9)	394/1482 (26.6)	0.94 (0.84, 1.05) 0.2994	0.91 (0.77, 1.09) 0.3187	-0.02 (-0.05, 0.01)*0.2926	
	> median	435/1427 (30.5)	476/1355 (35.1)	0.91 (0.83, 1.00) 0.0610	0.83 (0.70, 0.98) 0.0297	-0.05 (-0.08, -0.01)*0.0090	
	Gender						0.8535
	Male	459/1656 (27.7)	489/1625 (30.1)	0.94 (0.85, 1.03) 0.1831	0.90 (0.77, 1.06) 0.2202	-0.02 (-0.05, 0.01)*0.1334	
	Female	328/1186 (27.7)	381/1212 (31.4)	0.93 (0.83, 1.03) 0.1543	0.83 (0.69, 1.01) 0.0623	-0.04 (-0.07, -0.00)*0.0423	
	Race						0.7098
	White	568/2039 (27.9)	642/2058 (31.2)	0.93 (0.85, 1.01) 0.0736	0.87 (0.75, 1.00) 0.0527	-0.03 (-0.06, -0.01)*0.0191	
	Black or African	19/ 67 (28.4)	19/ 71 (26.8)	1.17 (0.71, 1.93) 0.5435	1.16 (0.53, 2.55) 0.7117	0.02 (-0.13, 0.17)*0.8337	
	Asian	170/ 558 (30.5)	177/ 555 (31.9)	0.95 (0.81, 1.12) 0.5297	0.92 (0.71, 1.20) 0.5537	-0.01 (-0.07, 0.04)*0.6076	
	Other	30/ 178 (16.9)	32/ 153 (20.9)	0.82 (0.55, 1.22) 0.3268	0.70 (0.38, 1.26) 0.2325	-0.04 (-0.13, 0.04)*0.3475	
	Geographic region						0.4797
	Asia	163/ 539 (30.2)	169/ 538 (31.4)	0.96 (0.81, 1.13) 0.5946	0.94 (0.72, 1.23) 0.6688	-0.01 (-0.07, 0.04)*0.6772	
	Europe and Saudi Arabia	386/1365 (28.3)	437/1394 (31.3)	0.94 (0.85, 1.04) 0.2507	0.89 (0.74, 1.06) 0.1892	-0.03 (-0.06, 0.00)*0.0777	
	North America	104/ 398 (26.1)	127/ 387 (32.8)	0.81 (0.66, 0.99) 0.0385	0.70 (0.51, 0.97) 0.0334	-0.07 (-0.13, -0.00)*0.0395	
	Latin America	134/ 540 (24.8)	137/ 518 (26.4)	1.01 (0.85, 1.20) 0.8950	0.92 (0.68, 1.24) 0.5880	-0.02 (-0.07, 0.04)*0.5431	
	NYHA class at enrolment						0.5298
	II	593/2113 (28.1)	679/2187 (31.0)	0.92 (0.85, 1.00) 0.0428	0.85 (0.74, 0.98) 0.0218	-0.03 (-0.06, -0.00)*0.0320	
	III or IV	194/ 729 (26.6)	190/ 649 (29.3)	0.96 (0.84, 1.10) 0.5893	0.91 (0.71, 1.18) 0.4947	-0.03 (-0.07, 0.02)*0.2715	
	LVEF at enrolment						0.3388
	<= 49	266/ 980 (27.1)	266/ 963 (27.6)	1.00 (0.88, 1.14) 0.9861	0.96 (0.78, 1.20) 0.7379	-0.00 (-0.04, 0.03)*0.8128	
	50-59	293/1029 (28.5)	330/1017 (32.4)	0.89 (0.79, 1.00) 0.0491	0.83 (0.68, 1.01) 0.0683	-0.04 (-0.08, 0.00)*0.0506	
	>= 60	228/ 833 (27.4)	274/ 857 (32.0)	0.90 (0.78, 1.02) 0.1092	0.83 (0.66, 1.04) 0.1027	-0.05 (-0.09, -0.00)*0.0381	
	NT-proBNP at enrolment						0.1589
	<= median	378/1418 (26.7)	444/1421 (31.2)	0.88 (0.80, 0.98) 0.0174	0.80 (0.67, 0.95) 0.0118	-0.05 (-0.08, -0.01)*0.0070	
	> median	409/1424 (28.7)	426/1415 (30.1)	0.98 (0.88, 1.08) 0.6688	0.95 (0.80, 1.13) 0.5652	-0.01 (-0.05, 0.02)*0.4183	
	Type 2 Diabetes Medical History						0.5485
	Yes	335/1250 (26.8)	390/1260 (31.0)	0.90 (0.81, 1.01) 0.0754	0.82 (0.69, 0.97)*0.0218	-0.04 (-0.08, -0.01)*0.0216	
	No	452/1592 (28.4)	480/1577 (30.4)	0.95 (0.86, 1.04) 0.2766	0.91 (0.78, 1.06)*0.2064	-0.02 (-0.05, 0.01)*0.2063	
	Atrial fibrillation or flutter at enrolment ECG						0.5924
	Yes	332/1199 (27.7)	356/1199 (29.7)	0.95 (0.85, 1.06) 0.3240	0.92 (0.76, 1.11) 0.3914	-0.02 (-0.06, 0.02)*0.2785	
	No	455/1643 (27.7)	514/1638 (31.4)	0.91 (0.82, 1.00) 0.0421	0.84 (0.71, 0.98) 0.0296	-0.04 (-0.07, -0.01)*0.0206	
	BMI (kg/m2) at enrolment						0.7793
	< 30	451/1571 (28.7)	502/1559 (32.2)	0.92 (0.83, 1.01) 0.0821	0.87 (0.74, 1.02) 0.0837	-0.03 (-0.07, -0.00)*0.0337	
	>= 30	335/1270 (26.4)	367/1275 (28.8)	0.94 (0.85, 1.05) 0.2980	0.88 (0.73, 1.06) 0.1719	-0.02 (-0.06, 0.01)*0.1743	
	Baseline eGFR (mL/min/1.73m^2)						0.0981
	< 60	416/1359 (30.6)	439/1396 (31.4)	0.98 (0.89, 1.09) 0.7601	0.97 (0.82, 1.16) 0.7588	-0.01 (-0.04, 0.03)*0.6352	
	>= 60	371/1483 (25.0)	430/1440 (29.9)	0.88 (0.79, 0.98) 0.0153	0.78 (0.66, 0.93) 0.0065	-0.05 (-0.08, -0.02)*0.0033	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.2819
	<= median	403/1424 (28.3)	440/1439 (30.6)	0.97 (0.88, 1.07) 0.5389	0.94 (0.79, 1.11) 0.4487	-0.02 (-0.06, 0.01)*0.1813	
	> median	384/1418 (27.1)	430/1398 (30.8)	0.89 (0.81, 0.99) 0.0345	0.82 (0.69, 0.97) 0.0230	-0.04 (-0.07, -0.00)*0.0313	
	LVEF at enrolment 2						0.1497
	<= 49	266/ 980 (27.1)	266/ 963 (27.6)	1.00 (0.88, 1.14) 0.9861	0.96 (0.78, 1.20) 0.7379	-0.00 (-0.04, 0.03)*0.8128	
	>= 50	521/1862 (28.0)	604/1874 (32.2)	0.90 (0.82, 0.98) 0.0131	0.83 (0.71, 0.96) 0.0152	-0.04 (-0.07, -0.01)*0.0046	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8644
	Yes	59/ 283 (20.8)	68/ 286 (23.8)	0.92 (0.71, 1.19) 0.5226	0.87 (0.57, 1.34) 0.5347	-0.03 (-0.10, 0.04)*0.4012	
	No	728/2559 (28.4)	802/2551 (31.4)	0.93 (0.86, 1.00) 0.0586	0.87 (0.77, 0.99) 0.0369	-0.03 (-0.06, -0.00)*0.0196	
	MRAs at baseline						0.8519
	Yes	337/1227 (27.5)	374/1224 (30.6)	0.92 (0.82, 1.03) 0.1300	0.87 (0.72, 1.04) 0.1322	-0.03 (-0.07, 0.01)*0.0917	
	No	450/1615 (27.9)	496/1613 (30.8)	0.93 (0.85, 1.03) 0.1657	0.88 (0.74, 1.03) 0.1086	-0.03 (-0.06, 0.00)*0.0715	
	ACEi+ARB at baseline						0.4087
	Yes	568/2065 (27.5)	647/2077 (31.2)	0.92 (0.84, 0.99) 0.0360	0.83 (0.72, 0.96) 0.0133	-0.04 (-0.06, -0.01)*0.0099	
	No	219/ 777 (28.2)	223/ 760 (29.3)	0.98 (0.85, 1.13) 0.7758	0.98 (0.78, 1.23) 0.8499	-0.00 (-0.04, 0.03) 0.9261	
	ARNI at baseline						0.0608
	Yes	41/ 153 (26.8)	28/ 126 (22.2)	1.32 (0.88, 1.99) 0.1776	1.45 (0.82, 2.57) 0.2072	0.07 (-0.03, 0.17) 0.1928	
	No	746/2689 (27.7)	842/2711 (31.1)	0.92 (0.85, 0.99) 0.0186	0.85 (0.75, 0.97) 0.0123	-0.03 (-0.06, -0.01)*0.0074	
	Beta Blocker at baseline						0.6508
	Yes	661/2360 (28.0)	731/2356 (31.0)	0.94 (0.87, 1.01) 0.0983	0.88 (0.77, 1.01) 0.0620	-0.03 (-0.06, -0.00)*0.0230	
	No	126/ 482 (26.1)	139/ 481 (28.9)	0.89 (0.75, 1.07) 0.2272	0.83 (0.61, 1.13) 0.2437	-0.03 (-0.08, 0.03)*0.3379	
	Diuretics at baseline						0.0492
	Yes	704/2536 (27.8)	791/2531 (31.3)	0.91 (0.84, 0.98) 0.0094	0.84 (0.74, 0.96) 0.0092	-0.03 (-0.06, -0.01)*0.0064	
	No	83/ 306 (27.1)	79/ 306 (25.8)	1.16 (0.90, 1.48) 0.2485	1.16 (0.80, 1.69) 0.4385	0.01 (-0.06, 0.08)*0.7140	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	707/2842 (24.9)	848/2837 (29.9)	0.84 (0.77, 0.91) <.0001	0.77 (0.68, 0.87) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Age						0.5924
	<= median	303/1415 (21.4)	388/1482 (26.2)	0.81 (0.71, 0.92) 0.0012	0.75 (0.63, 0.89) 0.0012	-0.05 (-0.08, -0.02)*0.0025	
	> median	404/1427 (28.3)	460/1355 (33.9)	0.85 (0.77, 0.94) 0.0025	0.78 (0.66, 0.92) 0.0035	-0.06 (-0.09, -0.02)*0.0013	
	Gender						0.3322
	Male	396/1656 (23.9)	484/1625 (29.8)	0.81 (0.72, 0.90) 0.0001	0.74 (0.63, 0.86) 0.0002	-0.06 (-0.09, -0.03)*0.0001	
	Female	311/1186 (26.2)	364/1212 (30.0)	0.88 (0.78, 0.99) 0.0364	0.82 (0.68, 0.99) 0.0383	-0.04 (-0.07, -0.00)*0.0378	
	Race						0.3206
	White	530/2039 (26.0)	631/2058 (30.7)	0.86 (0.78, 0.94) 0.0012	0.80 (0.69, 0.92) 0.0017	-0.05 (-0.07, -0.02)*0.0009	
	Black or African	18/ 67 (26.9)	17/ 71 (23.9)	1.08 (0.62, 1.88) 0.7978	1.16 (0.53, 2.54) 0.7177	-0.01 (-0.16, 0.14) 0.9384	
	Asian	135/ 558 (24.2)	164/ 555 (29.5)	0.81 (0.67, 0.98) 0.0324	0.74 (0.57, 0.97) 0.0314	-0.05 (-0.11, -0.00)*0.0435	
	Other	24/ 178 (13.5)	36/ 153 (23.5)	0.59 (0.37, 0.94) 0.0248	0.50 (0.28, 0.91) 0.0220	-0.10 (-0.18, -0.02) 0.0183	
	Geographic region						0.5851
	Asia	129/ 539 (23.9)	155/ 538 (28.8)	0.82 (0.68, 1.00) 0.0558	0.76 (0.58, 1.01) 0.0567	-0.05 (-0.10, 0.00)*0.0689	
	Europe and Saudi Arabia	368/1365 (27.0)	435/1394 (31.2)	0.89 (0.80, 0.99) 0.0302	0.82 (0.69, 0.98) 0.0265	-0.04 (-0.08, -0.01)*0.0140	
	North America	107/ 398 (26.9)	135/ 387 (34.9)	0.77 (0.62, 0.94) 0.0102	0.68 (0.49, 0.93) 0.0147	-0.08 (-0.14, -0.02)*0.0150	
	Latin America	103/ 540 (19.1)	123/ 518 (23.7)	0.80 (0.64, 1.00) 0.0492	0.74 (0.54, 1.00) 0.0480	-0.05 (-0.10, 0.00)*0.0639	
	NYHA class at enrolment						0.5988
	II	526/2113 (24.9)	659/2187 (30.1)	0.82 (0.75, 0.90) <.0001	0.75 (0.65, 0.86) <.0001	-0.05 (-0.08, -0.03)*0.0001	
	III or IV	181/ 729 (24.8)	189/ 649 (29.1)	0.87 (0.74, 1.02) 0.0813	0.80 (0.62, 1.03) 0.0879	-0.04 (-0.09, 0.00)*0.0732	
	LVEF at enrolment						0.8599
	<= 49	238/ 980 (24.3)	266/ 963 (27.6)	0.87 (0.75, 1.00) 0.0520	0.81 (0.66, 1.00) 0.0533	-0.03 (-0.07, 0.01)*0.0933	
	50-59	270/1029 (26.2)	323/1017 (31.8)	0.83 (0.73, 0.94) 0.0038	0.75 (0.62, 0.92) 0.0052	-0.06 (-0.09, -0.02)*0.0058	
	>= 60	199/ 833 (23.9)	259/ 857 (30.2)	0.82 (0.70, 0.95) 0.0104	0.75 (0.60, 0.93) 0.0103	-0.06 (-0.11, -0.02)*0.0033	
	NT-proBNP at enrolment						0.7598
	<= median	352/1418 (24.8)	412/1421 (29.0)	0.85 (0.75, 0.95) 0.0052	0.79 (0.67, 0.94) 0.0080	-0.04 (-0.07, -0.01)*0.0121	
	> median	355/1424 (24.9)	436/1415 (30.8)	0.83 (0.74, 0.93) 0.0012	0.75 (0.63, 0.89) 0.0009	-0.06 (-0.09, -0.03)*0.0005	
	Type 2 Diabetes Medical History						0.1264
	Yes	308/1250 (24.6)	401/1260 (31.8)	0.78 (0.69, 0.88) <.0001	0.70 (0.59, 0.83)*<.0001	-0.07 (-0.11, -0.04)*<.0001	
	No	399/1592 (25.1)	447/1577 (28.3)	0.89 (0.80, 0.99) 0.0383	0.85 (0.72, 0.99)*0.0369	-0.03 (-0.06, -0.00)*0.0367	
	Atrial fibrillation or flutter at enrolment ECG						0.6439
	Yes	284/1199 (23.7)	347/1199 (28.9)	0.82 (0.72, 0.93) 0.0022	0.75 (0.62, 0.91) 0.0034	-0.05 (-0.09, -0.02)*0.0034	
	No	423/1643 (25.7)	501/1638 (30.6)	0.85 (0.76, 0.94) 0.0023	0.78 (0.67, 0.91) 0.0022	-0.05 (-0.08, -0.02)*0.0020	
	BMI (kg/m2) at enrolment						0.6891
	< 30	387/1571 (24.6)	468/1559 (30.0)	0.83 (0.74, 0.92) 0.0008	0.76 (0.64, 0.89) 0.0008	-0.05 (-0.09, -0.02)*0.0007	
	>= 30	320/1270 (25.2)	378/1275 (29.6)	0.85 (0.76, 0.96) 0.0096	0.79 (0.66, 0.95) 0.0135	-0.04 (-0.08, -0.01)*0.0118	
	Baseline eGFR (mL/min/1.73m^2)						0.6596
	< 60	377/1359 (27.7)	457/1396 (32.7)	0.85 (0.77, 0.95) 0.0042	0.78 (0.66, 0.93) 0.0045	-0.05 (-0.08, -0.02)*0.0042	
	>= 60	330/1483 (22.3)	391/1440 (27.2)	0.82 (0.73, 0.93) 0.0021	0.76 (0.64, 0.91) 0.0023	-0.05 (-0.08, -0.02)*0.0021	

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Symptom Burden (LOCF)	SBP at randomisation						0.2220
	<= median	346/1424 (24.3)	451/1439 (31.3)	0.80 (0.71, 0.89) 0.0001	0.72 (0.61, 0.85) 0.0001	-0.07 (-0.10, -0.04)*<.0001	
	> median	361/1418 (25.5)	397/1398 (28.4)	0.88 (0.78, 0.99) 0.0308	0.83 (0.69, 0.98) 0.0317	-0.03 (-0.06, 0.00)*0.0786	
	LVEF at enrolment 2						0.6011
	<= 49	238/ 980 (24.3)	266/ 963 (27.6)	0.87 (0.75, 1.00) 0.0520	0.81 (0.66, 1.00) 0.0533	-0.03 (-0.07, 0.01)*0.0933	
	>= 50	469/1862 (25.2)	582/1874 (31.1)	0.82 (0.75, 0.91) 0.0001	0.75 (0.65, 0.87) 0.0002	-0.06 (-0.09, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7400
	Yes	54/ 283 (19.1)	65/ 286 (22.7)	0.76 (0.56, 1.02) 0.0655	0.70 (0.45, 1.08) 0.1053	-0.04 (-0.10, 0.03)*0.2843	
	No	653/2559 (25.5)	783/2551 (30.7)	0.84 (0.77, 0.91) <.0001	0.77 (0.68, 0.88) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	MRAs at baseline						0.1574
	Yes	290/1227 (23.6)	376/1224 (30.7)	0.78 (0.69, 0.88) 0.0001	0.70 (0.58, 0.84) 0.0001	-0.07 (-0.11, -0.04)*<.0001	
	No	417/1615 (25.8)	472/1613 (29.3)	0.88 (0.79, 0.98) 0.0200	0.83 (0.71, 0.98) 0.0240	-0.03 (-0.07, -0.00)*0.0285	
	ACEi+ARB at baseline						0.0375
	Yes	488/2065 (23.6)	630/2077 (30.3)	0.79 (0.72, 0.87) <.0001	0.71 (0.61, 0.82) <.0001	-0.07 (-0.09, -0.04)*<.0001	
	No	219/ 777 (28.2)	218/ 760 (28.7)	0.97 (0.83, 1.13) 0.6782	0.97 (0.77, 1.21) 0.7611	-0.00 (-0.05, 0.04)*0.8284	
	ARNI at baseline						0.0620
	Yes	47/ 153 (30.7)	31/ 126 (24.6)	1.17 (0.80, 1.72) 0.4117	1.26 (0.73, 2.18) 0.4087	0.04 (-0.06, 0.14) 0.4368	
	No	660/2689 (24.5)	817/2711 (30.1)	0.82 (0.76, 0.90) <.0001	0.75 (0.66, 0.85) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	Beta Blocker at baseline						0.6445
	Yes	598/2360 (25.3)	716/2356 (30.4)	0.84 (0.77, 0.92) 0.0002	0.78 (0.68, 0.89) 0.0002	-0.05 (-0.08, -0.02)*0.0001	
	No	109/ 482 (22.6)	132/ 481 (27.4)	0.80 (0.65, 0.99) 0.0408	0.72 (0.54, 0.98) 0.0368	-0.05 (-0.10, 0.01)*0.0832	
	Diuretics at baseline						0.3487
	Yes	648/2536 (25.6)	761/2531 (30.1)	0.85 (0.78, 0.92) 0.0001	0.79 (0.69, 0.89) 0.0002	-0.05 (-0.07, -0.02)*0.0003	
	No	59/ 306 (19.3)	87/ 306 (28.4)	0.74 (0.56, 0.98) 0.0381	0.63 (0.43, 0.93) 0.0215	-0.09 (-0.16, -0.02)*0.0076	

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Self Efficacy (LOCF)							
	Overall	716/2842 (25.2)	712/2837 (25.1)	1.01 (0.93, 1.10) 0.7275	1.01 (0.89, 1.15) 0.8601	0.00 (-0.02, 0.02)*0.9331	
	Age						0.1959
	<= median	343/1415 (24.2)	337/1482 (22.7)	1.07 (0.95, 1.21) 0.2680	1.09 (0.91, 1.31) 0.3464	0.02 (-0.02, 0.05)*0.3409	
	> median	373/1427 (26.1)	375/1355 (27.7)	0.96 (0.86, 1.08) 0.4931	0.93 (0.78, 1.11) 0.4456	-0.02 (-0.05, 0.02)*0.3611	
	Gender						0.6556
	Male	417/1656 (25.2)	395/1625 (24.3)	1.03 (0.92, 1.16) 0.5714	1.04 (0.88, 1.23) 0.6063	0.01 (-0.02, 0.04)*0.5621	
	Female	299/1186 (25.2)	317/1212 (26.2)	1.00 (0.88, 1.13) 0.9477	0.97 (0.80, 1.18) 0.7620	-0.01 (-0.04, 0.03)*0.5966	
	Race						0.9908
	White	497/2039 (24.4)	500/2058 (24.3)	1.02 (0.92, 1.13) 0.7117	1.02 (0.88, 1.18) 0.7899	0.00 (-0.03, 0.03)*0.9529	
	Black or African	16/ 67 (23.9)	17/ 71 (23.9)	0.93 (0.54, 1.58) 0.7795	0.86 (0.36, 2.03) 0.7321	-0.00 (-0.14, 0.14)*0.9931	
	Asian	168/ 558 (30.1)	166/ 555 (29.9)	1.01 (0.86, 1.18) 0.9231	0.97 (0.73, 1.28) 0.8268	0.00 (-0.05, 0.06)*0.9427	
	Other	35/ 178 (19.7)	29/ 153 (19.0)	1.04 (0.67, 1.61)*0.8708	1.04 (0.57, 1.90) 0.9011	0.01 (-0.08, 0.09)*0.8706	
	Geographic region						0.4324
	Asia	162/ 539 (30.1)	161/ 538 (29.9)	0.99 (0.84, 1.17) 0.9197	0.96 (0.72, 1.27) 0.7515	0.00 (-0.05, 0.06)*0.9629	
	Europe and Saudi Arabia	358/1365 (26.2)	354/1394 (25.4)	1.04 (0.93, 1.17) 0.4987	1.06 (0.88, 1.26) 0.5566	0.01 (-0.02, 0.04)*0.6173	
	North America	99/ 398 (24.9)	84/ 387 (21.7)	1.13 (0.88, 1.44) 0.3305	1.18 (0.84, 1.67) 0.3367	0.03 (-0.03, 0.09)*0.2931	
	Latin America	97/ 540 (18.0)	113/ 518 (21.8)	0.87 (0.69, 1.09) 0.2201	0.81 (0.59, 1.12) 0.2044	-0.04 (-0.09, 0.01)*0.1165	
	NYHA class at enrolment						0.2289
	II	541/2113 (25.6)	548/2187 (25.1)	1.04 (0.95, 1.15) 0.4007	1.04 (0.90, 1.21) 0.5644	0.01 (-0.02, 0.03)*0.6805	
	III or IV	175/ 729 (24.0)	164/ 649 (25.3)	0.92 (0.78, 1.09) 0.3599	0.90 (0.70, 1.17) 0.4489	-0.01 (-0.06, 0.03)*0.5869	
	LVEF at enrolment						0.4445
	<= 49	246/ 980 (25.1)	218/ 963 (22.6)	1.09 (0.93, 1.26) 0.2785	1.11 (0.90, 1.39) 0.3328	0.02 (-0.01, 0.06)*0.2024	
	50-59	269/1029 (26.1)	266/1017 (26.2)	1.00 (0.87, 1.14) 0.9969	1.01 (0.82, 1.25) 0.9180	-0.00 (-0.04, 0.04)*0.9945	
	>= 60	201/ 833 (24.1)	228/ 857 (26.6)	0.95 (0.82, 1.11) 0.5351	0.90 (0.72, 1.14) 0.3852	-0.02 (-0.07, 0.02)*0.2421	
	NT-proBNP at enrolment						0.3909
	<= median	353/1418 (24.9)	369/1421 (26.0)	0.98 (0.87, 1.10) 0.7044	0.95 (0.80, 1.14) 0.5809	-0.01 (-0.04, 0.02)*0.5113	
	> median	363/1424 (25.5)	343/1415 (24.2)	1.05 (0.93, 1.18) 0.3984	1.08 (0.90, 1.29) 0.4151	0.01 (-0.02, 0.04)*0.4405	
	Type 2 Diabetes Medical History						0.2646
	Yes	291/1250 (23.3)	312/1260 (24.8)	0.96 (0.84, 1.09) 0.5063	0.92 (0.77, 1.11)*0.3850	-0.01 (-0.05, 0.02)*0.3848	
	No	425/1592 (26.7)	400/1577 (25.4)	1.06 (0.95, 1.18) 0.3285	1.07 (0.91, 1.26)*0.3932	0.01 (-0.02, 0.04)*0.3930	
	Atrial fibrillation or flutter at enrolment ECG						0.5467
	Yes	324/1199 (27.0)	319/1199 (26.6)	1.05 (0.93, 1.18) 0.4740	1.06 (0.88, 1.29) 0.5226	0.00 (-0.03, 0.04)*0.8177	
	No	392/1643 (23.9)	393/1638 (24.0)	0.99 (0.88, 1.11) 0.8843	0.98 (0.82, 1.15) 0.7718	-0.00 (-0.03, 0.03)*0.9284	
	BMI (kg/m2) at enrolment						0.6382
	< 30	429/1571 (27.3)	423/1559 (27.1)	1.03 (0.93, 1.15) 0.5407	1.04 (0.88, 1.23) 0.6225	0.00 (-0.03, 0.03)*0.9126	
	>= 30	287/1270 (22.6)	289/1275 (22.7)	0.99 (0.86, 1.14) 0.8997	0.98 (0.80, 1.18) 0.8045	-0.00 (-0.03, 0.03)*0.9672	
	Baseline eGFR (mL/min/1.73m^2)						0.7868
	< 60	338/1359 (24.9)	342/1396 (24.5)	1.03 (0.91, 1.16) 0.6762	1.00 (0.84, 1.21) 0.9613	0.00 (-0.03, 0.04)*0.8206	
	>= 60	378/1483 (25.5)	370/1440 (25.7)	1.00 (0.89, 1.13) 0.9574	1.02 (0.85, 1.21) 0.8581	-0.00 (-0.03, 0.03)*0.8987	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.1826
	<= median	377/1424 (26.5)	361/1439 (25.1)	1.07 (0.95, 1.20) 0.2515	1.10 (0.92, 1.31) 0.3160	0.01 (-0.02, 0.05)*0.3959	
	> median	339/1418 (23.9)	351/1398 (25.1)	0.95 (0.85, 1.08) 0.4578	0.93 (0.78, 1.11) 0.4306	-0.01 (-0.04, 0.02)*0.4590	
	LVEF at enrolment 2						0.2358
	<= 49	246/ 980 (25.1)	218/ 963 (22.6)	1.09 (0.93, 1.26) 0.2785	1.11 (0.90, 1.39) 0.3328	0.02 (-0.01, 0.06)*0.2024	
	>= 50	470/1862 (25.2)	494/1874 (26.4)	0.98 (0.89, 1.09) 0.7143	0.96 (0.82, 1.13) 0.6379	-0.01 (-0.04, 0.02)*0.4344	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4423
	Yes	61/ 283 (21.6)	68/ 286 (23.8)	0.91 (0.68, 1.20) 0.4964	0.84 (0.55, 1.27) 0.4014	-0.02 (-0.09, 0.05)*0.5267	
	No	655/2559 (25.6)	644/2551 (25.2)	1.03 (0.94, 1.12) 0.5754	1.03 (0.90, 1.18) 0.6601	0.00 (-0.02, 0.03)*0.7733	
	MRAs at baseline						0.5614
	Yes	315/1227 (25.7)	321/1224 (26.2)	0.98 (0.87, 1.11) 0.7976	0.96 (0.79, 1.16) 0.6469	-0.01 (-0.04, 0.03)*0.7548	
	No	401/1615 (24.8)	391/1613 (24.2)	1.04 (0.93, 1.16) 0.5237	1.05 (0.89, 1.24) 0.5733	0.01 (-0.02, 0.04)*0.6973	
	ACEi+ARB at baseline						0.8761
	Yes	500/2065 (24.2)	509/2077 (24.5)	1.01 (0.92, 1.12) 0.8229	0.99 (0.85, 1.15) 0.8821	-0.00 (-0.03, 0.02)*0.8259	
	No	216/ 777 (27.8)	203/ 760 (26.7)	1.03 (0.88, 1.20) 0.7290	1.07 (0.84, 1.35) 0.5931	0.01 (-0.03, 0.06)*0.6317	
	ARNI at baseline						0.6190
	Yes	45/ 153 (29.4)	37/ 126 (29.4)	0.92 (0.64, 1.32) 0.6569	0.94 (0.54, 1.61) 0.8120	0.00 (-0.11, 0.11)*0.9932	
	No	671/2689 (25.0)	675/2711 (24.9)	1.02 (0.94, 1.11) 0.6409	1.02 (0.89, 1.16) 0.8186	0.00 (-0.02, 0.02)*0.9628	
	Beta Blocker at baseline						0.6531
	Yes	610/2360 (25.8)	601/2356 (25.5)	1.02 (0.93, 1.12) 0.6244	1.02 (0.89, 1.17) 0.7621	0.00 (-0.02, 0.03)*0.7904	
	No	106/ 482 (22.0)	111/ 481 (23.1)	0.97 (0.78, 1.20) 0.7604	0.96 (0.70, 1.31) 0.7760	-0.01 (-0.06, 0.04)*0.6869	
	Diuretics at baseline						0.5001
	Yes	645/2536 (25.4)	645/2531 (25.5)	1.00 (0.92, 1.10) 0.9179	1.00 (0.88, 1.14) 0.9975	-0.00 (-0.02, 0.02)*0.9673	
	No	71/ 306 (23.2)	67/ 306 (21.9)	1.12 (0.85, 1.47) 0.4151	1.13 (0.75, 1.69) 0.5632	0.01 (-0.05, 0.08)*0.6988	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	691/2842 (24.3)	829/2837 (29.2)	0.83 (0.77, 0.90) <.0001	0.76 (0.67, 0.86) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Age						0.9077
	<= median	315/1415 (22.3)	388/1482 (26.2)	0.84 (0.74, 0.95) 0.0049	0.78 (0.65, 0.93) 0.0055	-0.04 (-0.07, -0.01)*0.0137	
	> median	376/1427 (26.3)	441/1355 (32.5)	0.83 (0.74, 0.92) 0.0006	0.74 (0.62, 0.88) 0.0005	-0.06 (-0.10, -0.03)*0.0003	
	Gender						0.4710
	Male	405/1656 (24.5)	463/1625 (28.5)	0.85 (0.77, 0.95) 0.0048	0.80 (0.68, 0.93) 0.0053	-0.04 (-0.07, -0.01)*0.0087	
	Female	286/1186 (24.1)	366/1212 (30.2)	0.81 (0.71, 0.91) 0.0006	0.72 (0.60, 0.87) 0.0008	-0.06 (-0.10, -0.03)*0.0008	
	Race						0.1270
	White	513/2039 (25.2)	612/2058 (29.7)	0.86 (0.78, 0.94) 0.0015	0.79 (0.69, 0.92) 0.0016	-0.05 (-0.07, -0.02)*0.0010	
	Black or African	20/ 67 (29.9)	16/ 71 (22.5)	1.29 (0.76, 2.21) 0.3501	1.40 (0.63, 3.10) 0.4074	0.07 (-0.07, 0.22)*0.3276	
	Asian	133/ 558 (23.8)	168/ 555 (30.3)	0.77 (0.64, 0.94) 0.0094	0.70 (0.53, 0.92) 0.0091	-0.07 (-0.12, -0.02) 0.0078	
	Other	25/ 178 (14.0)	33/ 153 (21.6)	0.60 (0.39, 0.92) 0.0187	0.51 (0.27, 0.94) 0.0313	-0.08 (-0.16, 0.01)*0.0749	
	Geographic region						0.2751
	Asia	127/ 539 (23.6)	161/ 538 (29.9)	0.78 (0.64, 0.95) 0.0121	0.70 (0.54, 0.93) 0.0122	-0.06 (-0.12, -0.01) 0.0140	
	Europe and Saudi Arabia	345/1365 (25.3)	430/1394 (30.8)	0.84 (0.75, 0.94) 0.0020	0.76 (0.63, 0.90) 0.0017	-0.06 (-0.09, -0.02)*0.0011	
	North America	114/ 398 (28.6)	111/ 387 (28.7)	1.00 (0.81, 1.23) 0.9730	0.97 (0.71, 1.34) 0.8605	-0.00 (-0.06, 0.06)*0.9904	
	Latin America	105/ 540 (19.4)	127/ 518 (24.5)	0.77 (0.63, 0.95) 0.0144	0.69 (0.51, 0.95) 0.0229	-0.05 (-0.10, -0.00)*0.0462	
	NYHA class at enrolment						0.3614
	II	522/2113 (24.7)	654/2187 (29.9)	0.81 (0.74, 0.89) <.0001	0.74 (0.64, 0.85) <.0001	-0.05 (-0.08, -0.03)*0.0001	
	III or IV	169/ 729 (23.2)	175/ 649 (27.0)	0.89 (0.75, 1.06) 0.1872	0.82 (0.63, 1.06) 0.1259	-0.04 (-0.08, 0.01)*0.1061	
	LVEF at enrolment						0.9108
	<= 49	235/ 980 (24.0)	266/ 963 (27.6)	0.86 (0.74, 0.99) 0.0380	0.79 (0.64, 0.98) 0.0282	-0.04 (-0.08, 0.00)*0.0664	
	50-59	266/1029 (25.9)	313/1017 (30.8)	0.82 (0.72, 0.94) 0.0032	0.77 (0.63, 0.94) 0.0092	-0.05 (-0.09, -0.01)*0.0133	
	>= 60	190/ 833 (22.8)	250/ 857 (29.2)	0.82 (0.70, 0.96) 0.0113	0.73 (0.58, 0.92) 0.0067	-0.06 (-0.11, -0.02)*0.0028	
	NT-proBNP at enrolment						0.1936
	<= median	352/1418 (24.8)	394/1421 (27.7)	0.88 (0.78, 0.99) 0.0340	0.85 (0.71, 1.01) 0.0595	-0.03 (-0.06, 0.00)*0.0787	
	> median	339/1424 (23.8)	435/1415 (30.7)	0.79 (0.71, 0.89) <.0001	0.68 (0.58, 0.81) <.0001	-0.07 (-0.10, -0.04)*<.0001	
	Type 2 Diabetes Medical History						0.4320
	Yes	306/1250 (24.5)	384/1260 (30.5)	0.81 (0.71, 0.91) 0.0005	0.74 (0.62, 0.88)*0.0008	-0.06 (-0.09, -0.03)*0.0007	
	No	385/1592 (24.2)	445/1577 (28.2)	0.86 (0.77, 0.96) 0.0087	0.81 (0.69, 0.95)*0.0099	-0.04 (-0.07, -0.01)*0.0097	
	Atrial fibrillation or flutter at enrolment ECG						0.7094
	Yes	284/1199 (23.7)	344/1199 (28.7)	0.82 (0.72, 0.93) 0.0018	0.74 (0.61, 0.90) 0.0020	-0.05 (-0.09, -0.01)*0.0052	
	No	407/1643 (24.8)	485/1638 (29.6)	0.84 (0.76, 0.94) 0.0019	0.78 (0.66, 0.91) 0.0018	-0.05 (-0.08, -0.02)*0.0018	
	BMI (kg/m2) at enrolment						0.8079
	< 30	392/1571 (25.0)	470/1559 (30.1)	0.83 (0.74, 0.92) 0.0007	0.75 (0.64, 0.88) 0.0005	-0.05 (-0.08, -0.02)*0.0011	
	>= 30	299/1270 (23.5)	357/1275 (28.0)	0.85 (0.75, 0.96) 0.0077	0.78 (0.65, 0.95) 0.0109	-0.04 (-0.08, -0.01)*0.0101	
	Baseline eGFR (mL/min/1.73m^2)						0.9111
	< 60	356/1359 (26.2)	440/1396 (31.5)	0.83 (0.74, 0.93) 0.0010	0.75 (0.63, 0.89) 0.0012	-0.05 (-0.09, -0.02)*0.0020	
	>= 60	335/1483 (22.6)	389/1440 (27.0)	0.84 (0.74, 0.95) 0.0050	0.78 (0.65, 0.92) 0.0045	-0.04 (-0.08, -0.01)*0.0056	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)	SBP at randomisation						0.8745
	<= median	358/1424 (25.1)	435/1439 (30.2)	0.84 (0.75, 0.94) 0.0025	0.78 (0.66, 0.92) 0.0037	-0.05 (-0.08, -0.02)*0.0023	
	> median	333/1418 (23.5)	394/1398 (28.2)	0.83 (0.73, 0.93) 0.0019	0.75 (0.63, 0.89) 0.0013	-0.05 (-0.08, -0.01)*0.0043	
	LVEF at enrolment 2						0.6941
	<= 49	235/ 980 (24.0)	266/ 963 (27.6)	0.86 (0.74, 0.99) 0.0380	0.79 (0.64, 0.98) 0.0282	-0.04 (-0.08, 0.00)*0.0664	
	>= 50	456/1862 (24.5)	563/1874 (30.0)	0.82 (0.75, 0.91) 0.0001	0.75 (0.65, 0.87) 0.0002	-0.06 (-0.08, -0.03)*0.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6691
	Yes	57/ 283 (20.1)	61/ 286 (21.3)	0.85 (0.64, 1.13) 0.2641	0.72 (0.46, 1.13) 0.1519	-0.01 (-0.08, 0.05)*0.7268	
	No	634/2559 (24.8)	768/2551 (30.1)	0.83 (0.76, 0.90) <.0001	0.76 (0.67, 0.86) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	MRAs at baseline						0.6809
	Yes	299/1227 (24.4)	364/1224 (29.7)	0.81 (0.72, 0.92) 0.0012	0.74 (0.61, 0.89) 0.0015	-0.05 (-0.09, -0.02)*0.0027	
	No	392/1615 (24.3)	465/1613 (28.8)	0.85 (0.76, 0.94) 0.0029	0.78 (0.66, 0.91) 0.0024	-0.05 (-0.08, -0.02)*0.0033	
	ACEi+ARB at baseline						0.0790
	Yes	487/2065 (23.6)	621/2077 (29.9)	0.80 (0.72, 0.88) <.0001	0.71 (0.61, 0.82) <.0001	-0.06 (-0.09, -0.04)*<.0001	
	No	204/ 777 (26.3)	208/ 760 (27.4)	0.95 (0.81, 1.12) 0.5351	0.92 (0.73, 1.16) 0.5007	-0.02 (-0.07, 0.02) 0.2599	
	ARNI at baseline						0.1666
	Yes	38/ 153 (24.8)	25/ 126 (19.8)	1.17 (0.75, 1.83) 0.4936	1.25 (0.69, 2.24) 0.4616	0.05 (-0.05, 0.15)*0.3161	
	No	653/2689 (24.3)	804/2711 (29.7)	0.83 (0.76, 0.90) <.0001	0.75 (0.66, 0.85) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	Beta Blocker at baseline						0.1400
	Yes	584/2360 (24.7)	689/2356 (29.2)	0.86 (0.78, 0.94) 0.0008	0.79 (0.69, 0.91) 0.0007	-0.04 (-0.07, -0.02)*0.0005	
	No	107/ 482 (22.2)	140/ 481 (29.1)	0.72 (0.59, 0.89) 0.0020	0.63 (0.47, 0.85) 0.0029	-0.07 (-0.12, -0.01)*0.0138	
	Diuretics at baseline						0.1889
	Yes	635/2536 (25.0)	744/2531 (29.4)	0.85 (0.78, 0.92) 0.0002	0.78 (0.69, 0.89) 0.0001	-0.04 (-0.07, -0.02)*0.0005	
	No	56/ 306 (18.3)	85/ 306 (27.8)	0.70 (0.53, 0.93) 0.0129	0.61 (0.41, 0.91) 0.0152	-0.09 (-0.16, -0.03)*0.0051	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)							
	Overall	837/2669 (31.4)	862/2664 (32.4)	0.96 (0.89, 1.04) 0.3093	0.95 (0.84, 1.07) 0.3969	-0.01 (-0.03, 0.01) 0.4422	
	Age						0.0593
	<= median	378/1352 (28.0)	439/1422 (30.9)	0.89 (0.79, 0.99) 0.0332	0.84 (0.71, 1.00) 0.0500	-0.03 (-0.06, 0.00) 0.0806	
	> median	459/1317 (34.9)	423/1242 (34.1)	1.03 (0.93, 1.14) 0.5902	1.05 (0.89, 1.25) 0.5521	0.01 (-0.02, 0.04) 0.5706	
	Gender						0.9867
	Male	489/1568 (31.2)	483/1518 (31.8)	0.96 (0.87, 1.06) 0.4522	0.96 (0.82, 1.12) 0.5987	-0.01 (-0.03, 0.02) 0.7235	
	Female	348/1101 (31.6)	379/1146 (33.1)	0.96 (0.86, 1.08) 0.5354	0.94 (0.79, 1.13) 0.5400	-0.01 (-0.05, 0.02) 0.5025	
	Race						0.6543
	White	636/1925 (33.0)	665/1952 (34.1)	0.98 (0.90, 1.06) 0.5845	0.97 (0.85, 1.12) 0.6959	-0.00 (-0.03, 0.02) 0.7978	
	Black or African	25/ 61 (41.0)	24/ 67 (35.8)	1.09 (0.72, 1.64) 0.6844	1.18 (0.56, 2.50) 0.6629	0.00 (-0.17, 0.17) 0.9882	
	Asian	136/ 510 (26.7)	144/ 500 (28.8)	0.91 (0.75, 1.11) 0.3442	0.88 (0.67, 1.16) 0.3704	-0.02 (-0.08, 0.03) 0.4383	
	Other	40/ 173 (23.1)	29/ 145 (20.0)	1.09 (0.73, 1.63) 0.6716	1.08 (0.61, 1.89) 0.7985	0.00 (-0.09, 0.09) 0.9661	
	Geographic region						0.7507
	Asia	128/ 496 (25.8)	136/ 486 (28.0)	0.91 (0.74, 1.11) 0.3536	0.88 (0.66, 1.17) 0.3767	-0.02 (-0.08, 0.03) 0.4343	
	Europe and Saudi Arabia	437/1299 (33.6)	454/1323 (34.3)	1.00 (0.91, 1.10) 0.9961	1.00 (0.85, 1.19) 0.9561	0.01 (-0.02, 0.04) 0.6571	
	North America	138/ 372 (37.1)	133/ 359 (37.0)	0.99 (0.82, 1.18) 0.8710	0.97 (0.71, 1.32) 0.8378	-0.01 (-0.08, 0.06) 0.7790	
	Latin America	134/ 502 (26.7)	139/ 496 (28.0)	0.93 (0.77, 1.12) 0.4400	0.92 (0.68, 1.23) 0.5643	-0.02 (-0.07, 0.03) 0.4333	
	NYHA class at enrolment						0.7334
	II	606/1986 (30.5)	641/2059 (31.1)	0.96 (0.88, 1.05) 0.3764	0.95 (0.83, 1.09) 0.4988	-0.01 (-0.04, 0.01) 0.4208	
	III or IV	231/ 683 (33.8)	220/ 604 (36.4)	0.93 (0.82, 1.07) 0.3251	0.88 (0.69, 1.12) 0.2852	-0.02 (-0.07, 0.03) 0.3888	
	LVEF at enrolment						0.4268
	<= 49	285/ 928 (30.7)	262/ 912 (28.7)	1.03 (0.90, 1.18) 0.6537	1.05 (0.86, 1.29) 0.6266	0.01 (-0.03, 0.05) 0.6766	
	50-59	325/ 970 (33.5)	351/ 956 (36.7)	0.92 (0.82, 1.03) 0.1586	0.89 (0.74, 1.08) 0.2518	-0.02 (-0.06, 0.02) 0.2416	
	>= 60	227/ 771 (29.4)	249/ 796 (31.3)	0.95 (0.82, 1.09) 0.4653	0.91 (0.73, 1.14) 0.4266	-0.01 (-0.06, 0.03) 0.5271	
	NT-proBNP at enrolment						0.4440
	<= median	428/1334 (32.1)	429/1350 (31.8)	0.99 (0.89, 1.10) 0.8592	1.00 (0.85, 1.19) 0.9618	0.00 (-0.03, 0.04) 0.8002	
	> median	409/1335 (30.6)	433/1313 (33.0)	0.93 (0.84, 1.04) 0.2037	0.90 (0.76, 1.06) 0.2053	-0.02 (-0.05, 0.01) 0.1846	
	Type 2 Diabetes Medical History						0.9787
	Yes	366/1169 (31.3)	383/1186 (32.3)	0.96 (0.86, 1.08) 0.5042	0.96 (0.80, 1.14)*0.6080	-0.01 (-0.04, 0.03) 0.6294	
	No	471/1500 (31.4)	479/1478 (32.4)	0.96 (0.87, 1.07) 0.4662	0.95 (0.82, 1.11)*0.5549	-0.01 (-0.04, 0.02) 0.5510	
	Atrial fibrillation or flutter at enrolment ECG						0.7386
	Yes	334/1113 (30.0)	346/1123 (30.8)	0.98 (0.86, 1.10) 0.6841	0.96 (0.80, 1.16) 0.6704	-0.00 (-0.04, 0.03) 0.8095	
	No	503/1556 (32.3)	516/1541 (33.5)	0.95 (0.86, 1.05) 0.2895	0.94 (0.81, 1.10) 0.4431	-0.01 (-0.04, 0.02) 0.4178	
	BMI (kg/m2) at enrolment						0.1503
	< 30	445/1478 (30.1)	474/1451 (32.7)	0.92 (0.83, 1.01) 0.0910	0.88 (0.75, 1.03) 0.1180	-0.02 (-0.05, 0.01) 0.1528	
	>= 30	391/1190 (32.9)	388/1211 (32.0)	1.02 (0.91, 1.14) 0.7068	1.04 (0.87, 1.24) 0.6636	0.01 (-0.03, 0.04) 0.7170	
	Baseline eGFR (mL/min/1.73m^2)						0.6626
	< 60	429/1266 (33.9)	445/1297 (34.3)	0.98 (0.89, 1.09) 0.7244	0.97 (0.82, 1.15) 0.7554	-0.01 (-0.04, 0.03) 0.7002	
	>= 60	408/1403 (29.1)	416/1366 (30.5)	0.95 (0.85, 1.06) 0.3220	0.94 (0.79, 1.11) 0.4345	-0.01 (-0.04, 0.02) 0.6050	

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Social Limitation (LOCF)	SBP at randomisation						0.6357
	<= median	420/1344 (31.3)	427/1344 (31.8)	0.98 (0.88, 1.09) 0.7093	0.99 (0.84, 1.18) 0.9425	0.00 (-0.03, 0.03) 0.9917	
	> median	417/1325 (31.5)	435/1320 (33.0)	0.94 (0.85, 1.05) 0.2883	0.91 (0.77, 1.07) 0.2518	-0.02 (-0.05, 0.01) 0.2673	
	LVEF at enrolment 2						0.2179
	<= 49	285/ 928 (30.7)	262/ 912 (28.7)	1.03 (0.90, 1.18) 0.6537	1.05 (0.86, 1.29) 0.6266	0.01 (-0.03, 0.05) 0.6766	
	>= 50	552/1741 (31.7)	600/1752 (34.2)	0.93 (0.85, 1.02) 0.1291	0.90 (0.78, 1.05) 0.1750	-0.02 (-0.05, 0.01) 0.2194	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3630
	Yes	82/ 257 (31.9)	77/ 261 (29.5)	1.07 (0.85, 1.37) 0.5564	1.11 (0.75, 1.66) 0.5923	0.04 (-0.03, 0.11) 0.2499	
	No	755/2412 (31.3)	785/2403 (32.7)	0.95 (0.88, 1.03) 0.2225	0.94 (0.83, 1.06) 0.2959	-0.01 (-0.04, 0.01) 0.2730	
	MRAs at baseline						0.6034
	Yes	358/1155 (31.0)	368/1146 (32.1)	0.94 (0.84, 1.06) 0.3298	0.93 (0.78, 1.12) 0.4554	-0.01 (-0.04, 0.03) 0.6444	
	No	479/1514 (31.6)	494/1518 (32.5)	0.98 (0.89, 1.08) 0.6684	0.97 (0.82, 1.13) 0.6636	-0.01 (-0.04, 0.02) 0.4607	
	ACEi+ARB at baseline						0.6886
	Yes	596/1940 (30.7)	632/1959 (32.3)	0.95 (0.87, 1.04) 0.2691	0.93 (0.81, 1.07) 0.2937	-0.01 (-0.04, 0.01) 0.3521	
	No	241/ 729 (33.1)	230/ 705 (32.6)	1.00 (0.86, 1.15) 0.9543	1.01 (0.81, 1.27) 0.9186	0.00 (-0.04, 0.05) 0.8629	
	ARNI at baseline						0.9916
	Yes	47/ 149 (31.5)	37/ 116 (31.9)	1.02 (0.72, 1.46) 0.8971	1.03 (0.61, 1.76) 0.9094	0.00 (-0.11, 0.11) 0.9722	
	No	790/2520 (31.3)	825/2548 (32.4)	0.96 (0.89, 1.04) 0.3268	0.95 (0.84, 1.07) 0.4223	-0.01 (-0.03, 0.02) 0.5176	
	Beta Blocker at baseline						0.5619
	Yes	707/2232 (31.7)	725/2218 (32.7)	0.97 (0.90, 1.05) 0.4862	0.96 (0.84, 1.09) 0.5436	-0.01 (-0.03, 0.02) 0.5500	
	No	130/ 437 (29.7)	137/ 446 (30.7)	0.92 (0.76, 1.12) 0.4095	0.91 (0.67, 1.22) 0.5095	-0.01 (-0.07, 0.04) 0.6485	
	Diuretics at baseline						0.1784
	Yes	756/2391 (31.6)	787/2379 (33.1)	0.94 (0.87, 1.02) 0.1425	0.92 (0.81, 1.04) 0.1968	-0.01 (-0.04, 0.01) 0.2742	
	No	81/ 278 (29.1)	75/ 285 (26.3)	1.14 (0.88, 1.48) 0.3305	1.21 (0.83, 1.76) 0.3232	0.04 (-0.03, 0.11) 0.3093	

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Symptom Stability (LOCF)							
	Overall	652/2842 (22.9)	650/2837 (22.9)	1.05 (1.00, 1.11) 0.0577	1.07 (0.92, 1.24) 0.4026	0.00 (-0.02, 0.02)*0.9785	
	Age						0.7639
	<= median	312/1415 (22.0)	329/1482 (22.2)	1.06 (0.98, 1.14) 0.1249	1.03 (0.83, 1.29) 0.7666	-0.00 (-0.03, 0.03)*0.9224	
	> median	340/1427 (23.8)	321/1355 (23.7)	1.04 (0.97, 1.12) 0.2973	1.08 (0.87, 1.34) 0.4654	0.00 (-0.03, 0.03)*0.9328	
	Gender						0.3551
	Male	390/1656 (23.6)	376/1625 (23.1)	1.07 (1.00, 1.15) 0.0355	1.13 (0.92, 1.39) 0.2381	0.00 (-0.02, 0.03)*0.7802	
	Female	262/1186 (22.1)	274/1212 (22.6)	1.01 (0.93, 1.11) 0.7488	0.99 (0.79, 1.25) 0.9651	-0.01 (-0.04, 0.03)*0.7616	
	Race						0.5128*
	White	458/2039 (22.5)	477/2058 (23.2)	1.04 (0.98, 1.10) 0.2291	1.05 (0.88, 1.26) 0.5941	-0.01 (-0.03, 0.02)*0.5851	
	Black or African	18/ 67 (26.9)	15/ 71 (21.1)	1.27 (0.70, 2.31)*0.4312	1.80 (0.71, 4.55) 0.2161	0.06 (-0.09, 0.20)*0.4296	
	Asian	152/ 558 (27.2)	135/ 555 (24.3)	1.06 (0.93, 1.21) 0.3923	1.15 (0.83, 1.58) 0.4050	0.03 (-0.02, 0.08)*0.2659	
	Other	24/ 178 (13.5)	23/ 153 (15.0)	0.90 (0.53, 1.52)*0.6872	0.73 (0.33, 1.62) 0.4455	-0.02 (-0.09, 0.06)*0.6881	
	Geographic region						0.6625
	Asia	145/ 539 (26.9)	131/ 538 (24.3)	1.06 (0.93, 1.20) 0.3981	1.14 (0.82, 1.58) 0.4498	0.03 (-0.03, 0.08)*0.3372	
	Europe and Saudi Arabia	286/1365 (21.0)	312/1394 (22.4)	1.02 (0.94, 1.10) 0.6376	0.92 (0.73, 1.16) 0.4829	-0.01 (-0.05, 0.02)*0.3621	
	North America	97/ 398 (24.4)	96/ 387 (24.8)	1.09 (0.94, 1.27) 0.2615	1.23 (0.84, 1.81) 0.2890	-0.00 (-0.06, 0.06)*0.8876	
	Latin America	124/ 540 (23.0)	111/ 518 (21.4)	1.11 (1.00, 1.24) 0.0580	1.22 (0.84, 1.77) 0.2998	0.02 (-0.03, 0.07)*0.5481	
	NYHA class at enrolment						0.7627
	II	465/2113 (22.0)	471/2187 (21.5)	1.06 (0.99, 1.13) 0.1079	1.07 (0.89, 1.27) 0.4797	0.00 (-0.02, 0.03)*0.7087	
	III or IV	187/ 729 (25.7)	179/ 649 (27.6)	1.04 (0.96, 1.13) 0.3536	1.03 (0.76, 1.38) 0.8567	-0.02 (-0.07, 0.03)*0.4188	
	LVEF at enrolment						0.4314
	<= 49	216/ 980 (22.0)	224/ 963 (23.3)	1.02 (0.92, 1.12) 0.7397	0.91 (0.70, 1.18) 0.4797	-0.01 (-0.05, 0.03)*0.5207	
	50-59	243/1029 (23.6)	244/1017 (24.0)	1.05 (0.97, 1.13) 0.2079	1.09 (0.85, 1.40) 0.4877	-0.00 (-0.04, 0.03)*0.8413	
	>= 60	193/ 833 (23.2)	182/ 857 (21.2)	1.10 (1.00, 1.22) 0.0573	1.25 (0.94, 1.65) 0.1287	0.02 (-0.02, 0.06)*0.3392	
	NT-proBNP at enrolment						0.8004
	<= median	318/1418 (22.4)	304/1421 (21.4)	1.04 (0.97, 1.13) 0.2760	1.11 (0.89, 1.38) 0.3602	0.01 (-0.02, 0.04)*0.5060	
	> median	334/1424 (23.5)	346/1415 (24.5)	1.06 (0.98, 1.14) 0.1247	1.03 (0.83, 1.27) 0.7879	-0.01 (-0.04, 0.02)*0.5336	
	Type 2 Diabetes Medical History						0.0404
	Yes	312/1250 (25.0)	287/1260 (22.8)	1.10 (1.03, 1.19) 0.0087	1.13 (0.94, 1.36)*0.1998	0.02 (-0.01, 0.06)*0.1996	
	No	340/1592 (21.4)	363/1577 (23.0)	0.99 (0.91, 1.07) 0.7278	0.91 (0.77, 1.07)*0.2604	-0.02 (-0.05, 0.01)*0.2603	
	Atrial fibrillation or flutter at enrolment ECG						0.8369
	Yes	277/1199 (23.1)	275/1199 (22.9)	1.04 (0.97, 1.12) 0.2430	1.09 (0.86, 1.38) 0.4751	0.00 (-0.03, 0.04)*0.9227	
	No	375/1643 (22.8)	375/1638 (22.9)	1.07 (0.99, 1.15) 0.0900	1.05 (0.86, 1.28) 0.6424	-0.00 (-0.03, 0.03)*0.9621	
	BMI (kg/m2) at enrolment						0.3293
	< 30	364/1571 (23.2)	367/1559 (23.5)	1.03 (0.96, 1.11) 0.4055	1.03 (0.84, 1.27) 0.7583	-0.00 (-0.03, 0.03)*0.8063	
	>= 30	288/1270 (22.7)	283/1275 (22.2)	1.08 (1.01, 1.16) 0.0280	1.11 (0.88, 1.40) 0.3621	0.00 (-0.03, 0.04)*0.7711	
	Baseline eGFR (mL/min/1.73m^2)						0.0982
	< 60	355/1359 (26.1)	332/1396 (23.8)	1.10 (1.02, 1.18) 0.0128	1.26 (1.02, 1.56) 0.0322	0.02 (-0.01, 0.06)*0.1558	
	>= 60	297/1483 (20.0)	318/1440 (22.1)	1.01 (0.93, 1.09) 0.8393	0.90 (0.72, 1.12) 0.3485	-0.02 (-0.05, 0.01)*0.1728	

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Symptom Stability (LOCF)	SBP at randomisation						0.1266
	<= median	366/1424 (25.7)	350/1439 (24.3)	1.09 (1.02, 1.17) 0.0074	1.20 (0.97, 1.48) 0.0883	0.01 (-0.02, 0.05)*0.3940	
	> median	286/1418 (20.2)	300/1398 (21.5)	1.00 (0.91, 1.09) 0.9610	0.94 (0.75, 1.17) 0.5681	-0.01 (-0.04, 0.02)*0.3992	
	LVEF at enrolment 2						0.3059
	<= 49	216/ 980 (22.0)	224/ 963 (23.3)	1.02 (0.92, 1.12) 0.7397	0.91 (0.70, 1.18) 0.4797	-0.01 (-0.05, 0.03)*0.5207	
	>= 50	436/1862 (23.4)	426/1874 (22.7)	1.07 (1.01, 1.14) 0.0271	1.16 (0.96, 1.40) 0.1277	0.01 (-0.02, 0.03)*0.6200	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0590
	Yes	105/ 283 (37.1)	96/ 286 (33.6)	1.18 (1.03, 1.35) 0.0164	1.33 (0.86, 2.08) 0.2044	0.04 (-0.04, 0.11)*0.3773	
	No	547/2559 (21.4)	554/2551 (21.7)	1.02 (0.97, 1.08) 0.4256	1.04 (0.88, 1.22) 0.6530	-0.00 (-0.03, 0.02)*0.7666	
	MRAs at baseline						0.6318
	Yes	292/1227 (23.8)	290/1224 (23.7)	1.04 (0.95, 1.14) 0.3620	0.99 (0.79, 1.24) 0.9588	0.00 (-0.03, 0.03)*0.9513	
	No	360/1615 (22.3)	360/1613 (22.3)	1.06 (1.01, 1.13) 0.0298	1.14 (0.93, 1.41) 0.2127	-0.00 (-0.03, 0.03)*0.9850	
	ACEi+ARB at baseline						0.6326
	Yes	463/2065 (22.4)	466/2077 (22.4)	1.04 (0.98, 1.10) 0.2448	1.03 (0.86, 1.24) 0.7362	-0.00 (-0.03, 0.03)*0.9908	
	No	189/ 777 (24.3)	184/ 760 (24.2)	1.08 (0.98, 1.19) 0.1030	1.15 (0.87, 1.53) 0.3324	0.00 (-0.04, 0.04)*0.9585	
	ARNI at baseline						0.2168
	Yes	38/ 153 (24.8)	34/ 126 (27.0)	0.92 (0.62, 1.37)*0.6831	0.73 (0.38, 1.43) 0.3611	-0.02 (-0.12, 0.08)*0.6840	
	No	614/2689 (22.8)	616/2711 (22.7)	1.06 (1.01, 1.12) 0.0262	1.09 (0.93, 1.28) 0.2774	0.00 (-0.02, 0.02)*0.9222	
	Beta Blocker at baseline						0.6137
	Yes	533/2360 (22.6)	530/2356 (22.5)	1.06 (1.00, 1.12) 0.0663	1.12 (0.95, 1.33) 0.1892	0.00 (-0.02, 0.02)*0.9417	
	No	119/ 482 (24.7)	120/ 481 (24.9)	1.03 (0.93, 1.14) 0.5776	0.85 (0.60, 1.22) 0.3846	-0.00 (-0.06, 0.05)*0.9258	
	Diuretics at baseline						0.8730
	Yes	591/2536 (23.3)	587/2531 (23.2)	1.05 (1.00, 1.11) 0.0696	1.07 (0.91, 1.26) 0.3972	0.00 (-0.02, 0.02)*0.9248	
	No	61/ 306 (19.9)	63/ 306 (20.6)	1.06 (0.84, 1.32) 0.6295	1.01 (0.63, 1.63) 0.9527	-0.01 (-0.07, 0.06)*0.8406	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	705/2842 (24.8)	809/2837 (28.5)	0.87 (0.80, 0.94) 0.0009	0.82 (0.72, 0.92) 0.0013	-0.04 (-0.06, -0.01)*0.0016	
	Age						0.4073
	<= median	304/1415 (21.5)	376/1482 (25.4)	0.83 (0.73, 0.95) 0.0052	0.78 (0.65, 0.93) 0.0062	-0.04 (-0.07, -0.01)*0.0134	
	> median	401/1427 (28.1)	433/1355 (32.0)	0.89 (0.80, 1.00) 0.0402	0.84 (0.71, 1.00) 0.0496	-0.04 (-0.07, -0.00)*0.0266	
	Gender						0.6551
	Male	403/1656 (24.3)	462/1625 (28.4)	0.85 (0.77, 0.95) 0.0054	0.80 (0.68, 0.94) 0.0069	-0.04 (-0.07, -0.01)*0.0077	
	Female	302/1186 (25.5)	347/1212 (28.6)	0.89 (0.79, 1.01) 0.0634	0.85 (0.70, 1.02) 0.0822	-0.03 (-0.07, 0.00)*0.0807	
	Race						0.4497
	White	525/2039 (25.7)	609/2058 (29.6)	0.88 (0.80, 0.96) 0.0065	0.83 (0.72, 0.96) 0.0100	-0.04 (-0.07, -0.01)*0.0059	
	Black or African	19/ 67 (28.4)	15/ 71 (21.1)	1.28 (0.72, 2.26) 0.4004	1.44 (0.65, 3.23) 0.3714	0.07 (-0.07, 0.22)*0.3241	
	Asian	136/ 558 (24.4)	155/ 555 (27.9)	0.86 (0.71, 1.05) 0.1373	0.81 (0.62, 1.07) 0.1355	-0.04 (-0.09, 0.01) 0.1300	
	Other	25/ 178 (14.0)	30/ 153 (19.6)	0.72 (0.46, 1.14) 0.1578	0.63 (0.34, 1.17) 0.1471	-0.06 (-0.14, 0.03)*0.1784	
	Geographic region						0.9785
	Asia	130/ 539 (24.1)	148/ 538 (27.5)	0.87 (0.71, 1.06) 0.1648	0.82 (0.63, 1.09) 0.1698	-0.03 (-0.09, 0.02) 0.1910	
	Europe and Saudi Arabia	356/1365 (26.1)	417/1394 (29.9)	0.89 (0.79, 0.99) 0.0359	0.83 (0.70, 0.99) 0.0413	-0.04 (-0.07, -0.00)*0.0248	
	North America	109/ 398 (27.4)	121/ 387 (31.3)	0.87 (0.71, 1.07) 0.1952	0.81 (0.59, 1.11) 0.1955	-0.04 (-0.10, 0.02)*0.2323	
	Latin America	110/ 540 (20.4)	123/ 518 (23.7)	0.84 (0.68, 1.04) 0.1036	0.79 (0.58, 1.07) 0.1292	-0.03 (-0.08, 0.02)*0.1856	
	NYHA class at enrolment						0.6165
	II	532/2113 (25.2)	636/2187 (29.1)	0.85 (0.78, 0.94) 0.0011	0.80 (0.69, 0.92) 0.0013	-0.04 (-0.07, -0.01)*0.0040	
	III or IV	173/ 729 (23.7)	173/ 649 (26.7)	0.90 (0.76, 1.07) 0.2202	0.86 (0.67, 1.11) 0.2531	-0.03 (-0.08, 0.02)*0.2121	
	LVEF at enrolment						0.5384
	<= 49	239/ 980 (24.4)	253/ 963 (26.3)	0.92 (0.79, 1.06) 0.2454	0.87 (0.71, 1.08) 0.2126	-0.02 (-0.06, 0.02)*0.3396	
	50-59	273/1029 (26.5)	303/1017 (29.8)	0.88 (0.77, 1.00) 0.0470	0.84 (0.69, 1.03) 0.0866	-0.03 (-0.07, 0.01)*0.1007	
	>= 60	193/ 833 (23.2)	253/ 857 (29.5)	0.81 (0.70, 0.95) 0.0087	0.74 (0.59, 0.93) 0.0085	-0.06 (-0.11, -0.02)*0.0029	
	NT-proBNP at enrolment						0.5233
	<= median	360/1418 (25.4)	396/1421 (27.9)	0.89 (0.79, 1.01) 0.0614	0.87 (0.73, 1.03) 0.1083	-0.02 (-0.06, 0.01)*0.1348	
	> median	345/1424 (24.2)	413/1415 (29.2)	0.85 (0.76, 0.95) 0.0056	0.77 (0.65, 0.92) 0.0033	-0.05 (-0.08, -0.02)*0.0028	
	Type 2 Diabetes Medical History						0.2986
	Yes	316/1250 (25.3)	384/1260 (30.5)	0.83 (0.74, 0.94) 0.0026	0.77 (0.65, 0.92)*0.0037	-0.05 (-0.09, -0.02)*0.0036	
	No	389/1592 (24.4)	425/1577 (26.9)	0.91 (0.81, 1.02) 0.0960	0.88 (0.75, 1.03)*0.1053	-0.03 (-0.06, 0.01)*0.1051	
	Atrial fibrillation or flutter at enrolment ECG						0.8413
	Yes	283/1199 (23.6)	319/1199 (26.6)	0.88 (0.77, 1.00) 0.0523	0.84 (0.69, 1.01) 0.0689	-0.03 (-0.06, 0.00)*0.0898	
	No	422/1643 (25.7)	490/1638 (29.9)	0.86 (0.78, 0.96) 0.0064	0.80 (0.69, 0.94) 0.0070	-0.04 (-0.07, -0.01)*0.0068	
	BMI (kg/m2) at enrolment						0.8551
	< 30	391/1571 (24.9)	448/1559 (28.7)	0.87 (0.77, 0.97) 0.0118	0.81 (0.69, 0.95) 0.0117	-0.04 (-0.07, -0.01)*0.0150	
	>= 30	314/1270 (24.7)	359/1275 (28.2)	0.88 (0.78, 0.99) 0.0358	0.84 (0.70, 1.01) 0.0576	-0.03 (-0.07, -0.00)*0.0494	
	Baseline eGFR (mL/min/1.73m^2)						0.3361
	< 60	375/1359 (27.6)	425/1396 (30.4)	0.91 (0.81, 1.01) 0.0778	0.86 (0.73, 1.03) 0.0939	-0.03 (-0.06, 0.01)*0.0991	
	>= 60	330/1483 (22.3)	384/1440 (26.7)	0.84 (0.74, 0.95) 0.0046	0.78 (0.65, 0.93) 0.0051	-0.04 (-0.08, -0.01)*0.0055	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=5 point deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.3922
	<= median	350/1424 (24.6)	428/1439 (29.7)	0.84 (0.75, 0.94) 0.0031	0.78 (0.66, 0.93) 0.0046	-0.05 (-0.08, -0.02)*0.0019	
	> median	355/1418 (25.0)	381/1398 (27.3)	0.90 (0.80, 1.02) 0.0896	0.86 (0.72, 1.02) 0.0919	-0.02 (-0.05, 0.01)*0.1804	
	LVEF at enrolment 2						0.4179
	<= 49	239/ 980 (24.4)	253/ 963 (26.3)	0.92 (0.79, 1.06) 0.2454	0.87 (0.71, 1.08) 0.2126	-0.02 (-0.06, 0.02)*0.3396	
	>= 50	466/1862 (25.0)	556/1874 (29.7)	0.85 (0.77, 0.94) 0.0013	0.80 (0.68, 0.92) 0.0027	-0.05 (-0.07, -0.02)*0.0014	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6123
	Yes	58/ 283 (20.5)	59/ 286 (20.6)	0.90 (0.67, 1.21) 0.4936	0.83 (0.54, 1.30) 0.4180	-0.00 (-0.07, 0.07)*0.9683	
	No	647/2559 (25.3)	750/2551 (29.4)	0.86 (0.79, 0.94) 0.0009	0.81 (0.72, 0.92) 0.0014	-0.04 (-0.07, -0.02)*0.0010	
	MRAs at baseline						0.6206
	Yes	301/1227 (24.5)	354/1224 (28.9)	0.85 (0.75, 0.96) 0.0104	0.79 (0.66, 0.95) 0.0137	-0.04 (-0.08, -0.01)*0.0139	
	No	404/1615 (25.0)	455/1613 (28.2)	0.89 (0.79, 0.99) 0.0293	0.84 (0.71, 0.99) 0.0327	-0.03 (-0.06, -0.00)*0.0400	
	ACEi+ARB at baseline						0.0153
	Yes	486/2065 (23.5)	606/2077 (29.2)	0.82 (0.74, 0.90) <.0001	0.74 (0.64, 0.86) <.0001	-0.06 (-0.08, -0.03)*<.0001	
	No	219/ 777 (28.2)	203/ 760 (26.7)	1.04 (0.89, 1.22) 0.6408	1.06 (0.85, 1.33) 0.6014	0.00 (-0.04, 0.05) 0.8273	
	ARNI at baseline						0.0529
	Yes	42/ 153 (27.5)	24/ 126 (19.0)	1.33 (0.85, 2.09) 0.2086	1.48 (0.83, 2.65) 0.1857	0.08 (-0.01, 0.18)*0.0945	
	No	663/2689 (24.7)	785/2711 (29.0)	0.86 (0.79, 0.93) 0.0003	0.80 (0.71, 0.91) 0.0005	-0.04 (-0.07, -0.02)*0.0004	
	Beta Blocker at baseline						0.4238
	Yes	595/2360 (25.2)	678/2356 (28.8)	0.88 (0.81, 0.97) 0.0071	0.84 (0.73, 0.96) 0.0096	-0.04 (-0.06, -0.01)*0.0058	
	No	110/ 482 (22.8)	131/ 481 (27.2)	0.81 (0.65, 1.00) 0.0452	0.73 (0.54, 0.99) 0.0427	-0.04 (-0.10, 0.01)*0.1135	
	Diuretics at baseline						0.0741
	Yes	651/2536 (25.7)	724/2531 (28.6)	0.89 (0.82, 0.97) 0.0083	0.85 (0.74, 0.96) 0.0110	-0.03 (-0.05, -0.00)*0.0188	
	No	54/ 306 (17.6)	85/ 306 (27.8)	0.69 (0.52, 0.92) 0.0106	0.58 (0.39, 0.87) 0.0087	-0.10 (-0.17, -0.04)*0.0026	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	1174/2801 (41.9)	1033/2805 (36.8)	1.13 (1.06, 1.20) 0.0002	1.23 (1.10, 1.37) 0.0002	0.05 (0.02, 0.07) 0.0002	
	Age						0.6746
	<= median	633/1394 (45.4)	578/1471 (39.3)	1.15 (1.06, 1.25) 0.0009	1.29 (1.11, 1.50) 0.0008	0.06 (0.03, 0.10) 0.0006	
	> median	541/1407 (38.5)	455/1334 (34.1)	1.11 (1.00, 1.22) 0.0395	1.18 (1.01, 1.38) 0.0432	0.04 (0.00, 0.07) 0.0377	
	Gender						0.1624
	Male	701/1630 (43.0)	630/1608 (39.2)	1.08 (1.00, 1.17) 0.0510	1.17 (1.01, 1.34) 0.0334	0.04 (0.00, 0.07) 0.0250	
	Female	473/1171 (40.4)	403/1197 (33.7)	1.18 (1.06, 1.30) 0.0016	1.31 (1.11, 1.56) 0.0018	0.06 (0.02, 0.10) 0.0023	
	Race						0.8108*
	White	798/2006 (39.8)	698/2032 (34.4)	1.13 (1.05, 1.22) 0.0018	1.24 (1.09, 1.42) 0.0013	0.05 (0.02, 0.08) 0.0007	
	Black or African	29/ 64 (45.3)	30/ 70 (42.9)	1.14 (0.78, 1.66) 0.4891	1.14 (0.57, 2.28) 0.7148	0.02 (-0.14, 0.19) 0.7685	
	Asian	262/ 555 (47.2)	241/ 551 (43.7)	1.08 (0.95, 1.23) 0.2435	1.15 (0.91, 1.46) 0.2482	0.03 (-0.02, 0.09) 0.2485	
	Other	85/ 176 (48.3)	64/ 152 (42.1)	1.15 (0.90, 1.46)*0.2648	1.31 (0.83, 2.08) 0.2483	0.08 (-0.02, 0.18) 0.1277	
	Geographic region						0.7937*
	Asia	254/ 536 (47.4)	237/ 536 (44.2)	1.07 (0.94, 1.22) 0.2894	1.14 (0.89, 1.44) 0.2999	0.03 (-0.03, 0.09) 0.3008	
	Europe and Saudi Arabia	525/1341 (39.1)	465/1381 (33.7)	1.16 (1.05, 1.28)*0.0030	1.24 (1.06, 1.46) 0.0085	0.05 (0.02, 0.08) 0.0042	
	North America	134/ 393 (34.1)	113/ 376 (30.1)	1.14 (0.92, 1.39) 0.2254	1.20 (0.89, 1.63) 0.2346	0.04 (-0.03, 0.11) 0.2272	
	Latin America	261/ 531 (49.2)	218/ 512 (42.6)	1.15 (1.01, 1.32)*0.0339	1.32 (1.02, 1.70) 0.0327	0.07 (0.01, 0.13) 0.0187	
	NYHA class at enrolment						0.0101
	II	849/2083 (40.8)	813/2165 (37.6)	1.08 (1.00, 1.16) 0.0469	1.15 (1.01, 1.30) 0.0304	0.03 (0.00, 0.06) 0.0266	
	III or IV	325/ 718 (45.3)	220/ 639 (34.4)	1.31 (1.15, 1.50)*<.0001	1.56 (1.24, 1.96) 0.0002	0.11 (0.06, 0.15) <.0001	
	LVEF at enrolment						0.5645
	<= 49	396/ 959 (41.3)	360/ 950 (37.9)	1.09 (0.98, 1.21) 0.1259	1.17 (0.97, 1.41) 0.1001	0.04 (-0.00, 0.08) 0.0788	
	50-59	431/1017 (42.4)	375/1009 (37.2)	1.11 (1.00, 1.23) 0.0529	1.23 (1.02, 1.47) 0.0270	0.05 (0.01, 0.09) 0.0229	
	>= 60	347/ 825 (42.1)	298/ 846 (35.2)	1.18 (1.05, 1.33) 0.0064	1.30 (1.07, 1.59) 0.0094	0.06 (0.01, 0.11) 0.0104	
	NT-proBNP at enrolment						0.2837
	<= median	560/1396 (40.1)	511/1409 (36.3)	1.10 (1.00, 1.20) 0.0525	1.18 (1.01, 1.37) 0.0373	0.04 (0.00, 0.07) 0.0320	
	> median	614/1405 (43.7)	521/1395 (37.3)	1.16 (1.06, 1.26) 0.0007	1.28 (1.10, 1.49) 0.0018	0.06 (0.02, 0.09) 0.0014	
	Type 2 Diabetes Medical History						0.0872
	Yes	527/1231 (42.8)	442/1243 (35.6)	1.20 (1.09, 1.32) 0.0002	1.36 (1.15, 1.60)*0.0002	0.07 (0.03, 0.11) 0.0002	
	No	647/1570 (41.2)	591/1562 (37.8)	1.07 (0.98, 1.16) 0.1329	1.15 (1.00, 1.33)*0.0535	0.03 (-0.00, 0.06) 0.0749	
	Atrial fibrillation or flutter at enrolment ECG						0.3903
	Yes	505/1185 (42.6)	431/1188 (36.3)	1.16 (1.05, 1.28) 0.0025	1.30 (1.10, 1.54) 0.0020	0.06 (0.02, 0.10) 0.0016	
	No	669/1616 (41.4)	602/1617 (37.2)	1.10 (1.01, 1.20) 0.0237	1.18 (1.02, 1.36) 0.0238	0.04 (0.01, 0.07) 0.0207	
	BMI (kg/m2) at enrolment						0.9407
	< 30	681/1547 (44.0)	596/1541 (38.7)	1.13 (1.04, 1.23) 0.0036	1.24 (1.07, 1.43) 0.0035	0.05 (0.02, 0.09) 0.0032	
	>= 30	493/1253 (39.3)	436/1261 (34.6)	1.12 (1.02, 1.23) 0.0217	1.21 (1.02, 1.43) 0.0250	0.04 (0.01, 0.08) 0.0180	
	Baseline eGFR (mL/min/1.73m^2)						0.8690
	< 60	530/1338 (39.6)	476/1377 (34.6)	1.13 (1.03, 1.24) 0.0136	1.23 (1.05, 1.45) 0.0090	0.05 (0.01, 0.08) 0.0069	
	>= 60	644/1463 (44.0)	557/1427 (39.0)	1.12 (1.03, 1.21) 0.0093	1.21 (1.04, 1.41) 0.0119	0.05 (0.01, 0.08) 0.0108	

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AstraZeneca
Protocol: D169CC00001
Overall study population
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Full Analysis Set

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Clinical Summary Score (LOCF)	SBP at randomisation						0.1150
	<= median	583/1405 (41.5)	535/1420 (37.7)	1.08 (0.99, 1.18) 0.1013	1.15 (0.98, 1.33) 0.0818	0.03 (-0.00, 0.07) 0.0835	
	> median	591/1396 (42.3)	498/1385 (36.0)	1.19 (1.09, 1.30) 0.0002	1.33 (1.14, 1.55) 0.0003	0.07 (0.03, 0.10) 0.0002	
	LVEF at enrolment 2						0.4419
	<= 49	396/ 959 (41.3)	360/ 950 (37.9)	1.09 (0.98, 1.21) 0.1259	1.17 (0.97, 1.41) 0.1001	0.04 (-0.00, 0.08) 0.0788	
	>= 50	778/1842 (42.2)	673/1855 (36.3)	1.15 (1.06, 1.24) 0.0006	1.26 (1.10, 1.44) 0.0007	0.05 (0.02, 0.08) 0.0007	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1365
	Yes	127/ 280 (45.4)	129/ 281 (45.9)	0.99 (0.82, 1.18)*0.8959	1.01 (0.71, 1.43) 0.9647	-0.00 (-0.08, 0.08) 0.9809	
	No	1047/2521 (41.5)	904/2524 (35.8)	1.15 (1.07, 1.23) <.0001	1.26 (1.12, 1.41) <.0001	0.05 (0.03, 0.08) <.0001	
	MRAs at baseline						0.6480
	Yes	511/1216 (42.0)	436/1210 (36.0)	1.15 (1.04, 1.26) 0.0058	1.28 (1.08, 1.51) 0.0039	0.06 (0.02, 0.10) 0.0029	
	No	663/1585 (41.8)	597/1595 (37.4)	1.11 (1.02, 1.21) 0.0127	1.19 (1.03, 1.38) 0.0169	0.04 (0.01, 0.07) 0.0160	
	ACEi+ARB at baseline						0.2596
	Yes	858/2037 (42.1)	743/2059 (36.1)	1.15 (1.07, 1.23) 0.0003	1.27 (1.12, 1.45) 0.0002	0.06 (0.03, 0.09) 0.0002	
	No	316/ 764 (41.4)	290/ 746 (38.9)	1.06 (0.94, 1.20) 0.3451	1.11 (0.90, 1.37) 0.3123	0.03 (-0.02, 0.08) 0.2914	
	ARNI at baseline						0.5647
	Yes	64/ 149 (43.0)	53/ 125 (42.4)	1.02 (0.77, 1.34) 0.8914	1.06 (0.65, 1.72) 0.8280	0.02 (-0.10, 0.13) 0.8044	
	No	1110/2652 (41.9)	980/2680 (36.6)	1.13 (1.06, 1.20) 0.0003	1.23 (1.10, 1.38) 0.0002	0.05 (0.02, 0.08) 0.0002	
	Beta Blocker at baseline						0.4906
	Yes	960/2327 (41.3)	849/2330 (36.4)	1.12 (1.04, 1.20) 0.0022	1.21 (1.07, 1.36) 0.0022	0.04 (0.02, 0.07) 0.0020	
	No	214/ 474 (45.1)	184/ 475 (38.7)	1.18 (1.02, 1.37) 0.0257	1.34 (1.03, 1.74) 0.0280	0.07 (0.01, 0.13) 0.0215	
	Diuretics at baseline						0.8307
	Yes	1040/2500 (41.6)	917/2504 (36.6)	1.12 (1.05, 1.20) 0.0007	1.23 (1.10, 1.38) 0.0004	0.05 (0.02, 0.08) 0.0003	
	No	134/ 301 (44.5)	116/ 301 (38.5)	1.15 (0.95, 1.38) 0.1456	1.23 (0.88, 1.71) 0.2191	0.05 (-0.03, 0.13) 0.2245	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	1089/2801 (38.9)	971/2805 (34.6)	1.11 (1.04, 1.19) 0.0014	1.19 (1.06, 1.33) 0.0022	0.04 (0.01, 0.06) 0.0018	
	Age						0.9465
	<= median	571/1394 (41.0)	537/1471 (36.5)	1.12 (1.02, 1.23) 0.0127	1.21 (1.04, 1.41) 0.0138	0.05 (0.01, 0.08) 0.0108	
	> median	518/1407 (36.8)	434/1334 (32.5)	1.11 (1.00, 1.22) 0.0409	1.17 (1.00, 1.38) 0.0518	0.03 (-0.00, 0.07) 0.0548	
	Gender						0.2645
	Male	639/1630 (39.2)	581/1608 (36.1)	1.08 (0.99, 1.17) 0.0932	1.13 (0.98, 1.31) 0.0918	0.03 (-0.00, 0.06) 0.0585	
	Female	450/1171 (38.4)	390/1197 (32.6)	1.16 (1.04, 1.28) 0.0059	1.26 (1.06, 1.50) 0.0082	0.04 (0.01, 0.08) 0.0196	
	Race						0.9805*
	White	739/2006 (36.8)	667/2032 (32.8)	1.12 (1.03, 1.22)*0.0075	1.16 (1.02, 1.33) 0.0278	0.03 (0.01, 0.06) 0.0199	
	Black or African	29/ 64 (45.3)	27/ 70 (38.6)	1.18 (0.79, 1.75) 0.4242	1.33 (0.67, 2.68) 0.4162	0.07 (-0.09, 0.24) 0.3965	
	Asian	239/ 555 (43.1)	211/ 551 (38.3)	1.13 (0.98, 1.30) 0.1049	1.22 (0.96, 1.56) 0.0997	0.05 (-0.01, 0.11) 0.0962	
	Other	82/ 176 (46.6)	66/ 152 (43.4)	1.10 (0.88, 1.37) 0.3930	1.18 (0.74, 1.86) 0.4900	0.04 (-0.06, 0.14) 0.4416	
	Geographic region						0.8951*
	Asia	234/ 536 (43.7)	208/ 536 (38.8)	1.12 (0.97, 1.30) 0.1077	1.22 (0.96, 1.56) 0.1033	0.05 (-0.01, 0.11) 0.1004	
	Europe and Saudi Arabia	487/1341 (36.3)	436/1381 (31.6)	1.15 (1.04, 1.28)*0.0090	1.20 (1.02, 1.42) 0.0294	0.04 (0.01, 0.07) 0.0223	
	North America	131/ 393 (33.3)	115/ 376 (30.6)	1.08 (0.88, 1.33) 0.4414	1.13 (0.84, 1.54) 0.4191	0.03 (-0.04, 0.09) 0.3918	
	Latin America	237/ 531 (44.6)	212/ 512 (41.4)	1.08 (0.94, 1.24)*0.2934	1.13 (0.88, 1.47) 0.3393	0.03 (-0.02, 0.09) 0.2616	
	NYHA class at enrolment						0.1359*
	II	798/2083 (38.3)	761/2165 (35.2)	1.09 (1.01, 1.18) 0.0296	1.15 (1.01, 1.31) 0.0299	0.03 (0.00, 0.06) 0.0281	
	III or IV	291/ 718 (40.5)	210/ 639 (32.9)	1.23 (1.07, 1.42)*0.0038	1.35 (1.07, 1.71) 0.0116	0.07 (0.03, 0.12) 0.0022	
	LVEF at enrolment						0.2734
	<= 49	357/ 959 (37.2)	346/ 950 (36.4)	1.03 (0.92, 1.15) 0.6131	1.05 (0.87, 1.27) 0.6254	0.01 (-0.03, 0.05) 0.5722	
	50-59	414/1017 (40.7)	343/1009 (34.0)	1.15 (1.04, 1.29) 0.0091	1.31 (1.09, 1.57) 0.0044	0.06 (0.02, 0.10) 0.0049	
	>= 60	318/ 825 (38.5)	282/ 846 (33.3)	1.14 (1.01, 1.29) 0.0331	1.22 (0.99, 1.49) 0.0612	0.04 (-0.00, 0.09) 0.0556	
	NT-proBNP at enrolment						0.2006
	<= median	518/1396 (37.1)	485/1409 (34.4)	1.07 (0.97, 1.18) 0.1724	1.12 (0.96, 1.31) 0.1522	0.03 (-0.01, 0.06) 0.1351	
	> median	571/1405 (40.6)	485/1395 (34.8)	1.16 (1.06, 1.27) 0.0013	1.26 (1.08, 1.47) 0.0040	0.05 (0.02, 0.09) 0.0033	
	Type 2 Diabetes Medical History						0.0754
	Yes	468/1231 (38.0)	395/1243 (31.8)	1.20 (1.08, 1.33) 0.0008	1.32 (1.12, 1.55)*0.0011	0.06 (0.02, 0.10) 0.0016	
	No	621/1570 (39.6)	576/1562 (36.9)	1.06 (0.97, 1.15) 0.1842	1.12 (0.97, 1.29)*0.1231	0.02 (-0.01, 0.06) 0.1818	
	Atrial fibrillation or flutter at enrolment ECG						0.1493
	Yes	479/1185 (40.4)	400/1188 (33.7)	1.18 (1.06, 1.30) 0.0018	1.33 (1.12, 1.57) 0.0011	0.06 (0.03, 0.10) 0.0011	
	No	610/1616 (37.7)	571/1617 (35.3)	1.07 (0.98, 1.17) 0.1358	1.10 (0.95, 1.27) 0.2193	0.02 (-0.01, 0.05) 0.1872	
	BMI (kg/m2) at enrolment						0.6623
	< 30	623/1547 (40.3)	558/1541 (36.2)	1.10 (1.01, 1.20) 0.0265	1.17 (1.01, 1.36) 0.0329	0.04 (0.00, 0.07) 0.0302	
	>= 30	466/1253 (37.2)	411/1261 (32.6)	1.13 (1.02, 1.25) 0.0177	1.21 (1.02, 1.43) 0.0261	0.04 (0.01, 0.08) 0.0204	
	Baseline eGFR (mL/min/1.73m^2)						0.8435
	< 60	494/1338 (36.9)	448/1377 (32.5)	1.11 (1.01, 1.23) 0.0312	1.21 (1.03, 1.42) 0.0211	0.04 (0.01, 0.08) 0.0183	
	>= 60	595/1463 (40.7)	523/1427 (36.7)	1.11 (1.01, 1.21) 0.0231	1.16 (1.00, 1.35) 0.0533	0.04 (0.00, 0.07) 0.0459	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.4415
	<= median	542/1405 (38.6)	493/1420 (34.7)	1.09 (0.99, 1.19) 0.0769	1.15 (0.98, 1.34) 0.0864	0.03 (-0.00, 0.06) 0.0907	
	> median	547/1396 (39.2)	478/1385 (34.5)	1.14 (1.04, 1.25) 0.0049	1.24 (1.06, 1.45) 0.0085	0.05 (0.01, 0.08) 0.0058	
	LVEF at enrolment 2						0.1057
	<= 49	357/ 959 (37.2)	346/ 950 (36.4)	1.03 (0.92, 1.15) 0.6131	1.05 (0.87, 1.27) 0.6254	0.01 (-0.03, 0.05) 0.5722	
	>= 50	732/1842 (39.7)	625/1855 (33.7)	1.15 (1.06, 1.25) 0.0006	1.27 (1.10, 1.45) 0.0008	0.05 (0.02, 0.08) 0.0007	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2703
	Yes	127/ 280 (45.4)	128/ 281 (45.6)	1.00 (0.83, 1.19)*0.9631	1.01 (0.71, 1.45) 0.9393	0.01 (-0.06, 0.09) 0.7553	
	No	962/2521 (38.2)	843/2524 (33.4)	1.13 (1.05, 1.22) 0.0007	1.22 (1.08, 1.37) 0.0011	0.04 (0.02, 0.07) 0.0010	
	MRAs at baseline						0.5451
	Yes	475/1216 (39.1)	409/1210 (33.8)	1.14 (1.03, 1.26) 0.0106	1.25 (1.06, 1.48) 0.0098	0.05 (0.01, 0.09) 0.0067	
	No	614/1585 (38.7)	562/1595 (35.2)	1.09 (1.00, 1.19) 0.0448	1.14 (0.99, 1.32) 0.0743	0.03 (-0.00, 0.06) 0.0779	
	ACEi+ARB at baseline						0.3920
	Yes	799/2037 (39.2)	709/2059 (34.4)	1.13 (1.05, 1.22) 0.0015	1.21 (1.06, 1.38) 0.0039	0.04 (0.01, 0.07) 0.0039	
	No	290/ 764 (38.0)	262/ 746 (35.1)	1.07 (0.94, 1.22) 0.3345	1.13 (0.91, 1.39) 0.2604	0.03 (-0.02, 0.08) 0.2167	
	ARNI at baseline						0.7841
	Yes	53/ 149 (35.6)	43/ 125 (34.4)	1.06 (0.77, 1.47) 0.7217	1.11 (0.67, 1.85) 0.6812	0.03 (-0.09, 0.14) 0.6453	
	No	1036/2652 (39.1)	928/2680 (34.6)	1.11 (1.04, 1.19) 0.0015	1.19 (1.06, 1.34) 0.0023	0.04 (0.01, 0.07) 0.0018	
	Beta Blocker at baseline						0.7404
	Yes	894/2327 (38.4)	798/2330 (34.2)	1.11 (1.03, 1.19) 0.0062	1.17 (1.04, 1.33) 0.0099	0.04 (0.01, 0.06) 0.0097	
	No	195/ 474 (41.1)	173/ 475 (36.4)	1.16 (0.99, 1.35) 0.0598	1.27 (0.97, 1.66) 0.0811	0.06 (-0.00, 0.12) 0.0624	
	Diuretics at baseline						0.1509
	Yes	956/2500 (38.2)	866/2504 (34.6)	1.09 (1.02, 1.17) 0.0113	1.17 (1.04, 1.31) 0.0106	0.04 (0.01, 0.06) 0.0067	
	No	133/ 301 (44.2)	105/ 301 (34.9)	1.26 (1.04, 1.52) 0.0185	1.39 (0.99, 1.94) 0.0542	0.07 (-0.01, 0.15) 0.0760	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Full Analysis Set

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Physical Limitation (LOCF)							
	Overall	1103/2750 (40.1)	962/2758 (34.9)	1.14 (1.07, 1.22) 0.0001	1.24 (1.11, 1.38) 0.0001	0.05 (0.02, 0.08) 0.0001	
	Age						0.0879
	<= median	585/1382 (42.3)	562/1456 (38.6)	1.09 (1.00, 1.19) 0.0558	1.17 (1.01, 1.36) 0.0427	0.04 (0.00, 0.07) 0.0392	
	> median	518/1368 (37.9)	400/1302 (30.7)	1.22 (1.10, 1.36) 0.0002	1.35 (1.15, 1.59) 0.0003	0.07 (0.03, 0.10) 0.0003	
	Gender						0.1415
	Male	663/1611 (41.2)	589/1583 (37.2)	1.10 (1.01, 1.19) 0.0371	1.18 (1.02, 1.36) 0.0256	0.04 (0.01, 0.07) 0.0208	
	Female	440/1139 (38.6)	373/1175 (31.7)	1.20 (1.08, 1.34) 0.0009	1.32 (1.11, 1.57) 0.0017	0.06 (0.02, 0.09) 0.0035	
	Race						0.3627
	White	717/1970 (36.4)	653/1998 (32.7)	1.09 (1.01, 1.19) 0.0370	1.16 (1.01, 1.32) 0.0318	0.03 (0.00, 0.06) 0.0274	
	Black or African	30/ 63 (47.6)	24/ 66 (36.4)	1.34 (0.89, 2.03) 0.1610	1.62 (0.80, 3.29) 0.1824	0.11 (-0.06, 0.28) 0.1862	
	Asian	281/ 548 (51.3)	236/ 546 (43.2)	1.19 (1.05, 1.35) 0.0076	1.39 (1.10, 1.77) 0.0066	0.08 (0.02, 0.14) 0.0060	
	Other	75/ 169 (44.4)	49/ 148 (33.1)	1.34 (1.01, 1.78)*0.0435	1.73 (1.07, 2.80) 0.0244	0.12 (0.01, 0.22) 0.0255	
	Geographic region						0.6298
	Asia	272/ 530 (51.3)	233/ 531 (43.9)	1.17 (1.03, 1.33) 0.0153	1.36 (1.07, 1.73) 0.0133	0.08 (0.02, 0.14) 0.0124	
	Europe and Saudi Arabia	468/1323 (35.4)	434/1360 (31.9)	1.09 (0.99, 1.21) 0.0850	1.15 (0.98, 1.36) 0.0908	0.03 (-0.00, 0.06) 0.0933	
	North America	131/ 386 (33.9)	107/ 362 (29.6)	1.12 (0.91, 1.39) 0.2806	1.22 (0.89, 1.66) 0.2181	0.05 (-0.02, 0.11) 0.1607	
	Latin America	232/ 511 (45.4)	188/ 505 (37.2)	1.23 (1.08, 1.41) 0.0026	1.43 (1.11, 1.86) 0.0064	0.08 (0.02, 0.14) 0.0093	
	NYHA class at enrolment						0.5920
	II	838/2046 (41.0)	751/2136 (35.2)	1.16 (1.08, 1.25) 0.0001	1.28 (1.13, 1.45) 0.0001	0.06 (0.03, 0.09) 0.0001	
	III or IV	265/ 704 (37.6)	211/ 621 (34.0)	1.10 (0.96, 1.26) 0.1773	1.13 (0.90, 1.43) 0.2952	0.03 (-0.02, 0.08) 0.2369	
	LVEF at enrolment						0.1256
	<= 49	372/ 944 (39.4)	356/ 939 (37.9)	1.04 (0.93, 1.16) 0.5033	1.08 (0.89, 1.30) 0.4366	0.02 (-0.03, 0.06) 0.4005	
	50-59	393/1001 (39.3)	320/ 988 (32.4)	1.20 (1.07, 1.35) 0.0021	1.33 (1.11, 1.60) 0.0024	0.06 (0.02, 0.11) 0.0025	
	>= 60	338/ 805 (42.0)	286/ 831 (34.4)	1.20 (1.06, 1.35) 0.0038	1.34 (1.09, 1.64) 0.0048	0.07 (0.02, 0.11) 0.0049	
	NT-proBNP at enrolment						0.9700
	<= median	560/1371 (40.8)	492/1389 (35.4)	1.15 (1.04, 1.26) 0.0046	1.26 (1.08, 1.47) 0.0039	0.05 (0.02, 0.09) 0.0040	
	> median	543/1379 (39.4)	470/1368 (34.4)	1.14 (1.03, 1.25) 0.0084	1.22 (1.04, 1.43) 0.0123	0.05 (0.01, 0.08) 0.0091	
	Type 2 Diabetes Medical History						0.1130
	Yes	485/1213 (40.0)	398/1219 (32.6)	1.22 (1.10, 1.35) 0.0003	1.37 (1.16, 1.62)*0.0002	0.07 (0.04, 0.11) 0.0001	
	No	618/1537 (40.2)	564/1539 (36.6)	1.09 (1.00, 1.19) 0.0618	1.16 (1.01, 1.34)*0.0424	0.03 (-0.00, 0.07) 0.0746	
	Atrial fibrillation or flutter at enrolment ECG						0.3877
	Yes	465/1164 (39.9)	389/1164 (33.4)	1.18 (1.06, 1.31) 0.0021	1.32 (1.11, 1.57) 0.0014	0.07 (0.03, 0.10) 0.0008	
	No	638/1586 (40.2)	573/1594 (35.9)	1.11 (1.02, 1.22) 0.0158	1.19 (1.03, 1.37) 0.0197	0.04 (0.01, 0.07) 0.0216	
	BMI (kg/m2) at enrolment						0.1724
	< 30	651/1520 (42.8)	546/1517 (36.0)	1.19 (1.09, 1.30) 0.0001	1.33 (1.15, 1.54) 0.0001	0.07 (0.03, 0.10) 0.0002	
	>= 30	452/1229 (36.8)	416/1238 (33.6)	1.07 (0.96, 1.18) 0.2182	1.12 (0.95, 1.33) 0.1749	0.03 (-0.01, 0.06) 0.1432	
	Baseline eGFR (mL/min/1.73m^2)						0.3619
	< 60	499/1307 (38.2)	435/1345 (32.3)	1.18 (1.06, 1.30) 0.0019	1.29 (1.10, 1.51) 0.0021	0.06 (0.02, 0.09) 0.0020	
	>= 60	604/1443 (41.9)	527/1412 (37.3)	1.11 (1.01, 1.21) 0.0286	1.19 (1.02, 1.39) 0.0232	0.04 (0.01, 0.08) 0.0221	

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AstraZeneca
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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.4863
	<= median	556/1376 (40.4)	497/1395 (35.6)	1.12 (1.02, 1.23) 0.0209	1.20 (1.03, 1.40) 0.0209	0.04 (0.01, 0.08) 0.0212	
	> median	547/1374 (39.8)	465/1363 (34.1)	1.17 (1.06, 1.29) 0.0015	1.29 (1.10, 1.51) 0.0015	0.06 (0.02, 0.09) 0.0012	
	LVEF at enrolment 2						0.0427
	<= 49	372/ 944 (39.4)	356/ 939 (37.9)	1.04 (0.93, 1.16) 0.5033	1.08 (0.89, 1.30) 0.4366	0.02 (-0.03, 0.06) 0.4005	
	>= 50	731/1806 (40.5)	606/1819 (33.3)	1.20 (1.10, 1.31) <.0001	1.33 (1.16, 1.53) <.0001	0.07 (0.03, 0.10) <.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4610
	Yes	115/ 270 (42.6)	109/ 272 (40.1)	1.06 (0.88, 1.28) 0.5361	1.14 (0.80, 1.63) 0.4779	0.03 (-0.05, 0.11) 0.4050	
	No	988/2480 (39.8)	853/2486 (34.3)	1.15 (1.07, 1.24) 0.0001	1.26 (1.12, 1.41) 0.0001	0.05 (0.03, 0.08) 0.0001	
	MRAs at baseline						0.1769
	Yes	479/1191 (40.2)	394/1193 (33.0)	1.21 (1.09, 1.34) 0.0005	1.36 (1.15, 1.61) 0.0004	0.07 (0.03, 0.11) 0.0003	
	No	624/1559 (40.0)	568/1565 (36.3)	1.10 (1.00, 1.20) 0.0396	1.16 (1.00, 1.34) 0.0496	0.03 (-0.00, 0.07) 0.0509	
	ACEi+ARB at baseline						0.3267
	Yes	805/1999 (40.3)	696/2028 (34.3)	1.16 (1.07, 1.26) 0.0002	1.28 (1.12, 1.45) 0.0002	0.06 (0.03, 0.09) 0.0002	
	No	298/ 751 (39.7)	266/ 730 (36.4)	1.09 (0.95, 1.24) 0.2149	1.15 (0.93, 1.41) 0.2040	0.03 (-0.02, 0.08) 0.1958	
	ARNI at baseline						0.3787
	Yes	69/ 147 (46.9)	45/ 122 (36.9)	1.26 (0.94, 1.68) 0.1185	1.51 (0.92, 2.47) 0.1068	0.10 (-0.02, 0.22) 0.0990	
	No	1034/2603 (39.7)	917/2636 (34.8)	1.13 (1.05, 1.21) 0.0005	1.22 (1.09, 1.37) 0.0005	0.05 (0.02, 0.07) 0.0005	
	Beta Blocker at baseline						0.4303
	Yes	905/2289 (39.5)	795/2293 (34.7)	1.13 (1.05, 1.21) 0.0017	1.22 (1.08, 1.38) 0.0014	0.05 (0.02, 0.07) 0.0011	
	No	198/ 461 (43.0)	167/ 465 (35.9)	1.21 (1.03, 1.42) 0.0193	1.35 (1.03, 1.76) 0.0270	0.07 (0.01, 0.13) 0.0288	
	Diuretics at baseline						0.4963
	Yes	981/2458 (39.9)	861/2463 (35.0)	1.13 (1.05, 1.21) 0.0007	1.23 (1.09, 1.38) 0.0006	0.05 (0.02, 0.07) 0.0005	
	No	122/ 292 (41.8)	101/ 295 (34.2)	1.22 (0.99, 1.50) 0.0599	1.37 (0.98, 1.92) 0.0644	0.07 (-0.00, 0.15) 0.0662	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	1256/2801 (44.8)	1174/2805 (41.9)	1.05 (1.00, 1.11) 0.0545	1.10 (0.99, 1.23) 0.0778	0.02 (-0.00, 0.05) 0.0834	
	Age						0.0961
	<= median	618/1394 (44.3)	641/1471 (43.6)	1.01 (0.94, 1.09) 0.7198	1.02 (0.87, 1.18) 0.8293	0.01 (-0.03, 0.04) 0.7806	
	> median	638/1407 (45.3)	533/1334 (40.0)	1.13 (1.04, 1.24)*0.0045	1.20 (1.03, 1.41) 0.0213	0.04 (0.00, 0.08) 0.0291	
	Gender						0.8545*
	Male	745/1630 (45.7)	683/1608 (42.5)	1.07 (0.99, 1.14) 0.0769	1.12 (0.97, 1.29) 0.1237	0.03 (-0.01, 0.06) 0.1176	
	Female	511/1171 (43.6)	491/1197 (41.0)	1.03 (0.95, 1.12) 0.4077	1.08 (0.91, 1.28) 0.4035	0.01 (-0.02, 0.05) 0.4753	
	Race						0.6247
	White	888/2006 (44.3)	830/2032 (40.8)	1.07 (1.00, 1.14) 0.0405	1.12 (0.98, 1.27) 0.0975	0.02 (-0.00, 0.05) 0.1003	
	Black or African	35/ 64 (54.7)	35/ 70 (50.0)	1.11 (0.81, 1.52) 0.5267	1.19 (0.60, 2.36) 0.6271	0.04 (-0.12, 0.21) 0.6120	
	Asian	239/ 555 (43.1)	229/ 551 (41.6)	1.03 (0.90, 1.17) 0.7059	1.06 (0.83, 1.36) 0.6247	0.01 (-0.04, 0.07) 0.6751	
	Other	94/ 176 (53.4)	80/ 152 (52.6)	0.97 (0.80, 1.18) 0.7390	1.04 (0.66, 1.65) 0.8601	0.01 (-0.10, 0.11) 0.9246	
	Geographic region						0.7599
	Asia	233/ 536 (43.5)	225/ 536 (42.0)	1.03 (0.90, 1.17) 0.6882	1.06 (0.83, 1.36) 0.6519	0.01 (-0.05, 0.07) 0.7029	
	Europe and Saudi Arabia	576/1341 (43.0)	548/1381 (39.7)	1.08 (0.99, 1.18)*0.0832	1.11 (0.94, 1.30) 0.2096	0.02 (-0.02, 0.05) 0.3007	
	North America	189/ 393 (48.1)	163/ 376 (43.4)	1.10 (0.94, 1.27) 0.2238	1.21 (0.90, 1.61) 0.2027	0.05 (-0.02, 0.12) 0.1754	
	Latin America	258/ 531 (48.6)	238/ 512 (46.5)	1.00 (0.89, 1.11) 0.9373	1.04 (0.80, 1.34) 0.7730	0.01 (-0.05, 0.07) 0.7562	
	NYHA class at enrolment						0.0022
	II	915/2083 (43.9)	933/2165 (43.1)	1.01 (0.95, 1.08) 0.6785	1.03 (0.90, 1.16) 0.6963	0.01 (-0.02, 0.03) 0.7220	
	III or IV	341/ 718 (47.5)	241/ 639 (37.7)	1.17 (1.05, 1.31) 0.0055	1.45 (1.15, 1.83) 0.0016	0.08 (0.03, 0.13) 0.0016	
	LVEF at enrolment						0.4225*
	<= 49	414/ 959 (43.2)	400/ 950 (42.1)	1.01 (0.92, 1.11) 0.7776	1.04 (0.86, 1.25) 0.6830	0.01 (-0.03, 0.05) 0.7066	
	50-59	481/1017 (47.3)	424/1009 (42.0)	1.13 (1.02, 1.24)*0.0172	1.21 (1.01, 1.45) 0.0403	0.04 (0.00, 0.08) 0.0493	
	>= 60	361/ 825 (43.8)	350/ 846 (41.4)	1.06 (0.95, 1.18)*0.3240	1.05 (0.86, 1.28) 0.6294	0.01 (-0.03, 0.06) 0.5619	
	NT-proBNP at enrolment						0.2934
	<= median	623/1396 (44.6)	599/1409 (42.5)	1.02 (0.95, 1.11) 0.5261	1.06 (0.91, 1.24) 0.4447	0.01 (-0.02, 0.05) 0.4190	
	> median	633/1405 (45.1)	574/1395 (41.1)	1.08 (1.00, 1.16) 0.0458	1.15 (0.98, 1.34) 0.0788	0.03 (-0.01, 0.06) 0.1010	
	Type 2 Diabetes Medical History						0.0035
	Yes	568/1231 (46.1)	482/1243 (38.8)	1.17 (1.07, 1.28) 0.0004	1.35 (1.15, 1.59)*0.0002	0.06 (0.03, 0.10) 0.0010	
	No	688/1570 (43.8)	692/1562 (44.3)	0.99 (0.93, 1.06) 0.7951	0.98 (0.85, 1.13)*0.7865	-0.01 (-0.04, 0.02) 0.5296	
	Atrial fibrillation or flutter at enrolment ECG						0.0473
	Yes	551/1185 (46.5)	475/1188 (40.0)	1.11 (1.02, 1.21) 0.0165	1.28 (1.08, 1.52) 0.0040	0.05 (0.01, 0.09) 0.0066	
	No	705/1616 (43.6)	699/1617 (43.2)	1.00 (0.93, 1.08) 0.9069	0.99 (0.86, 1.14) 0.8964	-0.00 (-0.03, 0.03) 0.9496	
	BMI (kg/m2) at enrolment						0.0683
	< 30	675/1547 (43.6)	656/1541 (42.6)	1.01 (0.94, 1.08) 0.8099	1.01 (0.87, 1.16) 0.9427	0.00 (-0.03, 0.03) 0.9524	
	>= 30	581/1253 (46.4)	515/1261 (40.8)	1.11 (1.03, 1.20) 0.0094	1.25 (1.06, 1.47) 0.0083	0.05 (0.01, 0.09) 0.0089	
	Baseline eGFR (mL/min/1.73m^2)						0.7894
	< 60	596/1338 (44.5)	573/1377 (41.6)	1.04 (0.96, 1.13) 0.3125	1.11 (0.95, 1.30) 0.1799	0.02 (-0.01, 0.06) 0.1919	
	>= 60	660/1463 (45.1)	601/1427 (42.1)	1.06 (0.99, 1.14) 0.0960	1.09 (0.94, 1.27) 0.2708	0.02 (-0.01, 0.05) 0.2593	

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Quality of Life (LOCF)	SBP at randomisation						0.5740
	<= median	646/1405 (46.0)	598/1420 (42.1)	1.07 (0.99, 1.15) 0.0860	1.13 (0.96, 1.31) 0.1324	0.02 (-0.01, 0.06) 0.1678	
	> median	610/1396 (43.7)	576/1385 (41.6)	1.04 (0.96, 1.12) 0.3715	1.08 (0.93, 1.26) 0.3257	0.02 (-0.02, 0.05) 0.2906	
	LVEF at enrolment 2						0.2495
	<= 49	414/ 959 (43.2)	400/ 950 (42.1)	1.01 (0.92, 1.11) 0.7776	1.04 (0.86, 1.25) 0.6830	0.01 (-0.03, 0.05) 0.7066	
	>= 50	842/1842 (45.7)	774/1855 (41.7)	1.10 (1.02, 1.18)*0.0147	1.14 (0.99, 1.30) 0.0641	0.03 (-0.00, 0.06) 0.0649	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5618
	Yes	142/ 280 (50.7)	136/ 281 (48.4)	1.05 (0.89, 1.24)*0.5835	1.04 (0.72, 1.49) 0.8414	0.00 (-0.07, 0.08) 0.9912	
	No	1114/2521 (44.2)	1038/2524 (41.1)	1.06 (1.00, 1.12) 0.0463	1.11 (0.99, 1.24) 0.0752	0.02 (-0.00, 0.05) 0.0781	
	MRAs at baseline						0.5803
	Yes	540/1216 (44.4)	487/1210 (40.2)	1.07 (0.98, 1.16) 0.1229	1.17 (0.99, 1.39) 0.0616	0.03 (-0.00, 0.07) 0.0854	
	No	716/1585 (45.2)	687/1595 (43.1)	1.04 (0.97, 1.12) 0.2376	1.06 (0.91, 1.22) 0.4537	0.01 (-0.02, 0.05) 0.4210	
	ACEi+ARB at baseline						0.4597
	Yes	904/2037 (44.4)	845/2059 (41.0)	1.08 (1.01, 1.16)*0.0308	1.12 (0.99, 1.28) 0.0731	0.03 (-0.00, 0.05) 0.0860	
	No	352/ 764 (46.1)	329/ 746 (44.1)	1.03 (0.93, 1.15) 0.5317	1.05 (0.85, 1.29) 0.6359	0.01 (-0.04, 0.06) 0.6221	
	ARNI at baseline						0.3782
	Yes	58/ 149 (38.9)	51/ 125 (40.8)	0.93 (0.70, 1.23) 0.6058	0.83 (0.50, 1.37) 0.4575	-0.05 (-0.16, 0.07) 0.4423	
	No	1198/2652 (45.2)	1123/2680 (41.9)	1.06 (1.00, 1.12) 0.0368	1.12 (1.00, 1.25) 0.0466	0.03 (-0.00, 0.05) 0.0506	
	Beta Blocker at baseline						0.6484
	Yes	1020/2327 (43.8)	961/2330 (41.2)	1.04 (0.98, 1.10) 0.1876	1.08 (0.96, 1.22) 0.2204	0.02 (-0.01, 0.04) 0.2425	
	No	236/ 474 (49.8)	213/ 475 (44.8)	1.12 (1.00, 1.27) 0.0594	1.23 (0.95, 1.60) 0.1230	0.05 (-0.01, 0.11) 0.1092	
	Diuretics at baseline						0.7972
	Yes	1122/2500 (44.9)	1048/2504 (41.9)	1.06 (1.00, 1.12) 0.0535	1.11 (0.99, 1.25) 0.0698	0.02 (-0.00, 0.05) 0.0719	
	No	134/ 301 (44.5)	126/ 301 (41.9)	1.06 (0.89, 1.28)*0.5106	1.02 (0.73, 1.43) 0.9178	0.00 (-0.08, 0.08) 0.9909	

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Symptom Burden (LOCF)							
	Overall	1551/2801 (55.4)	1373/2805 (48.9)	1.12 (1.07, 1.18) <.0001	1.29 (1.16, 1.43) <.0001	0.06 (0.04, 0.09) <.0001	
	Age						0.1621
	<= median	818/1394 (58.7)	740/1471 (50.3)	1.16 (1.09, 1.24) <.0001	1.41 (1.21, 1.63) <.0001	0.08 (0.05, 0.12) <.0001	
	> median	733/1407 (52.1)	633/1334 (47.5)	1.08 (1.00, 1.16) 0.0444	1.19 (1.02, 1.38) 0.0250	0.04 (0.01, 0.08) 0.0261	
	Gender						0.8332
	Male	954/1630 (58.5)	825/1608 (51.3)	1.13 (1.06, 1.20) 0.0001	1.33 (1.16, 1.53) <.0001	0.07 (0.04, 0.10) <.0001	
	Female	597/1171 (51.0)	548/1197 (45.8)	1.10 (1.01, 1.19) 0.0212	1.22 (1.04, 1.44) 0.0155	0.05 (0.01, 0.09) 0.0169	
	Race						0.4270
	White	1083/2006 (54.0)	949/2032 (46.7)	1.13 (1.07, 1.20) <.0001	1.33 (1.17, 1.51) <.0001	0.07 (0.04, 0.10) <.0001	
	Black or African	41/ 64 (64.1)	40/ 70 (57.1)	1.15 (0.88, 1.52) 0.3033	1.37 (0.68, 2.77) 0.3769	0.08 (-0.09, 0.24) 0.3455	
	Asian	322/ 555 (58.0)	306/ 551 (55.5)	1.05 (0.94, 1.16) 0.3896	1.10 (0.87, 1.40) 0.4146	0.02 (-0.03, 0.08) 0.4081	
	Other	105/ 176 (59.7)	78/ 152 (51.3)	1.11 (0.93, 1.32) 0.2646	1.33 (0.84, 2.09) 0.2208	0.07 (-0.04, 0.17) 0.2054	
	Geographic region						0.3855
	Asia	312/ 536 (58.2)	299/ 536 (55.8)	1.05 (0.94, 1.16) 0.4072	1.10 (0.87, 1.40) 0.4294	0.02 (-0.04, 0.08) 0.4234	
	Europe and Saudi Arabia	723/1341 (53.9)	642/1381 (46.5)	1.11 (1.04, 1.20) 0.0033	1.33 (1.14, 1.55) 0.0003	0.07 (0.03, 0.10) 0.0003	
	North America	194/ 393 (49.4)	163/ 376 (43.4)	1.13 (0.97, 1.32) 0.1044	1.28 (0.96, 1.70) 0.0929	0.06 (-0.01, 0.13) 0.0877	
	Latin America	322/ 531 (60.6)	269/ 512 (52.5)	1.11 (1.00, 1.24) 0.0434	1.37 (1.07, 1.76) 0.0128	0.07 (0.01, 0.13) 0.0158	
	NYHA class at enrolment						0.0259
	II	1155/2083 (55.4)	1093/2165 (50.5)	1.10 (1.04, 1.16) 0.0015	1.22 (1.08, 1.38) 0.0011	0.05 (0.02, 0.08) 0.0012	
	III or IV	396/ 718 (55.2)	280/ 639 (43.8)	1.26 (1.13, 1.40)*<.0001	1.57 (1.26, 1.97) <.0001	0.11 (0.06, 0.16) <.0001	
	LVEF at enrolment						0.8579
	<= 49	542/ 959 (56.5)	470/ 950 (49.5)	1.13 (1.04, 1.23) 0.0029	1.34 (1.11, 1.60) 0.0017	0.07 (0.03, 0.12) 0.0017	
	50-59	572/1017 (56.2)	497/1009 (49.3)	1.12 (1.03, 1.21) 0.0081	1.32 (1.11, 1.58) 0.0019	0.07 (0.02, 0.11) 0.0023	
	>= 60	437/ 825 (53.0)	406/ 846 (48.0)	1.09 (0.99, 1.20) 0.0744	1.20 (0.99, 1.46) 0.0634	0.05 (-0.00, 0.09) 0.0625	
	NT-proBNP at enrolment						0.7143
	<= median	754/1396 (54.0)	678/1409 (48.1)	1.12 (1.04, 1.20) 0.0028	1.27 (1.09, 1.47) 0.0018	0.06 (0.02, 0.10) 0.0018	
	> median	797/1405 (56.7)	694/1395 (49.7)	1.13 (1.05, 1.20) 0.0005	1.31 (1.13, 1.52) 0.0005	0.07 (0.03, 0.10) 0.0004	
	Type 2 Diabetes Medical History						0.0453
	Yes	683/1231 (55.5)	575/1243 (46.3)	1.19 (1.10, 1.29) <.0001	1.45 (1.24, 1.70)*<.0001	0.09 (0.05, 0.13) <.0001	
	No	868/1570 (55.3)	798/1562 (51.1)	1.07 (1.00, 1.14) 0.0346	1.18 (1.03, 1.36)*0.0186	0.04 (0.00, 0.07) 0.0252	
	Atrial fibrillation or flutter at enrolment ECG						0.7869
	Yes	666/1185 (56.2)	584/1188 (49.2)	1.13 (1.05, 1.21) 0.0018	1.32 (1.12, 1.56) 0.0007	0.07 (0.03, 0.11) 0.0008	
	No	885/1616 (54.8)	789/1617 (48.8)	1.11 (1.04, 1.19) 0.0012	1.27 (1.10, 1.45) 0.0009	0.06 (0.02, 0.09) 0.0009	
	BMI (kg/m2) at enrolment						0.5801
	< 30	875/1547 (56.6)	778/1541 (50.5)	1.11 (1.04, 1.19) 0.0013	1.27 (1.10, 1.47) 0.0010	0.06 (0.02, 0.09) 0.0010	
	>= 30	676/1253 (54.0)	593/1261 (47.0)	1.13 (1.05, 1.22) 0.0013	1.32 (1.12, 1.54) 0.0007	0.07 (0.03, 0.11) 0.0006	
	Baseline eGFR (mL/min/1.73m^2)						0.6012
	< 60	701/1338 (52.4)	645/1377 (46.8)	1.10 (1.02, 1.19) 0.0095	1.24 (1.07, 1.45) 0.0047	0.05 (0.02, 0.09) 0.0049	
	>= 60	850/1463 (58.1)	728/1427 (51.0)	1.13 (1.06, 1.21) 0.0002	1.32 (1.14, 1.54) 0.0002	0.07 (0.03, 0.10) 0.0002	

N displays number of patients in the analysis, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)	SBP at randomisation						0.2852
	<= median	766/1405 (54.5)	699/1420 (49.2)	1.09 (1.02, 1.17) 0.0147	1.22 (1.05, 1.41) 0.0101	0.05 (0.01, 0.08) 0.0105	
	> median	785/1396 (56.2)	674/1385 (48.7)	1.15 (1.07, 1.23) <.0001	1.37 (1.18, 1.59) <.0001	0.08 (0.04, 0.11) <.0001	
	LVEF at enrolment 2						0.6894
	<= 49	542/ 959 (56.5)	470/ 950 (49.5)	1.13 (1.04, 1.23) 0.0029	1.34 (1.11, 1.60) 0.0017	0.07 (0.03, 0.12) 0.0017	
	>= 50	1009/1842 (54.8)	903/1855 (48.7)	1.11 (1.05, 1.18) 0.0006	1.26 (1.11, 1.44) 0.0004	0.06 (0.03, 0.09) 0.0004	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4188
	Yes	168/ 280 (60.0)	155/ 281 (55.2)	1.09 (0.94, 1.25)*0.2468	1.26 (0.89, 1.79) 0.1873	0.04 (-0.04, 0.12) 0.3157	
	No	1383/2521 (54.9)	1218/2524 (48.3)	1.13 (1.07, 1.19) <.0001	1.30 (1.16, 1.45) <.0001	0.06 (0.04, 0.09) <.0001	
	MRAs at baseline						0.6947
	Yes	678/1216 (55.8)	586/1210 (48.4)	1.13 (1.05, 1.22) 0.0013	1.33 (1.13, 1.56) 0.0005	0.07 (0.03, 0.11) 0.0006	
	No	873/1585 (55.1)	787/1595 (49.3)	1.11 (1.04, 1.19) 0.0016	1.25 (1.09, 1.44) 0.0015	0.06 (0.02, 0.09) 0.0014	
	ACEi+ARB at baseline						0.6065
	Yes	1123/2037 (55.1)	993/2059 (48.2)	1.13 (1.06, 1.19) <.0001	1.31 (1.16, 1.48) <.0001	0.07 (0.04, 0.10) <.0001	
	No	428/ 764 (56.0)	380/ 746 (50.9)	1.10 (1.00, 1.21) 0.0467	1.23 (1.01, 1.51) 0.0442	0.05 (0.00, 0.10) 0.0428	
	ARNI at baseline						0.4771
	Yes	84/ 149 (56.4)	68/ 125 (54.4)	1.04 (0.84, 1.29) 0.7265	1.10 (0.68, 1.79) 0.6952	0.02 (-0.10, 0.14) 0.7015	
	No	1467/2652 (55.3)	1305/2680 (48.7)	1.12 (1.07, 1.18) <.0001	1.30 (1.16, 1.44) <.0001	0.06 (0.04, 0.09) <.0001	
	Beta Blocker at baseline						0.2768
	Yes	1269/2327 (54.5)	1139/2330 (48.9)	1.11 (1.05, 1.17) 0.0003	1.24 (1.11, 1.40) 0.0002	0.05 (0.02, 0.08) 0.0002	
	No	282/ 474 (59.5)	234/ 475 (49.3)	1.18 (1.05, 1.33) 0.0043	1.55 (1.20, 2.01) 0.0010	0.10 (0.04, 0.17) 0.0011	
	Diuretics at baseline						0.1616
	Yes	1368/2500 (54.7)	1226/2504 (49.0)	1.11 (1.05, 1.17) 0.0002	1.26 (1.13, 1.41) <.0001	0.06 (0.03, 0.08) <.0001	
	No	183/ 301 (60.8)	147/ 301 (48.8)	1.23 (1.06, 1.42) 0.0051	1.58 (1.14, 2.18) 0.0063	0.11 (0.03, 0.19) 0.0056	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	1444/2801 (51.6)	1423/2805 (50.7)	1.02 (0.97, 1.07) 0.5374	1.03 (0.93, 1.15) 0.5429	0.01 (-0.02, 0.03) 0.5434	
	Age						0.6416
	<= median	744/1394 (53.4)	779/1471 (53.0)	1.01 (0.94, 1.08) 0.8579	1.02 (0.88, 1.18) 0.8203	0.00 (-0.03, 0.04) 0.8243	
	> median	700/1407 (49.8)	644/1334 (48.3)	1.03 (0.96, 1.11) 0.4205	1.06 (0.91, 1.23) 0.4572	0.01 (-0.02, 0.05) 0.4581	
	Gender						0.1162
	Male	864/1630 (53.0)	810/1608 (50.4)	1.05 (0.98, 1.12) 0.1385	1.11 (0.97, 1.28) 0.1320	0.03 (-0.01, 0.06) 0.1323	
	Female	580/1171 (49.5)	613/1197 (51.2)	0.97 (0.89, 1.05) 0.4317	0.93 (0.79, 1.10) 0.4063	-0.02 (-0.06, 0.02) 0.4049	
	Race						0.6276
	White	1069/2006 (53.3)	1066/2032 (52.5)	1.02 (0.96, 1.08) 0.5523	1.03 (0.91, 1.17) 0.5985	0.01 (-0.02, 0.04) 0.5935	
	Black or African	38/ 64 (59.4)	33/ 70 (47.1)	1.26 (0.91, 1.73) 0.1622	1.64 (0.82, 3.25) 0.1597	0.12 (-0.05, 0.29) 0.1556	
	Asian	252/ 555 (45.4)	250/ 551 (45.4)	1.00 (0.88, 1.14) 0.9891	1.02 (0.80, 1.29) 0.8828	0.00 (-0.05, 0.06) 0.9053	
	Other	85/ 176 (48.3)	74/ 152 (48.7)	0.99 (0.79, 1.24)*0.9440	1.02 (0.65, 1.60) 0.9358	0.00 (-0.10, 0.11) 0.9674	
	Geographic region						0.6460
	Asia	242/ 536 (45.1)	242/ 536 (45.1)	1.00 (0.88, 1.14) 0.9642	1.02 (0.80, 1.30) 0.8747	0.00 (-0.05, 0.06) 0.8901	
	Europe and Saudi Arabia	691/1341 (51.5)	679/1381 (49.2)	1.05 (0.97, 1.13) 0.2162	1.10 (0.94, 1.28) 0.2272	0.02 (-0.01, 0.06) 0.2265	
	North America	245/ 393 (62.3)	236/ 376 (62.8)	0.99 (0.89, 1.11) 0.9067	0.98 (0.73, 1.32) 0.9062	-0.00 (-0.07, 0.06) 0.9047	
	Latin America	266/ 531 (50.1)	266/ 512 (52.0)	0.97 (0.86, 1.10) 0.6505	0.93 (0.73, 1.19) 0.5905	-0.02 (-0.08, 0.04) 0.5935	
	NYHA class at enrolment						0.1336
	II	1059/2083 (50.8)	1108/2165 (51.2)	0.99 (0.94, 1.05) 0.8129	0.99 (0.87, 1.11) 0.8136	-0.00 (-0.03, 0.03) 0.8107	
	III or IV	385/ 718 (53.6)	315/ 639 (49.3)	1.09 (0.98, 1.21) 0.1030	1.19 (0.96, 1.48) 0.1068	0.04 (-0.01, 0.10) 0.1061	
	LVEF at enrolment						0.4100
	<= 49	487/ 959 (50.8)	496/ 950 (52.2)	0.97 (0.89, 1.06) 0.5212	0.94 (0.79, 1.13) 0.5268	-0.01 (-0.06, 0.03) 0.5263	
	50-59	525/1017 (51.6)	510/1009 (50.5)	1.02 (0.94, 1.11) 0.6571	1.04 (0.88, 1.24) 0.6356	0.01 (-0.03, 0.05) 0.6399	
	>= 60	432/ 825 (52.4)	417/ 846 (49.3)	1.06 (0.96, 1.16) 0.2431	1.13 (0.93, 1.37) 0.2232	0.03 (-0.02, 0.08) 0.2256	
	NT-proBNP at enrolment						0.7581
	<= median	713/1396 (51.1)	713/1409 (50.6)	1.01 (0.94, 1.08) 0.8260	1.02 (0.88, 1.18) 0.8097	0.00 (-0.03, 0.04) 0.8104	
	> median	731/1405 (52.0)	710/1395 (50.9)	1.02 (0.95, 1.10) 0.5020	1.05 (0.90, 1.21) 0.5458	0.01 (-0.03, 0.05) 0.5455	
	Type 2 Diabetes Medical History						0.0370
	Yes	669/1231 (54.3)	625/1243 (50.3)	1.08 (1.00, 1.16) 0.0485	1.18 (1.01, 1.38)*0.0431	0.04 (0.00, 0.08) 0.0449	
	No	775/1570 (49.4)	798/1562 (51.1)	0.97 (0.90, 1.04) 0.3375	0.93 (0.81, 1.07)*0.3343	-0.02 (-0.05, 0.02) 0.3428	
	Atrial fibrillation or flutter at enrolment ECG						0.0622
	Yes	607/1185 (51.2)	564/1188 (47.5)	1.08 (0.99, 1.17) 0.0744	1.16 (0.99, 1.36) 0.0723	0.04 (-0.00, 0.08) 0.0728	
	No	837/1616 (51.8)	859/1617 (53.1)	0.98 (0.91, 1.04) 0.4581	0.95 (0.83, 1.09) 0.4529	-0.01 (-0.05, 0.02) 0.4532	
	BMI (kg/m2) at enrolment						0.0134
	< 30	756/1547 (48.9)	785/1541 (50.9)	0.96 (0.89, 1.03) 0.2247	0.92 (0.80, 1.06) 0.2337	-0.02 (-0.06, 0.01) 0.2319	
	>= 30	688/1253 (54.9)	635/1261 (50.4)	1.09 (1.01, 1.18) 0.0210	1.20 (1.03, 1.40) 0.0226	0.05 (0.01, 0.08) 0.0223	
	Baseline eGFR (mL/min/1.73m^2)						0.6724
	< 60	667/1338 (49.9)	685/1377 (49.7)	1.00 (0.93, 1.08) 0.9524	1.00 (0.86, 1.16) 0.9803	0.00 (-0.04, 0.04) 0.9802	
	>= 60	777/1463 (53.1)	738/1427 (51.7)	1.02 (0.95, 1.09) 0.5500	1.05 (0.91, 1.22) 0.4890	0.01 (-0.02, 0.05) 0.4963	

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Self Efficacy (LOCF)	SBP at randomisation						0.1046
	<= median	706/1405 (50.2)	731/1420 (51.5)	0.97 (0.90, 1.04) 0.4388	0.95 (0.82, 1.10) 0.5137	-0.01 (-0.05, 0.02) 0.5086	
	> median	738/1396 (52.9)	692/1385 (50.0)	1.06 (0.99, 1.14) 0.1009	1.13 (0.97, 1.31) 0.1140	0.03 (-0.01, 0.07) 0.1131	
	LVEF at enrolment 2						0.2382
	<= 49	487/ 959 (50.8)	496/ 950 (52.2)	0.97 (0.89, 1.06) 0.5212	0.94 (0.79, 1.13) 0.5268	-0.01 (-0.06, 0.03) 0.5263	
	>= 50	957/1842 (52.0)	927/1855 (50.0)	1.04 (0.97, 1.11) 0.2463	1.08 (0.95, 1.23) 0.2356	0.02 (-0.01, 0.05) 0.2382	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9306
	Yes	135/ 280 (48.2)	134/ 281 (47.7)	1.00 (0.85, 1.19) 0.9743	1.00 (0.72, 1.40) 0.9972	0.00 (-0.08, 0.08) 0.9940	
	No	1309/2521 (51.9)	1289/2524 (51.1)	1.02 (0.96, 1.07) 0.5484	1.03 (0.93, 1.16) 0.5468	0.01 (-0.02, 0.04) 0.5473	
	MRAs at baseline						0.0384
	Yes	567/1216 (46.6)	592/1210 (48.9)	0.95 (0.88, 1.03) 0.2433	0.91 (0.78, 1.07) 0.2585	-0.02 (-0.06, 0.02) 0.2589	
	No	877/1585 (55.3)	831/1595 (52.1)	1.06 (1.00, 1.14) 0.0587	1.14 (0.99, 1.31) 0.0668	0.03 (-0.00, 0.07) 0.0660	
	ACEi+ARB at baseline						0.6807
	Yes	1032/2037 (50.7)	1020/2059 (49.5)	1.02 (0.96, 1.09) 0.4738	1.05 (0.93, 1.18) 0.4735	0.01 (-0.02, 0.04) 0.4741	
	No	412/ 764 (53.9)	403/ 746 (54.0)	1.00 (0.91, 1.10) 0.9806	0.99 (0.81, 1.22) 0.9584	-0.00 (-0.05, 0.05) 0.9614	
	ARNI at baseline						0.2165
	Yes	74/ 149 (49.7)	70/ 125 (56.0)	0.90 (0.72, 1.13) 0.3731	0.81 (0.50, 1.32) 0.3983	-0.05 (-0.17, 0.07) 0.3990	
	No	1370/2652 (51.7)	1353/2680 (50.5)	1.02 (0.97, 1.08) 0.3860	1.05 (0.94, 1.17) 0.3927	0.01 (-0.02, 0.04) 0.3939	
	Beta Blocker at baseline						0.3457
	Yes	1201/2327 (51.6)	1170/2330 (50.2)	1.03 (0.97, 1.09) 0.3376	1.06 (0.94, 1.19) 0.3444	0.01 (-0.01, 0.04) 0.3444	
	No	243/ 474 (51.3)	253/ 475 (53.3)	0.96 (0.85, 1.08) 0.4954	0.92 (0.71, 1.19) 0.5224	-0.02 (-0.08, 0.04) 0.5182	
	Diuretics at baseline						0.6398
	Yes	1288/2500 (51.5)	1264/2504 (50.5)	1.02 (0.97, 1.08) 0.4645	1.04 (0.93, 1.17) 0.4594	0.01 (-0.02, 0.04) 0.4616	
	No	156/ 301 (51.8)	159/ 301 (52.8)	0.98 (0.84, 1.14) 0.7995	0.97 (0.70, 1.33) 0.8318	-0.01 (-0.09, 0.07) 0.8298	

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Symptom Frequency (LOCF)							
	Overall	1355/2801 (48.4)	1235/2805 (44.0)	1.10 (1.04, 1.16) 0.0012	1.19 (1.07, 1.32) 0.0014	0.04 (0.02, 0.07) 0.0012	
	Age						0.4309
	<= median	724/1394 (51.9)	680/1471 (46.2)	1.12 (1.04, 1.21) 0.0017	1.27 (1.09, 1.47) 0.0018	0.06 (0.02, 0.09) 0.0017	
	> median	631/1407 (44.8)	555/1334 (41.6)	1.07 (0.98, 1.16) 0.1084	1.13 (0.97, 1.31) 0.1240	0.03 (-0.01, 0.07) 0.1179	
	Gender						0.3987
	Male	819/1630 (50.2)	750/1608 (46.6)	1.07 (1.00, 1.15) 0.0479	1.16 (1.01, 1.33) 0.0394	0.04 (0.00, 0.07) 0.0372	
	Female	536/1171 (45.8)	485/1197 (40.5)	1.12 (1.02, 1.22) 0.0130	1.23 (1.04, 1.45) 0.0162	0.05 (0.01, 0.09) 0.0171	
	Race						0.3883
	White	907/2006 (45.2)	832/2032 (40.9)	1.09 (1.02, 1.17) 0.0124	1.17 (1.03, 1.33) 0.0128	0.04 (0.01, 0.07) 0.0113	
	Black or African	31/ 64 (48.4)	36/ 70 (51.4)	0.95 (0.68, 1.34) 0.7691	0.90 (0.46, 1.78) 0.7588	-0.03 (-0.20, 0.14) 0.7583	
	Asian	310/ 555 (55.9)	293/ 551 (53.2)	1.05 (0.94, 1.17) 0.3704	1.11 (0.88, 1.41) 0.3711	0.03 (-0.03, 0.09) 0.3708	
	Other	107/ 176 (60.8)	74/ 152 (48.7)	1.25 (1.02, 1.53)*0.0309	1.69 (1.07, 2.67) 0.0254	0.13 (0.02, 0.23) 0.0181	
	Geographic region						0.3750
	Asia	303/ 536 (56.5)	286/ 536 (53.4)	1.06 (0.95, 1.18) 0.2912	1.14 (0.89, 1.45) 0.2953	0.03 (-0.03, 0.09) 0.2944	
	Europe and Saudi Arabia	593/1341 (44.2)	551/1381 (39.9)	1.08 (1.00, 1.18) 0.0565	1.17 (1.00, 1.37) 0.0444	0.04 (0.00, 0.07) 0.0386	
	North America	156/ 393 (39.7)	151/ 376 (40.2)	0.99 (0.84, 1.18) 0.9477	0.99 (0.74, 1.32) 0.9256	-0.00 (-0.07, 0.07) 0.9266	
	Latin America	303/ 531 (57.1)	247/ 512 (48.2)	1.16 (1.04, 1.30) 0.0067	1.45 (1.13, 1.87) 0.0035	0.09 (0.03, 0.15) 0.0030	
	NYHA class at enrolment						0.0321
	II	1007/2083 (48.3)	982/2165 (45.4)	1.06 (1.00, 1.13) 0.0597	1.13 (1.00, 1.28) 0.0425	0.03 (0.00, 0.06) 0.0426	
	III or IV	348/ 718 (48.5)	253/ 639 (39.6)	1.22 (1.09, 1.36) 0.0007	1.42 (1.14, 1.77) 0.0020	0.08 (0.03, 0.14) 0.0011	
	LVEF at enrolment						0.7293
	<= 49	469/ 959 (48.9)	422/ 950 (44.4)	1.10 (1.00, 1.20) 0.0587	1.21 (1.01, 1.45) 0.0410	0.05 (0.00, 0.09) 0.0401	
	50-59	486/1017 (47.8)	452/1009 (44.8)	1.07 (0.97, 1.17) 0.1578	1.12 (0.94, 1.34) 0.1925	0.03 (-0.01, 0.07) 0.1828	
	>= 60	400/ 825 (48.5)	361/ 846 (42.7)	1.13 (1.02, 1.25) 0.0199	1.24 (1.02, 1.51) 0.0276	0.05 (0.01, 0.10) 0.0268	
	NT-proBNP at enrolment						0.7452
	<= median	658/1396 (47.1)	598/1409 (42.4)	1.11 (1.02, 1.20) 0.0134	1.21 (1.04, 1.41) 0.0118	0.05 (0.01, 0.08) 0.0110	
	> median	697/1405 (49.6)	636/1395 (45.6)	1.09 (1.01, 1.17) 0.0338	1.16 (1.00, 1.35) 0.0463	0.04 (0.00, 0.07) 0.0443	
	Type 2 Diabetes Medical History						0.5364
	Yes	600/1231 (48.7)	542/1243 (43.6)	1.12 (1.03, 1.21) 0.0095	1.23 (1.05, 1.44)*0.0104	0.05 (0.01, 0.09) 0.0092	
	No	755/1570 (48.1)	693/1562 (44.4)	1.08 (1.00, 1.16) 0.0484	1.16 (1.01, 1.34)*0.0367	0.04 (0.00, 0.07) 0.0464	
	Atrial fibrillation or flutter at enrolment ECG						0.9024
	Yes	579/1185 (48.9)	528/1188 (44.4)	1.10 (1.01, 1.20) 0.0264	1.20 (1.02, 1.41) 0.0315	0.04 (0.00, 0.08) 0.0311	
	No	776/1616 (48.0)	707/1617 (43.7)	1.09 (1.02, 1.18) 0.0169	1.18 (1.03, 1.36) 0.0177	0.04 (0.01, 0.08) 0.0166	
	BMI (kg/m2) at enrolment						0.5710
	< 30	786/1547 (50.8)	723/1541 (46.9)	1.08 (1.01, 1.16) 0.0273	1.17 (1.01, 1.35) 0.0317	0.04 (0.00, 0.07) 0.0316	
	>= 30	569/1253 (45.4)	511/1261 (40.5)	1.11 (1.02, 1.21) 0.0166	1.21 (1.03, 1.43) 0.0181	0.05 (0.01, 0.09) 0.0138	
	Baseline eGFR (mL/min/1.73m^2)						0.6798
	< 60	620/1338 (46.3)	586/1377 (42.6)	1.08 (1.00, 1.17) 0.0648	1.16 (1.00, 1.36) 0.0525	0.04 (0.00, 0.07) 0.0489	
	>= 60	735/1463 (50.2)	649/1427 (45.5)	1.11 (1.03, 1.19) 0.0070	1.21 (1.04, 1.40) 0.0118	0.05 (0.01, 0.08) 0.0109	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)	SBP at randomisation						0.0954
	<= median	667/1405 (47.5)	635/1420 (44.7)	1.05 (0.97, 1.14) 0.2232	1.10 (0.95, 1.28) 0.1893	0.02 (-0.01, 0.06) 0.1943	
	> median	688/1396 (49.3)	600/1385 (43.3)	1.15 (1.07, 1.25) 0.0004	1.29 (1.11, 1.50) 0.0011	0.06 (0.03, 0.10) 0.0008	
	LVEF at enrolment 2						0.9876
	<= 49	469/ 959 (48.9)	422/ 950 (44.4)	1.10 (1.00, 1.20) 0.0587	1.21 (1.01, 1.45) 0.0410	0.05 (0.00, 0.09) 0.0401	
	>= 50	886/1842 (48.1)	813/1855 (43.8)	1.10 (1.02, 1.17) 0.0089	1.18 (1.03, 1.34) 0.0143	0.04 (0.01, 0.07) 0.0132	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3108
	Yes	143/ 280 (51.1)	141/ 281 (50.2)	1.00 (0.86, 1.16) 0.9834	1.12 (0.79, 1.57) 0.5347	0.02 (-0.06, 0.10) 0.5968	
	No	1212/2521 (48.1)	1094/2524 (43.3)	1.11 (1.04, 1.18) 0.0007	1.20 (1.08, 1.35) 0.0011	0.05 (0.02, 0.07) 0.0010	
	MRAs at baseline						0.8174
	Yes	590/1216 (48.5)	526/1210 (43.5)	1.10 (1.01, 1.20) 0.0245	1.23 (1.04, 1.44) 0.0136	0.05 (0.01, 0.09) 0.0134	
	No	765/1585 (48.3)	709/1595 (44.5)	1.09 (1.01, 1.17) 0.0215	1.16 (1.01, 1.34) 0.0345	0.04 (0.00, 0.07) 0.0322	
	ACEi+ARB at baseline						0.2204
	Yes	995/2037 (48.8)	890/2059 (43.2)	1.12 (1.05, 1.19) 0.0009	1.25 (1.10, 1.41) 0.0005	0.05 (0.02, 0.08) 0.0005	
	No	360/ 764 (47.1)	345/ 746 (46.2)	1.03 (0.92, 1.14) 0.6490	1.04 (0.85, 1.27) 0.7106	0.01 (-0.04, 0.06) 0.7102	
	ARNI at baseline						0.2623
	Yes	68/ 149 (45.6)	62/ 125 (49.6)	0.91 (0.71, 1.18) 0.4845	0.85 (0.52, 1.38) 0.5169	-0.04 (-0.16, 0.08) 0.5252	
	No	1287/2652 (48.5)	1173/2680 (43.8)	1.10 (1.04, 1.17) 0.0007	1.20 (1.08, 1.34) 0.0008	0.05 (0.02, 0.07) 0.0007	
	Beta Blocker at baseline						0.4769
	Yes	1116/2327 (48.0)	1020/2330 (43.8)	1.09 (1.02, 1.16) 0.0078	1.17 (1.04, 1.32) 0.0069	0.04 (0.01, 0.07) 0.0070	
	No	239/ 474 (50.4)	215/ 475 (45.3)	1.14 (1.00, 1.30) 0.0429	1.28 (0.98, 1.65) 0.0658	0.06 (-0.00, 0.13) 0.0507	
	Diuretics at baseline						0.2529
	Yes	1183/2500 (47.3)	1092/2504 (43.6)	1.08 (1.02, 1.15) 0.0085	1.16 (1.04, 1.30) 0.0079	0.04 (0.01, 0.06) 0.0070	
	No	172/ 301 (57.1)	143/ 301 (47.5)	1.20 (1.03, 1.39) 0.0181	1.42 (1.03, 1.97) 0.0337	0.09 (0.01, 0.17) 0.0309	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

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Social Limitation (LOCF)							
	Overall	1276/2625 (48.6)	1234/2625 (47.0)	1.04 (0.98, 1.10) 0.2241	1.07 (0.96, 1.19) 0.2537	0.02 (-0.01, 0.04) 0.2527	
	Age						0.9483
	<= median	673/1331 (50.6)	686/1409 (48.7)	1.04 (0.97, 1.12) 0.2969	1.08 (0.93, 1.26) 0.3053	0.02 (-0.02, 0.06) 0.3001	
	> median	603/1294 (46.6)	548/1216 (45.1)	1.04 (0.95, 1.13) 0.4198	1.06 (0.90, 1.24) 0.4811	0.01 (-0.03, 0.05) 0.4944	
	Gender						0.0451
	Male	755/1538 (49.1)	747/1500 (49.8)	0.99 (0.92, 1.06) 0.6881	0.97 (0.84, 1.12) 0.7082	-0.01 (-0.04, 0.03) 0.7108	
	Female	521/1087 (47.9)	487/1125 (43.3)	1.11 (1.01, 1.21) 0.0236	1.20 (1.01, 1.42) 0.0354	0.04 (0.00, 0.08) 0.0389	
	Race						0.8287
	White	879/1890 (46.5)	853/1921 (44.4)	1.04 (0.98, 1.12) 0.2133	1.08 (0.95, 1.23) 0.2589	0.02 (-0.01, 0.05) 0.2533	
	Black or African	24/ 58 (41.4)	32/ 66 (48.5)	0.88 (0.60, 1.31) 0.5322	0.76 (0.37, 1.55) 0.4462	-0.07 (-0.25, 0.10) 0.4275	
	Asian	291/ 506 (57.5)	279/ 494 (56.5)	1.01 (0.91, 1.12) 0.8423	1.03 (0.80, 1.33) 0.8090	0.01 (-0.05, 0.07) 0.8154	
	Other	82/ 171 (48.0)	70/ 144 (48.6)	1.02 (0.80, 1.28) 0.8960	1.00 (0.64, 1.57) 0.9879	0.00 (-0.11, 0.11) 0.9765	
	Geographic region						0.7527
	Asia	286/ 492 (58.1)	275/ 482 (57.1)	1.01 (0.91, 1.12) 0.8412	1.03 (0.80, 1.33) 0.8055	0.01 (-0.05, 0.07) 0.8129	
	Europe and Saudi Arabia	575/1273 (45.2)	564/1309 (43.1)	1.03 (0.94, 1.12) 0.5326	1.07 (0.91, 1.25) 0.4272	0.02 (-0.02, 0.05) 0.4182	
	North America	156/ 367 (42.5)	155/ 347 (44.7)	0.96 (0.81, 1.13) 0.6353	0.93 (0.69, 1.25) 0.6234	-0.02 (-0.09, 0.05) 0.6246	
	Latin America	259/ 493 (52.5)	240/ 487 (49.3)	1.09 (0.97, 1.23) 0.1642	1.14 (0.89, 1.47) 0.3032	0.03 (-0.03, 0.10) 0.2743	
	NYHA class at enrolment						0.7060
	II	989/1953 (50.6)	996/2031 (49.0)	1.04 (0.97, 1.10) 0.2733	1.07 (0.94, 1.21) 0.2953	0.02 (-0.01, 0.05) 0.2945	
	III or IV	287/ 672 (42.7)	238/ 593 (40.1)	1.06 (0.94, 1.20) 0.3564	1.11 (0.88, 1.40) 0.3733	0.02 (-0.03, 0.08) 0.3487	
	LVEF at enrolment						0.9428
	<= 49	451/ 907 (49.7)	432/ 896 (48.2)	1.04 (0.94, 1.14) 0.4657	1.07 (0.89, 1.29) 0.4531	0.02 (-0.03, 0.06) 0.4527	
	50-59	456/ 955 (47.7)	429/ 946 (45.3)	1.04 (0.95, 1.15) 0.3720	1.08 (0.90, 1.30) 0.3822	0.02 (-0.02, 0.06) 0.3851	
	>= 60	369/ 763 (48.4)	373/ 783 (47.6)	1.02 (0.92, 1.13) 0.7143	1.03 (0.84, 1.25) 0.7945	0.01 (-0.04, 0.06) 0.7925	
	NT-proBNP at enrolment						0.5598
	<= median	635/1312 (48.4)	635/1336 (47.5)	1.02 (0.94, 1.10) 0.6037	1.04 (0.89, 1.21) 0.6337	0.01 (-0.03, 0.05) 0.6277	
	> median	641/1313 (48.8)	598/1288 (46.4)	1.05 (0.97, 1.14) 0.2052	1.09 (0.94, 1.28) 0.2545	0.02 (-0.02, 0.06) 0.2539	
	Type 2 Diabetes Medical History						0.1807
	Yes	558/1150 (48.5)	529/1169 (45.3)	1.08 (0.99, 1.18) 0.0808	1.14 (0.97, 1.34)*0.1148	0.03 (-0.01, 0.07) 0.1169	
	No	718/1475 (48.7)	705/1456 (48.4)	1.00 (0.93, 1.08) 0.9965	1.01 (0.87, 1.17)*0.8890	0.00 (-0.03, 0.04) 0.9101	
	Atrial fibrillation or flutter at enrolment ECG						0.0544
	Yes	548/1097 (50.0)	500/1109 (45.1)	1.10 (1.01, 1.21) 0.0251	1.21 (1.03, 1.44) 0.0241	0.05 (0.01, 0.09) 0.0240	
	No	728/1528 (47.6)	734/1516 (48.4)	0.99 (0.92, 1.06) 0.7328	0.97 (0.84, 1.12) 0.6747	-0.01 (-0.04, 0.03) 0.6784	
	BMI (kg/m2) at enrolment						0.4893
	< 30	721/1452 (49.7)	697/1428 (48.8)	1.02 (0.94, 1.09) 0.6564	1.03 (0.89, 1.20) 0.6700	0.01 (-0.03, 0.04) 0.6682	
	>= 30	555/1172 (47.4)	536/1195 (44.9)	1.06 (0.97, 1.15) 0.1892	1.11 (0.94, 1.30) 0.2269	0.02 (-0.02, 0.06) 0.2265	
	Baseline eGFR (mL/min/1.73m^2)						0.2510
	< 60	572/1240 (46.1)	589/1270 (46.4)	1.00 (0.92, 1.09) 0.9797	0.99 (0.85, 1.16) 0.9118	-0.00 (-0.04, 0.04) 0.9001	
	>= 60	704/1385 (50.8)	645/1354 (47.6)	1.07 (0.99, 1.15) 0.0911	1.13 (0.98, 1.32) 0.1000	0.03 (-0.01, 0.07) 0.0983	

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Social Limitation (LOCF)	SBP at randomisation						0.2892
	<= median	637/1320 (48.3)	635/1323 (48.0)	1.00 (0.93, 1.09) 0.9069	1.00 (0.86, 1.17) 0.9955	0.00 (-0.04, 0.04) 0.9897	
	> median	639/1305 (49.0)	599/1302 (46.0)	1.07 (0.98, 1.16) 0.1130	1.13 (0.97, 1.32) 0.1169	0.03 (-0.01, 0.07) 0.1169	
	LVEF at enrolment 2						0.9929
	<= 49	451/ 907 (49.7)	432/ 896 (48.2)	1.04 (0.94, 1.14) 0.4657	1.07 (0.89, 1.29) 0.4531	0.02 (-0.03, 0.06) 0.4527	
	>= 50	825/1718 (48.0)	802/1729 (46.4)	1.03 (0.97, 1.11) 0.3354	1.06 (0.93, 1.21) 0.4022	0.01 (-0.02, 0.05) 0.4019	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5454
	Yes	128/ 252 (50.8)	131/ 256 (51.2)	0.95 (0.81, 1.11) 0.5110	1.02 (0.71, 1.47) 0.9082	0.00 (-0.08, 0.09) 0.9412	
	No	1148/2373 (48.4)	1103/2369 (46.6)	1.04 (0.98, 1.11) 0.1821	1.07 (0.96, 1.20) 0.2177	0.02 (-0.01, 0.05) 0.2178	
	MRAs at baseline						0.4381
	Yes	558/1144 (48.8)	547/1131 (48.4)	1.01 (0.93, 1.10) 0.8055	1.02 (0.86, 1.20) 0.8216	0.00 (-0.04, 0.05) 0.8248	
	No	718/1481 (48.5)	687/1494 (46.0)	1.06 (0.98, 1.14) 0.1626	1.10 (0.95, 1.27) 0.1937	0.02 (-0.01, 0.06) 0.1932	
	ACEi+ARB at baseline						0.6764
	Yes	921/1909 (48.2)	908/1934 (46.9)	1.03 (0.96, 1.10) 0.4181	1.05 (0.93, 1.19) 0.4463	0.01 (-0.02, 0.04) 0.4453	
	No	355/ 716 (49.6)	326/ 691 (47.2)	1.05 (0.95, 1.17) 0.3395	1.10 (0.89, 1.36) 0.3611	0.02 (-0.03, 0.08) 0.3607	
	ARNI at baseline						0.1695
	Yes	78/ 146 (53.4)	51/ 115 (44.3)	1.21 (0.94, 1.57) 0.1406	1.47 (0.89, 2.41) 0.1320	0.10 (-0.03, 0.22) 0.1283	
	No	1198/2479 (48.3)	1183/2510 (47.1)	1.03 (0.97, 1.09) 0.3845	1.05 (0.94, 1.17) 0.4213	0.01 (-0.02, 0.04) 0.4205	
	Beta Blocker at baseline						0.5189
	Yes	1053/2195 (48.0)	1020/2187 (46.6)	1.03 (0.97, 1.09) 0.4004	1.05 (0.93, 1.18) 0.4195	0.01 (-0.02, 0.04) 0.4191	
	No	223/ 430 (51.9)	214/ 438 (48.9)	1.07 (0.94, 1.23) 0.2872	1.14 (0.87, 1.49) 0.3348	0.03 (-0.03, 0.10) 0.3308	
	Diuretics at baseline						0.2171
	Yes	1139/2350 (48.5)	1086/2345 (46.3)	1.05 (0.99, 1.11) 0.1217	1.09 (0.97, 1.23) 0.1310	0.02 (-0.01, 0.05) 0.1293	
	No	137/ 275 (49.8)	148/ 280 (52.9)	0.94 (0.80, 1.11) 0.4762	0.89 (0.64, 1.24) 0.4931	-0.03 (-0.11, 0.05) 0.4922	

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Symptom Stability (LOCF)							
	Overall	893/2801 (31.9)	831/2805 (29.6)	1.08 (0.99, 1.16)*0.0674	1.11 (0.99, 1.25) 0.0853	0.02 (-0.00, 0.04) 0.1056	
	Age						0.7737*
	<= median	466/1394 (33.4)	451/1471 (30.7)	1.09 (0.98, 1.21)*0.1123	1.13 (0.96, 1.33) 0.1456	0.02 (-0.01, 0.05) 0.2220	
	> median	427/1407 (30.3)	380/1334 (28.5)	1.07 (0.95, 1.20)*0.2853	1.10 (0.93, 1.31) 0.2647	0.02 (-0.01, 0.05) 0.1670	
	Gender						0.0547*
	Male	482/1630 (29.6)	473/1608 (29.4)	1.01 (0.90, 1.12)*0.9229	1.00 (0.85, 1.16) 0.9562	-0.00 (-0.03, 0.03) 0.9620	
	Female	411/1171 (35.1)	358/1197 (29.9)	1.17 (1.04, 1.32)*0.0071	1.30 (1.08, 1.56) 0.0060	0.05 (0.01, 0.09)*0.0069	
	Race						0.8113*
	White	632/2006 (31.5)	601/2032 (29.6)	1.07 (0.97, 1.17)*0.1835	1.09 (0.95, 1.25) 0.2383	0.01 (-0.01, 0.04) 0.3965	
	Black or African	30/ 64 (46.9)	26/ 70 (37.1)	1.08 (0.72, 1.62) 0.7260	1.50 (0.71, 3.17) 0.2827	0.05 (-0.11, 0.21) 0.5137	
	Asian	142/ 555 (25.6)	136/ 551 (24.7)	1.04 (0.86, 1.26) 0.7078	1.05 (0.80, 1.39) 0.7282	0.02 (-0.03, 0.06) 0.5369	
	Other	89/ 176 (50.6)	68/ 152 (44.7)	1.13 (0.90, 1.42)*0.2949	1.42 (0.86, 2.32) 0.1672	0.06 (-0.05, 0.17)*0.2908	
	Geographic region						0.3658*
	Asia	134/ 536 (25.0)	129/ 536 (24.1)	1.04 (0.85, 1.26) 0.7296	1.05 (0.79, 1.40) 0.7298	0.02 (-0.03, 0.07) 0.5111	
	Europe and Saudi Arabia	409/1341 (30.5)	403/1381 (29.2)	1.05 (0.93, 1.17)*0.4525	1.08 (0.91, 1.29) 0.3897	0.01 (-0.02, 0.05)*0.4525	
	North America	107/ 393 (27.2)	104/ 376 (27.7)	0.98 (0.78, 1.24)*0.8930	0.90 (0.65, 1.26) 0.5538	-0.01 (-0.07, 0.04) 0.6177	
	Latin America	243/ 531 (45.8)	195/ 512 (38.1)	1.20 (1.04, 1.39)*0.0125	1.45 (1.11, 1.90) 0.0062	0.06 (0.00, 0.11) 0.0399	
	NYHA class at enrolment						0.1320*
	II	639/2083 (30.7)	641/2165 (29.6)	1.04 (0.95, 1.14)*0.4476	1.06 (0.92, 1.21) 0.4176	0.01 (-0.01, 0.04) 0.2821	
	III or IV	254/ 718 (35.4)	190/ 639 (29.7)	1.19 (1.02, 1.39)*0.0279	1.28 (1.00, 1.65) 0.0520	0.06 (0.01, 0.11)*0.0264	
	LVEF at enrolment						0.4517*
	<= 49	294/ 959 (30.7)	282/ 950 (29.7)	1.03 (0.90, 1.18)*0.6434	1.06 (0.86, 1.29) 0.6037	0.00 (-0.04, 0.04) 0.9454	
	50-59	331/1017 (32.5)	285/1009 (28.2)	1.15 (1.01, 1.32)*0.0357	1.23 (1.01, 1.50) 0.0424	0.04 (0.00, 0.07) 0.0492	
	>= 60	268/ 825 (32.5)	264/ 846 (31.2)	1.04 (0.90, 1.20)*0.5747	1.05 (0.85, 1.31) 0.6397	0.02 (-0.02, 0.05) 0.4338	
	NT-proBNP at enrolment						0.1007*
	<= median	429/1396 (30.7)	430/1409 (30.5)	1.01 (0.90, 1.13)*0.9028	1.01 (0.86, 1.20) 0.8706	0.01 (-0.02, 0.04) 0.7127	
	> median	464/1405 (33.0)	401/1395 (28.7)	1.15 (1.03, 1.28)*0.0145	1.22 (1.03, 1.44) 0.0242	0.03 (-0.00, 0.06) 0.0717	
	Type 2 Diabetes Medical History						0.5679*
	Yes	366/1231 (29.7)	353/1243 (28.4)	1.04 (0.96, 1.13) 0.3465	1.07 (0.90, 1.27)*0.4654	0.01 (-0.02, 0.04) 0.4147	
	No	527/1570 (33.6)	478/1562 (30.6)	1.10 (0.99, 1.21)*0.0758	1.15 (0.99, 1.33)*0.0756	0.02 (-0.01, 0.05) 0.1350	
	Atrial fibrillation or flutter at enrolment ECG						0.8291*
	Yes	359/1185 (30.3)	338/1188 (28.5)	1.06 (0.94, 1.21)*0.3242	1.10 (0.91, 1.32) 0.3320	0.01 (-0.02, 0.05) 0.3899	
	No	534/1616 (33.0)	493/1617 (30.5)	1.08 (0.98, 1.20)*0.1188	1.12 (0.96, 1.31) 0.1601	0.02 (-0.01, 0.05) 0.1614	
	BMI (kg/m2) at enrolment						0.2835*
	< 30	483/1547 (31.2)	429/1541 (27.8)	1.12 (1.01, 1.25)*0.0396	1.17 (0.99, 1.37) 0.0582	0.03 (-0.00, 0.06) 0.0793	
	>= 30	410/1253 (32.7)	401/1261 (31.8)	1.03 (0.92, 1.15)*0.6213	1.05 (0.88, 1.26) 0.5939	0.01 (-0.03, 0.05)*0.6212	
	Baseline eGFR (mL/min/1.73m^2)						0.3045*
	< 60	399/1338 (29.8)	399/1377 (29.0)	1.03 (0.92, 1.16)*0.6291	1.05 (0.88, 1.25) 0.5687	0.01 (-0.02, 0.04) 0.5762	
	>= 60	494/1463 (33.8)	431/1427 (30.2)	1.12 (1.00, 1.24)*0.0404	1.16 (0.99, 1.37) 0.0688	0.03 (-0.00, 0.06) 0.0773	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)	SBP at randomisation						0.3038*
	<= median	432/1405 (30.7)	423/1420 (29.8)	1.03 (0.92, 1.15)*0.5793	1.03 (0.87, 1.22) 0.7261	0.00 (-0.03, 0.03) 0.7870	
	> median	461/1396 (33.0)	408/1385 (29.5)	1.12 (1.00, 1.25)*0.0429	1.20 (1.02, 1.43) 0.0322	0.03 (0.00, 0.06) 0.0319	
	LVEF at enrolment 2						0.4672*
	<= 49	294/ 959 (30.7)	282/ 950 (29.7)	1.03 (0.90, 1.18)*0.6434	1.06 (0.86, 1.29) 0.6037	0.00 (-0.04, 0.04) 0.9454	
	>= 50	599/1842 (32.5)	549/1855 (29.6)	1.10 (1.00, 1.21)*0.0550	1.15 (0.99, 1.33) 0.0708	0.03 (0.00, 0.05) 0.0400	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3304*
	Yes	86/ 280 (30.7)	90/ 281 (32.0)	0.96 (0.75, 1.23)*0.7374	0.97 (0.66, 1.42) 0.8591	-0.02 (-0.08, 0.05) 0.5934	
	No	807/2521 (32.0)	741/2524 (29.4)	1.09 (1.00, 1.18)*0.0412	1.12 (0.99, 1.27) 0.0689	0.02 (0.00, 0.05) 0.0457	
	MRAs at baseline						0.1750*
	Yes	391/1216 (32.2)	384/1210 (31.7)	1.01 (0.90, 1.14)*0.8248	1.04 (0.87, 1.25) 0.6502	0.01 (-0.02, 0.04) 0.5753	
	No	502/1585 (31.7)	447/1595 (28.0)	1.13 (1.02, 1.26)*0.0248	1.17 (0.99, 1.37) 0.0630	0.02 (-0.01, 0.05) 0.1402	
	ACEi+ARB at baseline						0.6218*
	Yes	666/2037 (32.7)	618/2059 (30.0)	1.09 (0.99, 1.19)*0.0646	1.15 (1.00, 1.32) 0.0518	0.02 (-0.00, 0.05) 0.0790	
	No	227/ 764 (29.7)	213/ 746 (28.6)	1.04 (0.89, 1.22)*0.6201	1.02 (0.81, 1.29) 0.8482	0.01 (-0.04, 0.05) 0.7590	
	ARNI at baseline						0.6342*
	Yes	46/ 149 (30.9)	39/ 125 (31.2)	1.05 (0.75, 1.48) 0.7692	1.12 (0.66, 1.91) 0.6755	0.03 (-0.08, 0.13) 0.6160	
	No	847/2652 (31.9)	792/2680 (29.6)	1.08 (1.00, 1.17)*0.0592	1.11 (0.98, 1.26) 0.0887	0.02 (-0.01, 0.04) 0.1316	
	Beta Blocker at baseline						0.9032*
	Yes	740/2327 (31.8)	687/2330 (29.5)	1.08 (0.99, 1.18)*0.0867	1.09 (0.96, 1.25) 0.1785	0.02 (-0.01, 0.04) 0.1555	
	No	153/ 474 (32.3)	144/ 475 (30.3)	1.06 (0.88, 1.29)*0.5146	1.23 (0.92, 1.66) 0.1669	0.02 (-0.04, 0.08)*0.5143	
	Diuretics at baseline						0.7560*
	Yes	784/2500 (31.4)	733/2504 (29.3)	1.07 (0.98, 1.17)*0.1085	1.10 (0.97, 1.25) 0.1282	0.02 (-0.00, 0.04) 0.1077	
	No	109/ 301 (36.2)	98/ 301 (32.6)	1.11 (0.89, 1.39)*0.3458	1.16 (0.82, 1.66) 0.4045	0.03 (-0.04, 0.10) 0.3871	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	1344/2801 (48.0)	1218/2805 (43.4)	1.10 (1.04, 1.16) 0.0007	1.20 (1.08, 1.33) 0.0009	0.04 (0.02, 0.07) 0.0009	
	Age						0.3770
	<= median	718/1394 (51.5)	673/1471 (45.8)	1.14 (1.06, 1.22) 0.0007	1.27 (1.09, 1.47) 0.0017	0.06 (0.02, 0.09) 0.0015	
	> median	626/1407 (44.5)	545/1334 (40.9)	1.07 (0.98, 1.16) 0.1183	1.14 (0.98, 1.33) 0.0912	0.03 (-0.00, 0.07) 0.0898	
	Gender						0.9147
	Male	819/1630 (50.2)	737/1608 (45.8)	1.10 (1.02, 1.18) 0.0100	1.19 (1.04, 1.37) 0.0137	0.04 (0.01, 0.08) 0.0128	
	Female	525/1171 (44.8)	481/1197 (40.2)	1.09 (1.00, 1.19) 0.0573	1.20 (1.01, 1.41) 0.0349	0.04 (0.00, 0.08) 0.0383	
	Race						0.4284
	White	922/2006 (46.0)	831/2032 (40.9)	1.11 (1.04, 1.19) 0.0021	1.21 (1.07, 1.38) 0.0029	0.05 (0.02, 0.08) 0.0025	
	Black or African	32/ 64 (50.0)	34/ 70 (48.6)	1.04 (0.73, 1.48) 0.8201	1.07 (0.54, 2.11) 0.8480	0.02 (-0.15, 0.19) 0.8481	
	Asian	289/ 555 (52.1)	277/ 551 (50.3)	1.04 (0.93, 1.17) 0.5175	1.07 (0.85, 1.36) 0.5555	0.02 (-0.04, 0.08) 0.5533	
	Other	101/ 176 (57.4)	76/ 152 (50.0)	1.11 (0.92, 1.34) 0.2800	1.34 (0.85, 2.10) 0.2066	0.07 (-0.04, 0.18) 0.1960	
	Geographic region						0.0749
	Asia	282/ 536 (52.6)	269/ 536 (50.2)	1.05 (0.94, 1.18) 0.3931	1.10 (0.87, 1.40) 0.4298	0.02 (-0.04, 0.08) 0.4273	
	Europe and Saudi Arabia	607/1341 (45.3)	562/1381 (40.7)	1.11 (1.02, 1.21)*0.0161	1.18 (1.01, 1.38) 0.0371	0.04 (0.00, 0.08) 0.0348	
	North America	151/ 393 (38.4)	147/ 376 (39.1)	0.99 (0.83, 1.18) 0.9107	0.97 (0.73, 1.30) 0.8596	-0.01 (-0.07, 0.06) 0.8609	
	Latin America	304/ 531 (57.3)	240/ 512 (46.9)	1.22 (1.09, 1.37)*0.0009	1.53 (1.20, 1.97) 0.0008	0.10 (0.04, 0.16) 0.0006	
	NYHA class at enrolment						0.0071
	II	982/2083 (47.1)	966/2165 (44.6)	1.06 (0.99, 1.13) 0.0866	1.11 (0.98, 1.25) 0.0914	0.03 (-0.00, 0.06) 0.0955	
	III or IV	362/ 718 (50.4)	252/ 639 (39.4)	1.21 (1.08, 1.36) 0.0010	1.55 (1.24, 1.94) 0.0001	0.11 (0.06, 0.16) <.0001	
	LVEF at enrolment						0.9133
	<= 49	460/ 959 (48.0)	418/ 950 (44.0)	1.09 (0.99, 1.19) 0.0827	1.18 (0.98, 1.42) 0.0756	0.04 (-0.00, 0.08) 0.0729	
	50-59	491/1017 (48.3)	442/1009 (43.8)	1.09 (1.00, 1.19) 0.0615	1.19 (1.00, 1.42) 0.0511	0.04 (-0.00, 0.09) 0.0511	
	>= 60	393/ 825 (47.6)	358/ 846 (42.3)	1.12 (1.01, 1.24) 0.0376	1.22 (1.00, 1.48) 0.0470	0.05 (0.00, 0.10) 0.0477	
	NT-proBNP at enrolment						0.3327
	<= median	639/1396 (45.8)	599/1409 (42.5)	1.08 (0.99, 1.17) 0.0833	1.14 (0.98, 1.33) 0.0811	0.03 (-0.00, 0.07) 0.0795	
	> median	705/1405 (50.2)	618/1395 (44.3)	1.13 (1.05, 1.22) 0.0015	1.25 (1.08, 1.46) 0.0036	0.05 (0.02, 0.09) 0.0034	
	Type 2 Diabetes Medical History						0.1373
	Yes	610/1231 (49.6)	536/1243 (43.1)	1.15 (1.06, 1.25) 0.0008	1.30 (1.11, 1.52)*0.0013	0.06 (0.02, 0.10) 0.0014	
	No	734/1570 (46.8)	682/1562 (43.7)	1.06 (0.98, 1.14) 0.1515	1.13 (0.98, 1.30)*0.0824	0.03 (-0.01, 0.06) 0.1080	
	Atrial fibrillation or flutter at enrolment ECG						0.7438
	Yes	576/1185 (48.6)	527/1188 (44.4)	1.09 (1.00, 1.18) 0.0478	1.19 (1.01, 1.40) 0.0415	0.04 (0.00, 0.08) 0.0423	
	No	768/1616 (47.5)	691/1617 (42.7)	1.11 (1.03, 1.20) 0.0056	1.21 (1.05, 1.39) 0.0086	0.05 (0.01, 0.08) 0.0084	
	BMI (kg/m2) at enrolment						0.3967
	< 30	761/1547 (49.2)	699/1541 (45.4)	1.08 (1.01, 1.17) 0.0313	1.16 (1.01, 1.34) 0.0380	0.04 (0.00, 0.07) 0.0389	
	>= 30	583/1253 (46.5)	518/1261 (41.1)	1.12 (1.03, 1.22) 0.0070	1.24 (1.06, 1.46) 0.0085	0.05 (0.01, 0.09) 0.0071	
	Baseline eGFR (mL/min/1.73m^2)						0.7080
	< 60	613/1338 (45.8)	573/1377 (41.6)	1.09 (1.00, 1.18) 0.0512	1.18 (1.01, 1.38) 0.0341	0.04 (0.00, 0.08) 0.0334	
	>= 60	731/1463 (50.0)	645/1427 (45.2)	1.11 (1.03, 1.20) 0.0048	1.21 (1.04, 1.40) 0.0128	0.05 (0.01, 0.08) 0.0118	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.1045
	<= median	654/1405 (46.5)	617/1420 (43.5)	1.05 (0.97, 1.14) 0.1974	1.11 (0.96, 1.29) 0.1697	0.02 (-0.01, 0.06) 0.1838	
	> median	690/1396 (49.4)	601/1385 (43.4)	1.15 (1.07, 1.25) 0.0003	1.29 (1.11, 1.50) 0.0009	0.06 (0.03, 0.10) 0.0007	
	LVEF at enrolment 2						0.7730
	<= 49	460/ 959 (48.0)	418/ 950 (44.0)	1.09 (0.99, 1.19) 0.0827	1.18 (0.98, 1.42) 0.0756	0.04 (-0.00, 0.08) 0.0729	
	>= 50	884/1842 (48.0)	800/1855 (43.1)	1.11 (1.03, 1.19) 0.0040	1.20 (1.06, 1.37) 0.0056	0.04 (0.01, 0.08) 0.0056	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2773
	Yes	151/ 280 (53.9)	147/ 281 (52.3)	1.03 (0.88, 1.20)*0.7015	1.11 (0.78, 1.57) 0.5616	0.01 (-0.06, 0.09) 0.7130	
	No	1193/2521 (47.3)	1071/2524 (42.4)	1.11 (1.05, 1.18) 0.0004	1.21 (1.08, 1.35) 0.0008	0.05 (0.02, 0.07) 0.0008	
	MRAs at baseline						0.8225
	Yes	581/1216 (47.8)	524/1210 (43.3)	1.09 (1.00, 1.19) 0.0409	1.19 (1.01, 1.40) 0.0383	0.04 (0.00, 0.08) 0.0395	
	No	763/1585 (48.1)	694/1595 (43.5)	1.11 (1.03, 1.19) 0.0068	1.20 (1.04, 1.38) 0.0103	0.05 (0.01, 0.08) 0.0098	
	ACEi+ARB at baseline						0.2821
	Yes	987/2037 (48.5)	883/2059 (42.9)	1.12 (1.05, 1.19) 0.0006	1.24 (1.10, 1.41) 0.0007	0.05 (0.02, 0.08) 0.0007	
	No	357/ 764 (46.7)	335/ 746 (44.9)	1.05 (0.94, 1.17) 0.4273	1.08 (0.88, 1.32) 0.4573	0.02 (-0.03, 0.07) 0.4555	
	ARNI at baseline						0.1281
	Yes	65/ 149 (43.6)	63/ 125 (50.4)	0.85 (0.66, 1.10) 0.2109	0.74 (0.45, 1.20) 0.2158	-0.08 (-0.20, 0.04) 0.2165	
	No	1279/2652 (48.2)	1155/2680 (43.1)	1.11 (1.05, 1.18) 0.0003	1.22 (1.09, 1.36) 0.0003	0.05 (0.02, 0.07) 0.0003	
	Beta Blocker at baseline						0.3252
	Yes	1100/2327 (47.3)	1007/2330 (43.2)	1.09 (1.02, 1.16) 0.0072	1.16 (1.04, 1.31) 0.0107	0.04 (0.01, 0.06) 0.0114	
	No	244/ 474 (51.5)	211/ 475 (44.4)	1.16 (1.02, 1.33) 0.0215	1.38 (1.06, 1.79) 0.0154	0.08 (0.02, 0.14) 0.0132	
	Diuretics at baseline						0.6366
	Yes	1176/2500 (47.0)	1072/2504 (42.8)	1.09 (1.03, 1.16) 0.0029	1.19 (1.06, 1.33) 0.0027	0.04 (0.01, 0.07) 0.0025	
	No	168/ 301 (55.8)	146/ 301 (48.5)	1.14 (0.98, 1.33) 0.0813	1.29 (0.94, 1.79) 0.1193	0.06 (-0.02, 0.14) 0.1179	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	812/2801 (29.0)	733/2805 (26.1)	1.11 (1.02, 1.21)*0.0168	1.13 (0.98, 1.29) 0.0847	0.03 (0.01, 0.05)*0.0166	
	Age						0.4222*
	<= median	414/1394 (29.7)	406/1471 (27.6)	1.08 (0.96, 1.21)*0.2143	1.14 (0.94, 1.37) 0.1876	0.02 (-0.01, 0.05)*0.2144	
	> median	398/1407 (28.3)	327/1334 (24.5)	1.15 (1.02, 1.31)*0.0255	1.14 (0.94, 1.39) 0.1872	0.04 (0.00, 0.07)*0.0248	
	Gender						0.0551*
	Male	430/1630 (26.4)	412/1608 (25.6)	1.03 (0.92, 1.16)*0.6228	0.99 (0.82, 1.20) 0.9390	0.01 (-0.02, 0.04)*0.6227	
	Female	382/1171 (32.6)	321/1197 (26.8)	1.22 (1.07, 1.38)*0.0021	1.29 (1.06, 1.58) 0.0110	0.06 (0.02, 0.09)*0.0020	
	Race						0.9062*
	White	613/2006 (30.6)	551/2032 (27.1)	1.13 (1.02, 1.24)*0.0159	1.13 (0.97, 1.33) 0.1170	0.03 (0.01, 0.06)*0.0157	
	Black or African	24/ 64 (37.5)	26/ 70 (37.1)	1.01 (0.65, 1.57)*0.9659	1.03 (0.49, 2.19) 0.9314	-0.00 (-0.15, 0.15) 0.9731	
	Asian	105/ 555 (18.9)	100/ 551 (18.1)	1.04 (0.81, 1.33)*0.7418	1.05 (0.73, 1.51) 0.7911	0.01 (-0.04, 0.05)*0.7417	
	Other	70/ 176 (39.8)	56/ 152 (36.8)	1.08 (0.82, 1.42)*0.5873	1.21 (0.71, 2.04) 0.4818	0.03 (-0.08, 0.13)*0.5858	
	Geographic region						0.9280*
	Asia	101/ 536 (18.8)	96/ 536 (17.9)	1.05 (0.82, 1.35)*0.6934	1.04 (0.72, 1.51) 0.8274	0.01 (-0.04, 0.06)*0.6933	
	Europe and Saudi Arabia	407/1341 (30.4)	370/1381 (26.8)	1.13 (1.01, 1.28)*0.0401	1.15 (0.94, 1.39) 0.1697	0.04 (0.00, 0.07)*0.0398	
	North America	102/ 393 (26.0)	86/ 376 (22.9)	1.11 (0.89, 1.39) 0.3624	1.16 (0.81, 1.64) 0.4204	0.03 (-0.03, 0.09)*0.3194	
	Latin America	202/ 531 (38.0)	181/ 512 (35.4)	1.08 (0.92, 1.26)*0.3681	1.14 (0.84, 1.54) 0.3995	0.03 (-0.03, 0.09)*0.3673	
	NYHA class at enrolment						0.0542*
	II	526/2083 (25.3)	527/2165 (24.3)	1.04 (0.93, 1.15)*0.4922	1.06 (0.90, 1.24) 0.5041	0.01 (-0.02, 0.04)*0.4922	
	III or IV	286/ 718 (39.8)	206/ 639 (32.2)	1.24 (1.07, 1.43)*0.0040	1.36 (1.06, 1.74) 0.0153	0.08 (0.03, 0.13)*0.0035	
	LVEF at enrolment						0.0380*
	<= 49	262/ 959 (27.3)	261/ 950 (27.5)	0.99 (0.86, 1.15)*0.9400	1.02 (0.81, 1.29) 0.8632	-0.00 (-0.04, 0.04)*0.9400	
	50-59	297/1017 (29.2)	274/1009 (27.2)	1.08 (0.94, 1.24)*0.3059	1.02 (0.81, 1.28) 0.8800	0.02 (-0.02, 0.06)*0.3055	
	>= 60	253/ 825 (30.7)	198/ 846 (23.4)	1.31 (1.12, 1.54)*0.0009	1.41 (1.10, 1.80) 0.0062	0.07 (0.03, 0.12)*0.0008	
	NT-proBNP at enrolment						0.2622*
	<= median	363/1396 (26.0)	348/1409 (24.7)	1.05 (0.93, 1.20)*0.4272	1.07 (0.88, 1.30) 0.5027	0.01 (-0.02, 0.05)*0.4271	
	> median	449/1405 (32.0)	384/1395 (27.5)	1.16 (1.04, 1.30)*0.0105	1.18 (0.98, 1.43) 0.0861	0.04 (0.01, 0.08)*0.0102	
	Type 2 Diabetes Medical History						0.2104*
	Yes	379/1231 (30.8)	325/1243 (26.1)	1.18 (1.04, 1.33)*0.0107	1.26 (1.05, 1.50)*0.0106	0.05 (0.01, 0.08)*0.0104	
	No	433/1570 (27.6)	408/1562 (26.1)	1.06 (0.94, 1.19)*0.3570	1.08 (0.92, 1.26)*0.3569	0.01 (-0.02, 0.05)*0.3568	
	Atrial fibrillation or flutter at enrolment ECG						0.8537*
	Yes	354/1185 (29.9)	317/1188 (26.7)	1.12 (0.98, 1.27)*0.0848	1.16 (0.95, 1.43) 0.1531	0.03 (-0.00, 0.07)*0.0843	
	No	458/1616 (28.3)	416/1617 (25.7)	1.10 (0.98, 1.23)*0.0944	1.10 (0.92, 1.32) 0.2943	0.03 (-0.00, 0.06)*0.0940	
	BMI (kg/m2) at enrolment						0.8763*
	< 30	412/1547 (26.6)	372/1541 (24.1)	1.10 (0.98, 1.25)*0.1119	1.12 (0.92, 1.36) 0.2518	0.02 (-0.01, 0.06)*0.1115	
	>= 30	400/1253 (31.9)	360/1261 (28.5)	1.12 (0.99, 1.26)*0.0658	1.14 (0.94, 1.38) 0.1810	0.03 (-0.00, 0.07)*0.0653	
	Baseline eGFR (mL/min/1.73m^2)						0.8917*
	< 60	380/1338 (28.4)	355/1377 (25.8)	1.10 (0.97, 1.25)*0.1248	1.13 (0.93, 1.37) 0.2152	0.03 (-0.01, 0.06)*0.1245	
	>= 60	432/1463 (29.5)	378/1427 (26.5)	1.11 (0.99, 1.25)*0.0693	1.12 (0.92, 1.36) 0.2513	0.03 (-0.00, 0.06)*0.0687	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.3552*
	<= median	408/1405 (29.0)	357/1420 (25.1)	1.16 (1.02, 1.30)*0.0199	1.13 (0.93, 1.37) 0.2175	0.04 (0.01, 0.07)*0.0196	
	> median	404/1396 (28.9)	376/1385 (27.1)	1.07 (0.95, 1.20)*0.2931	1.13 (0.93, 1.37) 0.2114	0.02 (-0.02, 0.05)*0.2928	
	LVEF at enrolment 2						0.0710*
	<= 49	262/ 959 (27.3)	261/ 950 (27.5)	0.99 (0.86, 1.15)*0.9400	1.02 (0.81, 1.29) 0.8632	-0.00 (-0.04, 0.04)*0.9400	
	>= 50	550/1842 (29.9)	472/1855 (25.4)	1.17 (1.06, 1.30)*0.0028	1.19 (1.00, 1.40) 0.0452	0.04 (0.02, 0.07)*0.0027	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1394*
	Yes	108/ 280 (38.6)	113/ 281 (40.2)	0.96 (0.78, 1.18)*0.6907	0.98 (0.67, 1.45) 0.9350	-0.02 (-0.10, 0.06)*0.6906	
	No	704/2521 (27.9)	620/2524 (24.6)	1.14 (1.04, 1.25)*0.0067	1.15 (1.00, 1.33) 0.0576	0.03 (0.01, 0.06)*0.0066	
	MRAs at baseline						0.7443*
	Yes	348/1216 (28.6)	307/1210 (25.4)	1.13 (0.99, 1.29)*0.0721	1.15 (0.93, 1.41) 0.1923	0.03 (-0.00, 0.07)*0.0715	
	No	464/1585 (29.3)	426/1595 (26.7)	1.10 (0.98, 1.23)*0.1073	1.11 (0.93, 1.33) 0.2580	0.03 (-0.01, 0.06)*0.1069	
	ACEi+ARB at baseline						0.2922*
	Yes	618/2037 (30.3)	548/2059 (26.6)	1.14 (1.03, 1.26)*0.0084	1.16 (0.99, 1.36) 0.0588	0.04 (0.01, 0.06)*0.0082	
	No	194/ 764 (25.4)	185/ 746 (24.8)	1.02 (0.86, 1.22)*0.7902	1.03 (0.79, 1.35) 0.8193	0.01 (-0.04, 0.05)*0.7902	
	ARNI at baseline						0.2728*
	Yes	30/ 149 (20.1)	29/ 125 (23.2)	0.87 (0.55, 1.36)*0.5385	0.97 (0.50, 1.88) 0.9320	-0.03 (-0.13, 0.07)*0.5401	
	No	782/2652 (29.5)	704/2680 (26.3)	1.12 (1.03, 1.22)*0.0088	1.13 (0.99, 1.30) 0.0740	0.03 (0.01, 0.06)*0.0087	
	Beta Blocker at baseline						0.2223*
	Yes	682/2327 (29.3)	601/2330 (25.8)	1.14 (1.03, 1.25)*0.0074	1.14 (0.98, 1.32) 0.0823	0.04 (0.01, 0.06)*0.0072	
	No	130/ 474 (27.4)	132/ 475 (27.8)	0.99 (0.80, 1.21)*0.9004	1.07 (0.76, 1.50) 0.7087	-0.00 (-0.06, 0.05)*0.9004	
	Diuretics at baseline						0.3174*
	Yes	727/2500 (29.1)	666/2504 (26.6)	1.09 (1.00, 1.20)*0.0503	1.12 (0.98, 1.30) 0.1061	0.02 (-0.00, 0.05)*0.0500	
	No	85/ 301 (28.2)	67/ 301 (22.3)	1.27 (0.96, 1.67)*0.0928	1.11 (0.71, 1.73) 0.6506	0.06 (-0.01, 0.13)*0.0905	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	794/2801 (28.3)	703/2805 (25.1)	1.13 (1.04, 1.23)*0.0055	1.15 (1.01, 1.32) 0.0397	0.03 (0.01, 0.06)*0.0054	
	Age						0.2390*
	<= median	402/1394 (28.8)	393/1471 (26.7)	1.08 (0.96, 1.21)*0.2050	1.13 (0.94, 1.36) 0.2063	0.02 (-0.01, 0.05)*0.2051	
	> median	392/1407 (27.9)	310/1334 (23.2)	1.20 (1.05, 1.36)*0.0058	1.20 (0.98, 1.47) 0.0757	0.05 (0.01, 0.08)*0.0054	
	Gender						0.0195*
	Male	419/1630 (25.7)	401/1608 (24.9)	1.03 (0.92, 1.16)*0.6155	0.99 (0.82, 1.19) 0.9161	0.01 (-0.02, 0.04)*0.6154	
	Female	375/1171 (32.0)	302/1197 (25.2)	1.27 (1.12, 1.44)*0.0003	1.38 (1.12, 1.69) 0.0020	0.07 (0.03, 0.10)*0.0002	
	Race						0.9620*
	White	591/2006 (29.5)	529/2032 (26.0)	1.13 (1.02, 1.25)*0.0151	1.12 (0.96, 1.32) 0.1484	0.03 (0.01, 0.06)*0.0149	
	Black or African	23/ 64 (35.9)	25/ 70 (35.7)	1.03 (0.67, 1.59) 0.8840	1.01 (0.48, 2.12) 0.9880	-0.00 (-0.15, 0.15) 0.9890	
	Asian	108/ 555 (19.5)	93/ 551 (16.9)	1.15 (0.90, 1.48)*0.2664	1.23 (0.86, 1.75) 0.2555	0.03 (-0.02, 0.07)*0.2654	
	Other	72/ 176 (40.9)	56/ 152 (36.8)	1.11 (0.84, 1.46)*0.4532	1.32 (0.79, 2.22) 0.2871	0.04 (-0.06, 0.15)*0.4505	
	Geographic region						0.8981*
	Asia	105/ 536 (19.6)	90/ 536 (16.8)	1.17 (0.90, 1.51)*0.2358	1.23 (0.86, 1.76) 0.2605	0.03 (-0.02, 0.07)*0.2347	
	Europe and Saudi Arabia	392/1341 (29.2)	349/1381 (25.3)	1.16 (1.02, 1.31)*0.0205	1.17 (0.96, 1.43) 0.1234	0.04 (0.01, 0.07)*0.0203	
	North America	100/ 393 (25.4)	88/ 376 (23.4)	1.09 (0.85, 1.39)*0.5107	1.10 (0.77, 1.56) 0.6060	0.02 (-0.04, 0.08)*0.5099	
	Latin America	197/ 531 (37.1)	176/ 512 (34.4)	1.08 (0.92, 1.27)*0.3592	1.12 (0.83, 1.50) 0.4689	0.03 (-0.03, 0.09)*0.3584	
	NYHA class at enrolment						0.2647*
	II	524/2083 (25.2)	503/2165 (23.2)	1.08 (0.97, 1.20)*0.1435	1.13 (0.96, 1.34) 0.1339	0.02 (-0.01, 0.04)*0.1435	
	III or IV	270/ 718 (37.6)	200/ 639 (31.3)	1.20 (1.04, 1.39)*0.0155	1.27 (0.99, 1.63) 0.0563	0.06 (0.01, 0.11)*0.0144	
	LVEF at enrolment						0.0436*
	<= 49	248/ 959 (25.9)	254/ 950 (26.7)	0.97 (0.83, 1.12)*0.6636	0.97 (0.77, 1.23) 0.8084	-0.01 (-0.05, 0.03)*0.6636	
	50-59	310/1017 (30.5)	251/1009 (24.9)	1.23 (1.06, 1.41)*0.0050	1.27 (1.01, 1.59) 0.0425	0.06 (0.02, 0.09)*0.0047	
	>= 60	236/ 825 (28.6)	198/ 846 (23.4)	1.22 (1.04, 1.44)*0.0156	1.25 (0.97, 1.61) 0.0819	0.05 (0.01, 0.09)*0.0152	
	NT-proBNP at enrolment						0.2485*
	<= median	361/1396 (25.9)	340/1409 (24.1)	1.07 (0.94, 1.22)*0.2905	1.09 (0.90, 1.33) 0.3926	0.02 (-0.01, 0.05)*0.2902	
	> median	433/1405 (30.8)	362/1395 (25.9)	1.19 (1.06, 1.34)*0.0044	1.22 (1.01, 1.48) 0.0404	0.05 (0.02, 0.08)*0.0042	
	Type 2 Diabetes Medical History						0.1940*
	Yes	353/1231 (28.7)	295/1243 (23.7)	1.21 (1.06, 1.38)*0.0053	1.29 (1.08, 1.55)*0.0052	0.05 (0.01, 0.08)*0.0051	
	No	441/1570 (28.1)	408/1562 (26.1)	1.08 (0.96, 1.21)*0.2154	1.10 (0.94, 1.29)*0.2153	0.02 (-0.01, 0.05)*0.2151	
	Atrial fibrillation or flutter at enrolment ECG						0.3611*
	Yes	351/1185 (29.6)	297/1188 (25.0)	1.18 (1.04, 1.35)*0.0118	1.25 (1.02, 1.54) 0.0339	0.05 (0.01, 0.08)*0.0114	
	No	443/1616 (27.4)	406/1617 (25.1)	1.09 (0.97, 1.23)*0.1367	1.09 (0.91, 1.30) 0.3771	0.02 (-0.01, 0.05)*0.1363	
	BMI (kg/m2) at enrolment						0.9520*
	< 30	411/1547 (26.6)	362/1541 (23.5)	1.13 (1.00, 1.28)*0.0488	1.14 (0.94, 1.38) 0.1988	0.03 (0.00, 0.06)*0.0483	
	>= 30	383/1253 (30.6)	339/1261 (26.9)	1.14 (1.00, 1.29)*0.0416	1.18 (0.97, 1.43) 0.1007	0.04 (0.00, 0.07)*0.0411	
	Baseline eGFR (mL/min/1.73m^2)						0.5887*
	< 60	375/1338 (28.0)	333/1377 (24.2)	1.16 (1.02, 1.32)*0.0228	1.24 (1.02, 1.50) 0.0338	0.04 (0.01, 0.07)*0.0225	
	>= 60	419/1463 (28.6)	370/1427 (25.9)	1.10 (0.98, 1.24)*0.1023	1.08 (0.89, 1.30) 0.4531	0.03 (-0.01, 0.06)*0.1016	

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Overall Summary Score (LOCF)	SBP at randomisation						0.2527*
	<= median	405/1405 (28.8)	344/1420 (24.2)	1.19 (1.05, 1.35)*0.0057	1.18 (0.97, 1.43) 0.0915	0.05 (0.01, 0.08)*0.0056	
	> median	389/1396 (27.9)	359/1385 (25.9)	1.08 (0.95, 1.22)*0.2478	1.13 (0.93, 1.38) 0.2073	0.02 (-0.01, 0.05)*0.2474	
	LVEF at enrolment 2						0.0121*
	<= 49	248/ 959 (25.9)	254/ 950 (26.7)	0.97 (0.83, 1.12)*0.6636	0.97 (0.77, 1.23) 0.8084	-0.01 (-0.05, 0.03)*0.6636	
	>= 50	546/1842 (29.6)	449/1855 (24.2)	1.22 (1.10, 1.36)*0.0002	1.26 (1.06, 1.49) 0.0072	0.05 (0.03, 0.08)*0.0002	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0839*
	Yes	114/ 280 (40.7)	119/ 281 (42.3)	0.96 (0.79, 1.17)*0.6945	0.94 (0.64, 1.38) 0.7463	-0.02 (-0.10, 0.07)*0.6944	
	No	680/2521 (27.0)	584/2524 (23.1)	1.17 (1.06, 1.28)*0.0017	1.19 (1.03, 1.38) 0.0180	0.04 (0.01, 0.06)*0.0017	
	MRAs at baseline						0.9216*
	Yes	345/1216 (28.4)	302/1210 (25.0)	1.14 (1.00, 1.30)*0.0577	1.18 (0.96, 1.45) 0.1165	0.03 (-0.00, 0.07)*0.0571	
	No	449/1585 (28.3)	401/1595 (25.1)	1.13 (1.00, 1.26)*0.0425	1.13 (0.94, 1.36) 0.1797	0.03 (0.00, 0.06)*0.0422	
	ACEi+ARB at baseline						0.3817*
	Yes	599/2037 (29.4)	523/2059 (25.4)	1.16 (1.05, 1.28)*0.0041	1.19 (1.02, 1.40) 0.0302	0.04 (0.01, 0.07)*0.0040	
	No	195/ 764 (25.5)	180/ 746 (24.1)	1.06 (0.89, 1.26)*0.5307	1.06 (0.81, 1.38) 0.6851	0.01 (-0.03, 0.06)*0.5304	
	ARNI at baseline						0.5487*
	Yes	28/ 149 (18.8)	24/ 125 (19.2)	0.98 (0.60, 1.60)*0.9316	1.10 (0.55, 2.19) 0.7964	-0.00 (-0.10, 0.09)*0.9317	
	No	766/2652 (28.9)	679/2680 (25.3)	1.14 (1.04, 1.25)*0.0036	1.16 (1.01, 1.34) 0.0354	0.04 (0.01, 0.06)*0.0035	
	Beta Blocker at baseline						0.2371*
	Yes	663/2327 (28.5)	573/2330 (24.6)	1.16 (1.05, 1.28)*0.0026	1.17 (1.00, 1.35) 0.0445	0.04 (0.01, 0.06)*0.0026	
	No	131/ 474 (27.6)	130/ 475 (27.4)	1.01 (0.82, 1.24)*0.9261	1.11 (0.79, 1.55) 0.5500	0.00 (-0.05, 0.06)*0.9261	
	Diuretics at baseline						0.0051*
	Yes	694/2500 (27.8)	642/2504 (25.6)	1.08 (0.99, 1.19)*0.0901	1.10 (0.95, 1.27) 0.2107	0.02 (-0.00, 0.05)*0.0898	
	No	100/ 301 (33.2)	61/ 301 (20.3)	1.64 (1.24, 2.16)*0.0004	1.77 (1.14, 2.75) 0.0113	0.13 (0.06, 0.20)*0.0003	

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Physical Limitation (LOCF)							
	Overall	772/2750 (28.1)	676/2758 (24.5)	1.15 (1.05, 1.25)*0.0027	1.17 (1.03, 1.34) 0.0193	0.04 (0.01, 0.06)*0.0027	
	Age						0.0845*
	<= median	382/1382 (27.6)	378/1456 (26.0)	1.06 (0.94, 1.20)*0.3125	1.10 (0.91, 1.32) 0.3470	0.02 (-0.02, 0.05)*0.3127	
	> median	390/1368 (28.5)	298/1302 (22.9)	1.25 (1.09, 1.42)*0.0010	1.30 (1.07, 1.57) 0.0077	0.06 (0.02, 0.09)*0.0009	
	Gender						0.0397*
	Male	403/1611 (25.0)	376/1583 (23.8)	1.05 (0.93, 1.19)*0.4060	1.03 (0.86, 1.24) 0.7578	0.01 (-0.02, 0.04)*0.4058	
	Female	369/1139 (32.4)	300/1175 (25.5)	1.17 (1.05, 1.31) 0.0054	1.36 (1.12, 1.66) 0.0023	0.07 (0.03, 0.11)*0.0003	
	Race						0.6376*
	White	578/1970 (29.3)	525/1998 (26.3)	1.12 (1.01, 1.23)*0.0314	1.12 (0.96, 1.31) 0.1378	0.03 (0.00, 0.06)*0.0312	
	Black or African	21/ 63 (33.3)	18/ 66 (27.3)	1.31 (0.80, 2.14) 0.2883	1.41 (0.61, 3.24) 0.4205	0.06 (-0.10, 0.22)*0.4533	
	Asian	108/ 548 (19.7)	92/ 546 (16.8)	1.17 (0.91, 1.50)*0.2222	1.06 (0.74, 1.51) 0.7649	0.03 (-0.02, 0.07)*0.2210	
	Other	65/ 169 (38.5)	41/ 148 (27.7)	1.39 (1.01, 1.92)*0.0462	2.07 (1.19, 3.58) 0.0096	0.11 (0.00, 0.21)*0.0403	
	Geographic region						0.5307*
	Asia	102/ 530 (19.2)	89/ 531 (16.8)	1.15 (0.89, 1.49)*0.2929	1.02 (0.71, 1.48) 0.8990	0.02 (-0.02, 0.07)*0.2920	
	Europe and Saudi Arabia	381/1323 (28.8)	349/1360 (25.7)	1.12 (0.99, 1.27)*0.0682	1.15 (0.95, 1.39) 0.1407	0.03 (-0.00, 0.07)*0.0680	
	North America	95/ 386 (24.6)	87/ 362 (24.0)	1.02 (0.80, 1.32)*0.8539	0.95 (0.66, 1.35) 0.7616	0.01 (-0.06, 0.07)*0.8538	
	Latin America	194/ 511 (38.0)	151/ 505 (29.9)	1.27 (1.07, 1.51)*0.0070	1.57 (1.17, 2.12) 0.0028	0.08 (0.02, 0.14)*0.0064	
	NYHA class at enrolment						0.6995*
	II	534/2046 (26.1)	486/2136 (22.8)	1.15 (1.03, 1.28)*0.0118	1.22 (1.04, 1.43) 0.0141	0.03 (0.01, 0.06)*0.0118	
	III or IV	238/ 704 (33.8)	190/ 621 (30.6)	1.09 (0.96, 1.25) 0.1958	1.10 (0.85, 1.41) 0.4791	0.03 (-0.02, 0.08)*0.2113	
	LVEF at enrolment						0.0224*
	<= 49	248/ 944 (26.3)	255/ 939 (27.2)	0.97 (0.83, 1.12)*0.6642	0.99 (0.79, 1.24) 0.9069	-0.01 (-0.05, 0.03)*0.6642	
	50-59	273/1001 (27.3)	217/ 988 (22.0)	1.24 (1.06, 1.45)*0.0062	1.27 (1.01, 1.60) 0.0370	0.05 (0.02, 0.09)*0.0059	
	>= 60	251/ 805 (31.2)	204/ 831 (24.5)	1.27 (1.09, 1.49)*0.0029	1.32 (1.03, 1.68) 0.0276	0.07 (0.02, 0.11)*0.0027	
	NT-proBNP at enrolment						0.5008*
	<= median	372/1371 (27.1)	319/1389 (23.0)	1.18 (1.04, 1.34)*0.0117	1.27 (1.04, 1.54) 0.0173	0.04 (0.01, 0.07)*0.0114	
	> median	400/1379 (29.0)	357/1368 (26.1)	1.11 (0.98, 1.26)*0.0882	1.09 (0.91, 1.32) 0.3436	0.03 (-0.00, 0.06)*0.0877	
	Type 2 Diabetes Medical History						0.2787*
	Yes	347/1213 (28.6)	288/1219 (23.6)	1.21 (1.06, 1.39)*0.0053	1.30 (1.08, 1.55)*0.0052	0.05 (0.01, 0.08)*0.0051	
	No	425/1537 (27.7)	388/1539 (25.2)	1.10 (0.97, 1.23)*0.1252	1.13 (0.97, 1.33)*0.1250	0.02 (-0.01, 0.06)*0.1248	
	Atrial fibrillation or flutter at enrolment ECG						0.5634*
	Yes	329/1164 (28.3)	296/1164 (25.4)	1.11 (0.97, 1.27)*0.1231	1.14 (0.93, 1.40) 0.1989	0.03 (-0.01, 0.06)*0.1226	
	No	443/1586 (27.9)	380/1594 (23.8)	1.17 (1.04, 1.32)*0.0086	1.20 (1.00, 1.43) 0.0481	0.04 (0.01, 0.07)*0.0084	
	BMI (kg/m2) at enrolment						0.6143*
	< 30	400/1520 (26.3)	341/1517 (22.5)	1.17 (1.03, 1.33)*0.0140	1.22 (1.01, 1.47) 0.0393	0.04 (0.01, 0.07)*0.0137	
	>= 30	372/1229 (30.3)	335/1238 (27.1)	1.12 (0.99, 1.27)*0.0783	1.12 (0.92, 1.36) 0.2437	0.03 (-0.00, 0.07)*0.0779	
	Baseline eGFR (mL/min/1.73m^2)						0.7194*
	< 60	370/1307 (28.3)	327/1345 (24.3)	1.16 (1.02, 1.32)*0.0196	1.25 (1.03, 1.51) 0.0235	0.04 (0.01, 0.07)*0.0194	
	>= 60	402/1443 (27.9)	349/1412 (24.7)	1.13 (1.00, 1.27)*0.0570	1.09 (0.90, 1.32) 0.3686	0.03 (-0.00, 0.06)*0.0563	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.3455*
	<= median	396/1376 (28.8)	336/1395 (24.1)	1.19 (1.05, 1.35)*0.0052	1.17 (0.97, 1.42) 0.0967	0.05 (0.01, 0.08)*0.0050	
	> median	376/1374 (27.4)	340/1363 (24.9)	1.10 (0.97, 1.24)*0.1500	1.18 (0.97, 1.42) 0.0959	0.02 (-0.01, 0.06)*0.1495	
	LVEF at enrolment 2						0.0063*
	<= 49	248/ 944 (26.3)	255/ 939 (27.2)	0.97 (0.83, 1.12)*0.6642	0.99 (0.79, 1.24) 0.9069	-0.01 (-0.05, 0.03)*0.6642	
	>= 50	524/1806 (29.0)	421/1819 (23.1)	1.25 (1.12, 1.40)*<.0001	1.29 (1.09, 1.53) 0.0026	0.06 (0.03, 0.09)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2471*
	Yes	94/ 270 (34.8)	94/ 272 (34.6)	0.98 (0.81, 1.19) 0.8580	1.03 (0.69, 1.55) 0.8771	0.00 (-0.08, 0.08)*0.9501	
	No	678/2480 (27.3)	582/2486 (23.4)	1.17 (1.06, 1.29)*0.0015	1.20 (1.04, 1.38) 0.0137	0.04 (0.02, 0.06)*0.0015	
	MRAs at baseline						0.8828*
	Yes	325/1191 (27.3)	282/1193 (23.6)	1.15 (1.01, 1.33)*0.0412	1.20 (0.98, 1.48) 0.0835	0.04 (0.00, 0.07)*0.0406	
	No	447/1559 (28.7)	394/1565 (25.2)	1.14 (1.01, 1.28)*0.0278	1.15 (0.97, 1.38) 0.1124	0.03 (0.00, 0.07)*0.0275	
	ACEi+ARB at baseline						0.1216*
	Yes	585/1999 (29.3)	497/2028 (24.5)	1.19 (1.08, 1.32)*0.0007	1.26 (1.07, 1.47) 0.0043	0.05 (0.02, 0.07)*0.0007	
	No	187/ 751 (24.9)	179/ 730 (24.5)	1.02 (0.85, 1.21)*0.8656	0.97 (0.75, 1.27) 0.8452	0.00 (-0.04, 0.05)*0.8655	
	ARNI at baseline						0.8056*
	Yes	34/ 147 (23.1)	26/ 122 (21.3)	1.09 (0.69, 1.70)*0.7219	1.14 (0.60, 2.17) 0.6935	0.02 (-0.08, 0.12)*0.7206	
	No	738/2603 (28.4)	650/2636 (24.7)	1.15 (1.05, 1.26)*0.0025	1.17 (1.02, 1.35) 0.0223	0.04 (0.01, 0.06)*0.0024	
	Beta Blocker at baseline						0.6778*
	Yes	644/2289 (28.1)	568/2293 (24.8)	1.14 (1.03, 1.25)*0.0100	1.15 (0.99, 1.33) 0.0699	0.03 (0.01, 0.06)*0.0098	
	No	128/ 461 (27.8)	108/ 465 (23.2)	1.20 (0.96, 1.49)*0.1139	1.34 (0.96, 1.88) 0.0854	0.05 (-0.01, 0.10)*0.1126	
	Diuretics at baseline						0.9117*
	Yes	704/2458 (28.6)	617/2463 (25.1)	1.14 (1.04, 1.25)*0.0045	1.18 (1.03, 1.36) 0.0202	0.04 (0.01, 0.06)*0.0045	
	No	68/ 292 (23.3)	59/ 295 (20.0)	1.16 (0.85, 1.59)*0.3342	1.09 (0.70, 1.70) 0.7149	0.03 (-0.03, 0.10)*0.3332	

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AstraZeneca
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Full Analysis Set

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Quality of Life (LOCF)							
	Overall	1054/2801 (37.6)	975/2805 (34.8)	1.02 (0.98, 1.05) 0.3119	1.08 (0.96, 1.23) 0.2137	0.03 (0.00, 0.05)*0.0253	
	Age						0.0467*
	<= median	526/1394 (37.7)	547/1471 (37.2)	1.01 (0.95, 1.07) 0.8132	0.99 (0.84, 1.17) 0.9131	0.01 (-0.03, 0.04)*0.7622	
	> median	528/1407 (37.5)	428/1334 (32.1)	1.17 (1.05, 1.30)*0.0029	1.19 (0.99, 1.44) 0.0581	0.05 (0.02, 0.09)*0.0027	
	Gender						0.7872*
	Male	602/1630 (36.9)	553/1608 (34.4)	1.07 (0.98, 1.18)*0.1314	1.07 (0.90, 1.26) 0.4506	0.03 (-0.01, 0.06)*0.1309	
	Female	452/1171 (38.6)	422/1197 (35.3)	1.00 (0.94, 1.06) 0.9430	1.09 (0.90, 1.32) 0.3522	0.03 (-0.01, 0.07)*0.0916	
	Race						0.8475*
	White	751/2006 (37.4)	696/2032 (34.3)	1.09 (1.01, 1.19)*0.0349	1.08 (0.94, 1.25) 0.2849	0.03 (0.00, 0.06)*0.0347	
	Black or African	28/ 64 (43.8)	28/ 70 (40.0)	1.08 (0.77, 1.51) 0.6700	1.08 (0.50, 2.33) 0.8505	-0.00 (-0.16, 0.15) 0.9810	
	Asian	186/ 555 (33.5)	173/ 551 (31.4)	1.07 (0.90, 1.27)*0.4526	1.10 (0.82, 1.47) 0.5209	0.02 (-0.03, 0.08)*0.4522	
	Other	89/ 176 (50.6)	78/ 152 (51.3)	0.99 (0.80, 1.22)*0.8925	0.98 (0.61, 1.58) 0.9271	-0.01 (-0.12, 0.10)*0.8926	
	Geographic region						0.8742*
	Asia	182/ 536 (34.0)	169/ 536 (31.5)	1.08 (0.91, 1.28)*0.3978	1.11 (0.83, 1.49) 0.4683	0.02 (-0.03, 0.08)*0.3973	
	Europe and Saudi Arabia	504/1341 (37.6)	467/1381 (33.8)	1.11 (1.00, 1.23)*0.0404	1.13 (0.94, 1.35) 0.1878	0.04 (0.00, 0.07)*0.0401	
	North America	137/ 393 (34.9)	128/ 376 (34.0)	1.11 (0.96, 1.29) 0.1596	0.96 (0.68, 1.34) 0.7942	0.01 (-0.06, 0.08)*0.8115	
	Latin America	231/ 531 (43.5)	211/ 512 (41.2)	1.06 (0.92, 1.22)*0.4543	1.03 (0.77, 1.36) 0.8623	0.02 (-0.04, 0.08)*0.4538	
	NYHA class at enrolment						0.0088*
	II	729/2083 (35.0)	744/2165 (34.4)	1.02 (0.94, 1.11)*0.6649	1.00 (0.86, 1.16) 0.9921	0.01 (-0.02, 0.03)*0.6649	
	III or IV	325/ 718 (45.3)	231/ 639 (36.2)	1.25 (1.10, 1.43)*0.0007	1.42 (1.12, 1.81) 0.0043	0.09 (0.04, 0.14)*0.0006	
	LVEF at enrolment						0.3373*
	<= 49	348/ 959 (36.3)	340/ 950 (35.8)	1.01 (0.90, 1.14)*0.8206	1.01 (0.82, 1.25) 0.9121	0.00 (-0.04, 0.05)*0.8206	
	50-59	406/1017 (39.9)	351/1009 (34.8)	1.15 (1.02, 1.29)*0.0172	1.20 (0.97, 1.47) 0.0886	0.05 (0.01, 0.09)*0.0167	
	>= 60	300/ 825 (36.4)	284/ 846 (33.6)	1.08 (0.95, 1.23)*0.2313	1.03 (0.82, 1.30) 0.7968	0.03 (-0.02, 0.07)*0.2310	
	NT-proBNP at enrolment						0.1638*
	<= median	515/1396 (36.9)	504/1409 (35.8)	1.03 (0.94, 1.14)*0.5371	0.98 (0.82, 1.16) 0.7972	0.01 (-0.02, 0.05)*0.5370	
	> median	539/1405 (38.4)	470/1395 (33.7)	1.02 (0.97, 1.08) 0.4336	1.20 (1.01, 1.44) 0.0397	0.05 (0.01, 0.08)*0.0100	
	Type 2 Diabetes Medical History						0.0565
	Yes	485/1231 (39.4)	398/1243 (32.0)	1.09 (1.00, 1.19) 0.0473	1.38 (1.17, 1.63)*0.0001	0.07 (0.04, 0.11)*0.0001	
	No	569/1570 (36.2)	577/1562 (36.9)	1.00 (0.97, 1.04) 0.7771	0.97 (0.84, 1.12)*0.6852	-0.01 (-0.04, 0.03)*0.6852	
	Atrial fibrillation or flutter at enrolment ECG						0.4502
	Yes	470/1185 (39.7)	392/1188 (33.0)	1.20 (1.08, 1.34)*0.0008	1.33 (1.09, 1.61) 0.0041	0.07 (0.03, 0.11)*0.0007	
	No	584/1616 (36.1)	583/1617 (36.1)	1.00 (0.94, 1.07) 0.9388	0.94 (0.79, 1.10) 0.4201	0.00 (-0.03, 0.03)*0.9603	
	BMI (kg/m2) at enrolment						0.2650
	< 30	554/1547 (35.8)	527/1541 (34.2)	1.05 (0.95, 1.15)*0.3477	0.98 (0.82, 1.16) 0.7921	0.02 (-0.02, 0.05)*0.3475	
	>= 30	500/1253 (39.9)	445/1261 (35.3)	1.13 (1.02, 1.25)*0.0171	1.22 (1.02, 1.46) 0.0325	0.05 (0.01, 0.08)*0.0168	
	Baseline eGFR (mL/min/1.73m^2)						0.9155*
	< 60	492/1338 (36.8)	470/1377 (34.1)	1.08 (0.97, 1.19)*0.1507	1.10 (0.92, 1.31) 0.2975	0.03 (-0.01, 0.06)*0.1506	
	>= 60	562/1463 (38.4)	505/1427 (35.4)	1.03 (0.98, 1.09) 0.2237	1.06 (0.89, 1.26) 0.5075	0.03 (-0.00, 0.07)*0.0918	

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Quality of Life (LOCF)	SBP at randomisation						0.7454
	<= median	553/1405 (39.4)	490/1420 (34.5)	1.14 (1.04, 1.26)*0.0076	1.16 (0.97, 1.38) 0.1021	0.05 (0.01, 0.08)*0.0075	
	> median	501/1396 (35.9)	485/1385 (35.0)	1.02 (0.93, 1.13)*0.6315	1.01 (0.85, 1.21) 0.8980	0.01 (-0.03, 0.04)*0.6315	
	LVEF at enrolment 2						0.1861*
	<= 49	348/ 959 (36.3)	340/ 950 (35.8)	1.01 (0.90, 1.14)*0.8206	1.01 (0.82, 1.25) 0.9121	0.00 (-0.04, 0.05)*0.8206	
	>= 50	706/1842 (38.3)	635/1855 (34.2)	1.12 (1.03, 1.22)*0.0097	1.12 (0.96, 1.31) 0.1511	0.04 (0.01, 0.07)*0.0095	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9995*
	Yes	137/ 280 (48.9)	127/ 281 (45.2)	1.08 (0.91, 1.29)*0.3762	1.08 (0.74, 1.58) 0.6869	0.04 (-0.05, 0.12)*0.3755	
	No	917/2521 (36.4)	848/2524 (33.6)	1.02 (0.99, 1.06) 0.2375	1.08 (0.95, 1.23) 0.2387	0.03 (0.00, 0.05)*0.0386	
	MRAs at baseline						0.1155*
	Yes	471/1216 (38.7)	406/1210 (33.6)	1.02 (0.95, 1.10) 0.5702	1.26 (1.04, 1.51) 0.0175	0.05 (0.01, 0.09)*0.0078	
	No	583/1585 (36.8)	569/1595 (35.7)	1.03 (0.94, 1.13)*0.5156	0.96 (0.81, 1.14) 0.6530	0.01 (-0.02, 0.04)*0.5156	
	ACEi+ARB at baseline						0.5900*
	Yes	766/2037 (37.6)	707/2059 (34.3)	1.10 (1.01, 1.19)*0.0295	1.12 (0.97, 1.30) 0.1266	0.03 (0.00, 0.06)*0.0293	
	No	288/ 764 (37.7)	268/ 746 (35.9)	1.05 (0.92, 1.20)*0.4757	0.99 (0.78, 1.25) 0.9485	0.02 (-0.03, 0.07)*0.4754	
	ARNI at baseline						0.6225
	Yes	49/ 149 (32.9)	41/ 125 (32.8)	1.00 (0.71, 1.41)*0.9880	0.75 (0.42, 1.33) 0.3187	0.00 (-0.11, 0.11)*0.9880	
	No	1005/2652 (37.9)	934/2680 (34.9)	1.02 (0.99, 1.05) 0.2860	1.10 (0.97, 1.25) 0.1326	0.03 (0.00, 0.06)*0.0208	
	Beta Blocker at baseline						0.9925*
	Yes	864/2327 (37.1)	799/2330 (34.3)	1.08 (1.00, 1.17)*0.0435	1.06 (0.93, 1.22) 0.3656	0.03 (0.00, 0.06)*0.0432	
	No	190/ 474 (40.1)	176/ 475 (37.1)	1.08 (0.92, 1.27)*0.3377	1.18 (0.87, 1.59) 0.2938	0.03 (-0.03, 0.09)*0.3371	
	Diuretics at baseline						0.6251*
	Yes	939/2500 (37.6)	874/2504 (34.9)	1.02 (0.98, 1.06) 0.3032	1.09 (0.95, 1.24) 0.2076	0.03 (-0.00, 0.05)*0.0506	
	No	115/ 301 (38.2)	101/ 301 (33.6)	1.14 (0.92, 1.41)*0.2351	1.01 (0.68, 1.49) 0.9572	0.05 (-0.03, 0.12)*0.2336	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	1048/2801 (37.4)	908/2805 (32.4)	1.16 (1.08, 1.24)*<.0001	1.29 (1.13, 1.47) 0.0001	0.05 (0.03, 0.08)*<.0001	
	Age						0.7062*
	<= median	546/1394 (39.2)	491/1471 (33.4)	1.17 (1.06, 1.29)*0.0013	1.43 (1.19, 1.72) 0.0001	0.06 (0.02, 0.09)*0.0013	
	> median	502/1407 (35.7)	417/1334 (31.3)	1.14 (1.03, 1.27)*0.0146	1.17 (0.97, 1.42) 0.0928	0.04 (0.01, 0.08)*0.0141	
	Gender						0.8851*
	Male	587/1630 (36.0)	503/1608 (31.3)	1.15 (1.04, 1.27)*0.0045	1.28 (1.07, 1.53) 0.0062	0.05 (0.01, 0.08)*0.0043	
	Female	461/1171 (39.4)	405/1197 (33.8)	1.16 (1.05, 1.29)*0.0053	1.29 (1.06, 1.57) 0.0094	0.06 (0.02, 0.09)*0.0051	
	Race						0.9392*
	White	799/2006 (39.8)	692/2032 (34.1)	1.17 (1.08, 1.27)*0.0001	1.30 (1.12, 1.51) 0.0007	0.06 (0.03, 0.09)*0.0001	
	Black or African	30/ 64 (46.9)	30/ 70 (42.9)	1.09 (0.75, 1.59)*0.6402	1.19 (0.56, 2.51) 0.6508	0.04 (-0.13, 0.21)*0.6402	
	Asian	135/ 555 (24.3)	122/ 551 (22.1)	1.10 (0.89, 1.36)*0.3905	1.33 (0.93, 1.89) 0.1158	0.02 (-0.03, 0.07)*0.3899	
	Other	84/ 176 (47.7)	64/ 152 (42.1)	1.13 (0.89, 1.44)*0.3105	1.23 (0.74, 2.05) 0.4335	0.06 (-0.05, 0.16)*0.3064	
	Geographic region						0.9525*
	Asia	131/ 536 (24.4)	117/ 536 (21.8)	1.12 (0.90, 1.39)*0.3111	1.33 (0.93, 1.91) 0.1175	0.03 (-0.02, 0.08)*0.3104	
	Europe and Saudi Arabia	546/1341 (40.7)	477/1381 (34.5)	1.18 (1.07, 1.30)*0.0009	1.32 (1.10, 1.58) 0.0033	0.06 (0.03, 0.10)*0.0009	
	North America	136/ 393 (34.6)	116/ 376 (30.9)	1.12 (0.92, 1.37)*0.2684	1.16 (0.83, 1.63) 0.3795	0.04 (-0.03, 0.10)*0.2668	
	Latin America	235/ 531 (44.3)	198/ 512 (38.7)	1.14 (0.99, 1.32)*0.0682	1.33 (0.99, 1.79) 0.0558	0.06 (-0.00, 0.12)*0.0668	
	NYHA class at enrolment						0.2274*
	II	706/2083 (33.9)	659/2165 (30.4)	1.11 (1.02, 1.22)*0.0160	1.25 (1.07, 1.46) 0.0043	0.03 (0.01, 0.06)*0.0159	
	III or IV	342/ 718 (47.6)	249/ 639 (39.0)	1.22 (1.08, 1.38)*0.0015	1.45 (1.14, 1.86) 0.0030	0.09 (0.03, 0.14)*0.0012	
	LVEF at enrolment						0.4034*
	<= 49	356/ 959 (37.1)	316/ 950 (33.3)	1.12 (0.99, 1.26)*0.0780	1.29 (1.03, 1.61) 0.0290	0.04 (-0.00, 0.08)*0.0773	
	50-59	386/1017 (38.0)	341/1009 (33.8)	1.12 (1.00, 1.26)*0.0514	1.21 (0.97, 1.51) 0.0856	0.04 (-0.00, 0.08)*0.0508	
	>= 60	306/ 825 (37.1)	251/ 846 (29.7)	1.25 (1.09, 1.43)*0.0014	1.40 (1.10, 1.77) 0.0053	0.07 (0.03, 0.12)*0.0013	
	NT-proBNP at enrolment						0.3923*
	<= median	490/1396 (35.1)	442/1409 (31.4)	1.12 (1.01, 1.24)*0.0362	1.24 (1.04, 1.50) 0.0191	0.04 (0.00, 0.07)*0.0358	
	> median	558/1405 (39.7)	465/1395 (33.3)	1.19 (1.08, 1.31)*0.0005	1.34 (1.11, 1.61) 0.0022	0.06 (0.03, 0.10)*0.0004	
	Type 2 Diabetes Medical History						0.0592*
	Yes	480/1231 (39.0)	388/1243 (31.2)	1.25 (1.12, 1.39)*<.0001	1.41 (1.19, 1.66)*<.0001	0.08 (0.04, 0.12)*<.0001	
	No	568/1570 (36.2)	520/1562 (33.3)	1.09 (0.99, 1.20)*0.0899	1.14 (0.98, 1.32)*0.0898	0.03 (-0.00, 0.06)*0.0895	
	Atrial fibrillation or flutter at enrolment ECG						0.6397*
	Yes	462/1185 (39.0)	393/1188 (33.1)	1.18 (1.06, 1.31)*0.0028	1.38 (1.13, 1.69) 0.0018	0.06 (0.02, 0.10)*0.0027	
	No	586/1616 (36.3)	515/1617 (31.8)	1.14 (1.03, 1.25)*0.0082	1.23 (1.04, 1.46) 0.0183	0.04 (0.01, 0.08)*0.0080	
	BMI (kg/m2) at enrolment						0.7965*
	< 30	531/1547 (34.3)	461/1541 (29.9)	1.15 (1.04, 1.27)*0.0088	1.26 (1.04, 1.51) 0.0160	0.04 (0.01, 0.08)*0.0086	
	>= 30	517/1253 (41.3)	445/1261 (35.3)	1.17 (1.06, 1.29)*0.0021	1.33 (1.11, 1.61) 0.0022	0.06 (0.02, 0.10)*0.0020	
	Baseline eGFR (mL/min/1.73m^2)						0.7397*
	< 60	484/1338 (36.2)	437/1377 (31.7)	1.14 (1.03, 1.27)*0.0147	1.24 (1.03, 1.49) 0.0230	0.04 (0.01, 0.08)*0.0146	
	>= 60	564/1463 (38.6)	471/1427 (33.0)	1.17 (1.06, 1.29)*0.0019	1.34 (1.12, 1.62) 0.0017	0.06 (0.02, 0.09)*0.0018	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)	SBP at randomisation						0.4179*
	<= median	522/1405 (37.2)	443/1420 (31.2)	1.19 (1.07, 1.32)*0.0009	1.26 (1.04, 1.52) 0.0156	0.06 (0.02, 0.09)*0.0008	
	> median	526/1396 (37.7)	465/1385 (33.6)	1.12 (1.02, 1.24)*0.0240	1.32 (1.10, 1.58) 0.0033	0.04 (0.01, 0.08)*0.0237	
	LVEF at enrolment 2						0.4884*
	<= 49	356/ 959 (37.1)	316/ 950 (33.3)	1.12 (0.99, 1.26)*0.0780	1.29 (1.03, 1.61) 0.0290	0.04 (-0.00, 0.08)*0.0773	
	>= 50	692/1842 (37.6)	592/1855 (31.9)	1.18 (1.08, 1.29)*0.0003	1.29 (1.10, 1.52) 0.0016	0.06 (0.03, 0.09)*0.0003	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3231*
	Yes	139/ 280 (49.6)	131/ 281 (46.6)	1.06 (0.90, 1.26)*0.4738	1.24 (0.83, 1.83) 0.2927	0.03 (-0.05, 0.11)*0.4734	
	No	909/2521 (36.1)	777/2524 (30.8)	1.17 (1.08, 1.27)*<.0001	1.30 (1.13, 1.49) 0.0002	0.05 (0.03, 0.08)*<.0001	
	MRAs at baseline						0.1947*
	Yes	465/1216 (38.2)	379/1210 (31.3)	1.22 (1.09, 1.36)*0.0004	1.41 (1.15, 1.73) 0.0008	0.07 (0.03, 0.11)*0.0003	
	No	583/1585 (36.8)	529/1595 (33.2)	1.11 (1.01, 1.22)*0.0327	1.21 (1.02, 1.43) 0.0327	0.04 (0.00, 0.07)*0.0324	
	ACEi+ARB at baseline						0.5677*
	Yes	783/2037 (38.4)	676/2059 (32.8)	1.17 (1.08, 1.27)*0.0002	1.30 (1.12, 1.51) 0.0007	0.06 (0.03, 0.09)*0.0002	
	No	265/ 764 (34.7)	232/ 746 (31.1)	1.12 (0.97, 1.29)*0.1387	1.27 (0.98, 1.65) 0.0672	0.04 (-0.01, 0.08)*0.1377	
	ARNI at baseline						0.2207*
	Yes	38/ 149 (25.5)	35/ 125 (28.0)	0.91 (0.61, 1.35)*0.6413	1.00 (0.52, 1.94) 0.9969	-0.02 (-0.13, 0.08)*0.6422	
	No	1010/2652 (38.1)	873/2680 (32.6)	1.17 (1.09, 1.26)*<.0001	1.30 (1.14, 1.49) 0.0001	0.06 (0.03, 0.08)*<.0001	
	Beta Blocker at baseline						0.5207*
	Yes	875/2327 (37.6)	750/2330 (32.2)	1.17 (1.08, 1.26)*0.0001	1.28 (1.11, 1.47) 0.0008	0.05 (0.03, 0.08)*0.0001	
	No	173/ 474 (36.5)	158/ 475 (33.3)	1.10 (0.92, 1.31)*0.2963	1.38 (0.99, 1.91) 0.0588	0.03 (-0.03, 0.09)*0.2956	
	Diuretics at baseline						0.0475*
	Yes	937/2500 (37.5)	832/2504 (33.2)	1.13 (1.05, 1.22)*0.0017	1.26 (1.10, 1.45) 0.0009	0.04 (0.02, 0.07)*0.0016	
	No	111/ 301 (36.9)	76/ 301 (25.2)	1.46 (1.14, 1.86)*0.0024	1.55 (0.99, 2.42) 0.0535	0.12 (0.04, 0.19)*0.0019	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	763/2801 (27.2)	726/2805 (25.9)	1.05 (0.96, 1.15)*0.2498	1.10 (0.95, 1.27) 0.2077	0.01 (-0.01, 0.04)*0.2497	
	Age						0.5573*
	<= median	388/1394 (27.8)	398/1471 (27.1)	1.03 (0.91, 1.16)*0.6412	1.07 (0.88, 1.32) 0.4941	0.01 (-0.02, 0.04)*0.6413	
	> median	375/1407 (26.7)	328/1334 (24.6)	1.08 (0.95, 1.23)*0.2164	1.14 (0.92, 1.41) 0.2211	0.02 (-0.01, 0.05)*0.2155	
	Gender						0.9585*
	Male	452/1630 (27.7)	423/1608 (26.3)	1.05 (0.94, 1.18)*0.3617	1.14 (0.94, 1.38) 0.1830	0.01 (-0.02, 0.04)*0.3615	
	Female	311/1171 (26.6)	303/1197 (25.3)	1.05 (0.92, 1.20)*0.4894	1.04 (0.83, 1.31) 0.7153	0.01 (-0.02, 0.05)*0.4894	
	Race						0.9657*
	White	535/2006 (26.7)	517/2032 (25.4)	1.05 (0.94, 1.16)*0.3745	1.06 (0.89, 1.26) 0.5376	0.01 (-0.01, 0.04)*0.3744	
	Black or African	16/ 64 (25.0)	16/ 70 (22.9)	1.09 (0.60, 2.00)*0.7714	1.26 (0.47, 3.40) 0.6412	0.02 (-0.12, 0.17)*0.7716	
	Asian	146/ 555 (26.3)	142/ 551 (25.8)	1.02 (0.84, 1.25)*0.8394	1.16 (0.83, 1.61) 0.3946	0.01 (-0.05, 0.06)*0.8394	
	Other	66/ 176 (37.5)	51/ 152 (33.6)	1.12 (0.83, 1.50)*0.4584	1.39 (0.78, 2.46) 0.2639	0.04 (-0.06, 0.14)*0.4556	
	Geographic region						0.8338*
	Asia	139/ 536 (25.9)	139/ 536 (25.9)	1.00 (0.82, 1.22)*1.0000	1.13 (0.81, 1.59) 0.4662	0.00 (-0.05, 0.05)*1.0000	
	Europe and Saudi Arabia	378/1341 (28.2)	360/1381 (26.1)	1.08 (0.96, 1.22)*0.2137	1.14 (0.92, 1.40) 0.2235	0.02 (-0.01, 0.05)*0.2136	
	North America	81/ 393 (20.6)	80/ 376 (21.3)	0.97 (0.74, 1.27)*0.8205	0.95 (0.60, 1.51) 0.8398	-0.01 (-0.06, 0.05)*0.8206	
	Latin America	165/ 531 (31.1)	147/ 512 (28.7)	1.08 (0.90, 1.30)*0.4052	1.06 (0.76, 1.47) 0.7326	0.02 (-0.03, 0.08)*0.4045	
	NYHA class at enrolment						0.6352*
	II	555/2083 (26.6)	556/2165 (25.7)	1.04 (0.94, 1.15)*0.4753	1.08 (0.91, 1.28) 0.3666	0.01 (-0.02, 0.04)*0.4753	
	III or IV	208/ 718 (29.0)	170/ 639 (26.6)	1.09 (0.92, 1.29)*0.3327	1.18 (0.89, 1.57) 0.2557	0.02 (-0.02, 0.07)*0.3311	
	LVEF at enrolment						0.2184*
	<= 49	249/ 959 (26.0)	259/ 950 (27.3)	0.95 (0.82, 1.11)*0.5210	0.97 (0.76, 1.24) 0.8123	-0.01 (-0.05, 0.03)*0.5209	
	50-59	278/1017 (27.3)	257/1009 (25.5)	1.07 (0.93, 1.24)*0.3414	1.12 (0.88, 1.43) 0.3504	0.02 (-0.02, 0.06)*0.3410	
	>= 60	236/ 825 (28.6)	210/ 846 (24.8)	1.15 (0.98, 1.35)*0.0809	1.23 (0.93, 1.62) 0.1399	0.04 (-0.00, 0.08)*0.0804	
	NT-proBNP at enrolment						0.7026*
	<= median	374/1396 (26.8)	365/1409 (25.9)	1.03 (0.91, 1.17)*0.5944	1.02 (0.83, 1.25) 0.8371	0.01 (-0.02, 0.04)*0.5943	
	> median	389/1405 (27.7)	361/1395 (25.9)	1.07 (0.95, 1.21)*0.2801	1.19 (0.96, 1.46) 0.1124	0.02 (-0.01, 0.05)*0.2797	
	Type 2 Diabetes Medical History						0.1006*
	Yes	357/1231 (29.0)	316/1243 (25.4)	1.14 (1.00, 1.30)*0.0458	1.20 (1.00, 1.43)*0.0456	0.04 (0.00, 0.07)*0.0454	
	No	406/1570 (25.9)	410/1562 (26.2)	0.99 (0.88, 1.11)*0.8044	0.98 (0.84, 1.15)*0.8044	-0.00 (-0.03, 0.03)*0.8044	
	Atrial fibrillation or flutter at enrolment ECG						0.0860*
	Yes	330/1185 (27.8)	287/1188 (24.2)	1.15 (1.01, 1.32)*0.0408	1.23 (0.98, 1.55) 0.0710	0.04 (0.00, 0.07)*0.0403	
	No	433/1616 (26.8)	439/1617 (27.1)	0.99 (0.88, 1.11)*0.8204	1.01 (0.84, 1.23) 0.8882	-0.00 (-0.03, 0.03)*0.8204	
	BMI (kg/m2) at enrolment						0.6006*
	< 30	411/1547 (26.6)	396/1541 (25.7)	1.03 (0.92, 1.16)*0.5823	1.03 (0.84, 1.26) 0.7856	0.01 (-0.02, 0.04)*0.5822	
	>= 30	352/1253 (28.1)	327/1261 (25.9)	1.08 (0.95, 1.23)*0.2227	1.20 (0.97, 1.49) 0.0994	0.02 (-0.01, 0.06)*0.2224	
	Baseline eGFR (mL/min/1.73m^2)						0.6675*
	< 60	342/1338 (25.6)	342/1377 (24.8)	1.03 (0.90, 1.17)*0.6640	1.16 (0.94, 1.43) 0.1682	0.01 (-0.03, 0.04)*0.6640	
	>= 60	421/1463 (28.8)	384/1427 (26.9)	1.07 (0.95, 1.20)*0.2633	1.03 (0.84, 1.27) 0.7605	0.02 (-0.01, 0.05)*0.2628	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.1481*
	<= median	365/1405 (26.0)	374/1420 (26.3)	0.99 (0.87, 1.12)*0.8280	0.97 (0.78, 1.20) 0.7635	-0.00 (-0.04, 0.03)*0.8280	
	> median	398/1396 (28.5)	352/1385 (25.4)	1.12 (0.99, 1.27)*0.0663	1.24 (1.01, 1.52) 0.0392	0.03 (-0.00, 0.06)*0.0657	
	LVEF at enrolment 2						0.1055*
	<= 49	249/ 959 (26.0)	259/ 950 (27.3)	0.95 (0.82, 1.11)*0.5210	0.97 (0.76, 1.24) 0.8123	-0.01 (-0.05, 0.03)*0.5209	
	>= 50	514/1842 (27.9)	467/1855 (25.2)	1.11 (1.00, 1.23)*0.0604	1.17 (0.98, 1.41) 0.0904	0.03 (-0.00, 0.06)*0.0601	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6875*
	Yes	86/ 280 (30.7)	78/ 281 (27.8)	1.11 (0.85, 1.43)*0.4419	1.26 (0.81, 1.96) 0.2986	0.03 (-0.05, 0.10)*0.4412	
	No	677/2521 (26.9)	648/2524 (25.7)	1.05 (0.95, 1.15)*0.3407	1.08 (0.92, 1.26) 0.3376	0.01 (-0.01, 0.04)*0.3406	
	MRAs at baseline						0.0032*
	Yes	288/1216 (23.7)	319/1210 (26.4)	0.90 (0.78, 1.03)*0.1280	0.84 (0.67, 1.04) 0.1145	-0.03 (-0.06, 0.01)*0.1275	
	No	475/1585 (30.0)	407/1595 (25.5)	1.17 (1.05, 1.31)*0.0052	1.34 (1.10, 1.63) 0.0031	0.04 (0.01, 0.08)*0.0050	
	ACEi+ARB at baseline						0.8966*
	Yes	553/2037 (27.1)	533/2059 (25.9)	1.05 (0.95, 1.16)*0.3605	1.09 (0.92, 1.29) 0.3077	0.01 (-0.01, 0.04)*0.3605	
	No	210/ 764 (27.5)	193/ 746 (25.9)	1.06 (0.90, 1.26)*0.4782	1.11 (0.83, 1.48) 0.4761	0.02 (-0.03, 0.06)*0.4778	
	ARNI at baseline						0.0602*
	Yes	24/ 149 (16.1)	30/ 125 (24.0)	0.67 (0.41, 1.09)*0.1044	0.62 (0.29, 1.33) 0.2239	-0.08 (-0.17, 0.02)*0.1047	
	No	739/2652 (27.9)	696/2680 (26.0)	1.07 (0.98, 1.17)*0.1188	1.13 (0.97, 1.31) 0.1079	0.02 (-0.00, 0.04)*0.1186	
	Beta Blocker at baseline						0.7069*
	Yes	624/2327 (26.8)	589/2330 (25.3)	1.06 (0.96, 1.17)*0.2324	1.12 (0.96, 1.32) 0.1534	0.02 (-0.01, 0.04)*0.2321	
	No	139/ 474 (29.3)	137/ 475 (28.8)	1.02 (0.83, 1.24)*0.8699	0.98 (0.69, 1.39) 0.9121	0.00 (-0.05, 0.06)*0.8699	
	Diuretics at baseline						0.7921*
	Yes	676/2500 (27.0)	646/2504 (25.8)	1.05 (0.96, 1.15)*0.3195	1.11 (0.95, 1.29) 0.2084	0.01 (-0.01, 0.04)*0.3193	
	No	87/ 301 (28.9)	80/ 301 (26.6)	1.09 (0.84, 1.41)*0.5242	1.06 (0.70, 1.62) 0.7835	0.02 (-0.05, 0.09)*0.5238	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	889/2801 (31.7)	821/2805 (29.3)	1.08 (1.00, 1.17)*0.0448	1.12 (0.98, 1.28) 0.0905	0.02 (0.00, 0.05)*0.0446	
	Age						0.7820*
	<= median	451/1394 (32.4)	443/1471 (30.1)	1.07 (0.96, 1.20)*0.1964	1.16 (0.97, 1.40) 0.1111	0.02 (-0.01, 0.06)*0.1965	
	> median	438/1407 (31.1)	378/1334 (28.3)	1.10 (0.98, 1.23)*0.1103	1.10 (0.91, 1.33) 0.3497	0.03 (-0.01, 0.06)*0.1094	
	Gender						0.1820*
	Male	480/1630 (29.4)	458/1608 (28.5)	1.03 (0.93, 1.15)*0.5450	1.04 (0.87, 1.25) 0.6567	0.01 (-0.02, 0.04)*0.5449	
	Female	409/1171 (34.9)	363/1197 (30.3)	1.03 (0.95, 1.12) 0.4404	1.22 (1.00, 1.48) 0.0481	0.05 (0.01, 0.08)*0.0168	
	Race						0.6034*
	White	651/2006 (32.5)	597/2032 (29.4)	1.10 (1.01, 1.21)*0.0348	1.11 (0.95, 1.30) 0.1836	0.03 (0.00, 0.06)*0.0346	
	Black or African	23/ 64 (35.9)	30/ 70 (42.9)	0.84 (0.55, 1.28)*0.4162	0.76 (0.36, 1.58) 0.4636	-0.08 (-0.23, 0.08) 0.3323	
	Asian	134/ 555 (24.1)	130/ 551 (23.6)	1.02 (0.83, 1.26)*0.8299	1.17 (0.84, 1.65) 0.3483	0.01 (-0.04, 0.06)*0.8299	
	Other	81/ 176 (46.0)	64/ 152 (42.1)	1.09 (0.85, 1.40)*0.4778	1.31 (0.77, 2.21) 0.3208	0.04 (-0.07, 0.15)*0.4756	
	Geographic region						0.7266*
	Asia	131/ 536 (24.4)	123/ 536 (22.9)	1.07 (0.86, 1.32)*0.5657	1.23 (0.87, 1.74) 0.2349	0.01 (-0.04, 0.07)*0.5655	
	Europe and Saudi Arabia	421/1341 (31.4)	396/1381 (28.7)	1.09 (0.98, 1.23)*0.1219	1.07 (0.88, 1.31) 0.4704	0.03 (-0.01, 0.06)*0.1217	
	North America	115/ 393 (29.3)	113/ 376 (30.1)	1.03 (0.85, 1.25) 0.7386	0.98 (0.70, 1.37) 0.8918	-0.01 (-0.07, 0.06)*0.8103	
	Latin America	222/ 531 (41.8)	189/ 512 (36.9)	1.13 (0.97, 1.32)*0.1068	1.30 (0.96, 1.75) 0.0873	0.05 (-0.01, 0.11)*0.1053	
	NYHA class at enrolment						0.0581*
	II	595/2083 (28.6)	604/2165 (27.9)	1.02 (0.93, 1.13)*0.6296	1.07 (0.91, 1.25) 0.4353	0.01 (-0.02, 0.03)*0.6297	
	III or IV	294/ 718 (40.9)	217/ 639 (34.0)	1.21 (1.05, 1.39)*0.0085	1.34 (1.05, 1.71) 0.0207	0.07 (0.02, 0.12)*0.0077	
	LVEF at enrolment						0.2190*
	<= 49	288/ 959 (30.0)	276/ 950 (29.1)	1.03 (0.90, 1.19)*0.6394	1.10 (0.87, 1.39) 0.4257	0.01 (-0.03, 0.05)*0.6393	
	50-59	322/1017 (31.7)	308/1009 (30.5)	1.04 (0.91, 1.18)*0.5806	1.01 (0.81, 1.26) 0.9112	0.01 (-0.03, 0.05)*0.5805	
	>= 60	279/ 825 (33.8)	237/ 846 (28.0)	1.21 (1.05, 1.39)*0.0105	1.30 (1.02, 1.65) 0.0337	0.06 (0.01, 0.10)*0.0101	
	NT-proBNP at enrolment						0.7125*
	<= median	405/1396 (29.0)	383/1409 (27.2)	1.07 (0.95, 1.20)*0.2813	1.13 (0.93, 1.37) 0.2163	0.02 (-0.01, 0.05)*0.2811	
	> median	484/1405 (34.4)	437/1395 (31.3)	1.10 (0.99, 1.22)*0.0790	1.12 (0.93, 1.35) 0.2389	0.03 (-0.00, 0.07)*0.0785	
	Type 2 Diabetes Medical History						0.4128*
	Yes	412/1231 (33.5)	370/1243 (29.8)	1.12 (1.00, 1.26)*0.0480	1.19 (1.00, 1.41)*0.0478	0.04 (0.00, 0.07)*0.0475	
	No	477/1570 (30.4)	451/1562 (28.9)	1.05 (0.94, 1.17)*0.3553	1.08 (0.92, 1.25)*0.3552	0.02 (-0.02, 0.05)*0.3551	
	Atrial fibrillation or flutter at enrolment ECG						0.8816*
	Yes	390/1185 (32.9)	363/1188 (30.6)	1.08 (0.96, 1.21)*0.2179	1.12 (0.91, 1.37) 0.2797	0.02 (-0.01, 0.06)*0.2175	
	No	499/1616 (30.9)	458/1617 (28.3)	1.09 (0.98, 1.21)*0.1119	1.13 (0.94, 1.34) 0.1904	0.03 (-0.01, 0.06)*0.1115	
	BMI (kg/m2) at enrolment						0.8945*
	< 30	465/1547 (30.1)	429/1541 (27.8)	1.08 (0.97, 1.21)*0.1742	1.13 (0.94, 1.37) 0.1932	0.02 (-0.01, 0.05)*0.1738	
	>= 30	424/1253 (33.8)	391/1261 (31.0)	1.09 (0.97, 1.22)*0.1296	1.12 (0.93, 1.36) 0.2375	0.03 (-0.01, 0.06)*0.1292	
	Baseline eGFR (mL/min/1.73m^2)						0.7396*
	< 60	425/1338 (31.8)	409/1377 (29.7)	1.07 (0.96, 1.20)*0.2445	1.09 (0.91, 1.32) 0.3553	0.02 (-0.01, 0.06)*0.2444	
	>= 60	464/1463 (31.7)	412/1427 (28.9)	1.10 (0.98, 1.23)*0.0967	1.15 (0.95, 1.39) 0.1446	0.03 (-0.01, 0.06)*0.0960	

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Full Analysis Set

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Symptom Frequency (LOCF)	SBP at randomisation						0.8860*
	<= median	437/1405 (31.1)	405/1420 (28.5)	1.09 (0.97, 1.22)*0.1338	1.07 (0.88, 1.29) 0.5032	0.03 (-0.01, 0.06)*0.1335	
	> median	452/1396 (32.4)	416/1385 (30.0)	1.08 (0.97, 1.20)*0.1829	1.18 (0.98, 1.43) 0.0834	0.02 (-0.01, 0.06)*0.1824	
	LVEF at enrolment 2						0.4050*
	<= 49	288/ 959 (30.0)	276/ 950 (29.1)	1.03 (0.90, 1.19)*0.6394	1.10 (0.87, 1.39) 0.4257	0.01 (-0.03, 0.05)*0.6393	
	>= 50	601/1842 (32.6)	545/1855 (29.4)	1.11 (1.01, 1.22)*0.0330	1.13 (0.96, 1.33) 0.1294	0.03 (0.00, 0.06)*0.0327	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2307*
	Yes	117/ 280 (41.8)	121/ 281 (43.1)	0.97 (0.80, 1.18)*0.7600	1.09 (0.74, 1.61) 0.6578	-0.01 (-0.09, 0.07)*0.7600	
	No	772/2521 (30.6)	700/2524 (27.7)	1.10 (1.01, 1.20)*0.0241	1.13 (0.98, 1.30) 0.0964	0.03 (0.00, 0.05)*0.0239	
	MRAs at baseline						0.9442*
	Yes	374/1216 (30.8)	342/1210 (28.3)	1.09 (0.96, 1.23)*0.1787	1.12 (0.91, 1.38) 0.2874	0.02 (-0.01, 0.06)*0.1782	
	No	515/1585 (32.5)	479/1595 (30.0)	1.08 (0.98, 1.20)*0.1347	1.12 (0.94, 1.34) 0.1870	0.02 (-0.01, 0.06)*0.1343	
	ACEi+ARB at baseline						0.2182*
	Yes	673/2037 (33.0)	609/2059 (29.6)	1.12 (1.02, 1.22)*0.0170	1.16 (0.99, 1.35) 0.0636	0.03 (0.01, 0.06)*0.0169	
	No	216/ 764 (28.3)	212/ 746 (28.4)	0.99 (0.85, 1.17)*0.9498	1.02 (0.79, 1.33) 0.8545	-0.00 (-0.05, 0.04)*0.9498	
	ARNI at baseline						0.1106*
	Yes	28/ 149 (18.8)	31/ 125 (24.8)	0.76 (0.48, 1.19)*0.2293	0.92 (0.47, 1.81) 0.8018	-0.06 (-0.16, 0.04)*0.2310	
	No	861/2652 (32.5)	790/2680 (29.5)	1.10 (1.02, 1.19)*0.0184	1.13 (0.99, 1.30) 0.0698	0.03 (0.01, 0.05)*0.0182	
	Beta Blocker at baseline						0.2466*
	Yes	736/2327 (31.6)	665/2330 (28.5)	1.11 (1.02, 1.21)*0.0217	1.12 (0.97, 1.30) 0.1211	0.03 (0.00, 0.06)*0.0215	
	No	153/ 474 (32.3)	156/ 475 (32.8)	0.98 (0.82, 1.18)*0.8530	1.11 (0.81, 1.53) 0.5223	-0.01 (-0.07, 0.05)*0.8530	
	Diuretics at baseline						0.0382*
	Yes	780/2500 (31.2)	742/2504 (29.6)	1.05 (0.97, 1.14)*0.2283	1.09 (0.95, 1.25) 0.2351	0.02 (-0.01, 0.04)*0.2281	
	No	109/ 301 (36.2)	79/ 301 (26.2)	1.38 (1.08, 1.76)*0.0090	1.40 (0.90, 2.16) 0.1334	0.10 (0.03, 0.17)*0.0080	

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Social Limitation (LOCF)							
	Overall	825/2625 (31.4)	812/2625 (30.9)	1.01 (0.96, 1.07) 0.5763	1.01 (0.88, 1.15) 0.9317	0.00 (-0.02, 0.03)*0.6985	
	Age						0.3773*
	<= median	425/1331 (31.9)	457/1409 (32.4)	0.98 (0.88, 1.10)*0.7780	0.99 (0.82, 1.19) 0.9024	-0.01 (-0.04, 0.03)*0.7780	
	> median	400/1294 (30.9)	355/1216 (29.2)	1.03 (0.96, 1.11) 0.4176	1.04 (0.85, 1.27) 0.6924	0.02 (-0.02, 0.05)*0.3480	
	Gender						0.0093*
	Male	447/1538 (29.1)	471/1500 (31.4)	0.93 (0.83, 1.03)*0.1611	0.86 (0.71, 1.03) 0.0916	-0.02 (-0.06, 0.01)*0.1609	
	Female	378/1087 (34.8)	341/1125 (30.3)	1.06 (0.97, 1.16) 0.1920	1.23 (1.00, 1.50) 0.0480	0.04 (0.01, 0.08)*0.0250	
	Race						0.3806*
	White	624/1890 (33.0)	599/1921 (31.2)	1.00 (0.95, 1.06) 0.8747	1.05 (0.90, 1.23) 0.5411	0.02 (-0.01, 0.05)*0.2252	
	Black or African	19/ 58 (32.8)	24/ 66 (36.4)	0.91 (0.58, 1.43) 0.6889	0.84 (0.37, 1.90) 0.6746	-0.04 (-0.20, 0.13)*0.6732	
	Asian	120/ 506 (23.7)	131/ 494 (26.5)	0.89 (0.72, 1.11)*0.3072	0.88 (0.63, 1.24) 0.4697	-0.03 (-0.08, 0.03)*0.3067	
	Other	62/ 171 (36.3)	58/ 144 (40.3)	0.95 (0.73, 1.23) 0.6765	0.89 (0.54, 1.47) 0.6502	-0.04 (-0.15, 0.07)*0.4646	
	Geographic region						0.6328*
	Asia	117/ 492 (23.8)	128/ 482 (26.6)	0.90 (0.72, 1.11)*0.3186	0.88 (0.63, 1.23) 0.4473	-0.03 (-0.08, 0.03)*0.3182	
	Europe and Saudi Arabia	416/1273 (32.7)	409/1309 (31.2)	1.05 (0.93, 1.17)*0.4348	0.99 (0.82, 1.20) 0.9147	0.01 (-0.02, 0.05)*0.4348	
	North America	107/ 367 (29.2)	101/ 347 (29.1)	1.04 (0.86, 1.26) 0.6589	1.08 (0.75, 1.55) 0.6683	0.00 (-0.07, 0.07)*0.9886	
	Latin America	185/ 493 (37.5)	174/ 487 (35.7)	1.11 (0.98, 1.26) 0.1048	1.10 (0.82, 1.49) 0.5301	0.02 (-0.04, 0.08)*0.5594	
	NYHA class at enrolment						0.5223*
	II	577/1953 (29.5)	604/2031 (29.7)	0.99 (0.90, 1.09)*0.8930	1.00 (0.85, 1.17) 0.9971	-0.00 (-0.03, 0.03)*0.8930	
	III or IV	248/ 672 (36.9)	208/ 593 (35.1)	1.04 (0.92, 1.16) 0.5535	1.08 (0.83, 1.40) 0.5577	0.02 (-0.03, 0.07)*0.4986	
	LVEF at enrolment						0.7860*
	<= 49	292/ 907 (32.2)	294/ 896 (32.8)	1.00 (0.93, 1.09) 0.9049	1.05 (0.83, 1.31) 0.6966	-0.01 (-0.05, 0.04)*0.7792	
	50-59	307/ 955 (32.1)	290/ 946 (30.7)	1.00 (0.91, 1.09) 0.9195	0.97 (0.78, 1.21) 0.7928	0.01 (-0.03, 0.06)*0.4836	
	>= 60	226/ 763 (29.6)	228/ 783 (29.1)	1.02 (0.87, 1.19)*0.8287	1.00 (0.78, 1.30) 0.9728	0.01 (-0.04, 0.05)*0.8288	
	NT-proBNP at enrolment						0.1485*
	<= median	390/1312 (29.7)	415/1336 (31.1)	0.96 (0.85, 1.07)*0.4546	0.93 (0.77, 1.13) 0.4863	-0.01 (-0.05, 0.02)*0.4544	
	> median	435/1313 (33.1)	396/1288 (30.7)	1.04 (0.96, 1.12) 0.3047	1.09 (0.90, 1.31) 0.3938	0.02 (-0.01, 0.06)*0.1919	
	Type 2 Diabetes Medical History						0.0347*
	Yes	377/1150 (32.8)	342/1169 (29.3)	1.08 (0.98, 1.18) 0.1180	1.18 (0.99, 1.41)*0.0665	0.04 (-0.00, 0.07)*0.0662	
	No	448/1475 (30.4)	470/1456 (32.3)	0.94 (0.85, 1.05)*0.2658	0.92 (0.78, 1.07)*0.2657	-0.02 (-0.05, 0.01)*0.2656	
	Atrial fibrillation or flutter at enrolment ECG						0.1271*
	Yes	357/1097 (32.5)	330/1109 (29.8)	0.99 (0.91, 1.09) 0.8787	1.13 (0.92, 1.40) 0.2403	0.03 (-0.01, 0.07)*0.1575	
	No	468/1528 (30.6)	482/1516 (31.8)	0.96 (0.87, 1.07)*0.4876	0.92 (0.77, 1.10) 0.3721	-0.01 (-0.04, 0.02)*0.4876	
	BMI (kg/m2) at enrolment						0.2363*
	< 30	433/1452 (29.8)	438/1428 (30.7)	0.97 (0.87, 1.09)*0.6190	0.90 (0.75, 1.09) 0.2846	-0.01 (-0.04, 0.03)*0.6190	
	>= 30	392/1172 (33.4)	373/1195 (31.2)	1.03 (0.95, 1.12) 0.4680	1.12 (0.92, 1.37) 0.2398	0.02 (-0.02, 0.06)*0.2453	
	Baseline eGFR (mL/min/1.73m^2)						0.7314*
	< 60	390/1240 (31.5)	399/1270 (31.4)	1.00 (0.93, 1.08) 0.9176	1.00 (0.82, 1.21) 0.9832	0.00 (-0.04, 0.04)*0.9852	
	>= 60	435/1385 (31.4)	413/1354 (30.5)	1.03 (0.92, 1.15)*0.6083	1.01 (0.84, 1.22) 0.9343	0.01 (-0.03, 0.04)*0.6082	

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Social Limitation (LOCF)	SBP at randomisation						0.8185*
	<= median	428/1320 (32.4)	426/1323 (32.2)	1.00 (0.93, 1.08) 0.9106	0.92 (0.76, 1.11) 0.3936	0.00 (-0.03, 0.04)*0.9017	
	> median	397/1305 (30.4)	386/1302 (29.6)	1.03 (0.91, 1.15)*0.6661	1.10 (0.91, 1.34) 0.3189	0.01 (-0.03, 0.04)*0.6661	
	LVEF at enrolment 2						0.5264*
	<= 49	292/ 907 (32.2)	294/ 896 (32.8)	1.00 (0.93, 1.09) 0.9049	1.05 (0.83, 1.31) 0.6966	-0.01 (-0.05, 0.04)*0.7792	
	>= 50	533/1718 (31.0)	518/1729 (30.0)	1.04 (0.94, 1.15)*0.4971	0.99 (0.83, 1.17) 0.8671	0.01 (-0.02, 0.04)*0.4971	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6289*
	Yes	103/ 252 (40.9)	108/ 256 (42.2)	0.97 (0.79, 1.19)*0.7638	0.96 (0.64, 1.44) 0.8354	-0.01 (-0.10, 0.07)*0.7637	
	No	722/2373 (30.4)	704/2369 (29.7)	1.02 (0.94, 1.12)*0.5948	1.02 (0.88, 1.17) 0.8336	0.01 (-0.02, 0.03)*0.5948	
	MRAs at baseline						0.6757*
	Yes	372/1144 (32.5)	369/1131 (32.6)	0.99 (0.92, 1.07) 0.7468	1.00 (0.81, 1.22) 0.9804	-0.00 (-0.04, 0.04)*0.9560	
	No	453/1481 (30.6)	443/1494 (29.7)	1.03 (0.92, 1.15)*0.5782	1.01 (0.84, 1.21) 0.9072	0.01 (-0.02, 0.04)*0.5781	
	ACEi+ARB at baseline						0.7917*
	Yes	603/1909 (31.6)	605/1934 (31.3)	1.00 (0.94, 1.06) 0.9609	0.98 (0.84, 1.15) 0.8464	0.00 (-0.03, 0.03)*0.8387	
	No	222/ 716 (31.0)	207/ 691 (30.0)	1.04 (0.88, 1.21)*0.6692	1.07 (0.82, 1.38) 0.6326	0.01 (-0.04, 0.06)*0.6691	
	ARNI at baseline						0.6521*
	Yes	45/ 146 (30.8)	32/ 115 (27.8)	1.11 (0.76, 1.62)*0.5996	1.30 (0.71, 2.40) 0.3907	0.03 (-0.08, 0.14)*0.5968	
	No	780/2479 (31.5)	780/2510 (31.1)	1.01 (0.95, 1.06) 0.8219	0.99 (0.86, 1.14) 0.9206	0.00 (-0.02, 0.03)*0.7672	
	Beta Blocker at baseline						0.4897*
	Yes	691/2195 (31.5)	669/2187 (30.6)	1.01 (0.95, 1.07) 0.7156	1.00 (0.87, 1.16) 0.9565	0.01 (-0.02, 0.04)*0.5239	
	No	134/ 430 (31.2)	143/ 438 (32.6)	0.95 (0.79, 1.16)*0.6388	1.02 (0.73, 1.42) 0.9158	-0.01 (-0.08, 0.05)*0.6387	
	Diuretics at baseline						0.9076*
	Yes	742/2350 (31.6)	730/2345 (31.1)	1.01 (0.96, 1.07) 0.7429	1.03 (0.89, 1.18) 0.7187	0.00 (-0.02, 0.03)*0.7428	
	No	83/ 275 (30.2)	82/ 280 (29.3)	1.03 (0.80, 1.33)*0.8174	0.85 (0.56, 1.30) 0.4573	0.01 (-0.07, 0.09)*0.8174	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)							
	Overall	849/2801 (30.3)	790/2805 (28.2)	1.08 (0.99, 1.17)*0.0774	1.12 (0.98, 1.27) 0.0873	0.02 (-0.00, 0.05)*0.0772	
	Age						0.6510*
	<= median	441/1394 (31.6)	424/1471 (28.8)	1.10 (0.98, 1.23)*0.1014	1.14 (0.96, 1.36) 0.1377	0.03 (-0.01, 0.06)*0.1014	
	> median	408/1407 (29.0)	366/1334 (27.4)	1.06 (0.94, 1.19)*0.3643	1.10 (0.92, 1.32) 0.2964	0.02 (-0.02, 0.05)*0.3637	
	Gender						0.0711*
	Male	453/1630 (27.8)	444/1608 (27.6)	1.01 (0.90, 1.12)*0.9092	0.99 (0.84, 1.17) 0.9315	0.00 (-0.03, 0.03)*0.9092	
	Female	396/1171 (33.8)	346/1197 (28.9)	1.17 (1.04, 1.32)*0.0101	1.31 (1.08, 1.59) 0.0063	0.05 (0.01, 0.09)*0.0099	
	Race						0.6633*
	White	606/2006 (30.2)	574/2032 (28.2)	1.07 (0.97, 1.18)*0.1708	1.10 (0.95, 1.28) 0.1977	0.02 (-0.01, 0.05)*0.1706	
	Black or African	29/ 64 (45.3)	24/ 70 (34.3)	1.32 (0.87, 2.01)*0.1947	1.75 (0.78, 3.91) 0.1760	0.11 (-0.05, 0.28)*0.1904	
	Asian	127/ 555 (22.9)	126/ 551 (22.9)	1.00 (0.81, 1.24)*0.9951	0.98 (0.73, 1.32) 0.8790	0.00 (-0.05, 0.05)*0.9951	
	Other	87/ 176 (49.4)	66/ 152 (43.4)	1.14 (0.90, 1.44)*0.2797	1.50 (0.89, 2.53) 0.1253	0.06 (-0.05, 0.17)*0.2754	
	Geographic region						0.2740*
	Asia	120/ 536 (22.4)	120/ 536 (22.4)	1.00 (0.80, 1.25)*1.0000	0.98 (0.72, 1.33) 0.8848	0.00 (-0.05, 0.05)*1.0000	
	Europe and Saudi Arabia	395/1341 (29.5)	390/1381 (28.2)	1.04 (0.93, 1.17)*0.4841	1.08 (0.90, 1.30) 0.3892	0.01 (-0.02, 0.05)*0.4842	
	North America	98/ 393 (24.9)	94/ 376 (25.0)	1.00 (0.78, 1.27)*0.9837	0.89 (0.61, 1.29) 0.5416	-0.00 (-0.06, 0.06)*0.9837	
	Latin America	236/ 531 (44.4)	186/ 512 (36.3)	1.22 (1.05, 1.42)*0.0080	1.55 (1.17, 2.05) 0.0023	0.08 (0.02, 0.14)*0.0073	
	NYHA class at enrolment						0.0677*
	II	601/2083 (28.9)	609/2165 (28.1)	1.03 (0.93, 1.13)*0.6016	1.05 (0.91, 1.21) 0.5290	0.01 (-0.02, 0.03)*0.6016	
	III or IV	248/ 718 (34.5)	181/ 639 (28.3)	1.22 (1.04, 1.43)*0.0146	1.36 (1.05, 1.78) 0.0223	0.06 (0.01, 0.11)*0.0135	
	LVEF at enrolment						0.5319*
	<= 49	277/ 959 (28.9)	261/ 950 (27.5)	1.05 (0.91, 1.21)*0.4935	1.08 (0.87, 1.35) 0.4725	0.01 (-0.03, 0.05)*0.4933	
	50-59	314/1017 (30.9)	272/1009 (27.0)	1.15 (1.00, 1.31)*0.0522	1.23 (1.00, 1.53) 0.0539	0.04 (-0.00, 0.08)*0.0516	
	>= 60	258/ 825 (31.3)	257/ 846 (30.4)	1.03 (0.89, 1.19)*0.6922	1.04 (0.83, 1.30) 0.7486	0.01 (-0.04, 0.05)*0.6922	
	NT-proBNP at enrolment						0.0670*
	<= median	408/1396 (29.2)	413/1409 (29.3)	1.00 (0.89, 1.12)*0.9604	1.00 (0.84, 1.19) 0.9730	-0.00 (-0.03, 0.03)*0.9604	
	> median	441/1405 (31.4)	377/1395 (27.0)	1.16 (1.03, 1.30)*0.0113	1.25 (1.05, 1.50) 0.0144	0.04 (0.01, 0.08)*0.0110	
	Type 2 Diabetes Medical History						0.6022*
	Yes	350/1231 (28.4)	337/1243 (27.1)	1.03 (0.96, 1.10) 0.3944	1.07 (0.90, 1.27)*0.4635	0.01 (-0.02, 0.05)*0.4634	
	No	499/1570 (31.8)	453/1562 (29.0)	1.10 (0.99, 1.22)*0.0908	1.14 (0.98, 1.33)*0.0906	0.03 (-0.00, 0.06)*0.0904	
	Atrial fibrillation or flutter at enrolment ECG						0.8819*
	Yes	342/1185 (28.9)	321/1188 (27.0)	1.07 (0.94, 1.22)*0.3179	1.12 (0.92, 1.37) 0.2468	0.02 (-0.02, 0.05)*0.3177	
	No	507/1616 (31.4)	469/1617 (29.0)	1.08 (0.97, 1.20)*0.1425	1.11 (0.94, 1.31) 0.2185	0.02 (-0.01, 0.06)*0.1422	
	BMI (kg/m2) at enrolment						0.2243*
	< 30	454/1547 (29.3)	400/1541 (26.0)	1.13 (1.01, 1.27)*0.0355	1.18 (1.00, 1.40) 0.0537	0.03 (0.00, 0.07)*0.0351	
	>= 30	395/1253 (31.5)	389/1261 (30.8)	1.02 (0.91, 1.15)*0.7146	1.04 (0.86, 1.26) 0.6579	0.01 (-0.03, 0.04)*0.7146	
	Baseline eGFR (mL/min/1.73m^2)						0.3211*
	< 60	379/1338 (28.3)	379/1377 (27.5)	1.03 (0.91, 1.16)*0.6413	1.06 (0.88, 1.28) 0.5334	0.01 (-0.03, 0.04)*0.6413	
	>= 60	470/1463 (32.1)	410/1427 (28.7)	1.12 (1.00, 1.25)*0.0478	1.17 (0.98, 1.39) 0.0809	0.03 (0.00, 0.07)*0.0472	

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Symptom Stability (LOCF)	SBP at randomisation						0.4740*
	<= median	409/1405 (29.1)	396/1420 (27.9)	1.04 (0.93, 1.17)*0.4716	1.04 (0.87, 1.25) 0.6559	0.01 (-0.02, 0.05)*0.4715	
	> median	440/1396 (31.5)	394/1385 (28.4)	1.11 (0.99, 1.24)*0.0775	1.20 (1.00, 1.44) 0.0450	0.03 (-0.00, 0.06)*0.0770	
	LVEF at enrolment 2						0.6928*
	<= 49	277/ 959 (28.9)	261/ 950 (27.5)	1.05 (0.91, 1.21)*0.4935	1.08 (0.87, 1.35) 0.4725	0.01 (-0.03, 0.05)*0.4933	
	>= 50	572/1842 (31.1)	529/1855 (28.5)	1.09 (0.99, 1.20)*0.0920	1.14 (0.97, 1.33) 0.1012	0.03 (-0.00, 0.05)*0.0917	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5889*
	Yes	78/ 280 (27.9)	78/ 281 (27.8)	1.00 (0.77, 1.31)*0.9791	1.09 (0.70, 1.69) 0.6975	0.00 (-0.07, 0.08)*0.9791	
	No	771/2521 (30.6)	712/2524 (28.2)	1.08 (1.00, 1.18)*0.0644	1.12 (0.98, 1.27) 0.1069	0.02 (-0.00, 0.05)*0.0641	
	MRAs at baseline						0.1322*
	Yes	365/1216 (30.0)	362/1210 (29.9)	1.00 (0.89, 1.13)*0.9575	1.03 (0.85, 1.25) 0.7340	0.00 (-0.04, 0.04)*0.9575	
	No	484/1585 (30.5)	428/1595 (26.8)	1.14 (1.02, 1.27)*0.0212	1.18 (1.00, 1.40) 0.0501	0.04 (0.01, 0.07)*0.0209	
	ACEi+ARB at baseline						0.6876*
	Yes	638/2037 (31.3)	593/2059 (28.8)	1.09 (0.99, 1.19)*0.0788	1.16 (1.00, 1.34) 0.0519	0.03 (-0.00, 0.05)*0.0785	
	No	211/ 764 (27.6)	197/ 746 (26.4)	1.05 (0.89, 1.23)*0.5966	1.02 (0.79, 1.30) 0.9075	0.01 (-0.03, 0.06)*0.5964	
	ARNI at baseline						0.4490*
	Yes	40/ 149 (26.8)	36/ 125 (28.8)	0.93 (0.64, 1.37)*0.7187	1.04 (0.58, 1.85) 0.8978	-0.02 (-0.13, 0.09)*0.7194	
	No	809/2652 (30.5)	754/2680 (28.1)	1.08 (1.00, 1.18)*0.0573	1.12 (0.99, 1.28) 0.0782	0.02 (-0.00, 0.05)*0.0572	
	Beta Blocker at baseline						0.9833*
	Yes	700/2327 (30.1)	651/2330 (27.9)	1.08 (0.98, 1.18)*0.1075	1.08 (0.94, 1.25) 0.2517	0.02 (-0.00, 0.05)*0.1072	
	No	149/ 474 (31.4)	139/ 475 (29.3)	1.07 (0.89, 1.30)*0.4671	1.30 (0.96, 1.78) 0.0933	0.02 (-0.04, 0.08)*0.4668	
	Diuretics at baseline						0.5890*
	Yes	745/2500 (29.8)	699/2504 (27.9)	1.07 (0.98, 1.16)*0.1414	1.10 (0.96, 1.26) 0.1523	0.02 (-0.01, 0.04)*0.1412	
	No	104/ 301 (34.6)	91/ 301 (30.2)	1.14 (0.91, 1.44)*0.2584	1.22 (0.84, 1.79) 0.2962	0.04 (-0.03, 0.12)*0.2570	

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Total Symptom Score (LOCF)							
	Overall	875/2801 (31.2)	792/2805 (28.2)	1.11 (1.02, 1.20)*0.0140	1.15 (1.00, 1.32) 0.0427	0.03 (0.01, 0.05)*0.0138	
	Age						0.9342*
	<= median	451/1394 (32.4)	428/1471 (29.1)	1.11 (1.00, 1.24)*0.0589	1.25 (1.03, 1.51) 0.0250	0.03 (-0.00, 0.07)*0.0589	
	> median	424/1407 (30.1)	364/1334 (27.3)	1.10 (0.98, 1.24)*0.1000	1.08 (0.89, 1.31) 0.4463	0.03 (-0.01, 0.06)*0.0991	
	Gender						0.9209*
	Male	481/1630 (29.5)	430/1608 (26.7)	1.10 (0.99, 1.23)*0.0802	1.16 (0.96, 1.40) 0.1229	0.03 (-0.00, 0.06)*0.0797	
	Female	394/1171 (33.6)	362/1197 (30.2)	1.11 (0.99, 1.25)*0.0759	1.14 (0.93, 1.39) 0.2071	0.03 (-0.00, 0.07)*0.0755	
	Race						0.7626*
	White	659/2006 (32.9)	595/2032 (29.3)	1.12 (1.02, 1.23)*0.0143	1.14 (0.98, 1.34) 0.0980	0.04 (0.01, 0.06)*0.0142	
	Black or African	23/ 64 (35.9)	28/ 70 (40.0)	0.90 (0.58, 1.39)*0.6295	0.84 (0.40, 1.75) 0.6373	-0.07 (-0.22, 0.09) 0.4023	
	Asian	118/ 555 (21.3)	107/ 551 (19.4)	1.09 (0.87, 1.38)*0.4470	1.35 (0.93, 1.95) 0.1129	0.02 (-0.03, 0.07)*0.4466	
	Other	75/ 176 (42.6)	62/ 152 (40.8)	1.04 (0.81, 1.35)*0.7387	1.10 (0.64, 1.87) 0.7383	0.02 (-0.09, 0.13)*0.7382	
	Geographic region						0.4966*
	Asia	116/ 536 (21.6)	100/ 536 (18.7)	1.16 (0.91, 1.47)*0.2239	1.45 (0.99, 2.11) 0.0550	0.03 (-0.02, 0.08)*0.2228	
	Europe and Saudi Arabia	441/1341 (32.9)	405/1381 (29.3)	1.12 (1.00, 1.25)*0.0451	1.13 (0.93, 1.37) 0.2306	0.04 (0.00, 0.07)*0.0448	
	North America	107/ 393 (27.2)	109/ 376 (29.0)	0.94 (0.75, 1.18)*0.5867	0.89 (0.63, 1.25) 0.4993	-0.02 (-0.08, 0.05)*0.5867	
	Latin America	211/ 531 (39.7)	178/ 512 (34.8)	1.14 (0.98, 1.34)*0.0979	1.31 (0.97, 1.78) 0.0818	0.05 (-0.01, 0.11)*0.0964	
	NYHA class at enrolment						0.1339*
	II	573/2083 (27.5)	567/2165 (26.2)	1.05 (0.95, 1.16)*0.3321	1.11 (0.94, 1.30) 0.2298	0.01 (-0.01, 0.04)*0.3322	
	III or IV	302/ 718 (42.1)	225/ 639 (35.2)	1.19 (1.04, 1.37)*0.0103	1.32 (1.03, 1.70) 0.0276	0.07 (0.02, 0.12)*0.0094	
	LVEF at enrolment						0.1989*
	<= 49	280/ 959 (29.2)	271/ 950 (28.5)	1.02 (0.89, 1.18)*0.7464	1.06 (0.83, 1.35) 0.6351	0.01 (-0.03, 0.05)*0.7464	
	50-59	327/1017 (32.2)	298/1009 (29.5)	1.09 (0.96, 1.24)*0.2022	1.10 (0.87, 1.38) 0.4160	0.03 (-0.01, 0.07)*0.2016	
	>= 60	268/ 825 (32.5)	223/ 846 (26.4)	1.23 (1.06, 1.43)*0.0062	1.32 (1.04, 1.69) 0.0241	0.06 (0.02, 0.10)*0.0059	
	NT-proBNP at enrolment						0.2093*
	<= median	392/1396 (28.1)	378/1409 (26.8)	1.05 (0.93, 1.18)*0.4573	1.08 (0.89, 1.31) 0.4251	0.01 (-0.02, 0.05)*0.4573	
	> median	483/1405 (34.4)	413/1395 (29.6)	1.16 (1.04, 1.29)*0.0069	1.22 (1.01, 1.48) 0.0409	0.05 (0.01, 0.08)*0.0067	
	Type 2 Diabetes Medical History						0.0794*
	Yes	416/1231 (33.8)	351/1243 (28.2)	1.20 (1.06, 1.35)*0.0029	1.30 (1.09, 1.54)*0.0028	0.06 (0.02, 0.09)*0.0028	
	No	459/1570 (29.2)	441/1562 (28.2)	1.04 (0.93, 1.16)*0.5353	1.05 (0.90, 1.23)*0.5353	0.01 (-0.02, 0.04)*0.5352	
	Atrial fibrillation or flutter at enrolment ECG						0.6665*
	Yes	383/1185 (32.3)	354/1188 (29.8)	1.08 (0.96, 1.22)*0.1845	1.12 (0.91, 1.38) 0.2766	0.03 (-0.01, 0.06)*0.1841	
	No	492/1616 (30.4)	438/1617 (27.1)	1.12 (1.01, 1.25)*0.0352	1.18 (0.98, 1.41) 0.0802	0.03 (0.00, 0.06)*0.0348	
	BMI (kg/m2) at enrolment						0.8110*
	< 30	436/1547 (28.2)	396/1541 (25.7)	1.10 (0.98, 1.23)*0.1198	1.14 (0.93, 1.38) 0.2046	0.02 (-0.01, 0.06)*0.1193	
	>= 30	439/1253 (35.0)	395/1261 (31.3)	1.12 (1.00, 1.25)*0.0484	1.18 (0.97, 1.43) 0.0955	0.04 (0.00, 0.07)*0.0480	
	Baseline eGFR (mL/min/1.73m^2)						0.6067*
	< 60	411/1338 (30.7)	391/1377 (28.4)	1.08 (0.96, 1.22)*0.1850	1.10 (0.90, 1.33) 0.3463	0.02 (-0.01, 0.06)*0.1848	
	>= 60	464/1463 (31.7)	401/1427 (28.1)	1.13 (1.01, 1.26)*0.0342	1.21 (1.00, 1.47) 0.0537	0.04 (0.00, 0.07)*0.0337	

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Total Symptom Score (LOCF)	SBP at randomisation						0.3195*
	<= median	437/1405 (31.1)	383/1420 (27.0)	1.15 (1.03, 1.29)*0.0157	1.16 (0.95, 1.40) 0.1436	0.04 (0.01, 0.07)*0.0155	
	> median	438/1396 (31.4)	409/1385 (29.5)	1.06 (0.95, 1.19)*0.2908	1.15 (0.95, 1.40) 0.1559	0.02 (-0.02, 0.05)*0.2904	
	LVEF at enrolment 2						0.1835*
	<= 49	280/ 959 (29.2)	271/ 950 (28.5)	1.02 (0.89, 1.18)*0.7464	1.06 (0.83, 1.35) 0.6351	0.01 (-0.03, 0.05)*0.7464	
	>= 50	595/1842 (32.3)	521/1855 (28.1)	1.15 (1.04, 1.27)*0.0053	1.20 (1.02, 1.42) 0.0326	0.04 (0.01, 0.07)*0.0052	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1977*
	Yes	125/ 280 (44.6)	127/ 281 (45.2)	0.99 (0.82, 1.19)*0.8953	1.07 (0.72, 1.57) 0.7453	-0.01 (-0.09, 0.08)*0.8953	
	No	750/2521 (29.8)	665/2524 (26.3)	1.13 (1.03, 1.23)*0.0072	1.16 (1.00, 1.35) 0.0434	0.03 (0.01, 0.06)*0.0071	
	MRAs at baseline						0.5078*
	Yes	381/1216 (31.3)	332/1210 (27.4)	1.14 (1.01, 1.29)*0.0356	1.20 (0.98, 1.49) 0.0843	0.04 (0.00, 0.08)*0.0351	
	No	494/1585 (31.2)	460/1595 (28.8)	1.08 (0.97, 1.20)*0.1524	1.11 (0.93, 1.33) 0.2431	0.02 (-0.01, 0.06)*0.1521	
	ACEi+ARB at baseline						0.2416*
	Yes	669/2037 (32.8)	594/2059 (28.8)	1.14 (1.04, 1.25)*0.0057	1.19 (1.02, 1.39) 0.0315	0.04 (0.01, 0.07)*0.0056	
	No	206/ 764 (27.0)	198/ 746 (26.5)	1.02 (0.86, 1.20)*0.8531	1.05 (0.80, 1.38) 0.7121	0.00 (-0.04, 0.05)*0.8531	
	ARNI at baseline						0.0231*
	Yes	26/ 149 (17.4)	33/ 125 (26.4)	0.66 (0.42, 1.04)*0.0749	0.68 (0.34, 1.33) 0.2578	-0.09 (-0.19, 0.01)*0.0747	
	No	849/2652 (32.0)	759/2680 (28.3)	1.13 (1.04, 1.23)*0.0033	1.18 (1.03, 1.36) 0.0209	0.04 (0.01, 0.06)*0.0033	
	Beta Blocker at baseline						0.2537*
	Yes	725/2327 (31.2)	642/2330 (27.6)	1.13 (1.03, 1.24)*0.0070	1.15 (0.99, 1.34) 0.0609	0.04 (0.01, 0.06)*0.0069	
	No	150/ 474 (31.6)	150/ 475 (31.6)	1.00 (0.83, 1.21)*0.9824	1.14 (0.82, 1.58) 0.4479	0.00 (-0.06, 0.06)*0.9824	
	Diuretics at baseline						0.0590*
	Yes	772/2500 (30.9)	718/2504 (28.7)	1.08 (0.99, 1.17)*0.0881	1.13 (0.97, 1.30) 0.1065	0.02 (-0.00, 0.05)*0.0879	
	No	103/ 301 (34.2)	74/ 301 (24.6)	1.39 (1.08, 1.79)*0.0102	1.35 (0.86, 2.11) 0.1857	0.10 (0.02, 0.17)*0.0091	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	865/2842 (30.4)	769/2837 (27.1)	1.12 (1.03, 1.22)*0.0056	1.17 (1.02, 1.33) 0.0222	0.03 (0.01, 0.06)*0.0055	
	Age						0.4146*
	<= median	449/1415 (31.7)	431/1482 (29.1)	1.09 (0.98, 1.22)*0.1213	1.18 (0.98, 1.42) 0.0738	0.03 (-0.01, 0.06)*0.1212	
	> median	416/1427 (29.2)	338/1355 (24.9)	1.17 (1.03, 1.32)*0.0128	1.18 (0.97, 1.43) 0.0966	0.04 (0.01, 0.08)*0.0124	
	Gender						0.1682*
	Male	453/1656 (27.4)	417/1625 (25.7)	1.07 (0.95, 1.19)*0.2721	1.07 (0.90, 1.29) 0.4361	0.02 (-0.01, 0.05)*0.2717	
	Female	412/1186 (34.7)	352/1212 (29.0)	1.20 (1.06, 1.35)*0.0028	1.28 (1.05, 1.55) 0.0130	0.06 (0.02, 0.09)*0.0027	
	Race						0.8643*
	White	646/2039 (31.7)	584/2058 (28.4)	1.12 (1.02, 1.23)*0.0211	1.13 (0.97, 1.31) 0.1149	0.03 (0.00, 0.06)*0.0209	
	Black or African	25/ 67 (37.3)	25/ 71 (35.2)	1.06 (0.68, 1.65)*0.7973	1.13 (0.52, 2.45) 0.7536	0.02 (-0.14, 0.18)*0.7974	
	Asian	108/ 558 (19.4)	100/ 555 (18.0)	1.07 (0.84, 1.37)*0.5674	1.13 (0.79, 1.63) 0.5002	0.01 (-0.03, 0.06)*0.5672	
	Other	86/ 178 (48.3)	60/ 153 (39.2)	1.23 (0.96, 1.58)*0.1005	1.74 (1.04, 2.91) 0.0351	0.09 (-0.02, 0.20)*0.0945	
	Geographic region						0.7177*
	Asia	103/ 539 (19.1)	98/ 538 (18.2)	1.05 (0.82, 1.35)*0.7066	1.04 (0.72, 1.51) 0.8227	0.01 (-0.04, 0.06)*0.7066	
	Europe and Saudi Arabia	431/1365 (31.6)	382/1394 (27.4)	1.15 (1.03, 1.29)*0.0164	1.21 (1.00, 1.45) 0.0520	0.04 (0.01, 0.08)*0.0162	
	North America	110/ 398 (27.6)	89/ 387 (23.0)	1.20 (0.94, 1.53)*0.1364	1.27 (0.89, 1.81) 0.1803	0.05 (-0.01, 0.11)*0.1342	
	Latin America	221/ 540 (40.9)	200/ 518 (38.6)	1.06 (0.91, 1.23)*0.4421	1.13 (0.85, 1.50) 0.4015	0.02 (-0.04, 0.08)*0.4415	
	NYHA class at enrolment						0.3593*
	II	564/2113 (26.7)	540/2187 (24.7)	1.08 (0.98, 1.20)*0.1334	1.15 (0.98, 1.35) 0.0916	0.02 (-0.01, 0.05)*0.1333	
	III or IV	301/ 729 (41.3)	229/ 649 (35.3)	1.17 (1.02, 1.34)*0.0230	1.25 (0.99, 1.59) 0.0662	0.06 (0.01, 0.11)*0.0217	
	LVEF at enrolment						0.0364*
	<= 49	285/ 980 (29.1)	282/ 963 (29.3)	0.99 (0.86, 1.14)*0.9220	1.04 (0.83, 1.30) 0.7475	-0.00 (-0.04, 0.04)*0.9220	
	50-59	306/1029 (29.7)	270/1017 (26.5)	1.12 (0.97, 1.29)*0.1093	1.10 (0.89, 1.38) 0.3787	0.03 (-0.01, 0.07)*0.1085	
	>= 60	274/ 833 (32.9)	217/ 857 (25.3)	1.30 (1.12, 1.51)*0.0007	1.43 (1.12, 1.82) 0.0043	0.08 (0.03, 0.12)*0.0006	
	NT-proBNP at enrolment						0.8401*
	<= median	400/1418 (28.2)	360/1421 (25.3)	1.11 (0.99, 1.26)*0.0840	1.18 (0.98, 1.43) 0.0819	0.03 (-0.00, 0.06)*0.0836	
	> median	465/1424 (32.7)	408/1415 (28.8)	1.13 (1.01, 1.27)*0.0277	1.15 (0.95, 1.38) 0.1471	0.04 (0.00, 0.07)*0.0273	
	Type 2 Diabetes Medical History						0.8711*
	Yes	394/1250 (31.5)	351/1260 (27.9)	1.13 (1.00, 1.28)*0.0449	1.19 (1.00, 1.41)*0.0447	0.04 (0.00, 0.07)*0.0445	
	No	471/1592 (29.6)	418/1577 (26.5)	1.12 (1.00, 1.25)*0.0540	1.16 (1.00, 1.36)*0.0538	0.03 (-0.00, 0.06)*0.0535	
	Atrial fibrillation or flutter at enrolment ECG						0.7252*
	Yes	371/1199 (30.9)	336/1199 (28.0)	1.10 (0.98, 1.25)*0.1173	1.14 (0.93, 1.39) 0.1991	0.03 (-0.01, 0.07)*0.1168	
	No	494/1643 (30.1)	433/1638 (26.4)	1.14 (1.02, 1.27)*0.0211	1.19 (1.00, 1.42) 0.0558	0.04 (0.01, 0.07)*0.0207	
	BMI (kg/m2) at enrolment						0.5106*
	< 30	430/1571 (27.4)	369/1559 (23.7)	1.16 (1.03, 1.30)*0.0178	1.24 (1.03, 1.50) 0.0234	0.04 (0.01, 0.07)*0.0174	
	>= 30	435/1270 (34.3)	399/1275 (31.3)	1.09 (0.98, 1.22)*0.1122	1.11 (0.92, 1.33) 0.2832	0.03 (-0.01, 0.07)*0.1118	
	Baseline eGFR (mL/min/1.73m^2)						0.9141*
	< 60	406/1359 (29.9)	370/1396 (26.5)	1.13 (1.00, 1.27)*0.0495	1.20 (0.99, 1.45) 0.0582	0.03 (0.00, 0.07)*0.0492	
	>= 60	459/1483 (31.0)	399/1440 (27.7)	1.12 (1.00, 1.25)*0.0546	1.13 (0.94, 1.36) 0.1965	0.03 (-0.00, 0.07)*0.0540	

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Clinical Summary Score (LOCF)	SBP at randomisation						0.0793*
	<= median	428/1424 (30.1)	357/1439 (24.8)	1.21 (1.07, 1.37)*0.0017	1.25 (1.03, 1.51) 0.0228	0.05 (0.02, 0.09)*0.0016	
	> median	437/1418 (30.8)	412/1398 (29.5)	1.05 (0.93, 1.17)*0.4361	1.10 (0.91, 1.33) 0.3086	0.01 (-0.02, 0.05)*0.4359	
	LVEF at enrolment 2						0.0321*
	<= 49	285/ 980 (29.1)	282/ 963 (29.3)	0.99 (0.86, 1.14)*0.9220	1.04 (0.83, 1.30) 0.7475	-0.00 (-0.04, 0.04)*0.9220	
	>= 50	580/1862 (31.1)	487/1874 (26.0)	1.20 (1.08, 1.33)*0.0005	1.24 (1.05, 1.46) 0.0098	0.05 (0.02, 0.08)*0.0005	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4528*
	Yes	118/ 283 (41.7)	114/ 286 (39.9)	1.05 (0.86, 1.28)*0.6559	1.23 (0.84, 1.82) 0.2875	0.02 (-0.06, 0.10)*0.6558	
	No	747/2559 (29.2)	655/2551 (25.7)	1.14 (1.04, 1.24)*0.0049	1.16 (1.01, 1.34) 0.0353	0.04 (0.01, 0.06)*0.0048	
	MRAs at baseline						0.8870*
	Yes	374/1227 (30.5)	330/1224 (27.0)	1.13 (1.00, 1.28)*0.0545	1.18 (0.96, 1.45) 0.1086	0.04 (-0.00, 0.07)*0.0539	
	No	491/1615 (30.4)	439/1613 (27.2)	1.12 (1.00, 1.25)*0.0459	1.16 (0.97, 1.38) 0.0986	0.03 (0.00, 0.06)*0.0455	
	ACEi+ARB at baseline						0.1101*
	Yes	663/2065 (32.1)	571/2077 (27.5)	1.17 (1.06, 1.28)*0.0012	1.23 (1.06, 1.44) 0.0073	0.05 (0.02, 0.07)*0.0012	
	No	202/ 777 (26.0)	198/ 760 (26.1)	1.00 (0.84, 1.18)*0.9803	1.00 (0.77, 1.29) 0.9715	-0.00 (-0.04, 0.04)*0.9803	
	ARNI at baseline						0.3186*
	Yes	28/ 153 (18.3)	26/ 126 (20.6)	0.89 (0.55, 1.43)*0.6232	1.05 (0.51, 2.16) 0.9029	-0.02 (-0.12, 0.07)*0.6247	
	No	837/2689 (31.1)	743/2711 (27.4)	1.14 (1.05, 1.23)*0.0027	1.18 (1.03, 1.35) 0.0184	0.04 (0.01, 0.06)*0.0026	
	Beta Blocker at baseline						0.7623*
	Yes	718/2360 (30.4)	642/2356 (27.2)	1.12 (1.02, 1.22)*0.0163	1.12 (0.97, 1.29) 0.1261	0.03 (0.01, 0.06)*0.0161	
	No	147/ 482 (30.5)	127/ 481 (26.4)	1.16 (0.94, 1.41)*0.1599	1.45 (1.04, 2.01) 0.0274	0.04 (-0.02, 0.10)*0.1587	
	Diuretics at baseline						0.5825*
	Yes	769/2536 (30.3)	689/2531 (27.2)	1.11 (1.02, 1.21)*0.0149	1.17 (1.02, 1.35) 0.0242	0.03 (0.01, 0.06)*0.0147	
	No	96/ 306 (31.4)	80/ 306 (26.1)	1.20 (0.93, 1.54)*0.1543	1.06 (0.69, 1.63) 0.7896	0.05 (-0.02, 0.12)*0.1524	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	855/2842 (30.1)	769/2837 (27.1)	1.11 (1.02, 1.21)*0.0131	1.13 (0.99, 1.29) 0.0635	0.03 (0.01, 0.05)*0.0130	
	Age						0.4349*
	<= median	450/1415 (31.8)	436/1482 (29.4)	1.08 (0.97, 1.21)*0.1643	1.15 (0.96, 1.38) 0.1252	0.02 (-0.01, 0.06)*0.1643	
	> median	405/1427 (28.4)	333/1355 (24.6)	1.15 (1.02, 1.31)*0.0234	1.13 (0.93, 1.38) 0.2090	0.04 (0.01, 0.07)*0.0228	
	Gender						0.2312*
	Male	462/1656 (27.9)	427/1625 (26.3)	1.06 (0.95, 1.19)*0.2963	1.06 (0.89, 1.27) 0.4999	0.02 (-0.01, 0.05)*0.2959	
	Female	393/1186 (33.1)	342/1212 (28.2)	1.17 (1.04, 1.33)*0.0091	1.22 (1.00, 1.48) 0.0520	0.05 (0.01, 0.09)*0.0089	
	Race						0.5434*
	White	626/2039 (30.7)	581/2058 (28.2)	1.09 (0.99, 1.20)*0.0831	1.06 (0.91, 1.24) 0.4213	0.02 (-0.00, 0.05)*0.0828	
	Black or African	21/ 67 (31.3)	25/ 71 (35.2)	0.89 (0.55, 1.43)*0.6308	0.79 (0.35, 1.79) 0.5745	-0.04 (-0.20, 0.12)*0.6294	
	Asian	116/ 558 (20.8)	100/ 555 (18.0)	1.15 (0.91, 1.47)*0.2433	1.28 (0.90, 1.82) 0.1665	0.03 (-0.02, 0.07)*0.2422	
	Other	92/ 178 (51.7)	63/ 153 (41.2)	1.18 (0.95, 1.48) 0.1407	1.90 (1.14, 3.17) 0.0145	0.11 (-0.00, 0.21)*0.0545	
	Geographic region						0.9711*
	Asia	113/ 539 (21.0)	98/ 538 (18.2)	1.15 (0.90, 1.47)*0.2564	1.24 (0.86, 1.77) 0.2449	0.03 (-0.02, 0.07)*0.2554	
	Europe and Saudi Arabia	411/1365 (30.1)	377/1394 (27.0)	1.11 (0.99, 1.25)*0.0750	1.11 (0.92, 1.34) 0.2735	0.03 (-0.00, 0.06)*0.0746	
	North America	111/ 398 (27.9)	98/ 387 (25.3)	1.10 (0.87, 1.39)*0.4165	1.13 (0.80, 1.61) 0.4916	0.03 (-0.04, 0.09)*0.4156	
	Latin America	220/ 540 (40.7)	196/ 518 (37.8)	1.08 (0.93, 1.25)*0.3344	1.14 (0.86, 1.51) 0.3747	0.03 (-0.03, 0.09)*0.3335	
	NYHA class at enrolment						0.6135*
	II	569/2113 (26.9)	544/2187 (24.9)	1.08 (0.98, 1.20)*0.1243	1.14 (0.97, 1.33) 0.1065	0.02 (-0.01, 0.05)*0.1242	
	III or IV	286/ 729 (39.2)	225/ 649 (34.7)	1.13 (0.98, 1.30)*0.0812	1.16 (0.91, 1.48) 0.2226	0.05 (-0.01, 0.10)*0.0793	
	LVEF at enrolment						0.2096*
	<= 49	285/ 980 (29.1)	277/ 963 (28.8)	1.01 (0.88, 1.16)*0.8774	1.07 (0.86, 1.34) 0.5462	0.00 (-0.04, 0.04)*0.8774	
	50-59	314/1029 (30.5)	257/1017 (25.3)	1.21 (1.05, 1.39)*0.0084	1.23 (0.99, 1.54) 0.0664	0.05 (0.01, 0.09)*0.0081	
	>= 60	256/ 833 (30.7)	235/ 857 (27.4)	1.12 (0.97, 1.30)*0.1342	1.09 (0.86, 1.39) 0.4713	0.03 (-0.01, 0.08)*0.1338	
	NT-proBNP at enrolment						0.9842*
	<= median	396/1418 (27.9)	357/1421 (25.1)	1.11 (0.98, 1.26)*0.0910	1.16 (0.96, 1.40) 0.1203	0.03 (-0.00, 0.06)*0.0905	
	> median	459/1424 (32.2)	411/1415 (29.0)	1.11 (0.99, 1.24)*0.0658	1.11 (0.92, 1.33) 0.2881	0.03 (-0.00, 0.07)*0.0653	
	Type 2 Diabetes Medical History						0.7990*
	Yes	380/1250 (30.4)	341/1260 (27.1)	1.12 (0.99, 1.27)*0.0650	1.18 (0.99, 1.40)*0.0648	0.03 (-0.00, 0.07)*0.0646	
	No	475/1592 (29.8)	428/1577 (27.1)	1.10 (0.98, 1.23)*0.0930	1.14 (0.98, 1.33)*0.0928	0.03 (-0.00, 0.06)*0.0925	
	Atrial fibrillation or flutter at enrolment ECG						0.9382*
	Yes	366/1199 (30.5)	331/1199 (27.6)	1.11 (0.98, 1.25)*0.1158	1.12 (0.91, 1.37) 0.2827	0.03 (-0.01, 0.07)*0.1153	
	No	489/1643 (29.8)	438/1638 (26.7)	1.11 (1.00, 1.24)*0.0548	1.15 (0.96, 1.36) 0.1264	0.03 (-0.00, 0.06)*0.0544	
	BMI (kg/m2) at enrolment						0.1516*
	< 30	439/1571 (27.9)	369/1559 (23.7)	1.18 (1.05, 1.33)*0.0064	1.26 (1.04, 1.52) 0.0161	0.04 (0.01, 0.07)*0.0062	
	>= 30	416/1270 (32.8)	399/1275 (31.3)	1.05 (0.93, 1.17)*0.4294	1.02 (0.85, 1.23) 0.8127	0.01 (-0.02, 0.05)*0.4293	
	Baseline eGFR (mL/min/1.73m^2)						0.4524*
	< 60	397/1359 (29.2)	380/1396 (27.2)	1.07 (0.95, 1.21)*0.2455	1.10 (0.91, 1.33) 0.3176	0.02 (-0.01, 0.05)*0.2454	
	>= 60	458/1483 (30.9)	389/1440 (27.0)	1.14 (1.02, 1.28)*0.0214	1.16 (0.97, 1.40) 0.1129	0.04 (0.01, 0.07)*0.0209	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.0925*
	<= median	433/1424 (30.4)	367/1439 (25.5)	1.19 (1.06, 1.34)*0.0035	1.20 (1.00, 1.45) 0.0518	0.05 (0.02, 0.08)*0.0034	
	> median	422/1418 (29.8)	402/1398 (28.8)	1.03 (0.92, 1.16)*0.5579	1.07 (0.89, 1.29) 0.4889	0.01 (-0.02, 0.04)*0.5578	
	LVEF at enrolment 2						0.1058*
	<= 49	285/ 980 (29.1)	277/ 963 (28.8)	1.01 (0.88, 1.16)*0.8774	1.07 (0.86, 1.34) 0.5462	0.00 (-0.04, 0.04)*0.8774	
	>= 50	570/1862 (30.6)	492/1874 (26.3)	1.17 (1.05, 1.29)*0.0032	1.17 (0.99, 1.37) 0.0669	0.04 (0.01, 0.07)*0.0031	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3736*
	Yes	115/ 283 (40.6)	114/ 286 (39.9)	1.02 (0.83, 1.25)*0.8503	1.10 (0.75, 1.62) 0.6323	0.01 (-0.07, 0.09)*0.8503	
	No	740/2559 (28.9)	655/2551 (25.7)	1.13 (1.03, 1.23)*0.0094	1.14 (0.99, 1.31) 0.0654	0.03 (0.01, 0.06)*0.0093	
	MRAs at baseline						0.6412*
	Yes	371/1227 (30.2)	326/1224 (26.6)	1.14 (1.00, 1.29)*0.0484	1.20 (0.98, 1.46) 0.0826	0.04 (0.00, 0.07)*0.0479	
	No	484/1615 (30.0)	443/1613 (27.5)	1.09 (0.98, 1.22)*0.1161	1.08 (0.91, 1.29) 0.3612	0.03 (-0.01, 0.06)*0.1157	
	ACEi+ARB at baseline						0.9923*
	Yes	638/2065 (30.9)	578/2077 (27.8)	1.11 (1.01, 1.22)*0.0304	1.12 (0.96, 1.31) 0.1426	0.03 (0.00, 0.06)*0.0301	
	No	217/ 777 (27.9)	191/ 760 (25.1)	1.11 (0.94, 1.31)*0.2150	1.17 (0.90, 1.51) 0.2386	0.03 (-0.02, 0.07)*0.2141	
	ARNI at baseline						0.5487*
	Yes	28/ 153 (18.3)	24/ 126 (19.0)	0.96 (0.59, 1.57)*0.8733	0.97 (0.48, 1.97) 0.9387	-0.01 (-0.10, 0.08)*0.8735	
	No	827/2689 (30.8)	745/2711 (27.5)	1.12 (1.03, 1.22)*0.0082	1.14 (1.00, 1.31) 0.0524	0.03 (0.01, 0.06)*0.0081	
	Beta Blocker at baseline						0.9097*
	Yes	710/2360 (30.1)	640/2356 (27.2)	1.11 (1.01, 1.21)*0.0267	1.09 (0.95, 1.26) 0.2246	0.03 (0.00, 0.05)*0.0265	
	No	145/ 482 (30.1)	129/ 481 (26.8)	1.12 (0.92, 1.37)*0.2623	1.36 (0.98, 1.89) 0.0642	0.03 (-0.02, 0.09)*0.2614	
	Diuretics at baseline						0.2942*
	Yes	759/2536 (29.9)	693/2531 (27.4)	1.09 (1.00, 1.19)*0.0450	1.13 (0.98, 1.30) 0.0891	0.03 (0.00, 0.05)*0.0448	
	No	96/ 306 (31.4)	76/ 306 (24.8)	1.26 (0.98, 1.63)*0.0735	1.15 (0.76, 1.74) 0.5013	0.07 (-0.01, 0.14)*0.0713	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	843/2792 (30.2)	747/2792 (26.8)	1.13 (1.04, 1.23)*0.0045	1.16 (1.02, 1.32) 0.0278	0.03 (0.01, 0.06)*0.0044	
	Age						0.8043*
	<= median	435/1403 (31.0)	407/1469 (27.7)	1.12 (1.00, 1.25)*0.0524	1.22 (1.01, 1.46) 0.0381	0.03 (-0.00, 0.07)*0.0522	
	> median	408/1389 (29.4)	340/1323 (25.7)	1.07 (0.96, 1.18) 0.2078	1.13 (0.94, 1.36) 0.1847	0.04 (0.00, 0.07)*0.0320	
	Gender						0.0269*
	Male	440/1638 (26.9)	415/1602 (25.9)	1.04 (0.92, 1.16)*0.5367	1.01 (0.85, 1.21) 0.8785	0.01 (-0.02, 0.04)*0.5366	
	Female	403/1154 (34.9)	332/1190 (27.9)	1.15 (1.03, 1.27) 0.0090	1.34 (1.11, 1.63) 0.0024	0.07 (0.03, 0.11)*0.0002	
	Race						0.7200*
	White	633/2004 (31.6)	574/2025 (28.3)	1.04 (0.97, 1.11) 0.2751	1.13 (0.97, 1.31) 0.1059	0.03 (0.00, 0.06)*0.0247	
	Black or African	17/ 66 (25.8)	20/ 68 (29.4)	0.81 (0.49, 1.33) 0.4014	0.76 (0.33, 1.74) 0.5101	-0.04 (-0.19, 0.11)*0.6357	
	Asian	119/ 551 (21.6)	97/ 550 (17.6)	1.22 (0.96, 1.56)*0.0990	1.18 (0.83, 1.67) 0.3622	0.04 (-0.01, 0.09)*0.0975	
	Other	74/ 171 (43.3)	56/ 149 (37.6)	1.19 (0.95, 1.50) 0.1301	1.43 (0.87, 2.35) 0.1593	0.06 (-0.05, 0.16)*0.2996	
	Geographic region						0.8432*
	Asia	113/ 533 (21.2)	93/ 533 (17.4)	1.22 (0.95, 1.56)*0.1218	1.15 (0.81, 1.65) 0.4376	0.04 (-0.01, 0.08)*0.1204	
	Europe and Saudi Arabia	422/1347 (31.3)	388/1373 (28.3)	1.11 (0.99, 1.24)*0.0803	1.14 (0.95, 1.37) 0.1461	0.03 (-0.00, 0.07)*0.0800	
	North America	104/ 391 (26.6)	83/ 375 (22.1)	1.12 (0.90, 1.39) 0.3211	1.18 (0.83, 1.69) 0.3598	0.04 (-0.02, 0.11)*0.1493	
	Latin America	204/ 521 (39.2)	183/ 511 (35.8)	1.09 (0.93, 1.28)*0.2679	1.18 (0.89, 1.57) 0.2421	0.03 (-0.03, 0.09)*0.2670	
	NYHA class at enrolment						0.7510*
	II	571/2077 (27.5)	536/2159 (24.8)	1.11 (1.00, 1.23)*0.0485	1.16 (0.99, 1.35) 0.0642	0.03 (0.00, 0.05)*0.0485	
	III or IV	272/ 715 (38.0)	211/ 632 (33.4)	1.10 (0.97, 1.24) 0.1228	1.18 (0.93, 1.51) 0.1776	0.05 (-0.00, 0.10)*0.0745	
	LVEF at enrolment						0.4320*
	<= 49	292/ 967 (30.2)	272/ 952 (28.6)	1.06 (0.92, 1.21)*0.4348	1.16 (0.93, 1.44) 0.1832	0.02 (-0.02, 0.06)*0.4345	
	50-59	300/1013 (29.6)	245/ 998 (24.5)	1.21 (1.04, 1.39)*0.0109	1.23 (0.99, 1.53) 0.0651	0.05 (0.01, 0.09)*0.0104	
	>= 60	251/ 812 (30.9)	230/ 842 (27.3)	1.13 (0.97, 1.32)*0.1078	1.08 (0.85, 1.38) 0.5133	0.04 (-0.01, 0.08)*0.1074	
	NT-proBNP at enrolment						0.5900*
	<= median	419/1394 (30.1)	365/1402 (26.0)	1.15 (1.02, 1.30)*0.0181	1.23 (1.02, 1.48) 0.0321	0.04 (0.01, 0.07)*0.0178	
	> median	424/1398 (30.3)	382/1389 (27.5)	1.10 (0.98, 1.24)*0.1001	1.10 (0.91, 1.31) 0.3250	0.03 (-0.01, 0.06)*0.0996	
	Type 2 Diabetes Medical History						0.7332*
	Yes	386/1232 (31.3)	338/1237 (27.3)	1.15 (1.01, 1.30)*0.0290	1.21 (1.02, 1.44)*0.0289	0.04 (0.00, 0.08)*0.0286	
	No	457/1560 (29.3)	409/1555 (26.3)	1.11 (0.99, 1.25)*0.0626	1.16 (0.99, 1.36)*0.0624	0.03 (-0.00, 0.06)*0.0622	
	Atrial fibrillation or flutter at enrolment ECG						0.0715*
	Yes	347/1178 (29.5)	335/1175 (28.5)	1.03 (0.91, 1.17)*0.6131	1.01 (0.83, 1.23) 0.9070	0.01 (-0.03, 0.05)*0.6130	
	No	496/1614 (30.7)	412/1617 (25.5)	1.21 (1.08, 1.35)*0.0009	1.28 (1.08, 1.52) 0.0049	0.05 (0.02, 0.08)*0.0009	
	BMI (kg/m2) at enrolment						0.4897*
	< 30	440/1547 (28.4)	376/1535 (24.5)	1.16 (1.03, 1.31)*0.0132	1.22 (1.02, 1.47) 0.0300	0.04 (0.01, 0.07)*0.0129	
	>= 30	403/1244 (32.4)	371/1254 (29.6)	1.00 (0.91, 1.10) 0.9276	1.09 (0.90, 1.31) 0.3800	0.03 (-0.01, 0.06)*0.1287	
	Baseline eGFR (mL/min/1.73m^2)						0.9881*
	< 60	398/1328 (30.0)	363/1367 (26.6)	1.13 (1.00, 1.27)*0.0492	1.20 (0.99, 1.44) 0.0588	0.03 (0.00, 0.07)*0.0489	
	>= 60	445/1464 (30.4)	384/1424 (27.0)	1.13 (1.00, 1.27)*0.0420	1.10 (0.92, 1.32) 0.3082	0.03 (0.00, 0.07)*0.0414	

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Physical Limitation (LOCF)	SBP at randomisation						0.2760*
	<= median	426/1396 (30.5)	365/1414 (25.8)	1.18 (1.05, 1.33)*0.0057	1.18 (0.98, 1.41) 0.0848	0.05 (0.01, 0.08)*0.0055	
	> median	417/1396 (29.9)	382/1378 (27.7)	1.08 (0.96, 1.21)*0.2115	1.14 (0.95, 1.38) 0.1515	0.02 (-0.01, 0.06)*0.2111	
	LVEF at enrolment 2						0.2528*
	<= 49	292/ 967 (30.2)	272/ 952 (28.6)	1.06 (0.92, 1.21)*0.4348	1.16 (0.93, 1.44) 0.1832	0.02 (-0.02, 0.06)*0.4345	
	>= 50	551/1825 (30.2)	475/1840 (25.8)	1.17 (1.05, 1.30)*0.0032	1.16 (0.99, 1.36) 0.0736	0.04 (0.01, 0.07)*0.0031	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3697*
	Yes	99/ 273 (36.3)	98/ 277 (35.4)	1.03 (0.82, 1.28)*0.8287	1.07 (0.71, 1.59) 0.7524	0.01 (-0.07, 0.09)*0.8287	
	No	744/2519 (29.5)	649/2515 (25.8)	1.14 (1.05, 1.25)*0.0031	1.17 (1.02, 1.34) 0.0248	0.04 (0.01, 0.06)*0.0031	
	MRAs at baseline						0.7204*
	Yes	358/1200 (29.8)	325/1208 (26.9)	1.11 (0.98, 1.26)*0.1112	1.14 (0.94, 1.40) 0.1828	0.03 (-0.01, 0.07)*0.1107	
	No	485/1592 (30.5)	422/1584 (26.6)	1.14 (1.02, 1.28)*0.0173	1.17 (0.98, 1.39) 0.0762	0.04 (0.01, 0.07)*0.0170	
	ACEi+ARB at baseline						0.4366*
	Yes	639/2029 (31.5)	560/2047 (27.4)	1.15 (1.05, 1.27)*0.0038	1.20 (1.03, 1.39) 0.0207	0.04 (0.01, 0.07)*0.0037	
	No	204/ 763 (26.7)	187/ 745 (25.1)	1.07 (0.90, 1.26)*0.4688	1.06 (0.82, 1.37) 0.6601	0.02 (-0.03, 0.06)*0.4684	
	ARNI at baseline						0.8779*
	Yes	36/ 150 (24.0)	27/ 123 (22.0)	1.09 (0.71, 1.69)*0.6899	1.35 (0.70, 2.62) 0.3695	0.02 (-0.08, 0.12)*0.6883	
	No	807/2642 (30.5)	720/2669 (27.0)	1.13 (1.04, 1.23)*0.0041	1.16 (1.01, 1.32) 0.0327	0.04 (0.01, 0.06)*0.0040	
	Beta Blocker at baseline						0.7163*
	Yes	709/2323 (30.5)	632/2321 (27.2)	1.12 (1.02, 1.23)*0.0135	1.13 (0.98, 1.30) 0.0884	0.03 (0.01, 0.06)*0.0133	
	No	134/ 469 (28.6)	115/ 471 (24.4)	1.17 (0.94, 1.45)*0.1497	1.31 (0.95, 1.82) 0.1029	0.04 (-0.01, 0.10)*0.1485	
	Diuretics at baseline						0.1985*
	Yes	768/2493 (30.8)	668/2492 (26.8)	1.15 (1.05, 1.25)*0.0019	1.20 (1.05, 1.38) 0.0083	0.04 (0.01, 0.07)*0.0018	
	No	75/ 299 (25.1)	79/ 300 (26.3)	0.95 (0.73, 1.25)*0.7264	0.80 (0.52, 1.22) 0.2991	-0.01 (-0.08, 0.06)*0.7264	

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Quality of Life (LOCF)							
	Overall	1147/2842 (40.4)	1053/2837 (37.1)	1.02 (0.99, 1.04) 0.2801	1.11 (0.98, 1.26) 0.0889	0.03 (0.01, 0.06)*0.0121	
	Age						0.5216*
	<= median	608/1415 (43.0)	595/1482 (40.1)	1.03 (0.98, 1.07) 0.2834	1.13 (0.95, 1.33) 0.1617	0.03 (-0.01, 0.06)*0.1236	
	> median	539/1427 (37.8)	458/1355 (33.8)	1.12 (1.01, 1.23)*0.0294	1.10 (0.92, 1.32) 0.3045	0.04 (0.00, 0.08)*0.0288	
	Gender						0.4663*
	Male	649/1656 (39.2)	598/1625 (36.8)	1.06 (0.98, 1.16)*0.1586	1.07 (0.91, 1.25) 0.4403	0.02 (-0.01, 0.06)*0.1582	
	Female	498/1186 (42.0)	455/1212 (37.5)	1.01 (0.96, 1.06) 0.7266	1.17 (0.97, 1.41) 0.1064	0.04 (0.01, 0.08)*0.0259	
	Race						0.4555*
	White	816/2039 (40.0)	750/2058 (36.4)	1.10 (1.02, 1.19)*0.0186	1.12 (0.97, 1.29) 0.1298	0.04 (0.01, 0.07)*0.0184	
	Black or African	34/ 67 (50.7)	27/ 71 (38.0)	1.25 (0.86, 1.80) 0.2432	1.70 (0.77, 3.74) 0.1867	0.13 (-0.04, 0.29)*0.1298	
	Asian	189/ 558 (33.9)	191/ 555 (34.4)	0.98 (0.84, 1.16)*0.8484	0.95 (0.71, 1.27) 0.7129	-0.01 (-0.06, 0.05)*0.8484	
	Other	108/ 178 (60.7)	85/ 153 (55.6)	1.03 (0.85, 1.24) 0.7639	1.37 (0.83, 2.26) 0.2129	0.05 (-0.06, 0.16)*0.3463	
	Geographic region						0.7381*
	Asia	185/ 539 (34.3)	185/ 538 (34.4)	1.00 (0.85, 1.18)*0.9824	0.96 (0.72, 1.29) 0.7972	-0.00 (-0.06, 0.06)*0.9824	
	Europe and Saudi Arabia	541/1365 (39.6)	503/1394 (36.1)	1.10 (1.00, 1.21)*0.0547	1.13 (0.95, 1.35) 0.1729	0.04 (-0.00, 0.07)*0.0544	
	North America	158/ 398 (39.7)	139/ 387 (35.9)	1.08 (0.95, 1.24) 0.2433	1.12 (0.81, 1.56) 0.4868	0.04 (-0.03, 0.11)*0.2743	
	Latin America	263/ 540 (48.7)	226/ 518 (43.6)	1.12 (0.98, 1.27)*0.0989	1.22 (0.92, 1.61) 0.1705	0.05 (-0.01, 0.11)*0.0975	
	NYHA class at enrolment						0.2898*
	II	811/2113 (38.4)	792/2187 (36.2)	1.06 (0.98, 1.15)*0.1418	1.10 (0.95, 1.27) 0.1973	0.02 (-0.01, 0.05)*0.1417	
	III or IV	336/ 729 (46.1)	261/ 649 (40.2)	1.04 (0.96, 1.12) 0.3023	1.22 (0.95, 1.55) 0.1156	0.06 (0.01, 0.11)*0.0276	
	LVEF at enrolment						0.1446*
	<= 49	405/ 980 (41.3)	387/ 963 (40.2)	0.99 (0.94, 1.05) 0.7906	1.07 (0.87, 1.31) 0.5248	0.01 (-0.03, 0.06)*0.6092	
	50-59	421/1029 (40.9)	350/1017 (34.4)	1.19 (1.06, 1.33)*0.0025	1.29 (1.05, 1.59) 0.0157	0.06 (0.02, 0.11)*0.0024	
	>= 60	321/ 833 (38.5)	316/ 857 (36.9)	1.05 (0.92, 1.18)*0.4808	0.98 (0.78, 1.23) 0.8419	0.02 (-0.03, 0.06)*0.4807	
	NT-proBNP at enrolment						0.9014*
	<= median	568/1418 (40.1)	521/1421 (36.7)	1.09 (1.00, 1.20)*0.0633	1.11 (0.93, 1.32) 0.2455	0.03 (-0.00, 0.07)*0.0629	
	> median	579/1424 (40.7)	531/1415 (37.5)	1.00 (0.97, 1.04) 0.8183	1.12 (0.94, 1.33) 0.2078	0.03 (-0.00, 0.07)*0.0869	
	Type 2 Diabetes Medical History						0.5190
	Yes	516/1250 (41.3)	452/1260 (35.9)	1.03 (0.97, 1.11) 0.3250	1.26 (1.07, 1.48)*0.0054	0.05 (0.02, 0.09)*0.0053	
	No	631/1592 (39.6)	601/1577 (38.1)	1.01 (0.98, 1.04) 0.4457	1.07 (0.92, 1.23)*0.3785	0.02 (-0.02, 0.05)*0.3784	
	Atrial fibrillation or flutter at enrolment ECG						0.7586
	Yes	495/1199 (41.3)	442/1199 (36.9)	1.12 (1.01, 1.24)*0.0268	1.17 (0.97, 1.42) 0.1024	0.04 (0.01, 0.08)*0.0264	
	No	652/1643 (39.7)	611/1638 (37.3)	1.06 (0.98, 1.16)*0.1611	1.07 (0.91, 1.26) 0.3986	0.02 (-0.01, 0.06)*0.1608	
	BMI (kg/m2) at enrolment						0.5452*
	< 30	604/1571 (38.4)	561/1559 (36.0)	1.00 (0.97, 1.03) 0.9497	1.04 (0.88, 1.23) 0.6528	0.02 (-0.01, 0.06)*0.1540	
	>= 30	543/1270 (42.8)	490/1275 (38.4)	1.11 (1.01, 1.22)*0.0265	1.20 (1.00, 1.44) 0.0452	0.04 (0.01, 0.08)*0.0262	
	Baseline eGFR (mL/min/1.73m^2)						0.9047*
	< 60	520/1359 (38.3)	490/1396 (35.1)	1.09 (0.99, 1.20)*0.0851	1.15 (0.96, 1.38) 0.1242	0.03 (-0.00, 0.07)*0.0849	
	>= 60	627/1483 (42.3)	563/1440 (39.1)	1.02 (0.98, 1.07) 0.3244	1.07 (0.90, 1.27) 0.4279	0.03 (-0.00, 0.07)*0.0798	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.1262*
	<= median	605/1424 (42.5)	535/1439 (37.2)	1.01 (0.97, 1.05) 0.7340	1.20 (1.01, 1.43) 0.0410	0.05 (0.02, 0.09)*0.0037	
	> median	542/1418 (38.2)	518/1398 (37.1)	1.03 (0.94, 1.13)*0.5218	1.03 (0.87, 1.23) 0.7098	0.01 (-0.02, 0.05)*0.5217	
	LVEF at enrolment 2						0.2104*
	<= 49	405/ 980 (41.3)	387/ 963 (40.2)	0.99 (0.94, 1.05) 0.7906	1.07 (0.87, 1.31) 0.5248	0.01 (-0.03, 0.06)*0.6092	
	>= 50	742/1862 (39.8)	666/1874 (35.5)	1.12 (1.03, 1.22)*0.0066	1.14 (0.97, 1.32) 0.1042	0.04 (0.01, 0.07)*0.0065	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8696*
	Yes	144/ 283 (50.9)	132/ 286 (46.2)	1.10 (0.93, 1.31)*0.2596	1.20 (0.82, 1.75) 0.3529	0.05 (-0.03, 0.13)*0.2585	
	No	1003/2559 (39.2)	921/2551 (36.1)	1.02 (0.99, 1.05) 0.2139	1.11 (0.97, 1.26) 0.1294	0.03 (0.00, 0.06)*0.0225	
	MRAs at baseline						0.4095*
	Yes	504/1227 (41.1)	448/1224 (36.6)	1.00 (0.94, 1.07) 0.9946	1.21 (1.01, 1.46) 0.0427	0.04 (0.01, 0.08)*0.0229	
	No	643/1615 (39.8)	605/1613 (37.5)	1.06 (0.97, 1.16)*0.1787	1.04 (0.88, 1.23) 0.6515	0.02 (-0.01, 0.06)*0.1783	
	ACEi+ARB at baseline						0.7529*
	Yes	840/2065 (40.7)	772/2077 (37.2)	1.09 (1.01, 1.18)*0.0207	1.14 (0.99, 1.32) 0.0705	0.04 (0.01, 0.06)*0.0205	
	No	307/ 777 (39.5)	281/ 760 (37.0)	1.00 (0.94, 1.07) 0.8818	1.04 (0.82, 1.32) 0.7351	0.03 (-0.02, 0.07)*0.3059	
	ARNI at baseline						0.5156
	Yes	57/ 153 (37.3)	41/ 126 (32.5)	0.97 (0.70, 1.34) 0.8592	1.10 (0.63, 1.91) 0.7354	0.05 (-0.06, 0.16)*0.4096	
	No	1090/2689 (40.5)	1012/2711 (37.3)	1.02 (0.99, 1.05) 0.2086	1.12 (0.99, 1.27) 0.0758	0.03 (0.01, 0.06)*0.0156	
	Beta Blocker at baseline						0.6205*
	Yes	947/2360 (40.1)	876/2356 (37.2)	1.08 (1.00, 1.16)*0.0379	1.08 (0.94, 1.23) 0.2845	0.03 (0.00, 0.06)*0.0377	
	No	200/ 482 (41.5)	177/ 481 (36.8)	1.10 (0.97, 1.24) 0.1301	1.31 (0.97, 1.77) 0.0788	0.05 (-0.01, 0.11)*0.1351	
	Diuretics at baseline						0.9852*
	Yes	1020/2536 (40.2)	936/2531 (37.0)	1.02 (0.99, 1.05) 0.2765	1.13 (0.99, 1.29) 0.0657	0.03 (0.01, 0.06)*0.0178	
	No	127/ 306 (41.5)	117/ 306 (38.2)	1.09 (0.89, 1.32)*0.4094	0.98 (0.67, 1.42) 0.8978	0.03 (-0.04, 0.11)*0.4088	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	1075/2842 (37.8)	985/2837 (34.7)	1.09 (1.02, 1.17)*0.0150	1.15 (1.01, 1.31) 0.0323	0.03 (0.01, 0.06)*0.0149	
	Age						0.8934*
	<= median	576/1415 (40.7)	554/1482 (37.4)	1.09 (0.99, 1.19)*0.0667	1.24 (1.03, 1.48) 0.0199	0.03 (-0.00, 0.07)*0.0666	
	> median	499/1427 (35.0)	431/1355 (31.8)	1.10 (0.99, 1.22)*0.0778	1.09 (0.91, 1.32) 0.3501	0.03 (-0.00, 0.07)*0.0770	
	Gender						0.9681*
	Male	590/1656 (35.6)	530/1625 (32.6)	1.09 (0.99, 1.20)*0.0691	1.15 (0.97, 1.37) 0.1167	0.03 (-0.00, 0.06)*0.0686	
	Female	485/1186 (40.9)	455/1212 (37.5)	1.09 (0.99, 1.20)*0.0929	1.15 (0.95, 1.39) 0.1611	0.03 (-0.01, 0.07)*0.0926	
	Race						0.4893*
	White	804/2039 (39.4)	747/2058 (36.3)	1.09 (1.00, 1.18)*0.0388	1.12 (0.96, 1.29) 0.1428	0.03 (0.00, 0.06)*0.0386	
	Black or African	28/ 67 (41.8)	31/ 71 (43.7)	0.96 (0.65, 1.41)*0.8244	0.86 (0.40, 1.87) 0.7120	-0.02 (-0.18, 0.15)*0.8242	
	Asian	141/ 558 (25.3)	137/ 555 (24.7)	1.02 (0.84, 1.25)*0.8219	1.17 (0.83, 1.65) 0.3695	0.01 (-0.05, 0.06)*0.8219	
	Other	102/ 178 (57.3)	70/ 153 (45.8)	1.25 (1.01, 1.55)*0.0393	1.83 (1.09, 3.06) 0.0222	0.12 (0.01, 0.22)*0.0348	
	Geographic region						0.7190*
	Asia	137/ 539 (25.4)	133/ 538 (24.7)	1.03 (0.84, 1.26)*0.7921	1.12 (0.79, 1.59) 0.5186	0.01 (-0.04, 0.06)*0.7921	
	Europe and Saudi Arabia	546/1365 (40.0)	507/1394 (36.4)	1.10 (1.00, 1.21)*0.0499	1.15 (0.95, 1.38) 0.1433	0.04 (0.00, 0.07)*0.0496	
	North America	145/ 398 (36.4)	119/ 387 (30.7)	1.18 (0.97, 1.44)*0.0932	1.29 (0.93, 1.81) 0.1316	0.06 (-0.01, 0.12)*0.0912	
	Latin America	247/ 540 (45.7)	226/ 518 (43.6)	1.05 (0.92, 1.20)*0.4902	1.12 (0.84, 1.49) 0.4354	0.02 (-0.04, 0.08)*0.4897	
	NYHA class at enrolment						0.1164*
	II	715/2113 (33.8)	710/2187 (32.5)	1.04 (0.96, 1.13)*0.3388	1.09 (0.94, 1.28) 0.2457	0.01 (-0.01, 0.04)*0.3388	
	III or IV	360/ 729 (49.4)	274/ 649 (42.2)	1.17 (1.04, 1.31)*0.0082	1.36 (1.07, 1.73) 0.0127	0.07 (0.02, 0.12)*0.0075	
	LVEF at enrolment						0.1615*
	<= 49	363/ 980 (37.0)	358/ 963 (37.2)	1.00 (0.89, 1.12)*0.9510	1.02 (0.82, 1.27) 0.8362	-0.00 (-0.04, 0.04)*0.9510	
	50-59	387/1029 (37.6)	340/1017 (33.4)	1.12 (1.00, 1.26)*0.0488	1.21 (0.97, 1.50) 0.0928	0.04 (0.00, 0.08)*0.0481	
	>= 60	325/ 833 (39.0)	287/ 857 (33.5)	1.17 (1.03, 1.32)*0.0183	1.24 (0.99, 1.57) 0.0646	0.06 (0.01, 0.10)*0.0180	
	NT-proBNP at enrolment						0.2294*
	<= median	495/1418 (34.9)	476/1421 (33.5)	1.04 (0.94, 1.15)*0.4283	1.08 (0.90, 1.29) 0.4045	0.01 (-0.02, 0.05)*0.4281	
	> median	580/1424 (40.7)	508/1415 (35.9)	1.13 (1.03, 1.25)*0.0083	1.23 (1.02, 1.48) 0.0288	0.05 (0.01, 0.08)*0.0081	
	Type 2 Diabetes Medical History						0.5181*
	Yes	491/1250 (39.3)	443/1260 (35.2)	1.12 (1.01, 1.24)*0.0329	1.19 (1.01, 1.40)*0.0328	0.04 (0.00, 0.08)*0.0326	
	No	584/1592 (36.7)	542/1577 (34.4)	1.07 (0.97, 1.17)*0.1737	1.11 (0.96, 1.28)*0.1736	0.02 (-0.01, 0.06)*0.1733	
	Atrial fibrillation or flutter at enrolment ECG						0.8588*
	Yes	474/1199 (39.5)	432/1199 (36.0)	1.10 (0.99, 1.22)*0.0772	1.19 (0.98, 1.45) 0.0818	0.04 (-0.00, 0.07)*0.0767	
	No	601/1643 (36.6)	553/1638 (33.8)	1.08 (0.99, 1.19)*0.0911	1.12 (0.95, 1.33) 0.1839	0.03 (-0.00, 0.06)*0.0908	
	BMI (kg/m2) at enrolment						0.5493*
	< 30	541/1571 (34.4)	482/1559 (30.9)	1.11 (1.01, 1.23)*0.0361	1.20 (1.00, 1.45) 0.0474	0.04 (0.00, 0.07)*0.0357	
	>= 30	534/1270 (42.0)	502/1275 (39.4)	1.07 (0.97, 1.17)*0.1699	1.11 (0.92, 1.33) 0.2711	0.03 (-0.01, 0.06)*0.1695	
	Baseline eGFR (mL/min/1.73m^2)						0.7139*
	< 60	498/1359 (36.6)	476/1396 (34.1)	1.07 (0.97, 1.19)*0.1622	1.12 (0.93, 1.34) 0.2382	0.03 (-0.01, 0.06)*0.1620	
	>= 60	577/1483 (38.9)	508/1440 (35.3)	1.10 (1.00, 1.21)*0.0426	1.18 (0.99, 1.42) 0.0664	0.04 (0.00, 0.07)*0.0421	

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Symptom Burden (LOCF)	SBP at randomisation						0.0172*
	<= median	546/1424 (38.3)	465/1439 (32.3)	1.19 (1.07, 1.31)*0.0008	1.27 (1.06, 1.52) 0.0110	0.06 (0.03, 0.10)*0.0007	
	> median	529/1418 (37.3)	520/1398 (37.2)	1.00 (0.91, 1.10)*0.9518	1.05 (0.87, 1.26) 0.6268	0.00 (-0.03, 0.04)*0.9518	
	LVEF at enrolment 2						0.0624*
	<= 49	363/ 980 (37.0)	358/ 963 (37.2)	1.00 (0.89, 1.12)*0.9510	1.02 (0.82, 1.27) 0.8362	-0.00 (-0.04, 0.04)*0.9510	
	>= 50	712/1862 (38.2)	627/1874 (33.5)	1.14 (1.05, 1.25)*0.0024	1.22 (1.04, 1.44) 0.0125	0.05 (0.02, 0.08)*0.0023	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5465*
	Yes	145/ 283 (51.2)	141/ 286 (49.3)	1.04 (0.88, 1.22)*0.6443	1.23 (0.82, 1.84) 0.3118	0.02 (-0.06, 0.10)*0.6441	
	No	930/2559 (36.3)	844/2551 (33.1)	1.10 (1.02, 1.18)*0.0146	1.15 (1.00, 1.31) 0.0510	0.03 (0.01, 0.06)*0.0144	
	MRAs at baseline						0.3286*
	Yes	465/1227 (37.9)	409/1224 (33.4)	1.13 (1.02, 1.26)*0.0208	1.21 (1.00, 1.48) 0.0550	0.04 (0.01, 0.08)*0.0204	
	No	610/1615 (37.8)	576/1613 (35.7)	1.06 (0.97, 1.16)*0.2247	1.11 (0.93, 1.31) 0.2389	0.02 (-0.01, 0.05)*0.2245	
	ACEi+ARB at baseline						0.1872*
	Yes	813/2065 (39.4)	730/2077 (35.1)	1.12 (1.03, 1.21)*0.0050	1.20 (1.03, 1.39) 0.0184	0.04 (0.01, 0.07)*0.0049	
	No	262/ 777 (33.7)	255/ 760 (33.6)	1.00 (0.87, 1.16)*0.9448	1.03 (0.80, 1.32) 0.8288	0.00 (-0.05, 0.05)*0.9448	
	ARNI at baseline						0.3890*
	Yes	38/ 153 (24.8)	34/ 126 (27.0)	0.92 (0.62, 1.37)*0.6831	1.03 (0.54, 1.98) 0.9204	-0.02 (-0.12, 0.08)*0.6840	
	No	1037/2689 (38.6)	951/2711 (35.1)	1.10 (1.03, 1.18)*0.0080	1.16 (1.02, 1.32) 0.0281	0.03 (0.01, 0.06)*0.0079	
	Beta Blocker at baseline						0.9162*
	Yes	889/2360 (37.7)	816/2356 (34.6)	1.09 (1.01, 1.17)*0.0302	1.11 (0.96, 1.28) 0.1477	0.03 (0.00, 0.06)*0.0300	
	No	186/ 482 (38.6)	169/ 481 (35.1)	1.10 (0.93, 1.30)*0.2671	1.39 (1.01, 1.90) 0.0444	0.03 (-0.03, 0.10)*0.2663	
	Diuretics at baseline						0.6768*
	Yes	959/2536 (37.8)	883/2531 (34.9)	1.08 (1.01, 1.17)*0.0304	1.17 (1.02, 1.34) 0.0233	0.03 (0.00, 0.06)*0.0302	
	No	116/ 306 (37.9)	102/ 306 (33.3)	1.14 (0.92, 1.41)*0.2382	0.95 (0.63, 1.44) 0.8238	0.05 (-0.03, 0.12)*0.2368	

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Self Efficacy (LOCF)							
	Overall	825/2842 (29.0)	801/2837 (28.2)	1.03 (0.95, 1.12)*0.5077	1.05 (0.91, 1.21) 0.4801	0.01 (-0.02, 0.03)*0.5076	
	Age						0.3478*
	<= median	422/1415 (29.8)	445/1482 (30.0)	0.99 (0.89, 1.11)*0.9048	1.00 (0.82, 1.22) 0.9951	-0.00 (-0.04, 0.03)*0.9047	
	> median	403/1427 (28.2)	356/1355 (26.3)	1.07 (0.95, 1.21)*0.2445	1.13 (0.92, 1.39) 0.2475	0.02 (-0.01, 0.05)*0.2437	
	Gender						0.1218*
	Male	472/1656 (28.5)	476/1625 (29.3)	0.97 (0.87, 1.08)*0.6177	0.97 (0.81, 1.17) 0.7478	-0.01 (-0.04, 0.02)*0.6177	
	Female	353/1186 (29.8)	325/1212 (26.8)	1.11 (0.98, 1.26)*0.1092	1.18 (0.94, 1.48) 0.1449	0.03 (-0.01, 0.07)*0.1088	
	Race						0.3009*
	White	582/2039 (28.5)	565/2058 (27.5)	1.04 (0.94, 1.15)*0.4374	1.05 (0.89, 1.24) 0.5583	0.01 (-0.02, 0.04)*0.4374	
	Black or African	19/ 67 (28.4)	23/ 71 (32.4)	0.88 (0.53, 1.45)*0.6075	0.72 (0.25, 2.11) 0.5516	-0.04 (-0.19, 0.11)*0.6058	
	Asian	152/ 558 (27.2)	164/ 555 (29.5)	0.92 (0.76, 1.11)*0.3932	0.92 (0.67, 1.29) 0.6414	-0.02 (-0.08, 0.03)*0.3928	
	Other	72/ 178 (40.4)	49/ 153 (32.0)	1.26 (0.94, 1.69)*0.1166	1.85 (1.04, 3.30) 0.0363	0.08 (-0.02, 0.19)*0.1099	
	Geographic region						0.0244*
	Asia	144/ 539 (26.7)	158/ 538 (29.4)	0.91 (0.75, 1.10)*0.3331	0.92 (0.66, 1.29) 0.6476	-0.03 (-0.08, 0.03)*0.3325	
	Europe and Saudi Arabia	395/1365 (28.9)	399/1394 (28.6)	1.01 (0.90, 1.14)*0.8550	1.01 (0.83, 1.24) 0.8873	0.00 (-0.03, 0.04)*0.8550	
	North America	85/ 398 (21.4)	94/ 387 (24.3)	0.88 (0.68, 1.14)*0.3280	0.71 (0.44, 1.13) 0.1489	-0.03 (-0.09, 0.03)*0.3275	
	Latin America	201/ 540 (37.2)	150/ 518 (29.0)	1.29 (1.08, 1.53)*0.0046	1.58 (1.14, 2.18) 0.0055	0.08 (0.03, 0.14)*0.0041	
	NYHA class at enrolment						0.7617*
	II	599/2113 (28.3)	609/2187 (27.8)	1.02 (0.93, 1.12)*0.7143	1.04 (0.88, 1.23) 0.6534	0.01 (-0.02, 0.03)*0.7143	
	III or IV	226/ 729 (31.0)	192/ 649 (29.6)	1.05 (0.89, 1.23)*0.5681	1.11 (0.84, 1.46) 0.4768	0.01 (-0.03, 0.06)*0.5674	
	LVEF at enrolment						0.2026*
	<= 49	270/ 980 (27.6)	286/ 963 (29.7)	0.93 (0.81, 1.07)*0.2951	0.94 (0.74, 1.19) 0.6007	-0.02 (-0.06, 0.02)*0.2949	
	50-59	297/1029 (28.9)	273/1017 (26.8)	1.08 (0.94, 1.24)*0.3086	1.13 (0.89, 1.43) 0.3138	0.02 (-0.02, 0.06)*0.3082	
	>= 60	258/ 833 (31.0)	242/ 857 (28.2)	1.10 (0.95, 1.27)*0.2185	1.10 (0.85, 1.43) 0.4714	0.03 (-0.02, 0.07)*0.2182	
	NT-proBNP at enrolment						0.7860*
	<= median	404/1418 (28.5)	398/1421 (28.0)	1.02 (0.90, 1.14)*0.7753	0.99 (0.81, 1.21) 0.9127	0.00 (-0.03, 0.04)*0.7753	
	> median	421/1424 (29.6)	402/1415 (28.4)	1.04 (0.93, 1.17)*0.4978	1.13 (0.92, 1.39) 0.2337	0.01 (-0.02, 0.04)*0.4977	
	Type 2 Diabetes Medical History						0.2980*
	Yes	381/1250 (30.5)	356/1260 (28.3)	1.08 (0.96, 1.22)*0.2210	1.11 (0.94, 1.32)*0.2209	0.02 (-0.01, 0.06)*0.2207	
	No	444/1592 (27.9)	445/1577 (28.2)	0.99 (0.88, 1.10)*0.8368	0.98 (0.84, 1.15)*0.8368	-0.00 (-0.03, 0.03)*0.8368	
	Atrial fibrillation or flutter at enrolment ECG						0.1621*
	Yes	358/1199 (29.9)	325/1199 (27.1)	1.10 (0.97, 1.25)*0.1357	1.14 (0.92, 1.42) 0.2292	0.03 (-0.01, 0.06)*0.1352	
	No	467/1643 (28.4)	476/1638 (29.1)	0.98 (0.88, 1.09)*0.6872	0.99 (0.82, 1.20) 0.9395	-0.01 (-0.04, 0.02)*0.6872	
	BMI (kg/m2) at enrolment						0.4312*
	< 30	424/1571 (27.0)	422/1559 (27.1)	1.00 (0.89, 1.12)*0.9601	0.96 (0.79, 1.16) 0.6578	-0.00 (-0.03, 0.03)*0.9601	
	>= 30	401/1270 (31.6)	378/1275 (29.6)	1.07 (0.95, 1.20)*0.2916	1.18 (0.96, 1.46) 0.1198	0.02 (-0.02, 0.06)*0.2913	
	Baseline eGFR (mL/min/1.73m^2)						0.4644*
	< 60	379/1359 (27.9)	391/1396 (28.0)	1.00 (0.88, 1.12)*0.9439	1.09 (0.89, 1.34) 0.3914	-0.00 (-0.03, 0.03)*0.9438	
	>= 60	446/1483 (30.1)	409/1440 (28.4)	1.06 (0.95, 1.19)*0.3209	1.02 (0.84, 1.24) 0.8522	0.02 (-0.02, 0.05)*0.3205	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.9491*
	<= median	413/1424 (29.0)	407/1439 (28.3)	1.03 (0.91, 1.15)*0.6704	1.06 (0.86, 1.30) 0.5988	0.01 (-0.03, 0.04)*0.6704	
	> median	412/1418 (29.1)	394/1398 (28.2)	1.03 (0.92, 1.16)*0.6088	1.05 (0.86, 1.28) 0.6199	0.01 (-0.02, 0.04)*0.6087	
	LVEF at enrolment 2						0.0770*
	<= 49	270/ 980 (27.6)	286/ 963 (29.7)	0.93 (0.81, 1.07)*0.2951	0.94 (0.74, 1.19) 0.6007	-0.02 (-0.06, 0.02)*0.2949	
	>= 50	555/1862 (29.8)	515/1874 (27.5)	1.08 (0.98, 1.20)*0.1162	1.12 (0.94, 1.33) 0.2161	0.02 (-0.01, 0.05)*0.1159	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8969*
	Yes	95/ 283 (33.6)	92/ 286 (32.2)	1.04 (0.83, 1.32)*0.7221	1.16 (0.75, 1.80) 0.5034	0.01 (-0.06, 0.09)*0.7220	
	No	730/2559 (28.5)	709/2551 (27.8)	1.03 (0.94, 1.12)*0.5599	1.04 (0.89, 1.21) 0.6135	0.01 (-0.02, 0.03)*0.5598	
	MRAs at baseline						0.5361*
	Yes	345/1227 (28.1)	345/1224 (28.2)	1.00 (0.88, 1.13)*0.9697	1.03 (0.83, 1.28) 0.7866	-0.00 (-0.04, 0.03)*0.9697	
	No	480/1615 (29.7)	456/1613 (28.3)	1.05 (0.94, 1.17)*0.3637	1.07 (0.88, 1.29) 0.4915	0.01 (-0.02, 0.05)*0.3636	
	ACEi+ARB at baseline						0.1895*
	Yes	614/2065 (29.7)	581/2077 (28.0)	1.06 (0.97, 1.17)*0.2113	1.13 (0.96, 1.33) 0.1490	0.02 (-0.01, 0.05)*0.2111	
	No	211/ 777 (27.2)	220/ 760 (28.9)	0.94 (0.80, 1.10)*0.4344	0.86 (0.65, 1.14) 0.2866	-0.02 (-0.06, 0.03)*0.4343	
	ARNI at baseline						0.1500*
	Yes	28/ 153 (18.3)	31/ 126 (24.6)	0.74 (0.47, 1.17)*0.2007	0.64 (0.30, 1.37) 0.2484	-0.06 (-0.16, 0.03)*0.2029	
	No	797/2689 (29.6)	770/2711 (28.4)	1.04 (0.96, 1.13)*0.3169	1.08 (0.93, 1.24) 0.3202	0.01 (-0.01, 0.04)*0.3168	
	Beta Blocker at baseline						0.6695*
	Yes	671/2360 (28.4)	657/2356 (27.9)	1.02 (0.93, 1.12)*0.6768	1.04 (0.89, 1.22) 0.6088	0.01 (-0.02, 0.03)*0.6768	
	No	154/ 482 (32.0)	144/ 481 (29.9)	1.07 (0.88, 1.29)*0.4995	1.10 (0.80, 1.53) 0.5606	0.02 (-0.04, 0.08)*0.4992	
	Diuretics at baseline						0.6692*
	Yes	733/2536 (28.9)	707/2531 (27.9)	1.03 (0.95, 1.13)*0.4440	1.08 (0.93, 1.25) 0.3387	0.01 (-0.02, 0.03)*0.4439	
	No	92/ 306 (30.1)	94/ 306 (30.7)	0.98 (0.77, 1.24)*0.8605	0.89 (0.58, 1.37) 0.5968	-0.01 (-0.08, 0.07)*0.8605	

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AstraZeneca
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Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	937/2842 (33.0)	884/2837 (31.2)	1.06 (0.98, 1.14)*0.1441	1.09 (0.95, 1.24) 0.2091	0.02 (-0.01, 0.04)*0.1439	
	Age						0.9631*
	<= median	484/1415 (34.2)	479/1482 (32.3)	1.06 (0.95, 1.17)*0.2820	1.15 (0.96, 1.38) 0.1262	0.02 (-0.02, 0.05)*0.2820	
	> median	453/1427 (31.7)	405/1355 (29.9)	1.06 (0.95, 1.19)*0.2898	1.04 (0.86, 1.25) 0.7190	0.02 (-0.02, 0.05)*0.2892	
	Gender						0.5130*
	Male	498/1656 (30.1)	472/1625 (29.0)	1.04 (0.93, 1.15)*0.5196	1.06 (0.88, 1.26) 0.5437	0.01 (-0.02, 0.04)*0.5194	
	Female	439/1186 (37.0)	412/1212 (34.0)	1.09 (0.98, 1.21)*0.1223	1.12 (0.93, 1.36) 0.2366	0.03 (-0.01, 0.07)*0.1219	
	Race						0.4114*
	White	695/2039 (34.1)	651/2058 (31.6)	1.08 (0.99, 1.18)*0.0948	1.08 (0.93, 1.26) 0.3256	0.02 (-0.00, 0.05)*0.0946	
	Black or African	26/ 67 (38.8)	29/ 71 (40.8)	0.95 (0.63, 1.43)*0.8070	0.99 (0.47, 2.08) 0.9687	-0.02 (-0.18, 0.14)*0.8067	
	Asian	128/ 558 (22.9)	139/ 555 (25.0)	0.92 (0.74, 1.13)*0.4110	0.97 (0.69, 1.35) 0.8396	-0.02 (-0.07, 0.03)*0.4106	
	Other	88/ 178 (49.4)	65/ 153 (42.5)	1.16 (0.92, 1.47)*0.2095	1.64 (0.96, 2.78) 0.0690	0.07 (-0.04, 0.18)*0.2043	
	Geographic region						0.6531*
	Asia	125/ 539 (23.2)	133/ 538 (24.7)	0.94 (0.76, 1.16)*0.5565	0.97 (0.69, 1.37) 0.8526	-0.02 (-0.07, 0.04)*0.5563	
	Europe and Saudi Arabia	457/1365 (33.5)	437/1394 (31.3)	1.07 (0.96, 1.19)*0.2319	1.05 (0.86, 1.27) 0.6500	0.02 (-0.01, 0.06)*0.2317	
	North America	123/ 398 (30.9)	113/ 387 (29.2)	1.07 (0.90, 1.28) 0.4521	1.15 (0.82, 1.60) 0.4219	0.02 (-0.05, 0.08)*0.6022	
	Latin America	232/ 540 (43.0)	201/ 518 (38.8)	1.11 (0.96, 1.28)*0.1698	1.28 (0.96, 1.71) 0.0953	0.04 (-0.02, 0.10)*0.1684	
	NYHA class at enrolment						0.7864*
	II	620/2113 (29.3)	618/2187 (28.3)	1.04 (0.95, 1.14)*0.4324	1.10 (0.94, 1.29) 0.2157	0.01 (-0.02, 0.04)*0.4325	
	III or IV	317/ 729 (43.5)	266/ 649 (41.0)	1.06 (0.94, 1.20)*0.3496	1.07 (0.84, 1.36) 0.5702	0.02 (-0.03, 0.08)*0.3484	
	LVEF at enrolment						0.6639*
	<= 49	316/ 980 (32.2)	297/ 963 (30.8)	1.05 (0.92, 1.19)*0.5057	1.16 (0.92, 1.46) 0.2051	0.01 (-0.03, 0.06)*0.5055	
	50-59	334/1029 (32.5)	322/1017 (31.7)	1.03 (0.90, 1.16)*0.6994	1.00 (0.80, 1.24) 0.9860	0.01 (-0.03, 0.05)*0.6993	
	>= 60	287/ 833 (34.5)	265/ 857 (30.9)	1.11 (0.97, 1.28)*0.1220	1.13 (0.89, 1.44) 0.3129	0.04 (-0.01, 0.08)*0.1215	
	NT-proBNP at enrolment						0.9047*
	<= median	432/1418 (30.5)	411/1421 (28.9)	1.05 (0.94, 1.18)*0.3687	1.11 (0.92, 1.34) 0.2706	0.02 (-0.02, 0.05)*0.3685	
	> median	505/1424 (35.5)	472/1415 (33.4)	1.06 (0.96, 1.18)*0.2377	1.07 (0.89, 1.28) 0.4891	0.02 (-0.01, 0.06)*0.2373	
	Type 2 Diabetes Medical History						0.8392*
	Yes	431/1250 (34.5)	407/1260 (32.3)	1.07 (0.96, 1.19)*0.2474	1.10 (0.93, 1.30)*0.2473	0.02 (-0.02, 0.06)*0.2471	
	No	506/1592 (31.8)	477/1577 (30.2)	1.05 (0.95, 1.17)*0.3499	1.07 (0.92, 1.25)*0.3498	0.02 (-0.02, 0.05)*0.3497	
	Atrial fibrillation or flutter at enrolment ECG						0.2331*
	Yes	404/1199 (33.7)	402/1199 (33.5)	1.00 (0.90, 1.12)*0.9311	0.98 (0.81, 1.20) 0.8720	0.00 (-0.04, 0.04)*0.9311	
	No	533/1643 (32.4)	482/1638 (29.4)	1.10 (1.00, 1.22)*0.0620	1.17 (0.99, 1.40) 0.0696	0.03 (-0.00, 0.06)*0.0616	
	BMI (kg/m2) at enrolment						0.9697*
	< 30	470/1571 (29.9)	441/1559 (28.3)	1.06 (0.95, 1.18)*0.3157	1.11 (0.92, 1.34) 0.2667	0.02 (-0.02, 0.05)*0.3154	
	>= 30	467/1270 (36.8)	442/1275 (34.7)	1.06 (0.96, 1.18)*0.2680	1.08 (0.89, 1.30) 0.4384	0.02 (-0.02, 0.06)*0.2677	
	Baseline eGFR (mL/min/1.73m^2)						0.8697*
	< 60	446/1359 (32.8)	436/1396 (31.2)	1.05 (0.94, 1.17)*0.3723	1.08 (0.90, 1.30) 0.4265	0.02 (-0.02, 0.05)*0.3723	
	>= 60	491/1483 (33.1)	448/1440 (31.1)	1.06 (0.96, 1.18)*0.2479	1.09 (0.91, 1.31) 0.3527	0.02 (-0.01, 0.05)*0.2474	

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Symptom Frequency (LOCF)	SBP at randomisation						0.4278*
	<= median	458/1424 (32.2)	424/1439 (29.5)	1.09 (0.98, 1.22)*0.1182	1.08 (0.90, 1.31) 0.3959	0.03 (-0.01, 0.06)*0.1179	
	> median	479/1418 (33.8)	460/1398 (32.9)	1.03 (0.92, 1.14)*0.6221	1.09 (0.90, 1.31) 0.3730	0.01 (-0.03, 0.04)*0.6221	
	LVEF at enrolment 2						0.8241*
	<= 49	316/ 980 (32.2)	297/ 963 (30.8)	1.05 (0.92, 1.19)*0.5057	1.16 (0.92, 1.46) 0.2051	0.01 (-0.03, 0.06)*0.5055	
	>= 50	621/1862 (33.4)	587/1874 (31.3)	1.06 (0.97, 1.17)*0.1853	1.06 (0.90, 1.24) 0.5074	0.02 (-0.01, 0.05)*0.1851	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8291*
	Yes	140/ 283 (49.5)	136/ 286 (47.6)	1.04 (0.88, 1.23)*0.6473	1.44 (0.96, 2.14) 0.0768	0.02 (-0.06, 0.10)*0.6472	
	No	797/2559 (31.1)	748/2551 (29.3)	1.06 (0.98, 1.15)*0.1561	1.06 (0.92, 1.22) 0.4035	0.02 (-0.01, 0.04)*0.1559	
	MRAs at baseline						0.8750*
	Yes	396/1227 (32.3)	376/1224 (30.7)	1.05 (0.93, 1.18)*0.4074	1.06 (0.87, 1.31) 0.5447	0.02 (-0.02, 0.05)*0.4073	
	No	541/1615 (33.5)	508/1613 (31.5)	1.06 (0.96, 1.17)*0.2243	1.11 (0.93, 1.31) 0.2525	0.02 (-0.01, 0.05)*0.2240	
	ACEi+ARB at baseline						0.0590*
	Yes	713/2065 (34.5)	649/2077 (31.2)	1.10 (1.01, 1.21)*0.0248	1.15 (0.99, 1.34) 0.0682	0.03 (0.00, 0.06)*0.0245	
	No	224/ 777 (28.8)	235/ 760 (30.9)	0.93 (0.80, 1.09)*0.3704	0.92 (0.72, 1.19) 0.5472	-0.02 (-0.07, 0.02)*0.3702	
	ARNI at baseline						0.3745*
	Yes	33/ 153 (21.6)	31/ 126 (24.6)	0.88 (0.57, 1.35)*0.5483	1.24 (0.62, 2.50) 0.5426	-0.03 (-0.13, 0.07)*0.5501	
	No	904/2689 (33.6)	853/2711 (31.5)	1.07 (0.99, 1.15)*0.0913	1.09 (0.95, 1.24) 0.2225	0.02 (-0.00, 0.05)*0.0911	
	Beta Blocker at baseline						0.8245*
	Yes	776/2360 (32.9)	735/2356 (31.2)	1.05 (0.97, 1.15)*0.2153	1.04 (0.90, 1.20) 0.6086	0.02 (-0.01, 0.04)*0.2151	
	No	161/ 482 (33.4)	149/ 481 (31.0)	1.08 (0.90, 1.30)*0.4208	1.36 (0.99, 1.88) 0.0595	0.02 (-0.03, 0.08)*0.4204	
	Diuretics at baseline						0.3060*
	Yes	827/2536 (32.6)	791/2531 (31.3)	1.04 (0.96, 1.13)*0.3000	1.09 (0.95, 1.25) 0.2391	0.01 (-0.01, 0.04)*0.2998	
	No	110/ 306 (35.9)	93/ 306 (30.4)	1.18 (0.94, 1.48)*0.1456	1.03 (0.68, 1.57) 0.8778	0.06 (-0.02, 0.13)*0.1437	

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Social Limitation (LOCF)							
	Overall	884/2669 (33.1)	845/2664 (31.7)	1.03 (0.98, 1.09) 0.1999	1.07 (0.94, 1.22) 0.3232	0.01 (-0.01, 0.04)*0.2741	
	Age						0.3331*
	<= median	471/1352 (34.8)	457/1422 (32.1)	1.08 (0.98, 1.20)*0.1321	1.20 (1.00, 1.45) 0.0483	0.03 (-0.01, 0.06)*0.1321	
	> median	413/1317 (31.4)	388/1242 (31.2)	1.02 (0.94, 1.10) 0.6060	0.95 (0.78, 1.15) 0.5909	0.00 (-0.03, 0.04)*0.9482	
	Gender						0.7488
	Male	485/1568 (30.9)	466/1518 (30.7)	1.01 (0.91, 1.12)*0.8886	1.02 (0.85, 1.22) 0.8223	0.00 (-0.03, 0.03)*0.8886	
	Female	399/1101 (36.2)	379/1146 (33.1)	1.03 (0.95, 1.11) 0.4860	1.13 (0.93, 1.38) 0.2189	0.03 (-0.01, 0.07)*0.1145	
	Race						0.7583*
	White	659/1925 (34.2)	627/1952 (32.1)	1.01 (0.96, 1.06) 0.7574	1.07 (0.92, 1.25) 0.4038	0.02 (-0.01, 0.05)*0.1623	
	Black or African	19/ 61 (31.1)	23/ 67 (34.3)	1.07 (0.64, 1.76) 0.8029	0.84 (0.35, 1.99) 0.6901	-0.03 (-0.19, 0.13)*0.7014	
	Asian	129/ 510 (25.3)	132/ 500 (26.4)	0.96 (0.78, 1.18)*0.6881	1.03 (0.74, 1.44) 0.8398	-0.01 (-0.07, 0.04)*0.6881	
	Other	77/ 173 (44.5)	63/ 145 (43.4)	1.10 (0.87, 1.39) 0.4239	1.23 (0.73, 2.06) 0.4329	0.01 (-0.10, 0.12)*0.8495	
	Geographic region						0.8330*
	Asia	126/ 496 (25.4)	128/ 486 (26.3)	0.96 (0.78, 1.19)*0.7382	1.03 (0.73, 1.44) 0.8761	-0.01 (-0.06, 0.05)*0.7382	
	Europe and Saudi Arabia	446/1299 (34.3)	422/1323 (31.9)	1.08 (0.97, 1.20)*0.1851	1.06 (0.88, 1.28) 0.5220	0.02 (-0.01, 0.06)*0.1848	
	North America	114/ 372 (30.6)	105/ 359 (29.2)	1.10 (0.92, 1.32) 0.2860	1.16 (0.81, 1.67) 0.4157	0.01 (-0.05, 0.08)*0.6800	
	Latin America	198/ 502 (39.4)	190/ 496 (38.3)	1.03 (0.88, 1.20)*0.7129	1.06 (0.79, 1.44) 0.6861	0.01 (-0.05, 0.07)*0.7128	
	NYHA class at enrolment						0.6584*
	II	621/1986 (31.3)	627/2059 (30.5)	1.03 (0.94, 1.13)*0.5737	1.07 (0.91, 1.25) 0.3914	0.01 (-0.02, 0.04)*0.5738	
	III or IV	263/ 683 (38.5)	218/ 604 (36.1)	1.05 (0.94, 1.17) 0.3863	1.12 (0.87, 1.44) 0.3831	0.02 (-0.03, 0.08)*0.3712	
	LVEF at enrolment						0.5918
	<= 49	317/ 928 (34.2)	322/ 912 (35.3)	1.01 (0.93, 1.10) 0.8636	1.03 (0.83, 1.28) 0.7935	-0.01 (-0.05, 0.03)*0.6052	
	50-59	316/ 970 (32.6)	270/ 956 (28.2)	1.05 (0.96, 1.15) 0.3151	1.15 (0.91, 1.44) 0.2352	0.04 (0.00, 0.08)*0.0384	
	>= 60	251/ 771 (32.6)	253/ 796 (31.8)	1.02 (0.89, 1.18)*0.7439	1.03 (0.81, 1.32) 0.7914	0.01 (-0.04, 0.05)*0.7439	
	NT-proBNP at enrolment						0.1872*
	<= median	421/1334 (31.6)	430/1350 (31.9)	0.99 (0.89, 1.11)*0.8706	0.99 (0.82, 1.20) 0.9249	-0.00 (-0.04, 0.03)*0.8706	
	> median	463/1335 (34.7)	414/1313 (31.5)	1.06 (0.98, 1.13) 0.1400	1.16 (0.96, 1.40) 0.1282	0.03 (-0.00, 0.07)*0.0848	
	Type 2 Diabetes Medical History						0.7025
	Yes	400/1169 (34.2)	373/1186 (31.5)	1.05 (0.96, 1.14) 0.2738	1.13 (0.95, 1.35)*0.1529	0.03 (-0.01, 0.07)*0.1527	
	No	484/1500 (32.3)	472/1478 (31.9)	1.01 (0.91, 1.12)*0.8463	1.02 (0.87, 1.18)*0.8463	0.00 (-0.03, 0.04)*0.8463	
	Atrial fibrillation or flutter at enrolment ECG						0.3816
	Yes	391/1113 (35.1)	346/1123 (30.8)	1.06 (0.98, 1.15) 0.1542	1.25 (1.02, 1.53) 0.0324	0.04 (0.00, 0.08)*0.0296	
	No	493/1556 (31.7)	499/1541 (32.4)	1.01 (0.94, 1.08) 0.7470	0.95 (0.80, 1.14) 0.6000	-0.01 (-0.04, 0.03)*0.6773	
	BMI (kg/m2) at enrolment						0.5219
	< 30	468/1478 (31.7)	433/1451 (29.8)	1.06 (0.95, 1.18)*0.2854	1.09 (0.91, 1.31) 0.3555	0.02 (-0.02, 0.05)*0.2850	
	>= 30	416/1190 (35.0)	411/1211 (33.9)	1.02 (0.95, 1.09) 0.6316	1.04 (0.86, 1.27) 0.6570	0.01 (-0.03, 0.05)*0.5993	
	Baseline eGFR (mL/min/1.73m^2)						0.8459*
	< 60	407/1266 (32.1)	403/1297 (31.1)	1.03 (0.96, 1.12) 0.3970	1.08 (0.89, 1.30) 0.4487	0.01 (-0.03, 0.05)*0.5577	
	>= 60	477/1403 (34.0)	442/1366 (32.4)	1.05 (0.95, 1.17)*0.3593	1.05 (0.87, 1.27) 0.5935	0.02 (-0.02, 0.05)*0.3590	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)	SBP at randomisation						0.9788
	<= median	453/1344 (33.7)	434/1344 (32.3)	1.03 (0.96, 1.11) 0.3676	1.00 (0.83, 1.20) 0.9943	0.01 (-0.02, 0.05)*0.4357	
	> median	431/1325 (32.5)	411/1320 (31.1)	1.04 (0.93, 1.17)*0.4424	1.15 (0.95, 1.40) 0.1445	0.01 (-0.02, 0.05)*0.4422	
	LVEF at enrolment 2						0.3909
	<= 49	317/ 928 (34.2)	322/ 912 (35.3)	1.01 (0.93, 1.10) 0.8636	1.03 (0.83, 1.28) 0.7935	-0.01 (-0.05, 0.03)*0.6052	
	>= 50	567/1741 (32.6)	523/1752 (29.9)	1.05 (0.98, 1.11) 0.1581	1.09 (0.92, 1.29) 0.3057	0.03 (-0.00, 0.06)*0.0831	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7666*
	Yes	105/ 257 (40.9)	99/ 261 (37.9)	1.08 (0.87, 1.33)*0.4959	1.24 (0.82, 1.89) 0.3078	0.03 (-0.05, 0.11)*0.4956	
	No	779/2412 (32.3)	746/2403 (31.0)	1.04 (0.96, 1.13)*0.3504	1.05 (0.92, 1.21) 0.4686	0.01 (-0.01, 0.04)*0.3503	
	MRAs at baseline						0.4423
	Yes	386/1155 (33.4)	379/1146 (33.1)	1.02 (0.94, 1.10) 0.7058	1.04 (0.85, 1.27) 0.6975	0.00 (-0.04, 0.04)*0.8592	
	No	498/1514 (32.9)	466/1518 (30.7)	1.05 (0.98, 1.12) 0.1320	1.09 (0.92, 1.31) 0.3224	0.02 (-0.01, 0.06)*0.1943	
	ACEi+ARB at baseline						0.1183
	Yes	647/1940 (33.4)	638/1959 (32.6)	1.01 (0.95, 1.06) 0.8308	1.02 (0.87, 1.19) 0.8150	0.01 (-0.02, 0.04)*0.6031	
	No	237/ 729 (32.5)	207/ 705 (29.4)	1.11 (0.99, 1.25) 0.0673	1.22 (0.94, 1.58) 0.1281	0.03 (-0.02, 0.08)*0.1968	
	ARNI at baseline						0.4690*
	Yes	45/ 149 (30.2)	29/ 116 (25.0)	1.21 (0.81, 1.80)*0.3528	1.48 (0.82, 2.70) 0.1964	0.05 (-0.06, 0.16)*0.3448	
	No	839/2520 (33.3)	816/2548 (32.0)	1.03 (0.98, 1.08) 0.3312	1.05 (0.92, 1.21) 0.4636	0.01 (-0.01, 0.04)*0.3356	
	Beta Blocker at baseline						0.6305
	Yes	749/2232 (33.6)	709/2218 (32.0)	1.03 (0.97, 1.08) 0.3088	1.05 (0.91, 1.22) 0.4978	0.02 (-0.01, 0.04)*0.2579	
	No	135/ 437 (30.9)	136/ 446 (30.5)	1.08 (0.95, 1.24) 0.2530	1.16 (0.83, 1.61) 0.3824	0.00 (-0.06, 0.06)*0.8977	
	Diuretics at baseline						0.5260*
	Yes	799/2391 (33.4)	755/2379 (31.7)	1.03 (0.98, 1.09) 0.2352	1.11 (0.97, 1.28) 0.1362	0.02 (-0.01, 0.04)*0.2154	
	No	85/ 278 (30.6)	90/ 285 (31.6)	0.97 (0.76, 1.24)*0.7971	0.73 (0.48, 1.13) 0.1583	-0.01 (-0.09, 0.07)*0.7970	

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AstraZeneca
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Full Analysis Set

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Symptom Stability (LOCF)							
	Overall	767/2842 (27.0)	750/2837 (26.4)	1.02 (0.94, 1.11)*0.6385	1.02 (0.90, 1.16) 0.7506	0.01 (-0.02, 0.03)*0.6385	
	Age						0.0285*
	<= median	417/1415 (29.5)	390/1482 (26.3)	1.12 (1.00, 1.26)*0.0585	1.18 (0.99, 1.41) 0.0694	0.03 (-0.00, 0.06)*0.0584	
	> median	350/1427 (24.5)	360/1355 (26.6)	0.92 (0.81, 1.05)*0.2172	0.88 (0.73, 1.06) 0.1831	-0.02 (-0.05, 0.01)*0.2173	
	Gender						0.9887*
	Male	415/1656 (25.1)	398/1625 (24.5)	1.02 (0.91, 1.15)*0.7063	1.02 (0.86, 1.21) 0.8196	0.01 (-0.02, 0.04)*0.7063	
	Female	352/1186 (29.7)	352/1212 (29.0)	1.02 (0.90, 1.16)*0.7321	1.03 (0.84, 1.25) 0.7901	0.01 (-0.03, 0.04)*0.7321	
	Race						0.7176*
	White	558/2039 (27.4)	541/2058 (26.3)	1.04 (0.94, 1.15)*0.4359	1.05 (0.90, 1.23) 0.5072	0.01 (-0.02, 0.04)*0.4359	
	Black or African	26/ 67 (38.8)	31/ 71 (43.7)	0.89 (0.60, 1.33)*0.5637	0.74 (0.35, 1.57) 0.4370	-0.05 (-0.21, 0.12)*0.5619	
	Asian	116/ 558 (20.8)	124/ 555 (22.3)	0.93 (0.74, 1.16)*0.5287	0.87 (0.64, 1.19) 0.3887	-0.02 (-0.06, 0.03)*0.5285	
	Other	67/ 178 (37.6)	54/ 153 (35.3)	1.07 (0.80, 1.42)*0.6591	1.27 (0.74, 2.18) 0.3796	0.02 (-0.08, 0.13)*0.6581	
	Geographic region						0.5818*
	Asia	111/ 539 (20.6)	120/ 538 (22.3)	0.92 (0.73, 1.16)*0.4941	0.87 (0.63, 1.18) 0.3653	-0.02 (-0.07, 0.03)*0.4939	
	Europe and Saudi Arabia	378/1365 (27.7)	366/1394 (26.3)	1.05 (0.93, 1.19)*0.3952	1.10 (0.91, 1.32) 0.3185	0.01 (-0.02, 0.05)*0.3952	
	North America	96/ 398 (24.1)	101/ 387 (26.1)	0.92 (0.73, 1.18)*0.5230	0.79 (0.55, 1.14) 0.2051	-0.02 (-0.08, 0.04)*0.5229	
	Latin America	182/ 540 (33.7)	163/ 518 (31.5)	1.07 (0.90, 1.27)*0.4383	1.18 (0.88, 1.58) 0.2731	0.02 (-0.03, 0.08)*0.4376	
	NYHA class at enrolment						0.7711*
	II	542/2113 (25.7)	556/2187 (25.4)	1.01 (0.91, 1.12)*0.8640	1.02 (0.88, 1.19) 0.7798	0.00 (-0.02, 0.03)*0.8640	
	III or IV	225/ 729 (30.9)	193/ 649 (29.7)	1.04 (0.88, 1.22)*0.6501	1.00 (0.77, 1.31) 0.9884	0.01 (-0.04, 0.06)*0.6497	
	LVEF at enrolment						0.3159*
	<= 49	270/ 980 (27.6)	247/ 963 (25.6)	1.07 (0.93, 1.25)*0.3431	1.11 (0.89, 1.38) 0.3640	0.02 (-0.02, 0.06)*0.3426	
	50-59	272/1029 (26.4)	253/1017 (24.9)	1.06 (0.92, 1.23)*0.4205	1.09 (0.87, 1.35) 0.4637	0.02 (-0.02, 0.05)*0.4202	
	>= 60	225/ 833 (27.0)	250/ 857 (29.2)	0.93 (0.79, 1.08)*0.3236	0.87 (0.69, 1.10) 0.2563	-0.02 (-0.06, 0.02)*0.3229	
	NT-proBNP at enrolment						0.9263*
	<= median	388/1418 (27.4)	382/1421 (26.9)	1.02 (0.90, 1.15)*0.7736	1.03 (0.86, 1.24) 0.7137	0.00 (-0.03, 0.04)*0.7736	
	> median	379/1424 (26.6)	367/1415 (25.9)	1.03 (0.91, 1.16)*0.6812	1.01 (0.84, 1.21) 0.9237	0.01 (-0.03, 0.04)*0.6812	
	Type 2 Diabetes Medical History						0.3286*
	Yes	325/1250 (26.0)	337/1260 (26.7)	1.01 (0.96, 1.07) 0.6104	0.96 (0.81, 1.15)*0.6715	-0.01 (-0.04, 0.03)*0.6715	
	No	442/1592 (27.8)	413/1577 (26.2)	1.06 (0.95, 1.19)*0.3181	1.08 (0.93, 1.27)*0.3180	0.02 (-0.02, 0.05)*0.3178	
	Atrial fibrillation or flutter at enrolment ECG						0.1951*
	Yes	295/1199 (24.6)	310/1199 (25.9)	0.95 (0.83, 1.09)*0.4807	0.93 (0.76, 1.15) 0.5153	-0.01 (-0.05, 0.02)*0.4806	
	No	472/1643 (28.7)	440/1638 (26.9)	1.00 (0.95, 1.05) 0.8823	1.08 (0.91, 1.28) 0.3650	0.02 (-0.01, 0.05)*0.2328	
	BMI (kg/m2) at enrolment						0.5674*
	< 30	402/1571 (25.6)	381/1559 (24.4)	1.05 (0.93, 1.18)*0.4577	1.04 (0.87, 1.24) 0.6421	0.01 (-0.02, 0.04)*0.4575	
	>= 30	365/1270 (28.7)	368/1275 (28.9)	1.00 (0.88, 1.13)*0.9456	1.00 (0.83, 1.21) 0.9922	-0.00 (-0.04, 0.03)*0.9456	
	Baseline eGFR (mL/min/1.73m^2)						0.0061*
	< 60	324/1359 (23.8)	372/1396 (26.6)	0.89 (0.79, 1.02)*0.0905	0.84 (0.70, 1.02) 0.0808	-0.03 (-0.06, 0.00)*0.0898	
	>= 60	443/1483 (29.9)	377/1440 (26.2)	1.14 (1.02, 1.28)*0.0267	1.20 (1.00, 1.44) 0.0439	0.04 (0.00, 0.07)*0.0261	

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Symptom Stability (LOCF)	SBP at randomisation						0.1462*
	<= median	391/1424 (27.5)	363/1439 (25.2)	1.09 (0.96, 1.23)*0.1754	1.11 (0.92, 1.33) 0.2747	0.02 (-0.01, 0.05)*0.1751	
	> median	376/1418 (26.5)	387/1398 (27.7)	0.96 (0.85, 1.08)*0.4864	0.95 (0.79, 1.14) 0.5725	-0.01 (-0.04, 0.02)*0.4863	
	LVEF at enrolment 2						0.4063*
	<= 49	270/ 980 (27.6)	247/ 963 (25.6)	1.07 (0.93, 1.25)*0.3431	1.11 (0.89, 1.38) 0.3640	0.02 (-0.02, 0.06)*0.3426	
	>= 50	497/1862 (26.7)	503/1874 (26.8)	0.99 (0.89, 1.11)*0.9179	0.98 (0.84, 1.15) 0.8090	-0.00 (-0.03, 0.03)*0.9179	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4467*
	Yes	83/ 283 (29.3)	90/ 286 (31.5)	0.93 (0.73, 1.20)*0.5792	0.97 (0.62, 1.51) 0.8830	-0.02 (-0.10, 0.05)*0.5789	
	No	684/2559 (26.7)	660/2551 (25.9)	0.98 (0.93, 1.04) 0.5806	1.03 (0.90, 1.18) 0.6925	0.01 (-0.02, 0.03)*0.4866	
	MRAs at baseline						0.5709*
	Yes	339/1227 (27.6)	322/1224 (26.3)	1.05 (0.92, 1.20)*0.4613	1.11 (0.91, 1.36) 0.2846	0.01 (-0.02, 0.05)*0.4611	
	No	428/1615 (26.5)	428/1613 (26.5)	1.00 (0.89, 1.12)*0.9831	0.96 (0.80, 1.14) 0.6072	-0.00 (-0.03, 0.03)*0.9831	
	ACEi+ARB at baseline						0.5233*
	Yes	558/2065 (27.0)	559/2077 (26.9)	1.00 (0.91, 1.11)*0.9376	1.01 (0.87, 1.17) 0.9380	0.00 (-0.03, 0.03)*0.9376	
	No	209/ 777 (26.9)	191/ 760 (25.1)	1.07 (0.90, 1.27)*0.4302	1.07 (0.83, 1.38) 0.6185	0.02 (-0.03, 0.06)*0.4298	
	ARNI at baseline						0.7882*
	Yes	40/ 153 (26.1)	34/ 126 (27.0)	0.97 (0.65, 1.43)*0.8742	1.04 (0.58, 1.86) 0.8890	-0.01 (-0.11, 0.10)*0.8744	
	No	727/2689 (27.0)	716/2711 (26.4)	1.02 (0.94, 1.12)*0.6037	1.02 (0.89, 1.17) 0.7672	0.01 (-0.02, 0.03)*0.6037	
	Beta Blocker at baseline						0.6360*
	Yes	640/2360 (27.1)	620/2356 (26.3)	1.03 (0.94, 1.13)*0.5333	1.01 (0.87, 1.16) 0.9374	0.01 (-0.02, 0.03)*0.5333	
	No	127/ 482 (26.3)	130/ 481 (27.0)	0.97 (0.79, 1.20)*0.8119	1.11 (0.80, 1.52) 0.5354	-0.01 (-0.06, 0.05)*0.8119	
	Diuretics at baseline						0.3650*
	Yes	681/2536 (26.9)	675/2531 (26.7)	0.97 (0.92, 1.03) 0.3935	1.00 (0.87, 1.15) 0.9994	0.00 (-0.02, 0.03)*0.8824	
	No	86/ 306 (28.1)	75/ 306 (24.5)	1.15 (0.88, 1.50)*0.3133	1.23 (0.82, 1.86) 0.3136	0.04 (-0.03, 0.11)*0.3122	

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Total Symptom Score (LOCF)							
	Overall	920/2842 (32.4)	857/2837 (30.2)	1.07 (0.99, 1.16)*0.0789	1.10 (0.96, 1.26) 0.1675	0.02 (-0.00, 0.05)*0.0786	
	Age						0.8889*
	<= median	485/1415 (34.3)	475/1482 (32.1)	1.07 (0.96, 1.19)*0.2036	1.17 (0.97, 1.41) 0.0972	0.02 (-0.01, 0.06)*0.2036	
	> median	435/1427 (30.5)	382/1355 (28.2)	1.08 (0.96, 1.21)*0.1851	1.05 (0.86, 1.27) 0.6508	0.02 (-0.01, 0.06)*0.1843	
	Gender						0.7970*
	Male	497/1656 (30.0)	450/1625 (27.7)	1.08 (0.97, 1.21)*0.1429	1.13 (0.94, 1.36) 0.1906	0.02 (-0.01, 0.05)*0.1424	
	Female	423/1186 (35.7)	407/1212 (33.6)	1.06 (0.95, 1.19)*0.2833	1.06 (0.87, 1.29) 0.5499	0.02 (-0.02, 0.06)*0.2832	
	Race						0.3882*
	White	695/2039 (34.1)	645/2058 (31.3)	1.09 (1.00, 1.19)*0.0614	1.09 (0.94, 1.27) 0.2580	0.03 (-0.00, 0.06)*0.0611	
	Black or African	23/ 67 (34.3)	29/ 71 (40.8)	0.84 (0.54, 1.30)*0.4321	0.72 (0.34, 1.54) 0.3943	-0.07 (-0.23, 0.10)*0.4283	
	Asian	115/ 558 (20.6)	120/ 555 (21.6)	0.95 (0.76, 1.20)*0.6791	1.04 (0.73, 1.49) 0.8155	-0.01 (-0.06, 0.04)*0.6790	
	Other	87/ 178 (48.9)	63/ 153 (41.2)	1.19 (0.93, 1.51)*0.1646	1.60 (0.95, 2.70) 0.0788	0.08 (-0.03, 0.18)*0.1589	
	Geographic region						0.7497*
	Asia	111/ 539 (20.6)	115/ 538 (21.4)	0.96 (0.76, 1.21)*0.7528	1.01 (0.70, 1.45) 0.9730	-0.01 (-0.06, 0.04)*0.7527	
	Europe and Saudi Arabia	466/1365 (34.1)	431/1394 (30.9)	1.10 (0.99, 1.23)*0.0712	1.12 (0.92, 1.36) 0.2549	0.03 (-0.00, 0.07)*0.0709	
	North America	117/ 398 (29.4)	110/ 387 (28.4)	1.03 (0.83, 1.29)*0.7637	1.04 (0.74, 1.46) 0.8330	0.01 (-0.05, 0.07)*0.7636	
	Latin America	226/ 540 (41.9)	201/ 518 (38.8)	1.08 (0.93, 1.25)*0.3129	1.19 (0.89, 1.60) 0.2372	0.03 (-0.03, 0.09)*0.3119	
	NYHA class at enrolment						0.5415*
	II	604/2113 (28.6)	600/2187 (27.4)	1.04 (0.95, 1.15)*0.4011	1.10 (0.93, 1.29) 0.2599	0.01 (-0.02, 0.04)*0.4011	
	III or IV	316/ 729 (43.3)	257/ 649 (39.6)	1.09 (0.96, 1.24)*0.1601	1.14 (0.89, 1.45) 0.2980	0.04 (-0.01, 0.09)*0.1582	
	LVEF at enrolment						0.5896*
	<= 49	312/ 980 (31.8)	301/ 963 (31.3)	1.02 (0.89, 1.16)*0.7832	1.08 (0.86, 1.36) 0.5031	0.01 (-0.04, 0.05)*0.7832	
	50-59	327/1029 (31.8)	299/1017 (29.4)	1.08 (0.95, 1.23)*0.2435	1.08 (0.87, 1.35) 0.4859	0.02 (-0.02, 0.06)*0.2429	
	>= 60	281/ 833 (33.7)	257/ 857 (30.0)	1.12 (0.98, 1.29)*0.0988	1.14 (0.89, 1.44) 0.2938	0.04 (-0.01, 0.08)*0.0983	
	NT-proBNP at enrolment						0.3918*
	<= median	420/1418 (29.6)	407/1421 (28.6)	1.03 (0.92, 1.16)*0.5666	1.06 (0.88, 1.28) 0.5213	0.01 (-0.02, 0.04)*0.5666	
	> median	500/1424 (35.1)	449/1415 (31.7)	1.11 (1.00, 1.23)*0.0565	1.13 (0.94, 1.37) 0.1969	0.03 (-0.00, 0.07)*0.0560	
	Type 2 Diabetes Medical History						0.4675*
	Yes	431/1250 (34.5)	393/1260 (31.2)	1.11 (0.99, 1.24)*0.0796	1.16 (0.98, 1.37)*0.0794	0.03 (-0.00, 0.07)*0.0791	
	No	489/1592 (30.7)	464/1577 (29.4)	1.04 (0.94, 1.16)*0.4275	1.06 (0.91, 1.24)*0.4274	0.01 (-0.02, 0.04)*0.4273	
	Atrial fibrillation or flutter at enrolment ECG						0.3605*
	Yes	393/1199 (32.8)	382/1199 (31.9)	1.03 (0.92, 1.16)*0.6310	1.02 (0.83, 1.25) 0.8608	0.01 (-0.03, 0.05)*0.6310	
	No	527/1643 (32.1)	475/1638 (29.0)	1.11 (1.00, 1.23)*0.0560	1.16 (0.98, 1.39) 0.0925	0.03 (-0.00, 0.06)*0.0556	
	BMI (kg/m2) at enrolment						0.9561*
	< 30	452/1571 (28.8)	419/1559 (26.9)	1.07 (0.96, 1.20)*0.2370	1.11 (0.92, 1.34) 0.2801	0.02 (-0.01, 0.05)*0.2367	
	>= 30	468/1270 (36.9)	437/1275 (34.3)	1.08 (0.97, 1.19)*0.1749	1.10 (0.91, 1.33) 0.3260	0.03 (-0.01, 0.06)*0.1745	
	Baseline eGFR (mL/min/1.73m^2)						0.8041*
	< 60	436/1359 (32.1)	414/1396 (29.7)	1.08 (0.97, 1.21)*0.1682	1.12 (0.93, 1.36) 0.2354	0.02 (-0.01, 0.06)*0.1680	
	>= 60	484/1483 (32.6)	443/1440 (30.8)	1.06 (0.95, 1.18)*0.2770	1.07 (0.89, 1.30) 0.4557	0.02 (-0.02, 0.05)*0.2765	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.2280*
	<= median	452/1424 (31.7)	406/1439 (28.2)	1.13 (1.01, 1.26)*0.0396	1.12 (0.92, 1.35) 0.2516	0.04 (0.00, 0.07)*0.0393	
	> median	468/1418 (33.0)	451/1398 (32.3)	1.02 (0.92, 1.14)*0.6738	1.08 (0.90, 1.30) 0.4152	0.01 (-0.03, 0.04)*0.6738	
	LVEF at enrolment 2						0.3492*
	<= 49	312/ 980 (31.8)	301/ 963 (31.3)	1.02 (0.89, 1.16)*0.7832	1.08 (0.86, 1.36) 0.5031	0.01 (-0.04, 0.05)*0.7832	
	>= 50	608/1862 (32.7)	556/1874 (29.7)	1.10 (1.00, 1.21)*0.0491	1.11 (0.94, 1.30) 0.2182	0.03 (0.00, 0.06)*0.0489	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9221*
	Yes	140/ 283 (49.5)	133/ 286 (46.5)	1.06 (0.90, 1.26)*0.4790	1.41 (0.95, 2.10) 0.0904	0.03 (-0.05, 0.11)*0.4786	
	No	780/2559 (30.5)	724/2551 (28.4)	1.07 (0.99, 1.17)*0.0998	1.07 (0.93, 1.23) 0.3547	0.02 (-0.00, 0.05)*0.0995	
	MRAs at baseline						0.4672*
	Yes	403/1227 (32.8)	363/1224 (29.7)	1.11 (0.98, 1.25)*0.0890	1.16 (0.94, 1.42) 0.1646	0.03 (-0.00, 0.07)*0.0885	
	No	517/1615 (32.0)	494/1613 (30.6)	1.05 (0.94, 1.16)*0.3959	1.06 (0.89, 1.26) 0.5298	0.01 (-0.02, 0.05)*0.3958	
	ACEi+ARB at baseline						0.0185*
	Yes	712/2065 (34.5)	633/2077 (30.5)	1.13 (1.04, 1.24)*0.0060	1.19 (1.02, 1.40) 0.0243	0.04 (0.01, 0.07)*0.0059	
	No	208/ 777 (26.8)	224/ 760 (29.5)	0.91 (0.77, 1.07)*0.2387	0.86 (0.66, 1.12) 0.2681	-0.03 (-0.07, 0.02)*0.2383	
	ARNI at baseline						0.1773*
	Yes	30/ 153 (19.6)	31/ 126 (24.6)	0.80 (0.51, 1.24)*0.3155	0.95 (0.47, 1.95) 0.8941	-0.05 (-0.15, 0.05)*0.3180	
	No	890/2689 (33.1)	826/2711 (30.5)	1.09 (1.00, 1.17)*0.0381	1.11 (0.97, 1.27) 0.1380	0.03 (0.00, 0.05)*0.0379	
	Beta Blocker at baseline						0.5466*
	Yes	765/2360 (32.4)	705/2356 (29.9)	1.08 (1.00, 1.18)*0.0649	1.08 (0.93, 1.25) 0.2966	0.02 (-0.00, 0.05)*0.0646	
	No	155/ 482 (32.2)	152/ 481 (31.6)	1.02 (0.85, 1.22)*0.8529	1.18 (0.85, 1.63) 0.3151	0.01 (-0.05, 0.06)*0.8529	
	Diuretics at baseline						0.3037*
	Yes	813/2536 (32.1)	768/2531 (30.3)	1.06 (0.97, 1.15)*0.1879	1.10 (0.95, 1.27) 0.1892	0.02 (-0.01, 0.04)*0.1877	
	No	107/ 306 (35.0)	89/ 306 (29.1)	1.20 (0.95, 1.52)*0.1201	1.04 (0.68, 1.59) 0.8478	0.06 (-0.01, 0.13)*0.1182	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	1209/2842 (42.5)	1068/2837 (37.6)	1.12 (1.06, 1.19) 0.0002	1.22 (1.09, 1.36) 0.0003	0.05 (0.02, 0.07) 0.0002	
	Age						0.7799
	<= median	660/1415 (46.6)	614/1482 (41.4)	1.12 (1.04, 1.22) 0.0042	1.25 (1.07, 1.45) 0.0038	0.05 (0.02, 0.09) 0.0034	
	> median	549/1427 (38.5)	454/1355 (33.5)	1.13 (1.03, 1.24) 0.0103	1.21 (1.03, 1.42) 0.0178	0.04 (0.01, 0.08) 0.0145	
	Gender						0.0927
	Male	704/1656 (42.5)	640/1625 (39.4)	1.07 (0.99, 1.16) 0.0852	1.13 (0.99, 1.31) 0.0792	0.03 (-0.00, 0.06) 0.0702	
	Female	505/1186 (42.6)	428/1212 (35.3)	1.18 (1.08, 1.30) 0.0005	1.34 (1.13, 1.59) 0.0007	0.07 (0.03, 0.10) 0.0005	
	Race						0.7200*
	White	818/2039 (40.1)	727/2058 (35.3)	1.11 (1.03, 1.19) 0.0053	1.21 (1.06, 1.37) 0.0046	0.04 (0.01, 0.07) 0.0029	
	Black or African	27/ 67 (40.3)	29/ 71 (40.8)	1.08 (0.76, 1.53) 0.6691	1.01 (0.49, 2.07) 0.9860	-0.01 (-0.16, 0.15) 0.9240	
	Asian	263/ 558 (47.1)	241/ 555 (43.4)	1.09 (0.95, 1.24) 0.2091	1.16 (0.92, 1.47) 0.2082	0.04 (-0.02, 0.10) 0.2069	
	Other	101/ 178 (56.7)	71/ 153 (46.4)	1.29 (1.06, 1.58) 0.0129	1.57 (1.00, 2.49) 0.0520	0.12 (0.01, 0.22) 0.0282	
	Geographic region						0.7894*
	Asia	255/ 539 (47.3)	238/ 538 (44.2)	1.07 (0.94, 1.22) 0.3160	1.13 (0.89, 1.44) 0.3102	0.03 (-0.03, 0.09) 0.3078	
	Europe and Saudi Arabia	544/1365 (39.9)	480/1394 (34.4)	1.12 (1.02, 1.23) 0.0145	1.24 (1.06, 1.46) 0.0073	0.05 (0.01, 0.08) 0.0071	
	North America	140/ 398 (35.2)	117/ 387 (30.2)	1.16 (0.96, 1.42) 0.1314	1.25 (0.93, 1.69) 0.1442	0.05 (-0.02, 0.11) 0.1480	
	Latin America	270/ 540 (50.0)	233/ 518 (45.0)	1.11 (0.98, 1.26)*0.1031	1.24 (0.97, 1.60) 0.0913	0.06 (0.00, 0.12) 0.0408	
	NYHA class at enrolment						0.2243
	II	873/2113 (41.3)	817/2187 (37.4)	1.10 (1.02, 1.18) 0.0099	1.19 (1.05, 1.34) 0.0067	0.04 (0.01, 0.07) 0.0058	
	III or IV	336/ 729 (46.1)	251/ 649 (38.7)	1.19 (1.05, 1.35)*0.0058	1.33 (1.06, 1.66) 0.0126	0.07 (0.02, 0.12) 0.0075	
	LVEF at enrolment						0.2314
	<= 49	420/ 980 (42.9)	397/ 963 (41.2)	1.05 (0.94, 1.16) 0.3875	1.09 (0.90, 1.30) 0.3797	0.02 (-0.02, 0.06) 0.3618	
	50-59	434/1029 (42.2)	359/1017 (35.3)	1.17 (1.05, 1.30) 0.0042	1.32 (1.10, 1.58) 0.0027	0.07 (0.03, 0.11) 0.0016	
	>= 60	355/ 833 (42.6)	312/ 857 (36.4)	1.16 (1.04, 1.30) 0.0082	1.26 (1.03, 1.54) 0.0245	0.05 (0.01, 0.10) 0.0279	
	NT-proBNP at enrolment						0.8505
	<= median	590/1418 (41.6)	526/1421 (37.0)	1.12 (1.02, 1.23) 0.0130	1.21 (1.04, 1.41) 0.0127	0.05 (0.01, 0.08) 0.0115	
	> median	619/1424 (43.5)	541/1415 (38.2)	1.14 (1.04, 1.24)*0.0046	1.22 (1.05, 1.42) 0.0111	0.05 (0.01, 0.08) 0.0080	
	Type 2 Diabetes Medical History						0.4240
	Yes	531/1250 (42.5)	463/1260 (36.7)	1.16 (1.05, 1.27) 0.0025	1.27 (1.08, 1.49)*0.0033	0.06 (0.02, 0.09) 0.0029	
	No	678/1592 (42.6)	605/1577 (38.4)	1.10 (1.01, 1.19) 0.0257	1.19 (1.03, 1.37)*0.0155	0.04 (0.00, 0.07) 0.0258	
	Atrial fibrillation or flutter at enrolment ECG						0.6452
	Yes	515/1199 (43.0)	450/1199 (37.5)	1.14 (1.04, 1.25) 0.0063	1.25 (1.06, 1.47) 0.0088	0.05 (0.01, 0.09) 0.0072	
	No	694/1643 (42.2)	618/1638 (37.7)	1.11 (1.02, 1.20) 0.0134	1.20 (1.04, 1.38) 0.0133	0.04 (0.01, 0.08) 0.0119	
	BMI (kg/m2) at enrolment						0.3951
	< 30	687/1571 (43.7)	593/1559 (38.0)	1.16 (1.06, 1.26) 0.0007	1.26 (1.09, 1.46) 0.0015	0.06 (0.02, 0.09) 0.0015	
	>= 30	522/1270 (41.1)	474/1275 (37.2)	1.11 (1.00, 1.22)*0.0427	1.16 (0.98, 1.37) 0.0767	0.04 (-0.00, 0.07) 0.0534	
	Baseline eGFR (mL/min/1.73m^2)						0.8485
	< 60	543/1359 (40.0)	492/1396 (35.2)	1.12 (1.02, 1.23) 0.0135	1.22 (1.05, 1.43) 0.0120	0.05 (0.01, 0.08) 0.0103	
	>= 60	666/1483 (44.9)	576/1440 (40.0)	1.12 (1.03, 1.21) 0.0087	1.21 (1.04, 1.40) 0.0132	0.05 (0.01, 0.08) 0.0110	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.3442
	<= median	608/1424 (42.7)	520/1439 (36.1)	1.16 (1.06, 1.27) 0.0012	1.29 (1.11, 1.50) 0.0010	0.06 (0.03, 0.10) 0.0008	
	> median	601/1418 (42.4)	548/1398 (39.2)	1.09 (1.00, 1.19) 0.0438	1.16 (0.99, 1.35) 0.0643	0.03 (-0.00, 0.07) 0.0599	
	LVEF at enrolment 2						0.0887
	<= 49	420/ 980 (42.9)	397/ 963 (41.2)	1.05 (0.94, 1.16) 0.3875	1.09 (0.90, 1.30) 0.3797	0.02 (-0.02, 0.06) 0.3618	
	>= 50	789/1862 (42.4)	671/1874 (35.8)	1.16 (1.08, 1.26) 0.0001	1.29 (1.13, 1.48) 0.0002	0.06 (0.03, 0.09) 0.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7684
	Yes	137/ 283 (48.4)	129/ 286 (45.1)	1.07 (0.90, 1.28)*0.4298	1.22 (0.86, 1.73) 0.2546	0.04 (-0.03, 0.12) 0.2595	
	No	1072/2559 (41.9)	939/2551 (36.8)	1.13 (1.06, 1.21) 0.0004	1.22 (1.09, 1.37) 0.0005	0.05 (0.02, 0.07) 0.0004	
	MRAs at baseline						0.5258
	Yes	533/1227 (43.4)	460/1224 (37.6)	1.15 (1.05, 1.26) 0.0037	1.27 (1.08, 1.50) 0.0039	0.06 (0.02, 0.10) 0.0023	
	No	676/1615 (41.9)	608/1613 (37.7)	1.10 (1.02, 1.20) 0.0181	1.18 (1.02, 1.36) 0.0226	0.04 (0.01, 0.07) 0.0236	
	ACEi+ARB at baseline						0.0343
	Yes	896/2065 (43.4)	766/2077 (36.9)	1.17 (1.09, 1.25) <.0001	1.30 (1.14, 1.48) <.0001	0.06 (0.03, 0.09) <.0001	
	No	313/ 777 (40.3)	302/ 760 (39.7)	1.01 (0.90, 1.14) 0.8384	1.03 (0.84, 1.26) 0.8102	0.01 (-0.04, 0.06) 0.7972	
	ARNI at baseline						0.6313
	Yes	60/ 153 (39.2)	50/ 126 (39.7)	1.02 (0.76, 1.38) 0.8792	1.02 (0.62, 1.66) 0.9415	0.00 (-0.11, 0.12) 0.9612	
	No	1149/2689 (42.7)	1018/2711 (37.6)	1.12 (1.06, 1.20) 0.0002	1.23 (1.10, 1.37) 0.0003	0.05 (0.02, 0.07) 0.0002	
	Beta Blocker at baseline						0.0565
	Yes	983/2360 (41.7)	887/2356 (37.6)	1.09 (1.02, 1.17) 0.0119	1.16 (1.03, 1.31) 0.0126	0.04 (0.01, 0.06) 0.0103	
	No	226/ 482 (46.9)	181/ 481 (37.6)	1.27 (1.10, 1.47) 0.0011	1.51 (1.16, 1.96) 0.0019	0.10 (0.04, 0.16) 0.0017	
	Diuretics at baseline						0.8707
	Yes	1068/2536 (42.1)	947/2531 (37.4)	1.12 (1.05, 1.20) 0.0007	1.22 (1.08, 1.36) 0.0008	0.05 (0.02, 0.07) 0.0007	
	No	141/ 306 (46.1)	121/ 306 (39.5)	1.12 (0.94, 1.34) 0.1883	1.24 (0.89, 1.72) 0.2053	0.05 (-0.02, 0.13) 0.1789	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	1147/2842 (40.4)	1020/2837 (36.0)	1.11 (1.04, 1.18) 0.0013	1.20 (1.07, 1.33) 0.0014	0.04 (0.02, 0.07) 0.0008	
	Age						0.6860*
	<= median	620/1415 (43.8)	583/1482 (39.3)	1.11 (1.02, 1.21) 0.0133	1.21 (1.04, 1.41) 0.0125	0.05 (0.01, 0.08) 0.0098	
	> median	527/1427 (36.9)	437/1355 (32.3)	1.15 (1.03, 1.27)*0.0097	1.19 (1.02, 1.40) 0.0308	0.04 (0.01, 0.07) 0.0199	
	Gender						0.3003
	Male	668/1656 (40.3)	607/1625 (37.4)	1.08 (0.99, 1.17) 0.0813	1.13 (0.98, 1.30) 0.0975	0.03 (-0.00, 0.06) 0.0737	
	Female	479/1186 (40.4)	413/1212 (34.1)	1.19 (1.07, 1.32)*0.0014	1.29 (1.08, 1.53) 0.0041	0.06 (0.02, 0.09) 0.0027	
	Race						0.7103*
	White	772/2039 (37.9)	706/2058 (34.3)	1.10 (1.02, 1.20)*0.0179	1.14 (1.00, 1.30) 0.0538	0.03 (0.00, 0.06) 0.0213	
	Black or African	26/ 67 (38.8)	27/ 71 (38.0)	1.26 (0.80, 1.99) 0.3181	1.05 (0.51, 2.18) 0.8977	0.03 (-0.13, 0.18) 0.7352	
	Asian	247/ 558 (44.3)	217/ 555 (39.1)	1.14 (0.99, 1.31) 0.0715	1.24 (0.98, 1.57) 0.0781	0.05 (-0.01, 0.11) 0.0795	
	Other	102/ 178 (57.3)	70/ 153 (45.8)	1.23 (1.00, 1.51) 0.0531	1.75 (1.10, 2.80) 0.0189	0.12 (0.02, 0.22) 0.0180	
	Geographic region						0.9816*
	Asia	242/ 539 (44.9)	215/ 538 (40.0)	1.13 (0.98, 1.30) 0.0903	1.23 (0.96, 1.56) 0.1002	0.05 (-0.01, 0.11) 0.1021	
	Europe and Saudi Arabia	508/1365 (37.2)	458/1394 (32.9)	1.08 (0.98, 1.19) 0.1081	1.18 (1.01, 1.39) 0.0405	0.04 (0.01, 0.07) 0.0190	
	North America	144/ 398 (36.2)	125/ 387 (32.3)	1.12 (0.93, 1.36) 0.2289	1.19 (0.88, 1.61) 0.2462	0.04 (-0.02, 0.10) 0.2272	
	Latin America	253/ 540 (46.9)	222/ 518 (42.9)	1.09 (0.96, 1.25)*0.1924	1.18 (0.91, 1.53) 0.2052	0.05 (-0.01, 0.10) 0.1021	
	NYHA class at enrolment						0.8369*
	II	840/2113 (39.8)	779/2187 (35.6)	1.11 (1.03, 1.19) 0.0075	1.20 (1.06, 1.36) 0.0045	0.04 (0.01, 0.07) 0.0032	
	III or IV	307/ 729 (42.1)	241/ 649 (37.1)	1.13 (0.99, 1.29)*0.0606	1.19 (0.95, 1.50) 0.1377	0.04 (-0.01, 0.09) 0.0882	
	LVEF at enrolment						0.1947
	<= 49	391/ 980 (39.9)	362/ 963 (37.6)	1.06 (0.96, 1.18) 0.2491	1.13 (0.94, 1.36) 0.2103	0.03 (-0.01, 0.07) 0.1984	
	50-59	424/1029 (41.2)	337/1017 (33.1)	1.20 (1.07, 1.33) 0.0012	1.39 (1.16, 1.67) 0.0005	0.08 (0.04, 0.12) 0.0002	
	>= 60	332/ 833 (39.9)	321/ 857 (37.5)	1.07 (0.95, 1.20) 0.2533	1.07 (0.87, 1.31) 0.5144	0.02 (-0.03, 0.06) 0.4877	
	NT-proBNP at enrolment						0.9513
	<= median	558/1418 (39.4)	502/1421 (35.3)	1.11 (1.01, 1.22) 0.0279	1.19 (1.02, 1.38) 0.0304	0.04 (0.00, 0.07) 0.0263	
	> median	589/1424 (41.4)	517/1415 (36.5)	1.11 (1.02, 1.20) 0.0147	1.20 (1.03, 1.41) 0.0207	0.04 (0.01, 0.08) 0.0118	
	Type 2 Diabetes Medical History						0.6598
	Yes	492/1250 (39.4)	437/1260 (34.7)	1.13 (1.02, 1.24) 0.0159	1.22 (1.04, 1.44)*0.0153	0.05 (0.01, 0.08) 0.0124	
	No	655/1592 (41.1)	583/1577 (37.0)	1.10 (1.01, 1.19) 0.0293	1.19 (1.03, 1.37)*0.0161	0.04 (0.00, 0.07) 0.0267	
	Atrial fibrillation or flutter at enrolment ECG						0.7525
	Yes	487/1199 (40.6)	426/1199 (35.5)	1.12 (1.01, 1.23) 0.0243	1.23 (1.04, 1.46) 0.0164	0.05 (0.01, 0.09) 0.0134	
	No	660/1643 (40.2)	594/1638 (36.3)	1.10 (1.01, 1.19) 0.0251	1.17 (1.01, 1.35) 0.0327	0.04 (0.01, 0.07) 0.0229	
	BMI (kg/m2) at enrolment						0.1598
	< 30	648/1571 (41.2)	549/1559 (35.2)	1.16 (1.07, 1.27) 0.0006	1.28 (1.11, 1.49) 0.0008	0.06 (0.02, 0.09) 0.0008	
	>= 30	499/1270 (39.3)	470/1275 (36.9)	1.06 (0.97, 1.16) 0.2095	1.09 (0.92, 1.29) 0.3118	0.02 (-0.01, 0.06) 0.1814	
	Baseline eGFR (mL/min/1.73m^2)						0.2392*
	< 60	511/1359 (37.6)	489/1396 (35.0)	1.05 (0.96, 1.16) 0.2591	1.12 (0.95, 1.31) 0.1772	0.03 (-0.01, 0.06) 0.1459	
	>= 60	636/1483 (42.9)	531/1440 (36.9)	1.15 (1.06, 1.25) 0.0012	1.27 (1.09, 1.47) 0.0022	0.06 (0.02, 0.09) 0.0015	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.3891
	<= median	571/1424 (40.1)	495/1439 (34.4)	1.13 (1.04, 1.24) 0.0056	1.24 (1.06, 1.45) 0.0064	0.05 (0.01, 0.08) 0.0049	
	> median	576/1418 (40.6)	525/1398 (37.6)	1.08 (0.99, 1.18) 0.0882	1.15 (0.98, 1.34) 0.0804	0.03 (-0.00, 0.07) 0.0615	
	LVEF at enrolment 2						0.3607
	<= 49	391/ 980 (39.9)	362/ 963 (37.6)	1.06 (0.96, 1.18) 0.2491	1.13 (0.94, 1.36) 0.2103	0.03 (-0.01, 0.07) 0.1984	
	>= 50	756/1862 (40.6)	658/1874 (35.1)	1.13 (1.05, 1.22) 0.0021	1.23 (1.07, 1.41) 0.0028	0.05 (0.02, 0.08) 0.0015	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7649
	Yes	128/ 283 (45.2)	121/ 286 (42.3)	1.07 (0.89, 1.29)*0.4826	1.20 (0.84, 1.72) 0.3105	0.05 (-0.03, 0.12) 0.2054	
	No	1019/2559 (39.8)	899/2551 (35.2)	1.12 (1.04, 1.19) 0.0018	1.20 (1.07, 1.35) 0.0018	0.04 (0.02, 0.07) 0.0012	
	MRAs at baseline						0.1313
	Yes	503/1227 (41.0)	419/1224 (34.2)	1.17 (1.07, 1.29) 0.0011	1.33 (1.13, 1.58) 0.0008	0.07 (0.03, 0.11) 0.0003	
	No	644/1615 (39.9)	601/1613 (37.3)	1.06 (0.98, 1.15) 0.1503	1.10 (0.95, 1.27) 0.2068	0.02 (-0.01, 0.05) 0.1970	
	ACEi+ARB at baseline						0.5798
	Yes	838/2065 (40.6)	745/2077 (35.9)	1.13 (1.05, 1.22)*0.0018	1.21 (1.06, 1.37) 0.0046	0.04 (0.02, 0.07) 0.0021	
	No	309/ 777 (39.8)	275/ 760 (36.2)	1.09 (0.96, 1.23) 0.1880	1.16 (0.94, 1.43) 0.1540	0.04 (-0.01, 0.08) 0.1493	
	ARNI at baseline						0.5842
	Yes	51/ 153 (33.3)	43/ 126 (34.1)	0.99 (0.71, 1.39) 0.9594	0.97 (0.59, 1.61) 0.9198	-0.01 (-0.12, 0.11) 0.9010	
	No	1096/2689 (40.8)	977/2711 (36.0)	1.11 (1.04, 1.19) 0.0011	1.21 (1.08, 1.35) 0.0010	0.04 (0.02, 0.07) 0.0005	
	Beta Blocker at baseline						0.2089
	Yes	936/2360 (39.7)	842/2356 (35.7)	1.09 (1.01, 1.16) 0.0180	1.16 (1.03, 1.31) 0.0173	0.03 (0.01, 0.06) 0.0106	
	No	211/ 482 (43.8)	178/ 481 (37.0)	1.22 (1.05, 1.42) 0.0090	1.37 (1.06, 1.79) 0.0176	0.07 (0.01, 0.13) 0.0169	
	Diuretics at baseline						0.7447
	Yes	1012/2536 (39.9)	906/2531 (35.8)	1.10 (1.03, 1.18) 0.0040	1.19 (1.06, 1.33) 0.0037	0.04 (0.02, 0.07) 0.0019	
	No	135/ 306 (44.1)	114/ 306 (37.3)	1.16 (0.96, 1.41) 0.1129	1.27 (0.91, 1.76) 0.1534	0.06 (-0.02, 0.13) 0.1615	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	1147/2792 (41.1)	1023/2792 (36.6)	1.11 (1.04, 1.18) 0.0018	1.19 (1.07, 1.33) 0.0014	0.04 (0.02, 0.07) 0.0013	
	Age						0.9105
	<= median	629/1403 (44.8)	589/1469 (40.1)	1.11 (1.02, 1.21) 0.0128	1.22 (1.05, 1.42) 0.0095	0.05 (0.01, 0.08) 0.0092	
	> median	518/1389 (37.3)	434/1323 (32.8)	1.11 (1.01, 1.23) 0.0345	1.19 (1.01, 1.39) 0.0354	0.04 (0.00, 0.07) 0.0344	
	Gender						0.0232
	Male	673/1638 (41.1)	626/1602 (39.1)	1.04 (0.96, 1.13) 0.3530	1.08 (0.94, 1.25) 0.2749	0.02 (-0.01, 0.05) 0.2462	
	Female	474/1154 (41.1)	397/1190 (33.4)	1.20 (1.08, 1.33) 0.0006	1.36 (1.15, 1.61) 0.0005	0.07 (0.03, 0.11) 0.0005	
	Race						0.5347
	White	757/2004 (37.8)	700/2025 (34.6)	1.07 (0.99, 1.15) 0.1018	1.13 (0.99, 1.29) 0.0754	0.02 (-0.00, 0.05) 0.0882	
	Black or African	22/ 66 (33.3)	24/ 68 (35.3)	0.95 (0.60, 1.50) 0.8116	0.92 (0.45, 1.91) 0.8264	-0.02 (-0.18, 0.13) 0.7794	
	Asian	282/ 551 (51.2)	233/ 550 (42.4)	1.21 (1.07, 1.37) 0.0033	1.42 (1.12, 1.81) 0.0036	0.09 (0.03, 0.15) 0.0035	
	Other	86/ 171 (50.3)	66/ 149 (44.3)	1.14 (0.91, 1.44) 0.2471	1.28 (0.81, 2.01) 0.2878	0.06 (-0.05, 0.17) 0.2821	
	Geographic region						0.4634
	Asia	274/ 533 (51.4)	228/ 533 (42.8)	1.20 (1.06, 1.37) 0.0045	1.41 (1.11, 1.80) 0.0050	0.09 (0.03, 0.15) 0.0049	
	Europe and Saudi Arabia	497/1347 (36.9)	472/1373 (34.4)	1.05 (0.96, 1.16) 0.2727	1.10 (0.94, 1.29) 0.2446	0.02 (-0.02, 0.05) 0.3751	
	North America	136/ 391 (34.8)	101/ 375 (26.9)	1.25 (1.01, 1.55) 0.0409	1.42 (1.04, 1.95) 0.0267	0.08 (0.02, 0.14) 0.0147	
	Latin America	240/ 521 (46.1)	222/ 511 (43.4)	1.07 (0.94, 1.22) 0.2957	1.11 (0.86, 1.43) 0.4149	0.02 (-0.04, 0.08) 0.4330	
	NYHA class at enrolment						0.6662
	II	845/2077 (40.7)	792/2159 (36.7)	1.10 (1.02, 1.19) 0.0095	1.18 (1.04, 1.34) 0.0085	0.04 (0.01, 0.07) 0.0084	
	III or IV	302/ 715 (42.2)	231/ 632 (36.6)	1.12 (0.99, 1.27) 0.0716	1.24 (0.99, 1.56) 0.0640	0.05 (0.00, 0.10) 0.0408	
	LVEF at enrolment						0.1824
	<= 49	409/ 967 (42.3)	372/ 952 (39.1)	1.09 (0.98, 1.21) 0.1264	1.16 (0.97, 1.40) 0.1072	0.04 (-0.01, 0.08) 0.1059	
	50-59	414/1013 (40.9)	332/ 998 (33.3)	1.20 (1.07, 1.35) 0.0014	1.36 (1.13, 1.64) 0.0010	0.07 (0.03, 0.11) 0.0006	
	>= 60	324/ 812 (39.9)	319/ 842 (37.9)	1.03 (0.92, 1.16) 0.5902	1.05 (0.86, 1.28) 0.6427	0.01 (-0.04, 0.06) 0.6973	
	NT-proBNP at enrolment						0.8733
	<= median	594/1394 (42.6)	533/1402 (38.0)	1.11 (1.01, 1.21) 0.0260	1.20 (1.03, 1.40) 0.0170	0.04 (0.01, 0.08) 0.0168	
	> median	553/1398 (39.6)	490/1389 (35.3)	1.11 (1.01, 1.22) 0.0265	1.18 (1.01, 1.38) 0.0359	0.04 (0.00, 0.07) 0.0309	
	Type 2 Diabetes Medical History						0.3666
	Yes	507/1232 (41.2)	439/1237 (35.5)	1.14 (1.04, 1.26) 0.0072	1.27 (1.08, 1.50)*0.0038	0.06 (0.02, 0.09) 0.0031	
	No	640/1560 (41.0)	584/1555 (37.6)	1.08 (0.99, 1.18) 0.0722	1.16 (1.00, 1.34)*0.0475	0.03 (-0.00, 0.06) 0.0908	
	Atrial fibrillation or flutter at enrolment ECG						0.6186
	Yes	479/1178 (40.7)	434/1175 (36.9)	1.09 (0.98, 1.20) 0.0971	1.16 (0.98, 1.38) 0.0778	0.04 (-0.00, 0.08) 0.0591	
	No	668/1614 (41.4)	589/1617 (36.4)	1.12 (1.03, 1.22) 0.0068	1.22 (1.05, 1.40) 0.0074	0.04 (0.01, 0.08) 0.0096	
	BMI (kg/m2) at enrolment						0.1221
	< 30	674/1547 (43.6)	578/1535 (37.7)	1.16 (1.07, 1.26) 0.0005	1.27 (1.10, 1.47) 0.0011	0.06 (0.02, 0.09) 0.0013	
	>= 30	473/1244 (38.0)	445/1254 (35.5)	1.03 (0.94, 1.14) 0.5215	1.09 (0.92, 1.28) 0.3307	0.02 (-0.02, 0.06) 0.2725	
	Baseline eGFR (mL/min/1.73m^2)						0.7363
	< 60	511/1328 (38.5)	464/1367 (33.9)	1.11 (1.01, 1.23) 0.0307	1.21 (1.03, 1.42) 0.0178	0.04 (0.01, 0.08) 0.0150	
	>= 60	636/1464 (43.4)	559/1424 (39.3)	1.09 (1.00, 1.19) 0.0401	1.17 (1.00, 1.35) 0.0447	0.04 (0.00, 0.07) 0.0445	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.9168
	<= median	575/1396 (41.2)	514/1414 (36.4)	1.11 (1.01, 1.21) 0.0289	1.20 (1.03, 1.40) 0.0220	0.04 (0.01, 0.08) 0.0193	
	> median	572/1396 (41.0)	509/1378 (36.9)	1.11 (1.02, 1.22) 0.0216	1.20 (1.02, 1.40) 0.0236	0.04 (0.01, 0.08) 0.0245	
	LVEF at enrolment 2						0.6320
	<= 49	409/ 967 (42.3)	372/ 952 (39.1)	1.09 (0.98, 1.21) 0.1264	1.16 (0.97, 1.40) 0.1072	0.04 (-0.01, 0.08) 0.1059	
	>= 50	738/1825 (40.4)	651/1840 (35.4)	1.12 (1.03, 1.21) 0.0067	1.21 (1.05, 1.38) 0.0064	0.04 (0.01, 0.07) 0.0059	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8891
	Yes	123/ 273 (45.1)	113/ 277 (40.8)	1.09 (0.91, 1.31) 0.3515	1.22 (0.86, 1.74) 0.2645	0.05 (-0.03, 0.13) 0.2041	
	No	1024/2519 (40.7)	910/2515 (36.2)	1.11 (1.04, 1.19) 0.0025	1.19 (1.07, 1.34) 0.0024	0.04 (0.01, 0.07) 0.0024	
	MRAs at baseline						0.1975
	Yes	500/1200 (41.7)	425/1208 (35.2)	1.16 (1.05, 1.28) 0.0030	1.32 (1.11, 1.55) 0.0013	0.07 (0.03, 0.10) 0.0008	
	No	647/1592 (40.6)	598/1584 (37.8)	1.07 (0.98, 1.16) 0.1206	1.11 (0.96, 1.28) 0.1508	0.02 (-0.01, 0.06) 0.1672	
	ACEi+ARB at baseline						0.3654
	Yes	845/2029 (41.6)	746/2047 (36.4)	1.12 (1.04, 1.21) 0.0020	1.23 (1.08, 1.40) 0.0016	0.05 (0.02, 0.08) 0.0014	
	No	302/ 763 (39.6)	277/ 745 (37.2)	1.06 (0.93, 1.21) 0.3598	1.10 (0.90, 1.36) 0.3546	0.02 (-0.03, 0.07) 0.3554	
	ARNI at baseline						0.4455
	Yes	66/ 150 (44.0)	46/ 123 (37.4)	1.21 (0.91, 1.62) 0.1964	1.41 (0.86, 2.32) 0.1762	0.08 (-0.03, 0.20) 0.1597	
	No	1081/2642 (40.9)	977/2669 (36.6)	1.10 (1.03, 1.18) 0.0044	1.18 (1.06, 1.32) 0.0032	0.04 (0.01, 0.07) 0.0029	
	Beta Blocker at baseline						0.2625
	Yes	945/2323 (40.7)	853/2321 (36.8)	1.09 (1.01, 1.17) 0.0190	1.16 (1.03, 1.31) 0.0132	0.04 (0.01, 0.06) 0.0118	
	No	202/ 469 (43.1)	170/ 471 (36.1)	1.20 (1.03, 1.41) 0.0210	1.35 (1.04, 1.75) 0.0265	0.07 (0.01, 0.13) 0.0278	
	Diuretics at baseline						0.7626
	Yes	1022/2493 (41.0)	909/2492 (36.5)	1.11 (1.04, 1.19) 0.0025	1.20 (1.07, 1.35) 0.0021	0.04 (0.02, 0.07) 0.0021	
	No	125/ 299 (41.8)	114/ 300 (38.0)	1.09 (0.89, 1.32) 0.4080	1.16 (0.83, 1.61) 0.3807	0.04 (-0.04, 0.11) 0.3644	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	1340/2842 (47.1)	1229/2837 (43.3)	1.06 (1.01, 1.11) 0.0205	1.15 (1.03, 1.28) 0.0145	0.03 (0.01, 0.06) 0.0135	
	Age						0.3406
	<= median	698/1415 (49.3)	681/1482 (46.0)	1.06 (0.99, 1.13) 0.0846	1.14 (0.98, 1.33) 0.0878	0.03 (-0.00, 0.07) 0.0806	
	> median	642/1427 (45.0)	548/1355 (40.4)	1.11 (1.02, 1.21)*0.0157	1.16 (0.99, 1.36) 0.0694	0.03 (-0.00, 0.07) 0.0719	
	Gender						0.9787*
	Male	789/1656 (47.6)	712/1625 (43.8)	1.09 (1.01, 1.17)*0.0279	1.15 (1.00, 1.33) 0.0543	0.03 (0.00, 0.07) 0.0465	
	Female	551/1186 (46.5)	517/1212 (42.7)	1.04 (0.97, 1.12) 0.2365	1.13 (0.96, 1.35) 0.1514	0.02 (-0.01, 0.06) 0.1884	
	Race						0.7101*
	White	938/2039 (46.0)	864/2058 (42.0)	1.10 (1.02, 1.17)*0.0096	1.15 (1.01, 1.31) 0.0373	0.03 (0.00, 0.06) 0.0314	
	Black or African	38/ 67 (56.7)	33/ 71 (46.5)	1.22 (0.89, 1.67) 0.2114	1.46 (0.72, 2.95) 0.2910	0.09 (-0.08, 0.25) 0.2988	
	Asian	251/ 558 (45.0)	244/ 555 (44.0)	0.98 (0.87, 1.11) 0.8054	1.04 (0.82, 1.33) 0.7358	0.01 (-0.05, 0.07) 0.7580	
	Other	113/ 178 (63.5)	88/ 153 (57.5)	1.06 (0.89, 1.26) 0.5126	1.38 (0.85, 2.22) 0.1901	0.05 (-0.06, 0.15) 0.3754	
	Geographic region						0.7103*
	Asia	246/ 539 (45.6)	238/ 538 (44.2)	1.03 (0.90, 1.18)*0.6438	1.05 (0.82, 1.35) 0.6746	0.01 (-0.05, 0.07) 0.6757	
	Europe and Saudi Arabia	612/1365 (44.8)	574/1394 (41.2)	1.09 (1.00, 1.19)*0.0524	1.13 (0.97, 1.33) 0.1215	0.03 (-0.01, 0.06) 0.1521	
	North America	202/ 398 (50.8)	169/ 387 (43.7)	1.14 (0.99, 1.31) 0.0649	1.32 (0.99, 1.76) 0.0583	0.07 (0.00, 0.14) 0.0486	
	Latin America	280/ 540 (51.9)	248/ 518 (47.9)	1.05 (0.95, 1.17) 0.3417	1.14 (0.88, 1.48) 0.3201	0.02 (-0.03, 0.08) 0.3750	
	NYHA class at enrolment						0.3609*
	II	990/2113 (46.9)	956/2187 (43.7)	1.07 (1.00, 1.14)*0.0387	1.13 (1.00, 1.29) 0.0470	0.03 (0.00, 0.06) 0.0459	
	III or IV	350/ 729 (48.0)	273/ 649 (42.1)	1.05 (0.97, 1.15) 0.2210	1.22 (0.97, 1.54) 0.0941	0.03 (-0.01, 0.08) 0.1438	
	LVEF at enrolment						0.0418*
	<= 49	462/ 980 (47.1)	442/ 963 (45.9)	1.01 (0.94, 1.10) 0.7176	1.06 (0.88, 1.28) 0.5319	0.01 (-0.03, 0.05) 0.6173	
	50-59	498/1029 (48.4)	409/1017 (40.2)	1.20 (1.09, 1.33)*0.0002	1.38 (1.14, 1.65) 0.0007	0.07 (0.03, 0.11) 0.0005	
	>= 60	380/ 833 (45.6)	378/ 857 (44.1)	1.03 (0.93, 1.15)*0.5324	1.01 (0.83, 1.24) 0.8915	0.01 (-0.04, 0.05) 0.7628	
	NT-proBNP at enrolment						0.3754*
	<= median	678/1418 (47.8)	608/1421 (42.8)	1.12 (1.03, 1.21)*0.0072	1.20 (1.03, 1.40) 0.0185	0.04 (0.01, 0.08) 0.0158	
	> median	662/1424 (46.5)	620/1415 (43.8)	1.03 (0.97, 1.10) 0.2984	1.09 (0.93, 1.28) 0.2653	0.02 (-0.02, 0.05) 0.2827	
	Type 2 Diabetes Medical History						0.2598
	Yes	591/1250 (47.3)	529/1260 (42.0)	1.10 (1.02, 1.19) 0.0169	1.24 (1.06, 1.45)*0.0076	0.04 (0.01, 0.08) 0.0239	
	No	749/1592 (47.0)	700/1577 (44.4)	1.03 (0.98, 1.09) 0.2216	1.11 (0.97, 1.28)*0.1330	0.02 (-0.01, 0.05) 0.1945	
	Atrial fibrillation or flutter at enrolment ECG						0.7117
	Yes	574/1199 (47.9)	515/1199 (43.0)	1.07 (0.99, 1.15) 0.0909	1.20 (1.01, 1.42) 0.0384	0.04 (0.00, 0.08) 0.0352	
	No	766/1643 (46.6)	714/1638 (43.6)	1.05 (0.98, 1.12) 0.1448	1.11 (0.96, 1.28) 0.1479	0.02 (-0.01, 0.06) 0.1375	
	BMI (kg/m2) at enrolment						0.2489
	< 30	732/1571 (46.6)	672/1559 (43.1)	1.04 (0.97, 1.10) 0.2667	1.12 (0.97, 1.30) 0.1321	0.03 (-0.01, 0.06) 0.1133	
	>= 30	608/1270 (47.9)	555/1275 (43.5)	1.08 (1.01, 1.16) 0.0225	1.18 (1.01, 1.40) 0.0433	0.04 (-0.00, 0.07) 0.0516	
	Baseline eGFR (mL/min/1.73m^2)						0.6002
	< 60	610/1359 (44.9)	583/1396 (41.8)	1.07 (0.99, 1.17)*0.0982	1.13 (0.96, 1.32) 0.1320	0.03 (-0.01, 0.06) 0.1541	
	>= 60	730/1483 (49.2)	646/1440 (44.9)	1.06 (1.00, 1.13) 0.0636	1.15 (0.99, 1.34) 0.0650	0.03 (0.00, 0.07) 0.0497	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.7004
	<= median	688/1424 (48.3)	624/1439 (43.4)	1.05 (0.98, 1.12) 0.1671	1.18 (1.01, 1.38) 0.0354	0.03 (0.00, 0.07) 0.0468	
	> median	652/1418 (46.0)	605/1398 (43.3)	1.07 (1.00, 1.15) 0.0644	1.11 (0.95, 1.29) 0.1863	0.03 (-0.01, 0.06) 0.1552	
	LVEF at enrolment 2						0.1434*
	<= 49	462/ 980 (47.1)	442/ 963 (45.9)	1.01 (0.94, 1.10) 0.7176	1.06 (0.88, 1.28) 0.5319	0.01 (-0.03, 0.05) 0.6173	
	>= 50	878/1862 (47.2)	787/1874 (42.0)	1.12 (1.05, 1.21)*0.0015	1.19 (1.04, 1.37) 0.0100	0.04 (0.01, 0.07) 0.0064	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0006
	Yes	151/ 283 (53.4)	142/ 286 (49.7)	1.07 (0.92, 1.26)*0.3767	1.15 (0.80, 1.65) 0.4439	0.02 (-0.06, 0.09) 0.6152	
	No	1189/2559 (46.5)	1087/2551 (42.6)	1.07 (1.01, 1.12) 0.0130	1.15 (1.02, 1.29) 0.0189	0.03 (0.01, 0.06) 0.0161	
	MRAs at baseline						0.5709*
	Yes	574/1227 (46.8)	516/1224 (42.2)	1.06 (0.98, 1.15) 0.1432	1.20 (1.01, 1.41) 0.0342	0.04 (0.00, 0.08) 0.0399	
	No	766/1615 (47.4)	713/1613 (44.2)	1.07 (1.00, 1.16)*0.0660	1.11 (0.96, 1.28) 0.1611	0.03 (-0.01, 0.06) 0.1328	
	ACEi+ARB at baseline						0.7353*
	Yes	971/2065 (47.0)	892/2077 (42.9)	1.09 (1.02, 1.17)*0.0085	1.16 (1.02, 1.32) 0.0209	0.03 (0.00, 0.06) 0.0230	
	No	369/ 777 (47.5)	337/ 760 (44.3)	1.05 (0.95, 1.15) 0.3238	1.10 (0.90, 1.36) 0.3505	0.02 (-0.02, 0.07) 0.3153	
	ARNI at baseline						0.2724
	Yes	68/ 153 (44.4)	55/ 126 (43.7)	1.05 (0.80, 1.37) 0.7432	1.04 (0.64, 1.70) 0.8672	0.01 (-0.11, 0.12) 0.9058	
	No	1272/2689 (47.3)	1174/2711 (43.3)	1.06 (1.01, 1.11) 0.0129	1.16 (1.04, 1.30) 0.0100	0.03 (0.01, 0.06) 0.0080	
	Beta Blocker at baseline						0.4819
	Yes	1095/2360 (46.4)	1021/2356 (43.3)	1.07 (1.00, 1.14)*0.0346	1.10 (0.97, 1.24) 0.1237	0.02 (-0.01, 0.05) 0.1187	
	No	245/ 482 (50.8)	208/ 481 (43.2)	1.17 (1.04, 1.32) 0.0112	1.39 (1.07, 1.81) 0.0137	0.08 (0.02, 0.14) 0.0121	
	Diuretics at baseline						0.5163*
	Yes	1189/2536 (46.9)	1083/2531 (42.8)	1.06 (1.01, 1.12) 0.0202	1.17 (1.04, 1.31) 0.0089	0.04 (0.01, 0.06) 0.0072	
	No	151/ 306 (49.3)	146/ 306 (47.7)	1.03 (0.88, 1.22)*0.6860	1.00 (0.72, 1.39) 0.9905	-0.00 (-0.08, 0.08) 0.9817	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	1578/2842 (55.5)	1431/2837 (50.4)	1.09 (1.04, 1.14) 0.0006	1.22 (1.10, 1.36) 0.0002	0.05 (0.02, 0.07) 0.0002	
	Age						0.7276
	<= median	852/1415 (60.2)	806/1482 (54.4)	1.10 (1.04, 1.17) 0.0015	1.28 (1.10, 1.48) 0.0013	0.06 (0.02, 0.09) 0.0012	
	> median	726/1427 (50.9)	625/1355 (46.1)	1.07 (1.00, 1.16) 0.0611	1.19 (1.03, 1.39) 0.0224	0.04 (0.01, 0.08) 0.0225	
	Gender						0.8106
	Male	949/1656 (57.3)	841/1625 (51.8)	1.09 (1.03, 1.16) 0.0040	1.25 (1.09, 1.43) 0.0018	0.05 (0.02, 0.09) 0.0019	
	Female	629/1186 (53.0)	590/1212 (48.7)	1.07 (0.99, 1.15) 0.0808	1.18 (1.01, 1.39) 0.0425	0.04 (0.00, 0.08) 0.0428	
	Race						0.5917*
	White	1078/2039 (52.9)	995/2058 (48.3)	1.06 (1.00, 1.13) 0.0392	1.19 (1.05, 1.34) 0.0071	0.04 (0.01, 0.07) 0.0078	
	Black or African	38/ 67 (56.7)	38/ 71 (53.5)	1.13 (0.83, 1.53) 0.4326	1.14 (0.58, 2.26) 0.7054	0.04 (-0.12, 0.21) 0.6048	
	Asian	340/ 558 (60.9)	313/ 555 (56.4)	1.08 (0.98, 1.19) 0.1177	1.21 (0.95, 1.53) 0.1236	0.05 (-0.01, 0.10) 0.1214	
	Other	122/ 178 (68.5)	85/ 153 (55.6)	1.23 (1.05, 1.45) 0.0096	1.75 (1.10, 2.78) 0.0191	0.13 (0.03, 0.23) 0.0112	
	Geographic region						0.2298*
	Asia	331/ 539 (61.4)	308/ 538 (57.2)	1.07 (0.97, 1.19) 0.1589	1.19 (0.93, 1.52) 0.1650	0.04 (-0.02, 0.10) 0.1627	
	Europe and Saudi Arabia	711/1365 (52.1)	669/1394 (48.0)	1.09 (1.01, 1.17)*0.0315	1.16 (1.00, 1.35) 0.0548	0.03 (-0.00, 0.07) 0.0647	
	North America	206/ 398 (51.8)	157/ 387 (40.6)	1.26 (1.09, 1.47) 0.0025	1.58 (1.19, 2.10) 0.0017	0.11 (0.04, 0.18) 0.0013	
	Latin America	330/ 540 (61.1)	297/ 518 (57.3)	1.06 (0.96, 1.17) 0.2247	1.17 (0.91, 1.50) 0.2148	0.04 (-0.02, 0.10) 0.2053	
	NYHA class at enrolment						0.1664
	II	1168/2113 (55.3)	1118/2187 (51.1)	1.07 (1.02, 1.13) 0.0122	1.19 (1.05, 1.34) 0.0058	0.04 (0.01, 0.07) 0.0061	
	III or IV	410/ 729 (56.2)	312/ 649 (48.1)	1.17 (1.06, 1.30)*0.0027	1.38 (1.11, 1.72) 0.0041	0.08 (0.02, 0.13) 0.0034	
	LVEF at enrolment						0.0634
	<= 49	545/ 980 (55.6)	515/ 963 (53.5)	1.02 (0.95, 1.11) 0.5422	1.10 (0.92, 1.32) 0.3053	0.02 (-0.02, 0.07) 0.3343	
	50-59	577/1029 (56.1)	483/1017 (47.5)	1.16 (1.07, 1.26) 0.0003	1.41 (1.18, 1.68) 0.0001	0.08 (0.04, 0.13) 0.0001	
	>= 60	456/ 833 (54.7)	433/ 857 (50.5)	1.07 (0.98, 1.17) 0.1323	1.16 (0.96, 1.41) 0.1260	0.04 (-0.01, 0.08) 0.1229	
	NT-proBNP at enrolment						0.8482
	<= median	769/1418 (54.2)	705/1421 (49.6)	1.09 (1.01, 1.17) 0.0209	1.21 (1.04, 1.40) 0.0134	0.05 (0.01, 0.08) 0.0134	
	> median	809/1424 (56.8)	725/1415 (51.2)	1.08 (1.01, 1.15) 0.0208	1.24 (1.06, 1.44) 0.0057	0.05 (0.01, 0.09) 0.0063	
	Type 2 Diabetes Medical History						0.2349
	Yes	697/1250 (55.8)	615/1260 (48.8)	1.12 (1.05, 1.21) 0.0016	1.32 (1.13, 1.55)*0.0005	0.07 (0.03, 0.11) 0.0006	
	No	881/1592 (55.3)	816/1577 (51.7)	1.06 (1.00, 1.13) 0.0702	1.16 (1.00, 1.33)*0.0425	0.03 (-0.00, 0.07) 0.0558	
	Atrial fibrillation or flutter at enrolment ECG						0.8444
	Yes	681/1199 (56.8)	615/1199 (51.3)	1.09 (1.02, 1.17) 0.0147	1.25 (1.06, 1.47) 0.0081	0.05 (0.01, 0.09) 0.0082	
	No	897/1643 (54.6)	816/1638 (49.8)	1.08 (1.01, 1.15) 0.0157	1.21 (1.05, 1.39) 0.0079	0.05 (0.01, 0.08) 0.0079	
	BMI (kg/m2) at enrolment						0.2520
	< 30	897/1571 (57.1)	790/1559 (50.7)	1.12 (1.05, 1.20) 0.0004	1.29 (1.12, 1.49) 0.0004	0.06 (0.03, 0.10) 0.0004	
	>= 30	681/1270 (53.6)	640/1275 (50.2)	1.05 (0.98, 1.12) 0.2074	1.14 (0.97, 1.34) 0.1073	0.03 (-0.01, 0.07) 0.1062	
	Baseline eGFR (mL/min/1.73m^2)						0.4007
	< 60	709/1359 (52.2)	675/1396 (48.4)	1.06 (0.99, 1.14) 0.1211	1.16 (1.00, 1.35) 0.0529	0.04 (-0.00, 0.07) 0.0575	
	>= 60	869/1483 (58.6)	755/1440 (52.4)	1.11 (1.04, 1.18) 0.0013	1.28 (1.10, 1.48) 0.0012	0.06 (0.02, 0.10) 0.0010	

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Symptom Burden (LOCF)	SBP at randomisation						0.1955
	<= median	798/1424 (56.0)	703/1439 (48.9)	1.12 (1.05, 1.20) 0.0009	1.31 (1.13, 1.52) 0.0003	0.07 (0.03, 0.10) 0.0004	
	> median	780/1418 (55.0)	728/1398 (52.1)	1.05 (0.98, 1.12) 0.1355	1.14 (0.98, 1.32) 0.0966	0.03 (-0.01, 0.07) 0.0939	
	LVEF at enrolment 2						0.0634
	<= 49	545/ 980 (55.6)	515/ 963 (53.5)	1.02 (0.95, 1.11) 0.5422	1.10 (0.92, 1.32) 0.3053	0.02 (-0.02, 0.07) 0.3343	
	>= 50	1033/1862 (55.5)	916/1874 (48.9)	1.12 (1.06, 1.19) 0.0002	1.29 (1.13, 1.47) 0.0001	0.06 (0.03, 0.09) 0.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5704
	Yes	173/ 283 (61.1)	164/ 286 (57.3)	1.07 (0.93, 1.22)*0.3582	1.25 (0.88, 1.79) 0.2092	0.04 (-0.04, 0.12)*0.3575	
	No	1405/2559 (54.9)	1267/2551 (49.7)	1.10 (1.04, 1.15) 0.0005	1.23 (1.10, 1.37) 0.0003	0.05 (0.02, 0.08) 0.0003	
	MRAs at baseline						0.3437
	Yes	689/1227 (56.2)	609/1224 (49.8)	1.12 (1.04, 1.20) 0.0028	1.28 (1.09, 1.51) 0.0023	0.06 (0.02, 0.10) 0.0022	
	No	889/1615 (55.0)	822/1613 (51.0)	1.07 (1.00, 1.13) 0.0486	1.18 (1.02, 1.35) 0.0227	0.04 (0.01, 0.07) 0.0233	
	ACEi+ARB at baseline						0.4759
	Yes	1149/2065 (55.6)	1038/2077 (50.0)	1.10 (1.04, 1.16) 0.0013	1.25 (1.10, 1.41) 0.0005	0.05 (0.02, 0.08) 0.0005	
	No	429/ 777 (55.2)	393/ 760 (51.7)	1.06 (0.97, 1.16) 0.2169	1.15 (0.94, 1.41) 0.1616	0.04 (-0.01, 0.08) 0.1668	
	ARNI at baseline						0.3116
	Yes	79/ 153 (51.6)	69/ 126 (54.8)	0.96 (0.77, 1.21) 0.7488	0.92 (0.57, 1.49) 0.7364	-0.02 (-0.14, 0.10) 0.7359	
	No	1499/2689 (55.7)	1362/2711 (50.2)	1.09 (1.04, 1.15) 0.0004	1.24 (1.11, 1.38) 0.0001	0.05 (0.03, 0.08) 0.0001	
	Beta Blocker at baseline						0.1060
	Yes	1285/2360 (54.4)	1183/2356 (50.2)	1.07 (1.01, 1.12) 0.0173	1.17 (1.04, 1.32) 0.0070	0.04 (0.01, 0.07) 0.0072	
	No	293/ 482 (60.8)	248/ 481 (51.6)	1.18 (1.06, 1.32) 0.0024	1.49 (1.15, 1.93) 0.0023	0.10 (0.04, 0.16) 0.0021	
	Diuretics at baseline						0.9398
	Yes	1391/2536 (54.9)	1265/2531 (50.0)	1.09 (1.03, 1.14) 0.0016	1.22 (1.09, 1.36) 0.0006	0.05 (0.02, 0.08) 0.0005	
	No	187/ 306 (61.1)	166/ 306 (54.2)	1.10 (0.96, 1.26) 0.1830	1.28 (0.92, 1.77) 0.1406	0.06 (-0.02, 0.14) 0.1480	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	1475/2842 (51.9)	1479/2837 (52.1)	1.00 (0.95, 1.05) 0.9984	0.99 (0.89, 1.10) 0.8543	-0.00 (-0.03, 0.02) 0.8664	
	Age						0.2092
	<= median	761/1415 (53.8)	825/1482 (55.7)	0.97 (0.91, 1.04) 0.3732	0.93 (0.80, 1.07) 0.3153	-0.02 (-0.05, 0.02) 0.3232	
	> median	714/1427 (50.0)	654/1355 (48.3)	1.04 (0.96, 1.12) 0.3177	1.07 (0.92, 1.24) 0.3811	0.02 (-0.02, 0.05) 0.3822	
	Gender						0.3795
	Male	857/1656 (51.8)	860/1625 (52.9)	0.98 (0.92, 1.05) 0.5494	0.96 (0.83, 1.10) 0.5129	-0.01 (-0.05, 0.02) 0.5184	
	Female	618/1186 (52.1)	619/1212 (51.1)	1.03 (0.95, 1.11) 0.4645	1.04 (0.88, 1.22) 0.6399	0.01 (-0.03, 0.05) 0.6340	
	Race						0.3842
	White	1084/2039 (53.2)	1098/2058 (53.4)	1.00 (0.94, 1.06) 0.9698	0.99 (0.88, 1.12) 0.8813	-0.00 (-0.03, 0.03) 0.8920	
	Black or African	38/ 67 (56.7)	39/ 71 (54.9)	1.03 (0.77, 1.39)*0.8326	1.10 (0.55, 2.19) 0.7794	0.02 (-0.14, 0.18) 0.8059	
	Asian	257/ 558 (46.1)	271/ 555 (48.8)	0.94 (0.84, 1.06) 0.3148	0.91 (0.72, 1.16) 0.4380	-0.02 (-0.08, 0.03) 0.4083	
	Other	96/ 178 (53.9)	71/ 153 (46.4)	1.15 (0.92, 1.42) 0.2182	1.37 (0.88, 2.13) 0.1680	0.07 (-0.03, 0.18) 0.1766	
	Geographic region						0.2072
	Asia	248/ 539 (46.0)	260/ 538 (48.3)	0.95 (0.84, 1.07) 0.3780	0.93 (0.73, 1.19) 0.5632	-0.02 (-0.08, 0.04) 0.5365	
	Europe and Saudi Arabia	686/1365 (50.3)	703/1394 (50.4)	1.00 (0.93, 1.08) 0.9745	0.99 (0.85, 1.15) 0.9028	-0.00 (-0.04, 0.03) 0.9041	
	North America	235/ 398 (59.0)	245/ 387 (63.3)	0.94 (0.84, 1.05) 0.2420	0.84 (0.63, 1.12) 0.2263	-0.04 (-0.11, 0.03) 0.2302	
	Latin America	306/ 540 (56.7)	271/ 518 (52.3)	1.12 (1.00, 1.24) 0.0473	1.21 (0.94, 1.54) 0.1333	0.05 (-0.01, 0.11) 0.1088	
	NYHA class at enrolment						0.0528
	II	1083/2113 (51.3)	1156/2187 (52.9)	0.97 (0.92, 1.03) 0.3512	0.94 (0.83, 1.06) 0.2808	-0.02 (-0.05, 0.01) 0.2858	
	III or IV	392/ 729 (53.8)	322/ 649 (49.6)	1.09 (0.99, 1.21) 0.0927	1.19 (0.96, 1.47) 0.1099	0.04 (-0.01, 0.10) 0.1075	
	LVEF at enrolment						0.3586
	<= 49	498/ 980 (50.8)	516/ 963 (53.6)	0.95 (0.88, 1.04) 0.2729	0.90 (0.75, 1.07) 0.2361	-0.03 (-0.07, 0.02) 0.2390	
	50-59	536/1029 (52.1)	507/1017 (49.9)	1.05 (0.96, 1.14) 0.3049	1.09 (0.92, 1.30) 0.3152	0.02 (-0.02, 0.07) 0.3140	
	>= 60	441/ 833 (52.9)	456/ 857 (53.2)	1.00 (0.92, 1.10) 0.9523	0.99 (0.81, 1.19) 0.8821	-0.00 (-0.05, 0.04) 0.9016	
	NT-proBNP at enrolment						0.5928
	<= median	730/1418 (51.5)	743/1421 (52.3)	0.99 (0.92, 1.06) 0.7008	0.97 (0.83, 1.12) 0.6481	-0.01 (-0.05, 0.03) 0.6542	
	> median	745/1424 (52.3)	735/1415 (51.9)	1.02 (0.95, 1.09) 0.6631	1.02 (0.88, 1.18) 0.8207	0.00 (-0.03, 0.04) 0.8103	
	Type 2 Diabetes Medical History						0.2382
	Yes	685/1250 (54.8)	671/1260 (53.3)	1.03 (0.96, 1.11) 0.4240	1.06 (0.91, 1.25)*0.4371	0.02 (-0.02, 0.05) 0.4478	
	No	790/1592 (49.6)	808/1577 (51.2)	0.97 (0.91, 1.04) 0.4293	0.94 (0.82, 1.08)*0.3638	-0.02 (-0.05, 0.02) 0.3874	
	Atrial fibrillation or flutter at enrolment ECG						0.2639
	Yes	614/1199 (51.2)	595/1199 (49.6)	1.04 (0.96, 1.12) 0.3895	1.06 (0.90, 1.25) 0.4698	0.01 (-0.03, 0.05) 0.4671	
	No	861/1643 (52.4)	884/1638 (54.0)	0.98 (0.92, 1.04) 0.4551	0.94 (0.82, 1.08) 0.3811	-0.01 (-0.05, 0.02) 0.3898	
	BMI (kg/m2) at enrolment						0.0465
	< 30	753/1571 (47.9)	786/1559 (50.4)	0.95 (0.89, 1.02) 0.1913	0.90 (0.78, 1.04) 0.1462	-0.03 (-0.06, 0.01) 0.1488	
	>= 30	722/1270 (56.9)	692/1275 (54.3)	1.05 (0.98, 1.13) 0.1552	1.11 (0.95, 1.30) 0.1847	0.03 (-0.01, 0.06) 0.1796	
	Baseline eGFR (mL/min/1.73m^2)						0.3578
	< 60	688/1359 (50.6)	729/1396 (52.2)	0.98 (0.91, 1.05) 0.4996	0.94 (0.81, 1.09) 0.4053	-0.02 (-0.05, 0.02) 0.4063	
	>= 60	787/1483 (53.1)	749/1440 (52.0)	1.02 (0.95, 1.09) 0.5346	1.04 (0.90, 1.20) 0.6209	0.01 (-0.03, 0.05) 0.6053	

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Self Efficacy (LOCF)	SBP at randomisation						0.2027
	<= median	730/1424 (51.3)	764/1439 (53.1)	0.97 (0.90, 1.04) 0.3811	0.93 (0.80, 1.07) 0.3070	-0.02 (-0.06, 0.02) 0.3076	
	> median	745/1418 (52.5)	715/1398 (51.1)	1.03 (0.96, 1.11) 0.3886	1.06 (0.92, 1.23) 0.4257	0.02 (-0.02, 0.05) 0.4203	
	LVEF at enrolment 2						0.2122
	<= 49	498/ 980 (50.8)	516/ 963 (53.6)	0.95 (0.88, 1.04) 0.2729	0.90 (0.75, 1.07) 0.2361	-0.03 (-0.07, 0.02) 0.2390	
	>= 50	977/1862 (52.5)	963/1874 (51.4)	1.02 (0.96, 1.09) 0.4378	1.04 (0.92, 1.19) 0.5257	0.01 (-0.02, 0.04) 0.5178	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5309
	Yes	149/ 283 (52.7)	144/ 286 (50.3)	1.05 (0.90, 1.23) 0.5157	1.09 (0.78, 1.52) 0.6047	0.02 (-0.06, 0.10) 0.6088	
	No	1326/2559 (51.8)	1335/2551 (52.3)	0.99 (0.94, 1.05) 0.8227	0.98 (0.88, 1.09) 0.7086	-0.01 (-0.03, 0.02) 0.7192	
	MRAs at baseline						0.9290
	Yes	612/1227 (49.9)	615/1224 (50.2)	1.00 (0.92, 1.08) 0.9379	0.99 (0.84, 1.16) 0.8867	-0.00 (-0.04, 0.04) 0.8877	
	No	863/1615 (53.4)	864/1613 (53.6)	1.00 (0.94, 1.07) 0.9186	1.00 (0.87, 1.15) 0.9692	-0.00 (-0.03, 0.03) 0.9804	
	ACEi+ARB at baseline						0.3209
	Yes	1065/2065 (51.6)	1063/2077 (51.2)	1.02 (0.96, 1.08) 0.6069	1.02 (0.90, 1.15) 0.8007	0.00 (-0.03, 0.03) 0.7877	
	No	410/ 777 (52.8)	416/ 760 (54.7)	0.96 (0.88, 1.05) 0.3931	0.92 (0.75, 1.13) 0.4311	-0.02 (-0.07, 0.03) 0.4258	
	ARNI at baseline						0.8228
	Yes	82/ 153 (53.6)	65/ 126 (51.6)	1.05 (0.83, 1.31) 0.6992	1.11 (0.69, 1.80) 0.6568	0.03 (-0.09, 0.15) 0.6581	
	No	1393/2689 (51.8)	1414/2711 (52.2)	1.00 (0.95, 1.05) 0.9590	0.99 (0.89, 1.10) 0.7912	-0.00 (-0.03, 0.02) 0.8053	
	Beta Blocker at baseline						0.9192
	Yes	1210/2360 (51.3)	1217/2356 (51.7)	1.00 (0.95, 1.06) 0.9967	0.98 (0.88, 1.10) 0.7865	-0.00 (-0.03, 0.02) 0.8019	
	No	265/ 482 (55.0)	262/ 481 (54.5)	1.01 (0.90, 1.13) 0.8702	1.02 (0.79, 1.32) 0.8691	0.01 (-0.06, 0.07) 0.8688	
	Diuretics at baseline						0.2682
	Yes	1317/2536 (51.9)	1306/2531 (51.6)	1.01 (0.96, 1.06) 0.7157	1.01 (0.91, 1.13) 0.8058	0.00 (-0.02, 0.03) 0.7993	
	No	158/ 306 (51.6)	173/ 306 (56.5)	0.93 (0.80, 1.07) 0.3097	0.81 (0.59, 1.12) 0.2060	-0.05 (-0.13, 0.03) 0.2187	

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Symptom Frequency (LOCF)							
	Overall	1379/2842 (48.5)	1280/2837 (45.1)	1.07 (1.02, 1.13) 0.0114	1.15 (1.03, 1.27) 0.0112	0.03 (0.01, 0.06) 0.0099	
	Age						0.6317
	<= median	744/1415 (52.6)	717/1482 (48.4)	1.09 (1.02, 1.17) 0.0151	1.19 (1.03, 1.38) 0.0179	0.04 (0.01, 0.08) 0.0170	
	> median	635/1427 (44.5)	563/1355 (41.5)	1.05 (0.97, 1.14) 0.2289	1.11 (0.95, 1.30) 0.1762	0.03 (-0.01, 0.06) 0.1490	
	Gender						0.4281
	Male	810/1656 (48.9)	756/1625 (46.5)	1.05 (0.98, 1.13) 0.1607	1.10 (0.96, 1.27) 0.1622	0.02 (-0.01, 0.06) 0.1577	
	Female	569/1186 (48.0)	524/1212 (43.2)	1.09 (1.00, 1.18) 0.0466	1.20 (1.02, 1.42) 0.0294	0.04 (0.01, 0.08) 0.0243	
	Race						0.3203
	White	934/2039 (45.8)	880/2058 (42.8)	1.06 (0.99, 1.13) 0.0899	1.12 (0.98, 1.27) 0.0854	0.03 (-0.00, 0.06) 0.0804	
	Black or African	30/ 67 (44.8)	35/ 71 (49.3)	1.05 (0.73, 1.52) 0.7746	0.87 (0.44, 1.72) 0.6827	-0.03 (-0.20, 0.13) 0.6859	
	Asian	308/ 558 (55.2)	291/ 555 (52.4)	1.05 (0.94, 1.17) 0.3537	1.12 (0.89, 1.42) 0.3433	0.03 (-0.03, 0.09) 0.3440	
	Other	107/ 178 (60.1)	74/ 153 (48.4)	1.24 (1.01, 1.52)*0.0356	1.76 (1.11, 2.81) 0.0172	0.12 (0.01, 0.22)*0.0314	
	Geographic region						0.8439*
	Asia	301/ 539 (55.8)	285/ 538 (53.0)	1.05 (0.94, 1.18) 0.3478	1.13 (0.89, 1.43) 0.3342	0.03 (-0.03, 0.09) 0.3354	
	Europe and Saudi Arabia	629/1365 (46.1)	595/1394 (42.7)	1.08 (0.99, 1.17)*0.0726	1.13 (0.97, 1.32) 0.1239	0.03 (-0.01, 0.07) 0.1129	
	North America	158/ 398 (39.7)	150/ 387 (38.8)	1.04 (0.87, 1.23) 0.6856	1.06 (0.79, 1.41) 0.7156	0.01 (-0.06, 0.08) 0.7333	
	Latin America	291/ 540 (53.9)	250/ 518 (48.3)	1.12 (0.99, 1.26)*0.0681	1.29 (1.00, 1.66) 0.0469	0.06 (0.00, 0.12) 0.0360	
	NYHA class at enrolment						0.9334
	II	1011/2113 (47.8)	971/2187 (44.4)	1.07 (1.01, 1.14) 0.0281	1.16 (1.03, 1.31) 0.0166	0.04 (0.01, 0.07) 0.0166	
	III or IV	368/ 729 (50.5)	309/ 649 (47.6)	1.08 (0.98, 1.19) 0.1217	1.10 (0.89, 1.37) 0.3805	0.03 (-0.02, 0.08) 0.2917	
	LVEF at enrolment						0.9928
	<= 49	489/ 980 (49.9)	450/ 963 (46.7)	1.08 (0.98, 1.18) 0.1089	1.15 (0.96, 1.38) 0.1230	0.03 (-0.01, 0.08) 0.1213	
	50-59	480/1029 (46.6)	440/1017 (43.3)	1.07 (0.98, 1.17) 0.1475	1.14 (0.96, 1.37) 0.1378	0.03 (-0.01, 0.08) 0.1245	
	>= 60	410/ 833 (49.2)	390/ 857 (45.5)	1.07 (0.97, 1.18) 0.1852	1.14 (0.94, 1.38) 0.1878	0.03 (-0.01, 0.08) 0.1762	
	NT-proBNP at enrolment						0.6163
	<= median	677/1418 (47.7)	623/1421 (43.8)	1.09 (1.01, 1.18) 0.0362	1.18 (1.01, 1.36) 0.0333	0.04 (0.00, 0.08) 0.0306	
	> median	702/1424 (49.3)	656/1415 (46.4)	1.05 (0.98, 1.13) 0.1618	1.12 (0.96, 1.30) 0.1500	0.03 (-0.01, 0.06) 0.1483	
	Type 2 Diabetes Medical History						0.8948
	Yes	601/1250 (48.1)	568/1260 (45.1)	1.07 (0.99, 1.17) 0.0793	1.13 (0.96, 1.32)*0.1319	0.03 (-0.01, 0.07) 0.1073	
	No	778/1592 (48.9)	712/1577 (45.1)	1.07 (0.99, 1.15) 0.0774	1.16 (1.01, 1.34)*0.0359	0.04 (0.00, 0.07) 0.0453	
	Atrial fibrillation or flutter at enrolment ECG						0.6266
	Yes	591/1199 (49.3)	558/1199 (46.5)	1.05 (0.97, 1.14) 0.1955	1.12 (0.95, 1.32) 0.1738	0.03 (-0.01, 0.07) 0.1601	
	No	788/1643 (48.0)	722/1638 (44.1)	1.08 (1.01, 1.17) 0.0267	1.17 (1.02, 1.34) 0.0295	0.04 (0.00, 0.07) 0.0283	
	BMI (kg/m2) at enrolment						0.8363
	< 30	779/1571 (49.6)	716/1559 (45.9)	1.08 (1.01, 1.16) 0.0336	1.16 (1.01, 1.34) 0.0378	0.04 (0.00, 0.07) 0.0362	
	>= 30	600/1270 (47.2)	563/1275 (44.2)	1.06 (0.98, 1.15) 0.1388	1.13 (0.96, 1.32) 0.1481	0.03 (-0.01, 0.07) 0.1321	
	Baseline eGFR (mL/min/1.73m^2)						0.7806
	< 60	628/1359 (46.2)	603/1396 (43.2)	1.06 (0.98, 1.15) 0.1616	1.13 (0.97, 1.32) 0.1119	0.03 (-0.01, 0.07) 0.1130	
	>= 60	751/1483 (50.6)	677/1440 (47.0)	1.08 (1.00, 1.16) 0.0377	1.15 (1.00, 1.34) 0.0560	0.04 (0.00, 0.07) 0.0477	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Symptom Frequency (LOCF)	SBP at randomisation						0.8259
	<= median	676/1424 (47.5)	630/1439 (43.8)	1.06 (0.98, 1.15) 0.1188	1.15 (0.99, 1.33) 0.0730	0.03 (-0.00, 0.07) 0.0727	
	> median	703/1418 (49.6)	650/1398 (46.5)	1.08 (1.00, 1.16) 0.0489	1.14 (0.99, 1.33) 0.0774	0.03 (-0.00, 0.07) 0.0681	
	LVEF at enrolment 2						0.9170
	<= 49	489/ 980 (49.9)	450/ 963 (46.7)	1.08 (0.98, 1.18) 0.1089	1.15 (0.96, 1.38) 0.1230	0.03 (-0.01, 0.08) 0.1213	
	>= 50	890/1862 (47.8)	830/1874 (44.3)	1.07 (1.00, 1.14) 0.0511	1.14 (1.00, 1.30) 0.0496	0.03 (0.00, 0.06) 0.0428	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8198
	Yes	163/ 283 (57.6)	153/ 286 (53.5)	1.08 (0.93, 1.25)*0.3254	1.39 (0.97, 1.99) 0.0723	0.04 (-0.04, 0.12)*0.3246	
	No	1216/2559 (47.5)	1127/2551 (44.2)	1.07 (1.01, 1.14) 0.0207	1.14 (1.02, 1.27) 0.0226	0.03 (0.00, 0.06) 0.0203	
	MRAs at baseline						0.6136
	Yes	596/1227 (48.6)	542/1224 (44.3)	1.09 (1.00, 1.18) 0.0490	1.19 (1.01, 1.40) 0.0339	0.04 (0.00, 0.08) 0.0302	
	No	783/1615 (48.5)	738/1613 (45.8)	1.06 (0.99, 1.14) 0.1080	1.11 (0.97, 1.28) 0.1271	0.03 (-0.01, 0.06) 0.1228	
	ACEi+ARB at baseline						0.0389
	Yes	1015/2065 (49.2)	912/2077 (43.9)	1.10 (1.04, 1.17) 0.0019	1.23 (1.09, 1.39) 0.0012	0.05 (0.02, 0.08) 0.0010	
	No	364/ 777 (46.8)	368/ 760 (48.4)	0.97 (0.88, 1.08) 0.5801	0.94 (0.77, 1.15) 0.5744	-0.01 (-0.06, 0.04) 0.5755	
	ARNI at baseline						0.9129
	Yes	74/ 153 (48.4)	60/ 126 (47.6)	1.05 (0.82, 1.35) 0.7028	1.08 (0.66, 1.74) 0.7667	0.02 (-0.10, 0.14) 0.7725	
	No	1305/2689 (48.5)	1220/2711 (45.0)	1.07 (1.01, 1.13) 0.0133	1.15 (1.03, 1.28) 0.0132	0.03 (0.01, 0.06) 0.0115	
	Beta Blocker at baseline						0.0759
	Yes	1126/2360 (47.7)	1062/2356 (45.1)	1.05 (0.99, 1.11) 0.1196	1.10 (0.98, 1.24) 0.1026	0.02 (-0.00, 0.05) 0.0977	
	No	253/ 482 (52.5)	218/ 481 (45.3)	1.18 (1.04, 1.34) 0.0106	1.38 (1.07, 1.78) 0.0141	0.08 (0.02, 0.14) 0.0123	
	Diuretics at baseline						0.3660
	Yes	1207/2536 (47.6)	1136/2531 (44.9)	1.06 (1.00, 1.12) 0.0431	1.12 (1.00, 1.25) 0.0450	0.03 (0.00, 0.06) 0.0415	
	No	172/ 306 (56.2)	144/ 306 (47.1)	1.14 (0.98, 1.32) 0.0917	1.38 (1.00, 1.90) 0.0531	0.08 (-0.00, 0.16) 0.0540	

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Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)							
	Overall	1322/2669 (49.5)	1244/2664 (46.7)	1.06 (1.00, 1.12) 0.0352	1.12 (1.01, 1.25) 0.0387	0.03 (0.00, 0.06) 0.0365	
	Age						0.1311
	<= median	713/1352 (52.7)	677/1422 (47.6)	1.10 (1.03, 1.19) 0.0075	1.24 (1.06, 1.44) 0.0056	0.05 (0.02, 0.09) 0.0054	
	> median	609/1317 (46.2)	567/1242 (45.7)	1.01 (0.93, 1.10) 0.7399	1.02 (0.87, 1.19) 0.8505	0.00 (-0.03, 0.04) 0.8403	
	Gender						0.7085
	Male	780/1568 (49.7)	722/1518 (47.6)	1.05 (0.98, 1.13) 0.1833	1.10 (0.95, 1.26) 0.2062	0.02 (-0.01, 0.06) 0.1968	
	Female	542/1101 (49.2)	522/1146 (45.5)	1.07 (0.98, 1.17) 0.1152	1.15 (0.97, 1.36) 0.1024	0.03 (-0.01, 0.07) 0.1051	
	Race						0.9432
	White	897/1925 (46.6)	866/1952 (44.4)	1.04 (0.97, 1.11) 0.2284	1.08 (0.95, 1.23) 0.2314	0.02 (-0.01, 0.05) 0.2213	
	Black or African	27/ 61 (44.3)	29/ 67 (43.3)	1.13 (0.76, 1.68) 0.5481	1.09 (0.53, 2.24) 0.8129	0.03 (-0.14, 0.20) 0.7371	
	Asian	305/ 510 (59.8)	274/ 500 (54.8)	1.09 (0.98, 1.21) 0.1258	1.21 (0.94, 1.56) 0.1306	0.05 (-0.01, 0.11) 0.1299	
	Other	93/ 173 (53.8)	75/ 145 (51.7)	1.14 (0.93, 1.39) 0.2117	1.18 (0.74, 1.86) 0.4848	0.05 (-0.06, 0.15) 0.4031	
	Geographic region						0.9379
	Asia	300/ 496 (60.5)	269/ 486 (55.3)	1.09 (0.98, 1.21) 0.1206	1.22 (0.95, 1.58) 0.1242	0.05 (-0.01, 0.11) 0.1235	
	Europe and Saudi Arabia	590/1299 (45.4)	575/1323 (43.5)	1.04 (0.95, 1.12) 0.3973	1.06 (0.91, 1.24) 0.4525	0.01 (-0.02, 0.05) 0.4719	
	North America	164/ 372 (44.1)	153/ 359 (42.6)	1.05 (0.89, 1.23) 0.5653	1.08 (0.81, 1.46) 0.5963	0.02 (-0.05, 0.09) 0.5848	
	Latin America	268/ 502 (53.4)	247/ 496 (49.8)	1.09 (0.97, 1.22) 0.1522	1.16 (0.90, 1.50) 0.2456	0.04 (-0.02, 0.10) 0.1959	
	NYHA class at enrolment						0.9473
	II	1021/1986 (51.4)	995/2059 (48.3)	1.07 (1.00, 1.13) 0.0383	1.14 (1.00, 1.29) 0.0415	0.03 (0.00, 0.06) 0.0401	
	III or IV	301/ 683 (44.1)	249/ 604 (41.2)	1.06 (0.95, 1.20) 0.2970	1.12 (0.89, 1.42) 0.3155	0.03 (-0.02, 0.08) 0.2836	
	LVEF at enrolment						0.0858
	<= 49	459/ 928 (49.5)	449/ 912 (49.2)	1.02 (0.93, 1.11) 0.7133	1.03 (0.86, 1.24) 0.7622	0.01 (-0.04, 0.05) 0.7464	
	50-59	472/ 970 (48.7)	396/ 956 (41.4)	1.15 (1.05, 1.27) 0.0038	1.32 (1.10, 1.58) 0.0029	0.07 (0.02, 0.11) 0.0029	
	>= 60	391/ 771 (50.7)	399/ 796 (50.1)	1.02 (0.92, 1.12) 0.7525	1.02 (0.84, 1.25) 0.8237	0.01 (-0.04, 0.06) 0.8166	
	NT-proBNP at enrolment						0.3206
	<= median	651/1334 (48.8)	637/1350 (47.2)	1.03 (0.96, 1.12) 0.4170	1.07 (0.92, 1.25) 0.3792	0.02 (-0.02, 0.05) 0.3734	
	> median	671/1335 (50.3)	606/1313 (46.2)	1.09 (1.01, 1.18) 0.0278	1.18 (1.01, 1.37) 0.0401	0.04 (0.00, 0.08) 0.0377	
	Type 2 Diabetes Medical History						0.6739
	Yes	574/1169 (49.1)	542/1186 (45.7)	1.08 (0.99, 1.17) 0.0900	1.15 (0.97, 1.35)*0.0984	0.03 (-0.01, 0.07) 0.0950	
	No	748/1500 (49.9)	702/1478 (47.5)	1.05 (0.98, 1.13) 0.1894	1.10 (0.95, 1.27)*0.1958	0.02 (-0.01, 0.06) 0.1968	
	Atrial fibrillation or flutter at enrolment ECG						0.0757
	Yes	579/1113 (52.0)	521/1123 (46.4)	1.12 (1.03, 1.22) 0.0060	1.25 (1.06, 1.48) 0.0084	0.06 (0.01, 0.10) 0.0083	
	No	743/1556 (47.8)	723/1541 (46.9)	1.02 (0.94, 1.09) 0.6728	1.04 (0.90, 1.19) 0.6281	0.01 (-0.03, 0.04) 0.5967	
	BMI (kg/m2) at enrolment						0.1970
	< 30	759/1478 (51.4)	680/1451 (46.9)	1.10 (1.02, 1.18) 0.0139	1.20 (1.03, 1.38) 0.0154	0.04 (0.01, 0.08) 0.0148	
	>= 30	563/1190 (47.3)	563/1211 (46.5)	1.02 (0.94, 1.10) 0.6819	1.03 (0.88, 1.21) 0.6998	0.01 (-0.03, 0.05) 0.6841	
	Baseline eGFR (mL/min/1.73m^2)						0.6897
	< 60	591/1266 (46.7)	582/1297 (44.9)	1.05 (0.96, 1.14) 0.2886	1.08 (0.92, 1.26) 0.3306	0.02 (-0.02, 0.06) 0.3272	
	>= 60	731/1403 (52.1)	662/1366 (48.5)	1.07 (0.99, 1.15) 0.0686	1.15 (0.99, 1.34) 0.0634	0.04 (-0.00, 0.07) 0.0610	

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Social Limitation (LOCF)	SBP at randomisation						0.9277
	<= median	666/1344 (49.6)	628/1344 (46.7)	1.06 (0.98, 1.14) 0.1504	1.11 (0.95, 1.30) 0.1734	0.03 (-0.01, 0.06) 0.1633	
	> median	656/1325 (49.5)	616/1320 (46.7)	1.06 (0.98, 1.15) 0.1207	1.13 (0.97, 1.32) 0.1147	0.03 (-0.01, 0.07) 0.1147	
	LVEF at enrolment 2						0.2640
	<= 49	459/ 928 (49.5)	449/ 912 (49.2)	1.02 (0.93, 1.11) 0.7133	1.03 (0.86, 1.24) 0.7622	0.01 (-0.04, 0.05) 0.7464	
	>= 50	863/1741 (49.6)	795/1752 (45.4)	1.09 (1.01, 1.16) 0.0195	1.17 (1.03, 1.34) 0.0201	0.04 (0.01, 0.07) 0.0197	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9789
	Yes	127/ 257 (49.4)	121/ 261 (46.4)	1.00 (0.86, 1.17) 0.9763	1.19 (0.83, 1.71) 0.3473	0.03 (-0.05, 0.12) 0.4058	
	No	1195/2412 (49.5)	1123/2403 (46.7)	1.06 (1.00, 1.12) 0.0463	1.12 (1.00, 1.25) 0.0544	0.03 (-0.00, 0.06) 0.0517	
	MRAs at baseline						0.9431
	Yes	572/1155 (49.5)	535/1146 (46.7)	1.06 (0.97, 1.15) 0.1837	1.13 (0.96, 1.33) 0.1448	0.03 (-0.01, 0.07) 0.1373	
	No	750/1514 (49.5)	709/1518 (46.7)	1.06 (0.99, 1.14) 0.1020	1.11 (0.96, 1.29) 0.1412	0.03 (-0.01, 0.06) 0.1389	
	ACEi+ARB at baseline						0.1848
	Yes	947/1940 (48.8)	921/1959 (47.0)	1.04 (0.97, 1.10) 0.2861	1.07 (0.94, 1.22) 0.2810	0.02 (-0.01, 0.05) 0.2757	
	No	375/ 729 (51.4)	323/ 705 (45.8)	1.13 (1.01, 1.25) 0.0299	1.26 (1.02, 1.55) 0.0315	0.06 (0.01, 0.11) 0.0307	
	ARNI at baseline						0.2117
	Yes	75/ 149 (50.3)	48/ 116 (41.4)	1.20 (0.91, 1.57) 0.1888	1.44 (0.87, 2.36) 0.1526	0.09 (-0.03, 0.21) 0.1419	
	No	1247/2520 (49.5)	1196/2548 (46.9)	1.05 (1.00, 1.11) 0.0734	1.11 (0.99, 1.24) 0.0762	0.03 (-0.00, 0.05) 0.0723	
	Beta Blocker at baseline						0.2485
	Yes	1097/2232 (49.1)	1041/2218 (46.9)	1.04 (0.98, 1.11) 0.1519	1.09 (0.97, 1.22) 0.1658	0.02 (-0.01, 0.05) 0.1596	
	No	225/ 437 (51.5)	203/ 446 (45.5)	1.14 (0.99, 1.30) 0.0637	1.29 (0.99, 1.68) 0.0610	0.06 (-0.00, 0.13) 0.0597	
	Diuretics at baseline						0.0954
	Yes	1182/2391 (49.4)	1091/2379 (45.9)	1.08 (1.02, 1.14) 0.0118	1.16 (1.03, 1.30) 0.0111	0.04 (0.01, 0.06) 0.0105	
	No	140/ 278 (50.4)	153/ 285 (53.7)	0.94 (0.80, 1.10) 0.4181	0.87 (0.62, 1.21) 0.3933	-0.04 (-0.12, 0.05) 0.3958	

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Symptom Stability (LOCF)							
	Overall	797/2842 (28.0)	793/2837 (28.0)	1.00 (0.92, 1.09)*0.9387	0.99 (0.88, 1.12) 0.9015	-0.01 (-0.03, 0.01) 0.2982	
	Age						0.0369*
	<= median	435/1415 (30.7)	417/1482 (28.1)	1.09 (0.98, 1.22)*0.1242	1.13 (0.95, 1.34) 0.1566	0.01 (-0.02, 0.04) 0.6209	
	> median	362/1427 (25.4)	376/1355 (27.7)	0.91 (0.81, 1.03)*0.1552	0.87 (0.73, 1.04) 0.1224	-0.02 (-0.06, 0.01)*0.1552	
	Gender						0.8035*
	Male	435/1656 (26.3)	429/1625 (26.4)	0.97 (0.89, 1.06) 0.5168	0.98 (0.83, 1.15) 0.7985	-0.01 (-0.04, 0.01) 0.3062	
	Female	362/1186 (30.5)	364/1212 (30.0)	1.02 (0.90, 1.15)*0.7941	1.01 (0.84, 1.22) 0.8772	0.00 (-0.03, 0.04)*0.7941	
	Race						0.6340*
	White	576/2039 (28.2)	565/2058 (27.5)	1.00 (0.93, 1.08) 0.9664	1.03 (0.89, 1.19) 0.7034	-0.01 (-0.03, 0.02) 0.6372	
	Black or African	26/ 67 (38.8)	33/ 71 (46.5)	0.83 (0.56, 1.23)*0.3655	0.67 (0.32, 1.38) 0.2725	-0.08 (-0.24, 0.09)*0.3607	
	Asian	128/ 558 (22.9)	138/ 555 (24.9)	0.93 (0.77, 1.13) 0.4586	0.89 (0.67, 1.18) 0.4240	-0.02 (-0.07, 0.03) 0.3901	
	Other	67/ 178 (37.6)	57/ 153 (37.3)	1.01 (0.76, 1.34)*0.9424	1.10 (0.66, 1.84) 0.7109	0.00 (-0.10, 0.11)*0.9424	
	Geographic region						0.5857*
	Asia	122/ 539 (22.6)	133/ 538 (24.7)	0.92 (0.75, 1.12) 0.3909	0.88 (0.66, 1.17) 0.3880	-0.02 (-0.07, 0.03) 0.3786	
	Europe and Saudi Arabia	388/1365 (28.4)	380/1394 (27.3)	1.04 (0.92, 1.18)*0.4948	1.07 (0.90, 1.28) 0.4487	0.01 (-0.02, 0.05)*0.4948	
	North America	103/ 398 (25.9)	110/ 387 (28.4)	0.91 (0.72, 1.15)*0.4231	0.80 (0.58, 1.12) 0.1971	-0.04 (-0.09, 0.02) 0.1857	
	Latin America	184/ 540 (34.1)	170/ 518 (32.8)	1.04 (0.88, 1.23)*0.6654	1.09 (0.83, 1.45) 0.5330	0.01 (-0.04, 0.07)*0.6652	
	NYHA class at enrolment						0.7827*
	II	568/2113 (26.9)	592/2187 (27.1)	0.96 (0.90, 1.02) 0.2145	0.99 (0.86, 1.14) 0.9022	-0.01 (-0.03, 0.02) 0.5278	
	III or IV	229/ 729 (31.4)	200/ 649 (30.8)	1.02 (0.87, 1.19)*0.8115	0.97 (0.75, 1.25) 0.8267	0.01 (-0.04, 0.05)*0.8114	
	LVEF at enrolment						0.2399*
	<= 49	286/ 980 (29.2)	263/ 963 (27.3)	0.99 (0.88, 1.11) 0.8884	1.10 (0.89, 1.35) 0.3759	0.01 (-0.03, 0.04) 0.6729	
	50-59	280/1029 (27.2)	267/1017 (26.3)	1.04 (0.90, 1.20)*0.6248	1.04 (0.84, 1.28) 0.7137	-0.01 (-0.04, 0.02) 0.6360	
	>= 60	231/ 833 (27.7)	263/ 857 (30.7)	0.90 (0.78, 1.05)*0.1820	0.84 (0.67, 1.05) 0.1298	-0.04 (-0.07, -0.00) 0.0435	
	NT-proBNP at enrolment						0.8520*
	<= median	403/1418 (28.4)	399/1421 (28.1)	1.00 (0.91, 1.10) 0.9578	1.02 (0.86, 1.22) 0.7954	-0.00 (-0.03, 0.03) 0.8265	
	> median	394/1424 (27.7)	393/1415 (27.8)	1.00 (0.88, 1.12)*0.9500	0.96 (0.81, 1.15) 0.6811	-0.02 (-0.05, 0.01) 0.2360	
	Type 2 Diabetes Medical History						0.2038*
	Yes	332/1250 (26.6)	355/1260 (28.2)	1.01 (0.95, 1.08) 0.7735	0.92 (0.77, 1.10)*0.3644	-0.03 (-0.06, -0.00) 0.0426	
	No	465/1592 (29.2)	438/1577 (27.8)	1.05 (0.94, 1.17)*0.3713	1.07 (0.92, 1.25)*0.3712	0.01 (-0.02, 0.03) 0.6749	
	Atrial fibrillation or flutter at enrolment ECG						0.1853*
	Yes	303/1199 (25.3)	324/1199 (27.0)	0.94 (0.82, 1.07)*0.3293	0.90 (0.74, 1.10) 0.3050	-0.02 (-0.05, 0.02)*0.3290	
	No	494/1643 (30.1)	469/1638 (28.6)	1.00 (0.93, 1.07) 0.9771	1.06 (0.90, 1.24) 0.4980	-0.00 (-0.03, 0.03) 0.9573	
	BMI (kg/m2) at enrolment						0.5502*
	< 30	425/1571 (27.1)	410/1559 (26.3)	0.99 (0.91, 1.07) 0.7421	1.02 (0.86, 1.20) 0.8198	-0.00 (-0.03, 0.02) 0.8223	
	>= 30	372/1270 (29.3)	382/1275 (30.0)	0.98 (0.87, 1.10)*0.7115	0.97 (0.80, 1.16) 0.7212	-0.01 (-0.04, 0.03)*0.7115	
	Baseline eGFR (mL/min/1.73m^2)						0.0030*
	< 60	336/1359 (24.7)	395/1396 (28.3)	0.87 (0.77, 0.99)*0.0341	0.82 (0.68, 0.98) 0.0283	-0.04 (-0.07, -0.01) 0.0051	
	>= 60	461/1483 (31.1)	397/1440 (27.6)	1.13 (1.01, 1.26)*0.0372	1.17 (0.99, 1.39) 0.0658	0.02 (-0.01, 0.05) 0.2305	

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Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)	SBP at randomisation						0.2896*
	<= median	403/1424 (28.3)	388/1439 (27.0)	1.05 (0.93, 1.18)*0.4237	1.05 (0.88, 1.25) 0.5932	-0.01 (-0.04, 0.02) 0.3966	
	> median	394/1418 (27.8)	405/1398 (29.0)	0.98 (0.91, 1.06) 0.6253	0.95 (0.80, 1.12) 0.5223	-0.01 (-0.04, 0.02) 0.4792	
	LVEF at enrolment 2						0.2814*
	<= 49	286/ 980 (29.2)	263/ 963 (27.3)	0.99 (0.88, 1.11) 0.8884	1.10 (0.89, 1.35) 0.3759	0.01 (-0.03, 0.04) 0.6729	
	>= 50	511/1862 (27.4)	530/1874 (28.3)	0.97 (0.88, 1.08)*0.5678	0.94 (0.81, 1.10) 0.4409	-0.02 (-0.05, 0.00) 0.0812	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1516*
	Yes	89/ 283 (31.4)	105/ 286 (36.7)	0.86 (0.68, 1.08)*0.1865	0.80 (0.54, 1.18) 0.2538	-0.07 (-0.13, -0.01) 0.0253	
	No	708/2559 (27.7)	688/2551 (27.0)	0.98 (0.92, 1.05) 0.5827	1.02 (0.89, 1.16) 0.7851	-0.00 (-0.02, 0.02) 0.8304	
	MRAs at baseline						0.5929*
	Yes	360/1227 (29.3)	349/1224 (28.5)	0.99 (0.89, 1.09) 0.8140	1.06 (0.89, 1.28) 0.5090	0.00 (-0.03, 0.03) 0.9634	
	No	437/1615 (27.1)	444/1613 (27.5)	0.98 (0.88, 1.10)*0.7656	0.94 (0.79, 1.10) 0.4283	-0.00 (-0.04, 0.03)*0.7656	
	ACEi+ARB at baseline						0.6624*
	Yes	577/2065 (27.9)	585/2077 (28.2)	0.96 (0.89, 1.03) 0.2304	0.99 (0.85, 1.14) 0.8420	-0.01 (-0.03, 0.01) 0.4428	
	No	220/ 777 (28.3)	208/ 760 (27.4)	1.03 (0.88, 1.22)*0.6793	1.01 (0.80, 1.28) 0.9204	-0.01 (-0.05, 0.03) 0.5264	
	ARNI at baseline						0.9077*
	Yes	46/ 153 (30.1)	37/ 126 (29.4)	1.02 (0.71, 1.47)*0.8987	1.15 (0.67, 1.97) 0.6045	0.03 (-0.08, 0.13) 0.6045	
	No	751/2689 (27.9)	756/2711 (27.9)	1.00 (0.92, 1.09)*0.9724	0.99 (0.87, 1.12) 0.8184	-0.01 (-0.03, 0.01) 0.1927	
	Beta Blocker at baseline						0.6517*
	Yes	667/2360 (28.3)	658/2356 (27.9)	1.01 (0.92, 1.11)*0.7986	0.99 (0.86, 1.13) 0.8315	-0.01 (-0.03, 0.01) 0.3640	
	No	130/ 482 (27.0)	135/ 481 (28.1)	0.96 (0.78, 1.18)*0.7035	1.05 (0.77, 1.42) 0.7706	-0.01 (-0.05, 0.03) 0.6192	
	Diuretics at baseline						0.4658*
	Yes	705/2536 (27.8)	709/2531 (28.0)	0.97 (0.91, 1.03) 0.3030	0.98 (0.86, 1.11) 0.7246	-0.01 (-0.03, 0.01) 0.2453	
	No	92/ 306 (30.1)	84/ 306 (27.5)	1.10 (0.85, 1.41)*0.4753	1.13 (0.78, 1.62) 0.5271	0.01 (-0.06, 0.08) 0.8104	

N displays number of patients in the analysis, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	1378/2842 (48.5)	1253/2837 (44.2)	1.09 (1.03, 1.15) 0.0014	1.19 (1.07, 1.32) 0.0015	0.04 (0.02, 0.07) 0.0012	
	Age						0.8076
	<= median	748/1415 (52.9)	712/1482 (48.0)	1.11 (1.03, 1.19) 0.0038	1.22 (1.06, 1.42) 0.0073	0.05 (0.01, 0.09) 0.0065	
	> median	630/1427 (44.1)	541/1355 (39.9)	1.08 (0.99, 1.17) 0.0701	1.17 (1.00, 1.36) 0.0460	0.04 (0.00, 0.07) 0.0349	
	Gender						0.7423
	Male	813/1656 (49.1)	741/1625 (45.6)	1.08 (1.01, 1.16) 0.0271	1.15 (1.00, 1.32) 0.0491	0.03 (0.00, 0.07) 0.0446	
	Female	565/1186 (47.6)	512/1212 (42.2)	1.09 (1.00, 1.18) 0.0445	1.24 (1.05, 1.46) 0.0118	0.05 (0.01, 0.09) 0.0096	
	Race						0.5104*
	White	935/2039 (45.9)	860/2058 (41.8)	1.08 (1.01, 1.15) 0.0232	1.16 (1.03, 1.32) 0.0185	0.04 (0.01, 0.07) 0.0174	
	Black or African	31/ 67 (46.3)	35/ 71 (49.3)	0.98 (0.69, 1.39) 0.9091	0.89 (0.45, 1.74) 0.7330	-0.03 (-0.19, 0.14) 0.7393	
	Asian	303/ 558 (54.3)	282/ 555 (50.8)	1.07 (0.96, 1.20) 0.2412	1.15 (0.91, 1.46) 0.2381	0.04 (-0.02, 0.09) 0.2377	
	Other	109/ 178 (61.2)	76/ 153 (49.7)	1.24 (1.04, 1.48) 0.0181	1.67 (1.06, 2.63) 0.0285	0.12 (0.02, 0.22) 0.0228	
	Geographic region						0.8910*
	Asia	295/ 539 (54.7)	276/ 538 (51.3)	1.07 (0.95, 1.19) 0.2624	1.15 (0.90, 1.46) 0.2556	0.03 (-0.03, 0.09) 0.2555	
	Europe and Saudi Arabia	627/1365 (45.9)	579/1394 (41.5)	1.11 (1.02, 1.20)*0.0200	1.18 (1.01, 1.37) 0.0407	0.04 (0.00, 0.07) 0.0386	
	North America	155/ 398 (38.9)	142/ 387 (36.7)	1.06 (0.89, 1.27) 0.4906	1.10 (0.82, 1.48) 0.5155	0.02 (-0.05, 0.09) 0.5375	
	Latin America	301/ 540 (55.7)	256/ 518 (49.4)	1.12 (1.01, 1.24) 0.0288	1.31 (1.02, 1.69) 0.0320	0.07 (0.01, 0.12) 0.0247	
	NYHA class at enrolment						0.4394
	II	1009/2113 (47.8)	960/2187 (43.9)	1.08 (1.02, 1.15) 0.0153	1.18 (1.04, 1.33) 0.0087	0.04 (0.01, 0.07) 0.0086	
	III or IV	369/ 729 (50.6)	293/ 649 (45.1)	1.12 (1.00, 1.25)*0.0435	1.23 (0.99, 1.53) 0.0665	0.05 (0.00, 0.10) 0.0427	
	LVEF at enrolment						0.6398
	<= 49	492/ 980 (50.2)	455/ 963 (47.2)	1.07 (0.98, 1.16) 0.1565	1.14 (0.95, 1.36) 0.1592	0.03 (-0.01, 0.08) 0.1557	
	50-59	485/1029 (47.1)	420/1017 (41.3)	1.13 (1.03, 1.24) 0.0122	1.26 (1.06, 1.51) 0.0097	0.06 (0.01, 0.10) 0.0080	
	>= 60	401/ 833 (48.1)	378/ 857 (44.1)	1.08 (0.97, 1.19) 0.1472	1.15 (0.95, 1.40) 0.1591	0.03 (-0.01, 0.08) 0.1482	
	NT-proBNP at enrolment						0.8781
	<= median	670/1418 (47.2)	616/1421 (43.3)	1.09 (1.01, 1.18) 0.0361	1.17 (1.01, 1.36) 0.0351	0.04 (0.00, 0.08) 0.0319	
	> median	708/1424 (49.7)	636/1415 (44.9)	1.09 (1.01, 1.17) 0.0219	1.20 (1.03, 1.39) 0.0186	0.04 (0.01, 0.08) 0.0183	
	Type 2 Diabetes Medical History						0.7875
	Yes	613/1250 (49.0)	558/1260 (44.3)	1.10 (1.02, 1.19) 0.0176	1.21 (1.03, 1.42)*0.0170	0.05 (0.01, 0.09) 0.0152	
	No	765/1592 (48.1)	695/1577 (44.1)	1.08 (1.01, 1.16) 0.0299	1.17 (1.02, 1.35)*0.0246	0.04 (0.00, 0.07) 0.0311	
	Atrial fibrillation or flutter at enrolment ECG						0.4667
	Yes	581/1199 (48.5)	542/1199 (45.2)	1.07 (0.98, 1.16) 0.1164	1.14 (0.97, 1.34) 0.1180	0.03 (-0.01, 0.07) 0.1069	
	No	797/1643 (48.5)	711/1638 (43.4)	1.11 (1.03, 1.19) 0.0041	1.22 (1.06, 1.41) 0.0045	0.05 (0.02, 0.08) 0.0041	
	BMI (kg/m2) at enrolment						0.7140
	< 30	777/1571 (49.5)	696/1559 (44.6)	1.11 (1.03, 1.19) 0.0062	1.21 (1.05, 1.40) 0.0074	0.05 (0.01, 0.08) 0.0069	
	>= 30	601/1270 (47.3)	556/1275 (43.6)	1.07 (0.99, 1.16) 0.0739	1.15 (0.98, 1.35) 0.0821	0.03 (-0.00, 0.07) 0.0729	
	Baseline eGFR (mL/min/1.73m^2)						0.8887
	< 60	628/1359 (46.2)	584/1396 (41.8)	1.09 (1.01, 1.18) 0.0337	1.19 (1.02, 1.39) 0.0231	0.04 (0.01, 0.08) 0.0231	
	>= 60	750/1483 (50.6)	669/1440 (46.5)	1.09 (1.01, 1.17) 0.0218	1.17 (1.01, 1.36) 0.0329	0.04 (0.00, 0.08) 0.0269	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Total Symptom Score (LOCF)	SBP at randomisation						0.9995
	<= median	675/1424 (47.4)	617/1439 (42.9)	1.09 (1.01, 1.18) 0.0294	1.18 (1.02, 1.37) 0.0308	0.04 (0.00, 0.08) 0.0294	
	> median	703/1418 (49.6)	636/1398 (45.5)	1.09 (1.01, 1.18) 0.0192	1.20 (1.03, 1.39) 0.0194	0.04 (0.01, 0.08) 0.0170	
	LVEF at enrolment 2						0.4981
	<= 49	492/ 980 (50.2)	455/ 963 (47.2)	1.07 (0.98, 1.16) 0.1565	1.14 (0.95, 1.36) 0.1592	0.03 (-0.01, 0.08) 0.1557	
	>= 50	886/1862 (47.6)	798/1874 (42.6)	1.10 (1.03, 1.18) 0.0042	1.21 (1.06, 1.38) 0.0045	0.05 (0.02, 0.08) 0.0036	
	Randomised during hospitalisation for HF or within 30 days of discharge						1.0000
	Yes	163/ 283 (57.6)	150/ 286 (52.4)	1.10 (0.95, 1.27)*0.2176	1.39 (0.97, 1.98) 0.0723	0.05 (-0.03, 0.13)*0.2163	
	No	1215/2559 (47.5)	1103/2551 (43.2)	1.09 (1.03, 1.16) 0.0029	1.18 (1.05, 1.32) 0.0038	0.04 (0.01, 0.07) 0.0033	
	MRAs at baseline						0.5332
	Yes	604/1227 (49.2)	542/1224 (44.3)	1.11 (1.03, 1.21) 0.0088	1.21 (1.03, 1.43) 0.0181	0.05 (0.01, 0.09) 0.0153	
	No	774/1615 (47.9)	711/1613 (44.1)	1.08 (1.00, 1.16) 0.0417	1.17 (1.01, 1.34) 0.0302	0.04 (0.00, 0.07) 0.0292	
	ACEi+ARB at baseline						0.0342
	Yes	1016/2065 (49.2)	900/2077 (43.3)	1.13 (1.06, 1.20) 0.0002	1.26 (1.11, 1.43) 0.0003	0.06 (0.03, 0.09) 0.0002	
	No	362/ 777 (46.6)	353/ 760 (46.4)	1.00 (0.90, 1.11) 0.9388	1.01 (0.83, 1.23) 0.9281	0.00 (-0.05, 0.05) 0.9206	
	ARNI at baseline						0.7467
	Yes	73/ 153 (47.7)	60/ 126 (47.6)	1.00 (0.77, 1.28) 0.9746	1.00 (0.62, 1.61) 0.9847	-0.00 (-0.12, 0.12) 0.9856	
	No	1305/2689 (48.5)	1193/2711 (44.0)	1.09 (1.03, 1.15) 0.0016	1.19 (1.07, 1.33) 0.0015	0.04 (0.02, 0.07) 0.0013	
	Beta Blocker at baseline						0.1550
	Yes	1121/2360 (47.5)	1031/2356 (43.8)	1.07 (1.01, 1.14) 0.0234	1.15 (1.02, 1.29) 0.0194	0.03 (0.01, 0.06) 0.0181	
	No	257/ 482 (53.3)	222/ 481 (46.2)	1.18 (1.04, 1.33) 0.0112	1.37 (1.06, 1.77) 0.0154	0.08 (0.02, 0.14) 0.0136	
	Diuretics at baseline						0.4945
	Yes	1202/2536 (47.4)	1106/2531 (43.7)	1.08 (1.02, 1.15) 0.0074	1.17 (1.04, 1.30) 0.0076	0.04 (0.01, 0.06) 0.0066	
	No	176/ 306 (57.5)	147/ 306 (48.0)	1.16 (1.00, 1.35) 0.0455	1.40 (1.02, 1.94) 0.0391	0.08 (0.00, 0.16) 0.0376	

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AstraZeneca
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Clinical Summary Score (LOCF)							
	Overall	245/2801 (8.7)	337/2805 (12.0)	0.74 (0.63, 0.86) <.0001	0.70 (0.59, 0.84) <.0001	-0.03 (-0.05, -0.02)*<.0001	
	Age						0.7871
	<= median	111/1394 (8.0)	155/1471 (10.5)	0.75 (0.60, 0.94) 0.0140	0.72 (0.56, 0.93) 0.0130	-0.03 (-0.05, -0.00)*0.0171	
	> median	134/1407 (9.5)	182/1334 (13.6)	0.72 (0.58, 0.89) 0.0019	0.68 (0.54, 0.87) 0.0017	-0.04 (-0.07, -0.02)*0.0008	
	Gender						0.1379
	Male	132/1630 (8.1)	196/1608 (12.2)	0.67 (0.54, 0.82) 0.0001	0.63 (0.50, 0.80) 0.0001	-0.04 (-0.06, -0.02)*0.0001	
	Female	113/1171 (9.6)	141/1197 (11.8)	0.84 (0.67, 1.06) 0.1494	0.81 (0.62, 1.05) 0.1166	-0.02 (-0.05, 0.00)*0.0936	
	Race						0.6532
	White	181/2006 (9.0)	251/2032 (12.4)	0.75 (0.63, 0.89) 0.0013	0.71 (0.58, 0.87) 0.0012	-0.03 (-0.05, -0.01)*0.0006	
	Black or African	8/ 64 (12.5)	10/ 70 (14.3)	0.87 (0.37, 2.06) 0.7552	0.84 (0.31, 2.29) 0.7292	-0.02 (-0.13, 0.10)*0.7614	
	Asian	50/ 555 (9.0)	64/ 551 (11.6)	0.78 (0.55, 1.11) 0.1657	0.76 (0.51, 1.12) 0.1655	-0.03 (-0.06, 0.01) 0.1654	
	Other	6/ 176 (3.4)	12/ 152 (7.9)	0.41 (0.16, 1.05) 0.0619	0.37 (0.13, 1.04) 0.0586	-0.04 (-0.10, 0.01)*0.0821	
	Geographic region						0.7191
	Asia	46/ 536 (8.6)	63/ 536 (11.8)	0.73 (0.51, 1.05) 0.0921	0.71 (0.47, 1.06) 0.0917	-0.03 (-0.07, 0.01) 0.0943	
	Europe and Saudi Arabia	122/1341 (9.1)	166/1381 (12.0)	0.79 (0.64, 0.98) 0.0319	0.75 (0.58, 0.96) 0.0231	-0.03 (-0.05, -0.01)*0.0129	
	North America	41/ 393 (10.4)	51/ 376 (13.6)	0.76 (0.52, 1.12) 0.1681	0.74 (0.48, 1.15) 0.1863	-0.03 (-0.08, 0.01)*0.1817	
	Latin America	36/ 531 (6.8)	57/ 512 (11.1)	0.60 (0.41, 0.89) 0.0109	0.56 (0.36, 0.88) 0.0115	-0.04 (-0.08, -0.01)*0.0138	
	NYHA class at enrolment						0.5022
	II	187/2083 (9.0)	258/2165 (11.9)	0.75 (0.63, 0.90) 0.0016	0.72 (0.59, 0.88) 0.0014	-0.03 (-0.05, -0.01)*0.0017	
	III or IV	58/ 718 (8.1)	79/ 639 (12.4)	0.66 (0.49, 0.91) 0.0106	0.63 (0.44, 0.91) 0.0133	-0.04 (-0.08, -0.01)*0.0095	
	LVEF at enrolment						0.5740
	<= 49	77/ 959 (8.0)	98/ 950 (10.3)	0.78 (0.58, 1.03) 0.0782	0.75 (0.54, 1.02) 0.0681	-0.02 (-0.05, 0.00)*0.0834	
	50-59	99/1017 (9.7)	126/1009 (12.5)	0.78 (0.61, 1.00) 0.0519	0.75 (0.57, 1.00) 0.0499	-0.03 (-0.05, -0.00)*0.0485	
	>= 60	69/ 825 (8.4)	113/ 846 (13.4)	0.65 (0.49, 0.86) 0.0025	0.61 (0.45, 0.84) 0.0027	-0.05 (-0.08, -0.02)*0.0010	
	NT-proBNP at enrolment						0.5009
	<= median	128/1396 (9.2)	167/1409 (11.9)	0.78 (0.62, 0.96) 0.0211	0.75 (0.58, 0.95) 0.0195	-0.03 (-0.05, -0.00)*0.0204	
	> median	117/1405 (8.3)	170/1395 (12.2)	0.70 (0.56, 0.87) 0.0015	0.66 (0.52, 0.85) 0.0014	-0.04 (-0.06, -0.02)*0.0007	
	Type 2 Diabetes Medical History						0.2503
	Yes	102/1231 (8.3)	157/1243 (12.6)	0.66 (0.53, 0.84) 0.0006	0.62 (0.48, 0.81)*0.0005	-0.04 (-0.07, -0.02)*0.0004	
	No	143/1570 (9.1)	180/1562 (11.5)	0.80 (0.65, 0.98) 0.0318	0.77 (0.61, 0.97)*0.0266	-0.02 (-0.05, -0.00)*0.0262	
	Atrial fibrillation or flutter at enrolment ECG						0.6890
	Yes	103/1185 (8.7)	146/1188 (12.3)	0.71 (0.56, 0.90) 0.0044	0.67 (0.51, 0.88) 0.0040	-0.04 (-0.06, -0.01)*0.0042	
	No	142/1616 (8.8)	191/1617 (11.8)	0.76 (0.62, 0.93) 0.0072	0.73 (0.58, 0.91) 0.0065	-0.03 (-0.05, -0.01)*0.0046	
	BMI (kg/m2) at enrolment						0.3202
	< 30	143/1547 (9.2)	182/1541 (11.8)	0.79 (0.64, 0.97) 0.0240	0.76 (0.60, 0.96) 0.0230	-0.03 (-0.05, -0.00)*0.0200	
	>= 30	102/1253 (8.1)	155/1261 (12.3)	0.67 (0.53, 0.85) 0.0010	0.64 (0.49, 0.83) 0.0009	-0.04 (-0.07, -0.02)*0.0006	
	Baseline eGFR (mL/min/1.73m^2)						0.9598
	< 60	127/1338 (9.5)	180/1377 (13.1)	0.73 (0.59, 0.91) 0.0041	0.70 (0.55, 0.89) 0.0040	-0.04 (-0.06, -0.01)*0.0031	
	>= 60	118/1463 (8.1)	157/1427 (11.0)	0.74 (0.59, 0.93) 0.0093	0.71 (0.55, 0.92) 0.0084	-0.03 (-0.05, -0.01)*0.0072	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.5739
	<= median	120/1405 (8.5)	179/1420 (12.6)	0.70 (0.56, 0.87) 0.0015	0.67 (0.52, 0.85) 0.0013	-0.04 (-0.06, -0.02)*0.0004	
	> median	125/1396 (9.0)	158/1385 (11.4)	0.77 (0.62, 0.96) 0.0185	0.74 (0.57, 0.95) 0.0177	-0.02 (-0.05, -0.00)*0.0323	
	LVEF at enrolment 2						0.7141
	<= 49	77/ 959 (8.0)	98/ 950 (10.3)	0.78 (0.58, 1.03) 0.0782	0.75 (0.54, 1.02) 0.0681	-0.02 (-0.05, 0.00)*0.0834	
	>= 50	168/1842 (9.1)	239/1855 (12.9)	0.72 (0.60, 0.87) 0.0006	0.69 (0.56, 0.85) 0.0006	-0.04 (-0.06, -0.02)*0.0002	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3884
	Yes	17/ 280 (6.1)	28/ 281 (10.0)	0.61 (0.34, 1.09)*0.0938	0.51 (0.26, 0.97) 0.0401	-0.04 (-0.08, 0.01)*0.0887	
	No	228/2521 (9.0)	309/2524 (12.2)	0.75 (0.64, 0.88) 0.0005	0.72 (0.60, 0.86) 0.0004	-0.03 (-0.05, -0.01)*0.0002	
	MRAs at baseline						0.7188
	Yes	108/1216 (8.9)	143/1210 (11.8)	0.76 (0.60, 0.96) 0.0220	0.73 (0.56, 0.95) 0.0205	-0.03 (-0.05, -0.01)*0.0175	
	No	137/1585 (8.6)	194/1595 (12.2)	0.72 (0.59, 0.88) 0.0016	0.68 (0.54, 0.86) 0.0014	-0.04 (-0.06, -0.01)*0.0011	
	ACEi+ARB at baseline						0.2735
	Yes	166/2037 (8.1)	245/2059 (11.9)	0.70 (0.58, 0.84) 0.0001	0.66 (0.54, 0.81) 0.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	79/ 764 (10.3)	92/ 746 (12.3)	0.84 (0.63, 1.11) 0.2282	0.82 (0.59, 1.13) 0.2176	-0.02 (-0.05, 0.01)*0.2222	
	ARNI at baseline						0.2978
	Yes	14/ 149 (9.4)	10/ 125 (8.0)	1.16 (0.52, 2.55) 0.7206	1.17 (0.49, 2.78) 0.7193	0.01 (-0.06, 0.08) 0.7184	
	No	231/2652 (8.7)	327/2680 (12.2)	0.73 (0.62, 0.85) <.0001	0.69 (0.58, 0.83) <.0001	-0.03 (-0.05, -0.02)*<.0001	
	Beta Blocker at baseline						0.6698
	Yes	203/2327 (8.7)	278/2330 (11.9)	0.75 (0.63, 0.89) 0.0008	0.71 (0.59, 0.87) 0.0006	-0.03 (-0.05, -0.01)*0.0003	
	No	42/ 474 (8.9)	59/ 475 (12.4)	0.69 (0.47, 0.99) 0.0469	0.65 (0.43, 1.00) 0.0496	-0.04 (-0.07, 0.00)*0.0748	
	Diuretics at baseline						0.6781
	Yes	224/2500 (9.0)	310/2504 (12.4)	0.73 (0.62, 0.85) 0.0001	0.69 (0.58, 0.83) <.0001	-0.03 (-0.05, -0.02)*<.0001	
	No	21/ 301 (7.0)	27/ 301 (9.0)	0.81 (0.47, 1.40) 0.4604	0.79 (0.44, 1.44) 0.4474	-0.02 (-0.06, 0.02)*0.3663	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	234/2801 (8.4)	285/2805 (10.2)	0.83 (0.71, 0.98) 0.0285	0.81 (0.67, 0.97) 0.0239	-0.02 (-0.03, -0.00)*0.0196	
	Age						0.2585
	<= median	108/1394 (7.7)	124/1471 (8.4)	0.92 (0.72, 1.18) 0.5063	0.91 (0.69, 1.19) 0.4704	-0.01 (-0.03, 0.01)*0.5030	
	> median	126/1407 (9.0)	161/1334 (12.1)	0.76 (0.61, 0.95) 0.0148	0.73 (0.57, 0.94) 0.0136	-0.03 (-0.05, -0.01)*0.0079	
	Gender						0.3870
	Male	133/1630 (8.2)	168/1608 (10.4)	0.79 (0.63, 0.97) 0.0283	0.76 (0.60, 0.97) 0.0283	-0.02 (-0.04, -0.00)*0.0250	
	Female	101/1171 (8.6)	117/1197 (9.8)	0.91 (0.71, 1.17) 0.4593	0.88 (0.66, 1.17) 0.3799	-0.01 (-0.03, 0.01)*0.3331	
	Race						0.6848
	White	167/2006 (8.3)	219/2032 (10.8)	0.79 (0.66, 0.96) 0.0168	0.76 (0.62, 0.95) 0.0138	-0.02 (-0.04, -0.01)*0.0079	
	Black or African	6/ 64 (9.4)	8/ 70 (11.4)	0.79 (0.29, 2.12) 0.6377	0.77 (0.25, 2.39) 0.6512	-0.02 (-0.12, 0.08)*0.6966	
	Asian	51/ 555 (9.2)	50/ 551 (9.1)	1.02 (0.70, 1.48) 0.9274	1.02 (0.68, 1.53) 0.9351	-0.00 (-0.03, 0.03) 0.9931	
	Other	10/ 176 (5.7)	8/ 152 (5.3)	1.02 (0.42, 2.51) 0.9626	1.02 (0.39, 2.69) 0.9709	-0.02 (-0.08, 0.05) 0.5792	
	Geographic region						0.4865
	Asia	47/ 536 (8.8)	49/ 536 (9.1)	0.96 (0.66, 1.41) 0.8488	0.96 (0.63, 1.46) 0.8406	-0.01 (-0.04, 0.03) 0.7716	
	Europe and Saudi Arabia	117/1341 (8.7)	139/1381 (10.1)	0.91 (0.72, 1.14) 0.3957	0.88 (0.68, 1.15) 0.3501	-0.01 (-0.04, 0.01)*0.2305	
	North America	35/ 393 (8.9)	46/ 376 (12.2)	0.73 (0.48, 1.10) 0.1355	0.70 (0.44, 1.11) 0.1291	-0.04 (-0.09, 0.00) 0.0533	
	Latin America	35/ 531 (6.6)	51/ 512 (10.0)	0.66 (0.44, 0.99) 0.0455	0.63 (0.40, 0.99) 0.0469	-0.03 (-0.07, -0.00)*0.0483	
	NYHA class at enrolment						0.4758
	II	174/2083 (8.4)	211/2165 (9.7)	0.86 (0.71, 1.04) 0.1087	0.84 (0.68, 1.03) 0.0979	-0.01 (-0.03, 0.00)*0.1134	
	III or IV	60/ 718 (8.4)	74/ 639 (11.6)	0.72 (0.52, 1.00)*0.0480	0.71 (0.49, 1.03) 0.0705	-0.03 (-0.06, -0.00)*0.0484	
	LVEF at enrolment						0.2846
	<= 49	77/ 959 (8.0)	80/ 950 (8.4)	0.94 (0.70, 1.27) 0.7014	0.93 (0.67, 1.29) 0.6497	-0.00 (-0.03, 0.02)*0.7554	
	50-59	92/1017 (9.0)	104/1009 (10.3)	0.89 (0.68, 1.16) 0.3842	0.87 (0.65, 1.18) 0.3689	-0.01 (-0.04, 0.01)*0.3370	
	>= 60	65/ 825 (7.9)	101/ 846 (11.9)	0.68 (0.51, 0.92) 0.0118	0.65 (0.47, 0.90) 0.0106	-0.04 (-0.07, -0.01)*0.0053	
	NT-proBNP at enrolment						0.8003
	<= median	118/1396 (8.5)	141/1409 (10.0)	0.85 (0.67, 1.07) 0.1688	0.83 (0.64, 1.07) 0.1539	-0.02 (-0.04, 0.01)*0.1548	
	> median	116/1405 (8.3)	144/1395 (10.3)	0.82 (0.65, 1.03) 0.0864	0.79 (0.61, 1.03) 0.0798	-0.02 (-0.04, 0.00)*0.0595	
	Type 2 Diabetes Medical History						0.0145
	Yes	93/1231 (7.6)	144/1243 (11.6)	0.67 (0.52, 0.85) 0.0012	0.62 (0.47, 0.82)*0.0007	-0.04 (-0.06, -0.02)*0.0006	
	No	141/1570 (9.0)	141/1562 (9.0)	1.00 (0.81, 1.25) 0.9653	0.99 (0.78, 1.27)*0.9641	-0.00 (-0.02, 0.02)*0.9641	
	Atrial fibrillation or flutter at enrolment ECG						0.6278
	Yes	106/1185 (8.9)	123/1188 (10.4)	0.87 (0.68, 1.11) 0.2682	0.85 (0.64, 1.12) 0.2540	-0.01 (-0.04, 0.01)*0.2452	
	No	128/1616 (7.9)	162/1617 (10.0)	0.80 (0.64, 1.00) 0.0494	0.78 (0.61, 0.99) 0.0434	-0.02 (-0.04, -0.00)*0.0367	
	BMI (kg/m2) at enrolment						0.3403
	< 30	135/1547 (8.7)	152/1541 (9.9)	0.90 (0.72, 1.12) 0.3248	0.88 (0.69, 1.13) 0.3098	-0.01 (-0.03, 0.01)*0.2765	
	>= 30	99/1253 (7.9)	133/1261 (10.5)	0.76 (0.60, 0.98) 0.0316	0.73 (0.55, 0.96) 0.0247	-0.03 (-0.05, -0.00)*0.0217	
	Baseline eGFR (mL/min/1.73m^2)						0.2855
	< 60	114/1338 (8.5)	155/1377 (11.3)	0.76 (0.61, 0.96) 0.0197	0.73 (0.57, 0.95) 0.0185	-0.03 (-0.05, -0.00)*0.0167	
	>= 60	120/1463 (8.2)	130/1427 (9.1)	0.92 (0.72, 1.16) 0.4608	0.90 (0.69, 1.17) 0.4257	-0.01 (-0.03, 0.01)*0.3857	

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Overall Summary Score (LOCF)	SBP at randomisation						0.9074
	<= median	120/1405 (8.5)	149/1420 (10.5)	0.84 (0.67, 1.06) 0.1411	0.82 (0.64, 1.06) 0.1294	-0.02 (-0.04, 0.00)*0.0769	
	> median	114/1396 (8.2)	136/1385 (9.8)	0.83 (0.65, 1.04) 0.1105	0.80 (0.61, 1.04) 0.0969	-0.02 (-0.04, 0.00)*0.1275	
	LVEF at enrolment 2						0.3436
	<= 49	77/ 959 (8.0)	80/ 950 (8.4)	0.94 (0.70, 1.27) 0.7014	0.93 (0.67, 1.29) 0.6497	-0.00 (-0.03, 0.02)*0.7554	
	>= 50	157/1842 (8.5)	205/1855 (11.1)	0.79 (0.65, 0.96) 0.0193	0.76 (0.61, 0.95) 0.0171	-0.03 (-0.04, -0.01)*0.0096	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8274
	Yes	19/ 280 (6.8)	21/ 281 (7.5)	0.91 (0.50, 1.65)*0.7518	0.84 (0.43, 1.62) 0.6005	-0.01 (-0.05, 0.04)*0.7516	
	No	215/2521 (8.5)	264/2524 (10.5)	0.83 (0.70, 0.98) 0.0304	0.80 (0.67, 0.97) 0.0255	-0.02 (-0.04, -0.00)*0.0192	
	MRAs at baseline						0.6074
	Yes	102/1216 (8.4)	117/1210 (9.7)	0.87 (0.68, 1.12) 0.2903	0.86 (0.65, 1.13) 0.2740	-0.01 (-0.04, 0.01)*0.2708	
	No	132/1585 (8.3)	168/1595 (10.5)	0.80 (0.65, 1.00) 0.0462	0.78 (0.61, 0.99) 0.0404	-0.02 (-0.04, -0.00)*0.0333	
	ACEi+ARB at baseline						0.3138
	Yes	158/2037 (7.8)	206/2059 (10.0)	0.79 (0.65, 0.96) 0.0173	0.76 (0.61, 0.95) 0.0145	-0.02 (-0.04, -0.01)*0.0113	
	No	76/ 764 (9.9)	79/ 746 (10.6)	0.95 (0.71, 1.28) 0.7376	0.94 (0.67, 1.31) 0.7000	-0.01 (-0.04, 0.02)*0.6811	
	ARNI at baseline						0.3122
	Yes	14/ 149 (9.4)	9/ 125 (7.2)	1.28 (0.57, 2.91) 0.5487	1.31 (0.54, 3.18) 0.5505	0.02 (-0.04, 0.09)*0.5090	
	No	220/2652 (8.3)	276/2680 (10.3)	0.82 (0.69, 0.97) 0.0201	0.79 (0.66, 0.96) 0.0163	-0.02 (-0.04, -0.00)*0.0117	
	Beta Blocker at baseline						0.8773
	Yes	198/2327 (8.5)	242/2330 (10.4)	0.84 (0.70, 1.00) 0.0529	0.82 (0.67, 0.99) 0.0440	-0.02 (-0.04, -0.00)*0.0284	
	No	36/ 474 (7.6)	43/ 475 (9.1)	0.81 (0.53, 1.24) 0.3390	0.80 (0.50, 1.27) 0.3386	-0.01 (-0.05, 0.02)*0.4162	
	Diuretics at baseline						0.0456
	Yes	209/2500 (8.4)	267/2504 (10.7)	0.79 (0.67, 0.94) 0.0071	0.76 (0.63, 0.92) 0.0057	-0.02 (-0.04, -0.01)*0.0055	
	No	25/ 301 (8.3)	18/ 301 (6.0)	1.45 (0.81, 2.60) 0.2056	1.50 (0.80, 2.83) 0.2077	0.02 (-0.02, 0.06)*0.2675	

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Physical Limitation (LOCF)							
	Overall	395/2750 (14.4)	455/2758 (16.5)	0.88 (0.78, 0.99) 0.0366	0.86 (0.74, 1.00) 0.0437	-0.02 (-0.03, -0.00) 0.0442	
	Age						0.2378
	<= median	170/1382 (12.3)	221/1456 (15.2)	0.81 (0.67, 0.97) 0.0223	0.78 (0.62, 0.96) 0.0225	-0.03 (-0.05, -0.01) 0.0092	
	> median	225/1368 (16.4)	234/1302 (18.0)	0.93 (0.79, 1.10) 0.4080	0.93 (0.76, 1.14) 0.4726	-0.01 (-0.03, 0.02) 0.5671	
	Gender						0.7689
	Male	228/1611 (14.2)	250/1583 (15.8)	0.90 (0.76, 1.06) 0.1948	0.88 (0.73, 1.08) 0.2189	-0.01 (-0.04, 0.01) 0.2087	
	Female	167/1139 (14.7)	205/1175 (17.4)	0.87 (0.72, 1.04) 0.1224	0.84 (0.67, 1.05) 0.1271	-0.02 (-0.05, 0.00) 0.1141	
	Race						0.3088
	White	300/1970 (15.2)	346/1998 (17.3)	0.89 (0.78, 1.02) 0.0963	0.87 (0.74, 1.04) 0.1270	-0.02 (-0.04, 0.00)*0.0745	
	Black or African	14/ 63 (22.2)	13/ 66 (19.7)	1.13 (0.58, 2.21) 0.7151	1.16 (0.49, 2.72) 0.7372	0.02 (-0.13, 0.16) 0.8232	
	Asian	61/ 548 (11.1)	84/ 546 (15.4)	0.73 (0.54, 0.99) 0.0446	0.69 (0.49, 0.99) 0.0433	-0.04 (-0.08, -0.00) 0.0373	
	Other	20/ 169 (11.8)	12/ 148 (8.1)	1.30 (0.68, 2.47) 0.4232	1.43 (0.65, 3.15) 0.3768	0.04 (-0.03, 0.10)*0.2657	
	Geographic region						0.2870
	Asia	57/ 530 (10.8)	80/ 531 (15.1)	0.72 (0.52, 0.99) 0.0424	0.68 (0.48, 0.98) 0.0410	-0.04 (-0.08, -0.00) 0.0350	
	Europe and Saudi Arabia	204/1323 (15.4)	222/1360 (16.3)	0.95 (0.80, 1.13) 0.5726	0.96 (0.78, 1.19) 0.7090	-0.01 (-0.04, 0.02)*0.5216	
	North America	61/ 386 (15.8)	78/ 362 (21.5)	0.73 (0.54, 0.99) 0.0426	0.69 (0.47, 1.00) 0.0483	-0.05 (-0.11, 0.00) 0.0523	
	Latin America	73/ 511 (14.3)	75/ 505 (14.9)	0.96 (0.72, 1.28) 0.7711	0.94 (0.66, 1.35) 0.7348	-0.01 (-0.05, 0.04)*0.7983	
	NYHA class at enrolment						0.6884
	II	284/2046 (13.9)	337/2136 (15.8)	0.88 (0.76, 1.02) 0.0818	0.86 (0.72, 1.02) 0.0877	-0.01 (-0.03, 0.00) 0.1250	
	III or IV	111/ 704 (15.8)	118/ 621 (19.0)	0.83 (0.66, 1.04) 0.1068	0.81 (0.61, 1.09) 0.1678	-0.03 (-0.06, 0.01) 0.1130	
	LVEF at enrolment						0.1765
	<= 49	142/ 944 (15.0)	136/ 939 (14.5)	1.02 (0.82, 1.26) 0.8827	1.02 (0.79, 1.32) 0.8569	0.00 (-0.03, 0.03) 0.9954	
	50-59	146/1001 (14.6)	166/ 988 (16.8)	0.88 (0.72, 1.08) 0.2222	0.87 (0.68, 1.11) 0.2626	-0.01 (-0.04, 0.02) 0.5700	
	>= 60	107/ 805 (13.3)	153/ 831 (18.4)	0.75 (0.60, 0.94) 0.0120	0.70 (0.54, 0.92) 0.0114	-0.05 (-0.09, -0.02)*0.0044	
	NT-proBNP at enrolment						0.9771
	<= median	185/1371 (13.5)	214/1389 (15.4)	0.88 (0.73, 1.05) 0.1579	0.86 (0.69, 1.06) 0.1629	-0.01 (-0.03, 0.02) 0.5077	
	> median	210/1379 (15.2)	241/1368 (17.6)	0.87 (0.74, 1.03) 0.1136	0.86 (0.70, 1.05) 0.1396	-0.03 (-0.05, -0.00) 0.0455	
	Type 2 Diabetes Medical History						0.5961
	Yes	178/1213 (14.7)	210/1219 (17.2)	0.85 (0.71, 1.02) 0.0749	0.83 (0.66, 1.03)*0.0859	-0.02 (-0.05, 0.00) 0.0985	
	No	217/1537 (14.1)	245/1539 (15.9)	0.91 (0.77, 1.07) 0.2503	0.87 (0.71, 1.06)*0.1623	-0.01 (-0.03, 0.01) 0.2486	
	Atrial fibrillation or flutter at enrolment ECG						0.5401
	Yes	178/1164 (15.3)	194/1164 (16.7)	0.91 (0.76, 1.10) 0.3354	0.91 (0.72, 1.14) 0.4038	-0.01 (-0.04, 0.02)*0.3654	
	No	217/1586 (13.7)	261/1594 (16.4)	0.85 (0.72, 1.00) 0.0472	0.82 (0.67, 1.00) 0.0489	-0.02 (-0.05, 0.00) 0.0587	
	BMI (kg/m2) at enrolment						0.8856
	< 30	208/1520 (13.7)	241/1517 (15.9)	0.87 (0.73, 1.03) 0.1084	0.84 (0.69, 1.03) 0.1027	-0.02 (-0.05, 0.00) 0.0664	
	>= 30	187/1229 (15.2)	214/1238 (17.3)	0.89 (0.74, 1.05) 0.1728	0.88 (0.71, 1.10) 0.2575	-0.02 (-0.05, 0.01)*0.1632	
	Baseline eGFR (mL/min/1.73m^2)						0.8240
	< 60	200/1307 (15.3)	231/1345 (17.2)	0.89 (0.75, 1.06) 0.1891	0.88 (0.71, 1.08) 0.2299	-0.01 (-0.04, 0.01) 0.3450	
	>= 60	195/1443 (13.5)	224/1412 (15.9)	0.87 (0.73, 1.03) 0.1096	0.84 (0.68, 1.04) 0.1090	-0.02 (-0.05, -0.00) 0.0480	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)	SBP at randomisation						0.8718
	<= median	199/1376 (14.5)	235/1395 (16.8)	0.88 (0.74, 1.05) 0.1537	0.87 (0.70, 1.07) 0.1744	-0.01 (-0.04, 0.01) 0.2751	
	> median	196/1374 (14.3)	220/1363 (16.1)	0.87 (0.73, 1.03) 0.1037	0.84 (0.68, 1.04) 0.1109	-0.02 (-0.05, 0.01)*0.1716	
	LVEF at enrolment 2						0.1185
	<= 49	142/ 944 (15.0)	136/ 939 (14.5)	1.02 (0.82, 1.26) 0.8827	1.02 (0.79, 1.32) 0.8569	0.00 (-0.03, 0.03) 0.9954	
	>= 50	253/1806 (14.0)	319/1819 (17.5)	0.82 (0.71, 0.95) 0.0097	0.79 (0.66, 0.95) 0.0112	-0.03 (-0.05, -0.00) 0.0214	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3322
	Yes	46/ 270 (17.0)	44/ 272 (16.2)	1.03 (0.71, 1.49) 0.8641	1.04 (0.65, 1.66) 0.8609	0.01 (-0.05, 0.07)*0.7878	
	No	349/2480 (14.1)	411/2486 (16.5)	0.86 (0.76, 0.98) 0.0225	0.84 (0.72, 0.98) 0.0269	-0.02 (-0.04, -0.00) 0.0319	
	MRAs at baseline						0.1768
	Yes	160/1191 (13.4)	200/1193 (16.8)	0.80 (0.66, 0.96) 0.0187	0.77 (0.61, 0.97) 0.0244	-0.02 (-0.05, 0.00) 0.0693	
	No	235/1559 (15.1)	255/1565 (16.3)	0.94 (0.80, 1.11) 0.4818	0.93 (0.77, 1.13) 0.4809	-0.01 (-0.04, 0.01) 0.2349	
	ACEi+ARB at baseline						0.3174
	Yes	282/1999 (14.1)	342/2028 (16.9)	0.85 (0.73, 0.98) 0.0222	0.82 (0.69, 0.98) 0.0274	-0.02 (-0.04, -0.00) 0.0362	
	No	113/ 751 (15.0)	113/ 730 (15.5)	0.97 (0.76, 1.23) 0.8025	0.97 (0.73, 1.29) 0.8230	-0.00 (-0.04, 0.03) 0.7850	
	ARNI at baseline						0.7874
	Yes	20/ 147 (13.6)	17/ 122 (13.9)	0.93 (0.50, 1.70) 0.8061	0.92 (0.45, 1.86) 0.8113	-0.01 (-0.09, 0.07) 0.8331	
	No	375/2603 (14.4)	438/2636 (16.6)	0.88 (0.77, 0.99) 0.0398	0.86 (0.74, 1.00) 0.0491	-0.02 (-0.03, 0.00) 0.0618	
	Beta Blocker at baseline						0.8719
	Yes	327/2289 (14.3)	380/2293 (16.6)	0.87 (0.76, 1.00) 0.0486	0.85 (0.72, 1.00) 0.0553	-0.02 (-0.04, 0.00) 0.0505	
	No	68/ 461 (14.8)	75/ 465 (16.1)	0.91 (0.67, 1.22) 0.5220	0.89 (0.62, 1.28) 0.5314	-0.02 (-0.06, 0.03) 0.4341	
	Diuretics at baseline						0.7459
	Yes	363/2458 (14.8)	421/2463 (17.1)	0.87 (0.77, 0.99) 0.0362	0.85 (0.73, 0.99) 0.0409	-0.02 (-0.04, -0.00) 0.0316	
	No	32/ 292 (11.0)	34/ 295 (11.5)	0.94 (0.60, 1.48) 0.8041	0.95 (0.57, 1.59) 0.8428	-0.01 (-0.06, 0.05)*0.8280	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	454/2801 (16.2)	475/2805 (16.9)	0.98 (0.87, 1.10) 0.7070	0.97 (0.84, 1.12) 0.6789	-0.01 (-0.02, 0.01) 0.3403	
	Age						0.4403
	<= median	211/1394 (15.1)	219/1471 (14.9)	1.02 (0.87, 1.21) 0.7823	1.03 (0.84, 1.28) 0.7525	-0.00 (-0.02, 0.02) 0.8387	
	> median	243/1407 (17.3)	256/1334 (19.2)	0.94 (0.81, 1.09) 0.4098	0.91 (0.74, 1.11) 0.3489	-0.02 (-0.05, 0.01)*0.1934	
	Gender						0.1900
	Male	266/1630 (16.3)	257/1608 (16.0)	1.05 (0.90, 1.22) 0.5666	1.06 (0.87, 1.28) 0.5832	0.00 (-0.02, 0.03)*0.7948	
	Female	188/1171 (16.1)	218/1197 (18.2)	0.90 (0.76, 1.06) 0.2115	0.87 (0.70, 1.09) 0.2215	-0.01 (-0.03, 0.01) 0.4439	
	Race						0.9207
	White	327/2006 (16.3)	353/2032 (17.4)	0.97 (0.85, 1.10) 0.6362	0.96 (0.81, 1.14) 0.6257	-0.01 (-0.03, 0.01)*0.3631	
	Black or African	10/ 64 (15.6)	12/ 70 (17.1)	0.93 (0.43, 2.01) 0.8487	0.90 (0.36, 2.27) 0.8242	-0.03 (-0.16, 0.11) 0.7066	
	Asian	101/ 555 (18.2)	95/ 551 (17.2)	1.05 (0.82, 1.35) 0.6747	1.07 (0.78, 1.46) 0.6929	-0.00 (-0.04, 0.04) 0.9636	
	Other	16/ 176 (9.1)	15/ 152 (9.9)	0.81 (0.44, 1.49) 0.4953	0.78 (0.35, 1.73) 0.5397	-0.01 (-0.07, 0.06)*0.8108	
	Geographic region						0.5802
	Asia	97/ 536 (18.1)	91/ 536 (17.0)	1.07 (0.83, 1.38) 0.6148	1.08 (0.79, 1.49) 0.6259	0.00 (-0.04, 0.04) 0.9471	
	Europe and Saudi Arabia	221/1341 (16.5)	232/1381 (16.8)	1.02 (0.87, 1.20) 0.7628	1.03 (0.84, 1.28) 0.7531	-0.00 (-0.03, 0.02)*0.8231	
	North America	64/ 393 (16.3)	75/ 376 (19.9)	0.83 (0.62, 1.12) 0.2293	0.78 (0.54, 1.14) 0.1971	-0.05 (-0.10, 0.00) 0.0552	
	Latin America	72/ 531 (13.6)	77/ 512 (15.0)	0.93 (0.71, 1.23) 0.6342	0.89 (0.62, 1.28) 0.5332	-0.00 (-0.04, 0.03) 0.9043	
	NYHA class at enrolment						0.2492
	II	340/2083 (16.3)	352/2165 (16.3)	1.01 (0.89, 1.15) 0.8894	1.01 (0.85, 1.19) 0.9374	-0.00 (-0.02, 0.01) 0.7964	
	III or IV	114/ 718 (15.9)	122/ 639 (19.1)	0.87 (0.71, 1.08) 0.2085	0.83 (0.62, 1.12) 0.2347	-0.03 (-0.07, 0.01)*0.1201	
	LVEF at enrolment						0.6051
	<= 49	148/ 959 (15.4)	139/ 950 (14.6)	1.07 (0.88, 1.32) 0.4965	1.08 (0.83, 1.40) 0.5774	0.01 (-0.02, 0.04)*0.6243	
	50-59	169/1017 (16.6)	181/1009 (17.9)	0.94 (0.79, 1.13) 0.5386	0.92 (0.73, 1.17) 0.4999	-0.01 (-0.05, 0.02)*0.4316	
	>= 60	137/ 825 (16.6)	155/ 846 (18.3)	0.94 (0.77, 1.15) 0.5501	0.93 (0.72, 1.21) 0.6136	-0.02 (-0.05, 0.02)*0.3555	
	NT-proBNP at enrolment						0.7701
	<= median	221/1396 (15.8)	236/1409 (16.7)	0.96 (0.82, 1.13) 0.6332	0.95 (0.78, 1.17) 0.6471	-0.01 (-0.03, 0.01) 0.3716	
	> median	233/1405 (16.6)	239/1395 (17.1)	1.00 (0.85, 1.17) 0.9586	0.99 (0.80, 1.21) 0.8904	-0.01 (-0.03, 0.02)*0.6980	
	Type 2 Diabetes Medical History						0.0007
	Yes	179/1231 (14.5)	238/1243 (19.1)	0.78 (0.66, 0.93) 0.0053	0.72 (0.58, 0.89)*0.0023	-0.03 (-0.05, -0.00) 0.0293	
	No	275/1570 (17.5)	237/1562 (15.2)	1.17 (1.00, 1.36) 0.0454	1.19 (0.98, 1.44)*0.0764	0.00 (-0.01, 0.02) 0.5972	
	Atrial fibrillation or flutter at enrolment ECG						0.5705
	Yes	201/1185 (17.0)	201/1188 (16.9)	1.02 (0.86, 1.20) 0.8611	1.03 (0.82, 1.28) 0.8147	-0.01 (-0.03, 0.02) 0.5914	
	No	253/1616 (15.7)	274/1617 (16.9)	0.95 (0.81, 1.10) 0.4605	0.92 (0.76, 1.12) 0.4185	-0.01 (-0.04, 0.01)*0.3211	
	BMI (kg/m2) at enrolment						0.5915
	< 30	249/1547 (16.1)	256/1541 (16.6)	1.01 (0.86, 1.17) 0.9322	1.00 (0.82, 1.22) 0.9941	-0.01 (-0.03, 0.02)*0.6978	
	>= 30	204/1253 (16.3)	219/1261 (17.4)	0.94 (0.80, 1.11) 0.4902	0.93 (0.75, 1.15) 0.4930	-0.01 (-0.04, 0.02)*0.4666	
	Baseline eGFR (mL/min/1.73m^2)						0.1882
	< 60	222/1338 (16.6)	254/1377 (18.4)	0.91 (0.78, 1.06) 0.2277	0.89 (0.72, 1.09) 0.2585	-0.02 (-0.05, 0.01)*0.2036	
	>= 60	232/1463 (15.9)	220/1427 (15.4)	1.06 (0.90, 1.25) 0.4648	1.07 (0.87, 1.31) 0.5469	0.00 (-0.02, 0.03)*0.7442	

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Quality of Life (LOCF)	SBP at randomisation						0.2257
	<= median	232/1405 (16.5)	234/1420 (16.5)	1.05 (0.89, 1.23) 0.5483	1.05 (0.86, 1.29) 0.6264	0.00 (-0.03, 0.03)*0.9808	
	> median	222/1396 (15.9)	241/1385 (17.4)	0.91 (0.78, 1.07) 0.2596	0.89 (0.72, 1.10) 0.2816	-0.01 (-0.04, 0.01)*0.2889	
	LVEF at enrolment 2						0.3172
	<= 49	148/ 959 (15.4)	139/ 950 (14.6)	1.07 (0.88, 1.32) 0.4965	1.08 (0.83, 1.40) 0.5774	0.01 (-0.02, 0.04)*0.6243	
	>= 50	306/1842 (16.6)	336/1855 (18.1)	0.94 (0.82, 1.08) 0.3836	0.93 (0.78, 1.10) 0.3944	-0.02 (-0.04, 0.01)*0.2283	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7971
	Yes	38/ 280 (13.6)	39/ 281 (13.9)	0.98 (0.65, 1.48)*0.9157	1.05 (0.62, 1.75) 0.8644	-0.00 (-0.06, 0.05)*0.9157	
	No	416/2521 (16.5)	436/2524 (17.3)	0.97 (0.87, 1.10) 0.6715	0.96 (0.83, 1.12) 0.6356	-0.01 (-0.02, 0.01) 0.3031	
	MRAs at baseline						0.9623
	Yes	213/1216 (17.5)	220/1210 (18.2)	0.98 (0.83, 1.15) 0.7631	0.97 (0.78, 1.21) 0.8031	-0.00 (-0.03, 0.02) 0.9188	
	No	241/1585 (15.2)	255/1595 (16.0)	0.98 (0.84, 1.14) 0.7629	0.96 (0.79, 1.17) 0.6996	-0.01 (-0.03, 0.01) 0.4227	
	ACEi+ARB at baseline						0.5020
	Yes	330/2037 (16.2)	357/2059 (17.3)	0.96 (0.84, 1.09) 0.5084	0.93 (0.79, 1.11) 0.4338	-0.01 (-0.03, 0.01)*0.3295	
	No	124/ 764 (16.2)	118/ 746 (15.8)	1.05 (0.84, 1.32) 0.6579	1.07 (0.81, 1.42) 0.6233	0.00 (-0.03, 0.04)*0.8270	
	ARNI at baseline						0.3699
	Yes	25/ 149 (16.8)	18/ 125 (14.4)	1.26 (0.73, 2.17) 0.4027	1.38 (0.70, 2.75) 0.3551	0.02 (-0.06, 0.11)*0.5876	
	No	429/2652 (16.2)	457/2680 (17.1)	0.97 (0.86, 1.09) 0.5789	0.95 (0.82, 1.11) 0.5438	-0.01 (-0.02, 0.01) 0.2432	
	Beta Blocker at baseline						0.1608
	Yes	387/2327 (16.6)	394/2330 (16.9)	1.02 (0.90, 1.15) 0.7997	1.01 (0.86, 1.18) 0.8955	-0.01 (-0.02, 0.01) 0.3841	
	No	67/ 474 (14.1)	81/ 475 (17.1)	0.81 (0.61, 1.08) 0.1472	0.79 (0.55, 1.14) 0.2019	-0.02 (-0.06, 0.02) 0.2347	
	Diuretics at baseline						0.2513
	Yes	403/2500 (16.1)	428/2504 (17.1)	0.96 (0.85, 1.08) 0.4648	0.94 (0.81, 1.10) 0.4693	-0.01 (-0.02, 0.01) 0.2851	
	No	51/ 301 (16.9)	47/ 301 (15.6)	1.19 (0.84, 1.68) 0.3186	1.21 (0.77, 1.91) 0.3971	0.01 (-0.05, 0.07)*0.6587	

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Symptom Burden (LOCF)							
	Overall	368/2801 (13.1)	481/2805 (17.1)	0.77 (0.69, 0.88) <.0001	0.73 (0.63, 0.85) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Age						0.5841
	<= median	168/1394 (12.1)	220/1471 (15.0)	0.80 (0.67, 0.96) 0.0175	0.76 (0.61, 0.95) 0.0160	-0.03 (-0.05, -0.00)*0.0227	
	> median	200/1407 (14.2)	261/1334 (19.6)	0.75 (0.63, 0.88) 0.0006	0.69 (0.56, 0.85) 0.0004	-0.05 (-0.08, -0.03)*0.0002	
	Gender						0.0448
	Male	188/1630 (11.5)	270/1608 (16.8)	0.69 (0.58, 0.82) <.0001	0.65 (0.53, 0.79) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	Female	180/1171 (15.4)	211/1197 (17.6)	0.89 (0.75, 1.06) 0.2022	0.85 (0.68, 1.06) 0.1410	-0.02 (-0.05, 0.01)*0.1389	
	Race						0.6117
	White	275/2006 (13.7)	376/2032 (18.5)	0.76 (0.66, 0.87) <.0001	0.70 (0.59, 0.84) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Black or African	9/ 64 (14.1)	16/ 70 (22.9)	0.60 (0.29, 1.25) 0.1737	0.54 (0.22, 1.33) 0.1787	-0.09 (-0.22, 0.04)*0.1853	
	Asian	70/ 555 (12.6)	74/ 551 (13.4)	0.94 (0.69, 1.27) 0.6684	0.92 (0.65, 1.31) 0.6527	-0.01 (-0.05, 0.03)*0.6863	
	Other	14/ 176 (8.0)	15/ 152 (9.9)	0.85 (0.43, 1.69) 0.6390	0.84 (0.39, 1.82) 0.6536	-0.02 (-0.08, 0.04)*0.5453	
	Geographic region						0.5573
	Asia	67/ 536 (12.5)	71/ 536 (13.2)	0.94 (0.69, 1.28) 0.7065	0.93 (0.65, 1.34) 0.6966	-0.01 (-0.05, 0.03)*0.7153	
	Europe and Saudi Arabia	180/1341 (13.4)	258/1381 (18.7)	0.74 (0.63, 0.88) 0.0006	0.68 (0.55, 0.84) 0.0004	-0.05 (-0.08, -0.03)*0.0002	
	North America	67/ 393 (17.0)	79/ 376 (21.0)	0.82 (0.61, 1.09) 0.1666	0.77 (0.53, 1.11) 0.1609	-0.04 (-0.10, 0.02)*0.1616	
	Latin America	54/ 531 (10.2)	73/ 512 (14.3)	0.72 (0.52, 0.99) 0.0428	0.67 (0.46, 0.99) 0.0426	-0.04 (-0.08, -0.00)*0.0437	
	NYHA class at enrolment						0.0613
	II	281/2083 (13.5)	356/2165 (16.4)	0.82 (0.71, 0.94) 0.0059	0.78 (0.66, 0.93) 0.0050	-0.03 (-0.05, -0.01)*0.0069	
	III or IV	87/ 718 (12.1)	125/ 639 (19.6)	0.63 (0.49, 0.80) 0.0002	0.56 (0.41, 0.77) 0.0003	-0.07 (-0.11, -0.04)*0.0002	
	LVEF at enrolment						0.3152
	<= 49	112/ 959 (11.7)	157/ 950 (16.5)	0.70 (0.56, 0.88) 0.0017	0.65 (0.50, 0.85) 0.0016	-0.05 (-0.08, -0.02)*0.0023	
	50-59	150/1017 (14.7)	172/1009 (17.0)	0.87 (0.72, 1.06) 0.1688	0.83 (0.65, 1.06) 0.1440	-0.02 (-0.05, 0.01)*0.1572	
	>= 60	106/ 825 (12.8)	152/ 846 (18.0)	0.75 (0.60, 0.93) 0.0105	0.70 (0.53, 0.92) 0.0105	-0.05 (-0.09, -0.02)*0.0036	
	NT-proBNP at enrolment						0.2522
	<= median	194/1396 (13.9)	235/1409 (16.7)	0.83 (0.70, 0.99) 0.0366	0.80 (0.65, 0.98) 0.0341	-0.03 (-0.05, -0.00)*0.0405	
	> median	174/1405 (12.4)	246/1395 (17.6)	0.72 (0.61, 0.86) 0.0003	0.67 (0.54, 0.83) 0.0002	-0.05 (-0.08, -0.03)*<.0001	
	Type 2 Diabetes Medical History						0.0387
	Yes	156/1231 (12.7)	239/1243 (19.2)	0.67 (0.56, 0.81) <.0001	0.61 (0.49, 0.76)*<.0001	-0.07 (-0.09, -0.04)*<.0001	
	No	212/1570 (13.5)	242/1562 (15.5)	0.88 (0.74, 1.03) 0.1180	0.85 (0.70, 1.04)*0.1140	-0.02 (-0.04, 0.00)*0.1137	
	Atrial fibrillation or flutter at enrolment ECG						0.5569
	Yes	150/1185 (12.7)	203/1188 (17.1)	0.74 (0.61, 0.90) 0.0021	0.70 (0.55, 0.88) 0.0026	-0.04 (-0.07, -0.02)*0.0024	
	No	218/1616 (13.5)	278/1617 (17.2)	0.80 (0.68, 0.94) 0.0056	0.75 (0.62, 0.91) 0.0040	-0.04 (-0.06, -0.01)*0.0035	
	BMI (kg/m2) at enrolment						0.7246
	< 30	206/1547 (13.3)	262/1541 (17.0)	0.79 (0.67, 0.94) 0.0059	0.75 (0.61, 0.92) 0.0053	-0.04 (-0.06, -0.01)*0.0042	
	>= 30	162/1253 (12.9)	219/1261 (17.4)	0.76 (0.63, 0.91) 0.0028	0.70 (0.56, 0.88) 0.0022	-0.04 (-0.07, -0.02)*0.0019	
	Baseline eGFR (mL/min/1.73m^2)						0.1909
	< 60	185/1338 (13.8)	268/1377 (19.5)	0.72 (0.61, 0.85) 0.0001	0.66 (0.54, 0.81) 0.0001	-0.06 (-0.08, -0.03)*<.0001	
	>= 60	183/1463 (12.5)	213/1427 (14.9)	0.85 (0.71, 1.02) 0.0748	0.81 (0.66, 1.01) 0.0631	-0.02 (-0.05, 0.00)*0.0589	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)	SBP at randomisation						0.8797
	<= median	182/1405 (13.0)	244/1420 (17.2)	0.78 (0.65, 0.93) 0.0051	0.74 (0.60, 0.91) 0.0048	-0.04 (-0.07, -0.02)*0.0016	
	> median	186/1396 (13.3)	237/1385 (17.1)	0.77 (0.64, 0.91) 0.0025	0.71 (0.58, 0.88) 0.0019	-0.04 (-0.06, -0.01)*0.0054	
	LVEF at enrolment 2						0.2592
	<= 49	112/ 959 (11.7)	157/ 950 (16.5)	0.70 (0.56, 0.88) 0.0017	0.65 (0.50, 0.85) 0.0016	-0.05 (-0.08, -0.02)*0.0023	
	>= 50	256/1842 (13.9)	324/1855 (17.5)	0.81 (0.70, 0.94) 0.0064	0.77 (0.64, 0.93) 0.0053	-0.04 (-0.06, -0.01)*0.0028	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7181
	Yes	33/ 280 (11.8)	44/ 281 (15.7)	0.69 (0.46, 1.04) 0.0768	0.65 (0.39, 1.07) 0.0910	-0.04 (-0.10, 0.02)*0.1818	
	No	335/2521 (13.3)	437/2524 (17.3)	0.78 (0.69, 0.89) 0.0002	0.73 (0.63, 0.86) 0.0001	-0.04 (-0.06, -0.02)*<.0001	
	MRAs at baseline						0.5602
	Yes	158/1216 (13.0)	215/1210 (17.8)	0.74 (0.62, 0.90) 0.0019	0.70 (0.55, 0.87) 0.0018	-0.05 (-0.08, -0.02)*0.0011	
	No	210/1585 (13.2)	266/1595 (16.7)	0.80 (0.68, 0.94) 0.0077	0.76 (0.62, 0.92) 0.0064	-0.03 (-0.06, -0.01)*0.0067	
	ACEi+ARB at baseline						0.0823
	Yes	253/2037 (12.4)	360/2059 (17.5)	0.73 (0.63, 0.84) <.0001	0.67 (0.56, 0.80) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	No	115/ 764 (15.1)	121/ 746 (16.2)	0.92 (0.73, 1.17) 0.5032	0.91 (0.68, 1.20) 0.4950	-0.01 (-0.05, 0.02)*0.5323	
	ARNI at baseline						0.3872
	Yes	22/ 149 (14.8)	17/ 125 (13.6)	1.03 (0.57, 1.86) 0.9335	1.06 (0.53, 2.13) 0.8723	0.01 (-0.07, 0.09)*0.7827	
	No	346/2652 (13.0)	464/2680 (17.3)	0.77 (0.68, 0.87) <.0001	0.72 (0.62, 0.84) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Beta Blocker at baseline						0.2277
	Yes	311/2327 (13.4)	396/2330 (17.0)	0.80 (0.70, 0.92) 0.0014	0.76 (0.65, 0.90) 0.0011	-0.04 (-0.06, -0.02)*0.0005	
	No	57/ 474 (12.0)	85/ 475 (17.9)	0.66 (0.48, 0.89) 0.0073	0.60 (0.42, 0.87) 0.0071	-0.06 (-0.10, -0.01)*0.0110	
	Diuretics at baseline						0.1029
	Yes	326/2500 (13.0)	438/2504 (17.5)	0.75 (0.66, 0.85) <.0001	0.70 (0.60, 0.82) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	42/ 301 (14.0)	43/ 301 (14.3)	1.05 (0.71, 1.55) 0.8134	1.04 (0.66, 1.66) 0.8573	-0.00 (-0.06, 0.05)*0.9068	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	325/2801 (11.6)	333/2805 (11.9)	0.98 (0.86, 1.13) 0.8176	0.98 (0.83, 1.16) 0.8204	0.00 (-0.01, 0.01) 0.9045	
	Age						0.4451
	<= median	153/1394 (11.0)	158/1471 (10.7)	1.04 (0.85, 1.27) 0.7188	1.03 (0.81, 1.31) 0.8254	0.00 (-0.02, 0.03)*0.8401	
	> median	172/1407 (12.2)	175/1334 (13.1)	0.93 (0.77, 1.13) 0.4607	0.93 (0.74, 1.18) 0.5505	-0.01 (-0.03, 0.02)*0.4821	
	Gender						0.9343
	Male	198/1630 (12.1)	199/1608 (12.4)	0.98 (0.82, 1.17) 0.8016	0.97 (0.78, 1.21) 0.8112	-0.00 (-0.02, 0.02) 0.8032	
	Female	127/1171 (10.8)	134/1197 (11.2)	0.99 (0.79, 1.24) 0.9310	0.99 (0.76, 1.29) 0.9211	-0.00 (-0.03, 0.02)*0.7861	
	Race						0.9071
	White	215/2006 (10.7)	231/2032 (11.4)	0.96 (0.81, 1.14) 0.6371	0.95 (0.78, 1.17) 0.6416	-0.01 (-0.03, 0.01)*0.5097	
	Black or African	12/ 64 (18.8)	9/ 70 (12.9)	1.35 (0.61, 2.96) 0.4586	1.47 (0.57, 3.83) 0.4281	0.06 (-0.06, 0.18)*0.3503	
	Asian	84/ 555 (15.1)	80/ 551 (14.5)	1.01 (0.77, 1.33) 0.9232	1.02 (0.73, 1.44) 0.8968	0.01 (-0.03, 0.05) 0.6488	
	Other	14/ 176 (8.0)	13/ 152 (8.6)	0.97 (0.48, 1.93) 0.9225	0.93 (0.41, 2.16) 0.8743	-0.01 (-0.07, 0.05)*0.8446	
	Geographic region						0.9155
	Asia	82/ 536 (15.3)	80/ 536 (14.9)	0.99 (0.75, 1.30) 0.9416	0.99 (0.70, 1.40) 0.9657	-0.00 (-0.04, 0.04) 0.9585	
	Europe and Saudi Arabia	146/1341 (10.9)	161/1381 (11.7)	0.94 (0.77, 1.15) 0.5787	0.93 (0.73, 1.20) 0.5913	-0.01 (-0.03, 0.02)*0.5248	
	North America	38/ 393 (9.7)	32/ 376 (8.5)	1.11 (0.71, 1.74) 0.6370	1.13 (0.69, 1.86) 0.6307	0.01 (-0.03, 0.05)*0.5761	
	Latin America	59/ 531 (11.1)	60/ 512 (11.7)	1.02 (0.74, 1.42) 0.8864	1.02 (0.68, 1.52) 0.9275	-0.01 (-0.04, 0.03)*0.7577	
	NYHA class at enrolment						0.3687
	II	245/2083 (11.8)	254/2165 (11.7)	1.02 (0.87, 1.20) 0.8141	1.02 (0.84, 1.23) 0.8550	0.00 (-0.01, 0.02) 0.8128	
	III or IV	80/ 718 (11.1)	78/ 639 (12.2)	0.88 (0.66, 1.16) 0.3655	0.87 (0.62, 1.23) 0.4289	-0.01 (-0.04, 0.02)*0.5426	
	LVEF at enrolment						0.3055
	<= 49	110/ 959 (11.5)	102/ 950 (10.7)	1.05 (0.82, 1.34) 0.7082	1.04 (0.77, 1.40) 0.7906	0.01 (-0.02, 0.04)*0.6100	
	50-59	121/1017 (11.9)	113/1009 (11.2)	1.07 (0.85, 1.35) 0.5728	1.09 (0.82, 1.44) 0.5513	0.01 (-0.02, 0.03)*0.6228	
	>= 60	94/ 825 (11.4)	118/ 846 (13.9)	0.84 (0.66, 1.07) 0.1616	0.82 (0.61, 1.11) 0.1927	-0.03 (-0.06, 0.01)*0.1161	
	NT-proBNP at enrolment						0.9114
	<= median	164/1396 (11.7)	172/1409 (12.2)	0.98 (0.80, 1.19) 0.8108	0.97 (0.76, 1.22) 0.7751	-0.00 (-0.03, 0.02)*0.7079	
	> median	161/1405 (11.5)	161/1395 (11.5)	0.99 (0.81, 1.21) 0.9474	1.00 (0.78, 1.27) 0.9794	-0.00 (-0.02, 0.02)*0.9457	
	Type 2 Diabetes Medical History						0.0442
	Yes	129/1231 (10.5)	159/1243 (12.8)	0.84 (0.68, 1.03) 0.0974	0.80 (0.62, 1.02)*0.0734	-0.02 (-0.05, 0.00)*0.0727	
	No	196/1570 (12.5)	174/1562 (11.1)	1.12 (0.93, 1.34) 0.2473	1.14 (0.92, 1.41)*0.2440	0.01 (-0.01, 0.04)*0.2436	
	Atrial fibrillation or flutter at enrolment ECG						0.9360
	Yes	149/1185 (12.6)	156/1188 (13.1)	0.99 (0.81, 1.21) 0.9377	0.99 (0.77, 1.27) 0.9197	-0.01 (-0.03, 0.02)*0.6849	
	No	176/1616 (10.9)	177/1617 (10.9)	0.98 (0.81, 1.18) 0.8290	0.98 (0.78, 1.23) 0.8508	-0.00 (-0.02, 0.02)*0.9599	
	BMI (kg/m2) at enrolment						0.8442
	< 30	196/1547 (12.7)	201/1541 (13.0)	1.00 (0.84, 1.19) 0.9690	1.00 (0.80, 1.24) 0.9928	-0.01 (-0.03, 0.01) 0.6041	
	>= 30	129/1253 (10.3)	132/1261 (10.5)	0.97 (0.77, 1.21) 0.7777	0.96 (0.74, 1.25) 0.7575	-0.00 (-0.03, 0.02)*0.8872	
	Baseline eGFR (mL/min/1.73m^2)						0.5648
	< 60	156/1338 (11.7)	154/1377 (11.2)	1.03 (0.84, 1.26) 0.8077	1.04 (0.81, 1.32) 0.7644	0.00 (-0.02, 0.02) 0.9915	
	>= 60	169/1463 (11.6)	178/1427 (12.5)	0.95 (0.79, 1.15) 0.5910	0.93 (0.74, 1.18) 0.5552	-0.01 (-0.03, 0.01)*0.4459	

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Self Efficacy (LOCF)	SBP at randomisation						0.3912
	<= median	171/1405 (12.2)	166/1420 (11.7)	1.04 (0.86, 1.27) 0.6569	1.06 (0.84, 1.34) 0.6222	0.00 (-0.02, 0.03)*0.6935	
	> median	154/1396 (11.0)	167/1385 (12.1)	0.92 (0.76, 1.13) 0.4399	0.90 (0.71, 1.15) 0.4148	-0.01 (-0.03, 0.01)*0.3971	
	LVEF at enrolment 2						0.5124
	<= 49	110/ 959 (11.5)	102/ 950 (10.7)	1.05 (0.82, 1.34) 0.7082	1.04 (0.77, 1.40) 0.7906	0.01 (-0.02, 0.04)*0.6100	
	>= 50	215/1842 (11.7)	231/1855 (12.5)	0.95 (0.81, 1.13) 0.5742	0.95 (0.78, 1.17) 0.6340	0.00 (-0.01, 0.02) 0.7811	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3764
	Yes	36/ 280 (12.9)	30/ 281 (10.7)	1.20 (0.78, 1.83) 0.4070	1.25 (0.72, 2.18) 0.4272	0.02 (-0.03, 0.08)*0.4225	
	No	289/2521 (11.5)	303/2524 (12.0)	0.96 (0.83, 1.12) 0.6155	0.96 (0.80, 1.14) 0.6286	-0.00 (-0.02, 0.01) 0.8621	
	MRAs at baseline						0.7894
	Yes	153/1216 (12.6)	151/1210 (12.5)	1.00 (0.82, 1.23) 0.9792	1.00 (0.78, 1.28) 0.9936	0.00 (-0.02, 0.02) 0.7591	
	No	172/1585 (10.9)	182/1595 (11.4)	0.97 (0.80, 1.17) 0.7215	0.96 (0.77, 1.21) 0.7391	-0.01 (-0.03, 0.02)*0.6163	
	ACEi+ARB at baseline						0.0203
	Yes	221/2037 (10.8)	255/2059 (12.4)	0.89 (0.76, 1.05) 0.1585	0.86 (0.71, 1.05) 0.1377	-0.02 (-0.03, 0.00)*0.1250	
	No	104/ 764 (13.6)	78/ 746 (10.5)	1.30 (0.99, 1.69) 0.0568	1.39 (1.01, 1.92) 0.0431	0.03 (-0.00, 0.06)*0.0590	
	ARNI at baseline						0.0344
	Yes	25/ 149 (16.8)	10/ 125 (8.0)	2.15 (1.08, 4.28) 0.0284	2.47 (1.11, 5.52) 0.0272	0.09 (0.01, 0.16)*0.0246	
	No	300/2652 (11.3)	323/2680 (12.1)	0.95 (0.83, 1.10) 0.4925	0.94 (0.79, 1.12) 0.4980	-0.00 (-0.02, 0.01) 0.7204	
	Beta Blocker at baseline						0.4534
	Yes	276/2327 (11.9)	275/2330 (11.8)	1.01 (0.87, 1.17) 0.9297	1.01 (0.84, 1.21) 0.9271	0.00 (-0.01, 0.02) 0.7076	
	No	49/ 474 (10.3)	58/ 475 (12.2)	0.87 (0.61, 1.23) 0.4172	0.85 (0.56, 1.28) 0.4264	-0.02 (-0.06, 0.02)*0.3615	
	Diuretics at baseline						0.6325
	Yes	290/2500 (11.6)	293/2504 (11.7)	1.00 (0.86, 1.15) 0.9584	0.99 (0.83, 1.19) 0.9514	0.00 (-0.01, 0.01) 0.9406	
	No	35/ 301 (11.6)	40/ 301 (13.3)	0.90 (0.59, 1.35) 0.5992	0.88 (0.54, 1.45) 0.6215	-0.02 (-0.07, 0.04)*0.5371	

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Symptom Frequency (LOCF)							
	Overall	290/2801 (10.4)	405/2805 (14.4)	0.72 (0.63, 0.83) <.0001	0.68 (0.58, 0.80) <.0001	-0.03 (-0.05, -0.02) <.0001	
	Age						0.5579
	<= median	129/1394 (9.3)	196/1471 (13.3)	0.69 (0.56, 0.85) 0.0004	0.65 (0.51, 0.82) 0.0004	-0.04 (-0.06, -0.02) 0.0007	
	> median	161/1407 (11.4)	209/1334 (15.7)	0.75 (0.62, 0.90) 0.0023	0.70 (0.56, 0.88) 0.0019	-0.04 (-0.07, -0.02)*0.0012	
	Gender						0.7315
	Male	160/1630 (9.8)	222/1608 (13.8)	0.71 (0.59, 0.85) 0.0003	0.67 (0.54, 0.83) 0.0003	-0.04 (-0.06, -0.02)*0.0004	
	Female	130/1171 (11.1)	183/1197 (15.3)	0.74 (0.60, 0.91) 0.0048	0.69 (0.54, 0.88) 0.0032	-0.04 (-0.06, -0.01) 0.0071	
	Race						0.9166
	White	208/2006 (10.4)	297/2032 (14.6)	0.73 (0.62, 0.86) 0.0001	0.68 (0.56, 0.82) <.0001	-0.03 (-0.05, -0.01) 0.0010	
	Black or African	8/ 64 (12.5)	9/ 70 (12.9)	0.93 (0.39, 2.25) 0.8773	0.93 (0.33, 2.59) 0.8837	-0.00 (-0.12, 0.11)*0.9505	
	Asian	63/ 555 (11.4)	84/ 551 (15.2)	0.74 (0.54, 1.00) 0.0476	0.70 (0.49, 1.00) 0.0481	-0.04 (-0.08, 0.00) 0.0733	
	Other	11/ 176 (6.3)	15/ 152 (9.9)	0.62 (0.29, 1.30) 0.2045	0.59 (0.26, 1.33) 0.2025	-0.04 (-0.10, 0.02) 0.1574	
	Geographic region						0.7882
	Asia	60/ 536 (11.2)	82/ 536 (15.3)	0.73 (0.53, 0.99) 0.0424	0.69 (0.48, 0.99) 0.0426	-0.04 (-0.08, 0.00) 0.0602	
	Europe and Saudi Arabia	138/1341 (10.3)	196/1381 (14.2)	0.75 (0.62, 0.92) 0.0049	0.70 (0.55, 0.88) 0.0029	-0.04 (-0.06, -0.01)*0.0018	
	North America	47/ 393 (12.0)	57/ 376 (15.2)	0.77 (0.54, 1.11) 0.1580	0.74 (0.49, 1.13) 0.1646	-0.03 (-0.08, 0.02) 0.1995	
	Latin America	45/ 531 (8.5)	70/ 512 (13.7)	0.62 (0.44, 0.87) 0.0065	0.57 (0.38, 0.85) 0.0059	-0.05 (-0.09, -0.01)*0.0074	
	NYHA class at enrolment						0.4930
	II	222/2083 (10.7)	311/2165 (14.4)	0.74 (0.63, 0.86) 0.0002	0.69 (0.58, 0.84) 0.0001	-0.04 (-0.06, -0.02)*0.0003	
	III or IV	68/ 718 (9.5)	94/ 639 (14.7)	0.66 (0.49, 0.87) 0.0040	0.61 (0.44, 0.86) 0.0044	-0.05 (-0.08, -0.02) 0.0027	
	LVEF at enrolment						0.6931
	<= 49	90/ 959 (9.4)	111/ 950 (11.7)	0.79 (0.61, 1.03) 0.0827	0.76 (0.57, 1.03) 0.0740	-0.02 (-0.05, 0.00)*0.1016	
	50-59	106/1017 (10.4)	154/1009 (15.3)	0.68 (0.54, 0.86) 0.0011	0.64 (0.49, 0.83) 0.0010	-0.04 (-0.07, -0.01) 0.0062	
	>= 60	94/ 825 (11.4)	140/ 846 (16.5)	0.71 (0.56, 0.90) 0.0054	0.67 (0.50, 0.89) 0.0054	-0.05 (-0.08, -0.02)*0.0023	
	NT-proBNP at enrolment						0.7096
	<= median	140/1396 (10.0)	202/1409 (14.3)	0.70 (0.57, 0.86) 0.0005	0.66 (0.52, 0.83) 0.0004	-0.04 (-0.06, -0.02) 0.0005	
	> median	150/1405 (10.7)	203/1395 (14.6)	0.74 (0.61, 0.90) 0.0023	0.70 (0.55, 0.88) 0.0020	-0.04 (-0.06, -0.01)*0.0020	
	Type 2 Diabetes Medical History						0.6917
	Yes	130/1231 (10.6)	189/1243 (15.2)	0.70 (0.57, 0.86) 0.0007	0.66 (0.52, 0.84)*0.0006	-0.05 (-0.07, -0.02)*0.0005	
	No	160/1570 (10.2)	216/1562 (13.8)	0.74 (0.61, 0.89) 0.0018	0.71 (0.57, 0.88)*0.0018	-0.03 (-0.05, -0.00) 0.0184	
	Atrial fibrillation or flutter at enrolment ECG						0.8047
	Yes	130/1185 (11.0)	183/1188 (15.4)	0.70 (0.57, 0.87) 0.0008	0.66 (0.51, 0.84) 0.0008	-0.04 (-0.07, -0.02)*0.0014	
	No	160/1616 (9.9)	222/1617 (13.7)	0.73 (0.60, 0.88) 0.0011	0.69 (0.56, 0.86) 0.0009	-0.04 (-0.06, -0.01) 0.0009	
	BMI (kg/m2) at enrolment						0.7471
	< 30	160/1547 (10.3)	215/1541 (14.0)	0.74 (0.61, 0.89) 0.0017	0.70 (0.56, 0.87) 0.0016	-0.04 (-0.06, -0.01)*0.0021	
	>= 30	130/1253 (10.4)	189/1261 (15.0)	0.70 (0.57, 0.86) 0.0008	0.66 (0.52, 0.84) 0.0006	-0.04 (-0.06, -0.02) 0.0011	
	Baseline eGFR (mL/min/1.73m^2)						0.6156
	< 60	156/1338 (11.7)	216/1377 (15.7)	0.75 (0.62, 0.90) 0.0024	0.70 (0.56, 0.88) 0.0021	-0.04 (-0.07, -0.01)*0.0022	
	>= 60	134/1463 (9.2)	188/1427 (13.2)	0.70 (0.57, 0.86) 0.0007	0.66 (0.52, 0.84) 0.0006	-0.04 (-0.06, -0.02)*0.0006	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)	SBP at randomisation						0.4865
	<= median	157/1405 (11.2)	215/1420 (15.1)	0.76 (0.63, 0.91) 0.0038	0.71 (0.57, 0.89) 0.0029	-0.03 (-0.05, -0.01) 0.0156	
	> median	133/1396 (9.5)	190/1385 (13.7)	0.68 (0.56, 0.84) 0.0003	0.64 (0.51, 0.82) 0.0003	-0.04 (-0.07, -0.02)*0.0006	
	LVEF at enrolment 2						0.4043
	<= 49	90/ 959 (9.4)	111/ 950 (11.7)	0.79 (0.61, 1.03) 0.0827	0.76 (0.57, 1.03) 0.0740	-0.02 (-0.05, 0.00)*0.1016	
	>= 50	200/1842 (10.9)	294/1855 (15.8)	0.70 (0.59, 0.82) <.0001	0.65 (0.53, 0.79) <.0001	-0.04 (-0.06, -0.02) 0.0003	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2062
	Yes	20/ 280 (7.1)	35/ 281 (12.5)	0.57 (0.34, 0.97)*0.0375	0.42 (0.23, 0.77) 0.0053	-0.05 (-0.10, -0.00)*0.0336	
	No	270/2521 (10.7)	370/2524 (14.7)	0.74 (0.64, 0.85) <.0001	0.70 (0.59, 0.83) <.0001	-0.03 (-0.05, -0.02) <.0001	
	MRAs at baseline						0.4004
	Yes	113/1216 (9.3)	169/1210 (14.0)	0.67 (0.54, 0.84) 0.0004	0.62 (0.48, 0.80) 0.0003	-0.05 (-0.07, -0.02)*0.0003	
	No	177/1585 (11.2)	236/1595 (14.8)	0.76 (0.63, 0.91) 0.0023	0.72 (0.58, 0.89) 0.0023	-0.03 (-0.05, -0.01) 0.0110	
	ACEi+ARB at baseline						0.0480
	Yes	192/2037 (9.4)	299/2059 (14.5)	0.66 (0.56, 0.78) <.0001	0.61 (0.50, 0.74) <.0001	-0.04 (-0.06, -0.02) 0.0001	
	No	98/ 764 (12.8)	106/ 746 (14.2)	0.90 (0.70, 1.16) 0.4009	0.88 (0.65, 1.18) 0.3823	-0.02 (-0.06, 0.01) 0.1714	
	ARNI at baseline						0.9941
	Yes	14/ 149 (9.4)	15/ 125 (12.0)	0.78 (0.39, 1.57) 0.4888	0.75 (0.34, 1.64) 0.4670	-0.03 (-0.10, 0.05)*0.4890	
	No	276/2652 (10.4)	390/2680 (14.6)	0.72 (0.63, 0.83) <.0001	0.68 (0.58, 0.80) <.0001	-0.03 (-0.05, -0.02) <.0001	
	Beta Blocker at baseline						0.0312
	Yes	244/2327 (10.5)	320/2330 (13.7)	0.77 (0.66, 0.90) 0.0012	0.74 (0.62, 0.89) 0.0010	-0.02 (-0.04, -0.01) 0.0107	
	No	46/ 474 (9.7)	85/ 475 (17.9)	0.52 (0.38, 0.73) 0.0001	0.46 (0.31, 0.68) <.0001	-0.08 (-0.13, -0.04)*0.0002	
	Diuretics at baseline						0.3738
	Yes	266/2500 (10.6)	361/2504 (14.4)	0.73 (0.63, 0.85) <.0001	0.69 (0.59, 0.82) <.0001	-0.03 (-0.05, -0.01) 0.0003	
	No	24/ 301 (8.0)	44/ 301 (14.6)	0.59 (0.37, 0.95) 0.0289	0.54 (0.32, 0.92) 0.0238	-0.07 (-0.12, -0.02)*0.0096	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

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Social Limitation (LOCF)							
	Overall	441/2625 (16.8)	468/2625 (17.8)	0.94 (0.84, 1.06) 0.2982	0.93 (0.80, 1.07) 0.2953	-0.01 (-0.03, 0.01) 0.3660	
	Age						0.9725
	<= median	201/1331 (15.1)	224/1409 (15.9)	0.94 (0.79, 1.11) 0.4656	0.92 (0.75, 1.14) 0.4569	-0.01 (-0.03, 0.02) 0.4516	
	> median	240/1294 (18.5)	244/1216 (20.1)	0.93 (0.80, 1.09) 0.3795	0.91 (0.75, 1.12) 0.3744	-0.01 (-0.04, 0.02) 0.4025	
	Gender						0.8375
	Male	246/1538 (16.0)	254/1500 (16.9)	0.93 (0.80, 1.09) 0.3987	0.92 (0.76, 1.12) 0.4258	-0.01 (-0.03, 0.01) 0.4371	
	Female	195/1087 (17.9)	214/1125 (19.0)	0.96 (0.81, 1.14) 0.6148	0.94 (0.75, 1.17) 0.5540	-0.01 (-0.04, 0.02) 0.6645	
	Race						0.0511
	White	315/1890 (16.7)	371/1921 (19.3)	0.87 (0.77, 1.00) 0.0441	0.84 (0.71, 1.00) 0.0486	-0.02 (-0.04, 0.00) 0.1183	
	Black or African	16/ 58 (27.6)	9/ 66 (13.6)	1.98 (0.95, 4.14) 0.0686	2.40 (0.96, 6.00) 0.0611	0.13 (-0.01, 0.27) 0.0652	
	Asian	90/ 506 (17.8)	77/ 494 (15.6)	1.13 (0.86, 1.50) 0.3734	1.16 (0.83, 1.62) 0.3812	0.02 (-0.03, 0.07) 0.4120	
	Other	20/ 171 (11.7)	11/ 144 (7.6)	1.26 (0.63, 2.49) 0.5142	1.35 (0.60, 3.02) 0.4682	0.04 (-0.05, 0.12) 0.3919	
	Geographic region						0.5189
	Asia	85/ 492 (17.3)	73/ 482 (15.1)	1.14 (0.85, 1.51) 0.3796	1.16 (0.83, 1.64) 0.3898	0.02 (-0.03, 0.07) 0.4240	
	Europe and Saudi Arabia	223/1273 (17.5)	258/1309 (19.7)	0.91 (0.78, 1.06) 0.2354	0.89 (0.72, 1.09) 0.2618	0.00 (-0.02, 0.03) 0.9057	
	North America	65/ 367 (17.7)	59/ 347 (17.0)	1.03 (0.75, 1.42) 0.8636	1.03 (0.70, 1.52) 0.8752	0.00 (-0.05, 0.06) 0.9175	
	Latin America	68/ 493 (13.8)	78/ 487 (16.0)	0.85 (0.63, 1.14) 0.2744	0.83 (0.58, 1.18) 0.2975	-0.01 (-0.06, 0.03) 0.5065	
	NYHA class at enrolment						0.2688
	II	301/1953 (15.4)	348/2031 (17.1)	0.89 (0.78, 1.02) 0.1045	0.86 (0.73, 1.02) 0.0898	-0.02 (-0.04, 0.00) 0.0612	
	III or IV	140/ 672 (20.8)	119/ 593 (20.1)	1.02 (0.83, 1.26) 0.8149	1.05 (0.79, 1.39) 0.7390	0.01 (-0.03, 0.05) 0.5664	
	LVEF at enrolment						0.0771
	<= 49	155/ 907 (17.1)	130/ 896 (14.5)	1.13 (0.92, 1.40) 0.2389	1.17 (0.90, 1.51) 0.2364	0.02 (-0.01, 0.05) 0.2195	
	50-59	160/ 955 (16.8)	176/ 946 (18.6)	0.91 (0.76, 1.11) 0.3552	0.90 (0.71, 1.14) 0.3897	-0.01 (-0.04, 0.02) 0.5075	
	>= 60	126/ 763 (16.5)	162/ 783 (20.7)	0.81 (0.66, 1.00) 0.0486	0.75 (0.58, 0.98) 0.0357	-0.04 (-0.08, -0.01) 0.0229	
	NT-proBNP at enrolment						0.8321
	<= median	218/1312 (16.6)	236/1336 (17.7)	0.93 (0.79, 1.09) 0.3742	0.91 (0.74, 1.12) 0.3918	-0.01 (-0.03, 0.02) 0.5620	
	> median	223/1313 (17.0)	232/1288 (18.0)	0.95 (0.81, 1.12) 0.5273	0.93 (0.76, 1.15) 0.5204	-0.01 (-0.04, 0.02) 0.4588	
	Type 2 Diabetes Medical History						0.7255
	Yes	193/1150 (16.8)	213/1169 (18.2)	0.92 (0.77, 1.10) 0.3501	0.91 (0.73, 1.12)*0.3623	-0.01 (-0.04, 0.02) 0.3551	
	No	248/1475 (16.8)	255/1456 (17.5)	0.96 (0.82, 1.12) 0.5868	0.95 (0.79, 1.15)*0.6152	-0.01 (-0.03, 0.02) 0.6721	
	Atrial fibrillation or flutter at enrolment ECG						0.8783
	Yes	190/1097 (17.3)	202/1109 (18.2)	0.95 (0.80, 1.13) 0.5690	0.94 (0.75, 1.17) 0.5637	-0.00 (-0.03, 0.03) 0.9445	
	No	251/1528 (16.4)	266/1516 (17.5)	0.93 (0.80, 1.09) 0.3778	0.92 (0.76, 1.11) 0.3772	-0.01 (-0.04, 0.01) 0.3201	
	BMI (kg/m2) at enrolment						0.9509
	< 30	237/1452 (16.3)	248/1428 (17.4)	0.94 (0.81, 1.11) 0.4736	0.92 (0.76, 1.13) 0.4350	-0.01 (-0.03, 0.01) 0.3948	
	>= 30	204/1172 (17.4)	220/1195 (18.4)	0.94 (0.79, 1.11) 0.4631	0.93 (0.75, 1.15) 0.5020	-0.01 (-0.03, 0.02) 0.6605	
	Baseline eGFR (mL/min/1.73m^2)						0.8513
	< 60	226/1240 (18.2)	248/1270 (19.5)	0.93 (0.79, 1.09) 0.3766	0.91 (0.74, 1.12) 0.3682	-0.01 (-0.04, 0.02) 0.4118	
	>= 60	215/1385 (15.5)	220/1354 (16.2)	0.95 (0.80, 1.13) 0.5736	0.94 (0.77, 1.16) 0.5860	-0.01 (-0.03, 0.02) 0.6319	

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Social Limitation (LOCF)	SBP at randomisation						0.4161
	<= median	226/1320 (17.1)	233/1323 (17.6)	0.99 (0.84, 1.16) 0.8957	0.99 (0.80, 1.21) 0.8861	-0.00 (-0.03, 0.02) 0.8884	
	> median	215/1305 (16.5)	235/1302 (18.0)	0.90 (0.76, 1.06) 0.1964	0.87 (0.71, 1.07) 0.1909	-0.02 (-0.04, 0.01) 0.2516	
	LVEF at enrolment 2						0.0343
	<= 49	155/ 907 (17.1)	130/ 896 (14.5)	1.13 (0.92, 1.40) 0.2389	1.17 (0.90, 1.51) 0.2364	0.02 (-0.01, 0.05) 0.2195	
	>= 50	286/1718 (16.6)	338/1729 (19.5)	0.87 (0.75, 1.00) 0.0428	0.83 (0.70, 0.99) 0.0394	-0.02 (-0.05, 0.00) 0.0515	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1534
	Yes	46/ 252 (18.3)	37/ 256 (14.5)	1.22 (0.82, 1.79) 0.3243	1.32 (0.81, 2.16) 0.2687	0.04 (-0.03, 0.10)*0.2464	
	No	395/2373 (16.6)	431/2369 (18.2)	0.92 (0.81, 1.03) 0.1585	0.89 (0.77, 1.04) 0.1458	-0.02 (-0.04, 0.00) 0.1118	
	MRAs at baseline						0.2872
	Yes	200/1144 (17.5)	193/1131 (17.1)	1.01 (0.85, 1.21) 0.9074	1.02 (0.81, 1.27) 0.8873	0.01 (-0.02, 0.03) 0.6382	
	No	241/1481 (16.3)	275/1494 (18.4)	0.89 (0.76, 1.04) 0.1366	0.86 (0.71, 1.04) 0.1283	-0.02 (-0.04, 0.01) 0.1195	
	ACEi+ARB at baseline						0.1550
	Yes	307/1909 (16.1)	350/1934 (18.1)	0.89 (0.78, 1.02) 0.1014	0.86 (0.73, 1.02) 0.0927	-0.02 (-0.04, 0.00) 0.1188	
	No	134/ 716 (18.7)	118/ 691 (17.1)	1.08 (0.87, 1.35) 0.4981	1.11 (0.84, 1.46) 0.4671	0.02 (-0.02, 0.05) 0.3862	
	ARNI at baseline						0.6206
	Yes	25/ 146 (17.1)	18/ 115 (15.7)	1.11 (0.64, 1.94) 0.7090	1.13 (0.57, 2.21) 0.7279	0.01 (-0.09, 0.10) 0.8986	
	No	416/2479 (16.8)	450/2510 (17.9)	0.94 (0.83, 1.05) 0.2702	0.92 (0.79, 1.07) 0.2698	-0.01 (-0.03, 0.01) 0.3975	
	Beta Blocker at baseline						0.2656
	Yes	378/2195 (17.2)	391/2187 (17.9)	0.97 (0.85, 1.10) 0.6050	0.96 (0.82, 1.13) 0.6168	-0.00 (-0.02, 0.02) 0.7793	
	No	63/ 430 (14.7)	77/ 438 (17.6)	0.81 (0.60, 1.10) 0.1807	0.77 (0.53, 1.11) 0.1569	-0.04 (-0.09, 0.00) 0.0647	
	Diuretics at baseline						0.6731
	Yes	406/2350 (17.3)	432/2345 (18.4)	0.93 (0.83, 1.05) 0.2396	0.91 (0.78, 1.06) 0.2345	-0.01 (-0.03, 0.01) 0.3329	
	No	35/ 275 (12.7)	36/ 280 (12.9)	1.01 (0.66, 1.56) 0.9461	1.03 (0.62, 1.70) 0.9114	0.02 (-0.04, 0.07) 0.5874	

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Symptom Stability (LOCF)							
	Overall	556/2801 (19.9)	637/2805 (22.7)	0.95 (0.89, 1.01) 0.1136	0.82 (0.70, 0.95) 0.0108	-0.03 (-0.05, -0.01)*0.0089	
	Age						0.3509
	<= median	279/1394 (20.0)	327/1471 (22.2)	0.98 (0.89, 1.07) 0.6011	0.85 (0.68, 1.05) 0.1302	-0.02 (-0.05, 0.01)*0.1461	
	> median	277/1407 (19.7)	310/1334 (23.2)	0.92 (0.84, 1.00) 0.0523	0.78 (0.62, 0.97) 0.0269	-0.04 (-0.07, -0.00)*0.0236	
	Gender						0.2418
	Male	332/1630 (20.4)	354/1608 (22.0)	0.99 (0.91, 1.07) 0.7217	0.92 (0.74, 1.13) 0.4098	-0.02 (-0.04, 0.01)*0.2515	
	Female	224/1171 (19.1)	283/1197 (23.6)	0.89 (0.80, 1.00) 0.0409	0.71 (0.57, 0.90) 0.0041	-0.05 (-0.08, -0.01)*0.0073	
	Race						0.8258*
	White	383/2006 (19.1)	447/2032 (22.0)	0.96 (0.89, 1.04) 0.3373	0.85 (0.71, 1.02) 0.0807	-0.03 (-0.05, -0.00)*0.0222	
	Black or African	12/ 64 (18.8)	19/ 70 (27.1)	0.85 (0.51, 1.41) 0.5295	0.63 (0.25, 1.61) 0.3357	-0.08 (-0.23, 0.06)*0.2447	
	Asian	132/ 555 (23.8)	146/ 551 (26.5)	0.90 (0.79, 1.02) 0.1034	0.74 (0.53, 1.02) 0.0677	-0.03 (-0.08, 0.02)*0.2981	
	Other	29/ 176 (16.5)	25/ 152 (16.4)	1.00 (0.61, 1.63)*0.9942	0.94 (0.47, 1.91) 0.8745	0.00 (-0.08, 0.08)*0.9942	
	Geographic region						0.8273
	Asia	125/ 536 (23.3)	143/ 536 (26.7)	0.90 (0.79, 1.02) 0.0959	0.70 (0.50, 0.99) 0.0424	-0.03 (-0.09, 0.02)*0.2039	
	Europe and Saudi Arabia	260/1341 (19.4)	297/1381 (21.5)	0.97 (0.90, 1.06) 0.5018	0.85 (0.68, 1.07) 0.1686	-0.02 (-0.05, 0.01)*0.1706	
	North America	78/ 393 (19.8)	95/ 376 (25.3)	0.93 (0.76, 1.13) 0.4534	0.83 (0.56, 1.23) 0.3546	-0.05 (-0.11, 0.00)*0.0720	
	Latin America	93/ 531 (17.5)	102/ 512 (19.9)	1.00 (0.85, 1.18) 0.9804	0.83 (0.57, 1.19) 0.3078	-0.02 (-0.07, 0.02)*0.3189	
	NYHA class at enrolment						0.3773
	II	405/2083 (19.4)	467/2165 (21.6)	0.94 (0.87, 1.02) 0.1175	0.84 (0.70, 1.00) 0.0497	-0.02 (-0.05, 0.00)*0.0858	
	III or IV	151/ 718 (21.0)	170/ 639 (26.6)	0.98 (0.88, 1.10) 0.7916	0.75 (0.55, 1.01) 0.0619	-0.06 (-0.10, -0.01)*0.0162	
	LVEF at enrolment						0.1601
	<= 49	206/ 959 (21.5)	211/ 950 (22.2)	1.03 (0.92, 1.15) 0.5831	0.92 (0.71, 1.19) 0.5135	-0.01 (-0.04, 0.03)*0.6996	
	50-59	200/1017 (19.7)	240/1009 (23.8)	0.92 (0.83, 1.03) 0.1622	0.79 (0.62, 1.02) 0.0674	-0.04 (-0.08, -0.01)*0.0244	
	>= 60	150/ 825 (18.2)	186/ 846 (22.0)	0.83 (0.68, 1.00)*0.0531	0.74 (0.55, 1.00) 0.0469	-0.04 (-0.08, 0.00)*0.0519	
	NT-proBNP at enrolment						0.9629
	<= median	266/1396 (19.1)	290/1409 (20.6)	0.96 (0.87, 1.05) 0.3381	0.87 (0.70, 1.09) 0.2155	-0.02 (-0.04, 0.01)*0.3101	
	> median	290/1405 (20.6)	347/1395 (24.9)	0.95 (0.87, 1.04) 0.3029	0.77 (0.62, 0.96) 0.0181	-0.04 (-0.07, -0.01)*0.0075	
	Type 2 Diabetes Medical History						0.2844
	Yes	259/1231 (21.0)	279/1243 (22.4)	0.98 (0.89, 1.08) 0.6940	0.92 (0.76, 1.11)*0.3967	-0.01 (-0.05, 0.02)*0.3966	
	No	297/1570 (18.9)	358/1562 (22.9)	0.92 (0.84, 1.01) 0.0649	0.78 (0.66, 0.93)*0.0060	-0.04 (-0.07, -0.01)*0.0058	
	Atrial fibrillation or flutter at enrolment ECG						0.9822
	Yes	234/1185 (19.7)	268/1188 (22.6)	0.95 (0.87, 1.05) 0.3213	0.83 (0.65, 1.06) 0.1358	-0.03 (-0.06, 0.00)*0.0933	
	No	322/1616 (19.9)	369/1617 (22.8)	0.95 (0.87, 1.03) 0.2172	0.81 (0.66, 0.99) 0.0368	-0.03 (-0.06, -0.00)*0.0446	
	BMI (kg/m2) at enrolment						0.4781
	< 30	327/1547 (21.1)	361/1541 (23.4)	0.97 (0.89, 1.05) 0.4187	0.86 (0.70, 1.06) 0.1507	-0.02 (-0.05, 0.01)*0.1264	
	>= 30	229/1253 (18.3)	276/1261 (21.9)	0.93 (0.84, 1.03) 0.1551	0.77 (0.61, 0.97) 0.0264	-0.04 (-0.07, -0.00)*0.0237	
	Baseline eGFR (mL/min/1.73m^2)						0.4615
	< 60	296/1338 (22.1)	335/1377 (24.3)	0.96 (0.88, 1.05) 0.3690	0.86 (0.70, 1.07) 0.1759	-0.02 (-0.05, 0.01)*0.1734	
	>= 60	260/1463 (17.8)	302/1427 (21.2)	0.93 (0.84, 1.03) 0.1592	0.78 (0.62, 0.97) 0.0256	-0.03 (-0.06, -0.01)*0.0213	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)	SBP at randomisation						0.3660
	<= median	297/1405 (21.1)	338/1420 (23.8)	0.97 (0.89, 1.06) 0.5101	0.85 (0.68, 1.04) 0.1204	-0.03 (-0.06, 0.00)*0.0897	
	> median	259/1396 (18.6)	299/1385 (21.6)	0.92 (0.84, 1.01) 0.0827	0.79 (0.63, 0.99) 0.0429	-0.03 (-0.06, -0.00)*0.0456	
	LVEF at enrolment 2						0.0603
	<= 49	206/ 959 (21.5)	211/ 950 (22.2)	1.03 (0.92, 1.15) 0.5831	0.92 (0.71, 1.19) 0.5135	-0.01 (-0.04, 0.03)*0.6996	
	>= 50	350/1842 (19.0)	426/1855 (23.0)	0.91 (0.84, 0.98) 0.0159	0.77 (0.64, 0.93) 0.0078	-0.04 (-0.07, -0.01)*0.0030	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0365
	Yes	101/ 280 (36.1)	100/ 281 (35.6)	1.06 (0.92, 1.22) 0.4089	1.08 (0.70, 1.67) 0.7254	0.00 (-0.07, 0.08)*0.9048	
	No	455/2521 (18.0)	537/2524 (21.3)	0.92 (0.86, 0.99) 0.0255	0.79 (0.67, 0.93) 0.0049	-0.03 (-0.05, -0.01)*0.0039	
	MRAs at baseline						0.8852
	Yes	261/1216 (21.5)	285/1210 (23.6)	0.94 (0.85, 1.04) 0.2357	0.82 (0.65, 1.03) 0.0827	-0.02 (-0.05, 0.01)*0.2177	
	No	295/1585 (18.6)	352/1595 (22.1)	0.96 (0.89, 1.05) 0.3756	0.82 (0.67, 1.02) 0.0702	-0.03 (-0.06, -0.01)*0.0154	
	ACEi+ARB at baseline						0.8094
	Yes	397/2037 (19.5)	447/2059 (21.7)	0.96 (0.89, 1.03) 0.2441	0.83 (0.69, 1.00) 0.0508	-0.02 (-0.05, 0.00)*0.0788	
	No	159/ 764 (20.8)	190/ 746 (25.5)	0.93 (0.82, 1.05) 0.2355	0.78 (0.58, 1.04) 0.0858	-0.05 (-0.09, -0.00)*0.0317	
	ARNI at baseline						0.2947
	Yes	32/ 149 (21.5)	36/ 125 (28.8)	0.82 (0.61, 1.10) 0.1798	0.51 (0.26, 1.02) 0.0554	-0.07 (-0.18, 0.03)*0.1643	
	No	524/2652 (19.8)	601/2680 (22.4)	0.96 (0.90, 1.03) 0.2216	0.84 (0.72, 0.99) 0.0369	-0.03 (-0.05, -0.00)*0.0169	
	Beta Blocker at baseline						0.7860
	Yes	449/2327 (19.3)	523/2330 (22.4)	0.94 (0.87, 1.01) 0.0978	0.83 (0.70, 0.98) 0.0271	-0.03 (-0.05, -0.01)*0.0081	
	No	107/ 474 (22.6)	114/ 475 (24.0)	0.94 (0.75, 1.19)*0.6034	0.76 (0.52, 1.11) 0.1492	-0.01 (-0.07, 0.04)*0.6032	
	Diuretics at baseline						0.4562
	Yes	497/2500 (19.9)	570/2504 (22.8)	0.94 (0.88, 1.01) 0.0713	0.81 (0.69, 0.96) 0.0126	-0.03 (-0.05, -0.01)*0.0127	
	No	59/ 301 (19.6)	67/ 301 (22.3)	0.93 (0.76, 1.14) 0.4855	0.87 (0.55, 1.39) 0.5602	-0.03 (-0.09, 0.04)*0.4226	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	254/2801 (9.1)	368/2805 (13.1)	0.70 (0.60, 0.81) <.0001	0.66 (0.55, 0.78) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Age						0.7994
	<= median	113/1394 (8.1)	173/1471 (11.8)	0.68 (0.55, 0.85) 0.0007	0.64 (0.50, 0.83) 0.0006	-0.04 (-0.06, -0.01)*0.0010	
	> median	141/1407 (10.0)	195/1334 (14.6)	0.71 (0.58, 0.86) 0.0007	0.66 (0.52, 0.83) 0.0005	-0.05 (-0.07, -0.02)*0.0003	
	Gender						0.4829
	Male	134/1630 (8.2)	199/1608 (12.4)	0.67 (0.54, 0.82) 0.0001	0.63 (0.50, 0.80) 0.0001	-0.04 (-0.06, -0.02)*<.0001	
	Female	120/1171 (10.2)	169/1197 (14.1)	0.74 (0.60, 0.92) 0.0070	0.69 (0.54, 0.89) 0.0042	-0.04 (-0.06, -0.01)*0.0039	
	Race						0.8061
	White	185/2006 (9.2)	276/2032 (13.6)	0.70 (0.59, 0.83) <.0001	0.65 (0.53, 0.79) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Black or African	7/ 64 (10.9)	8/ 70 (11.4)	0.93 (0.36, 2.40) 0.8763	0.92 (0.31, 2.73) 0.8841	-0.00 (-0.11, 0.10)*0.9282	
	Asian	55/ 555 (9.9)	72/ 551 (13.1)	0.76 (0.54, 1.05) 0.0958	0.72 (0.50, 1.05) 0.0914	-0.03 (-0.07, 0.01)*0.0994	
	Other	7/ 176 (4.0)	12/ 152 (7.9)	0.49 (0.20, 1.21) 0.1206	0.45 (0.17, 1.19) 0.1089	-0.04 (-0.09, 0.01)*0.1374	
	Geographic region						0.8533
	Asia	52/ 536 (9.7)	71/ 536 (13.2)	0.73 (0.52, 1.02) 0.0683	0.70 (0.48, 1.02) 0.0648	-0.04 (-0.07, 0.00)*0.0682	
	Europe and Saudi Arabia	118/1341 (8.8)	182/1381 (13.2)	0.69 (0.56, 0.86) 0.0008	0.64 (0.50, 0.82) 0.0005	-0.04 (-0.07, -0.02)*0.0002	
	North America	43/ 393 (10.9)	52/ 376 (13.8)	0.79 (0.54, 1.15) 0.2125	0.75 (0.49, 1.17) 0.2053	-0.03 (-0.08, 0.02)*0.2243	
	Latin America	41/ 531 (7.7)	63/ 512 (12.3)	0.63 (0.43, 0.91) 0.0134	0.58 (0.38, 0.89) 0.0116	-0.05 (-0.08, -0.01)*0.0136	
	NYHA class at enrolment						0.0493
	II	201/2083 (9.6)	277/2165 (12.8)	0.75 (0.63, 0.89) 0.0009	0.71 (0.59, 0.87) 0.0007	-0.03 (-0.05, -0.01)*0.0011	
	III or IV	53/ 718 (7.4)	91/ 639 (14.2)	0.53 (0.39, 0.72) <.0001	0.48 (0.33, 0.69) <.0001	-0.07 (-0.10, -0.04)*<.0001	
	LVEF at enrolment						0.9332
	<= 49	76/ 959 (7.9)	102/ 950 (10.7)	0.73 (0.55, 0.97) 0.0290	0.70 (0.51, 0.96) 0.0267	-0.03 (-0.05, -0.00)*0.0345	
	50-59	97/1017 (9.5)	138/1009 (13.7)	0.70 (0.55, 0.89) 0.0039	0.65 (0.49, 0.86) 0.0027	-0.04 (-0.07, -0.01)*0.0036	
	>= 60	81/ 825 (9.8)	128/ 846 (15.1)	0.68 (0.52, 0.88) 0.0031	0.63 (0.47, 0.85) 0.0026	-0.05 (-0.08, -0.02)*0.0010	
	NT-proBNP at enrolment						0.4778
	<= median	131/1396 (9.4)	180/1409 (12.8)	0.74 (0.60, 0.91) 0.0044	0.70 (0.55, 0.89) 0.0037	-0.03 (-0.06, -0.01)*0.0042	
	> median	123/1405 (8.8)	188/1395 (13.5)	0.67 (0.54, 0.82) 0.0002	0.61 (0.48, 0.78) <.0001	-0.05 (-0.07, -0.02)*<.0001	
	Type 2 Diabetes Medical History						0.2721
	Yes	107/1231 (8.7)	173/1243 (13.9)	0.64 (0.51, 0.80) <.0001	0.59 (0.46, 0.76)*<.0001	-0.05 (-0.08, -0.03)*<.0001	
	No	147/1570 (9.4)	195/1562 (12.5)	0.75 (0.62, 0.92) 0.0054	0.72 (0.58, 0.91)*0.0052	-0.03 (-0.05, -0.01)*0.0051	
	Atrial fibrillation or flutter at enrolment ECG						0.4070
	Yes	109/1185 (9.2)	168/1188 (14.1)	0.65 (0.52, 0.81) 0.0002	0.60 (0.46, 0.78) 0.0001	-0.05 (-0.08, -0.02)*0.0002	
	No	145/1616 (9.0)	200/1617 (12.4)	0.74 (0.60, 0.90) 0.0029	0.70 (0.56, 0.88) 0.0022	-0.03 (-0.06, -0.01)*0.0017	
	BMI (kg/m2) at enrolment						0.6178
	< 30	141/1547 (9.1)	195/1541 (12.7)	0.73 (0.59, 0.89) 0.0019	0.69 (0.54, 0.87) 0.0015	-0.04 (-0.06, -0.01)*0.0016	
	>= 30	113/1253 (9.0)	173/1261 (13.7)	0.67 (0.54, 0.84) 0.0004	0.62 (0.48, 0.80) 0.0003	-0.05 (-0.07, -0.02)*0.0002	
	Baseline eGFR (mL/min/1.73m^2)						0.8764
	< 60	139/1338 (10.4)	205/1377 (14.9)	0.71 (0.58, 0.87) 0.0007	0.66 (0.52, 0.83) 0.0005	-0.04 (-0.07, -0.02)*0.0004	
	>= 60	115/1463 (7.9)	162/1427 (11.4)	0.70 (0.56, 0.87) 0.0016	0.66 (0.51, 0.85) 0.0014	-0.03 (-0.06, -0.01)*0.0014	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF)
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.8496
	<= median	132/1405 (9.4)	201/1420 (14.2)	0.69 (0.56, 0.85) 0.0004	0.64 (0.51, 0.81) 0.0002	-0.05 (-0.07, -0.02)*<.0001	
	> median	122/1396 (8.7)	167/1385 (12.1)	0.71 (0.57, 0.88) 0.0021	0.67 (0.52, 0.86) 0.0019	-0.03 (-0.06, -0.01)*0.0041	
	LVEF at enrolment 2						0.7431
	<= 49	76/ 959 (7.9)	102/ 950 (10.7)	0.73 (0.55, 0.97) 0.0290	0.70 (0.51, 0.96) 0.0267	-0.03 (-0.05, -0.00)*0.0345	
	>= 50	178/1842 (9.7)	266/1855 (14.3)	0.69 (0.58, 0.82) <.0001	0.64 (0.52, 0.79) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2362
	Yes	16/ 280 (5.7)	30/ 281 (10.7)	0.54 (0.30, 0.96)*0.0358	0.42 (0.22, 0.81) 0.0101	-0.05 (-0.09, -0.00)*0.0314	
	No	238/2521 (9.4)	338/2524 (13.4)	0.72 (0.61, 0.84) <.0001	0.68 (0.57, 0.81) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	MRAs at baseline						0.1833
	Yes	98/1216 (8.1)	160/1210 (13.2)	0.62 (0.49, 0.78) <.0001	0.57 (0.44, 0.75) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	No	156/1585 (9.8)	208/1595 (13.0)	0.76 (0.63, 0.92) 0.0054	0.72 (0.58, 0.90) 0.0044	-0.03 (-0.05, -0.01)*0.0046	
	ACEi+ARB at baseline						0.0126
	Yes	163/2037 (8.0)	273/2059 (13.3)	0.62 (0.51, 0.74) <.0001	0.57 (0.46, 0.70) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	No	91/ 764 (11.9)	95/ 746 (12.7)	0.93 (0.71, 1.22) 0.6079	0.92 (0.67, 1.25) 0.5795	-0.01 (-0.04, 0.02)*0.6264	
	ARNI at baseline						0.3695
	Yes	14/ 149 (9.4)	11/ 125 (8.8)	1.01 (0.47, 2.14) 0.9867	1.03 (0.44, 2.40) 0.9544	0.01 (-0.06, 0.07)*0.8642	
	No	240/2652 (9.0)	357/2680 (13.3)	0.69 (0.59, 0.81) <.0001	0.65 (0.54, 0.77) <.0001	-0.04 (-0.06, -0.03)*<.0001	
	Beta Blocker at baseline						0.5481
	Yes	212/2327 (9.1)	304/2330 (13.0)	0.71 (0.61, 0.84) <.0001	0.67 (0.56, 0.81) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	42/ 474 (8.9)	64/ 475 (13.5)	0.63 (0.44, 0.91) 0.0143	0.59 (0.39, 0.90) 0.0132	-0.05 (-0.09, -0.01)*0.0237	
	Diuretics at baseline						0.7569
	Yes	230/2500 (9.2)	333/2504 (13.3)	0.69 (0.59, 0.81) <.0001	0.65 (0.54, 0.78) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	24/ 301 (8.0)	35/ 301 (11.6)	0.75 (0.46, 1.22) 0.2499	0.70 (0.40, 1.22) 0.2090	-0.04 (-0.08, 0.01)*0.1309	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	245/2801 (8.7)	337/2805 (12.0)	0.74 (0.63, 0.86) <.0001	0.70 (0.59, 0.84) <.0001	-0.03 (-0.05, -0.02)*<.0001	
	Age						0.7871
	<= median	111/1394 (8.0)	155/1471 (10.5)	0.75 (0.60, 0.94) 0.0140	0.72 (0.56, 0.93) 0.0130	-0.03 (-0.05, -0.00)*0.0171	
	> median	134/1407 (9.5)	182/1334 (13.6)	0.72 (0.58, 0.89) 0.0019	0.68 (0.54, 0.87) 0.0017	-0.04 (-0.07, -0.02)*0.0008	
	Gender						0.1379
	Male	132/1630 (8.1)	196/1608 (12.2)	0.67 (0.54, 0.82) 0.0001	0.63 (0.50, 0.80) 0.0001	-0.04 (-0.06, -0.02)*0.0001	
	Female	113/1171 (9.6)	141/1197 (11.8)	0.84 (0.67, 1.06) 0.1494	0.81 (0.62, 1.05) 0.1166	-0.02 (-0.05, 0.00)*0.0936	
	Race						0.6532
	White	181/2006 (9.0)	251/2032 (12.4)	0.75 (0.63, 0.89) 0.0013	0.71 (0.58, 0.87) 0.0012	-0.03 (-0.05, -0.01)*0.0006	
	Black or African	8/ 64 (12.5)	10/ 70 (14.3)	0.87 (0.37, 2.06) 0.7552	0.84 (0.31, 2.29) 0.7292	-0.02 (-0.13, 0.10)*0.7614	
	Asian	50/ 555 (9.0)	64/ 551 (11.6)	0.78 (0.55, 1.11) 0.1657	0.76 (0.51, 1.12) 0.1655	-0.03 (-0.06, 0.01) 0.1654	
	Other	6/ 176 (3.4)	12/ 152 (7.9)	0.41 (0.16, 1.05) 0.0619	0.37 (0.13, 1.04) 0.0586	-0.04 (-0.10, 0.01)*0.0821	
	Geographic region						0.7191
	Asia	46/ 536 (8.6)	63/ 536 (11.8)	0.73 (0.51, 1.05) 0.0921	0.71 (0.47, 1.06) 0.0917	-0.03 (-0.07, 0.01) 0.0943	
	Europe and Saudi Arabia	122/1341 (9.1)	166/1381 (12.0)	0.79 (0.64, 0.98) 0.0319	0.75 (0.58, 0.96) 0.0231	-0.03 (-0.05, -0.01)*0.0129	
	North America	41/ 393 (10.4)	51/ 376 (13.6)	0.76 (0.52, 1.12) 0.1681	0.74 (0.48, 1.15) 0.1863	-0.03 (-0.08, 0.01)*0.1817	
	Latin America	36/ 531 (6.8)	57/ 512 (11.1)	0.60 (0.41, 0.89) 0.0109	0.56 (0.36, 0.88) 0.0115	-0.04 (-0.08, -0.01)*0.0138	
	NYHA class at enrolment						0.5022
	II	187/2083 (9.0)	258/2165 (11.9)	0.75 (0.63, 0.90) 0.0016	0.72 (0.59, 0.88) 0.0014	-0.03 (-0.05, -0.01)*0.0017	
	III or IV	58/ 718 (8.1)	79/ 639 (12.4)	0.66 (0.49, 0.91) 0.0106	0.63 (0.44, 0.91) 0.0133	-0.04 (-0.08, -0.01)*0.0095	
	LVEF at enrolment						0.5740
	<= 49	77/ 959 (8.0)	98/ 950 (10.3)	0.78 (0.58, 1.03) 0.0782	0.75 (0.54, 1.02) 0.0681	-0.02 (-0.05, 0.00)*0.0834	
	50-59	99/1017 (9.7)	126/1009 (12.5)	0.78 (0.61, 1.00) 0.0519	0.75 (0.57, 1.00) 0.0499	-0.03 (-0.05, -0.00)*0.0485	
	>= 60	69/ 825 (8.4)	113/ 846 (13.4)	0.65 (0.49, 0.86) 0.0025	0.61 (0.45, 0.84) 0.0027	-0.05 (-0.08, -0.02)*0.0010	
	NT-proBNP at enrolment						0.5009
	<= median	128/1396 (9.2)	167/1409 (11.9)	0.78 (0.62, 0.96) 0.0211	0.75 (0.58, 0.95) 0.0195	-0.03 (-0.05, -0.00)*0.0204	
	> median	117/1405 (8.3)	170/1395 (12.2)	0.70 (0.56, 0.87) 0.0015	0.66 (0.52, 0.85) 0.0014	-0.04 (-0.06, -0.02)*0.0007	
	Type 2 Diabetes Medical History						0.2503
	Yes	102/1231 (8.3)	157/1243 (12.6)	0.66 (0.53, 0.84) 0.0006	0.62 (0.48, 0.81)*0.0005	-0.04 (-0.07, -0.02)*0.0004	
	No	143/1570 (9.1)	180/1562 (11.5)	0.80 (0.65, 0.98) 0.0318	0.77 (0.61, 0.97)*0.0266	-0.02 (-0.05, -0.00)*0.0262	
	Atrial fibrillation or flutter at enrolment ECG						0.6890
	Yes	103/1185 (8.7)	146/1188 (12.3)	0.71 (0.56, 0.90) 0.0044	0.67 (0.51, 0.88) 0.0040	-0.04 (-0.06, -0.01)*0.0042	
	No	142/1616 (8.8)	191/1617 (11.8)	0.76 (0.62, 0.93) 0.0072	0.73 (0.58, 0.91) 0.0065	-0.03 (-0.05, -0.01)*0.0046	
	BMI (kg/m2) at enrolment						0.3202
	< 30	143/1547 (9.2)	182/1541 (11.8)	0.79 (0.64, 0.97) 0.0240	0.76 (0.60, 0.96) 0.0230	-0.03 (-0.05, -0.00)*0.0200	
	>= 30	102/1253 (8.1)	155/1261 (12.3)	0.67 (0.53, 0.85) 0.0010	0.64 (0.49, 0.83) 0.0009	-0.04 (-0.07, -0.02)*0.0006	
	Baseline eGFR (mL/min/1.73m^2)						0.9598
	< 60	127/1338 (9.5)	180/1377 (13.1)	0.73 (0.59, 0.91) 0.0041	0.70 (0.55, 0.89) 0.0040	-0.04 (-0.06, -0.01)*0.0031	
	>= 60	118/1463 (8.1)	157/1427 (11.0)	0.74 (0.59, 0.93) 0.0093	0.71 (0.55, 0.92) 0.0084	-0.03 (-0.05, -0.01)*0.0072	

N displays number of patients in the analysis, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.5739
	<= median	120/1405 (8.5)	179/1420 (12.6)	0.70 (0.56, 0.87) 0.0015	0.67 (0.52, 0.85) 0.0013	-0.04 (-0.06, -0.02)*0.0004	
	> median	125/1396 (9.0)	158/1385 (11.4)	0.77 (0.62, 0.96) 0.0185	0.74 (0.57, 0.95) 0.0177	-0.02 (-0.05, -0.00)*0.0323	
	LVEF at enrolment 2						0.7141
	<= 49	77/ 959 (8.0)	98/ 950 (10.3)	0.78 (0.58, 1.03) 0.0782	0.75 (0.54, 1.02) 0.0681	-0.02 (-0.05, 0.00)*0.0834	
	>= 50	168/1842 (9.1)	239/1855 (12.9)	0.72 (0.60, 0.87) 0.0006	0.69 (0.56, 0.85) 0.0006	-0.04 (-0.06, -0.02)*0.0002	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3884
	Yes	17/ 280 (6.1)	28/ 281 (10.0)	0.61 (0.34, 1.09)*0.0938	0.51 (0.26, 0.97) 0.0401	-0.04 (-0.08, 0.01)*0.0887	
	No	228/2521 (9.0)	309/2524 (12.2)	0.75 (0.64, 0.88) 0.0005	0.72 (0.60, 0.86) 0.0004	-0.03 (-0.05, -0.01)*0.0002	
	MRAs at baseline						0.7188
	Yes	108/1216 (8.9)	143/1210 (11.8)	0.76 (0.60, 0.96) 0.0220	0.73 (0.56, 0.95) 0.0205	-0.03 (-0.05, -0.01)*0.0175	
	No	137/1585 (8.6)	194/1595 (12.2)	0.72 (0.59, 0.88) 0.0016	0.68 (0.54, 0.86) 0.0014	-0.04 (-0.06, -0.01)*0.0011	
	ACEi+ARB at baseline						0.2735
	Yes	166/2037 (8.1)	245/2059 (11.9)	0.70 (0.58, 0.84) 0.0001	0.66 (0.54, 0.81) 0.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	79/ 764 (10.3)	92/ 746 (12.3)	0.84 (0.63, 1.11) 0.2282	0.82 (0.59, 1.13) 0.2176	-0.02 (-0.05, 0.01)*0.2222	
	ARNI at baseline						0.2978
	Yes	14/ 149 (9.4)	10/ 125 (8.0)	1.16 (0.52, 2.55) 0.7206	1.17 (0.49, 2.78) 0.7193	0.01 (-0.06, 0.08) 0.7184	
	No	231/2652 (8.7)	327/2680 (12.2)	0.73 (0.62, 0.85) <.0001	0.69 (0.58, 0.83) <.0001	-0.03 (-0.05, -0.02)*<.0001	
	Beta Blocker at baseline						0.6698
	Yes	203/2327 (8.7)	278/2330 (11.9)	0.75 (0.63, 0.89) 0.0008	0.71 (0.59, 0.87) 0.0006	-0.03 (-0.05, -0.01)*0.0003	
	No	42/ 474 (8.9)	59/ 475 (12.4)	0.69 (0.47, 0.99) 0.0469	0.65 (0.43, 1.00) 0.0496	-0.04 (-0.07, 0.00)*0.0748	
	Diuretics at baseline						0.6781
	Yes	224/2500 (9.0)	310/2504 (12.4)	0.73 (0.62, 0.85) 0.0001	0.69 (0.58, 0.83) <.0001	-0.03 (-0.05, -0.02)*<.0001	
	No	21/ 301 (7.0)	27/ 301 (9.0)	0.81 (0.47, 1.40) 0.4604	0.79 (0.44, 1.44) 0.4474	-0.02 (-0.06, 0.02)*0.3663	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Overall Summary Score (LOCF)							
	Overall	234/2801 (8.4)	282/2805 (10.1)	0.84 (0.71, 0.99) 0.0388	0.82 (0.68, 0.98) 0.0334	-0.02 (-0.03, -0.00)*0.0277	
	Age						0.2102
	<= median	108/1394 (7.7)	121/1471 (8.2)	0.94 (0.73, 1.20) 0.6271	0.93 (0.71, 1.22) 0.5919	-0.00 (-0.02, 0.02)*0.6368	
	> median	126/1407 (9.0)	161/1334 (12.1)	0.76 (0.61, 0.95) 0.0148	0.73 (0.57, 0.94) 0.0136	-0.03 (-0.05, -0.01)*0.0079	
	Gender						0.3535
	Male	133/1630 (8.2)	167/1608 (10.4)	0.79 (0.64, 0.98) 0.0322	0.77 (0.60, 0.98) 0.0327	-0.02 (-0.04, -0.00)*0.0289	
	Female	101/1171 (8.6)	115/1197 (9.6)	0.93 (0.72, 1.19) 0.5443	0.90 (0.68, 1.19) 0.4583	-0.01 (-0.03, 0.01)*0.4062	
	Race						0.6409
	White	167/2006 (8.3)	217/2032 (10.7)	0.80 (0.66, 0.97) 0.0216	0.77 (0.62, 0.96) 0.0183	-0.02 (-0.04, -0.01)*0.0107	
	Black or African	6/ 64 (9.4)	8/ 70 (11.4)	0.79 (0.29, 2.12) 0.6377	0.77 (0.25, 2.39) 0.6512	-0.02 (-0.12, 0.08)*0.6966	
	Asian	51/ 555 (9.2)	50/ 551 (9.1)	1.02 (0.70, 1.48) 0.9274	1.02 (0.68, 1.53) 0.9351	-0.00 (-0.03, 0.03) 0.9931	
	Other	10/ 176 (5.7)	7/ 152 (4.6)	1.12 (0.44, 2.84) 0.8053	1.15 (0.42, 3.17) 0.7871	0.01 (-0.04, 0.06)*0.6586	
	Geographic region						0.5644
	Asia	47/ 536 (8.8)	49/ 536 (9.1)	0.96 (0.66, 1.41) 0.8488	0.96 (0.63, 1.46) 0.8406	-0.01 (-0.04, 0.03) 0.7716	
	Europe and Saudi Arabia	117/1341 (8.7)	139/1381 (10.1)	0.91 (0.72, 1.14) 0.3957	0.88 (0.68, 1.15) 0.3501	-0.01 (-0.04, 0.01)*0.2305	
	North America	35/ 393 (8.9)	44/ 376 (11.7)	0.76 (0.50, 1.15) 0.1979	0.73 (0.46, 1.17) 0.1932	-0.03 (-0.07, 0.02)*0.2024	
	Latin America	35/ 531 (6.6)	50/ 512 (9.8)	0.67 (0.45, 1.01) 0.0556	0.64 (0.41, 1.01) 0.0578	-0.03 (-0.07, 0.00)*0.0614	
	NYHA class at enrolment						0.6115
	II	174/2083 (8.4)	211/2165 (9.7)	0.86 (0.71, 1.04) 0.1087	0.84 (0.68, 1.03) 0.0979	-0.01 (-0.03, 0.00)*0.1134	
	III or IV	60/ 718 (8.4)	71/ 639 (11.1)	0.75 (0.54, 1.04)*0.0875	0.75 (0.51, 1.08) 0.1248	-0.03 (-0.06, 0.00)*0.0883	
	LVEF at enrolment						0.2879
	<= 49	77/ 959 (8.0)	79/ 950 (8.3)	0.95 (0.71, 1.29) 0.7588	0.94 (0.67, 1.31) 0.7068	-0.00 (-0.03, 0.02)*0.8192	
	50-59	92/1017 (9.0)	103/1009 (10.2)	0.90 (0.69, 1.17) 0.4201	0.88 (0.65, 1.19) 0.4075	-0.01 (-0.04, 0.01)*0.3753	
	>= 60	65/ 825 (7.9)	100/ 846 (11.8)	0.69 (0.52, 0.93) 0.0146	0.66 (0.47, 0.92) 0.0133	-0.04 (-0.07, -0.01)*0.0067	
	NT-proBNP at enrolment						0.8318
	<= median	118/1396 (8.5)	140/1409 (9.9)	0.86 (0.68, 1.08) 0.1876	0.84 (0.65, 1.08) 0.1721	-0.01 (-0.04, 0.01)*0.1738	
	> median	116/1405 (8.3)	142/1395 (10.2)	0.83 (0.66, 1.04) 0.1105	0.81 (0.62, 1.05) 0.1043	-0.02 (-0.04, 0.00)*0.0785	
	Type 2 Diabetes Medical History						0.0165
	Yes	93/1231 (7.6)	142/1243 (11.4)	0.67 (0.53, 0.86) 0.0018	0.63 (0.48, 0.83)*0.0011	-0.04 (-0.06, -0.02)*0.0010	
	No	141/1570 (9.0)	140/1562 (9.0)	1.01 (0.81, 1.26) 0.9202	1.00 (0.78, 1.28)*0.9859	0.00 (-0.02, 0.02)*0.9859	
	Atrial fibrillation or flutter at enrolment ECG						0.7043
	Yes	106/1185 (8.9)	123/1188 (10.4)	0.87 (0.68, 1.11) 0.2682	0.85 (0.64, 1.12) 0.2540	-0.01 (-0.04, 0.01)*0.2452	
	No	128/1616 (7.9)	159/1617 (9.8)	0.82 (0.65, 1.02) 0.0728	0.79 (0.62, 1.01) 0.0656	-0.02 (-0.04, 0.00)*0.0558	
	BMI (kg/m2) at enrolment						0.4088
	< 30	135/1547 (8.7)	152/1541 (9.9)	0.90 (0.72, 1.12) 0.3248	0.88 (0.69, 1.13) 0.3098	-0.01 (-0.03, 0.01)*0.2765	
	>= 30	99/1253 (7.9)	130/1261 (10.3)	0.78 (0.61, 1.00) 0.0488	0.75 (0.57, 0.99) 0.0396	-0.02 (-0.05, -0.00)*0.0357	
	Baseline eGFR (mL/min/1.73m^2)						0.3002
	< 60	114/1338 (8.5)	153/1377 (11.1)	0.77 (0.62, 0.97) 0.0266	0.75 (0.58, 0.96) 0.0255	-0.03 (-0.05, -0.00)*0.0231	
	>= 60	120/1463 (8.2)	129/1427 (9.0)	0.92 (0.73, 1.17) 0.4989	0.91 (0.70, 1.18) 0.4641	-0.01 (-0.03, 0.01)*0.4226	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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Overall Summary Score (LOCF)	SBP at randomisation						0.9300
	<= median	120/1405 (8.5)	148/1420 (10.4)	0.85 (0.68, 1.07) 0.1600	0.83 (0.64, 1.07) 0.1479	-0.02 (-0.04, 0.00)*0.0876	
	> median	114/1396 (8.2)	134/1385 (9.7)	0.84 (0.66, 1.06) 0.1356	0.81 (0.62, 1.06) 0.1214	-0.02 (-0.04, 0.01)*0.1627	
	LVEF at enrolment 2						0.3403
	<= 49	77/ 959 (8.0)	79/ 950 (8.3)	0.95 (0.71, 1.29) 0.7588	0.94 (0.67, 1.31) 0.7068	-0.00 (-0.03, 0.02)*0.8192	
	>= 50	157/1842 (8.5)	203/1855 (10.9)	0.80 (0.66, 0.97) 0.0252	0.77 (0.62, 0.96) 0.0228	-0.02 (-0.04, -0.01)*0.0130	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8560
	Yes	19/ 280 (6.8)	21/ 281 (7.5)	0.91 (0.50, 1.65)*0.7518	0.84 (0.43, 1.62) 0.6005	-0.01 (-0.05, 0.04)*0.7516	
	No	215/2521 (8.5)	261/2524 (10.3)	0.84 (0.71, 0.99) 0.0418	0.82 (0.67, 0.99) 0.0361	-0.02 (-0.03, -0.00)*0.0276	
	MRAs at baseline						0.6199
	Yes	102/1216 (8.4)	116/1210 (9.6)	0.88 (0.68, 1.13) 0.3224	0.86 (0.65, 1.14) 0.3061	-0.01 (-0.03, 0.01)*0.3020	
	No	132/1585 (8.3)	166/1595 (10.4)	0.81 (0.66, 1.01) 0.0590	0.79 (0.62, 1.00) 0.0528	-0.02 (-0.04, -0.00)*0.0440	
	ACEi+ARB at baseline						0.3092
	Yes	158/2037 (7.8)	204/2059 (9.9)	0.80 (0.65, 0.97) 0.0224	0.77 (0.62, 0.96) 0.0191	-0.02 (-0.04, -0.00)*0.0152	
	No	76/ 764 (9.9)	78/ 746 (10.5)	0.96 (0.71, 1.30) 0.7985	0.95 (0.68, 1.33) 0.7630	-0.01 (-0.04, 0.03)*0.7443	
	ARNI at baseline						0.3258
	Yes	14/ 149 (9.4)	9/ 125 (7.2)	1.28 (0.57, 2.91) 0.5487	1.31 (0.54, 3.18) 0.5505	0.02 (-0.04, 0.09)*0.5090	
	No	220/2652 (8.3)	273/2680 (10.2)	0.83 (0.70, 0.98) 0.0279	0.80 (0.67, 0.97) 0.0234	-0.02 (-0.03, -0.00)*0.0170	
	Beta Blocker at baseline						0.9157
	Yes	198/2327 (8.5)	240/2330 (10.3)	0.85 (0.71, 1.01) 0.0655	0.82 (0.67, 1.00) 0.0556	-0.02 (-0.03, -0.00)*0.0361	
	No	36/ 474 (7.6)	42/ 475 (8.8)	0.83 (0.54, 1.27) 0.3830	0.81 (0.51, 1.30) 0.3872	-0.01 (-0.05, 0.02)*0.4841	
	Diuretics at baseline						0.0491
	Yes	209/2500 (8.4)	264/2504 (10.5)	0.80 (0.67, 0.95) 0.0103	0.77 (0.64, 0.94) 0.0085	-0.02 (-0.04, -0.01)*0.0083	
	No	25/ 301 (8.3)	18/ 301 (6.0)	1.45 (0.81, 2.60) 0.2056	1.50 (0.80, 2.83) 0.2077	0.02 (-0.02, 0.06)*0.2675	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	386/2750 (14.0)	445/2758 (16.1)	0.88 (0.78, 0.99) 0.0374	0.86 (0.74, 1.00) 0.0467	-0.02 (-0.04, -0.00)*0.0295	
	Age						0.2596
	<= median	168/1382 (12.2)	217/1456 (14.9)	0.81 (0.67, 0.97) 0.0257	0.78 (0.63, 0.97) 0.0267	-0.03 (-0.05, -0.00)*0.0321	
	> median	218/1368 (15.9)	228/1302 (17.5)	0.93 (0.79, 1.10) 0.4051	0.93 (0.75, 1.14) 0.4815	-0.02 (-0.04, 0.01)*0.2755	
	Gender						0.6994
	Male	225/1611 (14.0)	245/1583 (15.5)	0.90 (0.77, 1.06) 0.2217	0.89 (0.73, 1.09) 0.2585	-0.02 (-0.04, 0.01)*0.2284	
	Female	161/1139 (14.1)	200/1175 (17.0)	0.86 (0.72, 1.03) 0.1089	0.83 (0.66, 1.05) 0.1125	-0.03 (-0.06, 0.00)*0.0553	
	Race						0.1681
	White	292/1970 (14.8)	341/1998 (17.1)	0.88 (0.77, 1.01) 0.0735	0.86 (0.72, 1.03) 0.0974	-0.02 (-0.05, 0.00)*0.0533	
	Black or African	14/ 63 (22.2)	10/ 66 (15.2)	1.39 (0.68, 2.86) 0.3684	1.56 (0.62, 3.91) 0.3417	0.07 (-0.06, 0.20)*0.3019	
	Asian	60/ 548 (10.9)	83/ 546 (15.2)	0.73 (0.53, 0.99) 0.0460	0.69 (0.49, 0.99) 0.0442	-0.04 (-0.08, -0.00) 0.0344	
	Other	20/ 169 (11.8)	11/ 148 (7.4)	1.59 (0.79, 3.21)*0.1940	1.60 (0.71, 3.62) 0.2613	0.04 (-0.02, 0.11)*0.1809	
	Geographic region						0.3249
	Asia	56/ 530 (10.6)	79/ 531 (14.9)	0.72 (0.52, 0.99) 0.0437	0.68 (0.47, 0.99) 0.0417	-0.04 (-0.08, -0.00) 0.0324	
	Europe and Saudi Arabia	199/1323 (15.0)	219/1360 (16.1)	0.94 (0.80, 1.12) 0.5086	0.95 (0.77, 1.18) 0.6447	-0.01 (-0.04, 0.02)*0.4483	
	North America	59/ 386 (15.3)	74/ 362 (20.4)	0.75 (0.55, 1.01) 0.0585	0.70 (0.48, 1.04) 0.0745	-0.05 (-0.11, 0.00)*0.0656	
	Latin America	72/ 511 (14.1)	73/ 505 (14.5)	0.97 (0.72, 1.29) 0.8170	0.95 (0.66, 1.37) 0.7973	-0.00 (-0.05, 0.04)*0.8678	
	NYHA class at enrolment						0.7168
	II	280/2046 (13.7)	333/2136 (15.6)	0.88 (0.76, 1.01) 0.0779	0.86 (0.72, 1.02) 0.0838	-0.02 (-0.04, 0.00)*0.0812	
	III or IV	106/ 704 (15.1)	112/ 621 (18.0)	0.83 (0.66, 1.04) 0.1097	0.82 (0.60, 1.11) 0.1991	-0.03 (-0.07, 0.01)*0.1460	
	LVEF at enrolment						0.2015
	<= 49	139/ 944 (14.7)	133/ 939 (14.2)	1.01 (0.81, 1.26) 0.9172	1.02 (0.79, 1.32) 0.8841	0.01 (-0.03, 0.04)*0.7293	
	50-59	143/1001 (14.3)	163/ 988 (16.5)	0.88 (0.72, 1.08) 0.2200	0.87 (0.68, 1.11) 0.2650	-0.02 (-0.05, 0.01)*0.1715	
	>= 60	104/ 805 (12.9)	149/ 831 (17.9)	0.75 (0.60, 0.94) 0.0143	0.71 (0.54, 0.93) 0.0140	-0.05 (-0.08, -0.02)*0.0049	
	NT-proBNP at enrolment						0.8511
	<= median	181/1371 (13.2)	213/1389 (15.3)	0.87 (0.72, 1.04) 0.1169	0.84 (0.68, 1.04) 0.1151	-0.02 (-0.05, 0.00)*0.1090	
	> median	205/1379 (14.9)	232/1368 (17.0)	0.89 (0.75, 1.05) 0.1568	0.88 (0.71, 1.08) 0.2125	-0.02 (-0.05, 0.01)*0.1336	
	Type 2 Diabetes Medical History						0.5915
	Yes	174/1213 (14.3)	205/1219 (16.8)	0.85 (0.71, 1.02) 0.0761	0.83 (0.66, 1.03)*0.0931	-0.02 (-0.05, 0.00)*0.0925	
	No	212/1537 (13.8)	240/1539 (15.6)	0.91 (0.77, 1.07) 0.2551	0.87 (0.71, 1.06)*0.1585	-0.02 (-0.04, 0.01)*0.1581	
	Atrial fibrillation or flutter at enrolment ECG						0.5216
	Yes	175/1164 (15.0)	190/1164 (16.3)	0.92 (0.76, 1.10) 0.3461	0.91 (0.73, 1.15) 0.4316	-0.01 (-0.04, 0.02)*0.3925	
	No	211/1586 (13.3)	255/1594 (16.0)	0.84 (0.72, 1.00) 0.0463	0.82 (0.67, 1.00) 0.0482	-0.03 (-0.05, -0.00)*0.0316	
	BMI (kg/m2) at enrolment						0.9179
	< 30	204/1520 (13.4)	236/1517 (15.6)	0.87 (0.74, 1.04) 0.1180	0.85 (0.69, 1.04) 0.1121	-0.02 (-0.05, 0.00)*0.0944	
	>= 30	182/1229 (14.8)	209/1238 (16.9)	0.88 (0.74, 1.05) 0.1626	0.88 (0.70, 1.10) 0.2606	-0.02 (-0.05, 0.01)*0.1583	
	Baseline eGFR (mL/min/1.73m^2)						0.8196
	< 60	194/1307 (14.8)	224/1345 (16.7)	0.89 (0.75, 1.06) 0.1981	0.88 (0.71, 1.09) 0.2519	-0.02 (-0.05, 0.01)*0.2002	
	>= 60	192/1443 (13.3)	221/1412 (15.7)	0.87 (0.73, 1.03) 0.1079	0.84 (0.68, 1.04) 0.1079	-0.02 (-0.05, 0.00)*0.0749	

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Physical Limitation (LOCF)	SBP at randomisation						0.9559
	<= median	192/1376 (14.0)	230/1395 (16.5)	0.88 (0.74, 1.04) 0.1394	0.86 (0.70, 1.06) 0.1606	-0.03 (-0.05, 0.00)*0.0631	
	> median	194/1374 (14.1)	215/1363 (15.8)	0.87 (0.73, 1.04) 0.1228	0.85 (0.69, 1.05) 0.1378	-0.02 (-0.04, 0.01)*0.2247	
	LVEF at enrolment 2						0.1334
	<= 49	139/ 944 (14.7)	133/ 939 (14.2)	1.01 (0.81, 1.26) 0.9172	1.02 (0.79, 1.32) 0.8841	0.01 (-0.03, 0.04)*0.7293	
	>= 50	247/1806 (13.7)	312/1819 (17.2)	0.82 (0.71, 0.96) 0.0109	0.79 (0.66, 0.95) 0.0133	-0.03 (-0.06, -0.01)*0.0037	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2800
	Yes	46/ 270 (17.0)	43/ 272 (15.8)	1.05 (0.73, 1.53) 0.7788	1.08 (0.67, 1.72) 0.7615	0.01 (-0.05, 0.07)*0.6995	
	No	340/2480 (13.7)	402/2486 (16.2)	0.86 (0.75, 0.98) 0.0210	0.83 (0.71, 0.98) 0.0261	-0.02 (-0.04, -0.00)*0.0149	
	MRAs at baseline						0.1556
	Yes	156/1191 (13.1)	196/1193 (16.4)	0.79 (0.65, 0.96) 0.0162	0.76 (0.61, 0.96) 0.0220	-0.03 (-0.06, -0.00)*0.0217	
	No	230/1559 (14.8)	249/1565 (15.9)	0.95 (0.81, 1.11) 0.5143	0.94 (0.77, 1.14) 0.5241	-0.01 (-0.04, 0.01)*0.3692	
	ACEi+ARB at baseline						0.2843
	Yes	274/1999 (13.7)	334/2028 (16.5)	0.84 (0.73, 0.97) 0.0205	0.82 (0.69, 0.98) 0.0262	-0.03 (-0.05, -0.01)*0.0142	
	No	112/ 751 (14.9)	111/ 730 (15.2)	0.98 (0.77, 1.24) 0.8578	0.98 (0.73, 1.31) 0.8861	-0.00 (-0.04, 0.03)*0.8752	
	ARNI at baseline						0.6687
	Yes	20/ 147 (13.6)	16/ 122 (13.1)	0.99 (0.53, 1.84) 0.9742	0.99 (0.48, 2.03) 0.9746	-0.00 (-0.08, 0.08) 0.9588	
	No	366/2603 (14.1)	429/2636 (16.3)	0.88 (0.77, 0.99) 0.0379	0.86 (0.73, 1.00) 0.0487	-0.02 (-0.04, -0.00)*0.0254	
	Beta Blocker at baseline						0.7849
	Yes	320/2289 (14.0)	374/2293 (16.3)	0.87 (0.76, 1.00) 0.0440	0.85 (0.72, 1.00) 0.0505	-0.02 (-0.04, -0.00)*0.0277	
	No	66/ 461 (14.3)	71/ 465 (15.3)	0.92 (0.68, 1.25) 0.5931	0.91 (0.63, 1.32) 0.6293	-0.01 (-0.06, 0.04)*0.6832	
	Diuretics at baseline						0.8620
	Yes	355/2458 (14.4)	411/2463 (16.7)	0.88 (0.77, 0.99) 0.0416	0.85 (0.73, 1.00) 0.0490	-0.02 (-0.04, -0.00)*0.0298	
	No	31/ 292 (10.6)	34/ 295 (11.5)	0.91 (0.58, 1.44) 0.6998	0.91 (0.54, 1.54) 0.7319	-0.01 (-0.06, 0.04)*0.7256	

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Quality of Life (LOCF)							
	Overall	449/2801 (16.0)	467/2805 (16.6)	0.98 (0.88, 1.10) 0.7760	0.98 (0.84, 1.13) 0.7617	-0.01 (-0.03, 0.01)*0.5309	
	Age						0.3641
	<= median	207/1394 (14.8)	211/1471 (14.3)	1.04 (0.88, 1.23) 0.6600	1.06 (0.85, 1.31) 0.5976	0.01 (-0.02, 0.03)*0.7018	
	> median	242/1407 (17.2)	256/1334 (19.2)	0.94 (0.80, 1.09) 0.3901	0.90 (0.74, 1.11) 0.3236	-0.02 (-0.05, 0.01)*0.1770	
	Gender						0.1389
	Male	266/1630 (16.3)	253/1608 (15.7)	1.06 (0.91, 1.23) 0.4586	1.08 (0.89, 1.31) 0.4491	0.01 (-0.02, 0.03)*0.6499	
	Female	183/1171 (15.6)	214/1197 (17.9)	0.89 (0.75, 1.06) 0.1852	0.86 (0.68, 1.08) 0.1876	-0.02 (-0.05, 0.01)*0.1423	
	Race						0.8842
	White	325/2006 (16.2)	348/2032 (17.1)	0.98 (0.86, 1.11) 0.7183	0.97 (0.82, 1.15) 0.7253	-0.01 (-0.03, 0.01)*0.4305	
	Black or African	9/ 64 (14.1)	10/ 70 (14.3)	0.98 (0.43, 2.27)*0.9705	1.02 (0.37, 2.79) 0.9655	-0.00 (-0.12, 0.12)*0.9705	
	Asian	100/ 555 (18.0)	94/ 551 (17.1)	1.06 (0.82, 1.36) 0.6738	1.07 (0.78, 1.46) 0.6949	0.01 (-0.04, 0.05)*0.6752	
	Other	15/ 176 (8.5)	15/ 152 (9.9)	0.86 (0.44, 1.71)*0.6735	0.70 (0.31, 1.60) 0.3990	-0.01 (-0.08, 0.05)*0.6747	
	Geographic region						0.6032
	Asia	96/ 536 (17.9)	90/ 536 (16.8)	1.07 (0.83, 1.38) 0.6135	1.08 (0.79, 1.49) 0.6269	0.01 (-0.03, 0.06)*0.6284	
	Europe and Saudi Arabia	221/1341 (16.5)	231/1381 (16.7)	1.03 (0.88, 1.20) 0.7289	1.04 (0.84, 1.29) 0.7095	-0.00 (-0.03, 0.03)*0.8627	
	North America	63/ 393 (16.0)	73/ 376 (19.4)	0.84 (0.62, 1.13) 0.2486	0.79 (0.54, 1.15) 0.2214	-0.03 (-0.09, 0.02)*0.2192	
	Latin America	69/ 531 (13.0)	73/ 512 (14.3)	0.95 (0.72, 1.26) 0.7357	0.89 (0.61, 1.31) 0.5645	-0.01 (-0.05, 0.03)*0.5522	
	NYHA class at enrolment						0.3260
	II	337/2083 (16.2)	349/2165 (16.1)	1.01 (0.88, 1.15) 0.8949	1.01 (0.85, 1.19) 0.9475	0.00 (-0.02, 0.02)*0.9587	
	III or IV	112/ 718 (15.6)	117/ 639 (18.3)	0.89 (0.72, 1.10) 0.2944	0.86 (0.64, 1.17) 0.3505	-0.03 (-0.07, 0.01)*0.1846	
	LVEF at enrolment						0.5880
	<= 49	145/ 959 (15.1)	135/ 950 (14.2)	1.08 (0.88, 1.33) 0.4499	1.09 (0.83, 1.42) 0.5292	0.01 (-0.02, 0.04)*0.5743	
	50-59	168/1017 (16.5)	178/1009 (17.6)	0.95 (0.79, 1.14) 0.5977	0.93 (0.73, 1.19) 0.5701	-0.01 (-0.04, 0.02)*0.5022	
	>= 60	136/ 825 (16.5)	154/ 846 (18.2)	0.94 (0.77, 1.15) 0.5517	0.94 (0.72, 1.22) 0.6171	-0.02 (-0.05, 0.02)*0.3534	
	NT-proBNP at enrolment						0.7385
	<= median	218/1396 (15.6)	232/1409 (16.5)	0.96 (0.82, 1.13) 0.6587	0.96 (0.78, 1.18) 0.6804	-0.01 (-0.04, 0.02)*0.5398	
	> median	231/1405 (16.4)	235/1395 (16.8)	1.00 (0.86, 1.17) 0.9697	1.00 (0.81, 1.23) 0.9771	-0.00 (-0.03, 0.02)*0.7738	
	Type 2 Diabetes Medical History						0.0009
	Yes	177/1231 (14.4)	233/1243 (18.7)	0.79 (0.67, 0.94) 0.0081	0.73 (0.59, 0.90)*0.0036	-0.04 (-0.07, -0.01)*0.0034	
	No	272/1570 (17.3)	234/1562 (15.0)	1.17 (1.00, 1.36) 0.0458	1.19 (0.98, 1.44)*0.0749	0.02 (-0.00, 0.05)*0.0745	
	Atrial fibrillation or flutter at enrolment ECG						0.5486
	Yes	200/1185 (16.9)	198/1188 (16.7)	1.02 (0.86, 1.21) 0.7960	1.04 (0.83, 1.30) 0.7276	0.00 (-0.03, 0.03)*0.8906	
	No	249/1616 (15.4)	269/1617 (16.6)	0.95 (0.82, 1.10) 0.4875	0.93 (0.76, 1.13) 0.4420	-0.01 (-0.04, 0.01)*0.3414	
	BMI (kg/m2) at enrolment						0.6877
	< 30	246/1547 (15.9)	254/1541 (16.5)	1.00 (0.86, 1.17) 0.9554	1.00 (0.82, 1.22) 0.9742	-0.01 (-0.03, 0.02)*0.6612	
	>= 30	202/1253 (16.1)	213/1261 (16.9)	0.96 (0.81, 1.13) 0.5953	0.95 (0.76, 1.18) 0.6261	-0.01 (-0.04, 0.02)*0.6030	
	Baseline eGFR (mL/min/1.73m^2)						0.1559
	< 60	220/1338 (16.4)	252/1377 (18.3)	0.91 (0.78, 1.06) 0.2289	0.89 (0.72, 1.09) 0.2580	-0.02 (-0.05, 0.01)*0.2011	
	>= 60	229/1463 (15.7)	214/1427 (15.0)	1.07 (0.91, 1.26) 0.3844	1.09 (0.88, 1.34) 0.4383	0.01 (-0.02, 0.03)*0.6243	

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Quality of Life (LOCF)	SBP at randomisation						0.2794
	<= median	228/1405 (16.2)	231/1420 (16.3)	1.05 (0.89, 1.23) 0.5696	1.05 (0.85, 1.29) 0.6510	-0.00 (-0.03, 0.03)*0.9771	
	> median	221/1396 (15.8)	236/1385 (17.0)	0.92 (0.79, 1.08) 0.3301	0.91 (0.74, 1.12) 0.3731	-0.01 (-0.04, 0.02)*0.3897	
	LVEF at enrolment 2						0.3042
	<= 49	145/ 959 (15.1)	135/ 950 (14.2)	1.08 (0.88, 1.33) 0.4499	1.09 (0.83, 1.42) 0.5292	0.01 (-0.02, 0.04)*0.5743	
	>= 50	304/1842 (16.5)	332/1855 (17.9)	0.95 (0.83, 1.08) 0.4217	0.93 (0.78, 1.11) 0.4438	-0.01 (-0.04, 0.01)*0.2614	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8006
	Yes	38/ 280 (13.6)	39/ 281 (13.9)	0.98 (0.65, 1.48)*0.9157	1.05 (0.62, 1.75) 0.8644	-0.00 (-0.06, 0.05)*0.9157	
	No	411/2521 (16.3)	428/2524 (17.0)	0.98 (0.87, 1.10) 0.7413	0.97 (0.83, 1.13) 0.7176	-0.01 (-0.03, 0.01)*0.5327	
	MRAs at baseline						0.9380
	Yes	210/1216 (17.3)	215/1210 (17.8)	0.98 (0.83, 1.16) 0.8311	0.99 (0.79, 1.23) 0.8969	-0.00 (-0.04, 0.03)*0.7465	
	No	239/1585 (15.1)	252/1595 (15.8)	0.98 (0.84, 1.14) 0.7955	0.97 (0.79, 1.18) 0.7333	-0.01 (-0.03, 0.02)*0.5739	
	ACEi+ARB at baseline						0.5412
	Yes	327/2037 (16.1)	351/2059 (17.0)	0.96 (0.85, 1.10) 0.5825	0.94 (0.79, 1.12) 0.5069	-0.01 (-0.03, 0.01)*0.3919	
	No	122/ 764 (16.0)	116/ 746 (15.5)	1.05 (0.84, 1.32) 0.6637	1.08 (0.81, 1.43) 0.6106	0.00 (-0.03, 0.04)*0.8232	
	ARNI at baseline						0.4514
	Yes	24/ 149 (16.1)	18/ 125 (14.4)	1.21 (0.71, 2.08) 0.4847	1.32 (0.66, 2.64) 0.4390	0.02 (-0.07, 0.10)*0.6947	
	No	425/2652 (16.0)	449/2680 (16.8)	0.97 (0.87, 1.09) 0.6645	0.97 (0.83, 1.12) 0.6441	-0.01 (-0.03, 0.01)*0.4727	
	Beta Blocker at baseline						0.1653
	Yes	383/2327 (16.5)	388/2330 (16.7)	1.02 (0.90, 1.15) 0.7397	1.02 (0.87, 1.20) 0.8256	-0.00 (-0.02, 0.02)*0.8591	
	No	66/ 474 (13.9)	79/ 475 (16.6)	0.81 (0.61, 1.08) 0.1598	0.80 (0.55, 1.15) 0.2265	-0.03 (-0.07, 0.02)*0.2460	
	Diuretics at baseline						0.2535
	Yes	398/2500 (15.9)	420/2504 (16.8)	0.96 (0.85, 1.08) 0.5203	0.95 (0.81, 1.11) 0.5386	-0.01 (-0.03, 0.01)*0.4144	
	No	51/ 301 (16.9)	47/ 301 (15.6)	1.19 (0.84, 1.68) 0.3186	1.21 (0.77, 1.91) 0.3971	0.01 (-0.05, 0.07)*0.6587	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	368/2801 (13.1)	478/2805 (17.0)	0.78 (0.69, 0.88) <.0001	0.73 (0.63, 0.85) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Age						0.6032
	<= median	168/1394 (12.1)	219/1471 (14.9)	0.80 (0.67, 0.97) 0.0196	0.77 (0.62, 0.96) 0.0182	-0.03 (-0.05, -0.00)*0.0259	
	> median	200/1407 (14.2)	259/1334 (19.4)	0.75 (0.64, 0.89) 0.0008	0.70 (0.57, 0.86) 0.0007	-0.05 (-0.08, -0.02)*0.0003	
	Gender						0.0468
	Male	188/1630 (11.5)	268/1608 (16.7)	0.70 (0.59, 0.83) <.0001	0.65 (0.53, 0.80) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	Female	180/1171 (15.4)	210/1197 (17.5)	0.90 (0.75, 1.07) 0.2188	0.85 (0.68, 1.06) 0.1554	-0.02 (-0.05, 0.01)*0.1537	
	Race						0.6313
	White	275/2006 (13.7)	373/2032 (18.4)	0.76 (0.66, 0.87) 0.0001	0.71 (0.60, 0.84) 0.0001	-0.05 (-0.07, -0.02)*<.0001	
	Black or African	9/ 64 (14.1)	16/ 70 (22.9)	0.60 (0.29, 1.25) 0.1737	0.54 (0.22, 1.33) 0.1787	-0.09 (-0.22, 0.04)*0.1853	
	Asian	70/ 555 (12.6)	74/ 551 (13.4)	0.94 (0.69, 1.27) 0.6684	0.92 (0.65, 1.31) 0.6527	-0.01 (-0.05, 0.03)*0.6863	
	Other	14/ 176 (8.0)	15/ 152 (9.9)	0.85 (0.43, 1.69) 0.6390	0.84 (0.39, 1.82) 0.6536	-0.02 (-0.08, 0.04)*0.5453	
	Geographic region						0.5857
	Asia	67/ 536 (12.5)	71/ 536 (13.2)	0.94 (0.69, 1.28) 0.7065	0.93 (0.65, 1.34) 0.6966	-0.01 (-0.05, 0.03)*0.7153	
	Europe and Saudi Arabia	180/1341 (13.4)	255/1381 (18.5)	0.75 (0.64, 0.89) 0.0009	0.69 (0.56, 0.86) 0.0007	-0.05 (-0.08, -0.02)*0.0003	
	North America	67/ 393 (17.0)	79/ 376 (21.0)	0.82 (0.61, 1.09) 0.1666	0.77 (0.53, 1.11) 0.1609	-0.04 (-0.10, 0.02)*0.1616	
	Latin America	54/ 531 (10.2)	73/ 512 (14.3)	0.72 (0.52, 0.99) 0.0428	0.67 (0.46, 0.99) 0.0426	-0.04 (-0.08, -0.00)*0.0437	
	NYHA class at enrolment						0.0729
	II	281/2083 (13.5)	355/2165 (16.4)	0.82 (0.71, 0.95) 0.0066	0.78 (0.66, 0.93) 0.0056	-0.03 (-0.05, -0.01)*0.0078	
	III or IV	87/ 718 (12.1)	123/ 639 (19.2)	0.64 (0.50, 0.81) 0.0003	0.57 (0.42, 0.78) 0.0004	-0.07 (-0.11, -0.03)*0.0003	
	LVEF at enrolment						0.3514
	<= 49	112/ 959 (11.7)	155/ 950 (16.3)	0.71 (0.57, 0.88) 0.0024	0.66 (0.51, 0.86) 0.0023	-0.05 (-0.08, -0.02)*0.0034	
	50-59	150/1017 (14.7)	172/1009 (17.0)	0.87 (0.72, 1.06) 0.1688	0.83 (0.65, 1.06) 0.1440	-0.02 (-0.05, 0.01)*0.1572	
	>= 60	106/ 825 (12.8)	151/ 846 (17.8)	0.75 (0.60, 0.94) 0.0125	0.71 (0.54, 0.93) 0.0129	-0.05 (-0.08, -0.02)*0.0045	
	NT-proBNP at enrolment						0.2663
	<= median	194/1396 (13.9)	234/1409 (16.6)	0.84 (0.70, 0.99) 0.0405	0.80 (0.65, 0.99) 0.0383	-0.03 (-0.05, -0.00)*0.0457	
	> median	174/1405 (12.4)	244/1395 (17.5)	0.73 (0.61, 0.87) 0.0005	0.67 (0.54, 0.84) 0.0003	-0.05 (-0.08, -0.02)*0.0001	
	Type 2 Diabetes Medical History						0.0422
	Yes	156/1231 (12.7)	237/1243 (19.1)	0.68 (0.56, 0.81) <.0001	0.62 (0.49, 0.77)*<.0001	-0.06 (-0.09, -0.04)*<.0001	
	No	212/1570 (13.5)	241/1562 (15.4)	0.88 (0.74, 1.04) 0.1278	0.86 (0.70, 1.04)*0.1258	-0.02 (-0.04, 0.01)*0.1254	
	Atrial fibrillation or flutter at enrolment ECG						0.5457
	Yes	150/1185 (12.7)	202/1188 (17.0)	0.75 (0.62, 0.90) 0.0025	0.70 (0.56, 0.89) 0.0031	-0.04 (-0.07, -0.01)*0.0028	
	No	218/1616 (13.5)	276/1617 (17.1)	0.80 (0.68, 0.94) 0.0072	0.76 (0.62, 0.92) 0.0053	-0.04 (-0.06, -0.01)*0.0046	
	BMI (kg/m2) at enrolment						0.7121
	< 30	206/1547 (13.3)	260/1541 (16.9)	0.80 (0.68, 0.94) 0.0076	0.76 (0.62, 0.93) 0.0071	-0.04 (-0.06, -0.01)*0.0057	
	>= 30	162/1253 (12.9)	218/1261 (17.3)	0.76 (0.63, 0.91) 0.0032	0.71 (0.56, 0.89) 0.0026	-0.04 (-0.07, -0.02)*0.0022	
	Baseline eGFR (mL/min/1.73m^2)						0.1981
	< 60	185/1338 (13.8)	266/1377 (19.3)	0.72 (0.61, 0.85) 0.0002	0.67 (0.54, 0.82) 0.0002	-0.05 (-0.08, -0.03)*0.0001	
	>= 60	183/1463 (12.5)	212/1427 (14.9)	0.85 (0.71, 1.02) 0.0826	0.82 (0.66, 1.02) 0.0707	-0.02 (-0.05, 0.00)*0.0663	

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Symptom Burden (LOCF)	SBP at randomisation						0.8482
	<= median	182/1405 (13.0)	242/1420 (17.0)	0.79 (0.66, 0.94) 0.0070	0.75 (0.60, 0.92) 0.0068	-0.04 (-0.07, -0.01)*0.0023	
	> median	186/1396 (13.3)	236/1385 (17.0)	0.77 (0.65, 0.91) 0.0028	0.72 (0.58, 0.89) 0.0022	-0.04 (-0.06, -0.01)*0.0063	
	LVEF at enrolment 2						0.2841
	<= 49	112/ 959 (11.7)	155/ 950 (16.3)	0.71 (0.57, 0.88) 0.0024	0.66 (0.51, 0.86) 0.0023	-0.05 (-0.08, -0.02)*0.0034	
	>= 50	256/1842 (13.9)	323/1855 (17.4)	0.82 (0.70, 0.95) 0.0071	0.78 (0.65, 0.93) 0.0061	-0.04 (-0.06, -0.01)*0.0032	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6941
	Yes	33/ 280 (11.8)	44/ 281 (15.7)	0.69 (0.46, 1.04) 0.0768	0.65 (0.39, 1.07) 0.0910	-0.04 (-0.10, 0.02)*0.1818	
	No	335/2521 (13.3)	434/2524 (17.2)	0.78 (0.69, 0.89) 0.0002	0.74 (0.63, 0.87) 0.0002	-0.04 (-0.06, -0.02)*0.0001	
	MRAs at baseline						0.5500
	Yes	158/1216 (13.0)	214/1210 (17.7)	0.75 (0.62, 0.90) 0.0022	0.70 (0.56, 0.88) 0.0021	-0.05 (-0.08, -0.02)*0.0013	
	No	210/1585 (13.2)	264/1595 (16.6)	0.81 (0.68, 0.95) 0.0098	0.76 (0.63, 0.93) 0.0083	-0.03 (-0.06, -0.01)*0.0088	
	ACEi+ARB at baseline						0.0702
	Yes	253/2037 (12.4)	359/2059 (17.4)	0.73 (0.63, 0.84) <.0001	0.67 (0.56, 0.80) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	No	115/ 764 (15.1)	119/ 746 (16.0)	0.94 (0.74, 1.18) 0.5819	0.92 (0.70, 1.23) 0.5841	-0.01 (-0.05, 0.03)*0.6293	
	ARNI at baseline						0.4011
	Yes	22/ 149 (14.8)	17/ 125 (13.6)	1.03 (0.57, 1.86) 0.9335	1.06 (0.53, 2.13) 0.8723	0.01 (-0.07, 0.09)*0.7827	
	No	346/2652 (13.0)	461/2680 (17.2)	0.77 (0.68, 0.88) <.0001	0.72 (0.62, 0.85) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Beta Blocker at baseline						0.2689
	Yes	311/2327 (13.4)	395/2330 (17.0)	0.81 (0.70, 0.92) 0.0016	0.76 (0.65, 0.90) 0.0013	-0.04 (-0.06, -0.02)*0.0006	
	No	57/ 474 (12.0)	83/ 475 (17.5)	0.67 (0.49, 0.91) 0.0105	0.62 (0.43, 0.89) 0.0106	-0.05 (-0.10, -0.01)*0.0176	
	Diuretics at baseline						0.0881
	Yes	326/2500 (13.0)	436/2504 (17.4)	0.75 (0.66, 0.85) <.0001	0.70 (0.60, 0.82) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	42/ 301 (14.0)	42/ 301 (14.0)	1.07 (0.73, 1.59) 0.7171	1.08 (0.68, 1.73) 0.7476	0.00 (-0.06, 0.06)*1.0000	

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Self Efficacy (LOCF)							
	Overall	320/2801 (11.4)	330/2805 (11.8)	0.98 (0.85, 1.13) 0.7677	0.97 (0.82, 1.15) 0.7582	-0.00 (-0.02, 0.01)*0.6908	
	Age						0.4870
	<= median	150/1394 (10.8)	157/1471 (10.7)	1.03 (0.84, 1.26) 0.7884	1.01 (0.79, 1.29) 0.9251	0.00 (-0.02, 0.02)*0.9398	
	> median	170/1407 (12.1)	173/1334 (13.0)	0.93 (0.77, 1.13) 0.4604	0.93 (0.74, 1.18) 0.5572	-0.01 (-0.03, 0.02)*0.4838	
	Gender						0.9477
	Male	196/1630 (12.0)	198/1608 (12.3)	0.97 (0.82, 1.16) 0.7683	0.97 (0.78, 1.20) 0.7682	-0.00 (-0.03, 0.02)*0.8015	
	Female	124/1171 (10.6)	132/1197 (11.0)	0.98 (0.79, 1.23) 0.8915	0.98 (0.75, 1.28) 0.8742	-0.00 (-0.03, 0.02)*0.7312	
	Race						0.7218*
	White	213/2006 (10.6)	230/2032 (11.3)	0.96 (0.81, 1.13) 0.6085	0.95 (0.77, 1.16) 0.6076	-0.01 (-0.03, 0.01)*0.4761	
	Black or African	12/ 64 (18.8)	9/ 70 (12.9)	1.35 (0.61, 2.96) 0.4586	1.47 (0.57, 3.83) 0.4281	0.06 (-0.06, 0.18)*0.3503	
	Asian	81/ 555 (14.6)	78/ 551 (14.2)	1.00 (0.76, 1.32) 0.9937	1.00 (0.71, 1.42) 0.9818	0.00 (-0.04, 0.05)*0.8354	
	Other	14/ 176 (8.0)	13/ 152 (8.6)	0.97 (0.48, 1.93) 0.9225	0.93 (0.41, 2.16) 0.8743	-0.01 (-0.07, 0.05)*0.8446	
	Geographic region						0.9664
	Asia	80/ 536 (14.9)	78/ 536 (14.6)	0.99 (0.75, 1.30) 0.9252	0.99 (0.69, 1.41) 0.9471	0.00 (-0.04, 0.05)*0.8632	
	Europe and Saudi Arabia	146/1341 (10.9)	160/1381 (11.6)	0.95 (0.78, 1.16) 0.6120	0.94 (0.73, 1.21) 0.6344	-0.01 (-0.03, 0.02)*0.5640	
	North America	36/ 393 (9.2)	32/ 376 (8.5)	1.06 (0.67, 1.65) 0.8126	1.06 (0.64, 1.75) 0.8303	0.01 (-0.03, 0.05)*0.7509	
	Latin America	58/ 531 (10.9)	60/ 512 (11.7)	1.01 (0.73, 1.41) 0.9344	1.00 (0.67, 1.50) 0.9854	-0.01 (-0.05, 0.03)*0.6851	
	NYHA class at enrolment						0.3730
	II	240/2083 (11.5)	251/2165 (11.6)	1.01 (0.86, 1.19) 0.8583	1.01 (0.83, 1.23) 0.9175	-0.00 (-0.02, 0.02)*0.9418	
	III or IV	80/ 718 (11.1)	78/ 639 (12.2)	0.88 (0.66, 1.16) 0.3655	0.87 (0.62, 1.23) 0.4289	-0.01 (-0.04, 0.02)*0.5426	
	LVEF at enrolment						0.2285
	<= 49	110/ 959 (11.5)	101/ 950 (10.6)	1.06 (0.83, 1.35) 0.6641	1.05 (0.78, 1.42) 0.7374	0.01 (-0.02, 0.04)*0.5589	
	50-59	119/1017 (11.7)	111/1009 (11.0)	1.07 (0.85, 1.35) 0.5691	1.09 (0.82, 1.46) 0.5386	0.01 (-0.02, 0.03)*0.6194	
	>= 60	91/ 825 (11.0)	118/ 846 (13.9)	0.82 (0.64, 1.05) 0.1129	0.79 (0.58, 1.07) 0.1251	-0.03 (-0.06, 0.00)*0.0708	
	NT-proBNP at enrolment						0.8015
	<= median	160/1396 (11.5)	171/1409 (12.1)	0.96 (0.79, 1.17) 0.7031	0.94 (0.74, 1.20) 0.6385	-0.01 (-0.03, 0.02)*0.5795	
	> median	160/1405 (11.4)	159/1395 (11.4)	1.00 (0.82, 1.22) 0.9892	1.01 (0.79, 1.28) 0.9658	-0.00 (-0.02, 0.02)*0.9934	
	Type 2 Diabetes Medical History						0.0252
	Yes	125/1231 (10.2)	159/1243 (12.8)	0.82 (0.66, 1.01) 0.0620	0.77 (0.60, 0.99)*0.0400	-0.03 (-0.05, -0.00)*0.0394	
	No	195/1570 (12.4)	171/1562 (10.9)	1.13 (0.94, 1.36) 0.2093	1.15 (0.93, 1.44)*0.1998	0.01 (-0.01, 0.04)*0.1993	
	Atrial fibrillation or flutter at enrolment ECG						0.8672
	Yes	147/1185 (12.4)	154/1188 (13.0)	0.99 (0.81, 1.22) 0.9553	0.99 (0.77, 1.27) 0.9370	-0.01 (-0.03, 0.02)*0.6830	
	No	173/1616 (10.7)	176/1617 (10.9)	0.97 (0.80, 1.17) 0.7480	0.96 (0.77, 1.21) 0.7544	-0.00 (-0.02, 0.02)*0.8698	
	BMI (kg/m2) at enrolment						0.7593
	< 30	193/1547 (12.5)	198/1541 (12.8)	1.00 (0.84, 1.19) 0.9894	1.00 (0.80, 1.25) 0.9794	-0.00 (-0.03, 0.02)*0.7553	
	>= 30	127/1253 (10.1)	132/1261 (10.5)	0.96 (0.76, 1.19) 0.6864	0.94 (0.72, 1.23) 0.6484	-0.00 (-0.03, 0.02)*0.7841	
	Baseline eGFR (mL/min/1.73m^2)						0.5681
	< 60	153/1338 (11.4)	152/1377 (11.0)	1.02 (0.83, 1.25) 0.8446	1.03 (0.81, 1.32) 0.8044	0.00 (-0.02, 0.03)*0.7437	
	>= 60	167/1463 (11.4)	177/1427 (12.4)	0.95 (0.78, 1.14) 0.5593	0.92 (0.73, 1.17) 0.5146	-0.01 (-0.03, 0.01)*0.4120	

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Self Efficacy (LOCF)	SBP at randomisation						0.4720
	<= median	167/1405 (11.9)	165/1420 (11.6)	1.03 (0.85, 1.25) 0.7593	1.04 (0.82, 1.32) 0.7433	0.00 (-0.02, 0.03)*0.8260	
	> median	153/1396 (11.0)	165/1385 (11.9)	0.93 (0.76, 1.13) 0.4720	0.91 (0.71, 1.16) 0.4494	-0.01 (-0.03, 0.01)*0.4295	
	LVEF at enrolment 2						0.4351
	<= 49	110/ 959 (11.5)	101/ 950 (10.6)	1.06 (0.83, 1.35) 0.6641	1.05 (0.78, 1.42) 0.7374	0.01 (-0.02, 0.04)*0.5589	
	>= 50	210/1842 (11.4)	229/1855 (12.3)	0.94 (0.80, 1.12) 0.4932	0.94 (0.76, 1.15) 0.5363	-0.01 (-0.03, 0.01)*0.3747	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3693
	Yes	36/ 280 (12.9)	30/ 281 (10.7)	1.20 (0.78, 1.83) 0.4070	1.25 (0.72, 2.18) 0.4272	0.02 (-0.03, 0.08)*0.4225	
	No	284/2521 (11.3)	300/2524 (11.9)	0.96 (0.83, 1.11) 0.5694	0.95 (0.79, 1.14) 0.5702	-0.01 (-0.02, 0.01)*0.4909	
	MRAs at baseline						0.7378
	Yes	151/1216 (12.4)	149/1210 (12.3)	1.00 (0.82, 1.23) 0.9775	1.00 (0.78, 1.29) 0.9952	0.00 (-0.03, 0.03)*0.9382	
	No	169/1585 (10.7)	181/1595 (11.3)	0.96 (0.79, 1.16) 0.6532	0.95 (0.75, 1.19) 0.6542	-0.01 (-0.03, 0.01)*0.5368	
	ACEi+ARB at baseline						0.0149
	Yes	216/2037 (10.6)	253/2059 (12.3)	0.88 (0.75, 1.04) 0.1275	0.84 (0.69, 1.03) 0.0996	-0.02 (-0.04, 0.00)*0.0904	
	No	104/ 764 (13.6)	77/ 746 (10.3)	1.31 (1.00, 1.71) 0.0489	1.42 (1.03, 1.96) 0.0346	0.03 (0.00, 0.07)*0.0484	
	ARNI at baseline						0.0345
	Yes	25/ 149 (16.8)	10/ 125 (8.0)	2.15 (1.08, 4.28) 0.0284	2.47 (1.11, 5.52) 0.0272	0.09 (0.01, 0.16)*0.0246	
	No	295/2652 (11.1)	320/2680 (11.9)	0.95 (0.82, 1.09) 0.4530	0.93 (0.78, 1.11) 0.4473	-0.01 (-0.03, 0.01)*0.3505	
	Beta Blocker at baseline						0.5384
	Yes	271/2327 (11.6)	273/2330 (11.7)	1.00 (0.86, 1.16) 0.9815	1.00 (0.83, 1.20) 0.9624	-0.00 (-0.02, 0.02)*0.9400	
	No	49/ 474 (10.3)	57/ 475 (12.0)	0.88 (0.62, 1.25) 0.4740	0.86 (0.57, 1.31) 0.4936	-0.02 (-0.06, 0.02)*0.4161	
	Diuretics at baseline						0.5681
	Yes	286/2500 (11.4)	290/2504 (11.6)	0.99 (0.86, 1.15) 0.9346	0.99 (0.83, 1.19) 0.9202	-0.00 (-0.02, 0.02)*0.8754	
	No	34/ 301 (11.3)	40/ 301 (13.3)	0.88 (0.58, 1.33) 0.5300	0.85 (0.52, 1.41) 0.5383	-0.02 (-0.07, 0.03)*0.4562	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	286/2801 (10.2)	395/2805 (14.1)	0.73 (0.63, 0.84) <.0001	0.69 (0.58, 0.81) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Age						0.6530
	<= median	127/1394 (9.1)	188/1471 (12.8)	0.70 (0.57, 0.86) 0.0008	0.66 (0.52, 0.84) 0.0008	-0.04 (-0.06, -0.01)*0.0016	
	> median	159/1407 (11.3)	207/1334 (15.5)	0.75 (0.62, 0.90) 0.0023	0.70 (0.56, 0.88) 0.0019	-0.04 (-0.07, -0.02)*0.0012	
	Gender						0.7273
	Male	159/1630 (9.8)	218/1608 (13.6)	0.71 (0.59, 0.86) 0.0005	0.68 (0.54, 0.85) 0.0006	-0.04 (-0.06, -0.02)*0.0007	
	Female	127/1171 (10.8)	177/1197 (14.8)	0.75 (0.61, 0.93) 0.0072	0.70 (0.54, 0.90) 0.0047	-0.04 (-0.07, -0.01)*0.0040	
	Race						0.8923
	White	205/2006 (10.2)	290/2032 (14.3)	0.73 (0.62, 0.87) 0.0002	0.68 (0.56, 0.83) 0.0001	-0.04 (-0.06, -0.02)*<.0001	
	Black or African	8/ 64 (12.5)	8/ 70 (11.4)	1.03 (0.42, 2.55) 0.9501	1.06 (0.37, 3.05) 0.9173	0.01 (-0.10, 0.12)*0.8487	
	Asian	62/ 555 (11.2)	84/ 551 (15.2)	0.72 (0.53, 0.98) 0.0375	0.69 (0.48, 0.98) 0.0372	-0.04 (-0.08, -0.00)*0.0451	
	Other	11/ 176 (6.3)	13/ 152 (8.6)	0.68 (0.32, 1.47) 0.3284	0.66 (0.28, 1.54) 0.3326	-0.02 (-0.08, 0.03)*0.4290	
	Geographic region						0.8082
	Asia	59/ 536 (11.0)	82/ 536 (15.3)	0.71 (0.52, 0.97) 0.0333	0.68 (0.47, 0.97) 0.0327	-0.04 (-0.08, -0.00)*0.0373	
	Europe and Saudi Arabia	138/1341 (10.3)	195/1381 (14.1)	0.75 (0.62, 0.92) 0.0056	0.70 (0.55, 0.89) 0.0035	-0.04 (-0.06, -0.01)*0.0022	
	North America	44/ 393 (11.2)	51/ 376 (13.6)	0.80 (0.55, 1.16) 0.2402	0.78 (0.50, 1.20) 0.2594	-0.02 (-0.07, 0.02)*0.3191	
	Latin America	45/ 531 (8.5)	67/ 512 (13.1)	0.64 (0.45, 0.91) 0.0126	0.59 (0.39, 0.89) 0.0121	-0.05 (-0.08, -0.01)*0.0163	
	NYHA class at enrolment						0.7112
	II	220/2083 (10.6)	309/2165 (14.3)	0.73 (0.63, 0.86) 0.0001	0.69 (0.57, 0.83) <.0001	-0.04 (-0.06, -0.02)*0.0002	
	III or IV	66/ 718 (9.2)	86/ 639 (13.5)	0.69 (0.51, 0.92) 0.0120	0.65 (0.46, 0.93) 0.0171	-0.04 (-0.08, -0.01)*0.0135	
	LVEF at enrolment						0.6272
	<= 49	90/ 959 (9.4)	108/ 950 (11.4)	0.81 (0.63, 1.06) 0.1210	0.78 (0.58, 1.06) 0.1124	-0.02 (-0.05, 0.01)*0.1552	
	50-59	103/1017 (10.1)	149/1009 (14.8)	0.69 (0.54, 0.86) 0.0013	0.63 (0.48, 0.83) 0.0011	-0.05 (-0.08, -0.02)*0.0015	
	>= 60	93/ 825 (11.3)	138/ 846 (16.3)	0.72 (0.56, 0.91) 0.0065	0.67 (0.50, 0.89) 0.0065	-0.05 (-0.08, -0.02)*0.0027	
	NT-proBNP at enrolment						0.6898
	<= median	137/1396 (9.8)	196/1409 (13.9)	0.71 (0.58, 0.86) 0.0008	0.67 (0.53, 0.84) 0.0007	-0.04 (-0.06, -0.02)*0.0008	
	> median	149/1405 (10.6)	199/1395 (14.3)	0.75 (0.62, 0.91) 0.0035	0.70 (0.56, 0.89) 0.0031	-0.04 (-0.06, -0.01)*0.0033	
	Type 2 Diabetes Medical History						0.8433
	Yes	128/1231 (10.4)	181/1243 (14.6)	0.72 (0.58, 0.88) 0.0017	0.68 (0.53, 0.87)*0.0018	-0.04 (-0.07, -0.02)*0.0017	
	No	158/1570 (10.1)	214/1562 (13.7)	0.74 (0.61, 0.89) 0.0017	0.70 (0.57, 0.88)*0.0017	-0.04 (-0.06, -0.01)*0.0016	
	Atrial fibrillation or flutter at enrolment ECG						0.6722
	Yes	129/1185 (10.9)	182/1188 (15.3)	0.70 (0.57, 0.86) 0.0008	0.65 (0.51, 0.83) 0.0007	-0.04 (-0.07, -0.02)*0.0013	
	No	157/1616 (9.7)	213/1617 (13.2)	0.75 (0.62, 0.90) 0.0027	0.71 (0.57, 0.89) 0.0024	-0.03 (-0.06, -0.01)*0.0020	
	BMI (kg/m2) at enrolment						0.8415
	< 30	159/1547 (10.3)	213/1541 (13.8)	0.74 (0.61, 0.89) 0.0018	0.70 (0.56, 0.88) 0.0018	-0.04 (-0.06, -0.01)*0.0025	
	>= 30	127/1253 (10.1)	181/1261 (14.4)	0.72 (0.58, 0.89) 0.0019	0.67 (0.52, 0.86) 0.0015	-0.04 (-0.07, -0.02)*0.0012	
	Baseline eGFR (mL/min/1.73m^2)						0.7220
	< 60	153/1338 (11.4)	212/1377 (15.4)	0.75 (0.62, 0.90) 0.0026	0.70 (0.56, 0.88) 0.0022	-0.04 (-0.07, -0.01)*0.0024	
	>= 60	133/1463 (9.1)	182/1427 (12.8)	0.71 (0.58, 0.88) 0.0015	0.68 (0.53, 0.86) 0.0014	-0.04 (-0.06, -0.01)*0.0016	

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Symptom Frequency (LOCF)	SBP at randomisation						0.6145
	<= median	153/1405 (10.9)	211/1420 (14.9)	0.75 (0.62, 0.91) 0.0038	0.71 (0.56, 0.89) 0.0027	-0.04 (-0.06, -0.02)*0.0016	
	> median	133/1396 (9.5)	184/1385 (13.3)	0.70 (0.57, 0.86) 0.0008	0.66 (0.52, 0.85) 0.0009	-0.04 (-0.06, -0.01)*0.0018	
	LVEF at enrolment 2						0.3459
	<= 49	90/ 959 (9.4)	108/ 950 (11.4)	0.81 (0.63, 1.06) 0.1210	0.78 (0.58, 1.06) 0.1124	-0.02 (-0.05, 0.01)*0.1552	
	>= 50	196/1842 (10.6)	287/1855 (15.5)	0.70 (0.59, 0.83) <.0001	0.65 (0.53, 0.79) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1748
	Yes	20/ 280 (7.1)	35/ 281 (12.5)	0.57 (0.34, 0.97)*0.0375	0.42 (0.23, 0.77) 0.0053	-0.05 (-0.10, -0.00)*0.0336	
	No	266/2521 (10.6)	360/2524 (14.3)	0.75 (0.65, 0.87) <.0001	0.71 (0.60, 0.84) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	MRAs at baseline						0.4818
	Yes	113/1216 (9.3)	165/1210 (13.6)	0.68 (0.55, 0.85) 0.0008	0.64 (0.49, 0.83) 0.0006	-0.04 (-0.07, -0.02)*0.0008	
	No	173/1585 (10.9)	230/1595 (14.4)	0.76 (0.63, 0.91) 0.0028	0.72 (0.58, 0.89) 0.0027	-0.04 (-0.06, -0.01)*0.0029	
	ACEi+ARB at baseline						0.0454
	Yes	189/2037 (9.3)	292/2059 (14.2)	0.66 (0.56, 0.78) <.0001	0.61 (0.50, 0.75) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	No	97/ 764 (12.7)	103/ 746 (13.8)	0.91 (0.71, 1.18) 0.4710	0.89 (0.66, 1.21) 0.4567	-0.01 (-0.05, 0.02)*0.5245	
	ARNI at baseline						0.9008
	Yes	14/ 149 (9.4)	14/ 125 (11.2)	0.83 (0.41, 1.67) 0.5946	0.79 (0.36, 1.78) 0.5762	-0.02 (-0.09, 0.05)*0.6256	
	No	272/2652 (10.3)	381/2680 (14.2)	0.73 (0.63, 0.84) <.0001	0.69 (0.58, 0.81) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Beta Blocker at baseline						0.0591
	Yes	240/2327 (10.3)	315/2330 (13.5)	0.77 (0.66, 0.90) 0.0013	0.74 (0.62, 0.89) 0.0011	-0.03 (-0.05, -0.01)*0.0007	
	No	46/ 474 (9.7)	80/ 475 (16.8)	0.54 (0.39, 0.76) 0.0003	0.48 (0.32, 0.72) 0.0003	-0.07 (-0.11, -0.03)*0.0011	
	Diuretics at baseline						0.3740
	Yes	262/2500 (10.5)	351/2504 (14.0)	0.74 (0.64, 0.86) <.0001	0.70 (0.59, 0.84) <.0001	-0.04 (-0.05, -0.02)*0.0001	
	No	24/ 301 (8.0)	44/ 301 (14.6)	0.59 (0.37, 0.95) 0.0289	0.54 (0.32, 0.92) 0.0238	-0.07 (-0.12, -0.02)*0.0096	

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Social Limitation (LOCF)							
	Overall	421/2625 (16.0)	451/2625 (17.2)	0.93 (0.83, 1.05) 0.2293	0.91 (0.78, 1.06) 0.2133	-0.01 (-0.03, 0.01)*0.2659	
	Age						0.9152
	<= median	193/1331 (14.5)	215/1409 (15.3)	0.93 (0.78, 1.11) 0.4351	0.92 (0.74, 1.14) 0.4219	-0.01 (-0.03, 0.02)*0.5769	
	> median	228/1294 (17.6)	236/1216 (19.4)	0.92 (0.79, 1.08) 0.2975	0.89 (0.72, 1.10) 0.2741	-0.02 (-0.05, 0.01)*0.2492	
	Gender						0.9624
	Male	239/1538 (15.5)	244/1500 (16.3)	0.94 (0.80, 1.10) 0.4339	0.93 (0.76, 1.14) 0.4877	-0.01 (-0.03, 0.02)*0.5838	
	Female	182/1087 (16.7)	207/1125 (18.4)	0.93 (0.78, 1.11) 0.4337	0.89 (0.71, 1.12) 0.3145	-0.02 (-0.05, 0.02)*0.3058	
	Race						0.0863
	White	304/1890 (16.1)	360/1921 (18.7)	0.87 (0.76, 0.99) 0.0407	0.84 (0.70, 1.00) 0.0445	-0.03 (-0.05, -0.00)*0.0305	
	Black or African	14/ 58 (24.1)	8/ 66 (12.1)	1.82 (0.83, 3.97) 0.1334	2.27 (0.85, 6.06) 0.1023	0.12 (-0.02, 0.26)*0.0819	
	Asian	84/ 506 (16.6)	73/ 494 (14.8)	1.11 (0.83, 1.48) 0.4803	1.12 (0.79, 1.58) 0.5315	0.02 (-0.03, 0.06)*0.4277	
	Other	19/ 171 (11.1)	10/ 144 (6.9)	1.60 (0.77, 3.33)*0.2088	1.31 (0.55, 3.08) 0.5436	0.04 (-0.02, 0.10)*0.1934	
	Geographic region						0.6025
	Asia	79/ 492 (16.1)	69/ 482 (14.3)	1.11 (0.83, 1.49) 0.4861	1.12 (0.78, 1.59) 0.5416	0.02 (-0.03, 0.06)*0.4487	
	Europe and Saudi Arabia	219/1273 (17.2)	254/1309 (19.4)	0.91 (0.78, 1.06) 0.2327	0.89 (0.72, 1.09) 0.2599	-0.02 (-0.05, 0.01)*0.1480	
	North America	58/ 367 (15.8)	53/ 347 (15.3)	1.00 (0.71, 1.40) 0.9887	0.99 (0.65, 1.50) 0.9627	0.01 (-0.05, 0.06)*0.8450	
	Latin America	65/ 493 (13.2)	75/ 487 (15.4)	0.84 (0.63, 1.13) 0.2575	0.81 (0.56, 1.18) 0.2733	-0.02 (-0.07, 0.02)*0.3216	
	NYHA class at enrolment						0.3622
	II	296/1953 (15.2)	341/2031 (16.8)	0.89 (0.78, 1.03) 0.1086	0.86 (0.72, 1.02) 0.0922	-0.02 (-0.04, 0.01)*0.1592	
	III or IV	125/ 672 (18.6)	109/ 593 (18.4)	1.00 (0.82, 1.23) 0.9815	1.01 (0.74, 1.37) 0.9704	0.00 (-0.04, 0.05)*0.9198	
	LVEF at enrolment						0.1299
	<= 49	147/ 907 (16.2)	125/ 896 (14.0)	1.10 (0.89, 1.37) 0.3599	1.13 (0.87, 1.48) 0.3651	0.02 (-0.01, 0.06)*0.1804	
	50-59	150/ 955 (15.7)	167/ 946 (17.7)	0.90 (0.75, 1.10) 0.3082	0.89 (0.69, 1.14) 0.3486	-0.02 (-0.05, 0.01)*0.2549	
	>= 60	124/ 763 (16.3)	159/ 783 (20.3)	0.82 (0.66, 1.00) 0.0553	0.76 (0.58, 0.99) 0.0393	-0.04 (-0.08, -0.00)*0.0388	
	NT-proBNP at enrolment						0.8270
	<= median	210/1312 (16.0)	229/1336 (17.1)	0.92 (0.78, 1.08) 0.3160	0.90 (0.73, 1.11) 0.3246	-0.01 (-0.04, 0.02)*0.4323	
	> median	211/1313 (16.1)	222/1288 (17.2)	0.94 (0.80, 1.11) 0.4511	0.92 (0.74, 1.14) 0.4293	-0.01 (-0.04, 0.02)*0.4249	
	Type 2 Diabetes Medical History						0.5790
	Yes	180/1150 (15.7)	204/1169 (17.5)	0.90 (0.75, 1.07) 0.2312	0.88 (0.70, 1.09)*0.2442	-0.02 (-0.05, 0.01)*0.2437	
	No	241/1475 (16.3)	247/1456 (17.0)	0.96 (0.82, 1.12) 0.5948	0.96 (0.79, 1.16)*0.6496	-0.01 (-0.03, 0.02)*0.6496	
	Atrial fibrillation or flutter at enrolment ECG						0.9685
	Yes	182/1097 (16.6)	197/1109 (17.8)	0.93 (0.78, 1.12) 0.4502	0.91 (0.72, 1.14) 0.4170	-0.01 (-0.04, 0.02)*0.4651	
	No	239/1528 (15.6)	254/1516 (16.8)	0.93 (0.79, 1.09) 0.3495	0.91 (0.75, 1.11) 0.3460	-0.01 (-0.04, 0.02)*0.4045	
	BMI (kg/m2) at enrolment						0.8916
	< 30	229/1452 (15.8)	241/1428 (16.9)	0.94 (0.80, 1.10) 0.4285	0.91 (0.74, 1.12) 0.3778	-0.01 (-0.04, 0.02)*0.4223	
	>= 30	192/1172 (16.4)	210/1195 (17.6)	0.92 (0.78, 1.10) 0.3679	0.91 (0.73, 1.13) 0.3929	-0.01 (-0.04, 0.02)*0.4402	
	Baseline eGFR (mL/min/1.73m^2)						0.8815
	< 60	214/1240 (17.3)	237/1270 (18.7)	0.92 (0.79, 1.09) 0.3346	0.90 (0.73, 1.11) 0.3081	-0.01 (-0.04, 0.02)*0.3596	
	>= 60	207/1385 (14.9)	214/1354 (15.8)	0.94 (0.79, 1.12) 0.4872	0.93 (0.75, 1.15) 0.4843	-0.01 (-0.04, 0.02)*0.5331	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)	SBP at randomisation						0.4344
	<= median	213/1320 (16.1)	223/1323 (16.9)	0.98 (0.83, 1.16) 0.8026	0.97 (0.78, 1.20) 0.7703	-0.01 (-0.04, 0.02)*0.6184	
	> median	208/1305 (15.9)	228/1302 (17.5)	0.89 (0.75, 1.05) 0.1721	0.86 (0.70, 1.06) 0.1615	-0.02 (-0.04, 0.01)*0.2819	
	LVEF at enrolment 2						0.0558
	<= 49	147/ 907 (16.2)	125/ 896 (14.0)	1.10 (0.89, 1.37) 0.3599	1.13 (0.87, 1.48) 0.3651	0.02 (-0.01, 0.06)*0.1804	
	>= 50	274/1718 (15.9)	326/1729 (18.9)	0.86 (0.75, 0.99) 0.0412	0.82 (0.69, 0.99) 0.0353	-0.03 (-0.05, -0.00)*0.0243	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3560
	Yes	41/ 252 (16.3)	37/ 256 (14.5)	1.10 (0.74, 1.63) 0.6304	1.14 (0.68, 1.91) 0.6154	0.02 (-0.04, 0.08)*0.5701	
	No	380/2373 (16.0)	414/2369 (17.5)	0.92 (0.81, 1.04) 0.1593	0.89 (0.76, 1.04) 0.1442	-0.01 (-0.04, 0.01)*0.1774	
	MRAs at baseline						0.3051
	Yes	193/1144 (16.9)	188/1131 (16.6)	1.00 (0.84, 1.19) 0.9911	1.00 (0.80, 1.25) 0.9958	0.00 (-0.03, 0.03)*0.8741	
	No	228/1481 (15.4)	263/1494 (17.6)	0.88 (0.75, 1.03) 0.1116	0.84 (0.69, 1.03) 0.0963	-0.02 (-0.05, 0.00)*0.1044	
	ACEi+ARB at baseline						0.1798
	Yes	294/1909 (15.4)	338/1934 (17.5)	0.89 (0.77, 1.02) 0.0840	0.85 (0.71, 1.01) 0.0707	-0.02 (-0.04, 0.00)*0.0824	
	No	127/ 716 (17.7)	113/ 691 (16.4)	1.06 (0.85, 1.33) 0.6084	1.08 (0.82, 1.44) 0.5761	0.01 (-0.03, 0.05)*0.4898	
	ARNI at baseline						0.4979
	Yes	25/ 146 (17.1)	17/ 115 (14.8)	1.16 (0.66, 2.04) 0.6088	1.19 (0.60, 2.37) 0.6159	0.02 (-0.07, 0.11)*0.6067	
	No	396/2479 (16.0)	434/2510 (17.3)	0.92 (0.82, 1.04) 0.1931	0.90 (0.77, 1.05) 0.1770	-0.01 (-0.03, 0.01)*0.2117	
	Beta Blocker at baseline						0.3720
	Yes	360/2195 (16.4)	379/2187 (17.3)	0.95 (0.84, 1.08) 0.4538	0.94 (0.80, 1.10) 0.4380	-0.01 (-0.03, 0.01)*0.4116	
	No	61/ 430 (14.2)	72/ 438 (16.4)	0.83 (0.61, 1.12) 0.2208	0.78 (0.53, 1.14) 0.2007	-0.02 (-0.07, 0.03)*0.3565	
	Diuretics at baseline						0.7223
	Yes	388/2350 (16.5)	416/2345 (17.7)	0.92 (0.82, 1.04) 0.1862	0.90 (0.77, 1.05) 0.1693	-0.01 (-0.03, 0.01)*0.2636	
	No	33/ 275 (12.0)	35/ 280 (12.5)	1.00 (0.64, 1.54) 0.9827	1.01 (0.60, 1.69) 0.9809	-0.01 (-0.06, 0.05)*0.8574	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)							
	Overall	553/2801 (19.7)	634/2805 (22.6)	0.95 (0.89, 1.01) 0.1153	0.82 (0.70, 0.95) 0.0105	-0.03 (-0.05, -0.01)*0.0087	
	Age						0.3410
	<= median	278/1394 (19.9)	325/1471 (22.1)	0.98 (0.89, 1.07) 0.6166	0.85 (0.68, 1.06) 0.1411	-0.02 (-0.05, 0.01)*0.1574	
	> median	275/1407 (19.5)	309/1334 (23.2)	0.92 (0.85, 1.00) 0.0516	0.77 (0.62, 0.96) 0.0229	-0.04 (-0.07, -0.01)*0.0208	
	Gender						0.1750*
	Male	331/1630 (20.3)	352/1608 (21.9)	0.99 (0.91, 1.07) 0.7382	0.92 (0.75, 1.14) 0.4445	-0.02 (-0.04, 0.01)*0.2694	
	Female	222/1171 (19.0)	282/1197 (23.6)	0.80 (0.69, 0.94)*0.0064	0.70 (0.56, 0.89) 0.0031	-0.05 (-0.08, -0.01)*0.0061	
	Race						0.7423*
	White	383/2006 (19.1)	445/2032 (21.9)	0.96 (0.89, 1.04) 0.3574	0.86 (0.71, 1.03) 0.0985	-0.03 (-0.05, -0.00)*0.0270	
	Black or African	11/ 64 (17.2)	19/ 70 (27.1)	0.63 (0.33, 1.23)*0.1753	0.55 (0.20, 1.48) 0.2383	-0.10 (-0.24, 0.04)*0.1612	
	Asian	130/ 555 (23.4)	145/ 551 (26.3)	0.90 (0.79, 1.02) 0.0988	0.71 (0.51, 1.00) 0.0498	-0.03 (-0.08, 0.02)*0.2656	
	Other	29/ 176 (16.5)	25/ 152 (16.4)	1.00 (0.61, 1.63)*0.9942	0.94 (0.47, 1.91) 0.8745	0.00 (-0.08, 0.08)*0.9942	
	Geographic region						0.8026*
	Asia	123/ 536 (22.9)	142/ 536 (26.5)	0.90 (0.79, 1.02) 0.0915	0.68 (0.48, 0.96) 0.0299	-0.04 (-0.09, 0.02)*0.1782	
	Europe and Saudi Arabia	260/1341 (19.4)	297/1381 (21.5)	0.97 (0.90, 1.06) 0.5018	0.85 (0.68, 1.07) 0.1686	-0.02 (-0.05, 0.01)*0.1706	
	North America	77/ 393 (19.6)	95/ 376 (25.3)	0.92 (0.75, 1.13) 0.4298	0.82 (0.55, 1.21) 0.3167	-0.06 (-0.12, 0.00)*0.0590	
	Latin America	93/ 531 (17.5)	100/ 512 (19.5)	0.90 (0.69, 1.16)*0.4020	0.85 (0.59, 1.24) 0.3989	-0.02 (-0.07, 0.03)*0.4019	
	NYHA class at enrolment						0.3500
	II	402/2083 (19.3)	465/2165 (21.5)	0.94 (0.87, 1.01) 0.1127	0.83 (0.69, 0.99) 0.0432	-0.02 (-0.05, 0.00)*0.0778	
	III or IV	151/ 718 (21.0)	169/ 639 (26.4)	0.99 (0.88, 1.10) 0.8227	0.76 (0.56, 1.03) 0.0738	-0.05 (-0.10, -0.01)*0.0193	
	LVEF at enrolment						0.1605
	<= 49	205/ 959 (21.4)	210/ 950 (22.1)	1.03 (0.92, 1.15) 0.5835	0.92 (0.70, 1.19) 0.5118	-0.01 (-0.04, 0.03)*0.6995	
	50-59	200/1017 (19.7)	239/1009 (23.7)	0.93 (0.83, 1.03) 0.1705	0.80 (0.62, 1.03) 0.0774	-0.04 (-0.08, -0.00)*0.0279	
	>= 60	148/ 825 (17.9)	185/ 846 (21.9)	0.82 (0.68, 1.00)*0.0451	0.72 (0.53, 0.98) 0.0366	-0.04 (-0.08, -0.00)*0.0440	
	NT-proBNP at enrolment						0.9662
	<= median	265/1396 (19.0)	289/1409 (20.5)	0.96 (0.87, 1.05) 0.3389	0.87 (0.69, 1.09) 0.2139	-0.02 (-0.04, 0.01)*0.3092	
	> median	288/1405 (20.5)	345/1395 (24.7)	0.95 (0.87, 1.04) 0.3081	0.77 (0.62, 0.96) 0.0176	-0.04 (-0.07, -0.01)*0.0074	
	Type 2 Diabetes Medical History						0.2793
	Yes	257/1231 (20.9)	276/1243 (22.2)	0.98 (0.90, 1.08) 0.7164	0.92 (0.76, 1.12)*0.4222	-0.01 (-0.05, 0.02)*0.4220	
	No	296/1570 (18.9)	358/1562 (22.9)	0.92 (0.84, 1.00) 0.0624	0.78 (0.66, 0.93)*0.0052	-0.04 (-0.07, -0.01)*0.0051	
	Atrial fibrillation or flutter at enrolment ECG						0.9718
	Yes	233/1185 (19.7)	267/1188 (22.5)	0.95 (0.87, 1.05) 0.3257	0.83 (0.65, 1.06) 0.1346	-0.03 (-0.06, 0.00)*0.0928	
	No	320/1616 (19.8)	367/1617 (22.7)	0.95 (0.87, 1.03) 0.2177	0.80 (0.66, 0.99) 0.0358	-0.03 (-0.06, -0.00)*0.0441	
	BMI (kg/m2) at enrolment						0.4807
	< 30	325/1547 (21.0)	359/1541 (23.3)	0.97 (0.89, 1.05) 0.4244	0.86 (0.70, 1.06) 0.1504	-0.02 (-0.05, 0.01)*0.1257	
	>= 30	228/1253 (18.2)	275/1261 (21.8)	0.93 (0.84, 1.03) 0.1550	0.76 (0.60, 0.97) 0.0258	-0.04 (-0.07, -0.00)*0.0234	
	Baseline eGFR (mL/min/1.73m^2)						0.4536
	< 60	295/1338 (22.0)	334/1377 (24.3)	0.96 (0.88, 1.05) 0.3730	0.86 (0.69, 1.07) 0.1757	-0.02 (-0.05, 0.01)*0.1725	
	>= 60	258/1463 (17.6)	300/1427 (21.0)	0.93 (0.84, 1.03) 0.1590	0.77 (0.62, 0.97) 0.0244	-0.03 (-0.06, -0.01)*0.0210	

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Symptom Stability (LOCF)	SBP at randomisation						0.3756
	<= median	295/1405 (21.0)	337/1420 (23.7)	0.97 (0.89, 1.06) 0.5055	0.84 (0.68, 1.04) 0.1073	-0.03 (-0.06, 0.00)*0.0808	
	> median	258/1396 (18.5)	297/1385 (21.4)	0.86 (0.74, 1.00)*0.0510	0.79 (0.63, 1.00) 0.0482	-0.03 (-0.06, 0.00)*0.0505	
	LVEF at enrolment 2						0.0616
	<= 49	205/ 959 (21.4)	210/ 950 (22.1)	1.03 (0.92, 1.15) 0.5835	0.92 (0.70, 1.19) 0.5118	-0.01 (-0.04, 0.03)*0.6995	
	>= 50	348/1842 (18.9)	424/1855 (22.9)	0.91 (0.84, 0.98) 0.0164	0.77 (0.63, 0.93) 0.0076	-0.04 (-0.07, -0.01)*0.0030	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0418
	Yes	100/ 280 (35.7)	100/ 281 (35.6)	1.06 (0.92, 1.22) 0.4291	1.06 (0.68, 1.65) 0.7900	0.00 (-0.08, 0.08)*0.9749	
	No	453/2521 (18.0)	534/2524 (21.2)	0.92 (0.86, 0.99) 0.0272	0.79 (0.67, 0.93) 0.0053	-0.03 (-0.05, -0.01)*0.0043	
	MRAs at baseline						0.9032
	Yes	260/1216 (21.4)	283/1210 (23.4)	0.94 (0.85, 1.04) 0.2472	0.82 (0.65, 1.03) 0.0916	-0.02 (-0.05, 0.01)*0.2356	
	No	293/1585 (18.5)	351/1595 (22.0)	0.96 (0.89, 1.05) 0.3682	0.82 (0.66, 1.01) 0.0614	-0.04 (-0.06, -0.01)*0.0134	
	ACEi+ARB at baseline						0.8261
	Yes	394/2037 (19.3)	444/2059 (21.6)	0.96 (0.89, 1.03) 0.2436	0.83 (0.69, 1.00) 0.0483	-0.02 (-0.05, 0.00)*0.0778	
	No	159/ 764 (20.8)	190/ 746 (25.5)	0.93 (0.82, 1.05) 0.2355	0.78 (0.58, 1.04) 0.0858	-0.05 (-0.09, -0.00)*0.0317	
	ARNI at baseline						0.2964
	Yes	32/ 149 (21.5)	36/ 125 (28.8)	0.82 (0.61, 1.10) 0.1798	0.51 (0.26, 1.02) 0.0554	-0.07 (-0.18, 0.03)*0.1643	
	No	521/2652 (19.6)	598/2680 (22.3)	0.96 (0.90, 1.03) 0.2246	0.84 (0.72, 0.99) 0.0362	-0.03 (-0.05, -0.00)*0.0167	
	Beta Blocker at baseline						0.7322
	Yes	446/2327 (19.2)	521/2330 (22.4)	0.94 (0.87, 1.01) 0.0945	0.82 (0.69, 0.97) 0.0242	-0.03 (-0.06, -0.01)*0.0072	
	No	107/ 474 (22.6)	113/ 475 (23.8)	0.95 (0.75, 1.20)*0.6573	0.77 (0.52, 1.12) 0.1708	-0.01 (-0.07, 0.04)*0.6572	
	Diuretics at baseline						0.4979
	Yes	495/2500 (19.8)	567/2504 (22.6)	0.94 (0.88, 1.01) 0.0753	0.81 (0.69, 0.96) 0.0137	-0.03 (-0.05, -0.01)*0.0138	
	No	58/ 301 (19.3)	67/ 301 (22.3)	0.93 (0.76, 1.13) 0.4433	0.85 (0.53, 1.36) 0.4883	-0.03 (-0.09, 0.03)*0.3655	

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Total Symptom Score (LOCF)							
	Overall	254/2801 (9.1)	366/2805 (13.0)	0.70 (0.61, 0.82) <.0001	0.66 (0.56, 0.78) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Age						0.8454
	<= median	113/1394 (8.1)	171/1471 (11.6)	0.69 (0.55, 0.86) 0.0010	0.65 (0.51, 0.84) 0.0009	-0.04 (-0.06, -0.01)*0.0015	
	> median	141/1407 (10.0)	195/1334 (14.6)	0.71 (0.58, 0.86) 0.0007	0.66 (0.52, 0.83) 0.0005	-0.05 (-0.07, -0.02)*0.0003	
	Gender						0.5181
	Male	134/1630 (8.2)	197/1608 (12.3)	0.67 (0.55, 0.83) 0.0002	0.64 (0.50, 0.81) 0.0002	-0.04 (-0.06, -0.02)*0.0002	
	Female	120/1171 (10.2)	169/1197 (14.1)	0.74 (0.60, 0.92) 0.0070	0.69 (0.54, 0.89) 0.0042	-0.04 (-0.06, -0.01)*0.0039	
	Race						0.8125
	White	185/2006 (9.2)	274/2032 (13.5)	0.70 (0.59, 0.83) <.0001	0.65 (0.53, 0.80) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	Black or African	7/ 64 (10.9)	8/ 70 (11.4)	0.93 (0.36, 2.40) 0.8763	0.92 (0.31, 2.73) 0.8841	-0.00 (-0.11, 0.10)*0.9282	
	Asian	55/ 555 (9.9)	72/ 551 (13.1)	0.76 (0.54, 1.05) 0.0958	0.72 (0.50, 1.05) 0.0914	-0.03 (-0.07, 0.01)*0.0994	
	Other	7/ 176 (4.0)	12/ 152 (7.9)	0.49 (0.20, 1.21) 0.1206	0.45 (0.17, 1.19) 0.1089	-0.04 (-0.09, 0.01)*0.1374	
	Geographic region						0.8311
	Asia	52/ 536 (9.7)	71/ 536 (13.2)	0.73 (0.52, 1.02) 0.0683	0.70 (0.48, 1.02) 0.0648	-0.04 (-0.07, 0.00)*0.0682	
	Europe and Saudi Arabia	118/1341 (8.8)	181/1381 (13.1)	0.70 (0.56, 0.87) 0.0010	0.64 (0.50, 0.83) 0.0006	-0.04 (-0.07, -0.02)*0.0003	
	North America	43/ 393 (10.9)	51/ 376 (13.6)	0.80 (0.55, 1.17) 0.2468	0.77 (0.50, 1.19) 0.2429	-0.03 (-0.07, 0.02)*0.2677	
	Latin America	41/ 531 (7.7)	63/ 512 (12.3)	0.63 (0.43, 0.91) 0.0134	0.58 (0.38, 0.89) 0.0116	-0.05 (-0.08, -0.01)*0.0136	
	NYHA class at enrolment						0.0638
	II	201/2083 (9.6)	277/2165 (12.8)	0.75 (0.63, 0.89) 0.0009	0.71 (0.59, 0.87) 0.0007	-0.03 (-0.05, -0.01)*0.0011	
	III or IV	53/ 718 (7.4)	89/ 639 (13.9)	0.54 (0.39, 0.74) 0.0001	0.49 (0.34, 0.70) 0.0001	-0.07 (-0.10, -0.03)*<.0001	
	LVEF at enrolment						0.9198
	<= 49	76/ 959 (7.9)	101/ 950 (10.6)	0.74 (0.56, 0.98) 0.0340	0.71 (0.52, 0.97) 0.0317	-0.03 (-0.05, -0.00)*0.0414	
	50-59	97/1017 (9.5)	137/1009 (13.6)	0.71 (0.55, 0.90) 0.0046	0.66 (0.50, 0.87) 0.0032	-0.04 (-0.07, -0.01)*0.0044	
	>= 60	81/ 825 (9.8)	128/ 846 (15.1)	0.68 (0.52, 0.88) 0.0031	0.63 (0.47, 0.85) 0.0026	-0.05 (-0.08, -0.02)*0.0010	
	NT-proBNP at enrolment						0.4782
	<= median	131/1396 (9.4)	179/1409 (12.7)	0.74 (0.60, 0.91) 0.0052	0.70 (0.55, 0.90) 0.0044	-0.03 (-0.06, -0.01)*0.0050	
	> median	123/1405 (8.8)	187/1395 (13.4)	0.67 (0.54, 0.83) 0.0002	0.62 (0.48, 0.79) 0.0001	-0.05 (-0.07, -0.02)*<.0001	
	Type 2 Diabetes Medical History						0.2759
	Yes	107/1231 (8.7)	172/1243 (13.8)	0.64 (0.51, 0.80) <.0001	0.59 (0.46, 0.77)*<.0001	-0.05 (-0.08, -0.03)*<.0001	
	No	147/1570 (9.4)	194/1562 (12.4)	0.76 (0.62, 0.92) 0.0062	0.73 (0.58, 0.91)*0.0062	-0.03 (-0.05, -0.01)*0.0060	
	Atrial fibrillation or flutter at enrolment ECG						0.4088
	Yes	109/1185 (9.2)	167/1188 (14.1)	0.65 (0.52, 0.82) 0.0002	0.60 (0.47, 0.78) 0.0002	-0.05 (-0.07, -0.02)*0.0002	
	No	145/1616 (9.0)	199/1617 (12.3)	0.74 (0.61, 0.91) 0.0034	0.70 (0.56, 0.88) 0.0026	-0.03 (-0.05, -0.01)*0.0021	
	BMI (kg/m2) at enrolment						0.6230
	< 30	141/1547 (9.1)	194/1541 (12.6)	0.73 (0.60, 0.89) 0.0022	0.69 (0.55, 0.87) 0.0018	-0.03 (-0.06, -0.01)*0.0019	
	>= 30	113/1253 (9.0)	172/1261 (13.6)	0.67 (0.54, 0.84) 0.0005	0.62 (0.48, 0.81) 0.0003	-0.05 (-0.07, -0.02)*0.0002	
	Baseline eGFR (mL/min/1.73m^2)						0.9303
	< 60	139/1338 (10.4)	205/1377 (14.9)	0.71 (0.58, 0.87) 0.0007	0.66 (0.52, 0.83) 0.0005	-0.04 (-0.07, -0.02)*0.0004	
	>= 60	115/1463 (7.9)	160/1427 (11.2)	0.70 (0.56, 0.88) 0.0022	0.67 (0.52, 0.86) 0.0020	-0.03 (-0.05, -0.01)*0.0021	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at month 8 (LOCF) without ceiling correction
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.8524
	<= median	132/1405 (9.4)	200/1420 (14.1)	0.69 (0.56, 0.85) 0.0005	0.65 (0.51, 0.82) 0.0003	-0.05 (-0.07, -0.02)*0.0001	
	> median	122/1396 (8.7)	166/1385 (12.0)	0.71 (0.57, 0.89) 0.0025	0.68 (0.53, 0.87) 0.0022	-0.03 (-0.06, -0.01)*0.0049	
	LVEF at enrolment 2						0.7225
	<= 49	76/ 959 (7.9)	101/ 950 (10.6)	0.74 (0.56, 0.98) 0.0340	0.71 (0.52, 0.97) 0.0317	-0.03 (-0.05, -0.00)*0.0414	
	>= 50	178/1842 (9.7)	265/1855 (14.3)	0.69 (0.58, 0.83) <.0001	0.64 (0.52, 0.79) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2265
	Yes	16/ 280 (5.7)	30/ 281 (10.7)	0.54 (0.30, 0.96)*0.0358	0.42 (0.22, 0.81) 0.0101	-0.05 (-0.09, -0.00)*0.0314	
	No	238/2521 (9.4)	336/2524 (13.3)	0.72 (0.62, 0.84) <.0001	0.68 (0.57, 0.81) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	MRAs at baseline						0.1668
	Yes	98/1216 (8.1)	160/1210 (13.2)	0.62 (0.49, 0.78) <.0001	0.57 (0.44, 0.75) <.0001	-0.05 (-0.08, -0.03)*<.0001	
	No	156/1585 (9.8)	206/1595 (12.9)	0.77 (0.63, 0.93) 0.0071	0.73 (0.58, 0.91) 0.0059	-0.03 (-0.05, -0.01)*0.0063	
	ACEi+ARB at baseline						0.0116
	Yes	163/2037 (8.0)	272/2059 (13.2)	0.62 (0.52, 0.74) <.0001	0.57 (0.46, 0.70) <.0001	-0.05 (-0.07, -0.03)*<.0001	
	No	91/ 764 (11.9)	94/ 746 (12.6)	0.94 (0.72, 1.23) 0.6535	0.93 (0.68, 1.26) 0.6294	-0.01 (-0.04, 0.03)*0.6829	
	ARNI at baseline						0.3792
	Yes	14/ 149 (9.4)	11/ 125 (8.8)	1.01 (0.47, 2.14) 0.9867	1.03 (0.44, 2.40) 0.9544	0.01 (-0.06, 0.07)*0.8642	
	No	240/2652 (9.0)	355/2680 (13.2)	0.70 (0.60, 0.81) <.0001	0.65 (0.55, 0.78) <.0001	-0.04 (-0.06, -0.03)*<.0001	
	Beta Blocker at baseline						0.6385
	Yes	212/2327 (9.1)	304/2330 (13.0)	0.71 (0.61, 0.84) <.0001	0.67 (0.56, 0.81) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	42/ 474 (8.9)	62/ 475 (13.1)	0.65 (0.45, 0.94) 0.0204	0.61 (0.40, 0.92) 0.0196	-0.04 (-0.08, -0.00)*0.0383	
	Diuretics at baseline						0.7670
	Yes	230/2500 (9.2)	331/2504 (13.2)	0.70 (0.60, 0.81) <.0001	0.65 (0.55, 0.78) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	24/ 301 (8.0)	35/ 301 (11.6)	0.75 (0.46, 1.22) 0.2499	0.70 (0.40, 1.22) 0.2090	-0.04 (-0.08, 0.01)*0.1309	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	338/2842 (11.9)	408/2837 (14.4)	0.83 (0.73, 0.95) 0.0072	0.80 (0.69, 0.94) 0.0065	-0.02 (-0.04, -0.01)*0.0055	
	Age						0.4243
	<= median	139/1415 (9.8)	184/1482 (12.4)	0.78 (0.64, 0.96) 0.0186	0.75 (0.59, 0.95) 0.0178	-0.03 (-0.05, -0.00)*0.0262	
	> median	199/1427 (13.9)	224/1355 (16.5)	0.87 (0.73, 1.03) 0.1157	0.84 (0.68, 1.04) 0.1014	-0.03 (-0.05, 0.00)*0.0579	
	Gender						0.7495
	Male	194/1656 (11.7)	234/1625 (14.4)	0.82 (0.69, 0.98) 0.0258	0.79 (0.64, 0.97) 0.0233	-0.03 (-0.05, -0.00)*0.0224	
	Female	144/1186 (12.1)	174/1212 (14.4)	0.86 (0.70, 1.05) 0.1338	0.83 (0.65, 1.06) 0.1351	-0.02 (-0.05, 0.00)*0.1094	
	Race						0.9414
	White	251/2039 (12.3)	306/2058 (14.9)	0.84 (0.72, 0.98) 0.0257	0.81 (0.68, 0.98) 0.0266	-0.03 (-0.05, -0.00)*0.0168	
	Black or African	8/ 67 (11.9)	8/ 71 (11.3)	1.06 (0.43, 2.64) 0.8944	1.03 (0.36, 2.95) 0.9621	0.01 (-0.10, 0.11)*0.9019	
	Asian	66/ 558 (11.8)	81/ 555 (14.6)	0.81 (0.60, 1.10) 0.1707	0.79 (0.55, 1.11) 0.1736	-0.03 (-0.07, 0.01) 0.1962	
	Other	13/ 178 (7.3)	13/ 153 (8.5)	0.86 (0.42, 1.76) 0.6702	0.83 (0.36, 1.89) 0.6522	-0.01 (-0.07, 0.05)*0.6889	
	Geographic region						0.8246
	Asia	62/ 539 (11.5)	76/ 538 (14.1)	0.81 (0.59, 1.11) 0.1971	0.79 (0.55, 1.13) 0.1979	-0.03 (-0.07, 0.01) 0.2049	
	Europe and Saudi Arabia	161/1365 (11.8)	212/1394 (15.2)	0.81 (0.67, 0.97) 0.0236	0.75 (0.60, 0.95) 0.0151	-0.03 (-0.06, -0.01)*0.0086	
	North America	58/ 398 (14.6)	60/ 387 (15.5)	0.92 (0.67, 1.28) 0.6351	0.92 (0.62, 1.37) 0.6873	-0.01 (-0.06, 0.04)*0.7153	
	Latin America	57/ 540 (10.6)	60/ 518 (11.6)	0.90 (0.64, 1.26) 0.5393	0.89 (0.60, 1.31) 0.5432	-0.01 (-0.05, 0.03)*0.5945	
	NYHA class at enrolment						0.5465
	II	251/2113 (11.9)	319/2187 (14.6)	0.81 (0.70, 0.94) 0.0068	0.78 (0.65, 0.93) 0.0061	-0.03 (-0.05, -0.01)*0.0087	
	III or IV	87/ 729 (11.9)	89/ 649 (13.7)	0.89 (0.69, 1.17) 0.4065	0.86 (0.62, 1.20) 0.3838	-0.02 (-0.05, 0.02)*0.3248	
	LVEF at enrolment						0.5454
	<= 49	113/ 980 (11.5)	123/ 963 (12.8)	0.89 (0.70, 1.12) 0.3227	0.86 (0.65, 1.13) 0.2884	-0.01 (-0.04, 0.02)*0.4022	
	50-59	142/1029 (13.8)	163/1017 (16.0)	0.86 (0.70, 1.05) 0.1368	0.84 (0.66, 1.08) 0.1709	-0.02 (-0.05, 0.01)*0.1571	
	>= 60	83/ 833 (10.0)	122/ 857 (14.2)	0.74 (0.57, 0.95) 0.0200	0.69 (0.51, 0.94) 0.0167	-0.04 (-0.07, -0.01)*0.0069	
	NT-proBNP at enrolment						0.6568
	<= median	170/1418 (12.0)	197/1421 (13.9)	0.86 (0.71, 1.04) 0.1144	0.84 (0.67, 1.05) 0.1248	-0.02 (-0.04, 0.01)*0.1364	
	> median	168/1424 (11.8)	211/1415 (14.9)	0.81 (0.67, 0.98) 0.0272	0.77 (0.62, 0.96) 0.0212	-0.03 (-0.06, -0.01)*0.0146	
	Type 2 Diabetes Medical History						0.2702
	Yes	154/1250 (12.3)	202/1260 (16.0)	0.77 (0.64, 0.94) 0.0082	0.74 (0.59, 0.92)*0.0079	-0.04 (-0.06, -0.01)*0.0076	
	No	184/1592 (11.6)	206/1577 (13.1)	0.90 (0.75, 1.08) 0.2455	0.87 (0.70, 1.08)*0.1975	-0.02 (-0.04, 0.01)*0.1972	
	Atrial fibrillation or flutter at enrolment ECG						0.6561
	Yes	134/1199 (11.2)	167/1199 (13.9)	0.80 (0.65, 0.99) 0.0408	0.77 (0.60, 0.99) 0.0402	-0.03 (-0.05, -0.00)*0.0418	
	No	204/1643 (12.4)	241/1638 (14.7)	0.85 (0.72, 1.01) 0.0709	0.83 (0.67, 1.01) 0.0641	-0.02 (-0.05, 0.00)*0.0546	
	BMI (kg/m2) at enrolment						0.7540
	< 30	188/1571 (12.0)	221/1559 (14.2)	0.85 (0.71, 1.02) 0.0803	0.82 (0.67, 1.02) 0.0695	-0.02 (-0.05, 0.00)*0.0667	
	>= 30	150/1270 (11.8)	186/1275 (14.6)	0.82 (0.67, 0.99) 0.0423	0.79 (0.62, 1.00) 0.0497	-0.03 (-0.05, -0.00)*0.0383	
	Baseline eGFR (mL/min/1.73m^2)						0.1269
	< 60	185/1359 (13.6)	208/1396 (14.9)	0.92 (0.77, 1.11) 0.3899	0.90 (0.73, 1.12) 0.3615	-0.01 (-0.04, 0.01)*0.3339	
	>= 60	153/1483 (10.3)	200/1440 (13.9)	0.75 (0.62, 0.91) 0.0037	0.71 (0.57, 0.90) 0.0036	-0.04 (-0.06, -0.01)*0.0031	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)	SBP at randomisation						0.3331
	<= median	161/1424 (11.3)	215/1439 (14.9)	0.78 (0.64, 0.94) 0.0088	0.74 (0.60, 0.93) 0.0087	-0.04 (-0.06, -0.01)*0.0039	
	> median	177/1418 (12.5)	193/1398 (13.8)	0.89 (0.74, 1.07) 0.2122	0.86 (0.69, 1.08) 0.1972	-0.01 (-0.04, 0.01)*0.2988	
	LVEF at enrolment 2						0.5477
	<= 49	113/ 980 (11.5)	123/ 963 (12.8)	0.89 (0.70, 1.12) 0.3227	0.86 (0.65, 1.13) 0.2884	-0.01 (-0.04, 0.02)*0.4022	
	>= 50	225/1862 (12.1)	285/1874 (15.2)	0.81 (0.69, 0.95) 0.0112	0.78 (0.65, 0.95) 0.0116	-0.03 (-0.05, -0.01)*0.0054	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7103
	Yes	18/ 283 (6.4)	23/ 286 (8.0)	0.79 (0.44, 1.43)*0.4393	0.67 (0.35, 1.30) 0.2400	-0.02 (-0.06, 0.03)*0.4375	
	No	320/2559 (12.5)	385/2551 (15.1)	0.84 (0.73, 0.96) 0.0121	0.81 (0.69, 0.95) 0.0109	-0.03 (-0.04, -0.01)*0.0073	
	MRAs at baseline						0.3286
	Yes	141/1227 (11.5)	182/1224 (14.9)	0.77 (0.63, 0.94) 0.0120	0.74 (0.58, 0.94) 0.0133	-0.03 (-0.06, -0.01)*0.0133	
	No	197/1615 (12.2)	226/1613 (14.0)	0.88 (0.74, 1.05) 0.1672	0.86 (0.70, 1.05) 0.1436	-0.02 (-0.04, 0.01)*0.1268	
	ACEi+ARB at baseline						0.5067
	Yes	234/2065 (11.3)	295/2077 (14.2)	0.81 (0.69, 0.95) 0.0090	0.78 (0.64, 0.94) 0.0079	-0.03 (-0.05, -0.01)*0.0056	
	No	104/ 777 (13.4)	113/ 760 (14.9)	0.90 (0.70, 1.15) 0.3943	0.88 (0.66, 1.18) 0.3884	-0.02 (-0.05, 0.02) 0.3291	
	ARNI at baseline						0.4838
	Yes	18/ 153 (11.8)	13/ 126 (10.3)	1.05 (0.53, 2.09) 0.8851	1.07 (0.50, 2.31) 0.8656	0.02 (-0.06, 0.09) 0.6799	
	No	320/2689 (11.9)	395/2711 (14.6)	0.83 (0.72, 0.95) 0.0068	0.80 (0.68, 0.94) 0.0059	-0.03 (-0.04, -0.01)*0.0038	
	Beta Blocker at baseline						0.9475
	Yes	283/2360 (12.0)	345/2356 (14.6)	0.84 (0.73, 0.97) 0.0157	0.80 (0.68, 0.95) 0.0125	-0.03 (-0.05, -0.01)*0.0073	
	No	55/ 482 (11.4)	63/ 481 (13.1)	0.84 (0.60, 1.17) 0.2958	0.82 (0.56, 1.21) 0.3211	-0.02 (-0.06, 0.02)*0.4246	
	Diuretics at baseline						0.7309
	Yes	314/2536 (12.4)	375/2531 (14.8)	0.84 (0.73, 0.96) 0.0118	0.81 (0.69, 0.95) 0.0109	-0.02 (-0.04, -0.01)*0.0114	
	No	24/ 306 (7.8)	33/ 306 (10.8)	0.77 (0.47, 1.26) 0.2892	0.73 (0.42, 1.27) 0.2653	-0.03 (-0.08, 0.02)*0.2101	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	321/2842 (11.3)	380/2837 (13.4)	0.85 (0.74, 0.97) 0.0195	0.82 (0.70, 0.97) 0.0185	-0.02 (-0.04, -0.00)*0.0161	
	Age						0.5897
	<= median	129/1415 (9.1)	165/1482 (11.1)	0.81 (0.65, 1.00) 0.0540	0.78 (0.61, 1.00) 0.0532	-0.02 (-0.04, 0.00)*0.0716	
	> median	192/1427 (13.5)	215/1355 (15.9)	0.87 (0.73, 1.04) 0.1280	0.84 (0.68, 1.05) 0.1200	-0.02 (-0.05, 0.00)*0.0723	
	Gender						0.3868
	Male	195/1656 (11.8)	215/1625 (13.2)	0.89 (0.75, 1.07) 0.2142	0.88 (0.71, 1.08) 0.2158	-0.01 (-0.04, 0.01)*0.2076	
	Female	126/1186 (10.6)	165/1212 (13.6)	0.79 (0.64, 0.98) 0.0319	0.76 (0.59, 0.97) 0.0305	-0.03 (-0.06, -0.00)*0.0247	
	Race						0.4966
	White	228/2039 (11.2)	287/2058 (13.9)	0.82 (0.70, 0.96) 0.0154	0.79 (0.65, 0.95) 0.0137	-0.03 (-0.05, -0.01)*0.0076	
	Black or African	10/ 67 (14.9)	8/ 71 (11.3)	1.36 (0.59, 3.14) 0.4734	1.36 (0.49, 3.80) 0.5595	0.04 (-0.08, 0.15)*0.5245	
	Asian	68/ 558 (12.2)	75/ 555 (13.5)	0.90 (0.66, 1.22) 0.5055	0.89 (0.62, 1.26) 0.5047	-0.01 (-0.05, 0.03) 0.4967	
	Other	15/ 178 (8.4)	10/ 153 (6.5)	1.24 (0.59, 2.62) 0.5727	1.29 (0.55, 3.06) 0.5568	0.02 (-0.04, 0.08)*0.5123	
	Geographic region						0.6850
	Asia	63/ 539 (11.7)	70/ 538 (13.0)	0.90 (0.65, 1.24) 0.5085	0.88 (0.61, 1.27) 0.5083	-0.01 (-0.05, 0.03) 0.5097	
	Europe and Saudi Arabia	148/1365 (10.8)	199/1394 (14.3)	0.80 (0.66, 0.97) 0.0204	0.74 (0.59, 0.94) 0.0136	-0.03 (-0.06, -0.01)*0.0064	
	North America	55/ 398 (13.8)	54/ 387 (14.0)	0.96 (0.69, 1.35) 0.8317	0.97 (0.64, 1.47) 0.8842	-0.00 (-0.05, 0.05)*0.9566	
	Latin America	55/ 540 (10.2)	57/ 518 (11.0)	0.93 (0.66, 1.30) 0.6672	0.91 (0.61, 1.36) 0.6352	-0.01 (-0.05, 0.03)*0.6654	
	NYHA class at enrolment						0.3764
	II	233/2113 (11.0)	294/2187 (13.4)	0.81 (0.69, 0.95) 0.0112	0.78 (0.65, 0.94) 0.0102	-0.02 (-0.04, -0.00)*0.0155	
	III or IV	88/ 729 (12.1)	86/ 649 (13.3)	0.91 (0.69, 1.20)*0.5105	0.92 (0.66, 1.28) 0.6157	-0.01 (-0.05, 0.02)*0.5113	
	LVEF at enrolment						0.8098
	<= 49	103/ 980 (10.5)	109/ 963 (11.3)	0.90 (0.70, 1.16) 0.4221	0.88 (0.66, 1.18) 0.3871	-0.01 (-0.04, 0.02)*0.5677	
	50-59	134/1029 (13.0)	161/1017 (15.8)	0.82 (0.67, 1.01) 0.0679	0.80 (0.62, 1.03) 0.0833	-0.03 (-0.06, 0.00)*0.0705	
	>= 60	84/ 833 (10.1)	110/ 857 (12.8)	0.82 (0.63, 1.07) 0.1410	0.79 (0.58, 1.07) 0.1283	-0.03 (-0.06, 0.00)*0.0754	
	NT-proBNP at enrolment						0.6549
	<= median	152/1418 (10.7)	184/1421 (12.9)	0.82 (0.67, 1.00) 0.0552	0.80 (0.64, 1.01) 0.0615	-0.02 (-0.05, 0.00)*0.0658	
	> median	169/1424 (11.9)	196/1415 (13.9)	0.88 (0.73, 1.06) 0.1746	0.85 (0.68, 1.06) 0.1455	-0.02 (-0.04, 0.00)*0.1143	
	Type 2 Diabetes Medical History						0.8945
	Yes	145/1250 (11.6)	175/1260 (13.9)	0.84 (0.69, 1.03) 0.0985	0.81 (0.64, 1.03)*0.0860	-0.02 (-0.05, 0.00)*0.0853	
	No	176/1592 (11.1)	205/1577 (13.0)	0.86 (0.71, 1.04) 0.1106	0.83 (0.67, 1.03)*0.0928	-0.02 (-0.04, 0.00)*0.0924	
	Atrial fibrillation or flutter at enrolment ECG						0.5850
	Yes	130/1199 (10.8)	147/1199 (12.3)	0.89 (0.72, 1.11) 0.2976	0.87 (0.67, 1.12) 0.2832	-0.01 (-0.04, 0.01)*0.2773	
	No	191/1643 (11.6)	233/1638 (14.2)	0.82 (0.69, 0.98) 0.0299	0.79 (0.64, 0.98) 0.0298	-0.03 (-0.05, -0.00)*0.0264	
	BMI (kg/m2) at enrolment						0.4964
	< 30	175/1571 (11.1)	215/1559 (13.8)	0.82 (0.68, 0.98) 0.0318	0.78 (0.63, 0.97) 0.0275	-0.03 (-0.05, -0.00)*0.0247	
	>= 30	146/1270 (11.5)	164/1275 (12.9)	0.90 (0.73, 1.10) 0.3005	0.88 (0.69, 1.13) 0.3201	-0.01 (-0.04, 0.01)*0.2917	
	Baseline eGFR (mL/min/1.73m^2)						0.1951
	< 60	179/1359 (13.2)	200/1396 (14.3)	0.93 (0.77, 1.11) 0.4175	0.91 (0.73, 1.13) 0.3970	-0.01 (-0.04, 0.01)*0.3785	
	>= 60	142/1483 (9.6)	180/1440 (12.5)	0.77 (0.63, 0.95) 0.0131	0.74 (0.58, 0.94) 0.0127	-0.03 (-0.05, -0.01)*0.0116	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)	SBP at randomisation						0.9978
	<= median	155/1424 (10.9)	189/1439 (13.1)	0.85 (0.70, 1.03) 0.0963	0.83 (0.66, 1.04) 0.1108	-0.02 (-0.05, 0.00)*0.0639	
	> median	166/1418 (11.7)	191/1398 (13.7)	0.85 (0.70, 1.02) 0.0871	0.81 (0.64, 1.02) 0.0672	-0.02 (-0.04, 0.01)*0.1189	
	LVEF at enrolment 2						0.5413
	<= 49	103/ 980 (10.5)	109/ 963 (11.3)	0.90 (0.70, 1.16) 0.4221	0.88 (0.66, 1.18) 0.3871	-0.01 (-0.04, 0.02)*0.5677	
	>= 50	218/1862 (11.7)	271/1874 (14.5)	0.83 (0.70, 0.97) 0.0233	0.80 (0.66, 0.97) 0.0246	-0.03 (-0.05, -0.01)*0.0125	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4823
	Yes	17/ 283 (6.0)	24/ 286 (8.4)	0.72 (0.39, 1.30)*0.2742	0.66 (0.34, 1.28) 0.2189	-0.02 (-0.07, 0.02)*0.2705	
	No	304/2559 (11.9)	356/2551 (14.0)	0.86 (0.75, 0.99) 0.0363	0.84 (0.71, 0.99) 0.0358	-0.02 (-0.04, -0.00)*0.0269	
	MRAs at baseline						0.6062
	Yes	137/1227 (11.2)	167/1224 (13.6)	0.82 (0.66, 1.00) 0.0555	0.79 (0.62, 1.01) 0.0631	-0.02 (-0.05, 0.00)*0.0626	
	No	184/1615 (11.4)	213/1613 (13.2)	0.88 (0.73, 1.05) 0.1552	0.85 (0.68, 1.05) 0.1333	-0.02 (-0.04, 0.00)*0.1169	
	ACEi+ARB at baseline						0.0857
	Yes	214/2065 (10.4)	278/2077 (13.4)	0.78 (0.67, 0.92) 0.0037	0.75 (0.62, 0.91) 0.0031	-0.03 (-0.05, -0.01)*0.0026	
	No	107/ 777 (13.8)	102/ 760 (13.4)	1.03 (0.80, 1.32) 0.8375	1.03 (0.77, 1.39) 0.8296	0.00 (-0.03, 0.04)*0.8414	
	ARNI at baseline						0.5269
	Yes	14/ 153 (9.2)	10/ 126 (7.9)	1.11 (0.51, 2.44) 0.7904	1.13 (0.48, 2.67) 0.7831	0.01 (-0.05, 0.08)*0.7172	
	No	307/2689 (11.4)	370/2711 (13.6)	0.85 (0.74, 0.97) 0.0195	0.82 (0.70, 0.97) 0.0177	-0.02 (-0.04, -0.00)*0.0132	
	Beta Blocker at baseline						0.6628
	Yes	272/2360 (11.5)	322/2356 (13.7)	0.86 (0.74, 1.00) 0.0511	0.83 (0.70, 0.99) 0.0434	-0.02 (-0.04, -0.00)*0.0266	
	No	49/ 482 (10.2)	58/ 481 (12.1)	0.80 (0.56, 1.14) 0.2097	0.78 (0.52, 1.17) 0.2346	-0.02 (-0.06, 0.02)*0.3500	
	Diuretics at baseline						0.3227
	Yes	293/2536 (11.6)	353/2531 (13.9)	0.83 (0.72, 0.96) 0.0108	0.80 (0.68, 0.95) 0.0098	-0.02 (-0.04, -0.01)*0.0106	
	No	28/ 306 (9.2)	27/ 306 (8.8)	1.08 (0.65, 1.77) 0.7710	1.10 (0.63, 1.92) 0.7492	0.00 (-0.04, 0.05)*0.8876	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Physical Limitation (LOCF)							
	Overall	514/2792 (18.4)	579/2792 (20.7)	0.90 (0.81, 1.00) 0.0417	0.87 (0.76, 1.00) 0.0475	-0.02 (-0.04, -0.00)*0.0283	
	Age						0.5391
	<= median	219/1403 (15.6)	263/1469 (17.9)	0.86 (0.73, 1.01) 0.0659	0.83 (0.68, 1.02) 0.0744	-0.02 (-0.05, 0.00)*0.0995	
	> median	295/1389 (21.2)	316/1323 (23.9)	0.92 (0.81, 1.05) 0.2337	0.89 (0.74, 1.08) 0.2406	-0.03 (-0.06, 0.01)*0.0993	
	Gender						0.1332
	Male	321/1638 (19.6)	330/1602 (20.6)	0.96 (0.84, 1.10) 0.5259	0.94 (0.79, 1.12) 0.5167	-0.01 (-0.04, 0.02)*0.4767	
	Female	193/1154 (16.7)	249/1190 (20.9)	0.82 (0.69, 0.96) 0.0157	0.78 (0.63, 0.97) 0.0256	-0.04 (-0.07, -0.01)*0.0092	
	Race						0.8616
	White	391/2004 (19.5)	443/2025 (21.9)	0.91 (0.81, 1.02) 0.1065	0.88 (0.75, 1.03) 0.1238	-0.02 (-0.05, 0.00)*0.0637	
	Black or African	16/ 66 (24.2)	18/ 68 (26.5)	0.93 (0.55, 1.59) 0.7998	0.84 (0.36, 1.93) 0.6825	-0.02 (-0.17, 0.12)*0.7668	
	Asian	88/ 551 (16.0)	104/ 550 (18.9)	0.85 (0.66, 1.10) 0.2087	0.82 (0.60, 1.12) 0.2111	-0.03 (-0.07, 0.02) 0.2163	
	Other	19/ 171 (11.1)	14/ 149 (9.4)	1.18 (0.61, 2.28)*0.6156	1.15 (0.54, 2.47) 0.7129	0.02 (-0.05, 0.08)*0.6129	
	Geographic region						0.3610
	Asia	83/ 533 (15.6)	97/ 533 (18.2)	0.86 (0.66, 1.12) 0.2665	0.83 (0.60, 1.15) 0.2719	-0.02 (-0.07, 0.02) 0.2869	
	Europe and Saudi Arabia	253/1347 (18.8)	298/1373 (21.7)	0.88 (0.77, 1.02) 0.0923	0.85 (0.70, 1.03) 0.1013	-0.03 (-0.06, 0.00)*0.0577	
	North America	88/ 391 (22.5)	104/ 375 (27.7)	0.82 (0.65, 1.04) 0.0998	0.76 (0.54, 1.07) 0.1225	-0.05 (-0.11, 0.01)*0.0951	
	Latin America	90/ 521 (17.3)	80/ 511 (15.7)	1.12 (0.86, 1.45) 0.4199	1.13 (0.80, 1.58) 0.4932	0.02 (-0.03, 0.06)*0.4830	
	NYHA class at enrolment						0.7143
	II	383/2077 (18.4)	441/2159 (20.4)	0.90 (0.80, 1.02) 0.0947	0.88 (0.75, 1.03) 0.1066	-0.02 (-0.04, 0.00)*0.1022	
	III or IV	131/ 715 (18.3)	137/ 632 (21.7)	0.87 (0.71, 1.06) 0.1638	0.82 (0.62, 1.09) 0.1710	-0.03 (-0.08, 0.01)*0.1248	
	LVEF at enrolment						0.3713
	<= 49	186/ 967 (19.2)	180/ 952 (18.9)	0.99 (0.83, 1.19) 0.9284	0.99 (0.78, 1.24) 0.9048	0.00 (-0.03, 0.04)*0.8553	
	50-59	189/1013 (18.7)	226/ 998 (22.6)	0.84 (0.71, 0.99) 0.0342	0.80 (0.64, 1.00) 0.0550	-0.04 (-0.08, -0.00)*0.0270	
	>= 60	139/ 812 (17.1)	173/ 842 (20.5)	0.88 (0.72, 1.07) 0.1881	0.84 (0.65, 1.08) 0.1669	-0.03 (-0.07, 0.00)*0.0742	
	NT-proBNP at enrolment						0.2327
	<= median	241/1394 (17.3)	290/1402 (20.7)	0.84 (0.72, 0.98) 0.0240	0.80 (0.66, 0.97) 0.0245	-0.03 (-0.06, -0.00)*0.0219	
	> median	273/1398 (19.5)	289/1389 (20.8)	0.95 (0.83, 1.10) 0.5288	0.95 (0.78, 1.14) 0.5682	-0.01 (-0.04, 0.02)*0.4003	
	Type 2 Diabetes Medical History						0.6307
	Yes	236/1232 (19.2)	269/1237 (21.7)	0.87 (0.75, 1.02) 0.0821	0.85 (0.70, 1.04)*0.1108	-0.03 (-0.06, 0.01)*0.1104	
	No	278/1560 (17.8)	310/1555 (19.9)	0.92 (0.80, 1.06) 0.2518	0.87 (0.73, 1.04)*0.1316	-0.02 (-0.05, 0.01)*0.1313	
	Atrial fibrillation or flutter at enrolment ECG						0.7819
	Yes	220/1178 (18.7)	241/1175 (20.5)	0.91 (0.78, 1.07) 0.2612	0.90 (0.73, 1.10) 0.2999	-0.02 (-0.05, 0.01)*0.2621	
	No	294/1614 (18.2)	338/1617 (20.9)	0.89 (0.77, 1.02) 0.0807	0.85 (0.71, 1.02) 0.0822	-0.03 (-0.05, 0.00)*0.0540	
	BMI (kg/m2) at enrolment						0.2948
	< 30	268/1547 (17.3)	316/1535 (20.6)	0.85 (0.74, 0.99) 0.0312	0.81 (0.67, 0.97) 0.0247	-0.03 (-0.06, -0.00)*0.0208	
	>= 30	246/1244 (19.8)	263/1254 (21.0)	0.96 (0.82, 1.11) 0.5515	0.96 (0.79, 1.18) 0.6973	-0.01 (-0.04, 0.02)*0.4573	
	Baseline eGFR (mL/min/1.73m^2)						0.7007
	< 60	267/1328 (20.1)	299/1367 (21.9)	0.92 (0.80, 1.06) 0.2465	0.91 (0.75, 1.10) 0.3236	-0.02 (-0.05, 0.01)*0.2598	
	>= 60	247/1464 (16.9)	280/1424 (19.7)	0.88 (0.76, 1.02) 0.0951	0.84 (0.70, 1.02) 0.0838	-0.03 (-0.06, 0.00)*0.0522	

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Physical Limitation (LOCF)	SBP at randomisation						0.4945
	<= median	252/1396 (18.1)	284/1414 (20.1)	0.92 (0.80, 1.07) 0.2980	0.91 (0.75, 1.10) 0.3429	-0.02 (-0.05, 0.01)*0.1699	
	> median	262/1396 (18.8)	295/1378 (21.4)	0.86 (0.75, 1.00) 0.0454	0.82 (0.68, 0.99) 0.0431	-0.03 (-0.06, 0.00)*0.0826	
	LVEF at enrolment 2						0.1852
	<= 49	186/ 967 (19.2)	180/ 952 (18.9)	0.99 (0.83, 1.19) 0.9284	0.99 (0.78, 1.24) 0.9048	0.00 (-0.03, 0.04)*0.8553	
	>= 50	328/1825 (18.0)	399/1840 (21.7)	0.85 (0.75, 0.97) 0.0159	0.82 (0.69, 0.97) 0.0199	-0.04 (-0.06, -0.01)*0.0048	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4539
	Yes	40/ 273 (14.7)	51/ 277 (18.4)	0.79 (0.55, 1.15) 0.2241	0.75 (0.47, 1.19) 0.2262	-0.04 (-0.10, 0.02)*0.2346	
	No	474/2519 (18.8)	528/2515 (21.0)	0.91 (0.82, 1.01) 0.0815	0.89 (0.77, 1.02) 0.0926	-0.02 (-0.04, 0.00)*0.0530	
	MRAs at baseline						0.4737
	Yes	228/1200 (19.0)	265/1208 (21.9)	0.86 (0.74, 1.01) 0.0609	0.83 (0.68, 1.02) 0.0736	-0.03 (-0.06, 0.00)*0.0739	
	No	286/1592 (18.0)	314/1584 (19.8)	0.93 (0.81, 1.07) 0.3060	0.91 (0.76, 1.09) 0.3062	-0.02 (-0.05, 0.01)*0.1809	
	ACEi+ARB at baseline						0.0791
	Yes	358/2029 (17.6)	433/2047 (21.2)	0.85 (0.75, 0.96) 0.0085	0.81 (0.69, 0.95) 0.0094	-0.04 (-0.06, -0.01)*0.0046	
	No	156/ 763 (20.4)	146/ 745 (19.6)	1.05 (0.86, 1.28) 0.6631	1.06 (0.82, 1.37) 0.6559	0.01 (-0.03, 0.05) 0.5355	
	ARNI at baseline						0.6138
	Yes	28/ 150 (18.7)	22/ 123 (17.9)	0.96 (0.58, 1.59) 0.8796	0.95 (0.50, 1.78) 0.8620	-0.01 (-0.10, 0.08) 0.8122	
	No	486/2642 (18.4)	557/2669 (20.9)	0.90 (0.81, 1.00) 0.0414	0.87 (0.76, 1.00) 0.0497	-0.02 (-0.05, -0.00)*0.0232	
	Beta Blocker at baseline						0.4525
	Yes	425/2323 (18.3)	491/2321 (21.2)	0.88 (0.79, 0.99) 0.0316	0.85 (0.73, 0.98) 0.0307	-0.03 (-0.05, -0.01)*0.0143	
	No	89/ 469 (19.0)	88/ 471 (18.7)	0.99 (0.76, 1.28) 0.9347	1.00 (0.72, 1.40) 0.9794	0.00 (-0.05, 0.05)*0.9086	
	Diuretics at baseline						0.7284
	Yes	467/2493 (18.7)	530/2492 (21.3)	0.89 (0.80, 1.00) 0.0412	0.86 (0.75, 1.00) 0.0439	-0.03 (-0.05, -0.00)*0.0252	
	No	47/ 299 (15.7)	49/ 300 (16.3)	0.94 (0.66, 1.35) 0.7553	0.95 (0.61, 1.48) 0.8172	-0.01 (-0.06, 0.05)*0.8376	

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Quality of Life (LOCF)							
	Overall	483/2842 (17.0)	558/2837 (19.7)	0.88 (0.79, 0.98) 0.0152	0.84 (0.73, 0.97) 0.0154	-0.03 (-0.05, -0.01)*0.0092	
	Age						0.8259
	<= median	209/1415 (14.8)	246/1482 (16.6)	0.89 (0.76, 1.04) 0.1517	0.87 (0.70, 1.07) 0.1820	-0.02 (-0.04, 0.01)*0.1757	
	> median	274/1427 (19.2)	312/1355 (23.0)	0.87 (0.76, 1.00) 0.0435	0.81 (0.67, 0.98) 0.0304	-0.04 (-0.07, -0.01)*0.0135	
	Gender						0.6748
	Male	284/1656 (17.1)	314/1625 (19.3)	0.90 (0.78, 1.03) 0.1237	0.87 (0.72, 1.05) 0.1532	-0.02 (-0.05, 0.00)*0.1069	
	Female	199/1186 (16.8)	244/1212 (20.1)	0.86 (0.73, 1.01) 0.0635	0.80 (0.64, 0.99) 0.0442	-0.03 (-0.06, -0.00)*0.0341	
	Race						0.1602
	White	351/2039 (17.2)	404/2058 (19.6)	0.90 (0.80, 1.02) 0.0921	0.87 (0.73, 1.02) 0.0925	-0.02 (-0.05, -0.00)*0.0459	
	Black or African	14/ 67 (20.9)	9/ 71 (12.7)	1.80 (0.87, 3.73) 0.1161	2.02 (0.78, 5.27) 0.1501	0.08 (-0.04, 0.21)*0.1952	
	Asian	102/ 558 (18.3)	129/ 555 (23.2)	0.78 (0.62, 0.97) 0.0271	0.72 (0.53, 0.97) 0.0310	-0.05 (-0.10, -0.00)*0.0409	
	Other	16/ 178 (9.0)	16/ 153 (10.5)	0.86 (0.44, 1.66)*0.6523	0.77 (0.35, 1.68) 0.5065	-0.01 (-0.08, 0.05)*0.6537	
	Geographic region						0.3766
	Asia	97/ 539 (18.0)	123/ 538 (22.9)	0.78 (0.62, 0.98) 0.0316	0.73 (0.53, 0.99) 0.0407	-0.05 (-0.10, -0.00)*0.0473	
	Europe and Saudi Arabia	232/1365 (17.0)	269/1394 (19.3)	0.92 (0.79, 1.06) 0.2507	0.88 (0.72, 1.09) 0.2400	-0.02 (-0.05, 0.01)*0.1167	
	North America	71/ 398 (17.8)	87/ 387 (22.5)	0.80 (0.61, 1.04) 0.0958	0.72 (0.50, 1.04) 0.0828	-0.05 (-0.10, 0.01)*0.1047	
	Latin America	83/ 540 (15.4)	79/ 518 (15.3)	1.03 (0.80, 1.33) 0.7932	1.02 (0.71, 1.46) 0.9187	0.00 (-0.04, 0.04)*0.9570	
	NYHA class at enrolment						0.4324
	II	354/2113 (16.8)	429/2187 (19.6)	0.86 (0.76, 0.97) 0.0116	0.81 (0.69, 0.95) 0.0097	-0.03 (-0.05, -0.01)*0.0149	
	III or IV	129/ 729 (17.7)	128/ 649 (19.7)	0.94 (0.78, 1.14) 0.5465	0.91 (0.68, 1.22) 0.5361	-0.02 (-0.06, 0.02)*0.3359	
	LVEF at enrolment						0.7530
	<= 49	163/ 980 (16.6)	176/ 963 (18.3)	0.92 (0.77, 1.10) 0.3712	0.87 (0.68, 1.11) 0.2688	-0.02 (-0.05, 0.02)*0.3399	
	50-59	176/1029 (17.1)	206/1017 (20.3)	0.84 (0.71, 1.00) 0.0474	0.81 (0.64, 1.02) 0.0751	-0.03 (-0.07, 0.00)*0.0673	
	>= 60	144/ 833 (17.3)	176/ 857 (20.5)	0.88 (0.73, 1.06) 0.1840	0.84 (0.65, 1.09) 0.1867	-0.03 (-0.07, 0.00)*0.0877	
	NT-proBNP at enrolment						0.1636
	<= median	227/1418 (16.0)	280/1421 (19.7)	0.82 (0.70, 0.95) 0.0080	0.78 (0.63, 0.95) 0.0139	-0.04 (-0.07, -0.01)*0.0101	
	> median	256/1424 (18.0)	278/1415 (19.6)	0.95 (0.82, 1.09) 0.4428	0.90 (0.74, 1.10) 0.3215	-0.02 (-0.05, 0.01)*0.2551	
	Type 2 Diabetes Medical History						0.1896
	Yes	208/1250 (16.6)	265/1260 (21.0)	0.82 (0.70, 0.95) 0.0098	0.75 (0.61, 0.92)*0.0050	-0.04 (-0.07, -0.01)*0.0048	
	No	275/1592 (17.3)	293/1577 (18.6)	0.94 (0.82, 1.08) 0.3824	0.92 (0.76, 1.10)*0.3381	-0.01 (-0.04, 0.01)*0.3380	
	Atrial fibrillation or flutter at enrolment ECG						0.4931
	Yes	199/1199 (16.6)	222/1199 (18.5)	0.92 (0.78, 1.08) 0.2899	0.88 (0.71, 1.10) 0.2697	-0.02 (-0.05, 0.01)*0.2169	
	No	284/1643 (17.3)	336/1638 (20.5)	0.85 (0.74, 0.97) 0.0163	0.81 (0.67, 0.97) 0.0225	-0.03 (-0.06, -0.01)*0.0181	
	BMI (kg/m2) at enrolment						0.1412
	< 30	256/1571 (16.3)	318/1559 (20.4)	0.82 (0.71, 0.94) 0.0059	0.77 (0.64, 0.93) 0.0065	-0.04 (-0.07, -0.01)*0.0030	
	>= 30	226/1270 (17.8)	239/1275 (18.7)	0.96 (0.82, 1.12) 0.5949	0.94 (0.76, 1.16) 0.5393	-0.01 (-0.04, 0.02)*0.5352	
	Baseline eGFR (mL/min/1.73m^2)						0.2436
	< 60	262/1359 (19.3)	291/1396 (20.8)	0.93 (0.81, 1.07) 0.3205	0.91 (0.75, 1.11) 0.3474	-0.02 (-0.05, 0.01)*0.3045	
	>= 60	221/1483 (14.9)	267/1440 (18.5)	0.83 (0.71, 0.96) 0.0154	0.77 (0.62, 0.94) 0.0120	-0.04 (-0.06, -0.01)*0.0084	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.1652
	<= median	254/1424 (17.8)	280/1439 (19.5)	0.95 (0.82, 1.09) 0.4483	0.93 (0.76, 1.13) 0.4814	-0.02 (-0.04, 0.01)*0.2654	
	> median	229/1418 (16.1)	278/1398 (19.9)	0.82 (0.70, 0.95) 0.0080	0.76 (0.62, 0.93) 0.0068	-0.04 (-0.07, -0.01)*0.0098	
	LVEF at enrolment 2						0.5240
	<= 49	163/ 980 (16.6)	176/ 963 (18.3)	0.92 (0.77, 1.10) 0.3712	0.87 (0.68, 1.11) 0.2688	-0.02 (-0.05, 0.02)*0.3399	
	>= 50	320/1862 (17.2)	382/1874 (20.4)	0.86 (0.76, 0.97) 0.0184	0.82 (0.69, 0.98) 0.0272	-0.03 (-0.06, -0.01)*0.0122	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4761
	Yes	34/ 283 (12.0)	47/ 286 (16.4)	0.73 (0.49, 1.10)*0.1338	0.70 (0.42, 1.16) 0.1658	-0.04 (-0.10, 0.01)*0.1304	
	No	449/2559 (17.5)	511/2551 (20.0)	0.89 (0.80, 0.99) 0.0318	0.85 (0.74, 0.99) 0.0349	-0.02 (-0.05, -0.00)*0.0229	
	MRAs at baseline						0.9537
	Yes	212/1227 (17.3)	241/1224 (19.7)	0.88 (0.75, 1.03) 0.1097	0.86 (0.69, 1.06) 0.1607	-0.02 (-0.05, 0.01)*0.1239	
	No	271/1615 (16.8)	317/1613 (19.7)	0.88 (0.76, 1.01) 0.0615	0.83 (0.68, 1.00) 0.0450	-0.03 (-0.06, -0.00)*0.0344	
	ACEi+ARB at baseline						0.2297
	Yes	345/2065 (16.7)	416/2077 (20.0)	0.85 (0.75, 0.95) 0.0065	0.79 (0.67, 0.94) 0.0067	-0.03 (-0.06, -0.01)*0.0057	
	No	138/ 777 (17.8)	142/ 760 (18.7)	0.97 (0.80, 1.19) 0.8055	0.97 (0.74, 1.27) 0.8197	-0.01 (-0.05, 0.03)*0.6391	
	ARNI at baseline						0.0872
	Yes	25/ 153 (16.3)	15/ 126 (11.9)	1.46 (0.81, 2.62) 0.2076	1.63 (0.80, 3.33) 0.1757	0.04 (-0.04, 0.13)*0.2857	
	No	458/2689 (17.0)	543/2711 (20.0)	0.87 (0.78, 0.96) 0.0072	0.82 (0.71, 0.94) 0.0063	-0.03 (-0.05, -0.01)*0.0046	
	Beta Blocker at baseline						0.1950
	Yes	418/2360 (17.7)	473/2356 (20.1)	0.91 (0.81, 1.01) 0.0852	0.87 (0.75, 1.01) 0.0745	-0.02 (-0.05, -0.00)*0.0380	
	No	65/ 482 (13.5)	85/ 481 (17.7)	0.74 (0.56, 0.98) 0.0382	0.69 (0.48, 1.00) 0.0487	-0.04 (-0.09, 0.00)*0.0728	
	Diuretics at baseline						0.0621
	Yes	431/2536 (17.0)	511/2531 (20.2)	0.85 (0.76, 0.95) 0.0035	0.80 (0.69, 0.93) 0.0042	-0.03 (-0.05, -0.01)*0.0034	
	No	52/ 306 (17.0)	47/ 306 (15.4)	1.19 (0.84, 1.69) 0.3209	1.22 (0.78, 1.90) 0.3900	0.02 (-0.04, 0.07)*0.5830	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	431/2842 (15.2)	523/2837 (18.4)	0.83 (0.74, 0.93) 0.0010	0.79 (0.68, 0.91) 0.0010	-0.03 (-0.05, -0.01)*0.0010	
	Age						0.9446
	<= median	186/1415 (13.1)	233/1482 (15.7)	0.83 (0.69, 0.98) 0.0319	0.79 (0.64, 0.98) 0.0312	-0.03 (-0.05, -0.00)*0.0482	
	> median	245/1427 (17.2)	290/1355 (21.4)	0.82 (0.71, 0.95) 0.0089	0.77 (0.64, 0.94) 0.0096	-0.04 (-0.07, -0.01)*0.0047	
	Gender						0.5918
	Male	241/1656 (14.6)	297/1625 (18.3)	0.81 (0.69, 0.94) 0.0052	0.76 (0.63, 0.92) 0.0049	-0.04 (-0.06, -0.01)*0.0040	
	Female	190/1186 (16.0)	226/1212 (18.6)	0.86 (0.72, 1.01) 0.0738	0.82 (0.66, 1.03) 0.0828	-0.03 (-0.06, 0.00)*0.0890	
	Race						0.8728
	White	331/2039 (16.2)	399/2058 (19.4)	0.85 (0.75, 0.96) 0.0094	0.81 (0.68, 0.96) 0.0126	-0.03 (-0.05, -0.01)*0.0083	
	Black or African	10/ 67 (14.9)	12/ 71 (16.9)	0.88 (0.42, 1.86) 0.7337	0.83 (0.33, 2.13) 0.7057	-0.02 (-0.14, 0.10)*0.7509	
	Asian	77/ 558 (13.8)	94/ 555 (16.9)	0.81 (0.61, 1.07) 0.1341	0.77 (0.56, 1.07) 0.1242	-0.03 (-0.07, 0.01)*0.1464	
	Other	13/ 178 (7.3)	18/ 153 (11.8)	0.64 (0.33, 1.27) 0.2018	0.60 (0.28, 1.29) 0.1916	-0.03 (-0.10, 0.04) 0.3823	
	Geographic region						0.9795
	Asia	73/ 539 (13.5)	88/ 538 (16.4)	0.82 (0.62, 1.10) 0.1835	0.79 (0.56, 1.11) 0.1759	-0.03 (-0.07, 0.01)*0.1951	
	Europe and Saudi Arabia	217/1365 (15.9)	279/1394 (20.0)	0.82 (0.70, 0.96) 0.0110	0.76 (0.62, 0.93) 0.0086	-0.04 (-0.07, -0.01)*0.0048	
	North America	80/ 398 (20.1)	89/ 387 (23.0)	0.87 (0.67, 1.12) 0.2749	0.84 (0.59, 1.19) 0.3194	-0.03 (-0.09, 0.03)*0.3235	
	Latin America	61/ 540 (11.3)	67/ 518 (12.9)	0.86 (0.63, 1.18) 0.3522	0.84 (0.58, 1.23) 0.3691	-0.02 (-0.06, 0.02)*0.4145	
	NYHA class at enrolment						0.6153
	II	325/2113 (15.4)	402/2187 (18.4)	0.83 (0.73, 0.95) 0.0059	0.79 (0.67, 0.93) 0.0052	-0.03 (-0.05, -0.01)*0.0086	
	III or IV	106/ 729 (14.5)	121/ 649 (18.6)	0.78 (0.62, 0.97) 0.0283	0.74 (0.55, 0.99) 0.0462	-0.04 (-0.08, -0.00)*0.0412	
	LVEF at enrolment						0.8925
	<= 49	143/ 980 (14.6)	161/ 963 (16.7)	0.86 (0.70, 1.05) 0.1466	0.83 (0.64, 1.06) 0.1347	-0.02 (-0.05, 0.01)*0.1970	
	50-59	173/1029 (16.8)	208/1017 (20.5)	0.82 (0.69, 0.97) 0.0236	0.77 (0.61, 0.97) 0.0278	-0.04 (-0.07, -0.00)*0.0343	
	>= 60	115/ 833 (13.8)	154/ 857 (18.0)	0.80 (0.65, 1.00) 0.0450	0.76 (0.58, 1.00) 0.0475	-0.04 (-0.08, -0.01)*0.0189	
	NT-proBNP at enrolment						0.8665
	<= median	213/1418 (15.0)	254/1421 (17.9)	0.83 (0.71, 0.98) 0.0290	0.80 (0.65, 0.98) 0.0302	-0.03 (-0.06, -0.00)*0.0401	
	> median	218/1424 (15.3)	269/1415 (19.0)	0.82 (0.70, 0.96) 0.0148	0.78 (0.64, 0.95) 0.0144	-0.04 (-0.06, -0.01)*0.0088	
	Type 2 Diabetes Medical History						0.3771
	Yes	195/1250 (15.6)	253/1260 (20.1)	0.79 (0.67, 0.93) 0.0041	0.74 (0.60, 0.90)*0.0035	-0.04 (-0.07, -0.01)*0.0033	
	No	236/1592 (14.8)	270/1577 (17.1)	0.87 (0.74, 1.02) 0.0830	0.84 (0.70, 1.02)*0.0778	-0.02 (-0.05, 0.00)*0.0775	
	Atrial fibrillation or flutter at enrolment ECG						0.7246
	Yes	172/1199 (14.3)	214/1199 (17.8)	0.81 (0.67, 0.97) 0.0188	0.77 (0.61, 0.96) 0.0209	-0.04 (-0.06, -0.01)*0.0195	
	No	259/1643 (15.8)	309/1638 (18.9)	0.84 (0.73, 0.97) 0.0197	0.80 (0.66, 0.96) 0.0183	-0.03 (-0.06, -0.01)*0.0188	
	BMI (kg/m2) at enrolment						0.2892
	< 30	224/1571 (14.3)	286/1559 (18.3)	0.78 (0.67, 0.92) 0.0022	0.73 (0.60, 0.89) 0.0019	-0.04 (-0.07, -0.02)*0.0019	
	>= 30	207/1270 (16.3)	236/1275 (18.5)	0.89 (0.75, 1.04) 0.1464	0.86 (0.69, 1.06) 0.1599	-0.02 (-0.05, 0.01)*0.1412	
	Baseline eGFR (mL/min/1.73m^2)						0.7497
	< 60	233/1359 (17.1)	285/1396 (20.4)	0.84 (0.73, 0.98) 0.0277	0.80 (0.66, 0.98) 0.0296	-0.03 (-0.06, -0.00)*0.0278	
	>= 60	198/1483 (13.4)	238/1440 (16.5)	0.81 (0.69, 0.96) 0.0176	0.77 (0.63, 0.95) 0.0164	-0.03 (-0.06, -0.01)*0.0160	

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Symptom Burden (LOCF)	SBP at randomisation						0.0855
	<= median	199/1424 (14.0)	277/1439 (19.2)	0.75 (0.63, 0.88) 0.0004	0.70 (0.57, 0.85) 0.0005	-0.05 (-0.08, -0.03)*0.0001	
	> median	232/1418 (16.4)	246/1398 (17.6)	0.91 (0.78, 1.07) 0.2468	0.88 (0.72, 1.08) 0.2318	-0.01 (-0.04, 0.02)*0.3826	
	LVEF at enrolment 2						0.6722
	<= 49	143/ 980 (14.6)	161/ 963 (16.7)	0.86 (0.70, 1.05) 0.1466	0.83 (0.64, 1.06) 0.1347	-0.02 (-0.05, 0.01)*0.1970	
	>= 50	288/1862 (15.5)	362/1874 (19.3)	0.82 (0.71, 0.93) 0.0033	0.77 (0.65, 0.92) 0.0037	-0.04 (-0.06, -0.01)*0.0019	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1761
	Yes	28/ 283 (9.9)	42/ 286 (14.7)	0.57 (0.37, 0.87) 0.0094	0.52 (0.30, 0.90) 0.0187	-0.05 (-0.10, 0.01)*0.0808	
	No	403/2559 (15.7)	481/2551 (18.9)	0.85 (0.75, 0.95) 0.0051	0.81 (0.70, 0.94) 0.0048	-0.03 (-0.05, -0.01)*0.0033	
	MRAs at baseline						0.3773
	Yes	180/1227 (14.7)	233/1224 (19.0)	0.78 (0.65, 0.92) 0.0045	0.73 (0.59, 0.91) 0.0049	-0.04 (-0.07, -0.01)*0.0038	
	No	251/1615 (15.5)	290/1613 (18.0)	0.86 (0.74, 1.00) 0.0557	0.83 (0.69, 1.00) 0.0537	-0.02 (-0.05, 0.00)*0.0637	
	ACEi+ARB at baseline						0.1357
	Yes	287/2065 (13.9)	376/2077 (18.1)	0.78 (0.68, 0.90) 0.0004	0.73 (0.61, 0.87) 0.0003	-0.04 (-0.06, -0.02)*0.0002	
	No	144/ 777 (18.5)	147/ 760 (19.3)	0.95 (0.77, 1.16) 0.6074	0.94 (0.72, 1.21) 0.6230	-0.01 (-0.05, 0.03)*0.6856	
	ARNI at baseline						0.0715
	Yes	30/ 153 (19.6)	17/ 126 (13.5)	1.35 (0.78, 2.34) 0.2867	1.46 (0.75, 2.82) 0.2657	0.06 (-0.03, 0.15)*0.1668	
	No	401/2689 (14.9)	506/2711 (18.7)	0.81 (0.72, 0.91) 0.0004	0.76 (0.66, 0.89) 0.0003	-0.04 (-0.06, -0.02)*0.0002	
	Beta Blocker at baseline						0.2180
	Yes	372/2360 (15.8)	442/2356 (18.8)	0.85 (0.76, 0.96) 0.0111	0.82 (0.70, 0.95) 0.0108	-0.03 (-0.05, -0.01)*0.0064	
	No	59/ 482 (12.2)	81/ 481 (16.8)	0.70 (0.51, 0.95) 0.0208	0.65 (0.45, 0.94) 0.0220	-0.05 (-0.09, -0.00)*0.0425	
	Diuretics at baseline						0.6274
	Yes	396/2536 (15.6)	481/2531 (19.0)	0.82 (0.73, 0.92) 0.0007	0.78 (0.67, 0.90) 0.0010	-0.03 (-0.05, -0.01)*0.0014	
	No	35/ 306 (11.4)	42/ 306 (13.7)	0.91 (0.60, 1.37) 0.6420	0.87 (0.53, 1.41) 0.5596	-0.02 (-0.08, 0.03)*0.3933	

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Self Efficacy (LOCF)							
	Overall	415/2842 (14.6)	390/2837 (13.7)	1.07 (0.95, 1.21) 0.2906	1.09 (0.93, 1.27) 0.2927	0.01 (-0.01, 0.03)*0.3554	
	Age						0.0583
	<= median	204/1415 (14.4)	177/1482 (11.9)	1.20 (1.01, 1.44) 0.0414	1.26 (1.00, 1.58) 0.0465	0.02 (0.00, 0.05)*0.0492	
	> median	211/1427 (14.8)	213/1355 (15.7)	0.95 (0.81, 1.12) 0.5622	0.94 (0.76, 1.17) 0.6009	-0.01 (-0.04, 0.02)*0.4939	
	Gender						0.7761
	Male	234/1656 (14.1)	208/1625 (12.8)	1.09 (0.92, 1.28) 0.3197	1.12 (0.91, 1.39) 0.2739	0.01 (-0.01, 0.04)*0.2641	
	Female	181/1186 (15.3)	182/1212 (15.0)	1.05 (0.88, 1.26) 0.5760	1.05 (0.83, 1.33) 0.6871	0.00 (-0.03, 0.03)*0.8672	
	Race						0.4541
	White	294/2039 (14.4)	271/2058 (13.2)	1.11 (0.96, 1.28) 0.1785	1.14 (0.95, 1.38) 0.1567	0.01 (-0.01, 0.03)*0.2457	
	Black or African	11/ 67 (16.4)	7/ 71 (9.9)	1.48 (0.63, 3.49) 0.3660	1.65 (0.57, 4.73) 0.3551	0.07 (-0.05, 0.18)*0.2536	
	Asian	91/ 558 (16.3)	99/ 555 (17.8)	0.91 (0.72, 1.16) 0.4594	0.85 (0.61, 1.18) 0.3328	-0.02 (-0.06, 0.03)*0.4976	
	Other	19/ 178 (10.7)	13/ 153 (8.5)	1.26 (0.64, 2.46)*0.5055	1.34 (0.61, 2.93) 0.4703	0.02 (-0.04, 0.09)*0.5003	
	Geographic region						0.3071
	Asia	89/ 539 (16.5)	96/ 538 (17.8)	0.92 (0.72, 1.17) 0.4766	0.85 (0.61, 1.20) 0.3605	-0.01 (-0.06, 0.03)*0.5623	
	Europe and Saudi Arabia	217/1365 (15.9)	186/1394 (13.3)	1.18 (1.00, 1.41) 0.0533	1.26 (1.01, 1.58) 0.0394	0.03 (-0.00, 0.05)*0.0575	
	North America	45/ 398 (11.3)	39/ 387 (10.1)	1.12 (0.75, 1.66) 0.5823	1.12 (0.70, 1.78) 0.6404	0.01 (-0.03, 0.06)*0.5772	
	Latin America	64/ 540 (11.9)	69/ 518 (13.3)	0.94 (0.70, 1.27) 0.7060	0.94 (0.64, 1.38) 0.7494	-0.01 (-0.05, 0.03)*0.4717	
	NYHA class at enrolment						0.7260
	II	311/2113 (14.7)	304/2187 (13.9)	1.08 (0.94, 1.24) 0.2825	1.09 (0.91, 1.31) 0.3332	0.01 (-0.01, 0.03)*0.4438	
	III or IV	104/ 729 (14.3)	86/ 649 (13.3)	1.03 (0.80, 1.32) 0.8297	1.07 (0.77, 1.47) 0.7000	0.01 (-0.03, 0.05)*0.5847	
	LVEF at enrolment						0.1946
	<= 49	146/ 980 (14.9)	113/ 963 (11.7)	1.25 (1.00, 1.55) 0.0493	1.30 (0.98, 1.71) 0.0642	0.03 (0.00, 0.06)*0.0398	
	50-59	155/1029 (15.1)	145/1017 (14.3)	1.04 (0.85, 1.26) 0.7187	1.09 (0.84, 1.40) 0.5341	0.01 (-0.02, 0.04)*0.6065	
	>= 60	114/ 833 (13.7)	132/ 857 (15.4)	0.94 (0.75, 1.17) 0.5839	0.90 (0.68, 1.20) 0.4867	-0.02 (-0.05, 0.02)*0.3165	
	NT-proBNP at enrolment						0.8580
	<= median	214/1418 (15.1)	201/1421 (14.1)	1.08 (0.91, 1.28) 0.3768	1.10 (0.88, 1.37) 0.3979	0.01 (-0.02, 0.04)*0.4753	
	> median	201/1424 (14.1)	189/1415 (13.4)	1.05 (0.88, 1.25) 0.5662	1.08 (0.86, 1.35) 0.5223	0.01 (-0.02, 0.03)*0.5573	
	Type 2 Diabetes Medical History						0.1587
	Yes	161/1250 (12.9)	171/1260 (13.6)	0.96 (0.79, 1.16) 0.6675	0.94 (0.75, 1.19)*0.6092	-0.01 (-0.03, 0.02)*0.6091	
	No	254/1592 (16.0)	219/1577 (13.9)	1.15 (0.98, 1.34) 0.0897	1.18 (0.97, 1.43)*0.1027	0.02 (-0.00, 0.05)*0.1022	
	Atrial fibrillation or flutter at enrolment ECG						0.8326
	Yes	181/1199 (15.1)	173/1199 (14.4)	1.08 (0.90, 1.30) 0.3900	1.10 (0.87, 1.40) 0.4137	0.01 (-0.02, 0.04)*0.6451	
	No	234/1643 (14.2)	217/1638 (13.2)	1.05 (0.90, 1.24) 0.5215	1.08 (0.87, 1.32) 0.4937	0.01 (-0.01, 0.03)*0.4081	
	BMI (kg/m2) at enrolment						0.7226
	< 30	251/1571 (16.0)	244/1559 (15.7)	1.05 (0.90, 1.22) 0.5140	1.07 (0.87, 1.31) 0.5331	0.00 (-0.02, 0.03)*0.8026	
	>= 30	164/1270 (12.9)	146/1275 (11.5)	1.10 (0.90, 1.34) 0.3505	1.13 (0.88, 1.44) 0.3385	0.01 (-0.01, 0.04)*0.2593	
	Baseline eGFR (mL/min/1.73m^2)						0.9685
	< 60	187/1359 (13.8)	181/1396 (13.0)	1.06 (0.88, 1.27) 0.5315	1.06 (0.85, 1.34) 0.5964	0.01 (-0.02, 0.03)*0.5401	
	>= 60	228/1483 (15.4)	209/1440 (14.5)	1.07 (0.91, 1.26) 0.4373	1.10 (0.89, 1.37) 0.3631	0.01 (-0.02, 0.03)*0.5141	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.5646
	<= median	209/1424 (14.7)	195/1439 (13.6)	1.11 (0.93, 1.31) 0.2495	1.12 (0.90, 1.40) 0.3020	0.01 (-0.01, 0.04)*0.3869	
	> median	206/1418 (14.5)	195/1398 (13.9)	1.03 (0.87, 1.22) 0.7377	1.05 (0.84, 1.31) 0.6545	0.01 (-0.02, 0.03)*0.6602	
	LVEF at enrolment 2						0.0907
	<= 49	146/ 980 (14.9)	113/ 963 (11.7)	1.25 (1.00, 1.55) 0.0493	1.30 (0.98, 1.71) 0.0642	0.03 (0.00, 0.06)*0.0398	
	>= 50	269/1862 (14.4)	277/1874 (14.8)	0.99 (0.86, 1.15) 0.9376	1.00 (0.83, 1.21) 0.9924	-0.00 (-0.03, 0.02)*0.7724	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0447
	Yes	26/ 283 (9.2)	38/ 286 (13.3)	0.68 (0.44, 1.07) 0.0987	0.61 (0.35, 1.06) 0.0808	-0.04 (-0.09, 0.01)*0.1207	
	No	389/2559 (15.2)	352/2551 (13.8)	1.11 (0.98, 1.26) 0.1147	1.14 (0.97, 1.35) 0.1064	0.01 (-0.01, 0.03)*0.1544	
	MRAs at baseline						0.7768
	Yes	186/1227 (15.2)	170/1224 (13.9)	1.09 (0.91, 1.30) 0.3769	1.11 (0.88, 1.41) 0.3859	0.01 (-0.02, 0.04)*0.3722	
	No	229/1615 (14.2)	220/1613 (13.6)	1.05 (0.89, 1.24) 0.5509	1.07 (0.87, 1.31) 0.5518	0.01 (-0.02, 0.03)*0.6573	
	ACEi+ARB at baseline						0.3124
	Yes	287/2065 (13.9)	285/2077 (13.7)	1.03 (0.89, 1.18) 0.7247	1.03 (0.85, 1.23) 0.7893	0.00 (-0.02, 0.02)*0.8692	
	No	128/ 777 (16.5)	105/ 760 (13.8)	1.19 (0.95, 1.50) 0.1297	1.27 (0.95, 1.70) 0.1067	0.03 (-0.01, 0.06)*0.1457	
	ARNI at baseline						0.4616
	Yes	27/ 153 (17.6)	16/ 126 (12.7)	1.39 (0.80, 2.43) 0.2466	1.53 (0.76, 3.09) 0.2327	0.05 (-0.03, 0.13)*0.2473	
	No	388/2689 (14.4)	374/2711 (13.8)	1.06 (0.93, 1.20) 0.3759	1.07 (0.92, 1.26) 0.3808	0.01 (-0.01, 0.02)*0.5038	
	Beta Blocker at baseline						0.8868
	Yes	360/2360 (15.3)	337/2356 (14.3)	1.07 (0.94, 1.22) 0.3036	1.09 (0.92, 1.29) 0.3249	0.01 (-0.01, 0.03)*0.3578	
	No	55/ 482 (11.4)	53/ 481 (11.0)	1.04 (0.74, 1.46) 0.8312	1.07 (0.71, 1.63) 0.7383	0.00 (-0.04, 0.04)*0.8471	
	Diuretics at baseline						0.2281
	Yes	371/2536 (14.6)	356/2531 (14.1)	1.04 (0.92, 1.18) 0.5366	1.06 (0.90, 1.24) 0.5179	0.01 (-0.01, 0.02)*0.5671	
	No	44/ 306 (14.4)	34/ 306 (11.1)	1.36 (0.91, 2.03) 0.1278	1.44 (0.87, 2.37) 0.1578	0.03 (-0.02, 0.09)*0.2249	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	401/2842 (14.1)	456/2837 (16.1)	0.87 (0.77, 0.99) 0.0282	0.85 (0.73, 0.98) 0.0292	-0.02 (-0.04, -0.00)*0.0387	
	Age						0.8053
	<= median	177/1415 (12.5)	205/1482 (13.8)	0.89 (0.74, 1.06) 0.1966	0.86 (0.69, 1.07) 0.1878	-0.01 (-0.04, 0.01)*0.2919	
	> median	224/1427 (15.7)	251/1355 (18.5)	0.86 (0.73, 1.00) 0.0576	0.82 (0.67, 1.01) 0.0637	-0.03 (-0.06, -0.00)*0.0479	
	Gender						0.5969
	Male	224/1656 (13.5)	255/1625 (15.7)	0.85 (0.73, 1.00) 0.0528	0.82 (0.68, 1.01) 0.0578	-0.02 (-0.05, 0.00)*0.0790	
	Female	177/1186 (14.9)	201/1212 (16.6)	0.91 (0.76, 1.09) 0.3011	0.88 (0.70, 1.11) 0.2778	-0.02 (-0.05, 0.01)*0.2643	
	Race						0.2039
	White	288/2039 (14.1)	339/2058 (16.5)	0.87 (0.75, 1.00) 0.0446	0.84 (0.70, 1.00) 0.0471	-0.02 (-0.05, -0.00)*0.0367	
	Black or African	13/ 67 (19.4)	6/ 71 (8.5)	2.30 (0.93, 5.69)*0.0728	2.61 (0.88, 7.74) 0.0828	0.11 (-0.01, 0.22)*0.0612	
	Asian	84/ 558 (15.1)	95/ 555 (17.1)	0.87 (0.66, 1.13) 0.2925	0.84 (0.61, 1.16) 0.2831	-0.02 (-0.06, 0.02)*0.3487	
	Other	16/ 178 (9.0)	16/ 153 (10.5)	0.80 (0.42, 1.50) 0.4807	0.75 (0.35, 1.60) 0.4550	-0.01 (-0.08, 0.05)*0.6537	
	Geographic region						0.3376
	Asia	79/ 539 (14.7)	90/ 538 (16.7)	0.86 (0.66, 1.14) 0.2979	0.84 (0.60, 1.17) 0.2957	-0.02 (-0.06, 0.02)*0.3498	
	Europe and Saudi Arabia	196/1365 (14.4)	222/1394 (15.9)	0.93 (0.78, 1.10) 0.3740	0.89 (0.72, 1.11) 0.3116	-0.02 (-0.04, 0.01)*0.2509	
	North America	64/ 398 (16.1)	61/ 387 (15.8)	0.98 (0.72, 1.33) 0.8799	0.99 (0.66, 1.46) 0.9434	0.00 (-0.05, 0.05)*0.9031	
	Latin America	62/ 540 (11.5)	83/ 518 (16.0)	0.70 (0.52, 0.93) 0.0157	0.64 (0.45, 0.93) 0.0194	-0.05 (-0.09, -0.00)*0.0319	
	NYHA class at enrolment						0.4678
	II	303/2113 (14.3)	362/2187 (16.6)	0.85 (0.74, 0.97) 0.0191	0.82 (0.69, 0.97) 0.0193	-0.02 (-0.04, -0.00)*0.0445	
	III or IV	98/ 729 (13.4)	94/ 649 (14.5)	0.94 (0.73, 1.21) 0.6516	0.93 (0.68, 1.27) 0.6350	-0.01 (-0.05, 0.03)*0.5783	
	LVEF at enrolment						0.2972
	<= 49	131/ 980 (13.4)	124/ 963 (12.9)	1.02 (0.81, 1.28) 0.8729	1.01 (0.77, 1.32) 0.9470	0.00 (-0.03, 0.03)*0.7486	
	50-59	157/1029 (15.3)	184/1017 (18.1)	0.82 (0.68, 0.99) 0.0428	0.80 (0.63, 1.01) 0.0657	-0.03 (-0.06, 0.00)*0.0853	
	>= 60	113/ 833 (13.6)	148/ 857 (17.3)	0.82 (0.66, 1.02) 0.0791	0.78 (0.59, 1.02) 0.0687	-0.04 (-0.07, -0.00)*0.0346	
	NT-proBNP at enrolment						0.6969
	<= median	197/1418 (13.9)	218/1421 (15.3)	0.89 (0.75, 1.06) 0.2052	0.88 (0.71, 1.09) 0.2334	-0.01 (-0.04, 0.01)*0.2746	
	> median	204/1424 (14.3)	238/1415 (16.8)	0.86 (0.72, 1.01) 0.0690	0.82 (0.66, 1.01) 0.0606	-0.02 (-0.05, 0.00)*0.0668	
	Type 2 Diabetes Medical History						0.2193
	Yes	185/1250 (14.8)	229/1260 (18.2)	0.81 (0.68, 0.96) 0.0166	0.78 (0.63, 0.97)*0.0229	-0.03 (-0.06, -0.00)*0.0226	
	No	216/1592 (13.6)	227/1577 (14.4)	0.94 (0.80, 1.12) 0.5028	0.93 (0.76, 1.14)*0.5023	-0.01 (-0.03, 0.02)*0.5023	
	Atrial fibrillation or flutter at enrolment ECG						0.6392
	Yes	169/1199 (14.1)	183/1199 (15.3)	0.90 (0.75, 1.09) 0.2955	0.89 (0.70, 1.12) 0.3122	-0.01 (-0.04, 0.02)*0.4191	
	No	232/1643 (14.1)	273/1638 (16.7)	0.85 (0.73, 1.00) 0.0461	0.82 (0.67, 0.99) 0.0431	-0.03 (-0.05, -0.00)*0.0432	
	BMI (kg/m2) at enrolment						0.4362
	< 30	217/1571 (13.8)	255/1559 (16.4)	0.84 (0.72, 0.99) 0.0407	0.80 (0.66, 0.98) 0.0330	-0.03 (-0.05, -0.00)*0.0467	
	>= 30	184/1270 (14.5)	199/1275 (15.6)	0.92 (0.77, 1.10) 0.3839	0.92 (0.73, 1.15) 0.4654	-0.01 (-0.04, 0.02)*0.4295	
	Baseline eGFR (mL/min/1.73m^2)						0.2811
	< 60	228/1359 (16.8)	252/1396 (18.1)	0.93 (0.80, 1.09) 0.3812	0.91 (0.74, 1.11) 0.3362	-0.01 (-0.04, 0.02)*0.3777	
	>= 60	173/1483 (11.7)	204/1440 (14.2)	0.82 (0.68, 0.98) 0.0332	0.79 (0.63, 0.99) 0.0365	-0.03 (-0.05, -0.00)*0.0438	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)	SBP at randomisation						0.6933
	<= median	206/1424 (14.5)	246/1439 (17.1)	0.85 (0.72, 1.01) 0.0623	0.82 (0.67, 1.01) 0.0651	-0.03 (-0.05, 0.00)*0.0535	
	> median	195/1418 (13.8)	210/1398 (15.0)	0.90 (0.75, 1.07) 0.2175	0.87 (0.70, 1.08) 0.2210	-0.01 (-0.04, 0.01)*0.3371	
	LVEF at enrolment 2						0.1235
	<= 49	131/ 980 (13.4)	124/ 963 (12.9)	1.02 (0.81, 1.28) 0.8729	1.01 (0.77, 1.32) 0.9470	0.00 (-0.03, 0.03)*0.7486	
	>= 50	270/1862 (14.5)	332/1874 (17.7)	0.82 (0.71, 0.95) 0.0074	0.79 (0.66, 0.95) 0.0101	-0.03 (-0.06, -0.01)*0.0074	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2428
	Yes	24/ 283 (8.5)	33/ 286 (11.5)	0.73 (0.45, 1.21)*0.2269	0.53 (0.29, 0.96) 0.0349	-0.03 (-0.08, 0.02)*0.2235	
	No	377/2559 (14.7)	423/2551 (16.6)	0.89 (0.79, 1.01) 0.0723	0.87 (0.75, 1.02) 0.0786	-0.02 (-0.04, 0.00)*0.0688	
	MRAs at baseline						0.5001
	Yes	162/1227 (13.2)	192/1224 (15.7)	0.83 (0.69, 1.00) 0.0552	0.80 (0.64, 1.01) 0.0619	-0.02 (-0.05, 0.00)*0.0802	
	No	239/1615 (14.8)	264/1613 (16.4)	0.91 (0.77, 1.06) 0.2103	0.88 (0.72, 1.07) 0.1983	-0.02 (-0.04, 0.01)*0.2192	
	ACEi+ARB at baseline						0.4175
	Yes	273/2065 (13.2)	327/2077 (15.7)	0.84 (0.73, 0.97) 0.0203	0.81 (0.68, 0.97) 0.0216	-0.03 (-0.05, -0.00)*0.0209	
	No	128/ 777 (16.5)	129/ 760 (17.0)	0.95 (0.76, 1.19) 0.6649	0.94 (0.72, 1.24) 0.6666	-0.01 (-0.04, 0.03)*0.7928	
	ARNI at baseline						0.5569
	Yes	19/ 153 (12.4)	13/ 126 (10.3)	1.03 (0.53, 2.01) 0.9221	1.06 (0.49, 2.28) 0.8845	0.02 (-0.05, 0.10)*0.5805	
	No	382/2689 (14.2)	443/2711 (16.3)	0.87 (0.77, 0.99) 0.0303	0.84 (0.73, 0.98) 0.0298	-0.02 (-0.04, -0.00)*0.0291	
	Beta Blocker at baseline						0.0544
	Yes	345/2360 (14.6)	376/2356 (16.0)	0.92 (0.81, 1.05) 0.2248	0.91 (0.77, 1.07) 0.2304	-0.01 (-0.03, 0.01)*0.2008	
	No	56/ 482 (11.6)	80/ 481 (16.6)	0.67 (0.49, 0.91) 0.0110	0.60 (0.41, 0.88) 0.0089	-0.05 (-0.09, -0.01)*0.0251	
	Diuretics at baseline						0.2033
	Yes	370/2536 (14.6)	407/2531 (16.1)	0.90 (0.79, 1.02) 0.0860	0.87 (0.75, 1.02) 0.0874	-0.01 (-0.03, 0.00)*0.1408	
	No	31/ 306 (10.1)	49/ 306 (16.0)	0.69 (0.46, 1.03) 0.0713	0.63 (0.38, 1.03) 0.0637	-0.06 (-0.11, -0.01)*0.0303	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)							
	Overall	493/2669 (18.5)	524/2664 (19.7)	0.92 (0.83, 1.02) 0.1173	0.91 (0.79, 1.05) 0.1969	-0.01 (-0.03, 0.01)*0.2653	
	Age						0.3675
	<= median	213/1352 (15.8)	249/1422 (17.5)	0.86 (0.74, 1.02) 0.0754	0.85 (0.69, 1.04) 0.1165	-0.02 (-0.05, 0.01)*0.2140	
	> median	280/1317 (21.3)	275/1242 (22.1)	0.96 (0.83, 1.10) 0.5356	0.96 (0.79, 1.16) 0.6446	-0.01 (-0.04, 0.02)*0.5889	
	Gender						0.9885
	Male	285/1568 (18.2)	290/1518 (19.1)	0.92 (0.80, 1.06) 0.2594	0.92 (0.76, 1.11) 0.3844	-0.01 (-0.04, 0.02)*0.5081	
	Female	208/1101 (18.9)	234/1146 (20.4)	0.92 (0.79, 1.08) 0.3237	0.91 (0.73, 1.13) 0.3836	-0.02 (-0.05, 0.02)*0.3623	
	Race						0.0487
	White	362/1925 (18.8)	412/1952 (21.1)	0.89 (0.79, 1.00) 0.0558	0.87 (0.74, 1.03) 0.1053	-0.02 (-0.05, 0.00)*0.0729	
	Black or African	17/ 61 (27.9)	9/ 67 (13.4)	1.90 (0.93, 3.86) 0.0768	2.45 (0.96, 6.27) 0.0612	0.14 (0.01, 0.28)*0.0418	
	Asian	91/ 510 (17.8)	93/ 500 (18.6)	0.93 (0.72, 1.21) 0.5856	0.92 (0.67, 1.27) 0.6109	-0.01 (-0.05, 0.04) 0.8029	
	Other	23/ 173 (13.3)	10/ 145 (6.9)	1.93 (0.95, 3.92)*0.0696	1.63 (0.69, 3.84) 0.2685	0.06 (-0.00, 0.13)*0.0547	
	Geographic region						0.7947
	Asia	85/ 496 (17.1)	86/ 486 (17.7)	0.94 (0.72, 1.23) 0.6553	0.93 (0.67, 1.30) 0.6834	-0.00 (-0.05, 0.04) 0.8462	
	Europe and Saudi Arabia	260/1299 (20.0)	293/1323 (22.1)	0.92 (0.80, 1.06) 0.2471	0.90 (0.74, 1.10) 0.3047	-0.02 (-0.05, 0.01)*0.1808	
	North America	75/ 372 (20.2)	64/ 359 (17.8)	1.07 (0.80, 1.44) 0.6386	1.11 (0.76, 1.63) 0.5814	0.02 (-0.03, 0.08)*0.4209	
	Latin America	73/ 502 (14.5)	81/ 496 (16.3)	0.86 (0.65, 1.12) 0.2636	0.84 (0.58, 1.21) 0.3432	-0.02 (-0.06, 0.03)*0.4341	
	NYHA class at enrolment						0.1373
	II	346/1986 (17.4)	401/2059 (19.5)	0.87 (0.77, 0.98) 0.0274	0.84 (0.72, 0.99) 0.0419	-0.02 (-0.04, 0.00)*0.0921	
	III or IV	147/ 683 (21.5)	122/ 604 (20.2)	1.04 (0.86, 1.26) 0.6920	1.08 (0.81, 1.45) 0.6101	0.01 (-0.03, 0.06)*0.5593	
	LVEF at enrolment						0.5974
	<= 49	168/ 928 (18.1)	157/ 912 (17.2)	0.99 (0.82, 1.20) 0.9511	0.99 (0.78, 1.27) 0.9631	0.01 (-0.03, 0.04)*0.6172	
	50-59	188/ 970 (19.4)	205/ 956 (21.4)	0.89 (0.75, 1.06) 0.1888	0.90 (0.72, 1.14) 0.3843	-0.02 (-0.06, 0.02)*0.2615	
	>= 60	137/ 771 (17.8)	162/ 796 (20.4)	0.87 (0.72, 1.06) 0.1813	0.84 (0.65, 1.09) 0.1871	-0.03 (-0.06, 0.01)*0.1927	
	NT-proBNP at enrolment						0.7803
	<= median	257/1334 (19.3)	270/1350 (20.0)	0.93 (0.80, 1.08) 0.3501	0.93 (0.77, 1.14) 0.4953	-0.01 (-0.04, 0.02)*0.6319	
	> median	236/1335 (17.7)	254/1313 (19.3)	0.90 (0.78, 1.05) 0.1980	0.89 (0.72, 1.09) 0.2497	-0.02 (-0.05, 0.01)*0.2694	
	Type 2 Diabetes Medical History						0.1751
	Yes	227/1169 (19.4)	223/1186 (18.8)	1.00 (0.85, 1.17) 0.9644	1.04 (0.85, 1.28)*0.7040	0.01 (-0.03, 0.04)*0.7040	
	No	266/1500 (17.7)	301/1478 (20.4)	0.86 (0.75, 0.99) 0.0423	0.84 (0.70, 1.01)*0.0676	-0.03 (-0.05, 0.00)*0.0673	
	Atrial fibrillation or flutter at enrolment ECG						0.0562
	Yes	205/1113 (18.4)	196/1123 (17.5)	1.05 (0.88, 1.24) 0.6027	1.06 (0.85, 1.33) 0.5881	0.01 (-0.02, 0.04)*0.5519	
	No	288/1556 (18.5)	328/1541 (21.3)	0.84 (0.74, 0.97) 0.0133	0.82 (0.68, 0.99) 0.0346	-0.03 (-0.06, 0.00)*0.0529	
	BMI (kg/m2) at enrolment						0.0391
	< 30	255/1478 (17.3)	297/1451 (20.5)	0.83 (0.72, 0.96) 0.0119	0.79 (0.65, 0.96) 0.0161	-0.03 (-0.06, -0.00)*0.0261	
	>= 30	238/1190 (20.0)	227/1211 (18.7)	1.04 (0.89, 1.22) 0.6177	1.08 (0.88, 1.34) 0.4511	0.01 (-0.02, 0.04)*0.4365	
	Baseline eGFR (mL/min/1.73m^2)						0.0890
	< 60	271/1266 (21.4)	270/1297 (20.8)	1.01 (0.87, 1.16) 0.9199	1.03 (0.84, 1.25) 0.7873	0.01 (-0.03, 0.04)*0.7150	
	>= 60	222/1403 (15.8)	254/1366 (18.6)	0.83 (0.71, 0.97) 0.0218	0.80 (0.65, 0.99) 0.0368	-0.03 (-0.06, 0.00)*0.0534	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)	SBP at randomisation						0.3808
	<= median	238/1344 (17.7)	267/1344 (19.9)	0.88 (0.75, 1.02) 0.0970	0.88 (0.72, 1.07) 0.1947	-0.02 (-0.05, 0.01)*0.1520	
	> median	255/1325 (19.2)	257/1320 (19.5)	0.96 (0.83, 1.11) 0.5978	0.95 (0.77, 1.16) 0.5986	-0.00 (-0.03, 0.03)*0.8839	
	LVEF at enrolment 2						0.3229
	<= 49	168/ 928 (18.1)	157/ 912 (17.2)	0.99 (0.82, 1.20) 0.9511	0.99 (0.78, 1.27) 0.9631	0.01 (-0.03, 0.04)*0.6172	
	>= 50	325/1741 (18.7)	367/1752 (20.9)	0.89 (0.78, 1.01) 0.0670	0.87 (0.74, 1.04) 0.1294	-0.02 (-0.05, 0.00)*0.0908	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5388
	Yes	50/ 257 (19.5)	49/ 261 (18.8)	1.01 (0.73, 1.41) 0.9310	1.00 (0.62, 1.61) 0.9969	0.01 (-0.06, 0.07)*0.8437	
	No	443/2412 (18.4)	475/2403 (19.8)	0.91 (0.81, 1.02) 0.0982	0.90 (0.78, 1.05) 0.1726	-0.01 (-0.04, 0.01)*0.2161	
	MRAs at baseline						0.6892
	Yes	218/1155 (18.9)	221/1146 (19.3)	0.95 (0.81, 1.12) 0.5214	0.95 (0.77, 1.18) 0.6403	-0.00 (-0.04, 0.03)*0.8024	
	No	275/1514 (18.2)	303/1518 (20.0)	0.90 (0.78, 1.04) 0.1463	0.88 (0.73, 1.07) 0.2043	-0.02 (-0.05, 0.01)*0.2078	
	ACEi+ARB at baseline						0.0444
	Yes	333/1940 (17.2)	390/1959 (19.9)	0.86 (0.75, 0.97) 0.0151	0.82 (0.69, 0.97) 0.0191	-0.03 (-0.05, -0.00)*0.0274	
	No	160/ 729 (21.9)	134/ 705 (19.0)	1.10 (0.90, 1.34) 0.3400	1.19 (0.91, 1.55) 0.2038	0.03 (-0.01, 0.07)*0.1672	
	ARNI at baseline						0.3567
	Yes	30/ 149 (20.1)	19/ 116 (16.4)	1.24 (0.73, 2.09) 0.4263	1.30 (0.68, 2.47) 0.4269	0.03 (-0.06, 0.13) 0.4660	
	No	463/2520 (18.4)	505/2548 (19.8)	0.91 (0.82, 1.01) 0.0860	0.90 (0.78, 1.04) 0.1477	-0.01 (-0.04, 0.01)*0.1901	
	Beta Blocker at baseline						0.4584
	Yes	424/2232 (19.0)	446/2218 (20.1)	0.94 (0.83, 1.05) 0.2486	0.93 (0.80, 1.09) 0.3625	-0.01 (-0.03, 0.01)*0.3498	
	No	69/ 437 (15.8)	78/ 446 (17.5)	0.83 (0.62, 1.10) 0.1981	0.80 (0.55, 1.16) 0.2388	-0.02 (-0.07, 0.03)*0.4976	
	Diuretics at baseline						0.1862
	Yes	449/2391 (18.8)	485/2379 (20.4)	0.90 (0.80, 1.00) 0.0504	0.88 (0.76, 1.02) 0.0857	-0.02 (-0.04, 0.01)*0.1617	
	No	44/ 278 (15.8)	39/ 285 (13.7)	1.18 (0.80, 1.74) 0.4046	1.27 (0.79, 2.04) 0.3316	0.02 (-0.04, 0.08)*0.4734	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Symptom Stability (LOCF)							
	Overall	647/2842 (22.8)	648/2837 (22.8)	1.05 (1.00, 1.11) 0.0623	1.06 (0.91, 1.24) 0.4515	-0.00 (-0.02, 0.02)*0.9460	
	Age						0.7435
	<= median	311/1415 (22.0)	328/1482 (22.1)	1.06 (0.98, 1.14) 0.1254	1.03 (0.83, 1.29) 0.7609	-0.00 (-0.03, 0.03)*0.9207	
	> median	336/1427 (23.5)	320/1355 (23.6)	1.04 (0.97, 1.11) 0.3154	1.07 (0.86, 1.33) 0.5458	-0.00 (-0.03, 0.03)*0.9652	
	Gender						0.3560
	Male	386/1656 (23.3)	374/1625 (23.0)	1.07 (1.00, 1.15) 0.0375	1.13 (0.92, 1.39) 0.2556	0.00 (-0.03, 0.03)*0.8419	
	Female	261/1186 (22.0)	274/1212 (22.6)	1.01 (0.93, 1.10) 0.7691	0.99 (0.78, 1.25) 0.9200	-0.01 (-0.04, 0.03)*0.7239	
	Race						0.5838*
	White	456/2039 (22.4)	476/2058 (23.1)	1.04 (0.98, 1.10) 0.2304	1.05 (0.87, 1.26) 0.6147	-0.01 (-0.03, 0.02)*0.5590	
	Black or African	17/ 67 (25.4)	15/ 71 (21.1)	1.20 (0.65, 2.21)*0.5554	1.75 (0.66, 4.64) 0.2575	0.04 (-0.10, 0.18)*0.5549	
	Asian	150/ 558 (26.9)	134/ 555 (24.1)	1.06 (0.93, 1.20) 0.4182	1.14 (0.82, 1.58) 0.4495	0.03 (-0.02, 0.08)*0.2946	
	Other	24/ 178 (13.5)	23/ 153 (15.0)	0.90 (0.53, 1.52)*0.6872	0.73 (0.33, 1.62) 0.4455	-0.02 (-0.09, 0.06)*0.6881	
	Geographic region						0.6463
	Asia	143/ 539 (26.5)	130/ 538 (24.2)	1.05 (0.93, 1.20) 0.4225	1.12 (0.80, 1.57) 0.4956	0.02 (-0.03, 0.08)*0.3717	
	Europe and Saudi Arabia	285/1365 (20.9)	312/1394 (22.4)	1.02 (0.94, 1.10) 0.6446	0.91 (0.73, 1.15) 0.4456	-0.02 (-0.05, 0.02)*0.3377	
	North America	95/ 398 (23.9)	96/ 387 (24.8)	1.09 (0.93, 1.26) 0.2914	1.21 (0.82, 1.79) 0.3452	-0.01 (-0.07, 0.05)*0.7598	
	Latin America	124/ 540 (23.0)	110/ 518 (21.2)	1.11 (1.00, 1.24) 0.0556	1.25 (0.86, 1.82) 0.2511	0.02 (-0.03, 0.07)*0.4982	
	NYHA class at enrolment						0.7946
	II	461/2113 (21.8)	470/2187 (21.5)	1.05 (0.99, 1.12) 0.1192	1.06 (0.88, 1.26) 0.5561	0.00 (-0.02, 0.03)*0.7949	
	III or IV	186/ 729 (25.5)	178/ 649 (27.4)	1.04 (0.96, 1.13) 0.3466	1.03 (0.76, 1.40) 0.8279	-0.02 (-0.07, 0.03)*0.4221	
	LVEF at enrolment						0.4233
	<= 49	214/ 980 (21.8)	223/ 963 (23.2)	1.02 (0.92, 1.12) 0.7563	0.90 (0.69, 1.18) 0.4402	-0.01 (-0.05, 0.02)*0.4860	
	50-59	241/1029 (23.4)	244/1017 (24.0)	1.05 (0.97, 1.13) 0.2189	1.08 (0.84, 1.39) 0.5567	-0.01 (-0.04, 0.03)*0.7613	
	>= 60	192/ 833 (23.0)	181/ 857 (21.1)	1.10 (1.00, 1.22) 0.0583	1.25 (0.94, 1.67) 0.1216	0.02 (-0.02, 0.06)*0.3392	
	NT-proBNP at enrolment						0.8143
	<= median	317/1418 (22.4)	303/1421 (21.3)	1.04 (0.97, 1.12) 0.2766	1.11 (0.89, 1.38) 0.3531	0.01 (-0.02, 0.04)*0.5056	
	> median	330/1424 (23.2)	345/1415 (24.4)	1.06 (0.98, 1.14) 0.1354	1.02 (0.82, 1.26) 0.8911	-0.01 (-0.04, 0.02)*0.4498	
	Type 2 Diabetes Medical History						0.0346
	Yes	311/1250 (24.9)	285/1260 (22.6)	1.10 (1.03, 1.19) 0.0085	1.13 (0.94, 1.36)*0.1833	0.02 (-0.01, 0.06)*0.1831	
	No	336/1592 (21.1)	363/1577 (23.0)	0.98 (0.91, 1.06) 0.6748	0.89 (0.76, 1.06)*0.1942	-0.02 (-0.05, 0.01)*0.1941	
	Atrial fibrillation or flutter at enrolment ECG						0.8283
	Yes	274/1199 (22.9)	274/1199 (22.9)	1.04 (0.97, 1.12) 0.2553	1.08 (0.85, 1.38) 0.5380	0.00 (-0.03, 0.03)*1.0000	
	No	373/1643 (22.7)	374/1638 (22.8)	1.06 (0.99, 1.14) 0.0929	1.05 (0.86, 1.28) 0.6658	-0.00 (-0.03, 0.03)*0.9291	
	BMI (kg/m2) at enrolment						0.3336
	< 30	362/1571 (23.0)	366/1559 (23.5)	1.03 (0.96, 1.11) 0.4154	1.03 (0.84, 1.26) 0.7853	-0.00 (-0.03, 0.03)*0.7739	
	>= 30	285/1270 (22.4)	282/1275 (22.1)	1.08 (1.01, 1.16) 0.0296	1.10 (0.87, 1.40) 0.4080	0.00 (-0.03, 0.04)*0.8446	
	Baseline eGFR (mL/min/1.73m^2)						0.1012
	< 60	352/1359 (25.9)	331/1396 (23.7)	1.10 (1.02, 1.18) 0.0141	1.25 (1.01, 1.55) 0.0380	0.02 (-0.01, 0.05)*0.1831	
	>= 60	295/1483 (19.9)	317/1440 (22.0)	1.01 (0.93, 1.09) 0.8560	0.89 (0.71, 1.12) 0.3218	-0.02 (-0.05, 0.01)*0.1587	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Symptom Stability (LOCF)	SBP at randomisation						0.1353
	<= median	363/1424 (25.5)	350/1439 (24.3)	1.09 (1.02, 1.16) 0.0084	1.18 (0.96, 1.46) 0.1169	0.01 (-0.02, 0.04)*0.4695	
	> median	284/1418 (20.0)	298/1398 (21.3)	1.00 (0.92, 1.09) 0.9619	0.94 (0.75, 1.18) 0.5795	-0.01 (-0.04, 0.02)*0.3987	
	LVEF at enrolment 2						0.3048
	<= 49	214/ 980 (21.8)	223/ 963 (23.2)	1.02 (0.92, 1.12) 0.7563	0.90 (0.69, 1.18) 0.4402	-0.01 (-0.05, 0.02)*0.4860	
	>= 50	433/1862 (23.3)	425/1874 (22.7)	1.07 (1.01, 1.14) 0.0290	1.15 (0.95, 1.39) 0.1442	0.01 (-0.02, 0.03)*0.6757	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0604
	Yes	104/ 283 (36.7)	96/ 286 (33.6)	1.17 (1.03, 1.34) 0.0179	1.32 (0.84, 2.06) 0.2317	0.03 (-0.05, 0.11)*0.4264	
	No	543/2559 (21.2)	552/2551 (21.6)	1.02 (0.97, 1.08) 0.4396	1.03 (0.88, 1.22) 0.6943	-0.00 (-0.03, 0.02)*0.7149	
	MRAs at baseline						0.6425
	Yes	289/1227 (23.6)	288/1224 (23.5)	1.04 (0.95, 1.14) 0.3694	0.99 (0.79, 1.24) 0.9230	0.00 (-0.03, 0.03)*0.9888	
	No	358/1615 (22.2)	360/1613 (22.3)	1.06 (1.01, 1.13) 0.0319	1.13 (0.92, 1.40) 0.2467	-0.00 (-0.03, 0.03)*0.9176	
	ACEi+ARB at baseline						0.6162
	Yes	458/2065 (22.2)	464/2077 (22.3)	1.04 (0.97, 1.10) 0.2631	1.02 (0.85, 1.23) 0.8283	-0.00 (-0.03, 0.02)*0.9010	
	No	189/ 777 (24.3)	184/ 760 (24.2)	1.08 (0.98, 1.19) 0.1030	1.15 (0.87, 1.53) 0.3324	0.00 (-0.04, 0.04)*0.9585	
	ARNI at baseline						0.2182
	Yes	38/ 153 (24.8)	34/ 126 (27.0)	0.92 (0.62, 1.37)*0.6831	0.73 (0.38, 1.43) 0.3611	-0.02 (-0.12, 0.08)*0.6840	
	No	609/2689 (22.6)	614/2711 (22.6)	1.06 (1.01, 1.12) 0.0285	1.08 (0.93, 1.27) 0.3161	-0.00 (-0.02, 0.02)*0.9995	
	Beta Blocker at baseline						0.6504
	Yes	528/2360 (22.4)	529/2356 (22.5)	1.06 (0.99, 1.12) 0.0746	1.11 (0.93, 1.32) 0.2355	-0.00 (-0.02, 0.02)*0.9472	
	No	119/ 482 (24.7)	119/ 481 (24.7)	1.03 (0.93, 1.14) 0.5572	0.86 (0.60, 1.24) 0.4278	-0.00 (-0.06, 0.05)*0.9853	
	Diuretics at baseline						0.9074
	Yes	587/2536 (23.1)	585/2531 (23.1)	1.05 (1.00, 1.10) 0.0727	1.07 (0.91, 1.26) 0.4280	0.00 (-0.02, 0.02)*0.9776	
	No	60/ 306 (19.6)	63/ 306 (20.6)	0.95 (0.69, 1.31)*0.7622	0.99 (0.61, 1.60) 0.9652	-0.01 (-0.07, 0.05)*0.7622	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) without ceiling correction including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	334/2842 (11.8)	422/2837 (14.9)	0.79 (0.70, 0.90) 0.0005	0.76 (0.65, 0.88) 0.0005	-0.03 (-0.05, -0.01)*0.0005	
	Age						0.5099
	<= median	137/1415 (9.7)	188/1482 (12.7)	0.75 (0.61, 0.92) 0.0060	0.72 (0.57, 0.91) 0.0060	-0.03 (-0.05, -0.01)*0.0102	
	> median	197/1427 (13.8)	234/1355 (17.3)	0.82 (0.69, 0.97) 0.0228	0.78 (0.63, 0.96) 0.0185	-0.03 (-0.06, -0.01)*0.0117	
	Gender						0.5599
	Male	189/1656 (11.4)	226/1625 (13.9)	0.82 (0.69, 0.98) 0.0320	0.79 (0.64, 0.98) 0.0305	-0.02 (-0.05, -0.00)*0.0316	
	Female	145/1186 (12.2)	196/1212 (16.2)	0.76 (0.63, 0.92) 0.0059	0.72 (0.56, 0.91) 0.0054	-0.04 (-0.07, -0.01)*0.0055	
	Race						0.4012
	White	248/2039 (12.2)	310/2058 (15.1)	0.82 (0.70, 0.95) 0.0096	0.78 (0.65, 0.94) 0.0095	-0.03 (-0.05, -0.01)*0.0067	
	Black or African	9/ 67 (13.4)	6/ 71 (8.5)	1.53 (0.59, 3.95) 0.3814	1.62 (0.53, 4.99) 0.3979	0.05 (-0.05, 0.15)*0.3486	
	Asian	64/ 558 (11.5)	90/ 555 (16.2)	0.71 (0.52, 0.95) 0.0215	0.66 (0.47, 0.94) 0.0205	-0.05 (-0.09, -0.01) 0.0134	
	Other	13/ 178 (7.3)	16/ 153 (10.5)	0.67 (0.34, 1.34) 0.2602	0.63 (0.29, 1.37) 0.2404	-0.03 (-0.09, 0.03)*0.3167	
	Geographic region						0.5006
	Asia	60/ 539 (11.1)	85/ 538 (15.8)	0.70 (0.52, 0.96) 0.0247	0.66 (0.47, 0.95) 0.0236	-0.05 (-0.09, -0.01) 0.0166	
	Europe and Saudi Arabia	160/1365 (11.7)	214/1394 (15.4)	0.79 (0.66, 0.95) 0.0124	0.74 (0.59, 0.92) 0.0079	-0.04 (-0.06, -0.01)*0.0052	
	North America	59/ 398 (14.8)	58/ 387 (15.0)	0.97 (0.70, 1.35) 0.8632	0.97 (0.65, 1.44) 0.8759	-0.00 (-0.05, 0.05)*0.9489	
	Latin America	55/ 540 (10.2)	65/ 518 (12.5)	0.79 (0.57, 1.11) 0.1714	0.77 (0.52, 1.14) 0.1886	-0.02 (-0.06, 0.01)*0.2262	
	NYHA class at enrolment						0.7482
	II	256/2113 (12.1)	329/2187 (15.0)	0.80 (0.69, 0.93) 0.0031	0.76 (0.64, 0.91) 0.0028	-0.03 (-0.05, -0.01)*0.0050	
	III or IV	78/ 729 (10.7)	93/ 649 (14.3)	0.76 (0.58, 0.99) 0.0452	0.71 (0.51, 0.99) 0.0430	-0.04 (-0.07, -0.00)*0.0425	
	LVEF at enrolment						0.1938
	<= 49	110/ 980 (11.2)	115/ 963 (11.9)	0.92 (0.73, 1.18) 0.5278	0.91 (0.68, 1.20) 0.4885	-0.01 (-0.04, 0.02)*0.6213	
	50-59	138/1029 (13.4)	169/1017 (16.6)	0.80 (0.65, 0.98) 0.0302	0.77 (0.60, 0.98) 0.0360	-0.03 (-0.06, -0.00)*0.0422	
	>= 60	86/ 833 (10.3)	138/ 857 (16.1)	0.67 (0.52, 0.86) 0.0016	0.62 (0.46, 0.83) 0.0012	-0.06 (-0.09, -0.03)*0.0004	
	NT-proBNP at enrolment						0.9544
	<= median	163/1418 (11.5)	204/1421 (14.4)	0.79 (0.65, 0.95) 0.0139	0.76 (0.61, 0.95) 0.0178	-0.03 (-0.05, -0.00)*0.0230	
	> median	171/1424 (12.0)	218/1415 (15.4)	0.80 (0.67, 0.96) 0.0158	0.75 (0.60, 0.93) 0.0103	-0.03 (-0.06, -0.01)*0.0084	
	Type 2 Diabetes Medical History						0.2007
	Yes	148/1250 (11.8)	207/1260 (16.4)	0.73 (0.60, 0.88) 0.0010	0.68 (0.54, 0.86)*0.0010	-0.05 (-0.07, -0.02)*0.0009	
	No	186/1592 (11.7)	215/1577 (13.6)	0.86 (0.72, 1.03) 0.1057	0.84 (0.68, 1.03)*0.0990	-0.02 (-0.04, 0.00)*0.0987	
	Atrial fibrillation or flutter at enrolment ECG						0.7825
	Yes	133/1199 (11.1)	171/1199 (14.3)	0.78 (0.63, 0.95) 0.0163	0.74 (0.58, 0.94) 0.0156	-0.03 (-0.06, -0.01)*0.0195	
	No	201/1643 (12.2)	251/1638 (15.3)	0.80 (0.68, 0.95) 0.0118	0.77 (0.63, 0.94) 0.0105	-0.03 (-0.05, -0.01)*0.0102	
	BMI (kg/m2) at enrolment						0.8818
	< 30	180/1571 (11.5)	227/1559 (14.6)	0.79 (0.66, 0.95) 0.0105	0.75 (0.61, 0.93) 0.0086	-0.03 (-0.05, -0.01)*0.0098	
	>= 30	154/1270 (12.1)	193/1275 (15.1)	0.81 (0.67, 0.98) 0.0273	0.77 (0.61, 0.97) 0.0295	-0.03 (-0.06, -0.00)*0.0267	
	Baseline eGFR (mL/min/1.73m^2)						0.8075
	< 60	188/1359 (13.8)	241/1396 (17.3)	0.81 (0.68, 0.96) 0.0157	0.76 (0.62, 0.94) 0.0125	-0.03 (-0.06, -0.01)*0.0128	
	>= 60	146/1483 (9.8)	181/1440 (12.6)	0.78 (0.64, 0.96) 0.0178	0.75 (0.60, 0.95) 0.0182	-0.03 (-0.05, -0.00)*0.0196	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Full Analysis Set

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Total Symptom Score (LOCF)	SBP at randomisation						0.4430
	<= median	162/1424 (11.4)	223/1439 (15.5)	0.75 (0.63, 0.91) 0.0027	0.71 (0.57, 0.89) 0.0024	-0.04 (-0.07, -0.02)*0.0012	
	> median	172/1418 (12.1)	199/1398 (14.2)	0.83 (0.69, 1.01) 0.0585	0.81 (0.64, 1.01) 0.0571	-0.02 (-0.05, 0.00)*0.0987	
	LVEF at enrolment 2						0.1466
	<= 49	110/ 980 (11.2)	115/ 963 (11.9)	0.92 (0.73, 1.18) 0.5278	0.91 (0.68, 1.20) 0.4885	-0.01 (-0.04, 0.02)*0.6213	
	>= 50	224/1862 (12.0)	307/1874 (16.4)	0.75 (0.64, 0.87) 0.0002	0.70 (0.58, 0.85) 0.0002	-0.04 (-0.07, -0.02)*0.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1016
	Yes	17/ 283 (6.0)	31/ 286 (10.8)	0.55 (0.31, 0.98)*0.0418	0.40 (0.21, 0.77) 0.0061	-0.05 (-0.09, -0.00)*0.0371	
	No	317/2559 (12.4)	391/2551 (15.3)	0.82 (0.71, 0.94) 0.0034	0.78 (0.67, 0.92) 0.0031	-0.03 (-0.05, -0.01)*0.0023	
	MRAs at baseline						0.2353
	Yes	136/1227 (11.1)	189/1224 (15.4)	0.72 (0.59, 0.88) 0.0016	0.68 (0.54, 0.86) 0.0015	-0.04 (-0.07, -0.02)*0.0014	
	No	198/1615 (12.3)	233/1613 (14.4)	0.85 (0.71, 1.01) 0.0635	0.82 (0.67, 1.01) 0.0586	-0.02 (-0.05, 0.00)*0.0679	
	ACEi+ARB at baseline						0.0605
	Yes	217/2065 (10.5)	304/2077 (14.6)	0.73 (0.62, 0.85) <.0001	0.68 (0.56, 0.82) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	117/ 777 (15.1)	118/ 760 (15.5)	0.96 (0.76, 1.22) 0.7518	0.95 (0.72, 1.26) 0.7404	-0.01 (-0.04, 0.03) 0.6361	
	ARNI at baseline						0.1848
	Yes	21/ 153 (13.7)	13/ 126 (10.3)	1.17 (0.60, 2.25) 0.6463	1.22 (0.58, 2.59) 0.6019	0.03 (-0.04, 0.11)*0.3802	
	No	313/2689 (11.6)	409/2711 (15.1)	0.78 (0.68, 0.89) 0.0003	0.74 (0.63, 0.87) 0.0002	-0.03 (-0.05, -0.02)*0.0002	
	Beta Blocker at baseline						0.1871
	Yes	288/2360 (12.2)	354/2356 (15.0)	0.82 (0.72, 0.95) 0.0079	0.79 (0.67, 0.94) 0.0066	-0.03 (-0.05, -0.01)*0.0047	
	No	46/ 482 (9.5)	68/ 481 (14.1)	0.64 (0.45, 0.91) 0.0122	0.60 (0.40, 0.90) 0.0126	-0.05 (-0.09, -0.01)*0.0270	
	Diuretics at baseline						0.7078
	Yes	308/2536 (12.1)	383/2531 (15.1)	0.80 (0.70, 0.91) 0.0012	0.76 (0.65, 0.90) 0.0012	-0.03 (-0.05, -0.01)*0.0019	
	No	26/ 306 (8.5)	39/ 306 (12.7)	0.73 (0.46, 1.16) 0.1816	0.67 (0.40, 1.14) 0.1432	-0.04 (-0.09, 0.01)*0.0873	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Clinical Summary Score (LOCF)							
	Overall	338/2842 (11.9)	408/2837 (14.4)	0.83 (0.73, 0.95) 0.0072	0.80 (0.69, 0.94) 0.0065	-0.02 (-0.04, -0.01)*0.0055	
	Age						0.4243
	<= median	139/1415 (9.8)	184/1482 (12.4)	0.78 (0.64, 0.96) 0.0186	0.75 (0.59, 0.95) 0.0178	-0.03 (-0.05, -0.00)*0.0262	
	> median	199/1427 (13.9)	224/1355 (16.5)	0.87 (0.73, 1.03) 0.1157	0.84 (0.68, 1.04) 0.1014	-0.03 (-0.05, 0.00)*0.0579	
	Gender						0.7495
	Male	194/1656 (11.7)	234/1625 (14.4)	0.82 (0.69, 0.98) 0.0258	0.79 (0.64, 0.97) 0.0233	-0.03 (-0.05, -0.00)*0.0224	
	Female	144/1186 (12.1)	174/1212 (14.4)	0.86 (0.70, 1.05) 0.1338	0.83 (0.65, 1.06) 0.1351	-0.02 (-0.05, 0.00)*0.1094	
	Race						0.9414
	White	251/2039 (12.3)	306/2058 (14.9)	0.84 (0.72, 0.98) 0.0257	0.81 (0.68, 0.98) 0.0266	-0.03 (-0.05, -0.00)*0.0168	
	Black or African	8/ 67 (11.9)	8/ 71 (11.3)	1.06 (0.43, 2.64) 0.8944	1.03 (0.36, 2.95) 0.9621	0.01 (-0.10, 0.11)*0.9019	
	Asian	66/ 558 (11.8)	81/ 555 (14.6)	0.81 (0.60, 1.10) 0.1707	0.79 (0.55, 1.11) 0.1736	-0.03 (-0.07, 0.01) 0.1962	
	Other	13/ 178 (7.3)	13/ 153 (8.5)	0.86 (0.42, 1.76) 0.6702	0.83 (0.36, 1.89) 0.6522	-0.01 (-0.07, 0.05)*0.6889	
	Geographic region						0.8246
	Asia	62/ 539 (11.5)	76/ 538 (14.1)	0.81 (0.59, 1.11) 0.1971	0.79 (0.55, 1.13) 0.1979	-0.03 (-0.07, 0.01) 0.2049	
	Europe and Saudi Arabia	161/1365 (11.8)	212/1394 (15.2)	0.81 (0.67, 0.97) 0.0236	0.75 (0.60, 0.95) 0.0151	-0.03 (-0.06, -0.01)*0.0086	
	North America	58/ 398 (14.6)	60/ 387 (15.5)	0.92 (0.67, 1.28) 0.6351	0.92 (0.62, 1.37) 0.6873	-0.01 (-0.06, 0.04)*0.7153	
	Latin America	57/ 540 (10.6)	60/ 518 (11.6)	0.90 (0.64, 1.26) 0.5393	0.89 (0.60, 1.31) 0.5432	-0.01 (-0.05, 0.03)*0.5945	
	NYHA class at enrolment						0.5465
	II	251/2113 (11.9)	319/2187 (14.6)	0.81 (0.70, 0.94) 0.0068	0.78 (0.65, 0.93) 0.0061	-0.03 (-0.05, -0.01)*0.0087	
	III or IV	87/ 729 (11.9)	89/ 649 (13.7)	0.89 (0.69, 1.17) 0.4065	0.86 (0.62, 1.20) 0.3838	-0.02 (-0.05, 0.02)*0.3248	
	LVEF at enrolment						0.5454
	<= 49	113/ 980 (11.5)	123/ 963 (12.8)	0.89 (0.70, 1.12) 0.3227	0.86 (0.65, 1.13) 0.2884	-0.01 (-0.04, 0.02)*0.4022	
	50-59	142/1029 (13.8)	163/1017 (16.0)	0.86 (0.70, 1.05) 0.1368	0.84 (0.66, 1.08) 0.1709	-0.02 (-0.05, 0.01)*0.1571	
	>= 60	83/ 833 (10.0)	122/ 857 (14.2)	0.74 (0.57, 0.95) 0.0200	0.69 (0.51, 0.94) 0.0167	-0.04 (-0.07, -0.01)*0.0069	
	NT-proBNP at enrolment						0.6568
	<= median	170/1418 (12.0)	197/1421 (13.9)	0.86 (0.71, 1.04) 0.1144	0.84 (0.67, 1.05) 0.1248	-0.02 (-0.04, 0.01)*0.1364	
	> median	168/1424 (11.8)	211/1415 (14.9)	0.81 (0.67, 0.98) 0.0272	0.77 (0.62, 0.96) 0.0212	-0.03 (-0.06, -0.01)*0.0146	
	Type 2 Diabetes Medical History						0.2702
	Yes	154/1250 (12.3)	202/1260 (16.0)	0.77 (0.64, 0.94) 0.0082	0.74 (0.59, 0.92)*0.0079	-0.04 (-0.06, -0.01)*0.0076	
	No	184/1592 (11.6)	206/1577 (13.1)	0.90 (0.75, 1.08) 0.2455	0.87 (0.70, 1.08)*0.1975	-0.02 (-0.04, 0.01)*0.1972	
	Atrial fibrillation or flutter at enrolment ECG						0.6561
	Yes	134/1199 (11.2)	167/1199 (13.9)	0.80 (0.65, 0.99) 0.0408	0.77 (0.60, 0.99) 0.0402	-0.03 (-0.05, -0.00)*0.0418	
	No	204/1643 (12.4)	241/1638 (14.7)	0.85 (0.72, 1.01) 0.0709	0.83 (0.67, 1.01) 0.0641	-0.02 (-0.05, 0.00)*0.0546	
	BMI (kg/m2) at enrolment						0.7540
	< 30	188/1571 (12.0)	221/1559 (14.2)	0.85 (0.71, 1.02) 0.0803	0.82 (0.67, 1.02) 0.0695	-0.02 (-0.05, 0.00)*0.0667	
	>= 30	150/1270 (11.8)	186/1275 (14.6)	0.82 (0.67, 0.99) 0.0423	0.79 (0.62, 1.00) 0.0497	-0.03 (-0.05, -0.00)*0.0383	
	Baseline eGFR (mL/min/1.73m^2)						0.1269
	< 60	185/1359 (13.6)	208/1396 (14.9)	0.92 (0.77, 1.11) 0.3899	0.90 (0.73, 1.12) 0.3615	-0.01 (-0.04, 0.01)*0.3339	
	>= 60	153/1483 (10.3)	200/1440 (13.9)	0.75 (0.62, 0.91) 0.0037	0.71 (0.57, 0.90) 0.0036	-0.04 (-0.06, -0.01)*0.0031	

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Clinical Summary Score (LOCF)	SBP at randomisation						0.3331
	<= median	161/1424 (11.3)	215/1439 (14.9)	0.78 (0.64, 0.94) 0.0088	0.74 (0.60, 0.93) 0.0087	-0.04 (-0.06, -0.01)*0.0039	
	> median	177/1418 (12.5)	193/1398 (13.8)	0.89 (0.74, 1.07) 0.2122	0.86 (0.69, 1.08) 0.1972	-0.01 (-0.04, 0.01)*0.2988	
	LVEF at enrolment 2						0.5477
	<= 49	113/ 980 (11.5)	123/ 963 (12.8)	0.89 (0.70, 1.12) 0.3227	0.86 (0.65, 1.13) 0.2884	-0.01 (-0.04, 0.02)*0.4022	
	>= 50	225/1862 (12.1)	285/1874 (15.2)	0.81 (0.69, 0.95) 0.0112	0.78 (0.65, 0.95) 0.0116	-0.03 (-0.05, -0.01)*0.0054	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7103
	Yes	18/ 283 (6.4)	23/ 286 (8.0)	0.79 (0.44, 1.43)*0.4393	0.67 (0.35, 1.30) 0.2400	-0.02 (-0.06, 0.03)*0.4375	
	No	320/2559 (12.5)	385/2551 (15.1)	0.84 (0.73, 0.96) 0.0121	0.81 (0.69, 0.95) 0.0109	-0.03 (-0.04, -0.01)*0.0073	
	MRAs at baseline						0.3286
	Yes	141/1227 (11.5)	182/1224 (14.9)	0.77 (0.63, 0.94) 0.0120	0.74 (0.58, 0.94) 0.0133	-0.03 (-0.06, -0.01)*0.0133	
	No	197/1615 (12.2)	226/1613 (14.0)	0.88 (0.74, 1.05) 0.1672	0.86 (0.70, 1.05) 0.1436	-0.02 (-0.04, 0.01)*0.1268	
	ACEi+ARB at baseline						0.5067
	Yes	234/2065 (11.3)	295/2077 (14.2)	0.81 (0.69, 0.95) 0.0090	0.78 (0.64, 0.94) 0.0079	-0.03 (-0.05, -0.01)*0.0056	
	No	104/ 777 (13.4)	113/ 760 (14.9)	0.90 (0.70, 1.15) 0.3943	0.88 (0.66, 1.18) 0.3884	-0.02 (-0.05, 0.02) 0.3291	
	ARNI at baseline						0.4838
	Yes	18/ 153 (11.8)	13/ 126 (10.3)	1.05 (0.53, 2.09) 0.8851	1.07 (0.50, 2.31) 0.8656	0.02 (-0.06, 0.09) 0.6799	
	No	320/2689 (11.9)	395/2711 (14.6)	0.83 (0.72, 0.95) 0.0068	0.80 (0.68, 0.94) 0.0059	-0.03 (-0.04, -0.01)*0.0038	
	Beta Blocker at baseline						0.9475
	Yes	283/2360 (12.0)	345/2356 (14.6)	0.84 (0.73, 0.97) 0.0157	0.80 (0.68, 0.95) 0.0125	-0.03 (-0.05, -0.01)*0.0073	
	No	55/ 482 (11.4)	63/ 481 (13.1)	0.84 (0.60, 1.17) 0.2958	0.82 (0.56, 1.21) 0.3211	-0.02 (-0.06, 0.02)*0.4246	
	Diuretics at baseline						0.7309
	Yes	314/2536 (12.4)	375/2531 (14.8)	0.84 (0.73, 0.96) 0.0118	0.81 (0.69, 0.95) 0.0109	-0.02 (-0.04, -0.01)*0.0114	
	No	24/ 306 (7.8)	33/ 306 (10.8)	0.77 (0.47, 1.26) 0.2892	0.73 (0.42, 1.27) 0.2653	-0.03 (-0.08, 0.02)*0.2101	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall Summary Score (LOCF)							
	Overall	321/2842 (11.3)	382/2837 (13.5)	0.85 (0.74, 0.97) 0.0163	0.82 (0.70, 0.96) 0.0150	-0.02 (-0.04, -0.00)*0.0130	
	Age						0.5417
	<= median	129/1415 (9.1)	167/1482 (11.3)	0.80 (0.65, 0.99) 0.0433	0.78 (0.61, 0.99) 0.0417	-0.02 (-0.04, 0.00)*0.0552	
	> median	192/1427 (13.5)	215/1355 (15.9)	0.87 (0.73, 1.04) 0.1280	0.84 (0.68, 1.05) 0.1200	-0.02 (-0.05, 0.00)*0.0723	
	Gender						0.3817
	Male	195/1656 (11.8)	216/1625 (13.3)	0.89 (0.74, 1.06) 0.1985	0.87 (0.71, 1.07) 0.1976	-0.02 (-0.04, 0.01)*0.1895	
	Female	126/1186 (10.6)	166/1212 (13.7)	0.79 (0.64, 0.97) 0.0281	0.75 (0.59, 0.97) 0.0265	-0.03 (-0.06, -0.00)*0.0211	
	Race						0.4809
	White	228/2039 (11.2)	289/2058 (14.0)	0.82 (0.70, 0.96) 0.0124	0.78 (0.65, 0.94) 0.0106	-0.03 (-0.05, -0.01)*0.0058	
	Black or African	10/ 67 (14.9)	8/ 71 (11.3)	1.36 (0.59, 3.14) 0.4734	1.36 (0.49, 3.80) 0.5595	0.04 (-0.08, 0.15)*0.5245	
	Asian	68/ 558 (12.2)	75/ 555 (13.5)	0.90 (0.66, 1.22) 0.5055	0.89 (0.62, 1.26) 0.5047	-0.01 (-0.05, 0.03) 0.4967	
	Other	15/ 178 (8.4)	10/ 153 (6.5)	1.24 (0.59, 2.62) 0.5727	1.29 (0.55, 3.06) 0.5568	0.02 (-0.04, 0.08)*0.5123	
	Geographic region						0.7335
	Asia	63/ 539 (11.7)	70/ 538 (13.0)	0.90 (0.65, 1.24) 0.5085	0.88 (0.61, 1.27) 0.5083	-0.01 (-0.05, 0.03) 0.5097	
	Europe and Saudi Arabia	148/1365 (10.8)	199/1394 (14.3)	0.80 (0.66, 0.97) 0.0204	0.74 (0.59, 0.94) 0.0136	-0.03 (-0.06, -0.01)*0.0064	
	North America	55/ 398 (13.8)	56/ 387 (14.5)	0.94 (0.67, 1.32) 0.7119	0.93 (0.62, 1.40) 0.7304	-0.01 (-0.06, 0.04)*0.7935	
	Latin America	55/ 540 (10.2)	57/ 518 (11.0)	0.93 (0.66, 1.30) 0.6672	0.91 (0.61, 1.36) 0.6352	-0.01 (-0.05, 0.03)*0.6654	
	NYHA class at enrolment						0.4452
	II	233/2113 (11.0)	294/2187 (13.4)	0.81 (0.69, 0.95) 0.0112	0.78 (0.65, 0.94) 0.0102	-0.02 (-0.04, -0.00)*0.0155	
	III or IV	88/ 729 (12.1)	88/ 649 (13.6)	0.93 (0.71, 1.21) 0.5737	0.89 (0.64, 1.24) 0.4996	-0.01 (-0.05, 0.02)*0.4100	
	LVEF at enrolment						0.7858
	<= 49	103/ 980 (10.5)	109/ 963 (11.3)	0.90 (0.70, 1.16) 0.4221	0.88 (0.66, 1.18) 0.3871	-0.01 (-0.04, 0.02)*0.5677	
	50-59	134/1029 (13.0)	162/1017 (15.9)	0.82 (0.67, 1.01) 0.0612	0.79 (0.62, 1.02) 0.0735	-0.03 (-0.06, 0.00)*0.0615	
	>= 60	84/ 833 (10.1)	111/ 857 (13.0)	0.81 (0.62, 1.06) 0.1224	0.78 (0.58, 1.06) 0.1098	-0.03 (-0.06, 0.00)*0.0643	
	NT-proBNP at enrolment						0.6551
	<= median	152/1418 (10.7)	185/1421 (13.0)	0.82 (0.67, 1.00) 0.0497	0.80 (0.63, 1.00) 0.0545	-0.02 (-0.05, 0.00)*0.0580	
	> median	169/1424 (11.9)	197/1415 (13.9)	0.87 (0.72, 1.05) 0.1593	0.84 (0.67, 1.05) 0.1309	-0.02 (-0.05, 0.00)*0.1024	
	Type 2 Diabetes Medical History						0.8897
	Yes	145/1250 (11.6)	176/1260 (14.0)	0.84 (0.69, 1.03) 0.0888	0.81 (0.64, 1.02)*0.0760	-0.02 (-0.05, 0.00)*0.0754	
	No	176/1592 (11.1)	206/1577 (13.1)	0.86 (0.71, 1.03) 0.1007	0.83 (0.67, 1.03)*0.0830	-0.02 (-0.04, 0.00)*0.0826	
	Atrial fibrillation or flutter at enrolment ECG						0.5499
	Yes	130/1199 (10.8)	147/1199 (12.3)	0.89 (0.72, 1.11) 0.2976	0.87 (0.67, 1.12) 0.2832	-0.01 (-0.04, 0.01)*0.2773	
	No	191/1643 (11.6)	235/1638 (14.3)	0.82 (0.69, 0.97) 0.0240	0.79 (0.64, 0.97) 0.0232	-0.03 (-0.05, -0.00)*0.0203	
	BMI (kg/m2) at enrolment						0.5438
	< 30	175/1571 (11.1)	215/1559 (13.8)	0.82 (0.68, 0.98) 0.0318	0.78 (0.63, 0.97) 0.0275	-0.03 (-0.05, -0.00)*0.0247	
	>= 30	146/1270 (11.5)	166/1275 (13.0)	0.89 (0.73, 1.09) 0.2565	0.87 (0.68, 1.11) 0.2667	-0.02 (-0.04, 0.01)*0.2411	
	Baseline eGFR (mL/min/1.73m^2)						0.1936
	< 60	179/1359 (13.2)	201/1396 (14.4)	0.92 (0.77, 1.11) 0.3898	0.90 (0.73, 1.13) 0.3669	-0.01 (-0.04, 0.01)*0.3502	
	>= 60	142/1483 (9.6)	181/1440 (12.6)	0.77 (0.63, 0.94) 0.0115	0.73 (0.58, 0.93) 0.0109	-0.03 (-0.05, -0.01)*0.0099	

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Overall Summary Score (LOCF)	SBP at randomisation						0.9508
	<= median	155/1424 (10.9)	189/1439 (13.1)	0.85 (0.70, 1.03) 0.0963	0.83 (0.66, 1.04) 0.1108	-0.02 (-0.05, 0.00)*0.0639	
	> median	166/1418 (11.7)	193/1398 (13.8)	0.84 (0.69, 1.02) 0.0723	0.80 (0.64, 1.00) 0.0542	-0.02 (-0.05, 0.00)*0.0950	
	LVEF at enrolment 2						0.5116
	<= 49	103/ 980 (10.5)	109/ 963 (11.3)	0.90 (0.70, 1.16) 0.4221	0.88 (0.66, 1.18) 0.3871	-0.01 (-0.04, 0.02)*0.5677	
	>= 50	218/1862 (11.7)	273/1874 (14.6)	0.82 (0.70, 0.97) 0.0187	0.79 (0.65, 0.96) 0.0192	-0.03 (-0.05, -0.01)*0.0096	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4936
	Yes	17/ 283 (6.0)	24/ 286 (8.4)	0.72 (0.39, 1.30)*0.2742	0.66 (0.34, 1.28) 0.2189	-0.02 (-0.07, 0.02)*0.2705	
	No	304/2559 (11.9)	358/2551 (14.0)	0.86 (0.74, 0.99) 0.0305	0.83 (0.70, 0.98) 0.0293	-0.02 (-0.04, -0.00)*0.0218	
	MRAs at baseline						0.6475
	Yes	137/1227 (11.2)	167/1224 (13.6)	0.82 (0.66, 1.00) 0.0555	0.79 (0.62, 1.01) 0.0631	-0.02 (-0.05, 0.00)*0.0626	
	No	184/1615 (11.4)	215/1613 (13.3)	0.87 (0.73, 1.04) 0.1307	0.84 (0.68, 1.04) 0.1091	-0.02 (-0.04, 0.00)*0.0946	
	ACEi+ARB at baseline						0.0910
	Yes	214/2065 (10.4)	279/2077 (13.4)	0.78 (0.66, 0.92) 0.0032	0.74 (0.61, 0.90) 0.0027	-0.03 (-0.05, -0.01)*0.0023	
	No	107/ 777 (13.8)	103/ 760 (13.6)	1.02 (0.79, 1.31) 0.8889	1.02 (0.76, 1.37) 0.8876	0.00 (-0.03, 0.04)*0.9009	
	ARNI at baseline						0.5175
	Yes	14/ 153 (9.2)	10/ 126 (7.9)	1.11 (0.51, 2.44) 0.7904	1.13 (0.48, 2.67) 0.7831	0.01 (-0.05, 0.08)*0.7172	
	No	307/2689 (11.4)	372/2711 (13.7)	0.84 (0.73, 0.97) 0.0162	0.81 (0.69, 0.96) 0.0143	-0.02 (-0.04, -0.01)*0.0106	
	Beta Blocker at baseline						0.6228
	Yes	272/2360 (11.5)	323/2356 (13.7)	0.86 (0.74, 1.00) 0.0466	0.83 (0.70, 0.99) 0.0391	-0.02 (-0.04, -0.00)*0.0238	
	No	49/ 482 (10.2)	59/ 481 (12.3)	0.79 (0.55, 1.12) 0.1872	0.77 (0.51, 1.16) 0.2055	-0.02 (-0.06, 0.02)*0.3015	
	Diuretics at baseline						0.3141
	Yes	293/2536 (11.6)	355/2531 (14.0)	0.83 (0.72, 0.95) 0.0089	0.80 (0.67, 0.94) 0.0078	-0.02 (-0.04, -0.01)*0.0084	
	No	28/ 306 (9.2)	27/ 306 (8.8)	1.08 (0.65, 1.77) 0.7710	1.10 (0.63, 1.92) 0.7492	0.00 (-0.04, 0.05)*0.8876	

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Physical Limitation (LOCF)							
	Overall	523/2792 (18.7)	588/2792 (21.1)	0.90 (0.81, 1.00) 0.0429	0.87 (0.76, 1.00) 0.0480	-0.02 (-0.04, 0.00) 0.0700	
	Age						0.4925
	<= median	220/1403 (15.7)	266/1469 (18.1)	0.86 (0.73, 1.01) 0.0580	0.83 (0.68, 1.01) 0.0631	-0.02 (-0.05, 0.00)*0.0824	
	> median	303/1389 (21.8)	322/1323 (24.3)	0.92 (0.81, 1.06) 0.2439	0.90 (0.75, 1.08) 0.2533	-0.01 (-0.04, 0.01) 0.3108	
	Gender						0.1562
	Male	324/1638 (19.8)	334/1602 (20.8)	0.96 (0.84, 1.09) 0.5031	0.94 (0.79, 1.12) 0.4873	-0.01 (-0.04, 0.01) 0.2837	
	Female	199/1154 (17.2)	254/1190 (21.3)	0.82 (0.70, 0.97) 0.0188	0.79 (0.64, 0.98) 0.0299	-0.02 (-0.05, 0.01) 0.1709	
	Race						0.9158
	White	399/2004 (19.9)	449/2025 (22.2)	0.91 (0.81, 1.02) 0.1210	0.89 (0.76, 1.04) 0.1429	-0.02 (-0.05, 0.00)*0.0780	
	Black or African	16/ 66 (24.2)	19/ 68 (27.9)	0.90 (0.53, 1.54) 0.7038	0.79 (0.35, 1.78) 0.5648	-0.04 (-0.19, 0.11)*0.6255	
	Asian	89/ 551 (16.2)	105/ 550 (19.1)	0.85 (0.66, 1.10) 0.2082	0.82 (0.60, 1.12) 0.2099	-0.03 (-0.07, 0.02) 0.2145	
	Other	19/ 171 (11.1)	15/ 149 (10.1)	1.07 (0.58, 1.97) 0.8364	1.06 (0.51, 2.24) 0.8687	0.01 (-0.06, 0.08)*0.7617	
	Geographic region						0.4388
	Asia	84/ 533 (15.8)	98/ 533 (18.4)	0.86 (0.66, 1.12) 0.2662	0.83 (0.61, 1.15) 0.2698	-0.02 (-0.07, 0.02) 0.2798	
	Europe and Saudi Arabia	259/1347 (19.2)	302/1373 (22.0)	0.89 (0.77, 1.03) 0.1067	0.86 (0.71, 1.04) 0.1218	-0.03 (-0.06, 0.00)*0.0742	
	North America	89/ 391 (22.8)	105/ 375 (28.0)	0.82 (0.65, 1.04) 0.1019	0.77 (0.55, 1.07) 0.1216	-0.05 (-0.11, 0.01)*0.0955	
	Latin America	91/ 521 (17.5)	83/ 511 (16.2)	1.09 (0.84, 1.42) 0.5029	1.09 (0.78, 1.52) 0.6131	0.01 (-0.03, 0.06)*0.5994	
	NYHA class at enrolment						0.7064
	II	387/2077 (18.6)	445/2159 (20.6)	0.90 (0.80, 1.02) 0.0987	0.88 (0.76, 1.03) 0.1103	-0.01 (-0.03, 0.01) 0.2409	
	III or IV	136/ 715 (19.0)	142/ 632 (22.5)	0.87 (0.71, 1.06) 0.1581	0.82 (0.63, 1.08) 0.1656	-0.03 (-0.08, 0.01)*0.1198	
	LVEF at enrolment						0.3275
	<= 49	189/ 967 (19.5)	182/ 952 (19.1)	1.00 (0.83, 1.19) 0.9845	1.00 (0.79, 1.25) 0.9715	0.00 (-0.03, 0.04)*0.8126	
	50-59	191/1013 (18.9)	229/ 998 (22.9)	0.83 (0.71, 0.98) 0.0314	0.80 (0.64, 1.00) 0.0479	-0.02 (-0.05, 0.01) 0.1658	
	>= 60	143/ 812 (17.6)	177/ 842 (21.0)	0.87 (0.72, 1.06) 0.1768	0.84 (0.65, 1.07) 0.1586	-0.03 (-0.06, 0.01) 0.1283	
	NT-proBNP at enrolment						0.3060
	<= median	245/1394 (17.6)	291/1402 (20.8)	0.85 (0.73, 0.99) 0.0337	0.81 (0.67, 0.99) 0.0369	-0.01 (-0.04, 0.01) 0.3139	
	> median	278/1398 (19.9)	297/1389 (21.4)	0.95 (0.82, 1.09) 0.4514	0.93 (0.77, 1.12) 0.4597	-0.02 (-0.04, 0.01) 0.2310	
	Type 2 Diabetes Medical History						0.6963
	Yes	240/1232 (19.5)	272/1237 (22.0)	0.88 (0.76, 1.02) 0.0953	0.86 (0.71, 1.04)*0.1245	-0.02 (-0.05, 0.01) 0.1706	
	No	283/1560 (18.1)	316/1555 (20.3)	0.92 (0.80, 1.06) 0.2261	0.87 (0.73, 1.04)*0.1228	-0.01 (-0.04, 0.01) 0.2595	
	Atrial fibrillation or flutter at enrolment ECG						0.8640
	Yes	223/1178 (18.9)	246/1175 (20.9)	0.91 (0.78, 1.06) 0.2317	0.89 (0.72, 1.09) 0.2563	-0.02 (-0.05, 0.01)*0.2232	
	No	300/1614 (18.6)	342/1617 (21.2)	0.89 (0.78, 1.02) 0.0952	0.86 (0.72, 1.03) 0.0994	-0.02 (-0.04, 0.01) 0.1728	
	BMI (kg/m2) at enrolment						0.2826
	< 30	272/1547 (17.6)	320/1535 (20.8)	0.85 (0.74, 0.99) 0.0314	0.81 (0.68, 0.97) 0.0255	-0.03 (-0.06, -0.01) 0.0155	
	>= 30	251/1244 (20.2)	267/1254 (21.3)	0.96 (0.83, 1.11) 0.5819	0.96 (0.79, 1.18) 0.7206	0.00 (-0.03, 0.03) 0.9594	
	Baseline eGFR (mL/min/1.73m^2)						0.6414
	< 60	274/1328 (20.6)	305/1367 (22.3)	0.92 (0.80, 1.06) 0.2692	0.91 (0.76, 1.10) 0.3474	-0.00 (-0.03, 0.02) 0.7282	
	>= 60	249/1464 (17.0)	283/1424 (19.9)	0.88 (0.75, 1.02) 0.0881	0.84 (0.69, 1.02) 0.0760	-0.03 (-0.06, -0.00)*0.0471	

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Physical Limitation (LOCF)	SBP at randomisation						0.4785
	<= median	259/1396 (18.6)	290/1414 (20.5)	0.92 (0.80, 1.07) 0.3009	0.91 (0.75, 1.10) 0.3370	-0.01 (-0.04, 0.02) 0.4145	
	> median	264/1396 (18.9)	298/1378 (21.6)	0.86 (0.75, 1.00) 0.0438	0.82 (0.68, 0.99) 0.0413	-0.03 (-0.06, 0.00)*0.0753	
	LVEF at enrolment 2						0.1579
	<= 49	189/ 967 (19.5)	182/ 952 (19.1)	1.00 (0.83, 1.19) 0.9845	1.00 (0.79, 1.25) 0.9715	0.00 (-0.03, 0.04)*0.8126	
	>= 50	334/1825 (18.3)	406/1840 (22.1)	0.85 (0.75, 0.97) 0.0141	0.82 (0.69, 0.96) 0.0168	-0.03 (-0.05, -0.00) 0.0377	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4519
	Yes	40/ 273 (14.7)	51/ 277 (18.4)	0.79 (0.55, 1.15) 0.2241	0.75 (0.47, 1.19) 0.2262	-0.04 (-0.10, 0.02)*0.2346	
	No	483/2519 (19.2)	537/2515 (21.4)	0.91 (0.82, 1.01) 0.0831	0.89 (0.77, 1.02) 0.0921	-0.02 (-0.04, 0.00) 0.1072	
	MRAs at baseline						0.4919
	Yes	232/1200 (19.3)	269/1208 (22.3)	0.87 (0.74, 1.01) 0.0653	0.84 (0.68, 1.02) 0.0782	-0.02 (-0.05, 0.01) 0.1653	
	No	291/1592 (18.3)	319/1584 (20.1)	0.93 (0.81, 1.07) 0.3024	0.91 (0.76, 1.09) 0.2986	-0.02 (-0.05, 0.01)*0.1833	
	ACEi+ARB at baseline						0.0917
	Yes	366/2029 (18.0)	440/2047 (21.5)	0.85 (0.76, 0.96) 0.0097	0.81 (0.70, 0.95) 0.0110	-0.02 (-0.04, -0.00) 0.0372	
	No	157/ 763 (20.6)	148/ 745 (19.9)	1.04 (0.85, 1.27) 0.7065	1.05 (0.81, 1.35) 0.7093	0.01 (-0.03, 0.04) 0.7989	
	ARNI at baseline						0.8235
	Yes	28/ 150 (18.7)	24/ 123 (19.5)	0.88 (0.54, 1.43) 0.6049	0.86 (0.46, 1.59) 0.6218	-0.02 (-0.11, 0.08) 0.7336	
	No	495/2642 (18.7)	564/2669 (21.1)	0.90 (0.81, 1.00) 0.0482	0.88 (0.76, 1.00) 0.0583	-0.01 (-0.03, 0.00) 0.1482	
	Beta Blocker at baseline						0.4750
	Yes	432/2323 (18.6)	497/2321 (21.4)	0.88 (0.79, 0.99) 0.0336	0.85 (0.74, 0.99) 0.0334	-0.03 (-0.05, -0.01)*0.0164	
	No	91/ 469 (19.4)	91/ 471 (19.3)	0.99 (0.76, 1.28) 0.9200	1.00 (0.72, 1.38) 0.9769	-0.00 (-0.05, 0.05) 0.9714	
	Diuretics at baseline						0.7139
	Yes	475/2493 (19.1)	538/2492 (21.6)	0.89 (0.80, 1.00) 0.0414	0.87 (0.75, 1.00) 0.0438	-0.02 (-0.04, 0.00) 0.0636	
	No	48/ 299 (16.1)	50/ 300 (16.7)	0.95 (0.67, 1.36) 0.7874	0.96 (0.61, 1.49) 0.8398	-0.00 (-0.05, 0.05) 0.8978	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)							
	Overall	485/2842 (17.1)	565/2837 (19.9)	0.87 (0.79, 0.97) 0.0106	0.83 (0.72, 0.96) 0.0098	-0.01 (-0.03, -0.00) 0.0419	
	Age						0.9226
	<= median	211/1415 (14.9)	253/1482 (17.1)	0.88 (0.75, 1.03) 0.1040	0.85 (0.69, 1.04) 0.1187	-0.02 (-0.04, 0.00) 0.0866	
	> median	274/1427 (19.2)	312/1355 (23.0)	0.87 (0.76, 1.00) 0.0435	0.81 (0.67, 0.98) 0.0304	-0.04 (-0.07, -0.01)*0.0135	
	Gender						0.7284
	Male	284/1656 (17.1)	318/1625 (19.6)	0.89 (0.78, 1.02) 0.0927	0.86 (0.71, 1.03) 0.1069	-0.02 (-0.05, 0.00)*0.0734	
	Female	201/1186 (16.9)	247/1212 (20.4)	0.86 (0.73, 1.01) 0.0589	0.80 (0.64, 0.99) 0.0415	-0.02 (-0.04, 0.01) 0.2309	
	Race						0.3039
	White	351/2039 (17.2)	409/2058 (19.9)	0.89 (0.79, 1.01) 0.0654	0.85 (0.72, 1.01) 0.0593	-0.03 (-0.05, -0.00)*0.0284	
	Black or African	14/ 67 (20.9)	11/ 71 (15.5)	1.48 (0.73, 2.99) 0.2760	1.49 (0.61, 3.63) 0.3758	0.01 (-0.14, 0.16) 0.8976	
	Asian	103/ 558 (18.5)	129/ 555 (23.2)	0.78 (0.63, 0.98) 0.0321	0.73 (0.54, 0.98) 0.0384	-0.05 (-0.10, -0.00)*0.0491	
	Other	17/ 178 (9.6)	16/ 153 (10.5)	0.88 (0.48, 1.62) 0.6865	0.84 (0.39, 1.80) 0.6531	-0.01 (-0.07, 0.06)*0.7842	
	Geographic region						0.4161
	Asia	98/ 539 (18.2)	123/ 538 (22.9)	0.78 (0.62, 0.99) 0.0375	0.74 (0.54, 1.00) 0.0502	-0.05 (-0.09, 0.00)*0.0568	
	Europe and Saudi Arabia	232/1365 (17.0)	270/1394 (19.4)	0.91 (0.79, 1.06) 0.2345	0.88 (0.72, 1.08) 0.2197	-0.02 (-0.05, 0.01)*0.1060	
	North America	71/ 398 (17.8)	90/ 387 (23.3)	0.78 (0.60, 1.02) 0.0652	0.70 (0.49, 1.00) 0.0492	-0.05 (-0.11, 0.00)*0.0600	
	Latin America	84/ 540 (15.6)	82/ 518 (15.8)	1.02 (0.79, 1.31) 0.9078	0.99 (0.69, 1.40) 0.9431	-0.00 (-0.05, 0.04)*0.9023	
	NYHA class at enrolment						0.4628
	II	354/2113 (16.8)	432/2187 (19.8)	0.85 (0.76, 0.96) 0.0090	0.80 (0.68, 0.94) 0.0071	-0.03 (-0.05, -0.01)*0.0108	
	III or IV	131/ 729 (18.0)	132/ 649 (20.3)	0.93 (0.77, 1.13) 0.4635	0.89 (0.67, 1.19) 0.4293	-0.01 (-0.04, 0.01) 0.3289	
	LVEF at enrolment						0.7307
	<= 49	165/ 980 (16.8)	179/ 963 (18.6)	0.92 (0.77, 1.10) 0.3435	0.87 (0.68, 1.11) 0.2524	-0.02 (-0.05, 0.02)*0.3121	
	50-59	176/1029 (17.1)	209/1017 (20.6)	0.83 (0.70, 0.99) 0.0363	0.80 (0.63, 1.00) 0.0529	-0.03 (-0.07, -0.00)*0.0460	
	>= 60	144/ 833 (17.3)	177/ 857 (20.7)	0.88 (0.73, 1.06) 0.1675	0.84 (0.65, 1.08) 0.1662	-0.03 (-0.07, 0.00)*0.0772	
	NT-proBNP at enrolment						0.1439
	<= median	227/1418 (16.0)	284/1421 (20.0)	0.81 (0.70, 0.94) 0.0052	0.76 (0.62, 0.93) 0.0082	-0.04 (-0.07, -0.01)*0.0057	
	> median	258/1424 (18.1)	281/1415 (19.9)	0.94 (0.82, 1.09) 0.4149	0.90 (0.74, 1.10) 0.3013	-0.01 (-0.03, 0.01) 0.4918	
	Type 2 Diabetes Medical History						0.1918
	Yes	209/1250 (16.7)	268/1260 (21.3)	0.81 (0.70, 0.95) 0.0078	0.74 (0.61, 0.91)*0.0037	-0.02 (-0.05, 0.00) 0.1033	
	No	276/1592 (17.3)	297/1577 (18.8)	0.93 (0.81, 1.07) 0.3295	0.90 (0.75, 1.08)*0.2739	-0.01 (-0.03, 0.01) 0.1908	
	Atrial fibrillation or flutter at enrolment ECG						0.5286
	Yes	200/1199 (16.7)	226/1199 (18.8)	0.91 (0.77, 1.07) 0.2382	0.87 (0.70, 1.08) 0.2102	-0.02 (-0.05, 0.01)*0.1646	
	No	285/1643 (17.3)	339/1638 (20.7)	0.85 (0.74, 0.97) 0.0140	0.80 (0.67, 0.96) 0.0184	-0.03 (-0.06, -0.01)*0.0144	
	BMI (kg/m2) at enrolment						0.2036
	< 30	258/1571 (16.4)	319/1559 (20.5)	0.82 (0.71, 0.95) 0.0067	0.77 (0.64, 0.93) 0.0077	-0.01 (-0.04, 0.01) 0.2175	
	>= 30	226/1270 (17.8)	245/1275 (19.2)	0.94 (0.81, 1.10) 0.4398	0.91 (0.73, 1.12) 0.3604	-0.01 (-0.04, 0.02)*0.3561	
	Baseline eGFR (mL/min/1.73m^2)						0.2144
	< 60	262/1359 (19.3)	292/1396 (20.9)	0.93 (0.81, 1.07) 0.3024	0.91 (0.75, 1.10) 0.3229	-0.02 (-0.05, 0.01)*0.2832	
	>= 60	223/1483 (15.0)	273/1440 (19.0)	0.82 (0.70, 0.95) 0.0100	0.76 (0.62, 0.93) 0.0075	-0.04 (-0.07, -0.01)*0.0047	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Quality of Life (LOCF)	SBP at randomisation						0.1280
	<= median	256/1424 (18.0)	282/1439 (19.6)	0.95 (0.82, 1.09) 0.4525	0.93 (0.77, 1.13) 0.4828	-0.00 (-0.02, 0.02) 0.8495	
	> median	229/1418 (16.1)	283/1398 (20.2)	0.81 (0.69, 0.94) 0.0046	0.74 (0.61, 0.91) 0.0034	-0.04 (-0.07, -0.01)*0.0048	
	LVEF at enrolment 2						0.5033
	<= 49	165/ 980 (16.8)	179/ 963 (18.6)	0.92 (0.77, 1.10) 0.3435	0.87 (0.68, 1.11) 0.2524	-0.02 (-0.05, 0.02)*0.3121	
	>= 50	320/1862 (17.2)	386/1874 (20.6)	0.85 (0.75, 0.97) 0.0132	0.81 (0.69, 0.96) 0.0178	-0.03 (-0.06, -0.01)*0.0077	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4870
	Yes	34/ 283 (12.0)	47/ 286 (16.4)	0.73 (0.49, 1.10)*0.1338	0.70 (0.42, 1.16) 0.1658	-0.04 (-0.10, 0.01)*0.1304	
	No	451/2559 (17.6)	518/2551 (20.3)	0.88 (0.79, 0.98) 0.0226	0.84 (0.73, 0.98) 0.0229	-0.02 (-0.03, -0.00) 0.0402	
	MRAs at baseline						0.8945
	Yes	214/1227 (17.4)	244/1224 (19.9)	0.88 (0.75, 1.03) 0.1022	0.85 (0.69, 1.06) 0.1466	-0.01 (-0.03, 0.02) 0.6742	
	No	271/1615 (16.8)	321/1613 (19.9)	0.87 (0.76, 1.00) 0.0442	0.81 (0.67, 0.98) 0.0294	-0.03 (-0.06, -0.00)*0.0219	
	ACEi+ARB at baseline						0.1972
	Yes	345/2065 (16.7)	421/2077 (20.3)	0.84 (0.74, 0.95) 0.0041	0.78 (0.66, 0.92) 0.0037	-0.04 (-0.06, -0.01)*0.0031	
	No	140/ 777 (18.0)	144/ 760 (18.9)	0.98 (0.80, 1.19) 0.8067	0.97 (0.74, 1.26) 0.8141	-0.00 (-0.04, 0.03) 0.8451	
	ARNI at baseline						0.0618
	Yes	26/ 153 (17.0)	15/ 126 (11.9)	1.50 (0.84, 2.70) 0.1740	1.67 (0.83, 3.38) 0.1506	0.08 (-0.01, 0.16) 0.0788	
	No	459/2689 (17.1)	550/2711 (20.3)	0.86 (0.77, 0.95) 0.0044	0.81 (0.70, 0.93) 0.0034	-0.03 (-0.05, -0.01)*0.0024	
	Beta Blocker at baseline						0.2217
	Yes	419/2360 (17.8)	479/2356 (20.3)	0.90 (0.80, 1.01) 0.0617	0.86 (0.74, 1.00) 0.0491	-0.03 (-0.05, -0.00)*0.0242	
	No	66/ 482 (13.7)	86/ 481 (17.9)	0.75 (0.56, 0.99) 0.0399	0.70 (0.48, 1.00) 0.0521	-0.04 (-0.09, 0.00)*0.0744	
	Diuretics at baseline						0.0586
	Yes	433/2536 (17.1)	518/2531 (20.5)	0.84 (0.76, 0.94) 0.0023	0.80 (0.69, 0.92) 0.0025	-0.02 (-0.03, -0.00) 0.0284	
	No	52/ 306 (17.0)	47/ 306 (15.4)	1.19 (0.84, 1.69) 0.3209	1.22 (0.78, 1.90) 0.3900	0.02 (-0.04, 0.07)*0.5830	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)							
	Overall	431/2842 (15.2)	524/2837 (18.5)	0.83 (0.74, 0.92) 0.0009	0.79 (0.68, 0.91) 0.0009	-0.03 (-0.05, -0.01)*0.0009	
	Age						0.9246
	<= median	186/1415 (13.1)	233/1482 (15.7)	0.83 (0.69, 0.98) 0.0319	0.79 (0.64, 0.98) 0.0312	-0.03 (-0.05, -0.00)*0.0482	
	> median	245/1427 (17.2)	291/1355 (21.5)	0.82 (0.71, 0.95) 0.0079	0.77 (0.63, 0.94) 0.0084	-0.04 (-0.07, -0.01)*0.0040	
	Gender						0.6113
	Male	241/1656 (14.6)	297/1625 (18.3)	0.81 (0.69, 0.94) 0.0052	0.76 (0.63, 0.92) 0.0049	-0.04 (-0.06, -0.01)*0.0040	
	Female	190/1186 (16.0)	227/1212 (18.7)	0.85 (0.72, 1.01) 0.0679	0.82 (0.66, 1.02) 0.0745	-0.03 (-0.06, 0.00)*0.0797	
	Race						0.8122
	White	331/2039 (16.2)	399/2058 (19.4)	0.85 (0.75, 0.96) 0.0094	0.81 (0.68, 0.96) 0.0126	-0.03 (-0.05, -0.01)*0.0083	
	Black or African	10/ 67 (14.9)	12/ 71 (16.9)	0.88 (0.42, 1.86) 0.7337	0.83 (0.33, 2.13) 0.7057	-0.02 (-0.14, 0.10)*0.7509	
	Asian	77/ 558 (13.8)	94/ 555 (16.9)	0.81 (0.61, 1.07) 0.1341	0.77 (0.56, 1.07) 0.1242	-0.03 (-0.07, 0.01)*0.1464	
	Other	13/ 178 (7.3)	19/ 153 (12.4)	0.61 (0.31, 1.19) 0.1434	0.56 (0.27, 1.19) 0.1340	-0.05 (-0.11, 0.01) 0.1232	
	Geographic region						0.9840
	Asia	73/ 539 (13.5)	88/ 538 (16.4)	0.82 (0.62, 1.10) 0.1835	0.79 (0.56, 1.11) 0.1759	-0.03 (-0.07, 0.01)*0.1951	
	Europe and Saudi Arabia	217/1365 (15.9)	279/1394 (20.0)	0.82 (0.70, 0.96) 0.0110	0.76 (0.62, 0.93) 0.0086	-0.04 (-0.07, -0.01)*0.0048	
	North America	80/ 398 (20.1)	89/ 387 (23.0)	0.87 (0.67, 1.12) 0.2749	0.84 (0.59, 1.19) 0.3194	-0.03 (-0.09, 0.03)*0.3235	
	Latin America	61/ 540 (11.3)	68/ 518 (13.1)	0.85 (0.62, 1.17) 0.3137	0.83 (0.57, 1.21) 0.3229	-0.02 (-0.06, 0.02)*0.3633	
	NYHA class at enrolment						0.5820
	II	325/2113 (15.4)	402/2187 (18.4)	0.83 (0.73, 0.95) 0.0059	0.79 (0.67, 0.93) 0.0052	-0.03 (-0.05, -0.01)*0.0086	
	III or IV	106/ 729 (14.5)	122/ 649 (18.8)	0.77 (0.62, 0.97) 0.0247	0.73 (0.54, 0.98) 0.0387	-0.04 (-0.08, -0.00)*0.0345	
	LVEF at enrolment						0.8866
	<= 49	143/ 980 (14.6)	161/ 963 (16.7)	0.86 (0.70, 1.05) 0.1466	0.83 (0.64, 1.06) 0.1347	-0.02 (-0.05, 0.01)*0.1970	
	50-59	173/1029 (16.8)	209/1017 (20.6)	0.81 (0.68, 0.97) 0.0214	0.77 (0.61, 0.97) 0.0245	-0.04 (-0.07, -0.00)*0.0299	
	>= 60	115/ 833 (13.8)	154/ 857 (18.0)	0.80 (0.65, 1.00) 0.0450	0.76 (0.58, 1.00) 0.0475	-0.04 (-0.08, -0.01)*0.0189	
	NT-proBNP at enrolment						0.8457
	<= median	213/1418 (15.0)	254/1421 (17.9)	0.83 (0.71, 0.98) 0.0290	0.80 (0.65, 0.98) 0.0302	-0.03 (-0.06, -0.00)*0.0401	
	> median	218/1424 (15.3)	270/1415 (19.1)	0.82 (0.70, 0.96) 0.0133	0.77 (0.63, 0.95) 0.0126	-0.04 (-0.07, -0.01)*0.0077	
	Type 2 Diabetes Medical History						0.3906
	Yes	195/1250 (15.6)	253/1260 (20.1)	0.79 (0.67, 0.93) 0.0041	0.74 (0.60, 0.90)*0.0035	-0.04 (-0.07, -0.01)*0.0033	
	No	236/1592 (14.8)	271/1577 (17.2)	0.87 (0.74, 1.02) 0.0763	0.84 (0.69, 1.01)*0.0702	-0.02 (-0.05, 0.00)*0.0699	
	Atrial fibrillation or flutter at enrolment ECG						0.7003
	Yes	172/1199 (14.3)	215/1199 (17.9)	0.80 (0.67, 0.96) 0.0167	0.76 (0.61, 0.95) 0.0181	-0.04 (-0.07, -0.01)*0.0169	
	No	259/1643 (15.8)	309/1638 (18.9)	0.84 (0.73, 0.97) 0.0197	0.80 (0.66, 0.96) 0.0183	-0.03 (-0.06, -0.01)*0.0188	
	BMI (kg/m2) at enrolment						0.2783
	< 30	224/1571 (14.3)	287/1559 (18.4)	0.78 (0.67, 0.91) 0.0020	0.73 (0.60, 0.89) 0.0016	-0.04 (-0.07, -0.02)*0.0017	
	>= 30	207/1270 (16.3)	236/1275 (18.5)	0.89 (0.75, 1.04) 0.1464	0.86 (0.69, 1.06) 0.1599	-0.02 (-0.05, 0.01)*0.1412	
	Baseline eGFR (mL/min/1.73m^2)						0.7680
	< 60	233/1359 (17.1)	286/1396 (20.5)	0.84 (0.72, 0.98) 0.0251	0.80 (0.66, 0.97) 0.0263	-0.03 (-0.06, -0.00)*0.0246	
	>= 60	198/1483 (13.4)	238/1440 (16.5)	0.81 (0.69, 0.96) 0.0176	0.77 (0.63, 0.95) 0.0164	-0.03 (-0.06, -0.01)*0.0160	

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Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Burden (LOCF)	SBP at randomisation						0.0805
	<= median	199/1424 (14.0)	278/1439 (19.3)	0.74 (0.63, 0.88) 0.0004	0.69 (0.57, 0.85) 0.0004	-0.05 (-0.08, -0.03)*0.0001	
	> median	232/1418 (16.4)	246/1398 (17.6)	0.91 (0.78, 1.07) 0.2468	0.88 (0.72, 1.08) 0.2318	-0.01 (-0.04, 0.02)*0.3826	
	LVEF at enrolment 2						0.6580
	<= 49	143/ 980 (14.6)	161/ 963 (16.7)	0.86 (0.70, 1.05) 0.1466	0.83 (0.64, 1.06) 0.1347	-0.02 (-0.05, 0.01)*0.1970	
	>= 50	288/1862 (15.5)	363/1874 (19.4)	0.81 (0.71, 0.93) 0.0030	0.77 (0.65, 0.92) 0.0033	-0.04 (-0.06, -0.01)*0.0016	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1799
	Yes	28/ 283 (9.9)	42/ 286 (14.7)	0.57 (0.37, 0.87) 0.0094	0.52 (0.30, 0.90) 0.0187	-0.05 (-0.10, 0.01)*0.0808	
	No	403/2559 (15.7)	482/2551 (18.9)	0.84 (0.75, 0.95) 0.0046	0.81 (0.69, 0.93) 0.0043	-0.03 (-0.05, -0.01)*0.0029	
	MRAs at baseline						0.3614
	Yes	180/1227 (14.7)	234/1224 (19.1)	0.77 (0.65, 0.92) 0.0039	0.73 (0.59, 0.91) 0.0042	-0.04 (-0.07, -0.01)*0.0032	
	No	251/1615 (15.5)	290/1613 (18.0)	0.86 (0.74, 1.00) 0.0557	0.83 (0.69, 1.00) 0.0537	-0.02 (-0.05, 0.00)*0.0637	
	ACEi+ARB at baseline						0.1307
	Yes	287/2065 (13.9)	377/2077 (18.2)	0.78 (0.68, 0.89) 0.0003	0.73 (0.61, 0.86) 0.0003	-0.04 (-0.06, -0.02)*0.0002	
	No	144/ 777 (18.5)	147/ 760 (19.3)	0.95 (0.77, 1.16) 0.6074	0.94 (0.72, 1.21) 0.6230	-0.01 (-0.05, 0.03)*0.6856	
	ARNI at baseline						0.0701
	Yes	30/ 153 (19.6)	17/ 126 (13.5)	1.35 (0.78, 2.34) 0.2867	1.46 (0.75, 2.82) 0.2657	0.06 (-0.03, 0.15)*0.1668	
	No	401/2689 (14.9)	507/2711 (18.7)	0.81 (0.72, 0.91) 0.0003	0.76 (0.66, 0.88) 0.0003	-0.04 (-0.06, -0.02)*0.0002	
	Beta Blocker at baseline						0.1960
	Yes	372/2360 (15.8)	442/2356 (18.8)	0.85 (0.76, 0.96) 0.0111	0.82 (0.70, 0.95) 0.0108	-0.03 (-0.05, -0.01)*0.0064	
	No	59/ 482 (12.2)	82/ 481 (17.0)	0.69 (0.51, 0.94) 0.0178	0.64 (0.44, 0.93) 0.0184	-0.05 (-0.09, -0.00)*0.0345	
	Diuretics at baseline						0.6239
	Yes	396/2536 (15.6)	482/2531 (19.0)	0.82 (0.73, 0.92) 0.0007	0.77 (0.67, 0.90) 0.0009	-0.03 (-0.06, -0.01)*0.0012	
	No	35/ 306 (11.4)	42/ 306 (13.7)	0.91 (0.60, 1.37) 0.6420	0.87 (0.53, 1.41) 0.5596	-0.02 (-0.08, 0.03)*0.3933	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)							
	Overall	418/2842 (14.7)	396/2837 (14.0)	1.06 (0.94, 1.20) 0.3418	1.07 (0.92, 1.25) 0.3590	0.01 (-0.01, 0.03)*0.4202	
	Age						0.0469
	<= median	206/1415 (14.6)	179/1482 (12.1)	1.20 (1.01, 1.44) 0.0418	1.25 (1.00, 1.57) 0.0477	0.02 (0.00, 0.05)*0.0496	
	> median	212/1427 (14.9)	217/1355 (16.0)	0.94 (0.80, 1.11) 0.4668	0.93 (0.75, 1.15) 0.4807	-0.01 (-0.04, 0.02)*0.3981	
	Gender						0.7845
	Male	235/1656 (14.2)	211/1625 (13.0)	1.08 (0.92, 1.27) 0.3632	1.11 (0.90, 1.36) 0.3273	0.01 (-0.01, 0.04)*0.3132	
	Female	183/1186 (15.4)	185/1212 (15.3)	1.05 (0.87, 1.25) 0.6197	1.04 (0.82, 1.31) 0.7415	0.00 (-0.03, 0.03)*0.9102	
	Race						0.4989
	White	296/2039 (14.5)	277/2058 (13.5)	1.09 (0.94, 1.26) 0.2386	1.12 (0.93, 1.34) 0.2315	0.01 (-0.01, 0.03)*0.3293	
	Black or African	11/ 67 (16.4)	7/ 71 (9.9)	1.48 (0.63, 3.49) 0.3660	1.65 (0.57, 4.73) 0.3551	0.07 (-0.05, 0.18)*0.2536	
	Asian	92/ 558 (16.5)	99/ 555 (17.8)	0.92 (0.72, 1.17) 0.4964	0.86 (0.62, 1.20) 0.3820	-0.01 (-0.06, 0.03)*0.5502	
	Other	19/ 178 (10.7)	13/ 153 (8.5)	1.26 (0.64, 2.46)*0.5055	1.34 (0.61, 2.93) 0.4703	0.02 (-0.04, 0.09)*0.5003	
	Geographic region						0.3261
	Asia	90/ 539 (16.7)	96/ 538 (17.8)	0.92 (0.72, 1.18) 0.5156	0.87 (0.62, 1.22) 0.4128	-0.01 (-0.06, 0.03)*0.6187	
	Europe and Saudi Arabia	218/1365 (16.0)	188/1394 (13.5)	1.18 (0.99, 1.40) 0.0591	1.25 (1.00, 1.56) 0.0468	0.02 (-0.00, 0.05)*0.0656	
	North America	45/ 398 (11.3)	41/ 387 (10.6)	1.07 (0.72, 1.58) 0.7343	1.06 (0.67, 1.67) 0.8080	0.01 (-0.04, 0.05)*0.7493	
	Latin America	65/ 540 (12.0)	71/ 518 (13.7)	0.93 (0.69, 1.25) 0.6299	0.92 (0.63, 1.34) 0.6456	-0.02 (-0.06, 0.02)*0.4177	
	NYHA class at enrolment						0.7978
	II	314/2113 (14.9)	310/2187 (14.2)	1.07 (0.93, 1.23) 0.3492	1.08 (0.90, 1.28) 0.4199	0.01 (-0.01, 0.03)*0.5234	
	III or IV	104/ 729 (14.3)	86/ 649 (13.3)	1.03 (0.80, 1.32) 0.8297	1.07 (0.77, 1.47) 0.7000	0.01 (-0.03, 0.05)*0.5847	
	LVEF at enrolment						0.1714
	<= 49	146/ 980 (14.9)	114/ 963 (11.8)	1.24 (0.99, 1.54) 0.0560	1.28 (0.98, 1.69) 0.0748	0.03 (0.00, 0.06)*0.0472	
	50-59	158/1029 (15.4)	147/1017 (14.5)	1.04 (0.86, 1.27) 0.6709	1.09 (0.85, 1.41) 0.5019	0.01 (-0.02, 0.04)*0.5674	
	>= 60	114/ 833 (13.7)	135/ 857 (15.8)	0.92 (0.74, 1.15) 0.4589	0.88 (0.66, 1.16) 0.3594	-0.02 (-0.05, 0.01)*0.2301	
	NT-proBNP at enrolment						0.8322
	<= median	217/1418 (15.3)	205/1421 (14.4)	1.07 (0.91, 1.27) 0.4064	1.09 (0.88, 1.35) 0.4366	0.01 (-0.02, 0.03)*0.5114	
	> median	201/1424 (14.1)	191/1415 (13.5)	1.04 (0.88, 1.24) 0.6333	1.06 (0.85, 1.33) 0.6041	0.01 (-0.02, 0.03)*0.6337	
	Type 2 Diabetes Medical History						0.1653
	Yes	162/1250 (13.0)	173/1260 (13.7)	0.95 (0.79, 1.16) 0.6318	0.94 (0.74, 1.18)*0.5706	-0.01 (-0.03, 0.02)*0.5705	
	No	256/1592 (16.1)	223/1577 (14.1)	1.14 (0.97, 1.33) 0.1089	1.16 (0.96, 1.41)*0.1277	0.02 (-0.01, 0.04)*0.1272	
	Atrial fibrillation or flutter at enrolment ECG						0.8347
	Yes	183/1199 (15.3)	176/1199 (14.7)	1.08 (0.90, 1.29) 0.4333	1.09 (0.86, 1.38) 0.4677	0.01 (-0.02, 0.03)*0.6887	
	No	235/1643 (14.3)	220/1638 (13.4)	1.05 (0.89, 1.23) 0.5721	1.06 (0.87, 1.31) 0.5609	0.01 (-0.01, 0.03)*0.4698	
	BMI (kg/m2) at enrolment						0.5607
	< 30	252/1571 (16.0)	250/1559 (16.0)	1.03 (0.89, 1.20) 0.6728	1.03 (0.85, 1.26) 0.7430	0.00 (-0.03, 0.03)*0.9971	
	>= 30	166/1270 (13.1)	146/1275 (11.5)	1.11 (0.91, 1.36) 0.2974	1.15 (0.90, 1.46) 0.2774	0.02 (-0.01, 0.04)*0.2127	
	Baseline eGFR (mL/min/1.73m^2)						0.9729
	< 60	188/1359 (13.8)	182/1396 (13.0)	1.06 (0.88, 1.27) 0.5393	1.06 (0.85, 1.33) 0.6008	0.01 (-0.02, 0.03)*0.5400	
	>= 60	230/1483 (15.5)	214/1440 (14.9)	1.06 (0.90, 1.24) 0.5135	1.08 (0.88, 1.34) 0.4661	0.01 (-0.02, 0.03)*0.6255	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Self Efficacy (LOCF)	SBP at randomisation						0.4747
	<= median	211/1424 (14.8)	196/1439 (13.6)	1.11 (0.93, 1.32) 0.2363	1.13 (0.91, 1.40) 0.2818	0.01 (-0.01, 0.04)*0.3592	
	> median	207/1418 (14.6)	200/1398 (14.3)	1.01 (0.85, 1.21) 0.8678	1.03 (0.82, 1.27) 0.8238	0.00 (-0.02, 0.03)*0.8257	
	LVEF at enrolment 2						0.0911
	<= 49	146/ 980 (14.9)	114/ 963 (11.8)	1.24 (0.99, 1.54) 0.0560	1.28 (0.98, 1.69) 0.0748	0.03 (0.00, 0.06)*0.0472	
	>= 50	272/1862 (14.6)	282/1874 (15.0)	0.99 (0.85, 1.14) 0.8708	0.99 (0.82, 1.19) 0.9170	-0.00 (-0.03, 0.02)*0.7051	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0484
	Yes	26/ 283 (9.2)	38/ 286 (13.3)	0.68 (0.44, 1.07) 0.0987	0.61 (0.35, 1.06) 0.0808	-0.04 (-0.09, 0.01)*0.1207	
	No	392/2559 (15.3)	358/2551 (14.0)	1.10 (0.97, 1.25) 0.1433	1.13 (0.96, 1.33) 0.1430	0.01 (-0.01, 0.03)*0.1943	
	MRAs at baseline						0.6662
	Yes	188/1227 (15.3)	171/1224 (14.0)	1.09 (0.91, 1.31) 0.3542	1.12 (0.88, 1.41) 0.3576	0.01 (-0.01, 0.04)*0.3440	
	No	230/1615 (14.2)	225/1613 (13.9)	1.04 (0.88, 1.22) 0.6768	1.04 (0.85, 1.28) 0.7090	0.00 (-0.02, 0.03)*0.8114	
	ACEi+ARB at baseline						0.3150
	Yes	289/2065 (14.0)	289/2077 (13.9)	1.02 (0.88, 1.18) 0.7908	1.02 (0.85, 1.22) 0.8668	0.00 (-0.02, 0.02)*0.9401	
	No	129/ 777 (16.6)	107/ 760 (14.1)	1.18 (0.94, 1.49) 0.1467	1.25 (0.94, 1.66) 0.1296	0.03 (-0.01, 0.06)*0.1695	
	ARNI at baseline						0.4388
	Yes	27/ 153 (17.6)	16/ 126 (12.7)	1.39 (0.80, 2.43) 0.2466	1.53 (0.76, 3.09) 0.2327	0.05 (-0.03, 0.13)*0.2473	
	No	391/2689 (14.5)	380/2711 (14.0)	1.05 (0.93, 1.19) 0.4391	1.06 (0.91, 1.24) 0.4624	0.01 (-0.01, 0.02)*0.5823	
	Beta Blocker at baseline						0.8388
	Yes	362/2360 (15.3)	341/2356 (14.5)	1.07 (0.94, 1.21) 0.3406	1.08 (0.91, 1.27) 0.3735	0.01 (-0.01, 0.03)*0.4041	
	No	56/ 482 (11.6)	55/ 481 (11.4)	1.02 (0.73, 1.43) 0.9037	1.04 (0.69, 1.57) 0.8421	-0.01 (-0.04, 0.02) 0.6061	
	Diuretics at baseline						0.2193
	Yes	374/2536 (14.7)	362/2531 (14.3)	1.03 (0.91, 1.17) 0.6089	1.04 (0.89, 1.23) 0.6106	0.00 (-0.01, 0.02)*0.6531	
	No	44/ 306 (14.4)	34/ 306 (11.1)	1.36 (0.91, 2.03) 0.1278	1.44 (0.87, 2.37) 0.1578	0.03 (-0.02, 0.09)*0.2249	

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Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)							
	Overall	408/2842 (14.4)	465/2837 (16.4)	0.87 (0.77, 0.98) 0.0264	0.85 (0.73, 0.98) 0.0272	-0.02 (-0.04, -0.00)*0.0335	
	Age						0.8781
	<= median	180/1415 (12.7)	211/1482 (14.2)	0.88 (0.73, 1.06) 0.1677	0.86 (0.69, 1.06) 0.1600	-0.02 (-0.04, 0.00) 0.1033	
	> median	228/1427 (16.0)	254/1355 (18.7)	0.86 (0.74, 1.01) 0.0639	0.83 (0.68, 1.02) 0.0720	-0.03 (-0.06, 0.00)*0.0541	
	Gender						0.5583
	Male	226/1656 (13.6)	259/1625 (15.9)	0.85 (0.72, 1.00) 0.0457	0.82 (0.67, 1.00) 0.0487	-0.02 (-0.05, 0.00)*0.0645	
	Female	182/1186 (15.3)	206/1212 (17.0)	0.91 (0.76, 1.09) 0.3084	0.89 (0.71, 1.11) 0.2946	-0.02 (-0.05, 0.01)*0.2720	
	Race						0.2941
	White	294/2039 (14.4)	346/2058 (16.8)	0.87 (0.75, 1.00) 0.0433	0.84 (0.70, 1.00) 0.0457	-0.02 (-0.05, -0.00)*0.0347	
	Black or African	13/ 67 (19.4)	7/ 71 (9.9)	1.80 (0.79, 4.12) 0.1614	2.15 (0.77, 6.03) 0.1438	0.10 (-0.02, 0.21)*0.1110	
	Asian	85/ 558 (15.2)	95/ 555 (17.1)	0.88 (0.67, 1.15) 0.3342	0.85 (0.62, 1.18) 0.3292	-0.02 (-0.06, 0.02) 0.3362	
	Other	16/ 178 (9.0)	17/ 153 (11.1)	0.76 (0.41, 1.43) 0.4030	0.71 (0.34, 1.50) 0.3763	-0.02 (-0.09, 0.04)*0.5232	
	Geographic region						0.3494
	Asia	80/ 539 (14.8)	90/ 538 (16.7)	0.87 (0.66, 1.15) 0.3406	0.85 (0.61, 1.19) 0.3435	-0.02 (-0.06, 0.03) 0.4771	
	Europe and Saudi Arabia	197/1365 (14.4)	224/1394 (16.1)	0.92 (0.78, 1.09) 0.3503	0.89 (0.72, 1.10) 0.2895	-0.02 (-0.04, 0.01)*0.2316	
	North America	68/ 398 (17.1)	66/ 387 (17.1)	0.97 (0.72, 1.31) 0.8505	0.97 (0.67, 1.42) 0.8814	-0.01 (-0.06, 0.04) 0.7850	
	Latin America	63/ 540 (11.7)	85/ 518 (16.4)	0.69 (0.52, 0.93) 0.0137	0.64 (0.45, 0.93) 0.0173	-0.05 (-0.09, -0.01)*0.0263	
	NYHA class at enrolment						0.6025
	II	307/2113 (14.5)	365/2187 (16.7)	0.85 (0.74, 0.98) 0.0231	0.82 (0.70, 0.98) 0.0245	-0.02 (-0.04, 0.00)*0.0508	
	III or IV	101/ 729 (13.9)	100/ 649 (15.4)	0.92 (0.72, 1.18) 0.5104	0.89 (0.66, 1.21) 0.4680	-0.02 (-0.05, 0.01) 0.1620	
	LVEF at enrolment						0.3133
	<= 49	132/ 980 (13.5)	126/ 963 (13.1)	1.01 (0.81, 1.27) 0.9153	1.00 (0.77, 1.31) 0.9899	0.00 (-0.03, 0.03)*0.8024	
	50-59	161/1029 (15.6)	189/1017 (18.6)	0.83 (0.69, 1.00) 0.0461	0.80 (0.63, 1.01) 0.0661	-0.02 (-0.05, 0.01) 0.1257	
	>= 60	115/ 833 (13.8)	150/ 857 (17.5)	0.82 (0.66, 1.02) 0.0770	0.78 (0.59, 1.02) 0.0688	-0.04 (-0.07, -0.00)*0.0361	
	NT-proBNP at enrolment						0.7400
	<= median	201/1418 (14.2)	224/1421 (15.8)	0.89 (0.75, 1.06) 0.1836	0.87 (0.71, 1.08) 0.2042	-0.02 (-0.04, 0.01)*0.2354	
	> median	207/1424 (14.5)	241/1415 (17.0)	0.86 (0.73, 1.01) 0.0718	0.82 (0.67, 1.01) 0.0649	-0.02 (-0.05, 0.00)*0.0681	
	Type 2 Diabetes Medical History						0.2017
	Yes	189/1250 (15.1)	235/1260 (18.7)	0.81 (0.68, 0.96) 0.0144	0.78 (0.63, 0.96)*0.0184	-0.04 (-0.06, -0.01)*0.0181	
	No	219/1592 (13.8)	230/1577 (14.6)	0.95 (0.80, 1.12) 0.5128	0.93 (0.77, 1.14)*0.5038	-0.01 (-0.03, 0.01) 0.3607	
	Atrial fibrillation or flutter at enrolment ECG						0.5001
	Yes	173/1199 (14.4)	185/1199 (15.4)	0.92 (0.76, 1.11) 0.3641	0.91 (0.72, 1.14) 0.3978	-0.01 (-0.04, 0.02)*0.4916	
	No	235/1643 (14.3)	280/1638 (17.1)	0.84 (0.72, 0.99) 0.0319	0.81 (0.67, 0.98) 0.0280	-0.03 (-0.05, -0.00)*0.0279	
	BMI (kg/m2) at enrolment						0.4287
	< 30	218/1571 (13.9)	257/1559 (16.5)	0.84 (0.71, 0.99) 0.0377	0.80 (0.66, 0.98) 0.0304	-0.03 (-0.05, -0.00)*0.0419	
	>= 30	190/1270 (15.0)	206/1275 (16.2)	0.92 (0.78, 1.10) 0.3761	0.92 (0.74, 1.14) 0.4436	-0.01 (-0.03, 0.01) 0.3777	
	Baseline eGFR (mL/min/1.73m^2)						0.1682
	< 60	234/1359 (17.2)	254/1396 (18.2)	0.95 (0.81, 1.11) 0.4824	0.93 (0.76, 1.13) 0.4627	-0.01 (-0.04, 0.02)*0.5020	
	>= 60	174/1483 (11.7)	211/1440 (14.7)	0.80 (0.67, 0.96) 0.0176	0.77 (0.62, 0.95) 0.0173	-0.03 (-0.05, -0.00)*0.0197	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Frequency (LOCF)	SBP at randomisation						0.8209
	<= median	211/1424 (14.8)	249/1439 (17.3)	0.86 (0.73, 1.02) 0.0769	0.84 (0.68, 1.02) 0.0842	-0.02 (-0.05, 0.00)*0.0698	
	> median	197/1418 (13.9)	216/1398 (15.5)	0.89 (0.74, 1.05) 0.1707	0.86 (0.69, 1.06) 0.1654	-0.02 (-0.04, 0.01)*0.2427	
	LVEF at enrolment 2						0.1323
	<= 49	132/ 980 (13.5)	126/ 963 (13.1)	1.01 (0.81, 1.27) 0.9153	1.00 (0.77, 1.31) 0.9899	0.00 (-0.03, 0.03)*0.8024	
	>= 50	276/1862 (14.8)	339/1874 (18.1)	0.82 (0.72, 0.95) 0.0074	0.79 (0.66, 0.95) 0.0099	-0.03 (-0.06, -0.01)*0.0070	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2668
	Yes	24/ 283 (8.5)	33/ 286 (11.5)	0.73 (0.45, 1.21)*0.2269	0.53 (0.29, 0.96) 0.0349	-0.03 (-0.08, 0.02)*0.2235	
	No	384/2559 (15.0)	432/2551 (16.9)	0.89 (0.79, 1.01) 0.0661	0.87 (0.75, 1.01) 0.0705	-0.02 (-0.04, 0.00)*0.0598	
	MRAs at baseline						0.4523
	Yes	163/1227 (13.3)	195/1224 (15.9)	0.83 (0.68, 1.00) 0.0455	0.79 (0.63, 1.00) 0.0495	-0.03 (-0.05, 0.00)*0.0634	
	No	245/1615 (15.2)	270/1613 (16.7)	0.91 (0.78, 1.06) 0.2198	0.88 (0.73, 1.07) 0.2128	-0.01 (-0.03, 0.01) 0.1851	
	ACEi+ARB at baseline						0.4261
	Yes	278/2065 (13.5)	333/2077 (16.0)	0.84 (0.73, 0.97) 0.0199	0.81 (0.68, 0.97) 0.0214	-0.03 (-0.05, -0.00)*0.0196	
	No	130/ 777 (16.7)	132/ 760 (17.4)	0.95 (0.76, 1.18) 0.6407	0.94 (0.72, 1.23) 0.6367	-0.02 (-0.05, 0.02) 0.4084	
	ARNI at baseline						0.6749
	Yes	19/ 153 (12.4)	14/ 126 (11.1)	0.97 (0.51, 1.87) 0.9382	0.98 (0.46, 2.09) 0.9669	0.01 (-0.06, 0.09)*0.7353	
	No	389/2689 (14.5)	451/2711 (16.6)	0.87 (0.77, 0.99) 0.0302	0.85 (0.73, 0.98) 0.0300	-0.02 (-0.04, -0.00)*0.0277	
	Beta Blocker at baseline						0.0234
	Yes	352/2360 (14.9)	380/2356 (16.1)	0.93 (0.82, 1.06) 0.2727	0.92 (0.78, 1.08) 0.2897	-0.01 (-0.03, 0.01)*0.2497	
	No	56/ 482 (11.6)	85/ 481 (17.7)	0.64 (0.47, 0.87) 0.0046	0.57 (0.40, 0.83) 0.0033	-0.06 (-0.11, -0.02)*0.0077	
	Diuretics at baseline						0.1955
	Yes	377/2536 (14.9)	416/2531 (16.4)	0.89 (0.79, 1.01) 0.0824	0.87 (0.75, 1.02) 0.0840	-0.02 (-0.04, 0.00)*0.1239	
	No	31/ 306 (10.1)	49/ 306 (16.0)	0.69 (0.46, 1.03) 0.0713	0.63 (0.38, 1.03) 0.0637	-0.06 (-0.11, -0.01)*0.0303	

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AstraZeneca
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Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Social Limitation (LOCF)							
	Overall	510/2669 (19.1)	543/2664 (20.4)	0.92 (0.83, 1.02) 0.1326	0.91 (0.80, 1.05) 0.2019	-0.01 (-0.03, 0.01) 0.4271	
	Age						0.3445
	<= median	218/1352 (16.1)	257/1422 (18.1)	0.86 (0.74, 1.01) 0.0734	0.85 (0.69, 1.04) 0.1052	-0.01 (-0.04, 0.01) 0.2232	
	> median	292/1317 (22.2)	286/1242 (23.0)	0.96 (0.84, 1.10) 0.5782	0.96 (0.79, 1.16) 0.6675	-0.00 (-0.03, 0.03) 0.7869	
	Gender						0.9510
	Male	292/1568 (18.6)	299/1518 (19.7)	0.92 (0.80, 1.06) 0.2624	0.92 (0.76, 1.10) 0.3595	-0.01 (-0.03, 0.02) 0.6134	
	Female	218/1101 (19.8)	244/1146 (21.3)	0.93 (0.79, 1.09) 0.3613	0.92 (0.74, 1.13) 0.4239	-0.01 (-0.04, 0.02) 0.5748	
	Race						0.0426
	White	371/1925 (19.3)	425/1952 (21.8)	0.89 (0.79, 1.00) 0.0468	0.87 (0.74, 1.02) 0.0789	-0.01 (-0.03, 0.01) 0.2381	
	Black or African	18/ 61 (29.5)	10/ 67 (14.9)	1.91 (0.97, 3.77) 0.0605	2.34 (0.96, 5.69) 0.0607	0.13 (-0.03, 0.28) 0.1073	
	Asian	97/ 510 (19.0)	97/ 500 (19.4)	0.97 (0.75, 1.25) 0.7967	0.96 (0.70, 1.32) 0.8196	-0.00 (-0.05, 0.05) 0.9054	
	Other	24/ 173 (13.9)	11/ 145 (7.6)	1.46 (0.77, 2.77) 0.2472	1.63 (0.73, 3.64) 0.2296	0.06 (-0.00, 0.13)*0.0666	
	Geographic region						0.7047
	Asia	91/ 496 (18.3)	90/ 486 (18.5)	0.98 (0.75, 1.27) 0.8711	0.98 (0.71, 1.35) 0.8946	-0.00 (-0.05, 0.05) 0.9838	
	Europe and Saudi Arabia	264/1299 (20.3)	301/1323 (22.8)	0.91 (0.79, 1.05) 0.1942	0.89 (0.73, 1.08) 0.2208	-0.01 (-0.03, 0.02) 0.6481	
	North America	80/ 372 (21.5)	68/ 359 (18.9)	1.10 (0.83, 1.46) 0.5109	1.14 (0.79, 1.64) 0.4896	0.01 (-0.04, 0.07) 0.6403	
	Latin America	75/ 502 (14.9)	84/ 496 (16.9)	0.85 (0.65, 1.12) 0.2512	0.84 (0.59, 1.19) 0.3204	-0.02 (-0.05, 0.02) 0.3572	
	NYHA class at enrolment						0.1354
	II	350/1986 (17.6)	408/2059 (19.8)	0.87 (0.77, 0.98) 0.0256	0.84 (0.72, 0.99) 0.0368	-0.02 (-0.04, 0.00) 0.0508	
	III or IV	160/ 683 (23.4)	134/ 604 (22.2)	1.04 (0.86, 1.25) 0.7128	1.07 (0.82, 1.41) 0.6238	0.01 (-0.03, 0.05) 0.4935	
	LVEF at enrolment						0.6302
	<= 49	175/ 928 (18.9)	166/ 912 (18.2)	1.00 (0.83, 1.20) 0.9587	0.99 (0.78, 1.27) 0.9674	0.00 (-0.03, 0.03) 0.9421	
	50-59	195/ 970 (20.1)	213/ 956 (22.3)	0.90 (0.76, 1.06) 0.2099	0.90 (0.72, 1.13) 0.3554	-0.01 (-0.04, 0.02) 0.4899	
	>= 60	140/ 771 (18.2)	164/ 796 (20.6)	0.88 (0.72, 1.07) 0.2028	0.85 (0.66, 1.10) 0.2173	-0.01 (-0.05, 0.02) 0.4522	
	NT-proBNP at enrolment						0.7684
	<= median	264/1334 (19.8)	278/1350 (20.6)	0.94 (0.81, 1.08) 0.3747	0.94 (0.77, 1.14) 0.5020	-0.00 (-0.03, 0.02) 0.8181	
	> median	246/1335 (18.4)	265/1313 (20.2)	0.91 (0.78, 1.06) 0.2102	0.89 (0.73, 1.09) 0.2521	-0.01 (-0.04, 0.01) 0.3627	
	Type 2 Diabetes Medical History						0.1074
	Yes	238/1169 (20.4)	231/1186 (19.5)	1.02 (0.87, 1.19) 0.8482	1.06 (0.86, 1.29)*0.5921	0.01 (-0.02, 0.04) 0.3658	
	No	272/1500 (18.1)	312/1478 (21.1)	0.85 (0.74, 0.99) 0.0305	0.83 (0.69, 0.99)*0.0410	-0.02 (-0.05, 0.00) 0.0654	
	Atrial fibrillation or flutter at enrolment ECG						0.0549
	Yes	212/1113 (19.0)	203/1123 (18.1)	1.05 (0.89, 1.24) 0.5759	1.07 (0.86, 1.32) 0.5662	0.01 (-0.02, 0.04) 0.4647	
	No	298/1556 (19.2)	340/1541 (22.1)	0.85 (0.74, 0.97) 0.0151	0.82 (0.69, 0.98) 0.0335	-0.02 (-0.05, 0.00) 0.1039	
	BMI (kg/m2) at enrolment						0.0359
	< 30	264/1478 (17.9)	308/1451 (21.2)	0.83 (0.72, 0.96) 0.0128	0.80 (0.66, 0.96) 0.0164	-0.03 (-0.05, -0.00) 0.0457	
	>= 30	246/1190 (20.7)	235/1211 (19.4)	1.04 (0.89, 1.22) 0.5820	1.08 (0.88, 1.33) 0.4441	0.01 (-0.02, 0.04) 0.3961	
	Baseline eGFR (mL/min/1.73m^2)						0.1303
	< 60	281/1266 (22.2)	284/1297 (21.9)	1.00 (0.87, 1.15) 0.9906	1.01 (0.83, 1.22) 0.9132	0.00 (-0.03, 0.03) 0.9273	
	>= 60	229/1403 (16.3)	259/1366 (19.0)	0.84 (0.72, 0.99) 0.0335	0.82 (0.67, 1.01) 0.0563	-0.01 (-0.04, 0.01) 0.3018	

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Social Limitation (LOCF)	SBP at randomisation						0.4027
	<= median	250/1344 (18.6)	280/1344 (20.8)	0.89 (0.76, 1.03) 0.1147	0.88 (0.72, 1.07) 0.1881	-0.01 (-0.04, 0.02) 0.3696	
	> median	260/1325 (19.6)	263/1320 (19.9)	0.96 (0.83, 1.11) 0.6023	0.95 (0.78, 1.16) 0.6032	-0.00 (-0.03, 0.02) 0.8457	
	LVEF at enrolment 2						0.3490
	<= 49	175/ 928 (18.9)	166/ 912 (18.2)	1.00 (0.83, 1.20) 0.9587	0.99 (0.78, 1.27) 0.9674	0.00 (-0.03, 0.03) 0.9421	
	>= 50	335/1741 (19.2)	377/1752 (21.5)	0.89 (0.79, 1.01) 0.0778	0.88 (0.74, 1.04) 0.1361	-0.01 (-0.03, 0.01) 0.3314	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3640
	Yes	54/ 257 (21.0)	50/ 261 (19.2)	1.07 (0.77, 1.48) 0.7053	1.10 (0.70, 1.73) 0.6858	0.04 (-0.02, 0.10) 0.1928	
	No	456/2412 (18.9)	493/2403 (20.5)	0.91 (0.81, 1.02) 0.0907	0.90 (0.78, 1.04) 0.1403	-0.01 (-0.03, 0.01) 0.2320	
	MRAs at baseline						0.7221
	Yes	225/1155 (19.5)	230/1146 (20.1)	0.95 (0.81, 1.11) 0.5214	0.95 (0.77, 1.17) 0.6091	-0.00 (-0.03, 0.03) 0.8248	
	No	285/1514 (18.8)	313/1518 (20.6)	0.91 (0.79, 1.04) 0.1711	0.89 (0.74, 1.07) 0.2264	-0.01 (-0.04, 0.01) 0.2704	
	ACEi+ARB at baseline						0.0324
	Yes	343/1940 (17.7)	403/1959 (20.6)	0.86 (0.75, 0.97) 0.0142	0.82 (0.69, 0.97) 0.0174	-0.02 (-0.04, 0.00) 0.0647	
	No	167/ 729 (22.9)	140/ 705 (19.9)	1.12 (0.92, 1.36) 0.2693	1.19 (0.92, 1.54) 0.1807	0.03 (-0.01, 0.07) 0.0990	
	ARNI at baseline						0.4310
	Yes	30/ 149 (20.1)	20/ 116 (17.2)	1.19 (0.71, 1.99) 0.5097	1.23 (0.65, 2.33) 0.5176	0.03 (-0.07, 0.12) 0.5681	
	No	480/2520 (19.0)	523/2548 (20.5)	0.91 (0.82, 1.02) 0.1044	0.90 (0.78, 1.04) 0.1642	-0.01 (-0.03, 0.01) 0.4433	
	Beta Blocker at baseline						0.3812
	Yes	439/2232 (19.7)	460/2218 (20.7)	0.94 (0.84, 1.05) 0.2921	0.94 (0.81, 1.09) 0.4017	-0.00 (-0.03, 0.02) 0.6451	
	No	71/ 437 (16.2)	83/ 446 (18.6)	0.82 (0.62, 1.09) 0.1705	0.79 (0.55, 1.13) 0.1921	-0.02 (-0.07, 0.03)*0.3544	
	Diuretics at baseline						0.1899
	Yes	464/2391 (19.4)	502/2379 (21.1)	0.90 (0.81, 1.00) 0.0584	0.88 (0.76, 1.02) 0.0920	-0.01 (-0.03, 0.01) 0.3085	
	No	46/ 278 (16.5)	41/ 285 (14.4)	1.18 (0.80, 1.72) 0.4084	1.24 (0.78, 1.97) 0.3651	0.03 (-0.03, 0.09) 0.3254	

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Symptom Stability (LOCF)							
	Overall	652/2842 (22.9)	650/2837 (22.9)	1.05 (1.00, 1.11) 0.0577	1.07 (0.92, 1.24) 0.4026	0.00 (-0.02, 0.02)*0.9785	
	Age						0.7639
	<= median	312/1415 (22.0)	329/1482 (22.2)	1.06 (0.98, 1.14) 0.1249	1.03 (0.83, 1.29) 0.7666	-0.00 (-0.03, 0.03)*0.9224	
	> median	340/1427 (23.8)	321/1355 (23.7)	1.04 (0.97, 1.12) 0.2973	1.08 (0.87, 1.34) 0.4654	0.00 (-0.03, 0.03)*0.9328	
	Gender						0.3551
	Male	390/1656 (23.6)	376/1625 (23.1)	1.07 (1.00, 1.15) 0.0355	1.13 (0.92, 1.39) 0.2381	0.00 (-0.02, 0.03)*0.7802	
	Female	262/1186 (22.1)	274/1212 (22.6)	1.01 (0.93, 1.11) 0.7488	0.99 (0.79, 1.25) 0.9651	-0.01 (-0.04, 0.03)*0.7616	
	Race						0.5128*
	White	458/2039 (22.5)	477/2058 (23.2)	1.04 (0.98, 1.10) 0.2291	1.05 (0.88, 1.26) 0.5941	-0.01 (-0.03, 0.02)*0.5851	
	Black or African	18/ 67 (26.9)	15/ 71 (21.1)	1.27 (0.70, 2.31)*0.4312	1.80 (0.71, 4.55) 0.2161	0.06 (-0.09, 0.20)*0.4296	
	Asian	152/ 558 (27.2)	135/ 555 (24.3)	1.06 (0.93, 1.21) 0.3923	1.15 (0.83, 1.58) 0.4050	0.03 (-0.02, 0.08)*0.2659	
	Other	24/ 178 (13.5)	23/ 153 (15.0)	0.90 (0.53, 1.52)*0.6872	0.73 (0.33, 1.62) 0.4455	-0.02 (-0.09, 0.06)*0.6881	
	Geographic region						0.6625
	Asia	145/ 539 (26.9)	131/ 538 (24.3)	1.06 (0.93, 1.20) 0.3981	1.14 (0.82, 1.58) 0.4498	0.03 (-0.03, 0.08)*0.3372	
	Europe and Saudi Arabia	286/1365 (21.0)	312/1394 (22.4)	1.02 (0.94, 1.10) 0.6376	0.92 (0.73, 1.16) 0.4829	-0.01 (-0.05, 0.02)*0.3621	
	North America	97/ 398 (24.4)	96/ 387 (24.8)	1.09 (0.94, 1.27) 0.2615	1.23 (0.84, 1.81) 0.2890	-0.00 (-0.06, 0.06)*0.8876	
	Latin America	124/ 540 (23.0)	111/ 518 (21.4)	1.11 (1.00, 1.24) 0.0580	1.22 (0.84, 1.77) 0.2998	0.02 (-0.03, 0.07)*0.5481	
	NYHA class at enrolment						0.7627
	II	465/2113 (22.0)	471/2187 (21.5)	1.06 (0.99, 1.13) 0.1079	1.07 (0.89, 1.27) 0.4797	0.00 (-0.02, 0.03)*0.7087	
	III or IV	187/ 729 (25.7)	179/ 649 (27.6)	1.04 (0.96, 1.13) 0.3536	1.03 (0.76, 1.38) 0.8567	-0.02 (-0.07, 0.03)*0.4188	
	LVEF at enrolment						0.4314
	<= 49	216/ 980 (22.0)	224/ 963 (23.3)	1.02 (0.92, 1.12) 0.7397	0.91 (0.70, 1.18) 0.4797	-0.01 (-0.05, 0.03)*0.5207	
	50-59	243/1029 (23.6)	244/1017 (24.0)	1.05 (0.97, 1.13) 0.2079	1.09 (0.85, 1.40) 0.4877	-0.00 (-0.04, 0.03)*0.8413	
	>= 60	193/ 833 (23.2)	182/ 857 (21.2)	1.10 (1.00, 1.22) 0.0573	1.25 (0.94, 1.65) 0.1287	0.02 (-0.02, 0.06)*0.3392	
	NT-proBNP at enrolment						0.8004
	<= median	318/1418 (22.4)	304/1421 (21.4)	1.04 (0.97, 1.13) 0.2760	1.11 (0.89, 1.38) 0.3602	0.01 (-0.02, 0.04)*0.5060	
	> median	334/1424 (23.5)	346/1415 (24.5)	1.06 (0.98, 1.14) 0.1247	1.03 (0.83, 1.27) 0.7879	-0.01 (-0.04, 0.02)*0.5336	
	Type 2 Diabetes Medical History						0.0404
	Yes	312/1250 (25.0)	287/1260 (22.8)	1.10 (1.03, 1.19) 0.0087	1.13 (0.94, 1.36)*0.1998	0.02 (-0.01, 0.06)*0.1996	
	No	340/1592 (21.4)	363/1577 (23.0)	0.99 (0.91, 1.07) 0.7278	0.91 (0.77, 1.07)*0.2604	-0.02 (-0.05, 0.01)*0.2603	
	Atrial fibrillation or flutter at enrolment ECG						0.8369
	Yes	277/1199 (23.1)	275/1199 (22.9)	1.04 (0.97, 1.12) 0.2430	1.09 (0.86, 1.38) 0.4751	0.00 (-0.03, 0.04)*0.9227	
	No	375/1643 (22.8)	375/1638 (22.9)	1.07 (0.99, 1.15) 0.0900	1.05 (0.86, 1.28) 0.6424	-0.00 (-0.03, 0.03)*0.9621	
	BMI (kg/m2) at enrolment						0.3293
	< 30	364/1571 (23.2)	367/1559 (23.5)	1.03 (0.96, 1.11) 0.4055	1.03 (0.84, 1.27) 0.7583	-0.00 (-0.03, 0.03)*0.8063	
	>= 30	288/1270 (22.7)	283/1275 (22.2)	1.08 (1.01, 1.16) 0.0280	1.11 (0.88, 1.40) 0.3621	0.00 (-0.03, 0.04)*0.7711	
	Baseline eGFR (mL/min/1.73m^2)						0.0982
	< 60	355/1359 (26.1)	332/1396 (23.8)	1.10 (1.02, 1.18) 0.0128	1.26 (1.02, 1.56) 0.0322	0.02 (-0.01, 0.06)*0.1558	
	>= 60	297/1483 (20.0)	318/1440 (22.1)	1.01 (0.93, 1.09) 0.8393	0.90 (0.72, 1.12) 0.3485	-0.02 (-0.05, 0.01)*0.1728	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Symptom Stability (LOCF)	SBP at randomisation						0.1266
	<= median	366/1424 (25.7)	350/1439 (24.3)	1.09 (1.02, 1.17) 0.0074	1.20 (0.97, 1.48) 0.0883	0.01 (-0.02, 0.05)*0.3940	
	> median	286/1418 (20.2)	300/1398 (21.5)	1.00 (0.91, 1.09) 0.9610	0.94 (0.75, 1.17) 0.5681	-0.01 (-0.04, 0.02)*0.3992	
	LVEF at enrolment 2						0.3059
	<= 49	216/ 980 (22.0)	224/ 963 (23.3)	1.02 (0.92, 1.12) 0.7397	0.91 (0.70, 1.18) 0.4797	-0.01 (-0.05, 0.03)*0.5207	
	>= 50	436/1862 (23.4)	426/1874 (22.7)	1.07 (1.01, 1.14) 0.0271	1.16 (0.96, 1.40) 0.1277	0.01 (-0.02, 0.03)*0.6200	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0590
	Yes	105/ 283 (37.1)	96/ 286 (33.6)	1.18 (1.03, 1.35) 0.0164	1.33 (0.86, 2.08) 0.2044	0.04 (-0.04, 0.11)*0.3773	
	No	547/2559 (21.4)	554/2551 (21.7)	1.02 (0.97, 1.08) 0.4256	1.04 (0.88, 1.22) 0.6530	-0.00 (-0.03, 0.02)*0.7666	
	MRAs at baseline						0.6318
	Yes	292/1227 (23.8)	290/1224 (23.7)	1.04 (0.95, 1.14) 0.3620	0.99 (0.79, 1.24) 0.9588	0.00 (-0.03, 0.03)*0.9513	
	No	360/1615 (22.3)	360/1613 (22.3)	1.06 (1.01, 1.13) 0.0298	1.14 (0.93, 1.41) 0.2127	-0.00 (-0.03, 0.03)*0.9850	
	ACEi+ARB at baseline						0.6326
	Yes	463/2065 (22.4)	466/2077 (22.4)	1.04 (0.98, 1.10) 0.2448	1.03 (0.86, 1.24) 0.7362	-0.00 (-0.03, 0.03)*0.9908	
	No	189/ 777 (24.3)	184/ 760 (24.2)	1.08 (0.98, 1.19) 0.1030	1.15 (0.87, 1.53) 0.3324	0.00 (-0.04, 0.04)*0.9585	
	ARNI at baseline						0.2168
	Yes	38/ 153 (24.8)	34/ 126 (27.0)	0.92 (0.62, 1.37)*0.6831	0.73 (0.38, 1.43) 0.3611	-0.02 (-0.12, 0.08)*0.6840	
	No	614/2689 (22.8)	616/2711 (22.7)	1.06 (1.01, 1.12) 0.0262	1.09 (0.93, 1.28) 0.2774	0.00 (-0.02, 0.02)*0.9222	
	Beta Blocker at baseline						0.6137
	Yes	533/2360 (22.6)	530/2356 (22.5)	1.06 (1.00, 1.12) 0.0663	1.12 (0.95, 1.33) 0.1892	0.00 (-0.02, 0.02)*0.9417	
	No	119/ 482 (24.7)	120/ 481 (24.9)	1.03 (0.93, 1.14) 0.5776	0.85 (0.60, 1.22) 0.3846	-0.00 (-0.06, 0.05)*0.9258	
	Diuretics at baseline						0.8730
	Yes	591/2536 (23.3)	587/2531 (23.2)	1.05 (1.00, 1.11) 0.0696	1.07 (0.91, 1.26) 0.3972	0.00 (-0.02, 0.02)*0.9248	
	No	61/ 306 (19.9)	63/ 306 (20.6)	1.06 (0.84, 1.32) 0.6295	1.01 (0.63, 1.63) 0.9527	-0.01 (-0.07, 0.06)*0.8406	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)							
	Overall	334/2842 (11.8)	424/2837 (14.9)	0.79 (0.69, 0.90) 0.0004	0.75 (0.64, 0.88) 0.0004	-0.03 (-0.05, -0.01)*0.0004	
	Age						0.4708
	<= median	137/1415 (9.7)	190/1482 (12.8)	0.74 (0.61, 0.91) 0.0046	0.71 (0.56, 0.90) 0.0045	-0.03 (-0.05, -0.01)*0.0074	
	> median	197/1427 (13.8)	234/1355 (17.3)	0.82 (0.69, 0.97) 0.0228	0.78 (0.63, 0.96) 0.0185	-0.03 (-0.06, -0.01)*0.0117	
	Gender						0.5980
	Male	189/1656 (11.4)	228/1625 (14.0)	0.82 (0.68, 0.98) 0.0256	0.79 (0.64, 0.97) 0.0237	-0.03 (-0.05, -0.00)*0.0244	
	Female	145/1186 (12.2)	196/1212 (16.2)	0.76 (0.63, 0.92) 0.0059	0.72 (0.56, 0.91) 0.0054	-0.04 (-0.07, -0.01)*0.0055	
	Race						0.4080
	White	248/2039 (12.2)	312/2058 (15.2)	0.81 (0.70, 0.95) 0.0078	0.78 (0.65, 0.93) 0.0073	-0.03 (-0.05, -0.01)*0.0052	
	Black or African	9/ 67 (13.4)	6/ 71 (8.5)	1.53 (0.59, 3.95) 0.3814	1.62 (0.53, 4.99) 0.3979	0.05 (-0.05, 0.15)*0.3486	
	Asian	64/ 558 (11.5)	90/ 555 (16.2)	0.71 (0.52, 0.95) 0.0215	0.66 (0.47, 0.94) 0.0205	-0.05 (-0.09, -0.01) 0.0134	
	Other	13/ 178 (7.3)	16/ 153 (10.5)	0.67 (0.34, 1.34) 0.2602	0.63 (0.29, 1.37) 0.2404	-0.03 (-0.09, 0.03)*0.3167	
	Geographic region						0.5756
	Asia	60/ 539 (11.1)	85/ 538 (15.8)	0.70 (0.52, 0.96) 0.0247	0.66 (0.47, 0.95) 0.0236	-0.05 (-0.09, -0.01) 0.0166	
	Europe and Saudi Arabia	160/1365 (11.7)	214/1394 (15.4)	0.79 (0.66, 0.95) 0.0124	0.74 (0.59, 0.92) 0.0079	-0.04 (-0.06, -0.01)*0.0052	
	North America	59/ 398 (14.8)	60/ 387 (15.5)	0.94 (0.68, 1.31) 0.7285	0.93 (0.63, 1.38) 0.7245	-0.01 (-0.06, 0.04)*0.7907	
	Latin America	55/ 540 (10.2)	65/ 518 (12.5)	0.79 (0.57, 1.11) 0.1714	0.77 (0.52, 1.14) 0.1886	-0.02 (-0.06, 0.01)*0.2262	
	NYHA class at enrolment						0.7162
	II	256/2113 (12.1)	330/2187 (15.1)	0.80 (0.68, 0.92) 0.0027	0.76 (0.64, 0.91) 0.0025	-0.03 (-0.05, -0.01)*0.0044	
	III or IV	78/ 729 (10.7)	94/ 649 (14.5)	0.75 (0.57, 0.98) 0.0385	0.70 (0.50, 0.98) 0.0354	-0.04 (-0.07, -0.00)*0.0349	
	LVEF at enrolment						0.1918
	<= 49	110/ 980 (11.2)	115/ 963 (11.9)	0.92 (0.73, 1.18) 0.5278	0.91 (0.68, 1.20) 0.4885	-0.01 (-0.04, 0.02)*0.6213	
	50-59	138/1029 (13.4)	171/1017 (16.8)	0.79 (0.65, 0.97) 0.0240	0.76 (0.59, 0.97) 0.0274	-0.03 (-0.07, -0.00)*0.0315	
	>= 60	86/ 833 (10.3)	138/ 857 (16.1)	0.67 (0.52, 0.86) 0.0016	0.62 (0.46, 0.83) 0.0012	-0.06 (-0.09, -0.03)*0.0004	
	NT-proBNP at enrolment						0.9081
	<= median	163/1418 (11.5)	206/1421 (14.5)	0.78 (0.65, 0.95) 0.0109	0.75 (0.60, 0.94) 0.0135	-0.03 (-0.05, -0.01)*0.0173	
	> median	171/1424 (12.0)	218/1415 (15.4)	0.80 (0.67, 0.96) 0.0158	0.75 (0.60, 0.93) 0.0103	-0.03 (-0.06, -0.01)*0.0084	
	Type 2 Diabetes Medical History						0.2214
	Yes	148/1250 (11.8)	207/1260 (16.4)	0.73 (0.60, 0.88) 0.0010	0.68 (0.54, 0.86)*0.0010	-0.05 (-0.07, -0.02)*0.0009	
	No	186/1592 (11.7)	217/1577 (13.8)	0.85 (0.71, 1.02) 0.0877	0.83 (0.67, 1.02)*0.0796	-0.02 (-0.04, 0.00)*0.0793	
	Atrial fibrillation or flutter at enrolment ECG						0.7745
	Yes	133/1199 (11.1)	172/1199 (14.3)	0.77 (0.63, 0.95) 0.0143	0.73 (0.57, 0.94) 0.0135	-0.03 (-0.06, -0.01)*0.0167	
	No	201/1643 (12.2)	252/1638 (15.4)	0.80 (0.68, 0.95) 0.0105	0.76 (0.62, 0.94) 0.0092	-0.03 (-0.06, -0.01)*0.0088	
	BMI (kg/m2) at enrolment						0.9334
	< 30	180/1571 (11.5)	227/1559 (14.6)	0.79 (0.66, 0.95) 0.0105	0.75 (0.61, 0.93) 0.0086	-0.03 (-0.05, -0.01)*0.0098	
	>= 30	154/1270 (12.1)	195/1275 (15.3)	0.80 (0.66, 0.97) 0.0215	0.76 (0.60, 0.96) 0.0224	-0.03 (-0.06, -0.00)*0.0200	
	Baseline eGFR (mL/min/1.73m^2)						0.7553
	< 60	188/1359 (13.8)	241/1396 (17.3)	0.81 (0.68, 0.96) 0.0157	0.76 (0.62, 0.94) 0.0125	-0.03 (-0.06, -0.01)*0.0128	
	>= 60	146/1483 (9.8)	183/1440 (12.7)	0.78 (0.63, 0.95) 0.0138	0.75 (0.59, 0.94) 0.0137	-0.03 (-0.05, -0.01)*0.0144	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in KCCQ scores at study end (LOCF) including study closure visits
Full Analysis Set

Score	Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Total Symptom Score (LOCF)	SBP at randomisation						0.4771
	<= median	162/1424 (11.4)	223/1439 (15.5)	0.75 (0.63, 0.91) 0.0027	0.71 (0.57, 0.89) 0.0024	-0.04 (-0.07, -0.02)*0.0012	
	> median	172/1418 (12.1)	201/1398 (14.4)	0.83 (0.69, 1.00) 0.0482	0.80 (0.64, 1.00) 0.0458	-0.02 (-0.05, 0.00)*0.0785	
	LVEF at enrolment 2						0.1355
	<= 49	110/ 980 (11.2)	115/ 963 (11.9)	0.92 (0.73, 1.18) 0.5278	0.91 (0.68, 1.20) 0.4885	-0.01 (-0.04, 0.02)*0.6213	
	>= 50	224/1862 (12.0)	309/1874 (16.5)	0.74 (0.63, 0.87) 0.0002	0.70 (0.58, 0.84) 0.0002	-0.04 (-0.07, -0.02)*<.0001	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.1065
	Yes	17/ 283 (6.0)	31/ 286 (10.8)	0.55 (0.31, 0.98)*0.0418	0.40 (0.21, 0.77) 0.0061	-0.05 (-0.09, -0.00)*0.0371	
	No	317/2559 (12.4)	393/2551 (15.4)	0.81 (0.71, 0.93) 0.0027	0.78 (0.66, 0.92) 0.0024	-0.03 (-0.05, -0.01)*0.0018	
	MRAs at baseline						0.2562
	Yes	136/1227 (11.1)	189/1224 (15.4)	0.72 (0.59, 0.88) 0.0016	0.68 (0.54, 0.86) 0.0015	-0.04 (-0.07, -0.02)*0.0014	
	No	198/1615 (12.3)	235/1613 (14.6)	0.84 (0.71, 1.00) 0.0526	0.81 (0.66, 1.00) 0.0471	-0.02 (-0.05, 0.00)*0.0541	
	ACEi+ARB at baseline						0.0636
	Yes	217/2065 (10.5)	305/2077 (14.7)	0.73 (0.62, 0.85) <.0001	0.68 (0.56, 0.82) <.0001	-0.04 (-0.06, -0.02)*<.0001	
	No	117/ 777 (15.1)	119/ 760 (15.7)	0.96 (0.76, 1.21) 0.7078	0.95 (0.72, 1.25) 0.6919	-0.01 (-0.05, 0.02) 0.5057	
	ARNI at baseline						0.1792
	Yes	21/ 153 (13.7)	13/ 126 (10.3)	1.17 (0.60, 2.25) 0.6463	1.22 (0.58, 2.59) 0.6019	0.03 (-0.04, 0.11)*0.3802	
	No	313/2689 (11.6)	411/2711 (15.2)	0.78 (0.68, 0.89) 0.0002	0.74 (0.63, 0.86) 0.0002	-0.04 (-0.05, -0.02)*0.0001	
	Beta Blocker at baseline						0.1707
	Yes	288/2360 (12.2)	355/2356 (15.1)	0.82 (0.71, 0.95) 0.0071	0.79 (0.66, 0.93) 0.0059	-0.03 (-0.05, -0.01)*0.0041	
	No	46/ 482 (9.5)	69/ 481 (14.3)	0.64 (0.45, 0.90) 0.0103	0.59 (0.39, 0.88) 0.0104	-0.05 (-0.09, -0.01)*0.0213	
	Diuretics at baseline						0.7166
	Yes	308/2536 (12.1)	385/2531 (15.2)	0.79 (0.69, 0.91) 0.0009	0.76 (0.64, 0.89) 0.0009	-0.03 (-0.05, -0.01)*0.0015	
	No	26/ 306 (8.5)	39/ 306 (12.7)	0.73 (0.46, 1.16) 0.1816	0.67 (0.40, 1.14) 0.1432	-0.04 (-0.09, 0.01)*0.0873	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of EQ-5D VAS by visit
Full Analysis Set

		Dapa 10 mg (N=3131)		Placebo (N=3132)	
	Visit	n/ N#	Compliance	n/ N#	Compliance
EQ VAS Score	Visit 2 (Baseline)	2766/3131	88.34%	2797/3132	89.30%
	Visit 5 (8 Months)	2214/3030	73.07%	2221/3032	73.25%
	Study Closure Visit	2153/2621	82.14%	2145/2599	82.53%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of EQ-5D VAS by visit
Full Analysis Set

		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
EQ VAS Score	Visit 2 (Baseline)	2766	67.01 (17.21)			2797	67.16 (16.91)		
	Visit 5 (8 Months)	2214	70.64 (15.78)	2076	3.20 (17.05)	2221	69.71 (16.09)	2102	2.41 (17.01)

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of EQ-5D VAS
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
EQ VAS Score	Visit 5 (8 Months)		3.28 (0.31)		2.32 (0.31)	0.96 (0.11, 1.82)	0.0277	0.07 (0.01, 0.13)
	OVERALL	2076	3.28 (0.31)	2102	2.32 (0.31)	0.96 (0.11, 1.82)	0.0277	0.07 (0.01, 0.13)

N displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
OVERALL row displays model estimates over time.
LS Means and difference of LS Means estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of EQ-5D VAS - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
EQ VAS Score	Age												0.4013
	<= median	1370	66.96 (17.45)	1049	4.18 (0.44)	1461	67.39 (17.18)	1123	2.82 (0.43)	1.36 (0.16, 2.57)	0.0265	0.10 (0.01, 0.18)	
	> median	1396	67.05 (16.98)	1027	2.38 (0.43)	1336	66.91 (16.62)	979	1.75 (0.45)	0.63 (-0.59, 1.85)	0.3117	0.05 (-0.04, 0.13)	
	Gender												0.2483
	Male	1629	67.82 (16.91)	1227	3.47 (0.40)	1599	68.44 (16.65)	1199	2.08 (0.40)	1.38 (0.27, 2.49)	0.0146	0.10 (0.02, 0.18)	
	Female	1137	65.85 (17.58)	849	3.01 (0.49)	1198	65.46 (17.12)	903	2.65 (0.48)	0.36 (-0.99, 1.70)	0.6015	0.02 (-0.07, 0.12)	
	Race												0.5629
	White	1959	64.88 (17.35)	1405	3.03 (0.38)	2012	65.57 (16.86)	1474	2.20 (0.37)	0.83 (-0.20, 1.86)	0.1149	0.06 (-0.01, 0.13)	
	Black or African	68	68.31 (17.14)	43	6.34 (3.02)	70	63.99 (22.86)	45	4.05 (2.95)	2.29 (-6.13,10.70)	0.5904	0.11 (-0.30, 0.53)	
	Asian	559	73.11 (15.54)	499	2.65 (0.61)	556	72.14 (15.63)	478	1.49 (0.62)	1.16 (-0.55, 2.86)	0.1826	0.09 (-0.04, 0.21)	
	Other	180	70.67 (15.50)	129	6.80 (1.00)	159	71.26 (14.68)	105	7.98 (1.11)	-1.18 (-4.12, 1.76)	0.4299	-0.10 (-0.36, 0.15)	
	Geographic region												0.8247
	Asia	541	73.23 (15.58)	493	2.66 (0.61)	538	72.27 (15.64)	472	1.53 (0.62)	1.12 (-0.59, 2.83)	0.1977	0.08 (-0.04, 0.21)	
	Europe and Saudi Arabia	1277	63.57 (16.20)	960	2.20 (0.43)	1337	63.90 (16.12)	1020	1.79 (0.42)	0.41 (-0.78, 1.60)	0.4993	0.03 (-0.06, 0.12)	
	North America	404	68.39 (18.89)	255	2.47 (0.99)	395	68.58 (18.78)	252	1.30 (1.00)	1.17 (-1.60, 3.93)	0.4078	0.07 (-0.10, 0.25)	
	Latin America	544	67.86 (17.81)	368	7.23 (0.71)	527	69.14 (16.95)	358	5.90 (0.72)	1.33 (-0.64, 3.31)	0.1847	0.10 (-0.05, 0.24)	
	NYHA class at enrolment												0.1552
	II	2054	69.56 (16.24)	1567	2.42 (0.35)	2148	69.44 (16.00)	1628	1.77 (0.34)	0.65 (-0.30, 1.61)	0.1795	0.05 (-0.02, 0.12)	
	III or IV	712	59.63 (17.82)	509	6.17 (0.67)	648	59.56 (17.65)	473	3.98 (0.70)	2.19 (0.29, 4.08)	0.0236	0.14 (0.02, 0.27)	
	LVEF at enrolment												0.7776
	<= 49	955	66.48 (17.46)	703	4.17 (0.52)	949	66.00 (17.80)	723	2.99 (0.52)	1.18 (-0.26, 2.62)	0.1085	0.09 (-0.02, 0.19)	
	50-59	996	66.67 (17.63)	755	3.08 (0.52)	1004	66.59 (16.27)	771	2.55 (0.51)	0.53 (-0.90, 1.96)	0.4690	0.04 (-0.06, 0.14)	
	>= 60	815	68.04 (16.37)	618	2.46 (0.58)	844	69.14 (16.49)	608	1.29 (0.58)	1.17 (-0.44, 2.77)	0.1542	0.08 (-0.03, 0.19)	
	NT-proBNP at enrolment												0.6746
	<= median	1368	68.28 (16.69)	1046	2.75 (0.42)	1394	68.54 (16.36)	1048	1.98 (0.42)	0.77 (-0.41, 1.94)	0.1997	0.06 (-0.03, 0.14)	
	> median	1398	65.76 (17.63)	1030	3.81 (0.45)	1402	65.82 (17.32)	1053	2.67 (0.45)	1.13 (-0.12, 2.39)	0.0759	0.08 (-0.01, 0.16)	
	Type 2 Diabetes Medical History												0.6556
	Yes	1205	66.24 (17.46)	906	3.39 (0.48)	1231	66.14 (17.19)	908	2.19 (0.48)	1.20 (-0.13, 2.53)	0.0779	0.08 (-0.01, 0.17)	
	No	1561	67.60 (17.01)	1170	3.21 (0.41)	1566	67.96 (16.65)	1194	2.41 (0.40)	0.80 (-0.32, 1.92)	0.1602	0.06 (-0.02, 0.14)	
	Atrial fibrillation or flutter at enrolment ECG												0.2701
	Yes	1178	66.83 (16.96)	900	2.90 (0.48)	1183	66.20 (17.07)	915	2.47 (0.48)	0.43 (-0.91, 1.76)	0.5324	0.03 (-0.06, 0.12)	
	No	1588	67.14 (17.40)	1176	3.60 (0.40)	1614	67.86 (16.77)	1187	2.19 (0.40)	1.40 (0.29, 2.52)	0.0136	0.10 (0.02, 0.18)	
	BMI (kg/m2) at enrolment												0.5955
	< 30	1540	68.08 (17.15)	1179	3.03 (0.40)	1544	68.80 (16.23)	1172	2.25 (0.40)	0.78 (-0.33, 1.89)	0.1702	0.06 (-0.02, 0.14)	
	>= 30	1225	65.68 (17.20)	897	3.66 (0.48)	1250	65.17 (17.45)	928	2.41 (0.48)	1.25 (-0.09, 2.58)	0.0667	0.09 (-0.01, 0.18)	
	Baseline eGFR (mL/min/1.73m^2)												0.0593
	< 60	1335	66.67 (17.18)	964	2.48 (0.45)	1379	66.56 (17.02)	1009	2.39 (0.44)	0.09 (-1.15, 1.33)	0.8846	0.01 (-0.08, 0.09)	
	>= 60	1431	67.32 (17.24)	1112	3.99 (0.43)	1417	67.76 (16.79)	1092	2.25 (0.43)	1.74 (0.55, 2.93)	0.0041	0.12 (0.04, 0.21)	
	SBP at randomisation												0.5209
	<= median	1395	67.03 (17.81)	1031	3.88 (0.44)	1422	68.13 (17.09)	1079	2.62 (0.43)	1.25 (0.04, 2.47)	0.0430	0.09 (0.00, 0.17)	
	> median	1371	66.99 (16.60)	1045	2.70 (0.43)	1375	66.16 (16.68)	1023	2.01 (0.44)	0.69 (-0.52, 1.90)	0.2615	0.05 (-0.04, 0.14)	

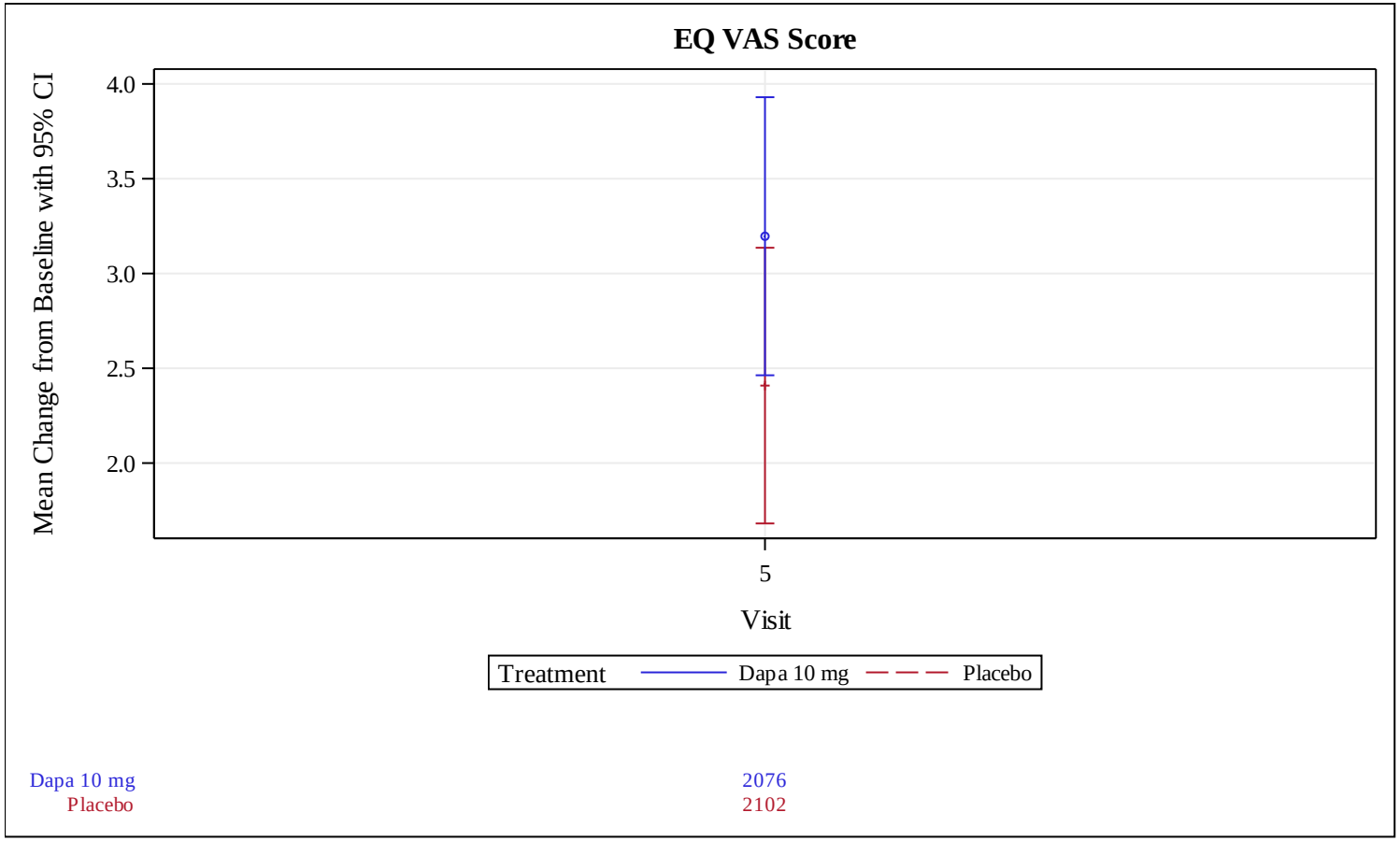
Repeated measures analysis displays overall results.
N* displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
LSMeans and difference of LSMeans estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.
p-Value for interaction from test for heterogeneity of the differences of LSMeans in the subgroups using Cochrane`s Q statistic.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of EQ-5D VAS - Subgroup analysis
Full Analysis Set

Subscale Score	Subgroup Level	Dapa 10 mg (N=3131) Baseline N	Dapa 10 mg (N=3131) Baseline Mean (SD)	Dapa 10 mg (N=3131) Overall N*	Dapa 10 mg (N=3131) Overall LSMean (SE)	Placebo (N=3132) Baseline N	Placebo (N=3132) Baseline Mean (SD)	Placebo (N=3132) Overall N*	Placebo (N=3132) Overall LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)	Interaction p-Value
EQ VAS Score	LVEF at enrolment 2												0.7011
	<= 49	955	66.48 (17.46)	703	4.17 (0.52)	949	66.00 (17.80)	723	2.99 (0.52)	1.18 (-0.26, 2.62)	0.1085	0.09 (-0.02, 0.19)	
	>= 50	1811	67.29 (17.08)	1373	2.81 (0.39)	1848	67.76 (16.41)	1379	1.98 (0.38)	0.83 (-0.24, 1.90)	0.1280	0.06 (-0.02, 0.13)	
	Randomised during hospitalisation for HF or within 30 days of discharge												0.0146
	Yes	285	61.94 (17.75)	197	6.94 (1.00)	286	59.78 (17.36)	210	2.75 (0.97)	4.20 (1.45, 6.94)	0.0029	0.30 (0.10, 0.49)	
	No	2481	67.59 (17.06)	1879	2.89 (0.33)	2511	68.00 (16.66)	1892	2.29 (0.32)	0.60 (-0.30, 1.50)	0.1916	0.04 (-0.02, 0.11)	
	MRAs at baseline												0.7576
	Yes	1181	67.02 (17.64)	918	3.09 (0.47)	1188	66.74 (17.06)	902	2.27 (0.47)	0.81 (-0.49, 2.12)	0.2222	0.06 (-0.03, 0.15)	
	No	1585	67.00 (16.90)	1158	3.44 (0.41)	1609	67.47 (16.80)	1200	2.36 (0.41)	1.09 (-0.05, 2.22)	0.0614	0.08 (-0.00, 0.16)	
	ACEi+ARB at baseline												0.5624
	Yes	2010	66.68 (17.07)	1498	3.11 (0.37)	2031	66.55 (16.78)	1541	2.02 (0.36)	1.09 (0.08, 2.11)	0.0353	0.08 (0.01, 0.15)	
	No	756	67.87 (17.57)	578	3.70 (0.57)	766	68.77 (17.16)	561	3.17 (0.58)	0.53 (-1.06, 2.12)	0.5102	0.04 (-0.08, 0.16)	
	ARNI at baseline												0.8864
	Yes	144	68.75 (18.11)	110	5.74 (1.16)	123	71.11 (16.64)	93	5.05 (1.26)	0.69 (-2.69, 4.07)	0.6885	0.06 (-0.22, 0.33)	
	No	2622	66.91 (17.16)	1966	3.14 (0.32)	2674	66.98 (16.91)	2009	2.20 (0.32)	0.94 (0.06, 1.82)	0.0368	0.07 (0.00, 0.13)	
	Beta Blocker at baseline												0.6887
	Yes	2293	66.48 (17.22)	1719	3.27 (0.34)	2329	66.91 (16.81)	1769	2.39 (0.34)	0.87 (-0.07, 1.81)	0.0687	0.06 (-0.00, 0.13)	
	No	473	69.55 (16.98)	357	3.32 (0.74)	468	68.38 (17.36)	333	1.98 (0.76)	1.34 (-0.75, 3.43)	0.2076	0.10 (-0.05, 0.25)	
	Diuretics at baseline												0.8741
	Yes	2476	66.85 (17.23)	1851	3.22 (0.33)	2495	67.00 (16.93)	1867	2.28 (0.33)	0.94 (0.02, 1.86)	0.0446	0.07 (0.00, 0.13)	
	No	290	68.35 (17.05)	225	3.80 (0.86)	302	68.46 (16.73)	235	2.66 (0.84)	1.14 (-1.21, 3.50)	0.3392	0.09 (-0.09, 0.27)	

Repeated measures analysis displays overall results.
N* displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
LSMeans and difference of LSMeans estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.
p-Value for interaction from test for heterogeneity of the differences of LSMeans in the subgroups using Cochrane`s Q statistic.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of EQ-5D VAS
Full Analysis Set



AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in EQ-5D VAS at month 8 (LOCF)
Full Analysis Set

Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	537/2076 (25.9)	485/2102 (23.1)	1.12 (1.01, 1.25)*0.0359	1.20 (1.03, 1.39) 0.0163	0.03 (0.01, 0.05) 0.0152	
Age						0.1392*
<= median	304/1049 (29.0)	269/1123 (24.0)	1.21 (1.05, 1.39)*0.0080	1.32 (1.08, 1.62) 0.0062	0.05 (0.02, 0.08) 0.0025	
> median	233/1027 (22.7)	216/ 979 (22.1)	1.03 (0.87, 1.21)*0.7375	1.08 (0.87, 1.34) 0.5043	0.01 (-0.03, 0.04) 0.7426	
Gender						0.0511*
Male	338/1227 (27.5)	270/1199 (22.5)	1.22 (1.06, 1.41)*0.0044	1.33 (1.09, 1.61) 0.0039	0.05 (0.02, 0.08) 0.0014	
Female	199/ 849 (23.4)	215/ 903 (23.8)	0.98 (0.83, 1.17)*0.8554	1.02 (0.81, 1.30) 0.8412	-0.01 (-0.04, 0.03) 0.6767	
Race						0.3264*
White	348/1405 (24.8)	312/1474 (21.2)	1.17 (1.02, 1.34)*0.0217	1.25 (1.04, 1.50) 0.0195	0.03 (0.00, 0.05) 0.0451	
Black or African	11/ 43 (25.6)	17/ 45 (37.8)	0.68 (0.36, 1.28)*0.2273	0.64 (0.24, 1.70) 0.3704	-0.10 (-0.28, 0.09) 0.3049	
Asian	132/ 499 (26.5)	123/ 478 (25.7)	1.03 (0.83, 1.27)*0.7977	1.07 (0.80, 1.44) 0.6309	0.02 (-0.03, 0.08) 0.4024	
Other	46/ 129 (35.7)	33/ 105 (31.4)	1.13 (0.79, 1.64)*0.4982	1.16 (0.66, 2.06) 0.6031	0.01 (-0.11, 0.12) 0.9118	
Geographic region						0.7155*
Asia	131/ 493 (26.6)	121/ 472 (25.6)	1.04 (0.84, 1.28)*0.7407	1.09 (0.81, 1.46) 0.5864	0.02 (-0.03, 0.08) 0.3661	
Europe and Saudi Arabia	200/ 960 (20.8)	196/1020 (19.2)	1.08 (0.91, 1.29)*0.3685	1.14 (0.90, 1.44) 0.2911	0.02 (-0.02, 0.05)*0.3688	
North America	77/ 255 (30.2)	61/ 252 (24.2)	1.25 (0.94, 1.66)*0.1315	1.38 (0.91, 2.07) 0.1267	0.05 (-0.02, 0.12) 0.1832	
Latin America	129/ 368 (35.1)	107/ 358 (29.9)	1.17 (0.95, 1.45)*0.1386	1.27 (0.91, 1.78) 0.1651	0.03 (-0.04, 0.09) 0.4075	
NYHA class at enrolment						0.0498*
II	375/1567 (23.9)	372/1628 (22.9)	1.05 (0.92, 1.19)*0.4705	1.09 (0.92, 1.30) 0.3029	0.02 (-0.01, 0.05) 0.1979	
III or IV	162/ 509 (31.8)	113/ 473 (23.9)	1.33 (1.09, 1.64)*0.0061	1.66 (1.21, 2.26) 0.0016	0.08 (0.02, 0.14)*0.0053	
LVEF at enrolment						0.3172*
<= 49	197/ 703 (28.0)	167/ 723 (23.1)	1.21 (1.02, 1.45)*0.0334	1.40 (1.09, 1.80) 0.0084	0.06 (0.01, 0.10) 0.0085	
50-59	190/ 755 (25.2)	192/ 771 (24.9)	1.01 (0.85, 1.20)*0.9057	1.03 (0.81, 1.31) 0.8218	0.01 (-0.03, 0.04) 0.7941	
>= 60	150/ 618 (24.3)	126/ 608 (20.7)	1.17 (0.95, 1.44)*0.1378	1.20 (0.90, 1.59) 0.2062	0.03 (-0.02, 0.07) 0.2149	
NT-proBNP at enrolment						0.8676*
<= median	261/1046 (25.0)	235/1048 (22.4)	1.11 (0.95, 1.30)*0.1740	1.19 (0.96, 1.46) 0.1052	0.03 (-0.00, 0.06) 0.0802	
> median	276/1030 (26.8)	249/1053 (23.6)	1.13 (0.98, 1.31)*0.0983	1.21 (0.98, 1.50) 0.0749	0.03 (-0.01, 0.06) 0.1306	
Type 2 Diabetes Medical History						0.8372*
Yes	239/ 906 (26.4)	211/ 908 (23.2)	1.14 (0.97, 1.33)*0.1218	1.18 (0.96, 1.47)*0.1215	0.04 (0.00, 0.07) 0.0479	
No	298/1170 (25.5)	274/1194 (22.9)	1.11 (0.96, 1.28)*0.1526	1.15 (0.95, 1.39)*0.1524	0.02 (-0.01, 0.06) 0.1397	
Atrial fibrillation or flutter at enrolment ECG						0.7501*
Yes	238/ 900 (26.4)	220/ 915 (24.0)	1.10 (0.94, 1.29)*0.2394	1.21 (0.97, 1.52) 0.0951	0.03 (0.00, 0.07) 0.0486	
No	299/1176 (25.4)	265/1187 (22.3)	1.14 (0.99, 1.32)*0.0775	1.20 (0.98, 1.46) 0.0753	0.03 (-0.01, 0.06) 0.1089	
BMI (kg/m2) at enrolment						0.8102*
< 30	311/1179 (26.4)	273/1172 (23.3)	1.13 (0.98, 1.30)*0.0839	1.17 (0.96, 1.42) 0.1122	0.03 (-0.01, 0.06) 0.1056	
>= 30	226/ 897 (25.2)	212/ 928 (22.8)	1.10 (0.94, 1.30)*0.2401	1.27 (1.00, 1.60) 0.0477	0.03 (-0.00, 0.06) 0.0682	
Baseline eGFR (mL/min/1.73m^2)						0.3037*
< 60	235/ 964 (24.4)	233/1009 (23.1)	1.06 (0.90, 1.24)*0.5023	1.14 (0.92, 1.42) 0.2381	0.02 (-0.01, 0.05) 0.2810	
>= 60	302/1112 (27.2)	251/1092 (23.0)	1.18 (1.02, 1.37)*0.0242	1.25 (1.02, 1.53) 0.0282	0.04 (0.00, 0.07) 0.0245	

N displays number of patients in the analysis, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with baseline value as a covariate and T2DM stratum.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in EQ-5D VAS at month 8 (LOCF)
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SBP at randomisation						0.1496*
<= median	300/1031 (29.1)	260/1079 (24.1)	1.21 (1.05, 1.39)*0.0095	1.30 (1.06, 1.59) 0.0118	0.04 (0.00, 0.07) 0.0261	
> median	237/1045 (22.7)	225/1023 (22.0)	1.03 (0.88, 1.21)*0.7084	1.11 (0.89, 1.38) 0.3527	0.02 (-0.01, 0.05) 0.2631	
LVEF at enrolment 2						0.2826*
<= 49	197/ 703 (28.0)	167/ 723 (23.1)	1.21 (1.02, 1.45)*0.0334	1.40 (1.09, 1.80) 0.0084	0.06 (0.01, 0.10) 0.0085	
>= 50	340/1373 (24.8)	318/1379 (23.1)	1.07 (0.94, 1.23)*0.2951	1.10 (0.91, 1.32) 0.3117	0.02 (-0.01, 0.04) 0.2895	
Randomised during hospitalisation for HF or within 30 days of discharge						0.3547*
Yes	64/ 197 (32.5)	53/ 210 (25.2)	1.29 (0.95, 1.75)*0.1078	1.89 (1.16, 3.06) 0.0101	0.07 (-0.02, 0.16)*0.1061	
No	473/1879 (25.2)	432/1892 (22.8)	1.10 (0.98, 1.24)*0.0927	1.15 (0.98, 1.34) 0.0843	0.02 (-0.00, 0.05) 0.0724	
MRAs at baseline						0.7301*
Yes	239/ 918 (26.0)	205/ 902 (22.7)	1.15 (0.97, 1.35)*0.1010	1.25 (1.00, 1.56) 0.0533	0.04 (0.00, 0.07) 0.0397	
No	298/1158 (25.7)	280/1200 (23.3)	1.10 (0.96, 1.27)*0.1757	1.16 (0.95, 1.42) 0.1333	0.02 (-0.01, 0.05) 0.1541	
ACEi+ARB at baseline						0.8797*
Yes	373/1498 (24.9)	341/1541 (22.1)	1.13 (0.99, 1.28)*0.0719	1.22 (1.02, 1.46) 0.0271	0.03 (-0.00, 0.05) 0.0652	
No	164/ 578 (28.4)	144/ 561 (25.7)	1.11 (0.91, 1.34)*0.3047	1.14 (0.86, 1.49) 0.3615	0.04 (-0.01, 0.08) 0.1378	
ARNI at baseline						0.5954*
Yes	37/ 110 (33.6)	25/ 93 (26.9)	1.25 (0.82, 1.92)*0.3021	1.34 (0.71, 2.52) 0.3688	0.06 (-0.06, 0.18) 0.3539	
No	500/1966 (25.4)	460/2009 (22.9)	1.11 (0.99, 1.24)*0.0620	1.19 (1.02, 1.38) 0.0288	0.03 (0.00, 0.05) 0.0284	
Beta Blocker at baseline						0.1314*
Yes	427/1719 (24.8)	408/1769 (23.1)	1.08 (0.96, 1.21)*0.2192	1.12 (0.95, 1.32) 0.1700	0.02 (-0.01, 0.04) 0.1779	
No	110/ 357 (30.8)	77/ 333 (23.1)	1.33 (1.04, 1.71)*0.0244	1.56 (1.10, 2.22) 0.0129	0.08 (0.02, 0.14) 0.0090	
Diuretics at baseline						0.6655*
Yes	474/1851 (25.6)	430/1867 (23.0)	1.11 (0.99, 1.25)*0.0673	1.18 (1.01, 1.39) 0.0368	0.03 (0.00, 0.05) 0.0442	
No	63/ 225 (28.0)	55/ 235 (23.4)	1.20 (0.88, 1.63)*0.2602	1.32 (0.86, 2.03) 0.2046	0.06 (-0.02, 0.14) 0.1242	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% improvement in EQ-5D VAS at study end (LOCF) including study closure visits
Full Analysis Set

Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	682/2498 (27.3)	633/2536 (25.0)	1.09 (1.00, 1.20)*0.0588	1.15 (1.01, 1.31) 0.0407	0.02 (-0.00, 0.04) 0.1214	
Age						0.7145*
<= median	373/1259 (29.6)	356/1340 (26.6)	1.12 (0.99, 1.26)*0.0828	1.17 (0.97, 1.40) 0.0987	0.02 (-0.01, 0.05) 0.1598	
> median	309/1239 (24.9)	277/1196 (23.2)	1.08 (0.93, 1.24)*0.3049	1.14 (0.94, 1.39) 0.1952	0.01 (-0.02, 0.04) 0.4690	
Gender						0.3638*
Male	406/1470 (27.6)	350/1439 (24.3)	1.14 (1.00, 1.28)*0.0430	1.19 (1.00, 1.42) 0.0495	0.02 (-0.01, 0.05) 0.1144	
Female	276/1028 (26.8)	283/1097 (25.8)	1.04 (0.90, 1.20)*0.5825	1.09 (0.89, 1.34) 0.4231	0.01 (-0.02, 0.04) 0.5717	
Race						0.8686*
White	457/1754 (26.1)	425/1808 (23.5)	1.11 (0.99, 1.24)*0.0783	1.14 (0.96, 1.34) 0.1299	0.00 (-0.02, 0.03) 0.6995	
Black or African	18/ 56 (32.1)	20/ 61 (32.8)	1.31 (0.74, 2.31) 0.3582	1.16 (0.51, 2.64) 0.7232	0.01 (-0.15, 0.17) 0.9300	
Asian	140/ 528 (26.5)	136/ 525 (25.9)	1.02 (0.84, 1.25)*0.8218	1.09 (0.82, 1.46) 0.5378	0.02 (-0.03, 0.07) 0.3935	
Other	67/ 160 (41.9)	52/ 142 (36.6)	1.14 (0.86, 1.52)*0.3532	1.21 (0.74, 1.99) 0.4430	0.02 (-0.09, 0.12) 0.7189	
Geographic region						0.9121*
Asia	139/ 517 (26.9)	132/ 509 (25.9)	1.04 (0.85, 1.27)*0.7293	1.12 (0.84, 1.50) 0.4509	0.02 (-0.02, 0.07) 0.3257	
Europe and Saudi Arabia	279/1164 (24.0)	263/1221 (21.5)	1.11 (0.96, 1.29)*0.1572	1.16 (0.94, 1.42) 0.1685	0.02 (-0.01, 0.06)*0.1572	
North America	90/ 336 (26.8)	85/ 331 (25.7)	1.04 (0.81, 1.35)*0.7455	1.07 (0.74, 1.54) 0.7345	0.00 (-0.06, 0.06) 0.9613	
Latin America	174/ 481 (36.2)	153/ 475 (32.2)	1.12 (0.94, 1.34)*0.1972	1.16 (0.87, 1.56) 0.3123	0.03 (-0.03, 0.08) 0.3150	
NYHA class at enrolment						0.0163*
II	473/1886 (25.1)	486/1970 (24.7)	1.02 (0.91, 1.13)*0.7687	1.04 (0.89, 1.22) 0.5925	0.00 (-0.02, 0.03) 0.7120	
III or IV	209/ 612 (34.2)	147/ 565 (26.0)	1.31 (1.10, 1.57)*0.0026	1.59 (1.21, 2.10) 0.0009	0.08 (0.03, 0.13)*0.0022	
LVEF at enrolment						0.7372*
<= 49	252/ 853 (29.5)	235/ 858 (27.4)	1.08 (0.93, 1.25)*0.3239	1.17 (0.94, 1.46) 0.1644	0.02 (-0.02, 0.05) 0.4097	
50-59	234/ 899 (26.0)	226/ 919 (24.6)	1.06 (0.90, 1.24)*0.4811	1.09 (0.87, 1.37) 0.4321	0.01 (-0.02, 0.05) 0.4467	
>= 60	196/ 746 (26.3)	172/ 759 (22.7)	1.16 (0.97, 1.39)*0.1036	1.19 (0.92, 1.53) 0.1788	0.02 (-0.02, 0.06) 0.2752	
NT-proBNP at enrolment						0.9881*
<= median	335/1256 (26.7)	315/1292 (24.4)	1.09 (0.96, 1.25)*0.1849	1.15 (0.95, 1.38) 0.1551	0.02 (-0.01, 0.05) 0.2184	
> median	347/1242 (27.9)	317/1243 (25.5)	1.10 (0.96, 1.25)*0.1703	1.16 (0.96, 1.40) 0.1350	0.01 (-0.02, 0.04) 0.3391	
Type 2 Diabetes Medical History						0.4746*
Yes	306/1081 (28.3)	278/1116 (24.9)	1.14 (0.99, 1.31)*0.0719	1.19 (0.98, 1.44)*0.0717	0.02 (-0.01, 0.05) 0.1809	
No	376/1417 (26.5)	355/1420 (25.0)	1.06 (0.94, 1.20)*0.3501	1.08 (0.92, 1.28)*0.3500	0.01 (-0.02, 0.04) 0.3735	
Atrial fibrillation or flutter at enrolment ECG						0.0775*
Yes	289/1062 (27.2)	294/1076 (27.3)	1.00 (0.87, 1.14)*0.9542	1.03 (0.84, 1.27) 0.7437	-0.00 (-0.03, 0.03) 0.9778	
No	393/1436 (27.4)	339/1460 (23.2)	1.18 (1.04, 1.34)*0.0104	1.25 (1.05, 1.49) 0.0143	0.03 (0.00, 0.06) 0.0398	
BMI (kg/m2) at enrolment						0.6661*
< 30	385/1399 (27.5)	345/1395 (24.7)	1.11 (0.98, 1.26)*0.0938	1.15 (0.96, 1.37) 0.1272	0.02 (-0.01, 0.05) 0.2151	
>= 30	297/1099 (27.0)	288/1138 (25.3)	1.07 (0.93, 1.23)*0.3557	1.15 (0.94, 1.41) 0.1752	0.01 (-0.02, 0.04) 0.4301	
Baseline eGFR (mL/min/1.73m^2)						0.2193*
< 60	303/1178 (25.7)	307/1225 (25.1)	1.03 (0.89, 1.18)*0.7100	1.08 (0.88, 1.31) 0.4606	0.00 (-0.03, 0.03) 0.8544	
>= 60	379/1320 (28.7)	326/1310 (24.9)	1.15 (1.02, 1.31)*0.0270	1.21 (1.01, 1.46) 0.0373	0.03 (-0.00, 0.06) 0.0537	

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Subgroup Level	Dapa 10 mg (N=3131) n/ N (%)	Placebo (N=3132) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SBP at randomisation						0.7042*
<= median	359/1243 (28.9)	335/1292 (25.9)	1.11 (0.98, 1.26)*0.0958	1.14 (0.95, 1.37) 0.1599	0.02 (-0.01, 0.05) 0.2718	
> median	323/1255 (25.7)	298/1244 (24.0)	1.07 (0.94, 1.23)*0.3029	1.16 (0.96, 1.41) 0.1227	0.02 (-0.01, 0.05) 0.1323	
LVEF at enrolment 2						0.8255*
<= 49	252/ 853 (29.5)	235/ 858 (27.4)	1.08 (0.93, 1.25)*0.3239	1.17 (0.94, 1.46) 0.1644	0.02 (-0.02, 0.05) 0.4097	
>= 50	430/1645 (26.1)	398/1678 (23.7)	1.10 (0.98, 1.24)*0.1069	1.14 (0.96, 1.34) 0.1323	0.02 (-0.01, 0.04) 0.1833	
Randomised during hospitalisation for HF or within 30 days of discharge						0.6701*
Yes	74/ 232 (31.9)	68/ 247 (27.5)	1.16 (0.88, 1.53)*0.2962	1.50 (0.97, 2.32) 0.0653	0.04 (-0.04, 0.13)*0.2958	
No	608/2266 (26.8)	565/2289 (24.7)	1.09 (0.98, 1.20)*0.0975	1.12 (0.97, 1.29) 0.1160	0.01 (-0.01, 0.04) 0.2032	
MRAs at baseline						0.0502*
Yes	313/1077 (29.1)	258/1080 (23.9)	1.22 (1.06, 1.40)*0.0066	1.38 (1.12, 1.69) 0.0020	0.05 (0.01, 0.08) 0.0045	
No	369/1421 (26.0)	375/1456 (25.8)	1.01 (0.89, 1.14)*0.8966	1.00 (0.84, 1.20) 0.9909	-0.01 (-0.03, 0.02) 0.6276	
ACEi+ARB at baseline						0.4552*
Yes	491/1827 (26.9)	466/1856 (25.1)	1.07 (0.96, 1.19)*0.2217	1.13 (0.97, 1.32) 0.1215	0.01 (-0.01, 0.04) 0.2975	
No	191/ 671 (28.5)	167/ 680 (24.6)	1.16 (0.97, 1.39)*0.1044	1.20 (0.93, 1.55) 0.1660	0.02 (-0.02, 0.07) 0.2326	
ARNI at baseline						0.3920*
Yes	45/ 130 (34.6)	29/ 108 (26.9)	1.29 (0.87, 1.91)*0.2028	1.31 (0.72, 2.36) 0.3756	0.06 (-0.05, 0.17) 0.2868	
No	637/2368 (26.9)	604/2428 (24.9)	1.08 (0.98, 1.19)*0.1097	1.14 (0.99, 1.30) 0.0679	0.01 (-0.01, 0.03) 0.2297	
Beta Blocker at baseline						0.5478*
Yes	550/2076 (26.5)	524/2132 (24.6)	1.08 (0.97, 1.20)*0.1543	1.11 (0.96, 1.29) 0.1651	0.01 (-0.01, 0.03) 0.4718	
No	132/ 422 (31.3)	109/ 404 (27.0)	1.16 (0.94, 1.44)*0.1754	1.31 (0.96, 1.80) 0.0873	0.05 (-0.01, 0.11) 0.0857	
Diuretics at baseline						0.8761*
Yes	604/2228 (27.1)	559/2250 (24.8)	1.09 (0.99, 1.20)*0.0841	1.15 (0.99, 1.32) 0.0611	0.02 (-0.01, 0.04) 0.1314	
No	78/ 270 (28.9)	74/ 286 (25.9)	1.12 (0.85, 1.46)*0.4256	1.19 (0.81, 1.75) 0.3801	0.02 (-0.05, 0.09) 0.5118	

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AstraZeneca
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Overall study population
Analysis of proportion of patients with >=15% deterioration in EQ-5D VAS at month 8 (LOCF)
Full Analysis Set

Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	242/2076 (11.7)	264/2102 (12.6)	0.92 (0.78, 1.07) 0.2674	0.90 (0.74, 1.09) 0.2904	-0.01 (-0.03, 0.01)*0.3712	
Age						0.7461*
<= median	108/1049 (10.3)	129/1123 (11.5)	0.90 (0.70, 1.14)*0.3739	0.87 (0.66, 1.15) 0.3321	-0.01 (-0.04, 0.01)*0.3726	
> median	134/1027 (13.0)	135/ 979 (13.8)	0.94 (0.76, 1.16) 0.5418	0.91 (0.70, 1.19) 0.4839	-0.01 (-0.04, 0.02)*0.6261	
Gender						0.0378*
Male	130/1227 (10.6)	159/1199 (13.3)	0.80 (0.65, 0.99) 0.0417	0.77 (0.60, 1.00) 0.0461	-0.03 (-0.05, -0.00)*0.0427	
Female	112/ 849 (13.2)	105/ 903 (11.6)	1.13 (0.88, 1.46)*0.3209	1.11 (0.83, 1.50) 0.4833	0.02 (-0.02, 0.05)*0.3213	
Race						0.0593*
White	185/1405 (13.2)	185/1474 (12.6)	1.05 (0.87, 1.27)*0.6213	1.07 (0.85, 1.34) 0.5887	0.01 (-0.02, 0.03)*0.6215	
Black or African	3/ 43 (7.0)	6/ 45 (13.3)	0.52 (0.14, 1.96)*0.3367	0.49 (0.11, 2.18) 0.3482	-0.06 (-0.19, 0.06)*0.3195	
Asian	45/ 499 (9.0)	68/ 478 (14.2)	0.61 (0.43, 0.85) 0.0044	0.57 (0.38, 0.85) 0.0066	-0.05 (-0.09, -0.01)*0.0110	
Other	9/ 129 (7.0)	5/ 105 (4.8)	1.47 (0.51, 4.24)*0.4811	1.74 (0.54, 5.57) 0.3513	0.02 (-0.04, 0.08)*0.4689	
Geographic region						0.1259*
Asia	45/ 493 (9.1)	67/ 472 (14.2)	0.62 (0.44, 0.87) 0.0060	0.58 (0.38, 0.87) 0.0090	-0.05 (-0.09, -0.01)*0.0141	
Europe and Saudi Arabia	124/ 960 (12.9)	126/1020 (12.4)	1.05 (0.83, 1.32)*0.7059	1.03 (0.78, 1.37) 0.8375	0.01 (-0.02, 0.03)*0.7060	
North America	41/ 255 (16.1)	37/ 252 (14.7)	1.06 (0.72, 1.58) 0.7561	1.12 (0.68, 1.83) 0.6666	0.01 (-0.05, 0.08)*0.6630	
Latin America	32/ 368 (8.7)	34/ 358 (9.5)	0.92 (0.58, 1.45)*0.7073	0.98 (0.58, 1.65) 0.9290	-0.01 (-0.05, 0.03)*0.7073	
NYHA class at enrolment						0.8207*
II	187/1567 (11.9)	207/1628 (12.7)	0.92 (0.77, 1.10) 0.3837	0.91 (0.73, 1.13) 0.3755	-0.01 (-0.03, 0.01)*0.5017	
III or IV	55/ 509 (10.8)	57/ 473 (12.1)	0.90 (0.63, 1.27)*0.5398	0.85 (0.56, 1.30) 0.4489	-0.01 (-0.05, 0.03)*0.5403	
LVEF at enrolment						0.4136*
<= 49	75/ 703 (10.7)	82/ 723 (11.3)	0.94 (0.70, 1.26)*0.6849	0.86 (0.61, 1.22) 0.4021	-0.01 (-0.04, 0.03)*0.6846	
50-59	93/ 755 (12.3)	91/ 771 (11.8)	1.04 (0.80, 1.37)*0.7574	1.01 (0.74, 1.39) 0.9439	0.01 (-0.03, 0.04)*0.7574	
>= 60	74/ 618 (12.0)	91/ 608 (15.0)	0.85 (0.65, 1.12) 0.2509	0.82 (0.58, 1.15) 0.2544	-0.03 (-0.07, 0.01)*0.1246	
NT-proBNP at enrolment						0.6759*
<= median	118/1046 (11.3)	132/1048 (12.6)	0.86 (0.69, 1.08) 0.1845	0.84 (0.64, 1.11) 0.2255	-0.01 (-0.04, 0.01)*0.3536	
> median	124/1030 (12.0)	132/1053 (12.5)	0.96 (0.76, 1.21)*0.7299	0.97 (0.74, 1.27) 0.8125	-0.00 (-0.03, 0.02)*0.7298	
Type 2 Diabetes Medical History						0.8549*
Yes	112/ 906 (12.4)	123/ 908 (13.5)	0.89 (0.71, 1.12) 0.3148	0.90 (0.68, 1.18)*0.4528	-0.01 (-0.04, 0.02)*0.4526	
No	130/1170 (11.1)	141/1194 (11.8)	0.94 (0.76, 1.17) 0.5743	0.93 (0.72, 1.20)*0.5944	-0.01 (-0.03, 0.02)*0.5942	
Atrial fibrillation or flutter at enrolment ECG						0.3041*
Yes	119/ 900 (13.2)	119/ 915 (13.0)	1.02 (0.80, 1.29)*0.8912	0.99 (0.74, 1.32) 0.9458	0.00 (-0.03, 0.03)*0.8912	
No	123/1176 (10.5)	145/1187 (12.2)	0.86 (0.68, 1.07)*0.1788	0.83 (0.64, 1.08) 0.1554	-0.02 (-0.04, 0.01)*0.1779	
BMI (kg/m2) at enrolment						0.4280*
< 30	126/1179 (10.7)	143/1172 (12.2)	0.88 (0.71, 1.10) 0.2687	0.87 (0.67, 1.13) 0.2817	-0.02 (-0.04, 0.01)*0.2487	
>= 30	116/ 897 (12.9)	120/ 928 (12.9)	1.00 (0.79, 1.27)*0.9995	0.95 (0.71, 1.27) 0.7334	0.00 (-0.03, 0.03)*0.9995	
Baseline eGFR (mL/min/1.73m^2)						0.5290*
< 60	129/ 964 (13.4)	138/1009 (13.7)	0.98 (0.78, 1.22)*0.8481	0.95 (0.72, 1.25) 0.7135	-0.00 (-0.03, 0.03)*0.8480	
>= 60	113/1112 (10.2)	126/1092 (11.5)	0.88 (0.69, 1.12)*0.2991	0.86 (0.65, 1.13) 0.2788	-0.01 (-0.04, 0.01)*0.2988	

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SBP at randomisation						0.0456*
<= median	105/1031 (10.2)	141/1079 (13.1)	0.78 (0.61, 0.99)*0.0399	0.76 (0.58, 1.00) 0.0527	-0.03 (-0.06, -0.00)*0.0384	
> median	137/1045 (13.1)	123/1023 (12.0)	1.09 (0.87, 1.37)*0.4564	1.05 (0.80, 1.38) 0.6983	0.01 (-0.02, 0.04)*0.4559	
LVEF at enrolment 2						0.9099*
<= 49	75/ 703 (10.7)	82/ 723 (11.3)	0.94 (0.70, 1.26)*0.6849	0.86 (0.61, 1.22) 0.4021	-0.01 (-0.04, 0.03)*0.6846	
>= 50	167/1373 (12.2)	182/1379 (13.2)	0.92 (0.76, 1.11) 0.4041	0.92 (0.73, 1.16) 0.4611	-0.01 (-0.04, 0.01)*0.4146	
Randomised during hospitalisation for HF or within 30 days of discharge						0.8937*
Yes	21/ 197 (10.7)	25/ 210 (11.9)	0.90 (0.52, 1.55)*0.6921	0.67 (0.34, 1.31) 0.2406	-0.01 (-0.07, 0.05)*0.6913	
No	221/1879 (11.8)	239/1892 (12.6)	0.93 (0.79, 1.10) 0.3952	0.92 (0.75, 1.13) 0.4247	-0.01 (-0.03, 0.01)*0.4140	
MRAs at baseline						0.3227*
Yes	113/ 918 (12.3)	109/ 902 (12.1)	1.02 (0.80, 1.30)*0.8834	0.99 (0.74, 1.33) 0.9546	0.00 (-0.03, 0.03)*0.8833	
No	129/1158 (11.1)	155/1200 (12.9)	0.86 (0.70, 1.06) 0.1659	0.84 (0.65, 1.08) 0.1739	-0.02 (-0.04, 0.01)*0.1844	
ACEi+ARB at baseline						0.6133*
Yes	181/1498 (12.1)	205/1541 (13.3)	0.91 (0.75, 1.09)*0.3128	0.86 (0.69, 1.08) 0.1884	-0.01 (-0.04, 0.01)*0.3121	
No	61/ 578 (10.6)	59/ 561 (10.5)	1.01 (0.73, 1.40) 0.9404	1.04 (0.70, 1.54) 0.8419	0.00 (-0.04, 0.04)*0.9839	
ARNI at baseline						0.7108*
Yes	8/ 110 (7.3)	6/ 93 (6.5)	1.13 (0.41, 3.13)*0.8183	1.47 (0.47, 4.63) 0.5109	0.01 (-0.06, 0.08)*0.8172	
No	234/1966 (11.9)	258/2009 (12.8)	0.93 (0.79, 1.09)*0.3685	0.90 (0.74, 1.09) 0.2754	-0.01 (-0.03, 0.01)*0.3681	
Beta Blocker at baseline						0.9742*
Yes	198/1719 (11.5)	220/1769 (12.4)	0.93 (0.77, 1.11)*0.4041	0.91 (0.74, 1.13) 0.3986	-0.01 (-0.03, 0.01)*0.4036	
No	44/ 357 (12.3)	44/ 333 (13.2)	0.86 (0.59, 1.24) 0.4149	0.87 (0.55, 1.39) 0.5635	-0.01 (-0.06, 0.04)*0.7269	
Diuretics at baseline						0.9054*
Yes	220/1851 (11.9)	240/1867 (12.9)	0.91 (0.78, 1.08) 0.2854	0.90 (0.73, 1.10) 0.3044	-0.01 (-0.03, 0.01)*0.3693	
No	22/ 225 (9.8)	24/ 235 (10.2)	0.96 (0.55, 1.66)*0.8765	0.94 (0.50, 1.80) 0.8628	-0.00 (-0.06, 0.05)*0.8764	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in EQ-5D VAS at study end (LOCF) including study closure visits
Full Analysis Set

Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	352/2498 (14.1)	399/2536 (15.7)	0.90 (0.80, 1.02) 0.1072	0.86 (0.73, 1.02) 0.0769	-0.02 (-0.04, 0.00)*0.1018	
Age						0.4454*
<= median	144/1259 (11.4)	183/1340 (13.7)	0.84 (0.68, 1.03)*0.0890	0.81 (0.63, 1.03) 0.0903	-0.02 (-0.05, 0.00)*0.0873	
> median	208/1239 (16.8)	216/1196 (18.1)	0.92 (0.78, 1.08) 0.3088	0.88 (0.71, 1.10) 0.2750	-0.01 (-0.04, 0.02)*0.4080	
Gender						0.2825
Male	198/1470 (13.5)	235/1439 (16.3)	0.85 (0.72, 1.00) 0.0546	0.79 (0.64, 0.98) 0.0323	-0.03 (-0.05, -0.00)*0.0302	
Female	154/1028 (15.0)	164/1097 (14.9)	0.97 (0.81, 1.18) 0.7829	0.97 (0.76, 1.25) 0.8334	0.00 (-0.03, 0.03)*0.9842	
Race						0.9460*
White	254/1754 (14.5)	288/1808 (15.9)	0.91 (0.78, 1.06)*0.2293	0.90 (0.74, 1.09) 0.2947	-0.01 (-0.04, 0.01)*0.2286	
Black or African	6/ 56 (10.7)	6/ 61 (9.8)	1.20 (0.41, 3.49) 0.7386	1.08 (0.32, 3.66) 0.9054	0.01 (-0.10, 0.12)*0.8759	
Asian	79/ 528 (15.0)	93/ 525 (17.7)	0.81 (0.62, 1.06) 0.1189	0.77 (0.55, 1.07) 0.1225	-0.03 (-0.07, 0.02)*0.2269	
Other	13/ 160 (8.1)	12/ 142 (8.5)	0.96 (0.45, 2.04)*0.9183	1.01 (0.42, 2.46) 0.9742	-0.00 (-0.07, 0.06)*0.9184	
Geographic region						0.2361*
Asia	77/ 517 (14.9)	88/ 509 (17.3)	0.83 (0.63, 1.08) 0.1633	0.79 (0.56, 1.11) 0.1728	-0.02 (-0.07, 0.02)*0.2964	
Europe and Saudi Arabia	155/1164 (13.3)	196/1221 (16.1)	0.83 (0.68, 1.01)*0.0600	0.79 (0.62, 1.00) 0.0533	-0.03 (-0.06, 0.00)*0.0587	
North America	71/ 336 (21.1)	58/ 331 (17.5)	1.18 (0.88, 1.58) 0.2765	1.28 (0.86, 1.92) 0.2254	0.04 (-0.02, 0.10)*0.2374	
Latin America	49/ 481 (10.2)	57/ 475 (12.0)	0.88 (0.62, 1.24) 0.4619	0.87 (0.57, 1.32) 0.5047	-0.02 (-0.06, 0.02)*0.3721	
NYHA class at enrolment						0.9235*
II	278/1886 (14.7)	322/1970 (16.3)	0.91 (0.79, 1.04) 0.1616	0.86 (0.72, 1.04) 0.1168	-0.02 (-0.04, 0.01)*0.1688	
III or IV	74/ 612 (12.1)	77/ 565 (13.6)	0.89 (0.66, 1.20)*0.4311	0.84 (0.58, 1.20) 0.3313	-0.02 (-0.05, 0.02)*0.4317	
LVEF at enrolment						0.3623
<= 49	109/ 853 (12.8)	113/ 858 (13.2)	0.97 (0.76, 1.24)*0.8095	0.92 (0.68, 1.23) 0.5626	-0.00 (-0.04, 0.03)*0.8095	
50-59	125/ 899 (13.9)	156/ 919 (17.0)	0.80 (0.66, 0.98) 0.0316	0.74 (0.56, 0.97) 0.0280	-0.03 (-0.06, 0.00)*0.0697	
>= 60	118/ 746 (15.8)	130/ 759 (17.1)	0.96 (0.78, 1.19) 0.7343	0.97 (0.73, 1.29) 0.8136	-0.01 (-0.05, 0.02)*0.4932	
NT-proBNP at enrolment						0.8104
<= median	180/1256 (14.3)	208/1292 (16.1)	0.89 (0.75, 1.06) 0.1886	0.86 (0.69, 1.08) 0.1866	-0.02 (-0.05, 0.01)*0.2139	
> median	172/1242 (13.8)	191/1243 (15.4)	0.90 (0.74, 1.09)*0.2846	0.87 (0.68, 1.10) 0.2334	-0.02 (-0.04, 0.01)*0.2841	
Type 2 Diabetes Medical History						0.4697
Yes	154/1081 (14.2)	190/1116 (17.0)	0.86 (0.72, 1.03) 0.1110	0.81 (0.64, 1.02)*0.0735	-0.03 (-0.06, 0.00)*0.0726	
No	198/1417 (14.0)	209/1420 (14.7)	0.94 (0.80, 1.12) 0.5124	0.94 (0.76, 1.16)*0.5714	-0.01 (-0.03, 0.02)*0.5713	
Atrial fibrillation or flutter at enrolment ECG						0.6772
Yes	151/1062 (14.2)	172/1076 (16.0)	0.88 (0.73, 1.06) 0.1667	0.82 (0.64, 1.05) 0.1160	-0.02 (-0.05, 0.01)*0.2538	
No	201/1436 (14.0)	227/1460 (15.5)	0.92 (0.78, 1.09) 0.3422	0.90 (0.72, 1.11) 0.3135	-0.02 (-0.04, 0.01)*0.2394	
BMI (kg/m2) at enrolment						0.3677
< 30	190/1399 (13.6)	225/1395 (16.1)	0.86 (0.73, 1.02) 0.0856	0.81 (0.65, 1.01) 0.0580	-0.03 (-0.05, 0.00)*0.0582	
>= 30	162/1099 (14.7)	173/1138 (15.2)	0.97 (0.81, 1.16) 0.7475	0.94 (0.74, 1.20) 0.6324	-0.00 (-0.03, 0.02)*0.7597	
Baseline eGFR (mL/min/1.73m^2)						0.1020
< 60	201/1178 (17.1)	209/1225 (17.1)	0.99 (0.85, 1.17) 0.9465	0.97 (0.78, 1.22) 0.8261	0.00 (-0.03, 0.03)*0.9992	
>= 60	151/1320 (11.4)	190/1310 (14.5)	0.81 (0.67, 0.98) 0.0271	0.76 (0.60, 0.96) 0.0207	-0.03 (-0.06, -0.00)*0.0193	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with >=15% deterioration in EQ-5D VAS at study end (LOCF) including study closure visits
Full Analysis Set

Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SBP at randomisation						0.3629
<= median	171/1243 (13.8)	217/1292 (16.8)	0.85 (0.72, 1.02) 0.0762	0.79 (0.63, 1.00) 0.0468	-0.03 (-0.06, -0.00)*0.0332	
> median	181/1255 (14.4)	182/1244 (14.6)	0.96 (0.80, 1.15) 0.6395	0.94 (0.75, 1.19) 0.6235	-0.00 (-0.03, 0.03)*0.8828	
LVEF at enrolment 2						0.5502
<= 49	109/ 853 (12.8)	113/ 858 (13.2)	0.97 (0.76, 1.24)*0.8095	0.92 (0.68, 1.23) 0.5626	-0.00 (-0.04, 0.03)*0.8095	
>= 50	243/1645 (14.8)	286/1678 (17.0)	0.88 (0.76, 1.02) 0.0933	0.84 (0.69, 1.02) 0.0865	-0.02 (-0.05, 0.00)*0.0732	
Randomised during hospitalisation for HF or within 30 days of discharge						0.1855
Yes	34/ 232 (14.7)	28/ 247 (11.3)	1.29 (0.81, 2.06)*0.2811	1.10 (0.61, 1.97) 0.7517	0.03 (-0.03, 0.09)*0.2805	
No	318/2266 (14.0)	371/2289 (16.2)	0.88 (0.77, 1.00) 0.0546	0.84 (0.71, 1.00) 0.0449	-0.02 (-0.04, -0.00)*0.0404	
MRAs at baseline						0.1571
Yes	147/1077 (13.6)	181/1080 (16.8)	0.81 (0.67, 1.00)*0.0449	0.74 (0.57, 0.94) 0.0158	-0.03 (-0.06, -0.00)*0.0441	
No	205/1421 (14.4)	218/1456 (15.0)	0.98 (0.83, 1.15) 0.7784	0.97 (0.78, 1.21) 0.8017	-0.01 (-0.03, 0.02)*0.6792	
ACEi+ARB at baseline						0.2463
Yes	246/1827 (13.5)	289/1856 (15.6)	0.86 (0.75, 1.00) 0.0490	0.81 (0.67, 0.98) 0.0329	-0.02 (-0.04, 0.00)*0.0694	
No	106/ 671 (15.8)	110/ 680 (16.2)	1.02 (0.81, 1.28) 0.8784	1.01 (0.74, 1.37) 0.9525	-0.00 (-0.04, 0.04)*0.8492	
ARNI at baseline						0.9078
Yes	12/ 130 (9.2)	12/ 108 (11.1)	0.83 (0.39, 1.77)*0.6318	0.98 (0.40, 2.37) 0.9616	-0.02 (-0.10, 0.06)*0.6339	
No	340/2368 (14.4)	387/2428 (15.9)	0.91 (0.80, 1.03) 0.1336	0.87 (0.73, 1.02) 0.0880	-0.02 (-0.04, 0.00)*0.1266	
Beta Blocker at baseline						0.7832
Yes	285/2076 (13.7)	333/2132 (15.6)	0.90 (0.78, 1.03) 0.1177	0.86 (0.72, 1.02) 0.0875	-0.02 (-0.04, 0.00)*0.0829	
No	67/ 422 (15.9)	66/ 404 (16.3)	0.95 (0.71, 1.27) 0.7204	0.91 (0.61, 1.34) 0.6230	-0.00 (-0.05, 0.05)*0.8574	
Diuretics at baseline						0.3701
Yes	320/2228 (14.4)	353/2250 (15.7)	0.92 (0.81, 1.05) 0.2091	0.89 (0.75, 1.05) 0.1725	-0.01 (-0.03, 0.01)*0.2142	
No	32/ 270 (11.9)	46/ 286 (16.1)	0.74 (0.48, 1.12)*0.1536	0.69 (0.41, 1.14) 0.1498	-0.04 (-0.10, 0.02)*0.1487	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of completion rates of PGIS Overall Status by visit
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) n/ N#	Dapa 10 mg (N=3131) Compliance	Placebo (N=3132) n/ N#	Placebo (N=3132) Compliance
PGI01-Severity	Visit 2 (Baseline)	2905/3131	92.78%	2899/3132	92.56%
	Visit 3 (1 Month)	2680/3130	85.62%	2686/3128	85.87%
	Visit 4 (4 Months)	2457/3087	79.59%	2435/3087	78.88%
	Visit 5 (8 Months)	2242/3030	73.99%	2246/3032	74.08%
	Study Closure Visit	2161/2621	82.45%	2157/2599	82.99%

N# is the number of patients, who have not died at time of beginning of PRO visit window.

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients without worsening of PGIS Overall Status at month 8 (LOCF)
Full Analysis Set

Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	2234/2802 (79.7)	2166/2811 (77.1)	1.03 (1.01, 1.06)*0.0150	1.17 (1.02, 1.35) 0.0251	0.03 (0.01, 0.05)*0.0149	
Age						0.5322*
<= median	1123/1392 (80.7)	1158/1474 (78.6)	1.03 (0.99, 1.07)*0.1601	1.14 (0.93, 1.39) 0.1977	0.02 (-0.01, 0.05)*0.1600	
> median	1111/1410 (78.8)	1008/1337 (75.4)	1.05 (1.00, 1.09)*0.0343	1.21 (1.00, 1.47) 0.0558	0.03 (0.00, 0.07)*0.0339	
Gender						0.8417*
Male	1320/1630 (81.0)	1259/1612 (78.1)	1.04 (1.00, 1.07)*0.0423	1.19 (0.99, 1.43) 0.0605	0.03 (0.00, 0.06)*0.0420	
Female	914/1172 (78.0)	907/1199 (75.6)	1.03 (0.99, 1.08)*0.1771	1.14 (0.92, 1.41) 0.2364	0.02 (-0.01, 0.06)*0.1768	
Race						0.8729*
White	1580/2006 (78.8)	1557/2038 (76.4)	1.03 (1.00, 1.07)*0.0714	1.12 (0.95, 1.31) 0.1906	0.02 (-0.00, 0.05)*0.0712	
Black or African	51/ 65 (78.5)	55/ 70 (78.6)	1.00 (0.84, 1.19)*0.9876	1.02 (0.40, 2.61) 0.9750	-0.00 (-0.14, 0.14)*0.9876	
Asian	446/ 555 (80.4)	427/ 551 (77.5)	1.04 (0.98, 1.10)*0.2432	1.25 (0.92, 1.69) 0.1528	0.03 (-0.02, 0.08)*0.2425	
Other	157/ 176 (89.2)	127/ 152 (83.6)	1.07 (0.98, 1.17)*0.1416	1.62 (0.81, 3.23) 0.1707	0.06 (-0.02, 0.13)*0.1379	
Geographic region						0.9637*
Asia	429/ 536 (80.0)	416/ 536 (77.6)	1.03 (0.97, 1.10)*0.3314	1.21 (0.88, 1.64) 0.2365	0.02 (-0.02, 0.07)*0.3309	
Europe and Saudi Arabia	1046/1341 (78.0)	1047/1381 (75.8)	1.03 (0.99, 1.07)*0.1758	1.10 (0.90, 1.35) 0.3287	0.02 (-0.01, 0.05)*0.1756	
North America	309/ 394 (78.4)	288/ 381 (75.6)	1.04 (0.96, 1.12)*0.3489	1.15 (0.81, 1.64) 0.4231	0.03 (-0.03, 0.09)*0.3482	
Latin America	450/ 531 (84.7)	415/ 513 (80.9)	1.05 (0.99, 1.11)*0.1001	1.29 (0.90, 1.85) 0.1684	0.04 (-0.01, 0.08)*0.0991	
NYHA class at enrolment						0.8908*
II	1652/2083 (79.3)	1665/2169 (76.8)	1.03 (1.00, 1.07)*0.0450	1.17 (1.00, 1.37) 0.0459	0.03 (0.00, 0.05)*0.0449	
III or IV	582/ 719 (80.9)	500/ 641 (78.0)	1.04 (0.98, 1.10)*0.1813	1.26 (0.93, 1.72) 0.1379	0.03 (-0.01, 0.07)*0.1802	
LVEF at enrolment						0.3021*
<= 49	768/ 958 (80.2)	751/ 951 (79.0)	1.02 (0.97, 1.06)*0.5165	1.06 (0.83, 1.36) 0.6273	0.01 (-0.02, 0.05)*0.5164	
50-59	799/1017 (78.6)	776/1013 (76.6)	1.03 (0.98, 1.07)*0.2898	1.16 (0.92, 1.45) 0.2011	0.02 (-0.02, 0.06)*0.2895	
>= 60	667/ 827 (80.7)	639/ 847 (75.4)	1.07 (1.02, 1.12)*0.0101	1.32 (1.03, 1.70) 0.0303	0.05 (0.01, 0.09)*0.0098	
NT-proBNP at enrolment						0.1404*
<= median	1113/1398 (79.6)	1110/1413 (78.6)	1.01 (0.98, 1.05)*0.4907	1.05 (0.86, 1.28) 0.6473	0.01 (-0.02, 0.04)*0.4906	
> median	1121/1404 (79.8)	1056/1397 (75.6)	1.06 (1.02, 1.10)*0.0069	1.30 (1.07, 1.58) 0.0077	0.04 (0.01, 0.07)*0.0068	
Type 2 Diabetes Medical History						0.0039*
Yes	1006/1233 (81.6)	938/1245 (75.3)	1.08 (1.04, 1.13)*0.0002	1.45 (1.20, 1.76)*0.0002	0.06 (0.03, 0.09)*0.0001	
No	1228/1569 (78.3)	1228/1566 (78.4)	1.00 (0.96, 1.04)*0.9188	0.99 (0.84, 1.17)*0.9188	-0.00 (-0.03, 0.03)*0.9188	
Atrial fibrillation or flutter at enrolment ECG						0.2043*
Yes	930/1183 (78.6)	924/1191 (77.6)	1.01 (0.97, 1.06)*0.5433	1.12 (0.91, 1.39) 0.2871	0.01 (-0.02, 0.04)*0.5433	
No	1304/1619 (80.5)	1242/1620 (76.7)	1.05 (1.01, 1.09)*0.0072	1.22 (1.01, 1.46) 0.0367	0.04 (0.01, 0.07)*0.0071	
BMI (kg/m2) at enrolment						0.0181*
< 30	1260/1548 (81.4)	1181/1547 (76.3)	1.07 (1.03, 1.11)*0.0006	1.33 (1.10, 1.61) 0.0029	0.05 (0.02, 0.08)*0.0006	
>= 30	973/1253 (77.7)	982/1261 (77.9)	1.00 (0.96, 1.04)*0.8940	1.01 (0.83, 1.25) 0.8876	-0.00 (-0.03, 0.03)*0.8940	
Baseline eGFR (mL/min/1.73m^2)						0.4308*
< 60	1048/1340 (78.2)	1033/1382 (74.7)	1.05 (1.00, 1.09)*0.0333	1.20 (0.99, 1.45) 0.0644	0.03 (0.00, 0.07)*0.0330	
>= 60	1186/1462 (81.1)	1132/1428 (79.3)	1.02 (0.99, 1.06)*0.2124	1.14 (0.93, 1.39) 0.2029	0.02 (-0.01, 0.05)*0.2121	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients without worsening of PGIS Overall Status at month 8 (LOCF)
Full Analysis Set

Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SBP at randomisation						0.3537*
<= median	1127/1406 (80.2)	1089/1424 (76.5)	1.05 (1.01, 1.09)*0.0176	1.18 (0.97, 1.43) 0.0992	0.04 (0.01, 0.07)*0.0174	
> median	1107/1396 (79.3)	1077/1387 (77.6)	1.02 (0.98, 1.06)*0.2903	1.16 (0.96, 1.42) 0.1306	0.02 (-0.01, 0.05)*0.2900	
LVEF at enrolment 2						0.3191*
<= 49	768/ 958 (80.2)	751/ 951 (79.0)	1.02 (0.97, 1.06)*0.5165	1.06 (0.83, 1.36) 0.6273	0.01 (-0.02, 0.05)*0.5164	
>= 50	1466/1844 (79.5)	1415/1860 (76.1)	1.05 (1.01, 1.08)*0.0122	1.23 (1.04, 1.45) 0.0168	0.03 (0.01, 0.06)*0.0121	
Randomised during hospitalisation for HF or within 30 days of discharge						0.2467*
Yes	239/ 281 (85.1)	221/ 281 (78.6)	1.08 (1.00, 1.17)*0.0497	1.67 (1.01, 2.76) 0.0465	0.06 (0.00, 0.13)*0.0481	
No	1995/2521 (79.1)	1945/2530 (76.9)	1.03 (1.00, 1.06)*0.0528	1.14 (0.98, 1.31) 0.0822	0.02 (-0.00, 0.05)*0.0527	
MRAs at baseline						0.8340*
Yes	970/1216 (79.8)	932/1213 (76.8)	1.04 (1.00, 1.08)*0.0795	1.15 (0.93, 1.42) 0.1983	0.03 (-0.00, 0.06)*0.0791	
No	1264/1586 (79.7)	1234/1598 (77.2)	1.03 (1.00, 1.07)*0.0894	1.19 (0.99, 1.43) 0.0674	0.02 (-0.00, 0.05)*0.0891	
ACEi+ARB at baseline						0.4225*
Yes	1625/2038 (79.7)	1576/2059 (76.5)	1.04 (1.01, 1.08)*0.0135	1.22 (1.04, 1.43) 0.0174	0.03 (0.01, 0.06)*0.0133	
No	609/ 764 (79.7)	590/ 752 (78.5)	1.02 (0.96, 1.07)*0.5483	1.05 (0.81, 1.37) 0.7097	0.01 (-0.03, 0.05)*0.5481	
ARNI at baseline						0.4406*
Yes	117/ 149 (78.5)	101/ 127 (79.5)	0.99 (0.87, 1.12)*0.8380	0.77 (0.40, 1.48) 0.4351	-0.01 (-0.11, 0.09)*0.8381	
No	2117/2653 (79.8)	2065/2684 (76.9)	1.04 (1.01, 1.07)*0.0112	1.19 (1.04, 1.38) 0.0147	0.03 (0.01, 0.05)*0.0111	
Beta Blocker at baseline						0.7219*
Yes	1853/2327 (79.6)	1793/2335 (76.8)	1.04 (1.01, 1.07)*0.0188	1.17 (1.00, 1.36) 0.0480	0.03 (0.00, 0.05)*0.0187	
No	381/ 475 (80.2)	373/ 476 (78.4)	1.02 (0.96, 1.09)*0.4818	1.20 (0.85, 1.68) 0.3015	0.02 (-0.03, 0.07)*0.4816	
Diuretics at baseline						0.2166*
Yes	1991/2500 (79.6)	1943/2509 (77.4)	1.03 (1.00, 1.06)*0.0581	1.14 (0.99, 1.32) 0.0778	0.02 (-0.00, 0.04)*0.0580	
No	243/ 302 (80.5)	223/ 302 (73.8)	1.09 (1.00, 1.19)*0.0534	1.44 (0.95, 2.18) 0.0847	0.07 (-0.00, 0.13)*0.0519	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients without worsening of PGIS Overall Status at study end (LOCF) including study closure visits
Full Analysis Set

Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	2154/2842 (75.8)	2088/2841 (73.5)	1.03 (1.00, 1.06)*0.0467	1.13 (0.99, 1.29) 0.0740	0.02 (0.00, 0.05)*0.0466	
Age						0.4050*
<= median	1098/1413 (77.7)	1131/1485 (76.2)	1.02 (0.98, 1.06)*0.3234	1.09 (0.90, 1.32) 0.3825	0.02 (-0.02, 0.05)*0.3234	
> median	1056/1429 (73.9)	957/1356 (70.6)	1.05 (1.00, 1.10)*0.0508	1.18 (0.98, 1.41) 0.0800	0.03 (-0.00, 0.07)*0.0503	
Gender						0.3848*
Male	1273/1656 (76.9)	1200/1628 (73.7)	1.04 (1.00, 1.08)*0.0359	1.19 (1.00, 1.41) 0.0496	0.03 (0.00, 0.06)*0.0356	
Female	881/1186 (74.3)	888/1213 (73.2)	1.01 (0.97, 1.06)*0.5491	1.04 (0.85, 1.28) 0.7097	0.01 (-0.02, 0.05)*0.5491	
Race						0.9670*
White	1520/2038 (74.6)	1488/2062 (72.2)	1.03 (1.00, 1.07)*0.0797	1.11 (0.95, 1.29) 0.2086	0.02 (-0.00, 0.05)*0.0795	
Black or African	49/ 68 (72.1)	51/ 71 (71.8)	1.00 (0.82, 1.23)*0.9762	1.00 (0.42, 2.38) 0.9945	0.00 (-0.15, 0.15)*0.9762	
Asian	432/ 558 (77.4)	419/ 555 (75.5)	1.03 (0.96, 1.09)*0.4496	1.17 (0.87, 1.56) 0.3002	0.02 (-0.03, 0.07)*0.4493	
Other	153/ 178 (86.0)	130/ 153 (85.0)	1.01 (0.93, 1.11)*0.7997	1.10 (0.56, 2.15) 0.7886	0.01 (-0.07, 0.09)*0.7995	
Geographic region						0.4135*
Asia	417/ 539 (77.4)	408/ 538 (75.8)	1.02 (0.95, 1.09)*0.5535	1.13 (0.84, 1.52) 0.4211	0.02 (-0.04, 0.07)*0.5534	
Europe and Saudi Arabia	1010/1365 (74.0)	975/1394 (69.9)	1.06 (1.01, 1.11)*0.0180	1.24 (1.02, 1.51) 0.0277	0.04 (0.01, 0.07)*0.0177	
North America	289/ 398 (72.6)	284/ 390 (72.8)	1.00 (0.92, 1.09)*0.9479	0.96 (0.69, 1.33) 0.7956	-0.00 (-0.06, 0.06)*0.9479	
Latin America	438/ 540 (81.1)	421/ 519 (81.1)	1.00 (0.94, 1.06)*0.9979	0.93 (0.66, 1.32) 0.6985	-0.00 (-0.05, 0.05)*0.9979	
NYHA class at enrolment						0.8638*
II	1588/2113 (75.2)	1595/2190 (72.8)	1.03 (1.00, 1.07)*0.0824	1.14 (0.98, 1.32) 0.0822	0.02 (-0.00, 0.05)*0.0823	
III or IV	566/ 729 (77.6)	492/ 650 (75.7)	1.03 (0.97, 1.09)*0.3940	1.15 (0.86, 1.54) 0.3517	0.02 (-0.03, 0.06)*0.3934	
LVEF at enrolment						0.7719*
<= 49	755/ 978 (77.2)	729/ 963 (75.7)	1.02 (0.97, 1.07)*0.4371	1.09 (0.86, 1.38) 0.4689	0.01 (-0.02, 0.05)*0.4369	
50-59	758/1029 (73.7)	731/1021 (71.6)	1.03 (0.98, 1.09)*0.2941	1.15 (0.93, 1.42) 0.2023	0.02 (-0.02, 0.06)*0.2938	
>= 60	641/ 835 (76.8)	628/ 857 (73.3)	1.05 (0.99, 1.11)*0.0976	1.15 (0.91, 1.47) 0.2491	0.03 (-0.01, 0.08)*0.0972	
NT-proBNP at enrolment						0.0563*
<= median	1061/1420 (74.7)	1063/1424 (74.6)	1.00 (0.96, 1.04)*0.9660	0.98 (0.81, 1.17) 0.7903	0.00 (-0.03, 0.03)*0.9660	
> median	1093/1422 (76.9)	1025/1416 (72.4)	1.06 (1.02, 1.11)*0.0062	1.30 (1.08, 1.57) 0.0056	0.04 (0.01, 0.08)*0.0061	
Type 2 Diabetes Medical History						0.5809*
Yes	966/1251 (77.2)	936/1262 (74.2)	1.04 (1.00, 1.09)*0.0748	1.18 (0.98, 1.42)*0.0749	0.03 (-0.00, 0.06)*0.0745	
No	1188/1591 (74.7)	1152/1579 (73.0)	1.02 (0.98, 1.07)*0.2730	1.09 (0.93, 1.28)*0.2729	0.02 (-0.01, 0.05)*0.2728	
Atrial fibrillation or flutter at enrolment ECG						0.3615*
Yes	899/1197 (75.1)	890/1202 (74.0)	1.01 (0.97, 1.06)*0.5507	1.12 (0.91, 1.37) 0.2711	0.01 (-0.02, 0.05)*0.5506	
No	1255/1645 (76.3)	1198/1639 (73.1)	1.04 (1.00, 1.09)*0.0352	1.14 (0.96, 1.35) 0.1463	0.03 (0.00, 0.06)*0.0349	
BMI (kg/m2) at enrolment						0.0367*
< 30	1218/1571 (77.5)	1142/1564 (73.0)	1.06 (1.02, 1.11)*0.0035	1.25 (1.05, 1.49) 0.0139	0.05 (0.01, 0.08)*0.0034	
>= 30	935/1270 (73.6)	943/1274 (74.0)	0.99 (0.95, 1.04)*0.8199	1.00 (0.82, 1.22) 0.9748	-0.00 (-0.04, 0.03)*0.8199	
Baseline eGFR (mL/min/1.73m^2)						0.9516*
< 60	1006/1360 (74.0)	1005/1399 (71.8)	1.03 (0.98, 1.08)*0.2074	1.10 (0.91, 1.32) 0.3177	0.02 (-0.01, 0.05)*0.2072	
>= 60	1148/1482 (77.5)	1082/1441 (75.1)	1.03 (0.99, 1.07)*0.1314	1.16 (0.96, 1.40) 0.1219	0.02 (-0.01, 0.05)*0.1310	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients without worsening of PGIS Overall Status at study end (LOCF) including study closure visits
Full Analysis Set

Subgroup Level	_Dapa 10 mg (N=3131)__ n/ N (%)	___Placebo (N=3132)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SBP at randomisation						0.5997*
<= median	1081/1424 (75.9)	1053/1442 (73.0)	1.04 (1.00, 1.09)*0.0762	1.10 (0.92, 1.32) 0.3035	0.03 (-0.00, 0.06)*0.0759	
> median	1073/1418 (75.7)	1035/1399 (74.0)	1.02 (0.98, 1.07)*0.3020	1.16 (0.96, 1.40) 0.1274	0.02 (-0.02, 0.05)*0.3018	
LVEF at enrolment 2						0.5961*
<= 49	755/ 978 (77.2)	729/ 963 (75.7)	1.02 (0.97, 1.07)*0.4371	1.09 (0.86, 1.38) 0.4689	0.01 (-0.02, 0.05)*0.4369	
>= 50	1399/1864 (75.1)	1359/1878 (72.4)	1.04 (1.00, 1.08)*0.0618	1.15 (0.98, 1.34) 0.0939	0.03 (-0.00, 0.06)*0.0615	
Randomised during hospitalisation for HF or within 30 days of discharge						0.5449*
Yes	230/ 284 (81.0)	219/ 286 (76.6)	1.06 (0.97, 1.15)*0.1983	1.39 (0.87, 2.22) 0.1673	0.04 (-0.02, 0.11)*0.1969	
No	1924/2558 (75.2)	1869/2555 (73.2)	1.03 (1.00, 1.06)*0.0918	1.11 (0.97, 1.27) 0.1439	0.02 (-0.00, 0.04)*0.0916	
MRAs at baseline						0.5049*
Yes	935/1226 (76.3)	896/1226 (73.1)	1.04 (1.00, 1.09)*0.0703	1.15 (0.94, 1.41) 0.1676	0.03 (-0.00, 0.07)*0.0699	
No	1219/1616 (75.4)	1192/1615 (73.8)	1.02 (0.98, 1.06)*0.2886	1.11 (0.93, 1.32) 0.2516	0.02 (-0.01, 0.05)*0.2885	
ACEi+ARB at baseline						0.2821*
Yes	1573/2066 (76.1)	1518/2077 (73.1)	1.04 (1.01, 1.08)*0.0241	1.19 (1.02, 1.39) 0.0291	0.03 (0.00, 0.06)*0.0240	
No	581/ 776 (74.9)	570/ 764 (74.6)	1.00 (0.95, 1.06)*0.9052	0.99 (0.77, 1.26) 0.9233	0.00 (-0.04, 0.05)*0.9052	
ARNI at baseline						0.4058*
Yes	114/ 153 (74.5)	97/ 127 (76.4)	0.98 (0.85, 1.12)*0.7171	0.79 (0.43, 1.45) 0.4469	-0.02 (-0.12, 0.08)*0.7173	
No	2040/2689 (75.9)	1991/2714 (73.4)	1.03 (1.00, 1.07)*0.0345	1.15 (1.00, 1.32) 0.0432	0.03 (0.00, 0.05)*0.0344	
Beta Blocker at baseline						0.5114*
Yes	1777/2360 (75.3)	1731/2360 (73.3)	1.03 (0.99, 1.06)*0.1255	1.08 (0.94, 1.25) 0.2753	0.02 (-0.01, 0.04)*0.1253	
No	377/ 482 (78.2)	357/ 481 (74.2)	1.05 (0.98, 1.13)*0.1459	1.34 (0.97, 1.84) 0.0722	0.04 (-0.01, 0.09)*0.1449	
Diuretics at baseline						0.4944*
Yes	1914/2536 (75.5)	1862/2535 (73.5)	1.03 (0.99, 1.06)*0.0989	1.11 (0.97, 1.28) 0.1264	0.02 (-0.00, 0.04)*0.0987	
No	240/ 306 (78.4)	226/ 306 (73.9)	1.06 (0.97, 1.16)*0.1849	1.25 (0.84, 1.87) 0.2726	0.05 (-0.02, 0.11)*0.1836	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, baseline value, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Estimates marked with * were calculated using unadjusted analyses with normal approximation (Wald).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of weight by visit
Full Analysis Set

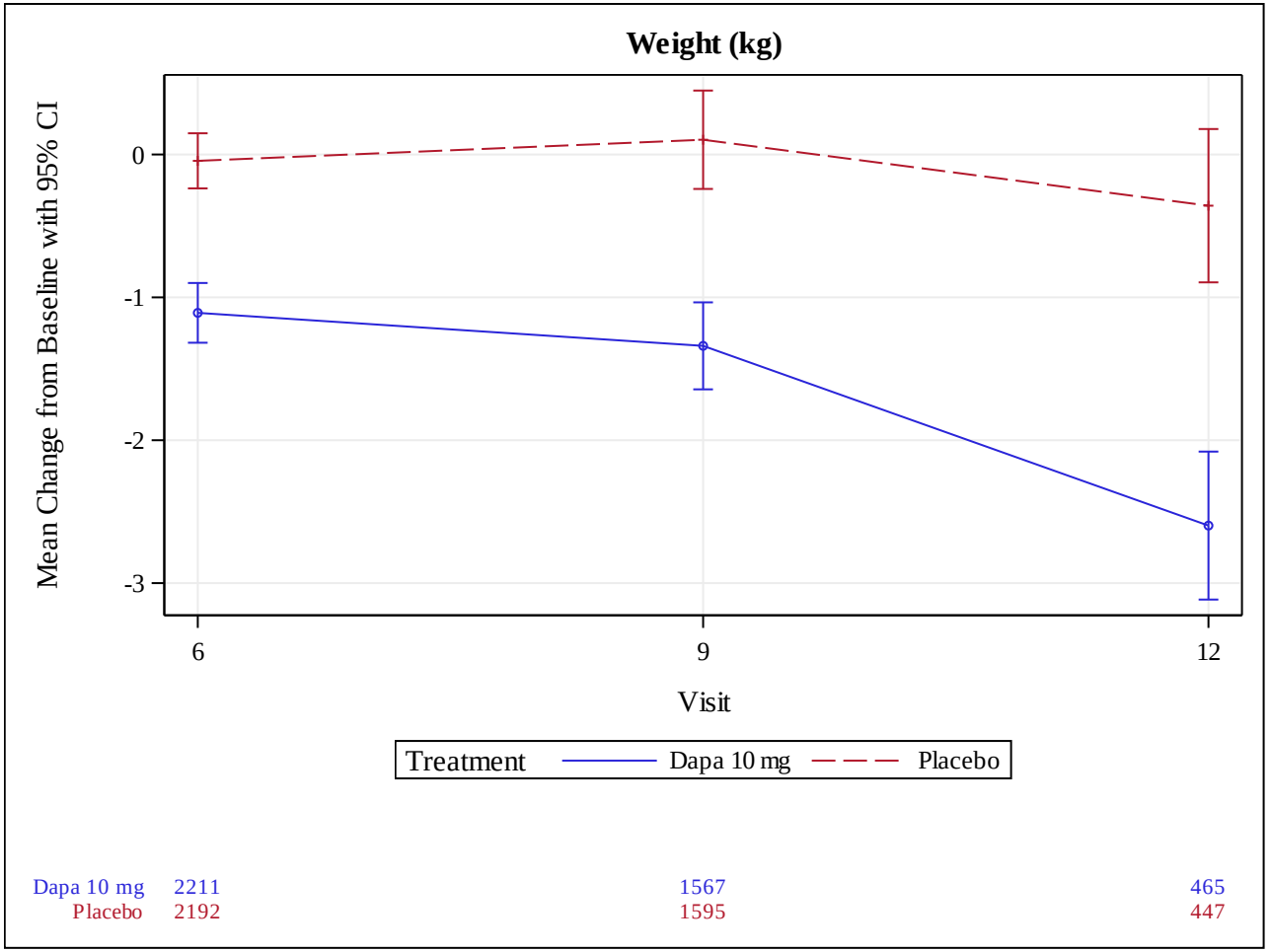
		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Weight (kg)	Visit 2 (Baseline)	3129	81.76 (20.33)			3131	81.56 (20.16)		
	Visit 6 (12 Months)	2211	79.78 (19.96)	2211	-1.11 (5.02)	2193	80.97 (20.27)	2192	-0.04 (4.61)
	Visit 9 (24 Months)	1567	81.02 (20.40)	1567	-1.34 (6.15)	1596	82.41 (21.10)	1595	0.10 (7.01)
	Visit 12 (36 Months)	465	78.39 (21.01)	465	-2.60 (5.70)	447	80.39 (20.74)	447	-0.36 (5.79)

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of weight
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Weight (kg)	Visit 6 (12 Months)		-1.11 (0.10)		-0.04 (0.10)	-1.07 (-1.34,-0.79)	<.0001	-0.23 (-0.29,-0.17)
	Visit 9 (24 Months)		-1.38 (0.16)		-0.04 (0.16)	-1.34 (-1.78,-0.90)	<.0001	-0.21 (-0.28,-0.14)
	Visit 12 (36 Months)		-2.07 (0.23)		-0.63 (0.23)	-1.45 (-2.08,-0.82)	<.0001	-0.30 (-0.43,-0.17)
	OVERALL	2466	-1.52 (0.13)	2464	-0.24 (0.13)	-1.28 (-1.64,-0.92)	<.0001	-0.20 (-0.26,-0.14)

N displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
OVERALL row displays model estimates over time.
LS Means and difference of LS Means estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of weight
Full Analysis Set



AstraZeneca
Protocol: D169CC00001
Overall study population
Summary of mean values and change from baseline of systolic blood pressure by visit
Full Analysis Set

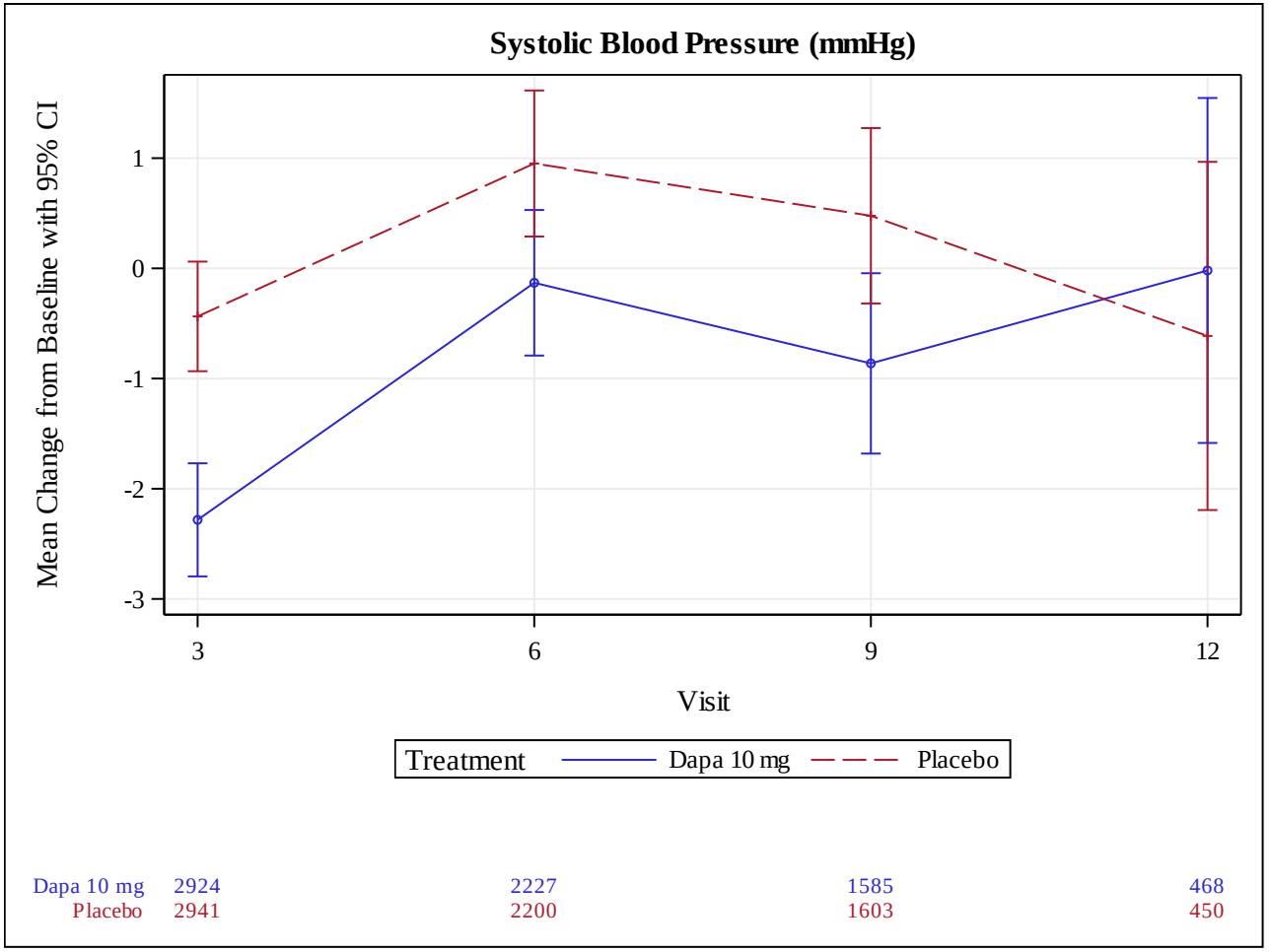
		Dapa 10 mg (N=3131)				Placebo (N=3132)			
		Value at Visit		Change from Baseline		Value at Visit		Change from Baseline	
	Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Systolic Blood Pressure (mmHg)	Visit 2 (Baseline)	3131	128.23 (15.42)			3132	128.23 (15.27)		
	Visit 3 (1 Month)	2924	126.02 (16.25)	2924	-2.28 (14.16)	2941	127.70 (16.33)	2941	-0.44 (13.76)
	Visit 6 (12 Months)	2227	127.96 (16.63)	2227	-0.13 (15.90)	2200	128.89 (17.02)	2200	0.95 (15.86)
	Visit 9 (24 Months)	1585	127.96 (16.20)	1585	-0.86 (16.62)	1603	130.19 (15.97)	1603	0.48 (16.25)
	Visit 12 (36 Months)	468	129.37 (17.72)	468	-0.02 (17.27)	450	130.27 (17.59)	450	-0.61 (17.10)

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of change from baseline of systolic blood pressure
Full Analysis Set

	Visit	Dapa 10 mg (N=3131) N	Dapa 10 mg (N=3131) LSMean (SE)	Placebo (N=3132) N	Placebo (N=3132) LSMean (SE)	Difference of LSMeans (95% CI)	p-Value	Hedge`s g (95% CI)
Systolic Blood Pressure (mmHg)	Visit 3 (1 Month)		-2.33 (0.24)		-0.58 (0.24)	-1.75 (-2.41,-1.09)	<.0001	-0.14 (-0.19,-0.08)
	Visit 6 (12 Months)		-0.20 (0.30)		0.84 (0.30)	-1.04 (-1.88,-0.20)	0.0147	-0.07 (-0.13,-0.01)
	Visit 9 (24 Months)		-0.80 (0.35)		0.51 (0.35)	-1.32 (-2.29,-0.35)	0.0077	-0.09 (-0.16,-0.02)
	Visit 12 (36 Months)		-0.01 (0.64)		0.34 (0.65)	-0.35 (-2.13, 1.43)	0.6992	-0.03 (-0.15, 0.10)
	OVERALL	3036	-0.84 (0.25)	3037	0.28 (0.26)	-1.12 (-1.82,-0.41)	0.0021	-0.08 (-0.13,-0.03)

N displays the number of subjects included in the regression model, e.g. all patients with non-missing values at baseline and at least one timepoint after baseline.
OVERALL row displays model estimates over time.
LS Means and difference of LS Means estimated from repeated measures model (MMRM) with terms for treatment group, baseline measurement, visit and visit by treatment group interaction.

AstraZeneca
Protocol: D169CC00001
Overall study population
Summary Plot of change from baseline of systolic blood pressure
Full Analysis Set



AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Event
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	2072/3126 (66.3)	2199/3127 (70.3)	0.94 (0.91, 0.97) 0.0003	0.83 (0.75, 0.92) 0.0006	-0.04 (-0.06, -0.02) 0.0004	
Age						0.6938
<= median	990/1544 (64.1)	1097/1602 (68.5)	0.93 (0.88, 0.98) 0.0044	0.82 (0.71, 0.95) 0.0095	-0.05 (-0.08, -0.01) 0.0064	
> median	1082/1582 (68.4)	1102/1525 (72.3)	0.95 (0.90, 0.99) 0.0162	0.83 (0.71, 0.97) 0.0182	-0.04 (-0.07, -0.01) 0.0168	
Gender						0.0233
Male	1170/1765 (66.3)	1269/1744 (72.8)	0.91 (0.87, 0.95) <.0001	0.73 (0.64, 0.85) <.0001	-0.07 (-0.10, -0.04) <.0001	
Female	902/1361 (66.3)	930/1383 (67.2)	0.98 (0.93, 1.04) 0.5564	0.96 (0.82, 1.12) 0.5963	-0.01 (-0.05, 0.03) 0.5762	
Race						0.2982
White	1468/2210 (66.4)	1568/2222 (70.6)	0.94 (0.90, 0.98) 0.0018	0.83 (0.73, 0.94) 0.0030	-0.04 (-0.07, -0.02) 0.0022	
Black or African	61/ 81 (75.3)	70/ 78 (89.7)	0.84 (0.73, 0.97) 0.0203	0.34 (0.14, 0.83) 0.0181	-0.14 (-0.26, -0.03) 0.0153	
Asian	416/ 629 (66.1)	451/ 643 (70.1)	0.94 (0.87, 1.01) 0.1144	0.83 (0.65, 1.05) 0.1214	-0.04 (-0.09, 0.01) 0.1169	
Other	127/ 206 (61.7)	110/ 184 (59.8)	1.03 (0.88, 1.21) 0.6703	1.11 (0.74, 1.67) 0.6200	0.02 (-0.07, 0.12) 0.6373	
Geographic region						0.8949
Asia	398/ 606 (65.7)	435/ 619 (70.3)	0.93 (0.86, 1.01) 0.0796	0.81 (0.64, 1.03) 0.0831	-0.05 (-0.10, 0.01) 0.0805	
Europe and Saudi Arabia	963/1491 (64.6)	1022/1508 (67.8)	0.95 (0.90, 1.00) 0.0474	0.87 (0.74, 1.01) 0.0622	-0.03 (-0.07, 0.00) 0.0543	
North America	320/ 427 (74.9)	343/ 422 (81.3)	0.92 (0.86, 0.99) 0.0203	0.69 (0.50, 0.96) 0.0255	-0.07 (-0.12, -0.01) 0.0209	
Latin America	391/ 602 (65.0)	399/ 578 (69.0)	0.94 (0.87, 1.02) 0.1299	0.84 (0.66, 1.08) 0.1750	-0.04 (-0.09, 0.01) 0.1497	
NYHA class at enrolment						0.2817
II	1545/2310 (66.9)	1679/2395 (70.1)	0.95 (0.91, 0.99) 0.0092	0.86 (0.76, 0.97) 0.0165	-0.03 (-0.06, -0.01) 0.0120	
III or IV	527/ 816 (64.6)	519/ 731 (71.0)	0.91 (0.85, 0.97) 0.0070	0.75 (0.60, 0.92) 0.0075	-0.06 (-0.11, -0.02) 0.0070	
LVEF at enrolment						0.8436
<= 49	676/1066 (63.4)	710/1047 (67.8)	0.93 (0.88, 0.99) 0.0256	0.82 (0.68, 0.98) 0.0295	-0.05 (-0.09, -0.01) 0.0272	
50-59	755/1132 (66.7)	798/1121 (71.2)	0.94 (0.88, 0.99) 0.0183	0.81 (0.68, 0.97) 0.0215	-0.05 (-0.08, -0.01) 0.0194	
>= 60	641/ 928 (69.1)	691/ 959 (72.1)	0.95 (0.90, 1.01) 0.1133	0.87 (0.71, 1.06) 0.1647	-0.03 (-0.07, 0.01) 0.1329	
NT-proBNP at enrolment						0.5338
<= median	990/1553 (63.7)	1053/1574 (66.9)	0.95 (0.90, 1.00) 0.0472	0.87 (0.75, 1.01) 0.0639	-0.03 (-0.07, 0.00) 0.0554	
> median	1082/1573 (68.8)	1145/1552 (73.8)	0.93 (0.89, 0.97) 0.0012	0.78 (0.67, 0.91) 0.0020	-0.05 (-0.08, -0.02) 0.0014	
Type 2 Diabetes Medical History						0.0246
Yes	945/1399 (67.5)	1047/1402 (74.7)	0.90 (0.86, 0.95)*<.0001	0.71 (0.60, 0.83)*<.0001	-0.07 (-0.10, -0.04)*<.0001	
No	1127/1727 (65.3)	1152/1725 (66.8)	0.98 (0.93, 1.03)*0.3443	0.93 (0.81, 1.08)*0.3443	-0.02 (-0.05, 0.02)*0.3442	
Atrial fibrillation or flutter at enrolment ECG						0.4643
Yes	880/1325 (66.4)	914/1317 (69.4)	0.96 (0.91, 1.01) 0.0891	0.87 (0.74, 1.03) 0.1017	-0.03 (-0.07, 0.01) 0.0948	
No	1191/1800 (66.2)	1284/1809 (71.0)	0.93 (0.89, 0.97) 0.0010	0.80 (0.69, 0.92) 0.0017	-0.05 (-0.08, -0.02) 0.0013	
BMI (kg/m2) at enrolment						0.3664
< 30	1139/1732 (65.8)	1193/1733 (68.8)	0.95 (0.91, 1.00) 0.0431	0.87 (0.75, 1.00) 0.0534	-0.03 (-0.06, -0.00) 0.0475	
>= 30	932/1392 (67.0)	1003/1390 (72.2)	0.93 (0.88, 0.97) 0.0020	0.78 (0.66, 0.92) 0.0029	-0.05 (-0.09, -0.02) 0.0023	
Baseline eGFR (mL/min/1.73m^2)						0.6069
< 60	1048/1514 (69.2)	1147/1551 (74.0)	0.93 (0.89, 0.97) 0.0020	0.79 (0.67, 0.92) 0.0031	-0.05 (-0.08, -0.02) 0.0023	
>= 60	1024/1612 (63.5)	1052/1575 (66.8)	0.95 (0.90, 1.00) 0.0464	0.87 (0.75, 1.00) 0.0556	-0.03 (-0.07, 0.00) 0.0510	
SBP at randomisation						0.0969
<= median	1053/1567 (67.2)	1100/1588 (69.3)	0.97 (0.92, 1.01) 0.1721	0.91 (0.78, 1.05) 0.1984	-0.02 (-0.05, 0.01) 0.1837	
> median	1019/1559 (65.4)	1099/1539 (71.4)	0.91 (0.87, 0.96) 0.0002	0.76 (0.65, 0.88) 0.0004	-0.06 (-0.09, -0.03) 0.0002	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Event
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.7658
<= 49	676/1066 (63.4)	710/1047 (67.8)	0.93 (0.88, 0.99) 0.0256	0.82 (0.68, 0.98) 0.0295	-0.05 (-0.09, -0.01) 0.0272	
>= 50	1396/2060 (67.8)	1489/2080 (71.6)	0.94 (0.91, 0.98) 0.0049	0.84 (0.73, 0.95) 0.0080	-0.04 (-0.07, -0.01) 0.0060	
Randomised during hospitalisation for HF or within 30 days of discharge						0.3879
Yes	205/ 328 (62.5)	226/ 326 (69.3)	0.90 (0.80, 1.00) 0.0543	0.73 (0.53, 1.01) 0.0589	-0.07 (-0.14, 0.00) 0.0553	
No	1867/2798 (66.7)	1973/2801 (70.4)	0.94 (0.91, 0.98) 0.0016	0.84 (0.75, 0.94) 0.0029	-0.04 (-0.06, -0.01) 0.0021	
MRAs at baseline						0.8635
Yes	868/1339 (64.8)	913/1325 (68.9)	0.94 (0.89, 0.99) 0.0195	0.83 (0.71, 0.98) 0.0237	-0.04 (-0.08, -0.01) 0.0213	
No	1204/1787 (67.4)	1286/1802 (71.4)	0.94 (0.90, 0.98) 0.0069	0.83 (0.72, 0.96) 0.0108	-0.04 (-0.07, -0.01) 0.0083	
ACEi+ARB at baseline						0.8254
Yes	1490/2259 (66.0)	1596/2276 (70.1)	0.94 (0.90, 0.98) 0.0016	0.83 (0.73, 0.94) 0.0027	-0.04 (-0.07, -0.02) 0.0020	
No	582/ 867 (67.1)	603/ 851 (70.9)	0.94 (0.89, 1.01) 0.0786	0.84 (0.68, 1.03) 0.0899	-0.04 (-0.08, 0.01) 0.0828	
ARNI at baseline						0.6393
Yes	105/ 165 (63.6)	95/ 136 (69.9)	0.90 (0.77, 1.06) 0.2126	0.73 (0.45, 1.19) 0.2060	-0.07 (-0.18, 0.04) 0.2067	
No	1967/2961 (66.4)	2104/2991 (70.3)	0.94 (0.91, 0.97) 0.0006	0.83 (0.75, 0.93) 0.0012	-0.04 (-0.06, -0.02) 0.0009	
Beta Blocker at baseline						0.5637
Yes	1706/2587 (65.9)	1798/2581 (69.7)	0.94 (0.91, 0.98) 0.0025	0.84 (0.75, 0.95) 0.0040	-0.04 (-0.06, -0.01) 0.0031	
No	366/ 539 (67.9)	401/ 546 (73.4)	0.92 (0.85, 1.00) 0.0400	0.77 (0.59, 1.00) 0.0462	-0.06 (-0.11, -0.00) 0.0420	
Diuretics at baseline						0.5253
Yes	1865/2789 (66.9)	1982/2783 (71.2)	0.94 (0.90, 0.97) 0.0002	0.82 (0.73, 0.91) 0.0004	-0.04 (-0.07, -0.02) 0.0003	
No	207/ 337 (61.4)	217/ 344 (63.1)	0.97 (0.87, 1.09) 0.6569	0.93 (0.68, 1.27) 0.6563	-0.02 (-0.09, 0.06) 0.6565	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Event excluding efficacy events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	1720/3126 (55.0)	1825/3127 (58.4)	0.94 (0.90, 0.98) 0.0071	0.87 (0.79, 0.96) 0.0077	-0.03 (-0.06, -0.01) 0.0075	
Age						0.9809
<= median	823/1544 (53.3)	907/1602 (56.6)	0.94 (0.88, 1.00) 0.0525	0.87 (0.76, 1.01) 0.0613	-0.03 (-0.07, 0.00) 0.0595	
> median	897/1582 (56.7)	918/1525 (60.2)	0.94 (0.89, 1.00) 0.0484	0.87 (0.75, 1.00) 0.0482	-0.03 (-0.07, -0.00) 0.0480	
Gender						0.0019
Male	941/1765 (53.3)	1048/1744 (60.1)	0.89 (0.84, 0.94) <.0001	0.76 (0.66, 0.87) <.0001	-0.07 (-0.10, -0.04) <.0001	
Female	779/1361 (57.2)	777/1383 (56.2)	1.02 (0.95, 1.09) 0.5665	1.04 (0.90, 1.21) 0.5802	0.01 (-0.03, 0.05) 0.5769	
Race						0.1967
White	1202/2210 (54.4)	1286/2222 (57.9)	0.94 (0.89, 0.99) 0.0186	0.87 (0.77, 0.98) 0.0194	-0.03 (-0.06, -0.01) 0.0191	
Black or African	52/ 81 (64.2)	61/ 78 (78.2)	0.82 (0.67, 1.00) 0.0512	0.49 (0.24, 0.99) 0.0466	-0.14 (-0.28, -0.00) 0.0432	
Asian	367/ 629 (58.3)	400/ 643 (62.2)	0.94 (0.86, 1.03) 0.1619	0.85 (0.68, 1.07) 0.1605	-0.04 (-0.09, 0.02) 0.1604	
Other	99/ 206 (48.1)	78/ 184 (42.4)	1.14 (0.92, 1.42) 0.2289	1.29 (0.86, 1.93) 0.2153	0.06 (-0.04, 0.16) 0.2114	
Geographic region						0.5512
Asia	355/ 606 (58.6)	386/ 619 (62.4)	0.94 (0.86, 1.03) 0.1799	0.85 (0.68, 1.07) 0.1779	-0.04 (-0.09, 0.02) 0.1781	
Europe and Saudi Arabia	772/1491 (51.8)	802/1508 (53.2)	0.97 (0.91, 1.04) 0.4392	0.95 (0.82, 1.09) 0.4407	-0.01 (-0.05, 0.02) 0.4405	
North America	286/ 427 (67.0)	312/ 422 (73.9)	0.90 (0.83, 0.99) 0.0219	0.71 (0.53, 0.96) 0.0262	-0.07 (-0.13, -0.01) 0.0229	
Latin America	307/ 602 (51.0)	325/ 578 (56.2)	0.91 (0.82, 1.02) 0.0980	0.82 (0.65, 1.03) 0.0912	-0.05 (-0.11, 0.01) 0.0915	
NYHA class at enrolment						0.9090
II	1314/2310 (56.9)	1437/2395 (60.0)	0.95 (0.90, 0.99) 0.0264	0.88 (0.78, 0.99) 0.0297	-0.03 (-0.06, -0.00) 0.0286	
III or IV	406/ 816 (49.8)	387/ 731 (52.9)	0.94 (0.85, 1.04) 0.2186	0.88 (0.72, 1.08) 0.2160	-0.03 (-0.08, 0.02) 0.2155	
LVEF at enrolment						0.4500
<= 49	528/1066 (49.5)	556/1047 (53.1)	0.93 (0.86, 1.01) 0.0970	0.87 (0.73, 1.03) 0.0979	-0.04 (-0.08, 0.01) 0.0974	
50-59	633/1132 (55.9)	680/1121 (60.7)	0.92 (0.86, 0.99) 0.0213	0.82 (0.70, 0.97) 0.0226	-0.05 (-0.09, -0.01) 0.0220	
>= 60	559/ 928 (60.2)	589/ 959 (61.4)	0.98 (0.91, 1.05) 0.5898	0.95 (0.79, 1.15) 0.6056	-0.01 (-0.06, 0.03) 0.6000	
NT-proBNP at enrolment						0.6133
<= median	847/1553 (54.5)	900/1574 (57.2)	0.95 (0.90, 1.01) 0.1306	0.90 (0.78, 1.03) 0.1372	-0.03 (-0.06, 0.01) 0.1357	
> median	873/1573 (55.5)	924/1552 (59.5)	0.93 (0.88, 0.99) 0.0217	0.85 (0.74, 0.98) 0.0224	-0.04 (-0.08, -0.01) 0.0220	
Type 2 Diabetes Medical History						0.1020
Yes	781/1399 (55.8)	863/1402 (61.6)	0.91 (0.85, 0.97)*0.0021	0.79 (0.68, 0.92)*0.0021	-0.06 (-0.09, -0.02)*0.0020	
No	939/1727 (54.4)	962/1725 (55.8)	0.97 (0.92, 1.04)*0.4096	0.95 (0.83, 1.08)*0.4096	-0.01 (-0.05, 0.02)*0.4095	
Atrial fibrillation or flutter at enrolment ECG						0.5368
Yes	712/1325 (53.7)	763/1317 (57.9)	0.93 (0.87, 0.99) 0.0315	0.84 (0.72, 0.98) 0.0294	-0.04 (-0.08, -0.00) 0.0296	
No	1007/1800 (55.9)	1061/1809 (58.7)	0.95 (0.90, 1.01) 0.0887	0.89 (0.78, 1.02) 0.0978	-0.03 (-0.06, 0.00) 0.0952	
BMI (kg/m2) at enrolment						0.1791
< 30	949/1732 (54.8)	980/1733 (56.5)	0.97 (0.91, 1.03) 0.2882	0.93 (0.81, 1.06) 0.2982	-0.02 (-0.05, 0.02) 0.2958	
>= 30	770/1392 (55.3)	842/1390 (60.6)	0.91 (0.86, 0.97) 0.0053	0.81 (0.69, 0.94) 0.0050	-0.05 (-0.09, -0.02) 0.0050	
Baseline eGFR (mL/min/1.73m^2)						0.8670
< 60	871/1514 (57.5)	949/1551 (61.2)	0.94 (0.89, 1.00) 0.0343	0.86 (0.74, 0.99) 0.0366	-0.04 (-0.07, -0.00) 0.0357	
>= 60	849/1612 (52.7)	876/1575 (55.6)	0.95 (0.89, 1.01) 0.0970	0.89 (0.77, 1.02) 0.0928	-0.03 (-0.06, 0.00) 0.0931	
SBP at randomisation						0.2777
<= median	875/1567 (55.8)	918/1588 (57.8)	0.97 (0.91, 1.03) 0.2659	0.92 (0.80, 1.06) 0.2650	-0.02 (-0.05, 0.01) 0.2651	
> median	845/1559 (54.2)	907/1539 (58.9)	0.92 (0.86, 0.98) 0.0078	0.83 (0.72, 0.95) 0.0085	-0.05 (-0.08, -0.01) 0.0082	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Event excluding efficacy events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.7384
<= 49	528/1066 (49.5)	556/1047 (53.1)	0.93 (0.86, 1.01) 0.0970	0.87 (0.73, 1.03) 0.0979	-0.04 (-0.08, 0.01) 0.0974	
>= 50	1192/2060 (57.9)	1269/2080 (61.0)	0.95 (0.90, 1.00) 0.0371	0.88 (0.78, 0.99) 0.0399	-0.03 (-0.06, -0.00) 0.0389	
Randomised during hospitalisation for HF or within 30 days of discharge						0.2259
Yes	147/ 328 (44.8)	170/ 326 (52.1)	0.86 (0.73, 1.01) 0.0601	0.74 (0.55, 1.01) 0.0585	-0.07 (-0.15, 0.00) 0.0575	
No	1573/2798 (56.2)	1655/2801 (59.1)	0.95 (0.91, 0.99) 0.0277	0.89 (0.80, 0.99) 0.0303	-0.03 (-0.05, -0.00) 0.0295	
MRAs at baseline						0.8651
Yes	706/1339 (52.7)	744/1325 (56.2)	0.94 (0.88, 1.01) 0.0729	0.87 (0.75, 1.01) 0.0744	-0.03 (-0.07, 0.00) 0.0739	
No	1014/1787 (56.7)	1081/1802 (60.0)	0.95 (0.89, 1.00) 0.0471	0.88 (0.77, 1.00) 0.0497	-0.03 (-0.06, -0.00) 0.0488	
ACEi+ARB at baseline						0.7366
Yes	1232/2259 (54.5)	1311/2276 (57.6)	0.95 (0.90, 1.00) 0.0373	0.88 (0.79, 0.99) 0.0377	-0.03 (-0.06, -0.00) 0.0375	
No	488/ 867 (56.3)	514/ 851 (60.4)	0.93 (0.86, 1.01) 0.0716	0.84 (0.70, 1.02) 0.0806	-0.04 (-0.09, 0.00) 0.0774	
ARNI at baseline						0.5193
Yes	86/ 165 (52.1)	80/ 136 (58.8)	0.88 (0.71, 1.08) 0.2155	0.75 (0.47, 1.19) 0.2239	-0.07 (-0.18, 0.04) 0.2203	
No	1634/2961 (55.2)	1745/2991 (58.3)	0.95 (0.90, 0.99) 0.0132	0.88 (0.79, 0.97) 0.0141	-0.03 (-0.06, -0.01) 0.0138	
Beta Blocker at baseline						0.5184
Yes	1413/2587 (54.6)	1505/2581 (58.3)	0.94 (0.89, 0.98) 0.0067	0.86 (0.77, 0.96) 0.0074	-0.04 (-0.06, -0.01) 0.0072	
No	307/ 539 (57.0)	320/ 546 (58.6)	0.97 (0.88, 1.08) 0.5832	0.93 (0.73, 1.19) 0.5811	-0.02 (-0.08, 0.04) 0.5816	
Diuretics at baseline						0.7309
Yes	1549/2789 (55.5)	1644/2783 (59.1)	0.94 (0.90, 0.98) 0.0071	0.87 (0.78, 0.96) 0.0077	-0.04 (-0.06, -0.01) 0.0075	
No	171/ 337 (50.7)	181/ 344 (52.6)	0.97 (0.83, 1.12) 0.6313	0.93 (0.69, 1.25) 0.6240	-0.02 (-0.09, 0.06) 0.6243	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	1454/3126 (46.5)	1508/3127 (48.2)	0.96 (0.91, 1.01) 0.1503	0.93 (0.84, 1.03) 0.1731	-0.02 (-0.04, 0.01) 0.1758	
Age						0.8482
<= median	689/1544 (44.6)	745/1602 (46.5)	0.95 (0.88, 1.03) 0.2305	0.93 (0.80, 1.07) 0.2830	-0.02 (-0.05, 0.02) 0.2957	
> median	765/1582 (48.4)	763/1525 (50.0)	0.97 (0.90, 1.04) 0.3427	0.93 (0.81, 1.08) 0.3479	-0.02 (-0.05, 0.02) 0.3471	
Gender						0.5044
Male	844/1765 (47.8)	878/1744 (50.3)	0.95 (0.89, 1.01) 0.1190	0.90 (0.79, 1.03) 0.1268	-0.03 (-0.06, 0.01) 0.1269	
Female	610/1361 (44.8)	630/1383 (45.6)	0.98 (0.90, 1.07) 0.6673	0.97 (0.84, 1.13) 0.7291	-0.01 (-0.04, 0.03) 0.7424	
Race						0.4441
White	1057/2210 (47.8)	1099/2222 (49.5)	0.96 (0.91, 1.02) 0.2277	0.94 (0.83, 1.05) 0.2761	-0.02 (-0.05, 0.01) 0.2792	
Black or African	43/ 81 (53.1)	44/ 78 (56.4)	0.93 (0.71, 1.24) 0.6369	0.86 (0.46, 1.61) 0.6413	-0.04 (-0.19, 0.12) 0.6400	
Asian	277/ 629 (44.0)	306/ 643 (47.6)	0.92 (0.82, 1.04) 0.1958	0.86 (0.69, 1.08) 0.1955	-0.04 (-0.09, 0.02) 0.1951	
Other	77/ 206 (37.4)	59/ 184 (32.1)	1.21 (0.92, 1.58) 0.1748	1.31 (0.86, 2.01) 0.2081	0.06 (-0.04, 0.15) 0.2435	
Geographic region						0.8358
Asia	264/ 606 (43.6)	294/ 619 (47.5)	0.92 (0.81, 1.04) 0.1641	0.85 (0.68, 1.07) 0.1631	-0.04 (-0.10, 0.02) 0.1625	
Europe and Saudi Arabia	717/1491 (48.1)	746/1508 (49.5)	0.97 (0.90, 1.04) 0.3797	0.94 (0.82, 1.09) 0.4228	-0.01 (-0.05, 0.02) 0.4252	
North America	233/ 427 (54.6)	233/ 422 (55.2)	0.98 (0.87, 1.10) 0.7062	0.97 (0.74, 1.27) 0.8246	-0.01 (-0.07, 0.06) 0.8021	
Latin America	240/ 602 (39.9)	235/ 578 (40.7)	0.98 (0.86, 1.13) 0.8301	0.98 (0.77, 1.24) 0.8523	-0.00 (-0.06, 0.05) 0.8635	
NYHA class at enrolment						0.6627
II	1039/2310 (45.0)	1111/2395 (46.4)	0.97 (0.91, 1.03) 0.2719	0.94 (0.84, 1.06) 0.3171	-0.01 (-0.04, 0.01) 0.3261	
III or IV	415/ 816 (50.9)	396/ 731 (54.2)	0.94 (0.86, 1.03) 0.2034	0.88 (0.72, 1.07) 0.2010	-0.03 (-0.08, 0.02) 0.2008	
LVEF at enrolment						0.9705
<= 49	506/1066 (47.5)	512/1047 (48.9)	0.97 (0.88, 1.05) 0.4373	0.94 (0.79, 1.11) 0.4672	-0.02 (-0.06, 0.03) 0.4695	
50-59	521/1132 (46.0)	534/1121 (47.6)	0.97 (0.89, 1.06) 0.4511	0.94 (0.79, 1.11) 0.4463	-0.02 (-0.06, 0.03) 0.4456	
>= 60	427/ 928 (46.0)	462/ 959 (48.2)	0.95 (0.87, 1.05) 0.3182	0.92 (0.77, 1.10) 0.3761	-0.02 (-0.06, 0.02) 0.3835	
NT-proBNP at enrolment						0.7189
<= median	662/1553 (42.6)	691/1574 (43.9)	0.97 (0.90, 1.05) 0.4636	0.95 (0.82, 1.09) 0.4711	-0.01 (-0.05, 0.02) 0.4738	
> median	792/1573 (50.3)	817/1552 (52.6)	0.95 (0.89, 1.02) 0.1578	0.91 (0.79, 1.05) 0.1954	-0.02 (-0.06, 0.01) 0.1926	
Type 2 Diabetes Medical History						0.4964
Yes	704/1399 (50.3)	745/1402 (53.1)	0.95 (0.88, 1.02)*0.1360	0.89 (0.77, 1.04)*0.1358	-0.03 (-0.07, 0.01)*0.1356	
No	750/1727 (43.4)	763/1725 (44.2)	0.98 (0.91, 1.06)*0.6341	0.97 (0.85, 1.11)*0.6341	-0.01 (-0.04, 0.03)*0.6341	
Atrial fibrillation or flutter at enrolment ECG						0.2501
Yes	629/1325 (47.5)	626/1317 (47.5)	1.00 (0.92, 1.08) 0.9450	1.00 (0.86, 1.16) 0.9922	-0.00 (-0.04, 0.04) 0.9967	
No	824/1800 (45.8)	882/1809 (48.8)	0.94 (0.87, 1.00) 0.0627	0.88 (0.78, 1.01) 0.0677	-0.03 (-0.06, 0.00) 0.0683	
BMI (kg/m2) at enrolment						0.4848
< 30	767/1732 (44.3)	811/1733 (46.8)	0.95 (0.88, 1.02) 0.1309	0.90 (0.79, 1.03) 0.1373	-0.03 (-0.06, 0.01) 0.1384	
>= 30	686/1392 (49.3)	696/1390 (50.1)	0.98 (0.91, 1.06) 0.6002	0.97 (0.83, 1.12) 0.6720	-0.01 (-0.04, 0.03) 0.6750	
Baseline eGFR (mL/min/1.73m^2)						0.5382
< 60	762/1514 (50.3)	819/1551 (52.8)	0.95 (0.89, 1.02) 0.1388	0.90 (0.78, 1.04) 0.1488	-0.03 (-0.06, 0.01) 0.1480	
>= 60	692/1612 (42.9)	689/1575 (43.7)	0.98 (0.91, 1.06) 0.6371	0.97 (0.84, 1.12) 0.6839	-0.01 (-0.04, 0.03) 0.6982	
SBP at randomisation						0.0694
<= median	731/1567 (46.6)	729/1588 (45.9)	1.01 (0.94, 1.09) 0.7827	1.02 (0.89, 1.18) 0.7306	0.01 (-0.03, 0.04) 0.7227	
> median	723/1559 (46.4)	779/1539 (50.6)	0.92 (0.85, 0.99) 0.0202	0.85 (0.74, 0.98) 0.0216	-0.04 (-0.08, -0.01) 0.0216	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.9179
<= 49	506/1066 (47.5)	512/1047 (48.9)	0.97 (0.88, 1.05) 0.4373	0.94 (0.79, 1.11) 0.4672	-0.02 (-0.06, 0.03) 0.4695	
>= 50	948/2060 (46.0)	996/2080 (47.9)	0.96 (0.90, 1.02) 0.2203	0.93 (0.82, 1.05) 0.2433	-0.02 (-0.05, 0.01) 0.2465	
Randomised during hospitalisation for HF or within 30 days of discharge						0.1846
Yes	169/ 328 (51.5)	190/ 326 (58.3)	0.88 (0.77, 1.01) 0.0737	0.75 (0.55, 1.02) 0.0694	-0.07 (-0.15, 0.01) 0.0689	
No	1285/2798 (45.9)	1318/2801 (47.1)	0.97 (0.92, 1.03) 0.3621	0.96 (0.86, 1.06) 0.4087	-0.01 (-0.04, 0.02) 0.4161	
MRAs at baseline						0.6405
Yes	593/1339 (44.3)	613/1325 (46.3)	0.95 (0.87, 1.03) 0.2394	0.92 (0.79, 1.07) 0.2806	-0.02 (-0.06, 0.02) 0.2894	
No	861/1787 (48.2)	895/1802 (49.7)	0.97 (0.91, 1.04) 0.4352	0.95 (0.83, 1.08) 0.4132	-0.01 (-0.05, 0.02) 0.4122	
ACEi+ARB at baseline						0.5966
Yes	1039/2259 (46.0)	1095/2276 (48.1)	0.95 (0.90, 1.01) 0.1346	0.92 (0.82, 1.03) 0.1557	-0.02 (-0.05, 0.01) 0.1587	
No	415/ 867 (47.9)	413/ 851 (48.5)	0.98 (0.89, 1.08) 0.7453	0.97 (0.80, 1.17) 0.7553	-0.01 (-0.05, 0.04) 0.7559	
ARNI at baseline						0.6379
Yes	72/ 165 (43.6)	57/ 136 (41.9)	1.01 (0.78, 1.31) 0.9539	1.00 (0.63, 1.60) 0.9884	0.00 (-0.11, 0.11) 0.9994	
No	1382/2961 (46.7)	1451/2991 (48.5)	0.96 (0.91, 1.01) 0.1408	0.93 (0.84, 1.03) 0.1631	-0.02 (-0.04, 0.01) 0.1655	
Beta Blocker at baseline						0.6827
Yes	1189/2587 (46.0)	1222/2581 (47.3)	0.97 (0.91, 1.02) 0.2589	0.94 (0.85, 1.05) 0.3048	-0.01 (-0.04, 0.01) 0.3121	
No	265/ 539 (49.2)	286/ 546 (52.4)	0.94 (0.83, 1.06) 0.2927	0.88 (0.69, 1.12) 0.2921	-0.03 (-0.09, 0.03) 0.2915	
Diuretics at baseline						0.5135
Yes	1321/2789 (47.4)	1360/2783 (48.9)	0.97 (0.92, 1.02) 0.2408	0.94 (0.85, 1.05) 0.2596	-0.02 (-0.04, 0.01) 0.2612	
No	133/ 337 (39.5)	148/ 344 (43.0)	0.92 (0.77, 1.10) 0.3432	0.86 (0.64, 1.17) 0.3458	-0.04 (-0.11, 0.04) 0.3460	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event excluding efficacy events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	947/3126 (30.3)	975/3127 (31.2)	0.97 (0.90, 1.05) 0.4429	0.96 (0.86, 1.07) 0.4462	-0.01 (-0.03, 0.01) 0.4507	
Age						0.5701
<= median	455/1544 (29.5)	476/1602 (29.7)	0.99 (0.89, 1.10) 0.8762	0.99 (0.85, 1.15) 0.8756	-0.00 (-0.03, 0.03) 0.8752	
> median	492/1582 (31.1)	499/1525 (32.7)	0.95 (0.86, 1.05) 0.3278	0.93 (0.80, 1.08) 0.3308	-0.02 (-0.05, 0.02) 0.3342	
Gender						0.1284
Male	528/1765 (29.9)	565/1744 (32.4)	0.92 (0.84, 1.02) 0.1129	0.89 (0.77, 1.03) 0.1093	-0.03 (-0.06, 0.01) 0.1051	
Female	419/1361 (30.8)	410/1383 (29.6)	1.04 (0.93, 1.16) 0.5263	1.06 (0.90, 1.25) 0.4967	0.01 (-0.02, 0.05) 0.4599	
Race						0.0319
White	678/2210 (30.7)	696/2222 (31.3)	0.98 (0.90, 1.07) 0.6252	0.97 (0.85, 1.10) 0.6424	-0.01 (-0.03, 0.02) 0.6643	
Black or African	31/ 81 (38.3)	31/ 78 (39.7)	0.96 (0.65, 1.42) 0.8455	0.94 (0.50, 1.78) 0.8434	-0.02 (-0.17, 0.14) 0.8422	
Asian	198/ 629 (31.5)	229/ 643 (35.6)	0.88 (0.76, 1.03) 0.1185	0.83 (0.66, 1.05) 0.1182	-0.04 (-0.09, 0.01) 0.1177	
Other	40/ 206 (19.4)	19/ 184 (10.3)	1.99 (1.20, 3.30) 0.0074	2.22 (1.22, 4.02) 0.0086	0.08 (0.01, 0.15) 0.0293	
Geographic region						0.6356
Asia	193/ 606 (31.8)	220/ 619 (35.5)	0.90 (0.77, 1.05) 0.1725	0.85 (0.67, 1.07) 0.1720	-0.04 (-0.09, 0.02) 0.1713	
Europe and Saudi Arabia	448/1491 (30.0)	449/1508 (29.8)	1.01 (0.90, 1.12) 0.9153	1.01 (0.86, 1.18) 0.8957	0.00 (-0.03, 0.04) 0.8692	
North America	176/ 427 (41.2)	182/ 422 (43.1)	0.95 (0.81, 1.11) 0.4802	0.92 (0.70, 1.21) 0.5559	-0.02 (-0.08, 0.05) 0.5858	
Latin America	130/ 602 (21.6)	124/ 578 (21.5)	1.01 (0.82, 1.26) 0.8941	1.02 (0.77, 1.34) 0.9142	0.00 (-0.05, 0.05) 0.9680	
NYHA class at enrolment						0.5194
II	694/2310 (30.0)	749/2395 (31.3)	0.96 (0.88, 1.04) 0.3309	0.94 (0.83, 1.07) 0.3521	-0.01 (-0.04, 0.01) 0.3804	
III or IV	253/ 816 (31.0)	225/ 731 (30.8)	1.01 (0.87, 1.18) 0.8609	1.01 (0.82, 1.26) 0.9018	0.00 (-0.04, 0.05) 0.9534	
LVEF at enrolment						0.9951
<= 49	300/1066 (28.1)	304/1047 (29.0)	0.97 (0.85, 1.11) 0.6260	0.95 (0.79, 1.15) 0.6189	-0.01 (-0.05, 0.03) 0.6086	
50-59	349/1132 (30.8)	354/1121 (31.6)	0.98 (0.86, 1.10) 0.7029	0.97 (0.81, 1.15) 0.7037	-0.01 (-0.05, 0.03) 0.7049	
>= 60	298/ 928 (32.1)	317/ 959 (33.1)	0.97 (0.85, 1.11) 0.6728	0.96 (0.79, 1.17) 0.6852	-0.01 (-0.05, 0.03) 0.6988	
NT-proBNP at enrolment						0.5432
<= median	460/1553 (29.6)	469/1574 (29.8)	0.99 (0.89, 1.11) 0.9111	0.99 (0.85, 1.16) 0.9138	-0.00 (-0.03, 0.03) 0.9176	
> median	487/1573 (31.0)	506/1552 (32.6)	0.95 (0.86, 1.05) 0.3171	0.93 (0.80, 1.08) 0.3204	-0.02 (-0.05, 0.02) 0.3246	
Type 2 Diabetes Medical History						0.9324
Yes	461/1399 (33.0)	477/1402 (34.0)	0.97 (0.87, 1.08)*0.5483	0.95 (0.81, 1.12)*0.5483	-0.01 (-0.05, 0.02)*0.5482	
No	486/1727 (28.1)	498/1725 (28.9)	0.97 (0.88, 1.08)*0.6356	0.96 (0.83, 1.12)*0.6356	-0.01 (-0.04, 0.02)*0.6355	
Atrial fibrillation or flutter at enrolment ECG						0.8870
Yes	391/1325 (29.5)	398/1317 (30.2)	0.98 (0.87, 1.10) 0.6917	0.97 (0.82, 1.14) 0.6970	-0.01 (-0.04, 0.03) 0.7044	
No	555/1800 (30.8)	577/1809 (31.9)	0.97 (0.88, 1.06) 0.4811	0.95 (0.83, 1.09) 0.4793	-0.01 (-0.04, 0.02) 0.4776	
BMI (kg/m2) at enrolment						0.2351
< 30	480/1732 (27.7)	516/1733 (29.8)	0.93 (0.84, 1.03) 0.1790	0.90 (0.78, 1.05) 0.1802	-0.02 (-0.05, 0.01) 0.1820	
>= 30	467/1392 (33.5)	458/1390 (32.9)	1.02 (0.92, 1.13) 0.7422	1.03 (0.88, 1.20) 0.7397	0.01 (-0.03, 0.04) 0.7374	
Baseline eGFR (mL/min/1.73m^2)						0.5103
< 60	506/1514 (33.4)	544/1551 (35.1)	0.95 (0.86, 1.05) 0.3146	0.92 (0.80, 1.07) 0.3055	-0.02 (-0.05, 0.02) 0.2975	
>= 60	441/1612 (27.4)	431/1575 (27.4)	1.00 (0.89, 1.12) 0.9985	1.00 (0.86, 1.17) 0.9917	0.00 (-0.03, 0.03) 0.9806	
SBP at randomisation						0.1207
<= median	481/1567 (30.7)	471/1588 (29.7)	1.03 (0.93, 1.15) 0.5586	1.05 (0.90, 1.22) 0.5444	0.01 (-0.02, 0.04) 0.5261	
> median	466/1559 (29.9)	504/1539 (32.7)	0.92 (0.83, 1.02) 0.1052	0.88 (0.75, 1.02) 0.0967	-0.03 (-0.06, 0.00) 0.0875	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event excluding efficacy events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.9341
<= 49	300/1066 (28.1)	304/1047 (29.0)	0.97 (0.85, 1.11) 0.6260	0.95 (0.79, 1.15) 0.6189	-0.01 (-0.05, 0.03) 0.6086	
>= 50	647/2060 (31.4)	671/2080 (32.3)	0.97 (0.89, 1.06) 0.5629	0.96 (0.84, 1.10) 0.5704	-0.01 (-0.04, 0.02) 0.5793	
Randomised during hospitalisation for HF or within 30 days of discharge						0.1316
Yes	93/ 328 (28.4)	112/ 326 (34.4)	0.82 (0.66, 1.03) 0.0942	0.75 (0.54, 1.04) 0.0878	-0.06 (-0.13, 0.01) 0.0798	
No	854/2798 (30.5)	863/2801 (30.8)	0.99 (0.92, 1.07) 0.8149	0.99 (0.88, 1.11) 0.8249	-0.00 (-0.03, 0.02) 0.8378	
MRAs at baseline						0.2439
Yes	361/1339 (27.0)	387/1325 (29.2)	0.92 (0.82, 1.04) 0.1851	0.89 (0.75, 1.06) 0.1889	-0.02 (-0.06, 0.01) 0.1949	
No	586/1787 (32.8)	588/1802 (32.6)	1.01 (0.92, 1.11) 0.8672	1.01 (0.88, 1.16) 0.8811	0.00 (-0.03, 0.03) 0.8963	
ACEi+ARB at baseline						0.4735
Yes	669/2259 (29.6)	683/2276 (30.0)	0.99 (0.90, 1.08) 0.7826	0.98 (0.86, 1.12) 0.7765	-0.00 (-0.03, 0.02) 0.7684	
No	278/ 867 (32.1)	292/ 851 (34.3)	0.93 (0.81, 1.06) 0.2908	0.90 (0.74, 1.10) 0.3099	-0.02 (-0.07, 0.02) 0.3300	
ARNI at baseline						0.9928
Yes	42/ 165 (25.5)	35/ 136 (25.7)	0.95 (0.64, 1.40) 0.7839	0.94 (0.55, 1.59) 0.8057	-0.01 (-0.11, 0.09) 0.8468	
No	905/2961 (30.6)	940/2991 (31.4)	0.97 (0.90, 1.05) 0.4802	0.96 (0.86, 1.07) 0.4811	-0.01 (-0.03, 0.02) 0.4825	
Beta Blocker at baseline						0.2206
Yes	760/2587 (29.4)	797/2581 (30.9)	0.95 (0.87, 1.03) 0.2275	0.93 (0.83, 1.05) 0.2330	-0.01 (-0.04, 0.01) 0.2410	
No	187/ 539 (34.7)	178/ 546 (32.6)	1.06 (0.90, 1.26) 0.4637	1.10 (0.85, 1.41) 0.4646	0.02 (-0.04, 0.08) 0.4653	
Diuretics at baseline						0.1173
Yes	863/2789 (30.9)	869/2783 (31.2)	0.99 (0.92, 1.07) 0.8143	0.99 (0.88, 1.11) 0.8190	-0.00 (-0.03, 0.02) 0.8250	
No	84/ 337 (24.9)	106/ 344 (30.8)	0.81 (0.63, 1.03) 0.0873	0.75 (0.53, 1.04) 0.0869	-0.06 (-0.13, 0.01) 0.0863	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event excluding Covid-19 events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	1297/3126 (41.5)	1379/3127 (44.1)	0.94 (0.89, 0.99) 0.0308	0.90 (0.81, 0.99) 0.0364	-0.03 (-0.05, -0.00) 0.0385	
Age						0.9217
<= median	608/1544 (39.4)	673/1602 (42.0)	0.93 (0.86, 1.01) 0.1056	0.90 (0.78, 1.03) 0.1285	-0.03 (-0.06, 0.01) 0.1419	
> median	689/1582 (43.6)	706/1525 (46.3)	0.94 (0.87, 1.02) 0.1196	0.89 (0.78, 1.03) 0.1230	-0.03 (-0.06, 0.01) 0.1237	
Gender						0.8987
Male	766/1765 (43.4)	803/1744 (46.0)	0.94 (0.87, 1.01) 0.1071	0.90 (0.78, 1.02) 0.1075	-0.03 (-0.06, 0.01) 0.1076	
Female	531/1361 (39.0)	576/1383 (41.6)	0.93 (0.85, 1.02) 0.1403	0.90 (0.77, 1.05) 0.1700	-0.02 (-0.06, 0.01) 0.1860	
Race						0.6237
White	925/2210 (41.9)	994/2222 (44.7)	0.93 (0.87, 1.00) 0.0406	0.89 (0.79, 1.00) 0.0527	-0.03 (-0.06, 0.00) 0.0571	
Black or African	39/ 81 (48.1)	38/ 78 (48.7)	0.99 (0.72, 1.35) 0.9439	0.95 (0.51, 1.79) 0.8783	-0.01 (-0.17, 0.14) 0.8706	
Asian	272/ 629 (43.2)	299/ 643 (46.5)	0.93 (0.82, 1.05) 0.2335	0.87 (0.70, 1.09) 0.2307	-0.03 (-0.09, 0.02) 0.2299	
Other	61/ 206 (29.6)	48/ 184 (26.1)	1.19 (0.86, 1.63) 0.2945	1.24 (0.79, 1.95) 0.3470	0.03 (-0.05, 0.12) 0.4496	
Geographic region						0.8263
Asia	259/ 606 (42.7)	287/ 619 (46.4)	0.92 (0.81, 1.04) 0.1981	0.86 (0.69, 1.08) 0.1950	-0.04 (-0.09, 0.02) 0.1940	
Europe and Saudi Arabia	625/1491 (41.9)	663/1508 (44.0)	0.95 (0.87, 1.03) 0.2154	0.92 (0.79, 1.06) 0.2386	-0.02 (-0.06, 0.01) 0.2470	
North America	222/ 427 (52.0)	223/ 422 (52.8)	0.97 (0.86, 1.10) 0.6845	0.96 (0.73, 1.26) 0.7770	-0.01 (-0.08, 0.06) 0.7675	
Latin America	191/ 602 (31.7)	206/ 578 (35.6)	0.89 (0.76, 1.05) 0.1686	0.85 (0.67, 1.08) 0.1810	-0.04 (-0.09, 0.02) 0.1945	
NYHA class at enrolment						0.7935
II	917/2310 (39.7)	1008/2395 (42.1)	0.94 (0.88, 1.01) 0.0733	0.90 (0.80, 1.02) 0.0895	-0.02 (-0.05, 0.00) 0.0977	
III or IV	380/ 816 (46.6)	370/ 731 (50.6)	0.92 (0.83, 1.02) 0.1214	0.85 (0.70, 1.04) 0.1180	-0.04 (-0.09, 0.01) 0.1174	
LVEF at enrolment						0.6998
<= 49	452/1066 (42.4)	469/1047 (44.8)	0.94 (0.86, 1.04) 0.2260	0.90 (0.76, 1.07) 0.2409	-0.02 (-0.07, 0.02) 0.2456	
50-59	475/1132 (42.0)	489/1121 (43.6)	0.96 (0.88, 1.06) 0.4374	0.93 (0.79, 1.10) 0.4286	-0.02 (-0.06, 0.02) 0.4259	
>= 60	370/ 928 (39.9)	421/ 959 (43.9)	0.91 (0.81, 1.01) 0.0676	0.85 (0.71, 1.02) 0.0852	-0.04 (-0.08, 0.01) 0.0930	
NT-proBNP at enrolment						0.9431
<= median	573/1553 (36.9)	621/1574 (39.5)	0.93 (0.86, 1.02) 0.1357	0.90 (0.78, 1.04) 0.1400	-0.03 (-0.06, 0.01) 0.1434	
> median	724/1573 (46.0)	758/1552 (48.8)	0.94 (0.87, 1.01) 0.0938	0.89 (0.78, 1.03) 0.1125	-0.03 (-0.06, 0.01) 0.1144	
Type 2 Diabetes Medical History						0.3967
Yes	630/1399 (45.0)	688/1402 (49.1)	0.92 (0.85, 0.99)*0.0324	0.85 (0.73, 0.99)*0.0322	-0.04 (-0.08, -0.00)*0.0320	
No	667/1727 (38.6)	691/1725 (40.1)	0.96 (0.89, 1.05)*0.3879	0.94 (0.82, 1.08)*0.3878	-0.01 (-0.05, 0.02)*0.3878	
Atrial fibrillation or flutter at enrolment ECG						0.3000
Yes	563/1325 (42.5)	575/1317 (43.7)	0.97 (0.89, 1.06) 0.5273	0.95 (0.82, 1.11) 0.5565	-0.01 (-0.05, 0.03) 0.5658	
No	733/1800 (40.7)	804/1809 (44.4)	0.91 (0.85, 0.99) 0.0195	0.86 (0.75, 0.98) 0.0215	-0.04 (-0.07, -0.01) 0.0223	
BMI (kg/m2) at enrolment						0.9798
< 30	704/1732 (40.6)	750/1733 (43.3)	0.94 (0.87, 1.01) 0.1095	0.90 (0.78, 1.03) 0.1165	-0.03 (-0.06, 0.01) 0.1192	
>= 30	592/1392 (42.5)	628/1390 (45.2)	0.94 (0.86, 1.02) 0.1378	0.90 (0.77, 1.04) 0.1557	-0.03 (-0.06, 0.01) 0.1623	
Baseline eGFR (mL/min/1.73m^2)						0.5568
< 60	692/1514 (45.7)	762/1551 (49.1)	0.93 (0.86, 1.00) 0.0448	0.87 (0.75, 1.00) 0.0495	-0.04 (-0.07, -0.00) 0.0499	
>= 60	605/1612 (37.5)	617/1575 (39.2)	0.96 (0.88, 1.05) 0.3464	0.94 (0.81, 1.08) 0.3722	-0.01 (-0.05, 0.02) 0.3886	
SBP at randomisation						0.0165
<= median	664/1567 (42.4)	664/1588 (41.8)	1.01 (0.93, 1.09) 0.8582	1.02 (0.88, 1.17) 0.8067	0.00 (-0.03, 0.04) 0.7881	
> median	633/1559 (40.6)	715/1539 (46.5)	0.88 (0.81, 0.95) 0.0012	0.79 (0.69, 0.91) 0.0013	-0.06 (-0.09, -0.02) 0.0013	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event excluding Covid-19 events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.9327
<= 49	452/1066 (42.4)	469/1047 (44.8)	0.94 (0.86, 1.04) 0.2260	0.90 (0.76, 1.07) 0.2409	-0.02 (-0.07, 0.02) 0.2456	
>= 50	845/2060 (41.0)	910/2080 (43.8)	0.94 (0.87, 1.01) 0.0723	0.90 (0.79, 1.01) 0.0816	-0.03 (-0.06, 0.00) 0.0853	
Randomised during hospitalisation for HF or within 30 days of discharge						0.4031
Yes	159/ 328 (48.5)	178/ 326 (54.6)	0.88 (0.76, 1.03) 0.1069	0.77 (0.57, 1.05) 0.1011	-0.06 (-0.14, 0.01) 0.1003	
No	1138/2798 (40.7)	1201/2801 (42.9)	0.95 (0.89, 1.01) 0.0832	0.91 (0.82, 1.02) 0.0981	-0.02 (-0.05, 0.00) 0.1048	
MRAs at baseline						0.8730
Yes	530/1339 (39.6)	557/1325 (42.0)	0.94 (0.85, 1.03) 0.1630	0.90 (0.77, 1.05) 0.1815	-0.02 (-0.06, 0.01) 0.1900	
No	767/1787 (42.9)	822/1802 (45.6)	0.94 (0.88, 1.02) 0.1220	0.90 (0.79, 1.03) 0.1208	-0.03 (-0.06, 0.01) 0.1207	
ACEi+ARB at baseline						0.8157
Yes	926/2259 (41.0)	996/2276 (43.8)	0.93 (0.87, 1.00) 0.0519	0.89 (0.79, 1.00) 0.0602	-0.03 (-0.06, 0.00) 0.0635	
No	371/ 867 (42.8)	383/ 851 (45.0)	0.95 (0.85, 1.05) 0.3278	0.91 (0.75, 1.10) 0.3310	-0.02 (-0.07, 0.02) 0.3321	
ARNI at baseline						0.8652
Yes	64/ 165 (38.8)	54/ 136 (39.7)	0.94 (0.71, 1.24) 0.6714	0.88 (0.55, 1.41) 0.5910	-0.03 (-0.14, 0.08) 0.5512	
No	1233/2961 (41.6)	1325/2991 (44.3)	0.94 (0.89, 1.00) 0.0339	0.90 (0.81, 1.00) 0.0406	-0.03 (-0.05, -0.00) 0.0431	
Beta Blocker at baseline						0.7772
Yes	1059/2587 (40.9)	1117/2581 (43.3)	0.94 (0.88, 1.00) 0.0674	0.91 (0.81, 1.01) 0.0825	-0.02 (-0.05, 0.00) 0.0893	
No	238/ 539 (44.2)	262/ 546 (48.0)	0.92 (0.81, 1.05) 0.2059	0.86 (0.67, 1.09) 0.2056	-0.04 (-0.10, 0.02) 0.2051	
Diuretics at baseline						0.8502
Yes	1172/2789 (42.0)	1242/2783 (44.6)	0.94 (0.89, 1.00) 0.0450	0.90 (0.81, 1.00) 0.0489	-0.03 (-0.05, 0.00) 0.0504	
No	125/ 337 (37.1)	137/ 344 (39.8)	0.93 (0.77, 1.13) 0.4641	0.89 (0.65, 1.21) 0.4636	-0.03 (-0.10, 0.05) 0.4624	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event excluding mild/moderate Covid-19 events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	1353/3126 (43.3)	1433/3127 (45.8)	0.94 (0.89, 1.00) 0.0340	0.90 (0.82, 1.00) 0.0421	-0.03 (-0.05, -0.00) 0.0444	
Age						0.6133
<= median	631/1544 (40.9)	704/1602 (43.9)	0.93 (0.85, 1.00) 0.0592	0.88 (0.76, 1.01) 0.0774	-0.03 (-0.06, 0.00) 0.0861	
> median	722/1582 (45.6)	729/1525 (47.8)	0.95 (0.88, 1.03) 0.2169	0.92 (0.80, 1.06) 0.2244	-0.02 (-0.06, 0.01) 0.2253	
Gender						0.9717
Male	798/1765 (45.2)	835/1744 (47.9)	0.94 (0.88, 1.01) 0.1016	0.90 (0.78, 1.02) 0.1061	-0.03 (-0.06, 0.01) 0.1067	
Female	555/1361 (40.8)	598/1383 (43.2)	0.94 (0.86, 1.03) 0.1656	0.91 (0.78, 1.06) 0.2050	-0.02 (-0.06, 0.01) 0.2218	
Race						0.6695
White	973/2210 (44.0)	1033/2222 (46.5)	0.94 (0.88, 1.01) 0.0709	0.90 (0.80, 1.02) 0.0988	-0.02 (-0.05, 0.01) 0.1059	
Black or African	39/ 81 (48.1)	41/ 78 (52.6)	0.92 (0.68, 1.25) 0.5995	0.82 (0.44, 1.53) 0.5272	-0.05 (-0.20, 0.10) 0.5243	
Asian	272/ 629 (43.2)	303/ 643 (47.1)	0.92 (0.81, 1.04) 0.1610	0.85 (0.68, 1.06) 0.1565	-0.04 (-0.09, 0.02) 0.1552	
Other	69/ 206 (33.5)	56/ 184 (30.4)	1.13 (0.85, 1.52) 0.3938	1.18 (0.77, 1.82) 0.4425	0.03 (-0.06, 0.12) 0.5028	
Geographic region						0.8992
Asia	259/ 606 (42.7)	291/ 619 (47.0)	0.91 (0.80, 1.03) 0.1324	0.84 (0.67, 1.05) 0.1287	-0.04 (-0.10, 0.01) 0.1276	
Europe and Saudi Arabia	660/1491 (44.3)	696/1508 (46.2)	0.95 (0.88, 1.03) 0.2338	0.92 (0.80, 1.07) 0.2751	-0.02 (-0.05, 0.02) 0.2849	
North America	223/ 427 (52.2)	227/ 422 (53.8)	0.96 (0.85, 1.09) 0.5411	0.93 (0.71, 1.23) 0.6210	-0.02 (-0.08, 0.05) 0.6107	
Latin America	211/ 602 (35.0)	219/ 578 (37.9)	0.93 (0.80, 1.08) 0.3238	0.89 (0.70, 1.13) 0.3445	-0.03 (-0.08, 0.03) 0.3608	
NYHA class at enrolment						0.6610
II	962/2310 (41.6)	1050/2395 (43.8)	0.95 (0.89, 1.01) 0.0953	0.91 (0.81, 1.02) 0.1201	-0.02 (-0.05, 0.01) 0.1297	
III or IV	391/ 816 (47.9)	382/ 731 (52.3)	0.92 (0.83, 1.02) 0.0963	0.84 (0.69, 1.03) 0.0940	-0.04 (-0.09, 0.01) 0.0936	
LVEF at enrolment						0.6882
<= 49	470/1066 (44.1)	482/1047 (46.0)	0.95 (0.87, 1.05) 0.3068	0.92 (0.77, 1.09) 0.3329	-0.02 (-0.06, 0.02) 0.3390	
50-59	492/1132 (43.5)	507/1121 (45.2)	0.96 (0.88, 1.05) 0.3995	0.93 (0.79, 1.10) 0.4020	-0.02 (-0.06, 0.02) 0.4027	
>= 60	391/ 928 (42.1)	444/ 959 (46.3)	0.91 (0.82, 1.00) 0.0607	0.85 (0.71, 1.02) 0.0776	-0.04 (-0.08, 0.01) 0.0824	
NT-proBNP at enrolment						0.9829
<= median	601/1553 (38.7)	647/1574 (41.1)	0.94 (0.86, 1.02) 0.1599	0.90 (0.78, 1.04) 0.1682	-0.02 (-0.06, 0.01) 0.1733	
> median	752/1573 (47.8)	786/1552 (50.6)	0.94 (0.88, 1.01) 0.0871	0.89 (0.77, 1.03) 0.1097	-0.03 (-0.06, 0.01) 0.1102	
Type 2 Diabetes Medical History						0.3463
Yes	657/1399 (47.0)	716/1402 (51.1)	0.92 (0.85, 0.99)*0.0299	0.85 (0.73, 0.98)*0.0297	-0.04 (-0.08, -0.00)*0.0295	
No	696/1727 (40.3)	717/1725 (41.6)	0.97 (0.89, 1.05)*0.4502	0.95 (0.83, 1.09)*0.4501	-0.01 (-0.05, 0.02)*0.4501	
Atrial fibrillation or flutter at enrolment ECG						0.4611
Yes	585/1325 (44.2)	602/1317 (45.7)	0.96 (0.89, 1.05) 0.4030	0.94 (0.81, 1.10) 0.4321	-0.01 (-0.05, 0.02) 0.4386	
No	767/1800 (42.6)	831/1809 (45.9)	0.92 (0.86, 0.99) 0.0346	0.87 (0.76, 0.99) 0.0403	-0.03 (-0.07, -0.00) 0.0421	
BMI (kg/m2) at enrolment						0.9673
< 30	731/1732 (42.2)	775/1733 (44.7)	0.94 (0.87, 1.02) 0.1277	0.90 (0.79, 1.03) 0.1353	-0.02 (-0.06, 0.01) 0.1374	
>= 30	621/1392 (44.6)	657/1390 (47.3)	0.94 (0.87, 1.02) 0.1282	0.90 (0.77, 1.04) 0.1571	-0.03 (-0.06, 0.01) 0.1641	
Baseline eGFR (mL/min/1.73m^2)						0.7576
< 60	723/1514 (47.8)	787/1551 (50.7)	0.94 (0.87, 1.01) 0.0744	0.88 (0.77, 1.02) 0.0841	-0.03 (-0.07, 0.00) 0.0843	
>= 60	630/1612 (39.1)	646/1575 (41.0)	0.95 (0.88, 1.04) 0.2643	0.93 (0.80, 1.07) 0.2927	-0.02 (-0.05, 0.02) 0.3077	
SBP at randomisation						0.0288
<= median	692/1567 (44.2)	696/1588 (43.8)	1.00 (0.93, 1.08) 0.9642	1.01 (0.88, 1.16) 0.9160	0.00 (-0.03, 0.04) 0.9033	
> median	661/1559 (42.4)	737/1539 (47.9)	0.89 (0.82, 0.96) 0.0023	0.80 (0.70, 0.93) 0.0026	-0.05 (-0.09, -0.02) 0.0027	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
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Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.7768
<= 49	470/1066 (44.1)	482/1047 (46.0)	0.95 (0.87, 1.05) 0.3068	0.92 (0.77, 1.09) 0.3329	-0.02 (-0.06, 0.02) 0.3390	
>= 50	883/2060 (42.9)	951/2080 (45.7)	0.94 (0.87, 1.00) 0.0596	0.89 (0.79, 1.01) 0.0697	-0.03 (-0.06, 0.00) 0.0726	
Randomised during hospitalisation for HF or within 30 days of discharge						0.3037
Yes	164/ 328 (50.0)	185/ 326 (56.7)	0.88 (0.76, 1.01) 0.0738	0.75 (0.55, 1.02) 0.0685	-0.07 (-0.15, 0.01) 0.0679	
No	1189/2798 (42.5)	1248/2801 (44.6)	0.95 (0.90, 1.01) 0.1025	0.92 (0.83, 1.02) 0.1247	-0.02 (-0.05, 0.01) 0.1321	
MRAs at baseline						0.7560
Yes	557/1339 (41.6)	585/1325 (44.2)	0.94 (0.86, 1.02) 0.1376	0.90 (0.77, 1.05) 0.1661	-0.03 (-0.06, 0.01) 0.1761	
No	796/1787 (44.5)	848/1802 (47.1)	0.95 (0.89, 1.02) 0.1592	0.91 (0.80, 1.04) 0.1508	-0.02 (-0.06, 0.01) 0.1494	
ACEi+ARB at baseline						0.6629
Yes	965/2259 (42.7)	1037/2276 (45.6)	0.93 (0.88, 1.00) 0.0436	0.89 (0.79, 1.00) 0.0547	-0.03 (-0.06, 0.00) 0.0582	
No	388/ 867 (44.8)	396/ 851 (46.5)	0.96 (0.87, 1.06) 0.4383	0.93 (0.77, 1.12) 0.4335	-0.02 (-0.07, 0.03) 0.4328	
ARNI at baseline						0.9167
Yes	66/ 165 (40.0)	56/ 136 (41.2)	0.94 (0.71, 1.23) 0.6330	0.87 (0.54, 1.39) 0.5584	-0.04 (-0.15, 0.08) 0.5274	
No	1287/2961 (43.5)	1377/2991 (46.0)	0.94 (0.89, 1.00) 0.0389	0.90 (0.81, 1.00) 0.0487	-0.03 (-0.05, 0.00) 0.0514	
Beta Blocker at baseline						0.6414
Yes	1107/2587 (42.8)	1160/2581 (44.9)	0.95 (0.89, 1.01) 0.0847	0.91 (0.82, 1.02) 0.1115	-0.02 (-0.05, 0.01) 0.1205	
No	246/ 539 (45.6)	273/ 546 (50.0)	0.91 (0.81, 1.03) 0.1507	0.84 (0.66, 1.07) 0.1504	-0.04 (-0.10, 0.02) 0.1499	
Diuretics at baseline						0.7136
Yes	1226/2789 (44.0)	1292/2783 (46.4)	0.95 (0.89, 1.00) 0.0552	0.90 (0.81, 1.01) 0.0634	-0.02 (-0.05, 0.00) 0.0654	
No	127/ 337 (37.7)	141/ 344 (41.0)	0.92 (0.76, 1.11) 0.3819	0.87 (0.64, 1.18) 0.3781	-0.03 (-0.11, 0.04) 0.3750	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event excluding efficacy events and mild/moderate Covid-19 events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	821/3126 (26.3)	878/3127 (28.1)	0.93 (0.86, 1.01) 0.1041	0.91 (0.82, 1.02) 0.1060	-0.02 (-0.04, 0.00) 0.1098	
Age						0.8645
<= median	386/1544 (25.0)	426/1602 (26.6)	0.94 (0.83, 1.06) 0.3044	0.92 (0.78, 1.08) 0.3032	-0.02 (-0.05, 0.01) 0.3029	
> median	435/1582 (27.5)	452/1525 (29.6)	0.93 (0.83, 1.04) 0.1827	0.90 (0.77, 1.05) 0.1852	-0.02 (-0.05, 0.01) 0.1892	
Gender						0.3111
Male	469/1765 (26.6)	514/1744 (29.5)	0.90 (0.81, 1.00) 0.0558	0.86 (0.75, 1.00) 0.0539	-0.03 (-0.06, 0.00) 0.0511	
Female	352/1361 (25.9)	364/1383 (26.3)	0.98 (0.87, 1.11) 0.7682	0.98 (0.83, 1.16) 0.8100	-0.00 (-0.04, 0.03) 0.8882	
Race						0.1152
White	571/2210 (25.8)	611/2222 (27.5)	0.94 (0.85, 1.03) 0.1954	0.92 (0.80, 1.05) 0.2107	-0.02 (-0.04, 0.01) 0.2409	
Black or African	27/ 81 (33.3)	27/ 78 (34.6)	0.97 (0.63, 1.49) 0.8750	0.93 (0.48, 1.80) 0.8295	-0.02 (-0.17, 0.13) 0.7832	
Asian	193/ 629 (30.7)	225/ 643 (35.0)	0.88 (0.75, 1.03) 0.1019	0.82 (0.65, 1.04) 0.1013	-0.04 (-0.09, 0.01) 0.1006	
Other	30/ 206 (14.6)	15/ 184 (8.2)	1.87 (1.04, 3.36) 0.0373	1.98 (1.03, 3.83) 0.0412	0.06 (-0.01, 0.12) 0.0877	
Geographic region						0.8559
Asia	188/ 606 (31.0)	216/ 619 (34.9)	0.89 (0.76, 1.04) 0.1501	0.84 (0.66, 1.07) 0.1494	-0.04 (-0.09, 0.01) 0.1485	
Europe and Saudi Arabia	372/1491 (24.9)	386/1508 (25.6)	0.97 (0.86, 1.10) 0.6190	0.96 (0.82, 1.14) 0.6532	-0.01 (-0.04, 0.03) 0.7245	
North America	164/ 427 (38.4)	174/ 422 (41.2)	0.92 (0.78, 1.09) 0.3408	0.88 (0.67, 1.17) 0.3822	-0.03 (-0.09, 0.04) 0.4061	
Latin America	97/ 602 (16.1)	102/ 578 (17.6)	0.91 (0.71, 1.18) 0.4899	0.90 (0.66, 1.22) 0.4881	-0.02 (-0.06, 0.03) 0.4803	
NYHA class at enrolment						0.4945
II	599/2310 (25.9)	673/2395 (28.1)	0.92 (0.84, 1.01) 0.0825	0.89 (0.79, 1.02) 0.0905	-0.02 (-0.05, 0.00) 0.1060	
III or IV	222/ 816 (27.2)	204/ 731 (27.9)	0.98 (0.83, 1.15) 0.8212	0.97 (0.77, 1.21) 0.7820	-0.01 (-0.05, 0.04) 0.7179	
LVEF at enrolment						0.8440
<= 49	249/1066 (23.4)	267/1047 (25.5)	0.91 (0.79, 1.06) 0.2389	0.89 (0.73, 1.08) 0.2332	-0.02 (-0.06, 0.01) 0.2225	
50-59	312/1132 (27.6)	320/1121 (28.5)	0.97 (0.85, 1.10) 0.6026	0.95 (0.79, 1.15) 0.6057	-0.01 (-0.05, 0.03) 0.6111	
>= 60	260/ 928 (28.0)	291/ 959 (30.3)	0.92 (0.80, 1.06) 0.2710	0.90 (0.73, 1.09) 0.2814	-0.02 (-0.06, 0.02) 0.2973	
NT-proBNP at enrolment						0.5478
<= median	389/1553 (25.0)	411/1574 (26.1)	0.96 (0.85, 1.08) 0.4890	0.95 (0.81, 1.11) 0.4951	-0.01 (-0.04, 0.02) 0.5078	
> median	432/1573 (27.5)	467/1552 (30.1)	0.91 (0.82, 1.02) 0.1021	0.88 (0.75, 1.03) 0.1033	-0.03 (-0.06, 0.01) 0.1054	
Type 2 Diabetes Medical History						0.6422
Yes	401/1399 (28.7)	438/1402 (31.2)	0.92 (0.82, 1.03)*0.1367	0.88 (0.75, 1.04)*0.1365	-0.03 (-0.06, 0.01)*0.1363	
No	420/1727 (24.3)	440/1725 (25.5)	0.95 (0.85, 1.07)*0.4200	0.94 (0.80, 1.10)*0.4199	-0.01 (-0.04, 0.02)*0.4198	
Atrial fibrillation or flutter at enrolment ECG						0.5396
Yes	338/1325 (25.5)	371/1317 (28.2)	0.91 (0.80, 1.03) 0.1242	0.87 (0.74, 1.04) 0.1251	-0.03 (-0.06, 0.01) 0.1268	
No	482/1800 (26.8)	507/1809 (28.0)	0.95 (0.86, 1.06) 0.3815	0.94 (0.81, 1.09) 0.3871	-0.01 (-0.04, 0.02) 0.3978	
BMI (kg/m2) at enrolment						0.7859
< 30	435/1732 (25.1)	470/1733 (27.1)	0.93 (0.83, 1.04) 0.1779	0.90 (0.77, 1.05) 0.1793	-0.02 (-0.05, 0.01) 0.1819	
>= 30	386/1392 (27.7)	407/1390 (29.3)	0.95 (0.84, 1.06) 0.3593	0.93 (0.79, 1.09) 0.3617	-0.02 (-0.05, 0.02) 0.3671	
Baseline eGFR (mL/min/1.73m^2)						0.8739
< 60	455/1514 (30.1)	499/1551 (32.2)	0.93 (0.84, 1.04) 0.1871	0.90 (0.77, 1.05) 0.1838	-0.02 (-0.06, 0.01) 0.1803	
>= 60	366/1612 (22.7)	379/1575 (24.1)	0.94 (0.83, 1.07) 0.3701	0.93 (0.79, 1.09) 0.3760	-0.01 (-0.04, 0.02) 0.3897	
SBP at randomisation						0.0909
<= median	427/1567 (27.2)	430/1588 (27.1)	1.00 (0.89, 1.12) 0.9630	1.01 (0.86, 1.18) 0.9471	0.00 (-0.03, 0.03) 0.9205	
> median	394/1559 (25.3)	448/1539 (29.1)	0.87 (0.78, 0.98) 0.0197	0.83 (0.71, 0.97) 0.0188	-0.04 (-0.07, -0.01) 0.0176	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Event excluding efficacy events and mild/moderate Covid-19 events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.7100
<= 49	249/1066 (23.4)	267/1047 (25.5)	0.91 (0.79, 1.06) 0.2389	0.89 (0.73, 1.08) 0.2332	-0.02 (-0.06, 0.01) 0.2225	
>= 50	572/2060 (27.8)	611/2080 (29.4)	0.95 (0.86, 1.04) 0.2544	0.93 (0.81, 1.06) 0.2622	-0.02 (-0.04, 0.01) 0.2747	
Randomised during hospitalisation for HF or within 30 days of discharge						0.2256
Yes	87/ 328 (26.5)	106/ 326 (32.5)	0.81 (0.64, 1.03) 0.0896	0.74 (0.53, 1.04) 0.0805	-0.06 (-0.13, 0.00) 0.0680	
No	734/2798 (26.2)	772/2801 (27.6)	0.95 (0.87, 1.04) 0.2598	0.94 (0.83, 1.05) 0.2680	-0.01 (-0.04, 0.01) 0.2831	
MRAs at baseline						0.2961
Yes	314/1339 (23.5)	349/1325 (26.3)	0.89 (0.78, 1.01) 0.0788	0.85 (0.72, 1.02) 0.0805	-0.03 (-0.06, 0.00) 0.0841	
No	507/1787 (28.4)	529/1802 (29.4)	0.97 (0.88, 1.07) 0.5568	0.96 (0.83, 1.11) 0.5492	-0.01 (-0.04, 0.02) 0.5387	
ACEi+ARB at baseline						0.4103
Yes	576/2259 (25.5)	608/2276 (26.7)	0.95 (0.87, 1.05) 0.3547	0.94 (0.82, 1.07) 0.3546	-0.01 (-0.04, 0.01) 0.3549	
No	245/ 867 (28.3)	270/ 851 (31.7)	0.89 (0.77, 1.02) 0.1019	0.84 (0.69, 1.04) 0.1093	-0.03 (-0.08, 0.01) 0.1203	
ARNI at baseline						0.3937
Yes	34/ 165 (20.6)	35/ 136 (25.7)	0.75 (0.50, 1.14) 0.1822	0.69 (0.40, 1.19) 0.1813	-0.06 (-0.16, 0.03) 0.1811	
No	787/2961 (26.6)	843/2991 (28.2)	0.94 (0.87, 1.02) 0.1674	0.92 (0.82, 1.03) 0.1700	-0.02 (-0.04, 0.01) 0.1749	
Beta Blocker at baseline						0.1682
Yes	656/2587 (25.4)	718/2581 (27.8)	0.91 (0.83, 1.00) 0.0406	0.88 (0.78, 1.00) 0.0431	-0.02 (-0.05, -0.00) 0.0485	
No	165/ 539 (30.6)	160/ 546 (29.3)	1.04 (0.87, 1.25) 0.6496	1.06 (0.82, 1.38) 0.6436	0.01 (-0.04, 0.07) 0.6353	
Diuretics at baseline						0.1984
Yes	748/2789 (26.8)	784/2783 (28.2)	0.95 (0.87, 1.04) 0.2524	0.93 (0.83, 1.05) 0.2577	-0.01 (-0.04, 0.01) 0.2675	
No	73/ 337 (21.7)	94/ 344 (27.3)	0.79 (0.61, 1.03) 0.0873	0.74 (0.52, 1.04) 0.0863	-0.06 (-0.12, 0.01) 0.0848	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Severe Adverse Events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	913/3126 (29.2)	962/3127 (30.8)	0.95 (0.88, 1.02) 0.1626	0.93 (0.83, 1.03) 0.1767	-0.01 (-0.04, 0.01) 0.1984	
Age						0.3681
<= median	412/1544 (26.7)	467/1602 (29.2)	0.91 (0.81, 1.02) 0.0953	0.88 (0.75, 1.03) 0.1190	-0.02 (-0.05, 0.01) 0.1722	
> median	501/1582 (31.7)	495/1525 (32.5)	0.98 (0.88, 1.08) 0.6440	0.96 (0.83, 1.12) 0.6326	-0.01 (-0.04, 0.02) 0.6205	
Gender						0.7959
Male	554/1765 (31.4)	571/1744 (32.7)	0.95 (0.87, 1.05) 0.3389	0.94 (0.81, 1.08) 0.3704	-0.01 (-0.04, 0.02) 0.4095	
Female	359/1361 (26.4)	391/1383 (28.3)	0.93 (0.83, 1.06) 0.2783	0.91 (0.77, 1.08) 0.2799	-0.02 (-0.05, 0.02) 0.2842	
Race						0.4891
White	657/2210 (29.7)	693/2222 (31.2)	0.95 (0.87, 1.04) 0.2564	0.93 (0.82, 1.06) 0.2900	-0.01 (-0.04, 0.01) 0.3395	
Black or African	25/ 81 (30.9)	33/ 78 (42.3)	0.73 (0.48, 1.11) 0.1394	0.61 (0.32, 1.16) 0.1319	-0.12 (-0.27, 0.03) 0.1231	
Asian	169/ 629 (26.9)	185/ 643 (28.8)	0.93 (0.78, 1.11) 0.4332	0.91 (0.71, 1.16) 0.4273	-0.02 (-0.07, 0.03) 0.4194	
Other	62/ 206 (30.1)	51/ 184 (27.7)	1.11 (0.81, 1.51) 0.5241	1.15 (0.74, 1.78) 0.5418	0.03 (-0.06, 0.12) 0.5694	
Geographic region						0.9570
Asia	158/ 606 (26.1)	178/ 619 (28.8)	0.90 (0.75, 1.09) 0.2818	0.87 (0.68, 1.12) 0.2812	-0.03 (-0.08, 0.02) 0.2811	
Europe and Saudi Arabia	428/1491 (28.7)	449/1508 (29.8)	0.96 (0.86, 1.07) 0.4718	0.95 (0.81, 1.11) 0.4871	-0.01 (-0.04, 0.02) 0.5117	
North America	151/ 427 (35.4)	157/ 422 (37.2)	0.95 (0.80, 1.13) 0.5736	0.92 (0.70, 1.22) 0.5625	-0.02 (-0.08, 0.05) 0.5551	
Latin America	176/ 602 (29.2)	178/ 578 (30.8)	0.95 (0.80, 1.13) 0.5702	0.94 (0.73, 1.20) 0.6070	-0.01 (-0.06, 0.04) 0.6585	
NYHA class at enrolment						0.7155
II	630/2310 (27.3)	697/2395 (29.1)	0.93 (0.85, 1.02) 0.1408	0.91 (0.80, 1.04) 0.1533	-0.02 (-0.04, 0.01) 0.1764	
III or IV	283/ 816 (34.7)	264/ 731 (36.1)	0.96 (0.84, 1.10) 0.5648	0.94 (0.76, 1.16) 0.5684	-0.01 (-0.06, 0.03) 0.5716	
LVEF at enrolment						0.6849
<= 49	329/1066 (30.9)	333/1047 (31.8)	0.97 (0.85, 1.09) 0.5798	0.95 (0.79, 1.14) 0.5914	-0.01 (-0.05, 0.03) 0.6068	
50-59	329/1132 (29.1)	336/1121 (30.0)	0.97 (0.85, 1.10) 0.6379	0.96 (0.80, 1.15) 0.6388	-0.01 (-0.05, 0.03) 0.6404	
>= 60	255/ 928 (27.5)	293/ 959 (30.6)	0.90 (0.78, 1.03) 0.1367	0.87 (0.71, 1.06) 0.1611	-0.03 (-0.07, 0.01) 0.2052	
NT-proBNP at enrolment						0.8186
<= median	381/1553 (24.5)	413/1574 (26.2)	0.93 (0.83, 1.05) 0.2714	0.91 (0.78, 1.07) 0.2716	-0.02 (-0.05, 0.01) 0.2751	
> median	532/1573 (33.8)	549/1552 (35.4)	0.95 (0.87, 1.05) 0.3220	0.93 (0.80, 1.08) 0.3556	-0.01 (-0.05, 0.02) 0.3878	
Type 2 Diabetes Medical History						0.3717
Yes	459/1399 (32.8)	501/1402 (35.7)	0.92 (0.83, 1.02)*0.1031	0.88 (0.75, 1.03)*0.1029	-0.03 (-0.06, 0.01)*0.1027	
No	454/1727 (26.3)	461/1725 (26.7)	0.98 (0.88, 1.10)*0.7715	0.98 (0.84, 1.14)*0.7715	-0.00 (-0.03, 0.03)*0.7715	
Atrial fibrillation or flutter at enrolment ECG						0.4921
Yes	384/1325 (29.0)	390/1317 (29.6)	0.98 (0.87, 1.10) 0.7066	0.97 (0.82, 1.15) 0.7358	-0.00 (-0.04, 0.03) 0.7774	
No	528/1800 (29.3)	572/1809 (31.6)	0.93 (0.84, 1.02) 0.1234	0.89 (0.78, 1.03) 0.1263	-0.02 (-0.05, 0.01) 0.1317	
BMI (kg/m2) at enrolment						0.4806
< 30	494/1732 (28.5)	535/1733 (30.9)	0.92 (0.83, 1.02) 0.1254	0.89 (0.77, 1.03) 0.1300	-0.02 (-0.05, 0.01) 0.1371	
>= 30	418/1392 (30.0)	427/1390 (30.7)	0.97 (0.87, 1.09) 0.6441	0.97 (0.82, 1.14) 0.6866	-0.01 (-0.04, 0.03) 0.7502	
Baseline eGFR (mL/min/1.73m^2)						0.7095
< 60	495/1514 (32.7)	539/1551 (34.8)	0.94 (0.85, 1.04) 0.2049	0.91 (0.78, 1.05) 0.2015	-0.02 (-0.06, 0.01) 0.1988	
>= 60	418/1612 (25.9)	423/1575 (26.9)	0.97 (0.86, 1.08) 0.5475	0.96 (0.82, 1.12) 0.5965	-0.01 (-0.04, 0.02) 0.6886	
SBP at randomisation						0.3842
<= median	473/1567 (30.2)	486/1588 (30.6)	0.98 (0.88, 1.09) 0.6932	0.97 (0.84, 1.13) 0.7344	-0.00 (-0.04, 0.03) 0.7888	
> median	440/1559 (28.2)	476/1539 (30.9)	0.92 (0.82, 1.02) 0.1112	0.88 (0.76, 1.03) 0.1135	-0.03 (-0.06, 0.01) 0.1179	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Severe Adverse Events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.7139
<= 49	329/1066 (30.9)	333/1047 (31.8)	0.97 (0.85, 1.09) 0.5798	0.95 (0.79, 1.14) 0.5914	-0.01 (-0.05, 0.03) 0.6068	
>= 50	584/2060 (28.3)	629/2080 (30.2)	0.94 (0.85, 1.03) 0.1791	0.91 (0.80, 1.05) 0.1936	-0.02 (-0.05, 0.01) 0.2171	
Randomised during hospitalisation for HF or within 30 days of discharge						0.5733
Yes	115/ 328 (35.1)	113/ 326 (34.7)	1.00 (0.81, 1.24) 0.9670	1.01 (0.73, 1.39) 0.9691	0.00 (-0.07, 0.07) 0.9710	
No	798/2798 (28.5)	849/2801 (30.3)	0.94 (0.87, 1.02) 0.1335	0.92 (0.82, 1.03) 0.1473	-0.02 (-0.04, 0.01) 0.1698	
MRAs at baseline						0.3623
Yes	387/1339 (28.9)	417/1325 (31.5)	0.91 (0.81, 1.02) 0.1167	0.88 (0.75, 1.04) 0.1314	-0.03 (-0.06, 0.01) 0.1531	
No	526/1787 (29.4)	545/1802 (30.2)	0.98 (0.88, 1.08) 0.6525	0.97 (0.84, 1.12) 0.6489	-0.01 (-0.04, 0.02) 0.6453	
ACEi+ARB at baseline						0.9003
Yes	649/2259 (28.7)	691/2276 (30.4)	0.94 (0.86, 1.03) 0.2083	0.93 (0.81, 1.05) 0.2329	-0.01 (-0.04, 0.01) 0.2738	
No	264/ 867 (30.4)	271/ 851 (31.8)	0.96 (0.83, 1.10) 0.5220	0.94 (0.76, 1.15) 0.5199	-0.01 (-0.06, 0.03) 0.5177	
ARNI at baseline						0.3413
Yes	45/ 165 (27.3)	45/ 136 (33.1)	0.81 (0.57, 1.15) 0.2322	0.73 (0.44, 1.21) 0.2256	-0.07 (-0.17, 0.04) 0.2158	
No	868/2961 (29.3)	917/2991 (30.7)	0.96 (0.88, 1.03) 0.2473	0.94 (0.84, 1.05) 0.2700	-0.01 (-0.04, 0.01) 0.3045	
Beta Blocker at baseline						0.9579
Yes	743/2587 (28.7)	780/2581 (30.2)	0.95 (0.87, 1.03) 0.1992	0.93 (0.82, 1.05) 0.2252	-0.01 (-0.04, 0.01) 0.2685	
No	170/ 539 (31.5)	182/ 546 (33.3)	0.95 (0.80, 1.12) 0.5327	0.92 (0.71, 1.19) 0.5310	-0.02 (-0.07, 0.04) 0.5290	
Diuretics at baseline						0.7854
Yes	823/2789 (29.5)	862/2783 (31.0)	0.95 (0.88, 1.03) 0.2119	0.93 (0.83, 1.05) 0.2319	-0.01 (-0.04, 0.01) 0.2623	
No	90/ 337 (26.7)	100/ 344 (29.1)	0.92 (0.72, 1.17) 0.4930	0.89 (0.64, 1.24) 0.4923	-0.02 (-0.09, 0.04) 0.4911	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Non-Severe Adverse Events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	1749/3126 (56.0)	1861/3127 (59.5)	0.94 (0.90, 0.98) 0.0039	0.86 (0.78, 0.96) 0.0043	-0.04 (-0.06, -0.01) 0.0042	
Age						0.7743
<= median	836/1544 (54.1)	917/1602 (57.2)	0.94 (0.89, 1.00) 0.0620	0.88 (0.77, 1.02) 0.0797	-0.03 (-0.07, 0.00) 0.0757	
> median	913/1582 (57.7)	944/1525 (61.9)	0.93 (0.88, 0.99) 0.0173	0.84 (0.73, 0.97) 0.0173	-0.04 (-0.08, -0.01) 0.0171	
Gender						0.0123
Male	965/1765 (54.7)	1064/1744 (61.0)	0.89 (0.85, 0.95) 0.0001	0.77 (0.67, 0.88) 0.0001	-0.06 (-0.10, -0.03) 0.0001	
Female	784/1361 (57.6)	797/1383 (57.6)	1.00 (0.94, 1.07) 0.9928	1.00 (0.86, 1.16) 0.9889	-0.00 (-0.04, 0.04) 0.9899	
Race						0.3547
White	1237/2210 (56.0)	1344/2222 (60.5)	0.93 (0.88, 0.97) 0.0023	0.83 (0.74, 0.94) 0.0023	-0.05 (-0.07, -0.02) 0.0023	
Black or African	54/ 81 (66.7)	60/ 78 (76.9)	0.85 (0.70, 1.03) 0.1007	0.59 (0.29, 1.19) 0.1403	-0.11 (-0.25, 0.03) 0.1096	
Asian	363/ 629 (57.7)	377/ 643 (58.6)	0.98 (0.90, 1.08) 0.7249	0.96 (0.77, 1.20) 0.7287	-0.01 (-0.06, 0.04) 0.7276	
Other	95/ 206 (46.1)	80/ 184 (43.5)	1.07 (0.86, 1.34) 0.5264	1.14 (0.76, 1.71) 0.5160	0.03 (-0.07, 0.13) 0.5137	
Geographic region						0.6810
Asia	348/ 606 (57.4)	361/ 619 (58.3)	0.98 (0.89, 1.08) 0.7455	0.96 (0.77, 1.21) 0.7470	-0.01 (-0.06, 0.05) 0.7465	
Europe and Saudi Arabia	792/1491 (53.1)	852/1508 (56.5)	0.94 (0.88, 1.00) 0.0630	0.87 (0.76, 1.01) 0.0630	-0.03 (-0.07, 0.00) 0.0628	
North America	296/ 427 (69.3)	316/ 422 (74.9)	0.92 (0.85, 1.01) 0.0676	0.76 (0.56, 1.02) 0.0709	-0.06 (-0.12, 0.00) 0.0680	
Latin America	313/ 602 (52.0)	332/ 578 (57.4)	0.91 (0.82, 1.01) 0.0829	0.81 (0.65, 1.02) 0.0783	-0.05 (-0.11, 0.01) 0.0784	
NYHA class at enrolment						0.5053
II	1325/2310 (57.4)	1445/2395 (60.3)	0.95 (0.91, 1.00) 0.0350	0.88 (0.79, 0.99) 0.0379	-0.03 (-0.06, -0.00) 0.0369	
III or IV	424/ 816 (52.0)	415/ 731 (56.8)	0.92 (0.84, 1.01) 0.0677	0.83 (0.68, 1.01) 0.0623	-0.05 (-0.10, 0.00) 0.0627	
LVEF at enrolment						0.4355
<= 49	554/1066 (52.0)	571/1047 (54.5)	0.95 (0.88, 1.03) 0.2327	0.90 (0.76, 1.07) 0.2320	-0.03 (-0.07, 0.02) 0.2316	
50-59	637/1132 (56.3)	694/1121 (61.9)	0.91 (0.85, 0.97) 0.0059	0.79 (0.67, 0.94) 0.0066	-0.06 (-0.10, -0.02) 0.0062	
>= 60	558/ 928 (60.1)	596/ 959 (62.1)	0.97 (0.90, 1.04) 0.3596	0.92 (0.76, 1.11) 0.3743	-0.02 (-0.06, 0.02) 0.3688	
NT-proBNP at enrolment						0.7613
<= median	855/1553 (55.1)	915/1574 (58.1)	0.95 (0.89, 1.01) 0.0809	0.88 (0.77, 1.02) 0.0826	-0.03 (-0.07, 0.00) 0.0821	
> median	894/1573 (56.8)	945/1552 (60.9)	0.93 (0.88, 0.99) 0.0209	0.85 (0.73, 0.97) 0.0210	-0.04 (-0.08, -0.01) 0.0208	
Type 2 Diabetes Medical History						0.3336
Yes	798/1399 (57.0)	870/1402 (62.1)	0.92 (0.86, 0.98)*0.0070	0.81 (0.70, 0.94)*0.0069	-0.05 (-0.09, -0.01)*0.0068	
No	951/1727 (55.1)	991/1725 (57.4)	0.96 (0.90, 1.02)*0.1584	0.91 (0.79, 1.04)*0.1583	-0.02 (-0.06, 0.01)*0.1581	
Atrial fibrillation or flutter at enrolment ECG						0.5718
Yes	732/1325 (55.2)	785/1317 (59.6)	0.93 (0.87, 0.99) 0.0238	0.84 (0.72, 0.98) 0.0234	-0.04 (-0.08, -0.01) 0.0233	
No	1017/1800 (56.5)	1075/1809 (59.4)	0.95 (0.90, 1.00) 0.0647	0.89 (0.78, 1.01) 0.0730	-0.03 (-0.06, 0.00) 0.0704	
BMI (kg/m2) at enrolment						0.0759
< 30	956/1732 (55.2)	982/1733 (56.7)	0.97 (0.92, 1.03) 0.3838	0.94 (0.82, 1.08) 0.3841	-0.01 (-0.05, 0.02) 0.3840	
>= 30	792/1392 (56.9)	876/1390 (63.0)	0.90 (0.85, 0.96) 0.0011	0.77 (0.67, 0.90) 0.0010	-0.06 (-0.10, -0.02) 0.0010	
Baseline eGFR (mL/min/1.73m^2)						0.5424
< 60	896/1514 (59.2)	963/1551 (62.1)	0.95 (0.90, 1.01) 0.0873	0.88 (0.76, 1.02) 0.0912	-0.03 (-0.06, 0.00) 0.0895	
>= 60	853/1612 (52.9)	898/1575 (57.0)	0.93 (0.87, 0.99) 0.0209	0.85 (0.74, 0.97) 0.0194	-0.04 (-0.08, -0.01) 0.0196	
SBP at randomisation						0.1923
<= median	883/1567 (56.3)	925/1588 (58.2)	0.97 (0.91, 1.03) 0.2781	0.93 (0.80, 1.07) 0.2797	-0.02 (-0.05, 0.02) 0.2792	
> median	866/1559 (55.5)	936/1539 (60.8)	0.91 (0.86, 0.97) 0.0029	0.81 (0.70, 0.93) 0.0033	-0.05 (-0.09, -0.02) 0.0031	

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Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Non-Severe Adverse Events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.6910
<= 49	554/1066 (52.0)	571/1047 (54.5)	0.95 (0.88, 1.03) 0.2327	0.90 (0.76, 1.07) 0.2320	-0.03 (-0.07, 0.02) 0.2316	
>= 50	1195/2060 (58.0)	1290/2080 (62.0)	0.93 (0.89, 0.98) 0.0076	0.85 (0.75, 0.96) 0.0087	-0.04 (-0.07, -0.01) 0.0083	
Randomised during hospitalisation for HF or within 30 days of discharge						0.0876
Yes	158/ 328 (48.2)	188/ 326 (57.7)	0.83 (0.72, 0.96) 0.0132	0.68 (0.50, 0.92) 0.0135	-0.10 (-0.17, -0.02) 0.0128	
No	1591/2798 (56.9)	1673/2801 (59.7)	0.95 (0.91, 0.99) 0.0279	0.89 (0.80, 0.99) 0.0300	-0.03 (-0.05, -0.00) 0.0293	
MRAs at baseline						0.7627
Yes	716/1339 (53.5)	759/1325 (57.3)	0.93 (0.87, 1.00) 0.0474	0.86 (0.74, 1.00) 0.0477	-0.04 (-0.08, -0.00) 0.0474	
No	1033/1787 (57.8)	1102/1802 (61.2)	0.94 (0.90, 1.00) 0.0396	0.87 (0.76, 1.00) 0.0432	-0.03 (-0.07, -0.00) 0.0419	
ACEi+ARB at baseline						0.2596
Yes	1250/2259 (55.3)	1360/2276 (59.8)	0.93 (0.88, 0.97) 0.0026	0.83 (0.74, 0.94) 0.0026	-0.04 (-0.07, -0.02) 0.0026	
No	499/ 867 (57.6)	501/ 851 (58.9)	0.98 (0.90, 1.06) 0.5468	0.94 (0.78, 1.14) 0.5630	-0.01 (-0.06, 0.03) 0.5581	
ARNI at baseline						0.9679
Yes	90/ 165 (54.5)	79/ 136 (58.1)	0.93 (0.76, 1.13) 0.4620	0.84 (0.53, 1.33) 0.4517	-0.04 (-0.16, 0.07) 0.4530	
No	1659/2961 (56.0)	1782/2991 (59.6)	0.94 (0.90, 0.98) 0.0052	0.86 (0.78, 0.96) 0.0057	-0.04 (-0.06, -0.01) 0.0055	
Beta Blocker at baseline						0.6807
Yes	1445/2587 (55.9)	1527/2581 (59.2)	0.94 (0.90, 0.99) 0.0142	0.87 (0.78, 0.97) 0.0159	-0.03 (-0.06, -0.01) 0.0153	
No	304/ 539 (56.4)	334/ 546 (61.2)	0.92 (0.83, 1.02) 0.1124	0.82 (0.64, 1.04) 0.1086	-0.05 (-0.11, 0.01) 0.1090	
Diuretics at baseline						0.2918
Yes	1582/2789 (56.7)	1693/2783 (60.8)	0.93 (0.89, 0.97) 0.0016	0.84 (0.76, 0.94) 0.0018	-0.04 (-0.07, -0.02) 0.0017	
No	167/ 337 (49.6)	168/ 344 (48.8)	1.01 (0.87, 1.18) 0.8538	1.03 (0.76, 1.39) 0.8504	0.01 (-0.07, 0.08) 0.8503	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events leading to discontinuation of study drug
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	183/3126 (5.9)	181/3127 (5.8)	1.01 (0.83, 1.24) 0.9068	1.01 (0.82, 1.25) 0.9104	0.00 (-0.01, 0.01) 0.9656	
Age						0.9504
<= median	74/1544 (4.8)	77/1602 (4.8)	1.00 (0.73, 1.36) 0.9859	1.00 (0.72, 1.38) 0.9857	-0.00 (-0.02, 0.01) 0.9828	
> median	109/1582 (6.9)	104/1525 (6.8)	1.01 (0.78, 1.31) 0.9326	1.01 (0.77, 1.34) 0.9348	0.00 (-0.02, 0.02) 0.9641	
Gender						0.0805
Male	84/1765 (4.8)	98/1744 (5.6)	0.85 (0.64, 1.13) 0.2528	0.84 (0.62, 1.13) 0.2526	-0.01 (-0.02, 0.01) 0.2511	
Female	99/1361 (7.3)	83/1383 (6.0)	1.21 (0.91, 1.60) 0.1846	1.23 (0.91, 1.66) 0.1872	0.01 (-0.01, 0.03) 0.2306	
Race						0.0638
White	143/2210 (6.5)	122/2222 (5.5)	1.18 (0.93, 1.49) 0.1684	1.19 (0.93, 1.53) 0.1692	0.01 (-0.00, 0.02) 0.1834	
Black or African	3/ 81 (3.7)	6/ 78 (7.7)	0.47 (0.12, 1.80) 0.2696	0.45 (0.11, 1.88) 0.2754	-0.04 (-0.12, 0.04) 0.3528	
Asian	35/ 629 (5.6)	47/ 643 (7.3)	0.76 (0.50, 1.17) 0.2110	0.75 (0.48, 1.18) 0.2097	-0.02 (-0.04, 0.01) 0.1958	
Other	2/ 206 (1.0)	6/ 184 (3.3)	0.28 (0.06, 1.38) 0.1181	0.27 (0.05, 1.37) 0.1153	-0.02 (-0.05, 0.01)*0.1210	
Geographic region						0.0141
Asia	34/ 606 (5.6)	47/ 619 (7.6)	0.74 (0.48, 1.13) 0.1676	0.72 (0.46, 1.14) 0.1664	-0.02 (-0.05, 0.01) 0.1527	
Europe and Saudi Arabia	106/1491 (7.1)	76/1508 (5.0)	1.41 (1.06, 1.88) 0.0176	1.44 (1.07, 1.96) 0.0176	0.02 (0.00, 0.04) 0.0194	
North America	35/ 427 (8.2)	45/ 422 (10.7)	0.77 (0.50, 1.17) 0.2212	0.75 (0.47, 1.19) 0.2208	-0.02 (-0.06, 0.01) 0.2209	
Latin America	8/ 602 (1.3)	13/ 578 (2.2)	0.57 (0.24, 1.38) 0.2139	0.57 (0.23, 1.38) 0.2103	-0.01 (-0.03, 0.00) 0.0530	
NYHA class at enrolment						0.6397
II	151/2310 (6.5)	150/2395 (6.3)	1.05 (0.84, 1.30) 0.6858	1.05 (0.83, 1.32) 0.6934	0.00 (-0.01, 0.02) 0.8021	
III or IV	32/ 816 (3.9)	31/ 731 (4.2)	0.93 (0.57, 1.50) 0.7601	0.92 (0.56, 1.53) 0.7583	-0.00 (-0.02, 0.02) 0.7157	
LVEF at enrolment						0.2566
<= 49	56/1066 (5.3)	62/1047 (5.9)	0.89 (0.63, 1.26) 0.5131	0.88 (0.61, 1.28) 0.5138	-0.01 (-0.03, 0.01) 0.5269	
50-59	72/1132 (6.4)	56/1121 (5.0)	1.27 (0.91, 1.79) 0.1626	1.29 (0.90, 1.85) 0.1632	0.01 (-0.01, 0.03) 0.1762	
>= 60	55/ 928 (5.9)	63/ 959 (6.6)	0.90 (0.63, 1.28) 0.5549	0.89 (0.61, 1.30) 0.5489	-0.01 (-0.03, 0.01) 0.4667	
NT-proBNP at enrolment						0.0927
<= median	83/1553 (5.3)	68/1574 (4.3)	1.24 (0.91, 1.69) 0.1807	1.25 (0.90, 1.74) 0.1821	0.01 (-0.01, 0.02) 0.2170	
> median	100/1573 (6.4)	113/1552 (7.3)	0.87 (0.67, 1.13) 0.3071	0.86 (0.65, 1.14) 0.3065	-0.01 (-0.03, 0.01) 0.2995	
Type 2 Diabetes Medical History						0.2434
Yes	78/1399 (5.6)	88/1402 (6.3)	0.89 (0.66, 1.19)*0.4322	0.88 (0.64, 1.21)*0.4321	-0.01 (-0.02, 0.01)*0.4318	
No	105/1727 (6.1)	93/1725 (5.4)	1.13 (0.86, 1.48)*0.3847	1.14 (0.85, 1.51)*0.3846	0.01 (-0.01, 0.02)*0.3842	
Atrial fibrillation or flutter at enrolment ECG						0.4759
Yes	79/1325 (6.0)	71/1317 (5.4)	1.11 (0.81, 1.51) 0.5257	1.11 (0.80, 1.55) 0.5258	0.01 (-0.01, 0.02) 0.5265	
No	104/1800 (5.8)	110/1809 (6.1)	0.95 (0.74, 1.24) 0.7235	0.95 (0.72, 1.25) 0.7117	-0.00 (-0.02, 0.01) 0.5464	
BMI (kg/m2) at enrolment						0.5839
< 30	99/1732 (5.7)	103/1733 (5.9)	0.96 (0.74, 1.26) 0.7792	0.96 (0.72, 1.27) 0.7743	-0.00 (-0.02, 0.01) 0.6996	
>= 30	84/1392 (6.0)	78/1390 (5.6)	1.08 (0.80, 1.45) 0.6340	1.08 (0.79, 1.48) 0.6339	0.00 (-0.01, 0.02) 0.6325	
Baseline eGFR (mL/min/1.73m^2)						0.1199
< 60	108/1514 (7.1)	123/1551 (7.9)	0.90 (0.71, 1.16) 0.4291	0.90 (0.68, 1.17) 0.4242	-0.01 (-0.03, 0.01) 0.3725	
>= 60	75/1612 (4.7)	58/1575 (3.7)	1.26 (0.90, 1.76) 0.1789	1.27 (0.90, 1.80) 0.1790	0.01 (-0.00, 0.02) 0.1850	
SBP at randomisation						0.5611
<= median	96/1567 (6.1)	91/1588 (5.7)	1.07 (0.81, 1.42) 0.6153	1.08 (0.80, 1.45) 0.6099	0.01 (-0.01, 0.02) 0.5321	
> median	87/1559 (5.6)	90/1539 (5.8)	0.95 (0.72, 1.27) 0.7449	0.95 (0.70, 1.29) 0.7418	-0.00 (-0.02, 0.01) 0.6917	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events leading to discontinuation of study drug
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.3814
<= 49	56/1066 (5.3)	62/1047 (5.9)	0.89 (0.63, 1.26) 0.5131	0.88 (0.61, 1.28) 0.5138	-0.01 (-0.03, 0.01) 0.5269	
>= 50	127/2060 (6.2)	119/2080 (5.7)	1.08 (0.84, 1.37) 0.5506	1.08 (0.84, 1.40) 0.5554	0.00 (-0.01, 0.02) 0.6300	
Randomised during hospitalisation for HF or within 30 days of discharge						0.1133
Yes	16/ 328 (4.9)	25/ 326 (7.7)	0.62 (0.34, 1.14) 0.1272	0.60 (0.31, 1.15) 0.1219	-0.03 (-0.07, 0.00) 0.0624	
No	167/2798 (6.0)	156/2801 (5.6)	1.07 (0.87, 1.32) 0.5240	1.07 (0.86, 1.35) 0.5292	0.00 (-0.01, 0.02) 0.6175	
MRAs at baseline						0.2972
Yes	64/1339 (4.8)	72/1325 (5.4)	0.89 (0.64, 1.23) 0.4663	0.88 (0.62, 1.24) 0.4715	-0.00 (-0.02, 0.01) 0.5779	
No	119/1787 (6.7)	109/1802 (6.0)	1.10 (0.86, 1.41) 0.4569	1.11 (0.85, 1.45) 0.4603	0.01 (-0.01, 0.02) 0.5060	
ACEi+ARB at baseline						0.6837
Yes	123/2259 (5.4)	126/2276 (5.5)	0.98 (0.77, 1.25) 0.8900	0.98 (0.76, 1.27) 0.8904	-0.00 (-0.01, 0.01) 0.8961	
No	60/ 867 (6.9)	55/ 851 (6.5)	1.08 (0.76, 1.53) 0.6868	1.08 (0.74, 1.58) 0.6953	0.00 (-0.02, 0.03) 0.8111	
ARNI at baseline						0.1605
Yes	7/ 165 (4.2)	11/ 136 (8.1)	0.56 (0.22, 1.43) 0.2265	0.54 (0.20, 1.45) 0.2201	-0.04 (-0.09, 0.02) 0.1656	
No	176/2961 (5.9)	170/2991 (5.7)	1.05 (0.85, 1.28) 0.6717	1.05 (0.84, 1.30) 0.6742	0.00 (-0.01, 0.01) 0.7134	
Beta Blocker at baseline						0.0666
Yes	149/2587 (5.8)	133/2581 (5.2)	1.12 (0.89, 1.40) 0.3341	1.13 (0.88, 1.43) 0.3351	0.01 (-0.01, 0.02) 0.3527	
No	34/ 539 (6.3)	48/ 546 (8.8)	0.72 (0.47, 1.09) 0.1196	0.69 (0.44, 1.09) 0.1162	-0.03 (-0.06, 0.00) 0.0862	
Diuretics at baseline						0.4444
Yes	164/2789 (5.9)	166/2783 (6.0)	0.99 (0.80, 1.22) 0.8992	0.98 (0.79, 1.23) 0.8941	-0.00 (-0.01, 0.01) 0.8174	
No	19/ 337 (5.6)	15/ 344 (4.4)	1.29 (0.67, 2.50) 0.4485	1.31 (0.66, 2.63) 0.4437	0.02 (-0.02, 0.05) 0.3509	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events leading to discontinuation of study drug
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	79/3126 (2.5)	100/3127 (3.2)	0.79 (0.59, 1.06) 0.1124	0.78 (0.58, 1.06) 0.1126	-0.01 (-0.01, 0.00) 0.1220	
Age						0.7558
<= median	30/1544 (1.9)	42/1602 (2.6)	0.74 (0.47, 1.18) 0.2053	0.74 (0.46, 1.18) 0.2044	-0.01 (-0.02, 0.00) 0.1667	
> median	49/1582 (3.1)	58/1525 (3.8)	0.81 (0.56, 1.18) 0.2818	0.81 (0.55, 1.19) 0.2824	-0.01 (-0.02, 0.01) 0.3037	
Gender						0.4772
Male	43/1765 (2.4)	59/1744 (3.4)	0.72 (0.49, 1.06) 0.0972	0.71 (0.48, 1.06) 0.0974	-0.01 (-0.02, 0.00) 0.1069	
Female	36/1361 (2.6)	41/1383 (3.0)	0.89 (0.57, 1.39) 0.6103	0.89 (0.56, 1.40) 0.6104	-0.00 (-0.02, 0.01) 0.6142	
Race						0.0127
White	64/2210 (2.9)	64/2222 (2.9)	1.01 (0.71, 1.41) 0.9748	1.01 (0.71, 1.43) 0.9752	0.00 (-0.01, 0.01) 0.9902	
Black or African	1/ 81 (1.2)	5/ 78 (6.4)	0.18 (0.02, 1.54) 0.1181	0.17 (0.02, 1.51) 0.1122	-0.05 (-0.11, 0.01)*0.0879	
Asian	14/ 629 (2.2)	27/ 643 (4.2)	0.53 (0.28, 1.01) 0.0533	0.52 (0.27, 1.01) 0.0531	-0.02 (-0.04, 0.00) 0.0734	
Other	0/ 206 (0.0)	4/ 184 (2.2)	0.00 (0.00,) 0.9999	0.10 (0.01, 1.82)*0.1186	-0.02 (-0.04, -0.00)*0.0432	
Geographic region						0.0004
Asia	13/ 606 (2.1)	27/ 619 (4.4)	0.50 (0.26, 0.95) 0.0348	0.48 (0.25, 0.95) 0.0343	-0.02 (-0.04, -0.00) 0.0412	
Europe and Saudi Arabia	52/1491 (3.5)	35/1508 (2.3)	1.50 (0.98, 2.29) 0.0603	1.52 (0.98, 2.34) 0.0601	0.01 (-0.00, 0.02) 0.0629	
North America	11/ 427 (2.6)	30/ 422 (7.1)	0.36 (0.18, 0.71) 0.0033	0.35 (0.17, 0.70) 0.0031	-0.05 (-0.08, -0.02) 0.0011	
Latin America	3/ 602 (0.5)	8/ 578 (1.4)	0.35 (0.09, 1.33) 0.1241	0.35 (0.09, 1.33) 0.1230	-0.01 (-0.02, 0.00)*0.1165	
NYHA class at enrolment						0.3163
II	66/2310 (2.9)	80/2395 (3.3)	0.86 (0.62, 1.18) 0.3409	0.85 (0.61, 1.19) 0.3413	-0.00 (-0.01, 0.01) 0.3543	
III or IV	13/ 816 (1.6)	20/ 731 (2.7)	0.58 (0.29, 1.16) 0.1251	0.58 (0.28, 1.17) 0.1248	-0.01 (-0.03, 0.00) 0.1123	
LVEF at enrolment						0.8045
<= 49	26/1066 (2.4)	36/1047 (3.4)	0.71 (0.43, 1.17) 0.1752	0.70 (0.42, 1.17) 0.1747	-0.01 (-0.03, 0.00) 0.1528	
50-59	29/1132 (2.6)	32/1121 (2.9)	0.90 (0.55, 1.47) 0.6688	0.89 (0.54, 1.49) 0.6688	-0.00 (-0.02, 0.01) 0.6660	
>= 60	24/ 928 (2.6)	32/ 959 (3.3)	0.77 (0.46, 1.30) 0.3280	0.76 (0.45, 1.31) 0.3271	-0.01 (-0.02, 0.01) 0.3052	
NT-proBNP at enrolment						0.2691
<= median	31/1553 (2.0)	32/1574 (2.0)	0.98 (0.60, 1.60) 0.9419	0.98 (0.60, 1.62) 0.9415	-0.00 (-0.01, 0.01) 0.9218	
> median	48/1573 (3.1)	68/1552 (4.4)	0.70 (0.48, 1.00) 0.0507	0.69 (0.47, 1.00) 0.0506	-0.01 (-0.03, 0.00) 0.0526	
Type 2 Diabetes Medical History						0.4202
Yes	41/1399 (2.9)	46/1402 (3.3)	0.89 (0.59, 1.35)*0.5933	0.89 (0.58, 1.36)*0.5932	-0.00 (-0.02, 0.01)*0.5930	
No	38/1727 (2.2)	54/1725 (3.1)	0.70 (0.47, 1.06)*0.0916	0.70 (0.46, 1.06)*0.0914	-0.01 (-0.02, 0.00)*0.0897	
Atrial fibrillation or flutter at enrolment ECG						0.8393
Yes	33/1325 (2.5)	40/1317 (3.0)	0.82 (0.52, 1.29) 0.3929	0.82 (0.51, 1.30) 0.3927	-0.01 (-0.02, 0.01) 0.3889	
No	46/1800 (2.6)	60/1809 (3.3)	0.77 (0.53, 1.13) 0.1779	0.77 (0.52, 1.13) 0.1788	-0.01 (-0.02, 0.00) 0.2112	
BMI (kg/m2) at enrolment						0.5384
< 30	43/1732 (2.5)	59/1733 (3.4)	0.73 (0.49, 1.07) 0.1095	0.72 (0.48, 1.08) 0.1098	-0.01 (-0.02, 0.00) 0.1251	
>= 30	36/1392 (2.6)	41/1390 (2.9)	0.88 (0.56, 1.36) 0.5598	0.87 (0.55, 1.38) 0.5589	-0.00 (-0.02, 0.01) 0.5255	
Baseline eGFR (mL/min/1.73m^2)						0.5294
< 60	46/1514 (3.0)	64/1551 (4.1)	0.74 (0.51, 1.07) 0.1099	0.73 (0.50, 1.07) 0.1105	-0.01 (-0.02, 0.00) 0.1284	
>= 60	33/1612 (2.0)	36/1575 (2.3)	0.89 (0.56, 1.43) 0.6398	0.89 (0.55, 1.44) 0.6399	-0.00 (-0.01, 0.01) 0.6459	
SBP at randomisation						0.3343
<= median	43/1567 (2.7)	48/1588 (3.0)	0.91 (0.61, 1.37) 0.6545	0.91 (0.60, 1.38) 0.6594	-0.00 (-0.01, 0.01) 0.8305	
> median	36/1559 (2.3)	52/1539 (3.4)	0.68 (0.45, 1.04) 0.0767	0.68 (0.44, 1.04) 0.0765	-0.01 (-0.02, 0.00) 0.0740	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events leading to discontinuation of study drug
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.6032
<= 49	26/1066 (2.4)	36/1047 (3.4)	0.71 (0.43, 1.17) 0.1752	0.70 (0.42, 1.17) 0.1747	-0.01 (-0.03, 0.00) 0.1528	
>= 50	53/2060 (2.6)	64/2080 (3.1)	0.83 (0.58, 1.20) 0.3244	0.83 (0.57, 1.20) 0.3246	-0.00 (-0.02, 0.01) 0.3356	
Randomised during hospitalisation for HF or within 30 days of discharge						0.9397
Yes	10/ 328 (3.0)	13/ 326 (4.0)	0.74 (0.33, 1.67) 0.4692	0.73 (0.31, 1.69) 0.4592	-0.02 (-0.04, 0.01) 0.1838	
No	69/2798 (2.5)	87/2801 (3.1)	0.79 (0.58, 1.08) 0.1441	0.79 (0.57, 1.09) 0.1448	-0.01 (-0.01, 0.00) 0.1717	
MRAs at baseline						0.3213
Yes	24/1339 (1.8)	37/1325 (2.8)	0.64 (0.39, 1.07) 0.0900	0.64 (0.38, 1.07) 0.0905	-0.01 (-0.02, 0.00) 0.1186	
No	55/1787 (3.1)	63/1802 (3.5)	0.88 (0.62, 1.26) 0.4804	0.88 (0.61, 1.27) 0.4805	-0.00 (-0.02, 0.01) 0.4822	
ACEi+ARB at baseline						0.9530
Yes	56/2259 (2.5)	71/2276 (3.1)	0.79 (0.56, 1.12) 0.1921	0.79 (0.55, 1.13) 0.1921	-0.01 (-0.02, 0.00) 0.1888	
No	23/ 867 (2.7)	29/ 851 (3.4)	0.78 (0.46, 1.34) 0.3680	0.77 (0.44, 1.35) 0.3678	-0.01 (-0.02, 0.01) 0.3717	
ARNI at baseline						0.7920
Yes	4/ 165 (2.4)	5/ 136 (3.7)	0.71 (0.19, 2.61) 0.6018	0.70 (0.18, 2.70) 0.6043	-0.01 (-0.05, 0.03) 0.7128	
No	75/2961 (2.5)	95/2991 (3.2)	0.80 (0.59, 1.07) 0.1364	0.79 (0.58, 1.08) 0.1365	-0.01 (-0.01, 0.00) 0.1429	
Beta Blocker at baseline						0.1060
Yes	65/2587 (2.5)	72/2581 (2.8)	0.90 (0.65, 1.25) 0.5356	0.90 (0.64, 1.26) 0.5357	-0.00 (-0.01, 0.01) 0.5375	
No	14/ 539 (2.6)	28/ 546 (5.1)	0.50 (0.27, 0.95) 0.0332	0.49 (0.26, 0.94) 0.0325	-0.03 (-0.05, -0.00) 0.0269	
Diuretics at baseline						0.5265
Yes	74/2789 (2.7)	91/2783 (3.3)	0.81 (0.60, 1.10) 0.1751	0.81 (0.59, 1.10) 0.1754	-0.01 (-0.01, 0.00) 0.1897	
No	5/ 337 (1.5)	9/ 344 (2.6)	0.57 (0.19, 1.68) 0.3056	0.56 (0.19, 1.69) 0.3033	-0.02 (-0.04, 0.01) 0.1572	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events leading to death
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	507/3126 (16.2)	529/3127 (16.9)	0.96 (0.86, 1.07) 0.4505	0.95 (0.83, 1.09) 0.4562	-0.01 (-0.03, 0.01) 0.4810	
Age						0.5960
<= median	205/1544 (13.3)	231/1602 (14.4)	0.92 (0.77, 1.09) 0.3332	0.91 (0.74, 1.11) 0.3490	-0.01 (-0.03, 0.01) 0.4508	
> median	302/1582 (19.1)	298/1525 (19.5)	0.98 (0.85, 1.13) 0.7503	0.97 (0.81, 1.16) 0.7487	-0.00 (-0.03, 0.02) 0.7439	
Gender						0.6732
Male	318/1765 (18.0)	334/1744 (19.2)	0.94 (0.82, 1.08) 0.3713	0.93 (0.78, 1.10) 0.3788	-0.01 (-0.04, 0.01) 0.4054	
Female	189/1361 (13.9)	195/1383 (14.1)	0.99 (0.82, 1.19) 0.8881	0.98 (0.79, 1.22) 0.8868	-0.00 (-0.03, 0.02) 0.8801	
Race						0.4514
White	387/2210 (17.5)	402/2222 (18.1)	0.97 (0.85, 1.10) 0.6055	0.96 (0.82, 1.12) 0.6133	-0.01 (-0.03, 0.02) 0.6422	
Black or African	10/ 81 (12.3)	17/ 78 (21.8)	0.57 (0.28, 1.16) 0.1190	0.50 (0.21, 1.18) 0.1142	-0.10 (-0.21, 0.02) 0.0994	
Asian	68/ 629 (10.8)	67/ 643 (10.4)	1.03 (0.75, 1.42) 0.8375	1.04 (0.72, 1.48) 0.8470	0.00 (-0.03, 0.04) 0.9192	
Other	42/ 206 (20.4)	43/ 184 (23.4)	0.87 (0.60, 1.27) 0.4861	0.84 (0.52, 1.37) 0.4873	-0.03 (-0.11, 0.05) 0.4908	
Geographic region						0.6122
Asia	59/ 606 (9.7)	66/ 619 (10.7)	0.91 (0.65, 1.27) 0.5779	0.90 (0.62, 1.30) 0.5766	-0.01 (-0.04, 0.02) 0.5693	
Europe and Saudi Arabia	271/1491 (18.2)	270/1508 (17.9)	1.01 (0.87, 1.18) 0.8657	1.02 (0.84, 1.22) 0.8627	0.00 (-0.02, 0.03) 0.8524	
North America	63/ 427 (14.8)	77/ 422 (18.2)	0.81 (0.60, 1.10) 0.1722	0.77 (0.54, 1.11) 0.1678	-0.04 (-0.09, 0.01) 0.1525	
Latin America	114/ 602 (18.9)	116/ 578 (20.1)	0.94 (0.75, 1.19) 0.6229	0.93 (0.70, 1.24) 0.6222	-0.01 (-0.06, 0.03) 0.6190	
NYHA class at enrolment						0.8845
II	331/2310 (14.3)	364/2395 (15.2)	0.94 (0.82, 1.08) 0.3858	0.93 (0.79, 1.10) 0.3914	-0.01 (-0.03, 0.01) 0.4214	
III or IV	176/ 816 (21.6)	165/ 731 (22.6)	0.96 (0.79, 1.15) 0.6316	0.94 (0.74, 1.20) 0.6316	-0.01 (-0.05, 0.03) 0.6317	
LVEF at enrolment						0.5212
<= 49	197/1066 (18.5)	207/1047 (19.8)	0.93 (0.78, 1.11) 0.4326	0.92 (0.74, 1.14) 0.4343	-0.01 (-0.05, 0.02) 0.4405	
50-59	178/1132 (15.7)	169/1121 (15.1)	1.04 (0.86, 1.27) 0.6666	1.05 (0.84, 1.32) 0.6692	0.01 (-0.02, 0.04) 0.6805	
>= 60	132/ 928 (14.2)	153/ 959 (16.0)	0.89 (0.72, 1.10) 0.2913	0.88 (0.68, 1.13) 0.3192	-0.01 (-0.04, 0.02) 0.4765	
NT-proBNP at enrolment						0.9547
<= median	182/1553 (11.7)	194/1574 (12.3)	0.95 (0.79, 1.15) 0.5954	0.94 (0.76, 1.17) 0.6021	-0.01 (-0.03, 0.02) 0.6475	
> median	325/1573 (20.7)	335/1552 (21.6)	0.96 (0.84, 1.09) 0.5184	0.95 (0.80, 1.12) 0.5222	-0.01 (-0.04, 0.02) 0.5337	
Type 2 Diabetes Medical History						0.7954
Yes	246/1399 (17.6)	261/1402 (18.6)	0.94 (0.81, 1.11)*0.4781	0.93 (0.77, 1.13)*0.4781	-0.01 (-0.04, 0.02)*0.4780	
No	261/1727 (15.1)	268/1725 (15.5)	0.97 (0.83, 1.14)*0.7299	0.97 (0.80, 1.16)*0.7299	-0.00 (-0.03, 0.02)*0.7299	
Atrial fibrillation or flutter at enrolment ECG						0.4304
Yes	229/1325 (17.3)	226/1317 (17.2)	1.01 (0.85, 1.19) 0.9291	1.01 (0.83, 1.24) 0.9217	0.00 (-0.03, 0.03) 0.8940	
No	278/1800 (15.4)	303/1809 (16.7)	0.92 (0.79, 1.07) 0.2780	0.91 (0.76, 1.08) 0.2796	-0.01 (-0.04, 0.01) 0.2878	
BMI (kg/m2) at enrolment						0.4937
< 30	278/1732 (16.1)	301/1733 (17.4)	0.92 (0.80, 1.07) 0.2931	0.91 (0.76, 1.09) 0.2986	-0.01 (-0.04, 0.01) 0.3216	
>= 30	228/1392 (16.4)	228/1390 (16.4)	1.00 (0.84, 1.18) 0.9838	1.00 (0.82, 1.22) 0.9843	-0.00 (-0.03, 0.03) 0.9862	
Baseline eGFR (mL/min/1.73m^2)						0.7200
< 60	296/1514 (19.6)	309/1551 (19.9)	0.98 (0.85, 1.13) 0.7716	0.97 (0.82, 1.16) 0.7756	-0.00 (-0.03, 0.02) 0.7882	
>= 60	211/1612 (13.1)	220/1575 (14.0)	0.94 (0.79, 1.12) 0.4839	0.93 (0.76, 1.14) 0.4893	-0.01 (-0.03, 0.02) 0.5207	
SBP at randomisation						0.9589
<= median	266/1567 (17.0)	281/1588 (17.7)	0.96 (0.82, 1.11) 0.5592	0.95 (0.79, 1.14) 0.5626	-0.01 (-0.03, 0.02) 0.5763	
> median	241/1559 (15.5)	248/1539 (16.1)	0.96 (0.82, 1.13) 0.6343	0.96 (0.79, 1.16) 0.6408	-0.01 (-0.03, 0.02) 0.6705	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events leading to death
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.7084
<= 49	197/1066 (18.5)	207/1047 (19.8)	0.93 (0.78, 1.11) 0.4326	0.92 (0.74, 1.14) 0.4343	-0.01 (-0.05, 0.02) 0.4405	
>= 50	310/2060 (15.0)	322/2080 (15.5)	0.97 (0.84, 1.12) 0.7069	0.97 (0.82, 1.15) 0.7149	-0.00 (-0.03, 0.02) 0.7529	
Randomised during hospitalisation for HF or within 30 days of discharge						0.8121
Yes	77/ 328 (23.5)	82/ 326 (25.2)	0.93 (0.71, 1.22) 0.6086	0.91 (0.64, 1.30) 0.6056	-0.02 (-0.08, 0.05) 0.5992	
No	430/2798 (15.4)	447/2801 (16.0)	0.96 (0.85, 1.09) 0.5414	0.96 (0.83, 1.11) 0.5510	-0.01 (-0.02, 0.01) 0.5948	
MRAs at baseline						0.6069
Yes	224/1339 (16.7)	238/1325 (18.0)	0.93 (0.79, 1.10) 0.3842	0.92 (0.75, 1.12) 0.3881	-0.01 (-0.04, 0.02) 0.4035	
No	283/1787 (15.8)	291/1802 (16.1)	0.98 (0.85, 1.14) 0.8305	0.98 (0.82, 1.17) 0.8331	-0.00 (-0.03, 0.02) 0.8453	
ACEi+ARB at baseline						0.9067
Yes	362/2259 (16.0)	379/2276 (16.7)	0.96 (0.84, 1.10) 0.5607	0.96 (0.82, 1.12) 0.5724	-0.01 (-0.03, 0.02) 0.6239	
No	145/ 867 (16.7)	150/ 851 (17.6)	0.95 (0.77, 1.17) 0.6159	0.94 (0.73, 1.20) 0.6139	-0.01 (-0.05, 0.03) 0.6065	
ARNI at baseline						0.4150
Yes	24/ 165 (14.5)	25/ 136 (18.4)	0.79 (0.47, 1.32) 0.3663	0.75 (0.40, 1.39) 0.3644	-0.04 (-0.13, 0.05) 0.3516	
No	483/2961 (16.3)	504/2991 (16.9)	0.97 (0.86, 1.08) 0.5772	0.96 (0.84, 1.10) 0.5872	-0.00 (-0.02, 0.01) 0.6295	
Beta Blocker at baseline						0.1245
Yes	421/2587 (16.3)	420/2581 (16.3)	1.00 (0.88, 1.13) 0.9821	1.00 (0.86, 1.16) 0.9879	0.00 (-0.02, 0.02) 0.9880	
No	86/ 539 (16.0)	109/ 546 (20.0)	0.80 (0.62, 1.03) 0.0861	0.76 (0.55, 1.04) 0.0821	-0.04 (-0.09, 0.00) 0.0690	
Diuretics at baseline						0.8612
Yes	468/2789 (16.8)	486/2783 (17.5)	0.96 (0.86, 1.08) 0.4917	0.95 (0.83, 1.10) 0.4978	-0.01 (-0.03, 0.01) 0.5228	
No	39/ 337 (11.6)	43/ 344 (12.5)	0.93 (0.62, 1.39) 0.7121	0.92 (0.58, 1.45) 0.7109	-0.01 (-0.06, 0.04) 0.7034	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events of Special Interest: Major Hypoglycaemic Events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	8/3126 (0.3)	7/3127 (0.2)	1.14 (0.41, 3.14) 0.7986	1.14 (0.41, 3.16) 0.7973	0.00 (-0.00, 0.00)*0.7955	
Age						NC
<= median	4/1544 (0.3)	3/1602 (0.2)	NC	NC	NC	
> median	4/1582 (0.3)	4/1525 (0.3)	NC	NC	NC	
Gender						NC
Male	3/1765 (0.2)	3/1744 (0.2)	NC	NC	NC	
Female	5/1361 (0.4)	4/1383 (0.3)	NC	NC	NC	
Race						NC
White	4/2210 (0.2)	4/2222 (0.2)	NC	NC	NC	
Black or African	1/ 81 (1.2)	1/ 78 (1.3)	NC	NC	NC	
Asian	2/ 629 (0.3)	2/ 643 (0.3)	NC	NC	NC	
Other	1/ 206 (0.5)	0/ 184 (0.0)	NC	NC	NC	
Geographic region						NC
Asia	2/ 606 (0.3)	2/ 619 (0.3)	NC	NC	NC	
Europe and Saudi Arabia	2/1491 (0.1)	1/1508 (0.1)	NC	NC	NC	
North America	3/ 427 (0.7)	2/ 422 (0.5)	NC	NC	NC	
Latin America	1/ 602 (0.2)	2/ 578 (0.3)	NC	NC	NC	
NYHA class at enrolment						NC
II	4/2310 (0.2)	5/2395 (0.2)	NC	NC	NC	
III or IV	4/ 816 (0.5)	2/ 731 (0.3)	NC	NC	NC	
LVEF at enrolment						NC
<= 49	2/1066 (0.2)	2/1047 (0.2)	NC	NC	NC	
50-59	4/1132 (0.4)	3/1121 (0.3)	NC	NC	NC	
>= 60	2/ 928 (0.2)	2/ 959 (0.2)	NC	NC	NC	
NT-proBNP at enrolment						NC
<= median	3/1553 (0.2)	4/1574 (0.3)	NC	NC	NC	
> median	5/1573 (0.3)	3/1552 (0.2)	NC	NC	NC	
Type 2 Diabetes Medical History						0.2847
Yes	6/1399 (0.4)	7/1402 (0.5)	0.86 (0.29, 2.55)*0.7842	0.86 (0.29, 2.56)*0.7842	-0.00 (-0.01, 0.00)*0.7840	
No	2/1727 (0.1)	0/1725 (0.0)	4.99 (0.24,104.0)*0.2991	5.00 (0.24,104.2)*0.2990	0.00 (-0.00, 0.00)*0.1571	
Atrial fibrillation or flutter at enrolment ECG						NC
Yes	4/1325 (0.3)	2/1317 (0.2)	NC	NC	NC	
No	4/1800 (0.2)	5/1809 (0.3)	NC	NC	NC	
BMI (kg/m2) at enrolment						NC
< 30	4/1732 (0.2)	4/1733 (0.2)	NC	NC	NC	
>= 30	4/1392 (0.3)	3/1390 (0.2)	NC	NC	NC	
Baseline eGFR (mL/min/1.73m^2)						0.4686
< 60	6/1514 (0.4)	4/1551 (0.3)	1.49 (0.42, 5.25) 0.5380	1.49 (0.42, 5.30) 0.5371	0.00 (-0.00, 0.01)*0.5028	
>= 60	2/1612 (0.1)	3/1575 (0.2)	0.67 (0.11, 3.98) 0.6569	0.67 (0.11, 4.00) 0.6576	-0.00 (-0.00, 0.00)*0.6366	
SBP at randomisation						0.7348
<= median	3/1567 (0.2)	2/1588 (0.1)	1.45 (0.24, 8.68) 0.6811	1.52 (0.25, 9.12)*0.6462	0.00 (-0.00, 0.00)*0.6442	
> median	5/1559 (0.3)	5/1539 (0.3)	1.01 (0.29, 3.47) 0.9901	1.01 (0.29, 3.50) 0.9883	-0.00 (-0.00, 0.00)*0.9837	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events of Special Interest: Major Hypoglycaemic Events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.8266
<= 49	2/1066 (0.2)	2/1047 (0.2)	0.96 (0.14, 6.81) 0.9685	0.96 (0.14, 6.85) 0.9693	-0.00 (-0.00, 0.00)*0.9856	
>= 50	6/2060 (0.3)	5/2080 (0.2)	1.23 (0.38, 4.02) 0.7316	1.23 (0.38, 4.05) 0.7307	0.00 (-0.00, 0.00)*0.7506	
Randomised during hospitalisation for HF or within 30 days of discharge						0.2637
Yes	1/ 328 (0.3)	0/ 326 (0.0)	2.98 (0.12,72.93)*0.5030	2.99 (0.12,73.69)*0.5028	0.00 (-0.00, 0.01)*0.3166	
No	7/2798 (0.3)	7/2801 (0.2)	1.01 (0.35, 2.87) 0.9895	1.01 (0.35, 2.88) 0.9879	0.00 (-0.00, 0.00)*0.9984	
MRAs at baseline						0.1579
Yes	1/1339 (0.1)	3/1325 (0.2)	0.31 (0.03, 3.01) 0.3146	0.33 (0.03, 3.17)*0.3364	-0.00 (-0.00, 0.00)*0.3131	
No	7/1787 (0.4)	4/1802 (0.2)	1.80 (0.53, 6.13) 0.3483	1.80 (0.53, 6.18) 0.3474	0.00 (-0.00, 0.01)*0.3582	
ACEi+ARB at baseline						0.2583
Yes	7/2259 (0.3)	7/2276 (0.3)	1.01 (0.36, 2.87) 0.9851	1.01 (0.35, 2.89) 0.9833	0.00 (-0.00, 0.00)*0.9888	
No	1/ 867 (0.1)	0/ 851 (0.0)	2.94 (0.12,72.18)*0.5082	2.95 (0.12,72.47)*0.5081	0.00 (-0.00, 0.00)*0.3170	
ARNI at baseline						1.0000
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NE	NE	NE	
No	8/2961 (0.3)	7/2991 (0.2)	1.16 (0.42, 3.20) 0.7693	1.17 (0.42, 3.22) 0.7680	0.00 (-0.00, 0.00)*0.7810	
Beta Blocker at baseline						1.0000
Yes	8/2587 (0.3)	7/2581 (0.3)	1.13 (0.41, 3.11) 0.8110	1.13 (0.41, 3.13) 0.8094	0.00 (-0.00, 0.00)*0.7994	
No	0/ 539 (0.0)	0/ 546 (0.0)	NE	NE	NE	
Diuretics at baseline						0.9290
Yes	7/2789 (0.3)	6/2783 (0.2)	1.16 (0.39, 3.45) 0.7862	1.16 (0.39, 3.47) 0.7850	0.00 (-0.00, 0.00)*0.7842	
No	1/ 337 (0.3)	1/ 344 (0.3)	1.01 (0.06,16.05) 0.9925	1.02 (0.06,16.39)*0.9884	0.00 (-0.01, 0.01)*0.9884	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events of Special Interest: Major Hypoglycaemic Events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	5/3126 (0.2)	1/3127 (0.0)	5.00 (0.58,42.72) 0.1418	5.01 (0.58,42.87) 0.1417	0.00 (-0.00, 0.00)*0.1022	
Age						NC
<= median	2/1544 (0.1)	0/1602 (0.0)	NC	NC	NC	
> median	3/1582 (0.2)	1/1525 (0.1)	NC	NC	NC	
Gender						NC
Male	3/1765 (0.2)	0/1744 (0.0)	NC	NC	NC	
Female	2/1361 (0.1)	1/1383 (0.1)	NC	NC	NC	
Race						NC
White	3/2210 (0.1)	1/2222 (0.0)	NC	NC	NC	
Black or African	0/ 81 (0.0)	0/ 78 (0.0)	NC	NC	NC	
Asian	2/ 629 (0.3)	0/ 643 (0.0)	NC	NC	NC	
Other	0/ 206 (0.0)	0/ 184 (0.0)	NC	NC	NC	
Geographic region						NC
Asia	2/ 606 (0.3)	0/ 619 (0.0)	NC	NC	NC	
Europe and Saudi Arabia	1/1491 (0.1)	1/1508 (0.1)	NC	NC	NC	
North America	2/ 427 (0.5)	0/ 422 (0.0)	NC	NC	NC	
Latin America	0/ 602 (0.0)	0/ 578 (0.0)	NC	NC	NC	
NYHA class at enrolment						NC
II	2/2310 (0.1)	1/2395 (0.0)	NC	NC	NC	
III or IV	3/ 816 (0.4)	0/ 731 (0.0)	NC	NC	NC	
LVEF at enrolment						NC
<= 49	1/1066 (0.1)	0/1047 (0.0)	NC	NC	NC	
50-59	3/1132 (0.3)	0/1121 (0.0)	NC	NC	NC	
>= 60	1/ 928 (0.1)	1/ 959 (0.1)	NC	NC	NC	
NT-proBNP at enrolment						NC
<= median	2/1553 (0.1)	1/1574 (0.1)	NC	NC	NC	
> median	3/1573 (0.2)	0/1552 (0.0)	NC	NC	NC	
Type 2 Diabetes Medical History						NC
Yes	4/1399 (0.3)	1/1402 (0.1)	NC	NC	NC	
No	1/1727 (0.1)	0/1725 (0.0)	NC	NC	NC	
Atrial fibrillation or flutter at enrolment ECG						NC
Yes	3/1325 (0.2)	0/1317 (0.0)	NC	NC	NC	
No	2/1800 (0.1)	1/1809 (0.1)	NC	NC	NC	
BMI (kg/m2) at enrolment						NC
< 30	2/1732 (0.1)	0/1733 (0.0)	NC	NC	NC	
>= 30	3/1392 (0.2)	1/1390 (0.1)	NC	NC	NC	
Baseline eGFR (mL/min/1.73m^2)						NC
< 60	4/1514 (0.3)	1/1551 (0.1)	NC	NC	NC	
>= 60	1/1612 (0.1)	0/1575 (0.0)	NC	NC	NC	
SBP at randomisation						NC
<= median	2/1567 (0.1)	0/1588 (0.0)	NC	NC	NC	
> median	3/1559 (0.2)	1/1539 (0.1)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events of Special Interest: Major Hypoglycaemic Events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						NC
<= 49	1/1066 (0.1)	0/1047 (0.0)	NC	NC	NC	
>= 50	4/2060 (0.2)	1/2080 (0.0)	NC	NC	NC	
Randomised during hospitalisation for HF or within 30 days of discharge						NC
Yes	0/ 328 (0.0)	0/ 326 (0.0)	NC	NC	NC	
No	5/2798 (0.2)	1/2801 (0.0)	NC	NC	NC	
MRAs at baseline						NC
Yes	0/1339 (0.0)	1/1325 (0.1)	NC	NC	NC	
No	5/1787 (0.3)	0/1802 (0.0)	NC	NC	NC	
ACEi+ARB at baseline						NC
Yes	4/2259 (0.2)	1/2276 (0.0)	NC	NC	NC	
No	1/ 867 (0.1)	0/ 851 (0.0)	NC	NC	NC	
ARNI at baseline						NC
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NC	NC	NC	
No	5/2961 (0.2)	1/2991 (0.0)	NC	NC	NC	
Beta Blocker at baseline						NC
Yes	5/2587 (0.2)	1/2581 (0.0)	NC	NC	NC	
No	0/ 539 (0.0)	0/ 546 (0.0)	NC	NC	NC	
Diuretics at baseline						NC
Yes	5/2789 (0.2)	1/2783 (0.0)	NC	NC	NC	
No	0/ 337 (0.0)	0/ 344 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Severe Adverse Events of Special Interest: Major Hypoglycaemic Events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	2/3126 (0.1)	2/3127 (0.1)	1.00 (0.14, 7.09) 0.9994	1.00 (0.14, 7.10) 0.9996	0.00 (-0.00, 0.00)*0.9997	
Age						NC
<= median	0/1544 (0.0)	1/1602 (0.1)	NC	NC	NC	
> median	2/1582 (0.1)	1/1525 (0.1)	NC	NC	NC	
Gender						NC
Male	1/1765 (0.1)	1/1744 (0.1)	NC	NC	NC	
Female	1/1361 (0.1)	1/1383 (0.1)	NC	NC	NC	
Race						NC
White	0/2210 (0.0)	2/2222 (0.1)	NC	NC	NC	
Black or African	0/ 81 (0.0)	0/ 78 (0.0)	NC	NC	NC	
Asian	1/ 629 (0.2)	0/ 643 (0.0)	NC	NC	NC	
Other	1/ 206 (0.5)	0/ 184 (0.0)	NC	NC	NC	
Geographic region						NC
Asia	1/ 606 (0.2)	0/ 619 (0.0)	NC	NC	NC	
Europe and Saudi Arabia	0/1491 (0.0)	1/1508 (0.1)	NC	NC	NC	
North America	0/ 427 (0.0)	0/ 422 (0.0)	NC	NC	NC	
Latin America	1/ 602 (0.2)	1/ 578 (0.2)	NC	NC	NC	
NYHA class at enrolment						NC
II	2/2310 (0.1)	1/2395 (0.0)	NC	NC	NC	
III or IV	0/ 816 (0.0)	1/ 731 (0.1)	NC	NC	NC	
LVEF at enrolment						NC
<= 49	1/1066 (0.1)	1/1047 (0.1)	NC	NC	NC	
50-59	0/1132 (0.0)	0/1121 (0.0)	NC	NC	NC	
>= 60	1/ 928 (0.1)	1/ 959 (0.1)	NC	NC	NC	
NT-proBNP at enrolment						NC
<= median	1/1553 (0.1)	1/1574 (0.1)	NC	NC	NC	
> median	1/1573 (0.1)	1/1552 (0.1)	NC	NC	NC	
Type 2 Diabetes Medical History						NC
Yes	1/1399 (0.1)	2/1402 (0.1)	NC	NC	NC	
No	1/1727 (0.1)	0/1725 (0.0)	NC	NC	NC	
Atrial fibrillation or flutter at enrolment ECG						NC
Yes	1/1325 (0.1)	0/1317 (0.0)	NC	NC	NC	
No	1/1800 (0.1)	2/1809 (0.1)	NC	NC	NC	
BMI (kg/m2) at enrolment						NC
< 30	2/1732 (0.1)	1/1733 (0.1)	NC	NC	NC	
>= 30	0/1392 (0.0)	1/1390 (0.1)	NC	NC	NC	
Baseline eGFR (mL/min/1.73m^2)						NC
< 60	2/1514 (0.1)	2/1551 (0.1)	NC	NC	NC	
>= 60	0/1612 (0.0)	0/1575 (0.0)	NC	NC	NC	
SBP at randomisation						NC
<= median	1/1567 (0.1)	1/1588 (0.1)	NC	NC	NC	
> median	1/1559 (0.1)	1/1539 (0.1)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Severe Adverse Events of Special Interest: Major Hypoglycaemic Events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						NC
<= 49	1/1066 (0.1)	1/1047 (0.1)	NC	NC	NC	
>= 50	1/2060 (0.0)	1/2080 (0.0)	NC	NC	NC	
Randomised during hospitalisation for HF or within 30 days of discharge						NC
Yes	0/ 328 (0.0)	0/ 326 (0.0)	NC	NC	NC	
No	2/2798 (0.1)	2/2801 (0.1)	NC	NC	NC	
MRAs at baseline						NC
Yes	1/1339 (0.1)	2/1325 (0.2)	NC	NC	NC	
No	1/1787 (0.1)	0/1802 (0.0)	NC	NC	NC	
ACEi+ARB at baseline						NC
Yes	2/2259 (0.1)	2/2276 (0.1)	NC	NC	NC	
No	0/ 867 (0.0)	0/ 851 (0.0)	NC	NC	NC	
ARNI at baseline						NC
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NC	NC	NC	
No	2/2961 (0.1)	2/2991 (0.1)	NC	NC	NC	
Beta Blocker at baseline						NC
Yes	2/2587 (0.1)	2/2581 (0.1)	NC	NC	NC	
No	0/ 539 (0.0)	0/ 546 (0.0)	NC	NC	NC	
Diuretics at baseline						NC
Yes	1/2789 (0.0)	2/2783 (0.1)	NC	NC	NC	
No	1/ 337 (0.3)	0/ 344 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Non-Severe Adverse Events of Special Interest: Major Hypoglycaemic Events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	6/3126 (0.2)	5/3127 (0.2)	1.20 (0.37, 3.92) 0.7649	1.20 (0.37, 3.94) 0.7642	0.00 (-0.00, 0.00)*0.7624	
Age						NC
<= median	4/1544 (0.3)	2/1602 (0.1)	NC	NC	NC	
> median	2/1582 (0.1)	3/1525 (0.2)	NC	NC	NC	
Gender						NC
Male	2/1765 (0.1)	2/1744 (0.1)	NC	NC	NC	
Female	4/1361 (0.3)	3/1383 (0.2)	NC	NC	NC	
Race						NC
White	4/2210 (0.2)	2/2222 (0.1)	NC	NC	NC	
Black or African	1/ 81 (1.2)	1/ 78 (1.3)	NC	NC	NC	
Asian	1/ 629 (0.2)	2/ 643 (0.3)	NC	NC	NC	
Other	0/ 206 (0.0)	0/ 184 (0.0)	NC	NC	NC	
Geographic region						NC
Asia	1/ 606 (0.2)	2/ 619 (0.3)	NC	NC	NC	
Europe and Saudi Arabia	2/1491 (0.1)	0/1508 (0.0)	NC	NC	NC	
North America	3/ 427 (0.7)	2/ 422 (0.5)	NC	NC	NC	
Latin America	0/ 602 (0.0)	1/ 578 (0.2)	NC	NC	NC	
NYHA class at enrolment						NC
II	2/2310 (0.1)	4/2395 (0.2)	NC	NC	NC	
III or IV	4/ 816 (0.5)	1/ 731 (0.1)	NC	NC	NC	
LVEF at enrolment						NC
<= 49	1/1066 (0.1)	1/1047 (0.1)	NC	NC	NC	
50-59	4/1132 (0.4)	3/1121 (0.3)	NC	NC	NC	
>= 60	1/ 928 (0.1)	1/ 959 (0.1)	NC	NC	NC	
NT-proBNP at enrolment						NC
<= median	2/1553 (0.1)	3/1574 (0.2)	NC	NC	NC	
> median	4/1573 (0.3)	2/1552 (0.1)	NC	NC	NC	
Type 2 Diabetes Medical History						0.5315
Yes	5/1399 (0.4)	5/1402 (0.4)	1.00 (0.29, 3.45)*0.9973	1.00 (0.29, 3.47)*0.9973	0.00 (-0.00, 0.00)*0.9973	
No	1/1727 (0.1)	0/1725 (0.0)	3.00 (0.12,73.51)*0.5015	3.00 (0.12,73.65)*0.5014	0.00 (-0.00, 0.00)*0.3172	
Atrial fibrillation or flutter at enrolment ECG						NC
Yes	3/1325 (0.2)	2/1317 (0.2)	NC	NC	NC	
No	3/1800 (0.2)	3/1809 (0.2)	NC	NC	NC	
BMI (kg/m2) at enrolment						NC
< 30	2/1732 (0.1)	3/1733 (0.2)	NC	NC	NC	
>= 30	4/1392 (0.3)	2/1390 (0.1)	NC	NC	NC	
Baseline eGFR (mL/min/1.73m^2)						NC
< 60	4/1514 (0.3)	2/1551 (0.1)	NC	NC	NC	
>= 60	2/1612 (0.1)	3/1575 (0.2)	NC	NC	NC	
SBP at randomisation						NC
<= median	2/1567 (0.1)	1/1588 (0.1)	NC	NC	NC	
> median	4/1559 (0.3)	4/1539 (0.3)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Non-Severe Adverse Events of Special Interest: Major Hypoglycaemic Events
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						NC
<= 49	1/1066 (0.1)	1/1047 (0.1)	NC	NC	NC	
>= 50	5/2060 (0.2)	4/2080 (0.2)	NC	NC	NC	
Randomised during hospitalisation for HF or within 30 days of discharge						0.2694
Yes	1/ 328 (0.3)	0/ 326 (0.0)	2.98 (0.12,72.93)*0.5030	2.99 (0.12,73.69)*0.5028	0.00 (-0.00, 0.01)*0.3166	
No	5/2798 (0.2)	5/2801 (0.2)	1.01 (0.29, 3.48) 0.9895	1.01 (0.29, 3.49) 0.9888	0.00 (-0.00, 0.00)*0.9986	
MRAs at baseline						0.1805
Yes	0/1339 (0.0)	1/1325 (0.1)	0.33 (0.01, 8.09)*0.4969	0.33 (0.01, 8.10)*0.4968	-0.00 (-0.00, 0.00)*0.3171	
No	6/1787 (0.3)	4/1802 (0.2)	1.55 (0.44, 5.48) 0.4964	1.55 (0.44, 5.52) 0.4956	0.00 (-0.00, 0.00)*0.5182	
ACEi+ARB at baseline						0.2632
Yes	5/2259 (0.2)	5/2276 (0.2)	1.01 (0.29, 3.48) 0.9862	1.01 (0.29, 3.50) 0.9853	0.00 (-0.00, 0.00)*0.9905	
No	1/ 867 (0.1)	0/ 851 (0.0)	2.94 (0.12,72.18)*0.5082	2.95 (0.12,72.47)*0.5081	0.00 (-0.00, 0.00)*0.3170	
ARNI at baseline						1.0000
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NE	NE	NE	
No	6/2961 (0.2)	5/2991 (0.2)	1.22 (0.37, 4.00) 0.7387	1.22 (0.37, 4.02) 0.7380	0.00 (-0.00, 0.00)*0.7502	
Beta Blocker at baseline						1.0000
Yes	6/2587 (0.2)	5/2581 (0.2)	1.19 (0.36, 3.88) 0.7760	1.19 (0.36, 3.90) 0.7753	0.00 (-0.00, 0.00)*0.7657	
No	0/ 539 (0.0)	0/ 546 (0.0)	NE	NE	NE	
Diuretics at baseline						0.1946
Yes	6/2789 (0.2)	4/2783 (0.1)	1.50 (0.42, 5.29) 0.5325	1.50 (0.42, 5.32) 0.5320	0.00 (-0.00, 0.00)*0.5288	
No	0/ 337 (0.0)	1/ 344 (0.3)	0.34 (0.01, 8.32)*0.5087	0.34 (0.01, 8.36)*0.5085	-0.00 (-0.01, 0.00)*0.3166	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events of Special Interest: Diabetic Ketoacidosis (DKA)
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	2/3126 (0.1)	0/3127 (0.0)	5.00 (0.24,104.1)*0.2987	5.00 (0.24,104.3)*0.2986	0.00 (-0.00, 0.00)*0.1572	
Age						NC
<= median	2/1544 (0.1)	0/1602 (0.0)	NC	NC	NC	
> median	0/1582 (0.0)	0/1525 (0.0)	NC	NC	NC	
Gender						NC
Male	0/1765 (0.0)	0/1744 (0.0)	NC	NC	NC	
Female	2/1361 (0.1)	0/1383 (0.0)	NC	NC	NC	
Race						NC
White	1/2210 (0.0)	0/2222 (0.0)	NC	NC	NC	
Black or African	0/ 81 (0.0)	0/ 78 (0.0)	NC	NC	NC	
Asian	0/ 629 (0.0)	0/ 643 (0.0)	NC	NC	NC	
Other	1/ 206 (0.5)	0/ 184 (0.0)	NC	NC	NC	
Geographic region						NC
Asia	0/ 606 (0.0)	0/ 619 (0.0)	NC	NC	NC	
Europe and Saudi Arabia	0/1491 (0.0)	0/1508 (0.0)	NC	NC	NC	
North America	2/ 427 (0.5)	0/ 422 (0.0)	NC	NC	NC	
Latin America	0/ 602 (0.0)	0/ 578 (0.0)	NC	NC	NC	
NYHA class at enrolment						NC
II	0/2310 (0.0)	0/2395 (0.0)	NC	NC	NC	
III or IV	2/ 816 (0.2)	0/ 731 (0.0)	NC	NC	NC	
LVEF at enrolment						NC
<= 49	0/1066 (0.0)	0/1047 (0.0)	NC	NC	NC	
50-59	1/1132 (0.1)	0/1121 (0.0)	NC	NC	NC	
>= 60	1/ 928 (0.1)	0/ 959 (0.0)	NC	NC	NC	
NT-proBNP at enrolment						NC
<= median	1/1553 (0.1)	0/1574 (0.0)	NC	NC	NC	
> median	1/1573 (0.1)	0/1552 (0.0)	NC	NC	NC	
Type 2 Diabetes Medical History						NC
Yes	2/1399 (0.1)	0/1402 (0.0)	NC	NC	NC	
No	0/1727 (0.0)	0/1725 (0.0)	NC	NC	NC	
Atrial fibrillation or flutter at enrolment ECG						NC
Yes	0/1325 (0.0)	0/1317 (0.0)	NC	NC	NC	
No	2/1800 (0.1)	0/1809 (0.0)	NC	NC	NC	
BMI (kg/m2) at enrolment						NC
< 30	0/1732 (0.0)	0/1733 (0.0)	NC	NC	NC	
>= 30	2/1392 (0.1)	0/1390 (0.0)	NC	NC	NC	
Baseline eGFR (mL/min/1.73m^2)						NC
< 60	2/1514 (0.1)	0/1551 (0.0)	NC	NC	NC	
>= 60	0/1612 (0.0)	0/1575 (0.0)	NC	NC	NC	
SBP at randomisation						NC
<= median	0/1567 (0.0)	0/1588 (0.0)	NC	NC	NC	
> median	2/1559 (0.1)	0/1539 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events of Special Interest: Diabetic Ketoacidosis (DKA)
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						NC
<= 49	0/1066 (0.0)	0/1047 (0.0)	NC	NC	NC	
>= 50	2/2060 (0.1)	0/2080 (0.0)	NC	NC	NC	
Randomised during hospitalisation for HF or within 30 days of discharge						NC
Yes	1/ 328 (0.3)	0/ 326 (0.0)	NC	NC	NC	
No	1/2798 (0.0)	0/2801 (0.0)	NC	NC	NC	
MRAs at baseline						NC
Yes	0/1339 (0.0)	0/1325 (0.0)	NC	NC	NC	
No	2/1787 (0.1)	0/1802 (0.0)	NC	NC	NC	
ACEi+ARB at baseline						NC
Yes	1/2259 (0.0)	0/2276 (0.0)	NC	NC	NC	
No	1/ 867 (0.1)	0/ 851 (0.0)	NC	NC	NC	
ARNI at baseline						NC
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NC	NC	NC	
No	2/2961 (0.1)	0/2991 (0.0)	NC	NC	NC	
Beta Blocker at baseline						NC
Yes	2/2587 (0.1)	0/2581 (0.0)	NC	NC	NC	
No	0/ 539 (0.0)	0/ 546 (0.0)	NC	NC	NC	
Diuretics at baseline						NC
Yes	2/2789 (0.1)	0/2783 (0.0)	NC	NC	NC	
No	0/ 337 (0.0)	0/ 344 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events of Special Interest: Diabetic Ketoacidosis (DKA)
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	2/3126 (0.1)	0/3127 (0.0)	5.00 (0.24,104.1)*0.2987	5.00 (0.24,104.3)*0.2986	0.00 (-0.00, 0.00)*0.1572	
Age						NC
<= median	2/1544 (0.1)	0/1602 (0.0)	NC	NC	NC	
> median	0/1582 (0.0)	0/1525 (0.0)	NC	NC	NC	
Gender						NC
Male	0/1765 (0.0)	0/1744 (0.0)	NC	NC	NC	
Female	2/1361 (0.1)	0/1383 (0.0)	NC	NC	NC	
Race						NC
White	1/2210 (0.0)	0/2222 (0.0)	NC	NC	NC	
Black or African	0/ 81 (0.0)	0/ 78 (0.0)	NC	NC	NC	
Asian	0/ 629 (0.0)	0/ 643 (0.0)	NC	NC	NC	
Other	1/ 206 (0.5)	0/ 184 (0.0)	NC	NC	NC	
Geographic region						NC
Asia	0/ 606 (0.0)	0/ 619 (0.0)	NC	NC	NC	
Europe and Saudi Arabia	0/1491 (0.0)	0/1508 (0.0)	NC	NC	NC	
North America	2/ 427 (0.5)	0/ 422 (0.0)	NC	NC	NC	
Latin America	0/ 602 (0.0)	0/ 578 (0.0)	NC	NC	NC	
NYHA class at enrolment						NC
II	0/2310 (0.0)	0/2395 (0.0)	NC	NC	NC	
III or IV	2/ 816 (0.2)	0/ 731 (0.0)	NC	NC	NC	
LVEF at enrolment						NC
<= 49	0/1066 (0.0)	0/1047 (0.0)	NC	NC	NC	
50-59	1/1132 (0.1)	0/1121 (0.0)	NC	NC	NC	
>= 60	1/ 928 (0.1)	0/ 959 (0.0)	NC	NC	NC	
NT-proBNP at enrolment						NC
<= median	1/1553 (0.1)	0/1574 (0.0)	NC	NC	NC	
> median	1/1573 (0.1)	0/1552 (0.0)	NC	NC	NC	
Type 2 Diabetes Medical History						NC
Yes	2/1399 (0.1)	0/1402 (0.0)	NC	NC	NC	
No	0/1727 (0.0)	0/1725 (0.0)	NC	NC	NC	
Atrial fibrillation or flutter at enrolment ECG						NC
Yes	0/1325 (0.0)	0/1317 (0.0)	NC	NC	NC	
No	2/1800 (0.1)	0/1809 (0.0)	NC	NC	NC	
BMI (kg/m2) at enrolment						NC
< 30	0/1732 (0.0)	0/1733 (0.0)	NC	NC	NC	
>= 30	2/1392 (0.1)	0/1390 (0.0)	NC	NC	NC	
Baseline eGFR (mL/min/1.73m^2)						NC
< 60	2/1514 (0.1)	0/1551 (0.0)	NC	NC	NC	
>= 60	0/1612 (0.0)	0/1575 (0.0)	NC	NC	NC	
SBP at randomisation						NC
<= median	0/1567 (0.0)	0/1588 (0.0)	NC	NC	NC	
> median	2/1559 (0.1)	0/1539 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events of Special Interest: Diabetic Ketoacidosis (DKA)
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						NC
<= 49	0/1066 (0.0)	0/1047 (0.0)	NC	NC	NC	
>= 50	2/2060 (0.1)	0/2080 (0.0)	NC	NC	NC	
Randomised during hospitalisation for HF or within 30 days of discharge						NC
Yes	1/ 328 (0.3)	0/ 326 (0.0)	NC	NC	NC	
No	1/2798 (0.0)	0/2801 (0.0)	NC	NC	NC	
MRAs at baseline						NC
Yes	0/1339 (0.0)	0/1325 (0.0)	NC	NC	NC	
No	2/1787 (0.1)	0/1802 (0.0)	NC	NC	NC	
ACEi+ARB at baseline						NC
Yes	1/2259 (0.0)	0/2276 (0.0)	NC	NC	NC	
No	1/ 867 (0.1)	0/ 851 (0.0)	NC	NC	NC	
ARNI at baseline						NC
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NC	NC	NC	
No	2/2961 (0.1)	0/2991 (0.0)	NC	NC	NC	
Beta Blocker at baseline						NC
Yes	2/2587 (0.1)	0/2581 (0.0)	NC	NC	NC	
No	0/ 539 (0.0)	0/ 546 (0.0)	NC	NC	NC	
Diuretics at baseline						NC
Yes	2/2789 (0.1)	0/2783 (0.0)	NC	NC	NC	
No	0/ 337 (0.0)	0/ 344 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Severe Adverse Events of Special Interest: Diabetic Ketoacidosis (DKA)
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	1/3126 (0.0)	0/3127 (0.0)	3.00 (0.12,73.64)*0.5009	3.00 (0.12,73.72)*0.5009	0.00 (-0.00, 0.00)*0.3172	
Age						NC
<= median	1/1544 (0.1)	0/1602 (0.0)	NC	NC	NC	
> median	0/1582 (0.0)	0/1525 (0.0)	NC	NC	NC	
Gender						NC
Male	0/1765 (0.0)	0/1744 (0.0)	NC	NC	NC	
Female	1/1361 (0.1)	0/1383 (0.0)	NC	NC	NC	
Race						NC
White	1/2210 (0.0)	0/2222 (0.0)	NC	NC	NC	
Black or African	0/ 81 (0.0)	0/ 78 (0.0)	NC	NC	NC	
Asian	0/ 629 (0.0)	0/ 643 (0.0)	NC	NC	NC	
Other	0/ 206 (0.0)	0/ 184 (0.0)	NC	NC	NC	
Geographic region						NC
Asia	0/ 606 (0.0)	0/ 619 (0.0)	NC	NC	NC	
Europe and Saudi Arabia	0/1491 (0.0)	0/1508 (0.0)	NC	NC	NC	
North America	1/ 427 (0.2)	0/ 422 (0.0)	NC	NC	NC	
Latin America	0/ 602 (0.0)	0/ 578 (0.0)	NC	NC	NC	
NYHA class at enrolment						NC
II	0/2310 (0.0)	0/2395 (0.0)	NC	NC	NC	
III or IV	1/ 816 (0.1)	0/ 731 (0.0)	NC	NC	NC	
LVEF at enrolment						NC
<= 49	0/1066 (0.0)	0/1047 (0.0)	NC	NC	NC	
50-59	0/1132 (0.0)	0/1121 (0.0)	NC	NC	NC	
>= 60	1/ 928 (0.1)	0/ 959 (0.0)	NC	NC	NC	
NT-proBNP at enrolment						NC
<= median	0/1553 (0.0)	0/1574 (0.0)	NC	NC	NC	
> median	1/1573 (0.1)	0/1552 (0.0)	NC	NC	NC	
Type 2 Diabetes Medical History						NC
Yes	1/1399 (0.1)	0/1402 (0.0)	NC	NC	NC	
No	0/1727 (0.0)	0/1725 (0.0)	NC	NC	NC	
Atrial fibrillation or flutter at enrolment ECG						NC
Yes	0/1325 (0.0)	0/1317 (0.0)	NC	NC	NC	
No	1/1800 (0.1)	0/1809 (0.0)	NC	NC	NC	
BMI (kg/m2) at enrolment						NC
< 30	0/1732 (0.0)	0/1733 (0.0)	NC	NC	NC	
>= 30	1/1392 (0.1)	0/1390 (0.0)	NC	NC	NC	
Baseline eGFR (mL/min/1.73m^2)						NC
< 60	1/1514 (0.1)	0/1551 (0.0)	NC	NC	NC	
>= 60	0/1612 (0.0)	0/1575 (0.0)	NC	NC	NC	
SBP at randomisation						NC
<= median	0/1567 (0.0)	0/1588 (0.0)	NC	NC	NC	
> median	1/1559 (0.1)	0/1539 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Severe Adverse Events of Special Interest: Diabetic Ketoacidosis (DKA)
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						NC
<= 49	0/1066 (0.0)	0/1047 (0.0)	NC	NC	NC	
>= 50	1/2060 (0.0)	0/2080 (0.0)	NC	NC	NC	
Randomised during hospitalisation for HF or within 30 days of discharge						NC
Yes	1/ 328 (0.3)	0/ 326 (0.0)	NC	NC	NC	
No	0/2798 (0.0)	0/2801 (0.0)	NC	NC	NC	
MRAs at baseline						NC
Yes	0/1339 (0.0)	0/1325 (0.0)	NC	NC	NC	
No	1/1787 (0.1)	0/1802 (0.0)	NC	NC	NC	
ACEi+ARB at baseline						NC
Yes	0/2259 (0.0)	0/2276 (0.0)	NC	NC	NC	
No	1/ 867 (0.1)	0/ 851 (0.0)	NC	NC	NC	
ARNI at baseline						NC
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NC	NC	NC	
No	1/2961 (0.0)	0/2991 (0.0)	NC	NC	NC	
Beta Blocker at baseline						NC
Yes	1/2587 (0.0)	0/2581 (0.0)	NC	NC	NC	
No	0/ 539 (0.0)	0/ 546 (0.0)	NC	NC	NC	
Diuretics at baseline						NC
Yes	1/2789 (0.0)	0/2783 (0.0)	NC	NC	NC	
No	0/ 337 (0.0)	0/ 344 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Non-Severe Adverse Events of Special Interest: Diabetic Ketoacidosis (DKA)
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	1/3126 (0.0)	0/3127 (0.0)	3.00 (0.12,73.64)*0.5009	3.00 (0.12,73.72)*0.5009	0.00 (-0.00, 0.00)*0.3172	
Age						NC
<= median	1/1544 (0.1)	0/1602 (0.0)	NC	NC	NC	
> median	0/1582 (0.0)	0/1525 (0.0)	NC	NC	NC	
Gender						NC
Male	0/1765 (0.0)	0/1744 (0.0)	NC	NC	NC	
Female	1/1361 (0.1)	0/1383 (0.0)	NC	NC	NC	
Race						NC
White	0/2210 (0.0)	0/2222 (0.0)	NC	NC	NC	
Black or African	0/ 81 (0.0)	0/ 78 (0.0)	NC	NC	NC	
Asian	0/ 629 (0.0)	0/ 643 (0.0)	NC	NC	NC	
Other	1/ 206 (0.5)	0/ 184 (0.0)	NC	NC	NC	
Geographic region						NC
Asia	0/ 606 (0.0)	0/ 619 (0.0)	NC	NC	NC	
Europe and Saudi Arabia	0/1491 (0.0)	0/1508 (0.0)	NC	NC	NC	
North America	1/ 427 (0.2)	0/ 422 (0.0)	NC	NC	NC	
Latin America	0/ 602 (0.0)	0/ 578 (0.0)	NC	NC	NC	
NYHA class at enrolment						NC
II	0/2310 (0.0)	0/2395 (0.0)	NC	NC	NC	
III or IV	1/ 816 (0.1)	0/ 731 (0.0)	NC	NC	NC	
LVEF at enrolment						NC
<= 49	0/1066 (0.0)	0/1047 (0.0)	NC	NC	NC	
50-59	1/1132 (0.1)	0/1121 (0.0)	NC	NC	NC	
>= 60	0/ 928 (0.0)	0/ 959 (0.0)	NC	NC	NC	
NT-proBNP at enrolment						NC
<= median	1/1553 (0.1)	0/1574 (0.0)	NC	NC	NC	
> median	0/1573 (0.0)	0/1552 (0.0)	NC	NC	NC	
Type 2 Diabetes Medical History						NC
Yes	1/1399 (0.1)	0/1402 (0.0)	NC	NC	NC	
No	0/1727 (0.0)	0/1725 (0.0)	NC	NC	NC	
Atrial fibrillation or flutter at enrolment ECG						NC
Yes	0/1325 (0.0)	0/1317 (0.0)	NC	NC	NC	
No	1/1800 (0.1)	0/1809 (0.0)	NC	NC	NC	
BMI (kg/m2) at enrolment						NC
< 30	0/1732 (0.0)	0/1733 (0.0)	NC	NC	NC	
>= 30	1/1392 (0.1)	0/1390 (0.0)	NC	NC	NC	
Baseline eGFR (mL/min/1.73m^2)						NC
< 60	1/1514 (0.1)	0/1551 (0.0)	NC	NC	NC	
>= 60	0/1612 (0.0)	0/1575 (0.0)	NC	NC	NC	
SBP at randomisation						NC
<= median	0/1567 (0.0)	0/1588 (0.0)	NC	NC	NC	
> median	1/1559 (0.1)	0/1539 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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AstraZeneca
Protocol: D169CC00001
Overall study population
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Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						NC
<= 49	0/1066 (0.0)	0/1047 (0.0)	NC	NC	NC	
>= 50	1/2060 (0.0)	0/2080 (0.0)	NC	NC	NC	
Randomised during hospitalisation for HF or within 30 days of discharge						NC
Yes	0/ 328 (0.0)	0/ 326 (0.0)	NC	NC	NC	
No	1/2798 (0.0)	0/2801 (0.0)	NC	NC	NC	
MRAs at baseline						NC
Yes	0/1339 (0.0)	0/1325 (0.0)	NC	NC	NC	
No	1/1787 (0.1)	0/1802 (0.0)	NC	NC	NC	
ACEi+ARB at baseline						NC
Yes	1/2259 (0.0)	0/2276 (0.0)	NC	NC	NC	
No	0/ 867 (0.0)	0/ 851 (0.0)	NC	NC	NC	
ARNI at baseline						NC
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NC	NC	NC	
No	1/2961 (0.0)	0/2991 (0.0)	NC	NC	NC	
Beta Blocker at baseline						NC
Yes	1/2587 (0.0)	0/2581 (0.0)	NC	NC	NC	
No	0/ 539 (0.0)	0/ 546 (0.0)	NC	NC	NC	
Diuretics at baseline						NC
Yes	1/2789 (0.0)	0/2783 (0.0)	NC	NC	NC	
No	0/ 337 (0.0)	0/ 344 (0.0)	NC	NC	NC	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events of Special Interest: Events leading to Amputation
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	19/3126 (0.6)	26/3127 (0.8)	0.73 (0.41, 1.31) 0.2944	0.73 (0.40, 1.32) 0.2951	-0.00 (-0.00, 0.00) 0.6260	
Age						0.4217
<= median	14/1544 (0.9)	22/1602 (1.4)	0.66 (0.34, 1.28) 0.2176	0.65 (0.33, 1.28) 0.2170	-0.00 (-0.01, 0.00) 0.3962	
> median	5/1582 (0.3)	4/1525 (0.3)	1.21 (0.32, 4.48) 0.7805	1.21 (0.32, 4.50) 0.7806	0.00 (-0.00, 0.00) 0.7900	
Gender						0.4330
Male	14/1765 (0.8)	16/1744 (0.9)	0.85 (0.42, 1.74) 0.6662	0.85 (0.41, 1.75) 0.6654	-0.00 (-0.01, 0.00) 0.6062	
Female	5/1361 (0.4)	10/1383 (0.7)	0.51 (0.18, 1.50) 0.2226	0.51 (0.17, 1.50) 0.2236	-0.00 (-0.01, 0.00) 0.8350	
Race						0.1981
White	16/2210 (0.7)	23/2222 (1.0)	0.70 (0.37, 1.32) 0.2683	0.70 (0.37, 1.32) 0.2692	-0.00 (-0.01, 0.00) 0.5612	
Black or African	1/ 81 (1.2)	2/ 78 (2.6)	0.45 (0.04, 4.77) 0.5057	0.48 (0.04, 5.35)*0.5467	-0.01 (-0.06, 0.03)*0.5401	
Asian	0/ 629 (0.0)	1/ 643 (0.2)	0.34 (0.01, 8.35)*0.5095	0.34 (0.01, 8.37)*0.5093	-0.00 (-0.00, 0.00)*0.3169	
Other	2/ 206 (1.0)	0/ 184 (0.0)	4.47 (0.22,92.48)*0.3328	4.51 (0.22,94.58)*0.3319	0.01 (-0.00, 0.02)*0.1553	
Geographic region						0.4205
Asia	0/ 606 (0.0)	1/ 619 (0.2)	0.34 (0.01, 8.34)*0.5091	0.34 (0.01, 8.36)*0.5090	-0.00 (-0.00, 0.00)*0.3169	
Europe and Saudi Arabia	10/1491 (0.7)	17/1508 (1.1)	0.59 (0.27, 1.28) 0.1798	0.58 (0.27, 1.28) 0.1794	-0.00 (-0.01, 0.00) 0.2303	
North America	4/ 427 (0.9)	5/ 422 (1.2)	0.78 (0.21, 2.86) 0.7043	0.78 (0.21, 2.93) 0.7090	-0.00 (-0.02, 0.01)*0.7243	
Latin America	5/ 602 (0.8)	3/ 578 (0.5)	1.71 (0.41, 7.11) 0.4612	1.72 (0.41, 7.25) 0.4597	0.00 (-0.01, 0.01)*0.5124	
NYHA class at enrolment						0.2909
II	16/2310 (0.7)	19/2395 (0.8)	0.87 (0.45, 1.68) 0.6702	0.87 (0.44, 1.69) 0.6722	0.00 (-0.00, 0.00) 0.9203	
III or IV	3/ 816 (0.4)	7/ 731 (1.0)	0.40 (0.10, 1.52) 0.1779	0.39 (0.10, 1.53) 0.1768	-0.01 (-0.01, 0.00)*0.1580	
LVEF at enrolment						0.8221
<= 49	7/1066 (0.7)	10/1047 (1.0)	0.67 (0.26, 1.76) 0.4179	0.67 (0.25, 1.77) 0.4187	-0.00 (-0.01, 0.01) 0.6550	
50-59	6/1132 (0.5)	6/1121 (0.5)	0.99 (0.32, 3.07) 0.9927	0.99 (0.32, 3.08)*0.9865	-0.00 (-0.01, 0.01)*0.9865	
>= 60	6/ 928 (0.6)	10/ 959 (1.0)	0.63 (0.23, 1.73) 0.3717	0.63 (0.23, 1.74) 0.3726	-0.00 (-0.01, 0.01) 0.6173	
NT-proBNP at enrolment						0.4875
<= median	6/1553 (0.4)	11/1574 (0.7)	0.55 (0.20, 1.49) 0.2397	0.55 (0.20, 1.49) 0.2406	-0.00 (-0.01, 0.00)*0.2337	
> median	13/1573 (0.8)	15/1552 (1.0)	0.85 (0.41, 1.78) 0.6728	0.85 (0.40, 1.80) 0.6721	-0.00 (-0.01, 0.00) 0.6406	
Type 2 Diabetes Medical History						0.6267
Yes	15/1399 (1.1)	22/1402 (1.6)	0.68 (0.36, 1.31)*0.2523	0.68 (0.35, 1.32)*0.2522	-0.00 (-0.01, 0.00)*0.2492	
No	4/1727 (0.2)	4/1725 (0.2)	1.00 (0.25, 3.99)*0.9987	1.00 (0.25, 4.00)*0.9987	-0.00 (-0.00, 0.00)*0.9987	
Atrial fibrillation or flutter at enrolment ECG						0.4696
Yes	4/1325 (0.3)	8/1317 (0.6)	0.50 (0.15, 1.66) 0.2588	0.50 (0.15, 1.66) 0.2585	-0.00 (-0.01, 0.00) 0.3527	
No	15/1800 (0.8)	18/1809 (1.0)	0.83 (0.42, 1.64) 0.5895	0.83 (0.42, 1.65) 0.5916	0.00 (-0.00, 0.00) 0.9330	
BMI (kg/m2) at enrolment						0.2958
< 30	11/1732 (0.6)	11/1733 (0.6)	1.00 (0.44, 2.30) 0.9996	1.00 (0.43, 2.32) 0.9981	0.00 (-0.00, 0.00) 0.7460	
>= 30	8/1392 (0.6)	15/1390 (1.1)	0.53 (0.23, 1.25) 0.1471	0.53 (0.22, 1.25) 0.1468	-0.00 (-0.01, 0.00) 0.2764	
Baseline eGFR (mL/min/1.73m^2)						0.8346
< 60	13/1514 (0.9)	17/1551 (1.1)	0.76 (0.37, 1.56) 0.4538	0.76 (0.37, 1.57) 0.4548	-0.00 (-0.01, 0.00) 0.7789	
>= 60	6/1612 (0.4)	9/1575 (0.6)	0.66 (0.24, 1.86) 0.4358	0.66 (0.24, 1.87) 0.4363	-0.00 (-0.01, 0.00) 0.6462	
SBP at randomisation						0.6236
<= median	4/1567 (0.3)	7/1588 (0.4)	0.57 (0.17, 1.93) 0.3641	0.57 (0.17, 1.94) 0.3640	-0.00 (-0.01, 0.00) 0.4155	
> median	15/1559 (1.0)	19/1539 (1.2)	0.80 (0.41, 1.56) 0.5133	0.80 (0.40, 1.58) 0.5155	-0.00 (-0.01, 0.01) 0.9827	

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AstraZeneca
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Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.8257
<= 49	7/1066 (0.7)	10/1047 (1.0)	0.67 (0.26, 1.76) 0.4179	0.67 (0.25, 1.77) 0.4187	-0.00 (-0.01, 0.01) 0.6550	
>= 50	12/2060 (0.6)	16/2080 (0.8)	0.77 (0.36, 1.62) 0.4865	0.77 (0.36, 1.62) 0.4870	-0.00 (-0.00, 0.00) 0.7726	
Randomised during hospitalisation for HF or within 30 days of discharge						0.8547
Yes	2/ 328 (0.6)	3/ 326 (0.9)	0.61 (0.10, 3.59) 0.5820	0.66 (0.11, 3.98)*0.6508	-0.00 (-0.02, 0.01)*0.6487	
No	17/2798 (0.6)	23/2801 (0.8)	0.74 (0.40, 1.39) 0.3527	0.74 (0.40, 1.39) 0.3535	-0.00 (-0.00, 0.00) 0.6418	
MRAs at baseline						0.1688
Yes	4/1339 (0.3)	10/1325 (0.8)	0.38 (0.12, 1.22) 0.1046	0.38 (0.12, 1.22) 0.1045	-0.00 (-0.01, 0.00) 0.2667	
No	15/1787 (0.8)	16/1802 (0.9)	0.96 (0.48, 1.94) 0.9198	0.96 (0.47, 1.96) 0.9215	0.00 (-0.00, 0.01) 0.7969	
ACEi+ARB at baseline						0.5049
Yes	16/2259 (0.7)	20/2276 (0.9)	0.81 (0.42, 1.55) 0.5217	0.81 (0.42, 1.56) 0.5245	0.00 (-0.00, 0.00) 0.7791	
No	3/ 867 (0.3)	6/ 851 (0.7)	0.48 (0.12, 1.93) 0.3035	0.48 (0.12, 1.93) 0.3019	-0.00 (-0.01, 0.00)*0.3041	
ARNI at baseline						0.2218
Yes	0/ 165 (0.0)	1/ 136 (0.7)	0.28 (0.01, 6.70)*0.4282	0.27 (0.01, 6.75)*0.4276	-0.01 (-0.02, 0.01)*0.3155	
No	19/2961 (0.6)	25/2991 (0.8)	0.77 (0.43, 1.40) 0.3958	0.77 (0.42, 1.41) 0.3973	-0.00 (-0.00, 0.00) 0.9220	
Beta Blocker at baseline						0.2861
Yes	17/2587 (0.7)	20/2581 (0.8)	0.84 (0.44, 1.60) 0.6018	0.84 (0.44, 1.61) 0.6024	-0.00 (-0.00, 0.00) 0.8191	
No	2/ 539 (0.4)	6/ 546 (1.1)	0.34 (0.07, 1.69) 0.1892	0.34 (0.07, 1.70) 0.1894	-0.00 (-0.02, 0.01) 0.4571	
Diuretics at baseline						0.2951
Yes	19/2789 (0.7)	25/2783 (0.9)	0.76 (0.42, 1.37) 0.3583	0.76 (0.41, 1.38) 0.3599	-0.00 (-0.00, 0.00) 0.8900	
No	0/ 337 (0.0)	1/ 344 (0.3)	0.34 (0.01, 8.32)*0.5087	0.34 (0.01, 8.36)*0.5085	-0.00 (-0.01, 0.00)*0.3166	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	18/3126 (0.6)	24/3127 (0.8)	0.75 (0.41, 1.38) 0.3527	0.75 (0.40, 1.38) 0.3526	-0.00 (-0.00, 0.00) 0.4937	
Age						0.7195
<= median	14/1544 (0.9)	20/1602 (1.2)	0.72 (0.37, 1.43) 0.3508	0.72 (0.36, 1.43) 0.3500	-0.00 (-0.01, 0.00) 0.4434	
> median	4/1582 (0.3)	4/1525 (0.3)	0.96 (0.24, 3.85) 0.9582	0.96 (0.24, 3.86) 0.9582	-0.00 (-0.00, 0.00) 0.9587	
Gender						0.3182
Male	14/1765 (0.8)	15/1744 (0.9)	0.91 (0.44, 1.88) 0.8033	0.91 (0.44, 1.89) 0.8022	-0.00 (-0.01, 0.00) 0.6673	
Female	4/1361 (0.3)	9/1383 (0.7)	0.46 (0.14, 1.48) 0.1926	0.46 (0.14, 1.49) 0.1927	-0.00 (-0.01, 0.00) 0.5989	
Race						0.2075
White	15/2210 (0.7)	22/2222 (1.0)	0.69 (0.36, 1.32) 0.2565	0.68 (0.35, 1.32) 0.2566	-0.00 (-0.01, 0.00) 0.4173	
Black or African	1/ 81 (1.2)	1/ 78 (1.3)	0.90 (0.06,13.89) 0.9373	0.96 (0.06,15.66)*0.9786	-0.00 (-0.04, 0.03)*0.9786	
Asian	0/ 629 (0.0)	1/ 643 (0.2)	0.34 (0.01, 8.35)*0.5095	0.34 (0.01, 8.37)*0.5093	-0.00 (-0.00, 0.00)*0.3169	
Other	2/ 206 (1.0)	0/ 184 (0.0)	4.47 (0.22,92.48)*0.3328	4.51 (0.22,94.58)*0.3319	0.01 (-0.00, 0.02)*0.1553	
Geographic region						0.3795
Asia	0/ 606 (0.0)	1/ 619 (0.2)	0.34 (0.01, 8.34)*0.5091	0.34 (0.01, 8.36)*0.5090	-0.00 (-0.00, 0.00)*0.3169	
Europe and Saudi Arabia	9/1491 (0.6)	16/1508 (1.1)	0.56 (0.25, 1.27) 0.1643	0.56 (0.25, 1.27) 0.1632	-0.00 (-0.01, 0.00) 0.1166	
North America	4/ 427 (0.9)	4/ 422 (0.9)	0.97 (0.25, 3.85) 0.9679	0.98 (0.24, 3.94) 0.9721	-0.00 (-0.01, 0.01)*0.9866	
Latin America	5/ 602 (0.8)	3/ 578 (0.5)	1.71 (0.41, 7.11) 0.4612	1.72 (0.41, 7.25) 0.4597	0.00 (-0.01, 0.01)*0.5124	
NYHA class at enrolment						0.2675
II	15/2310 (0.6)	17/2395 (0.7)	0.91 (0.45, 1.81) 0.7839	0.91 (0.45, 1.82) 0.7844	-0.00 (-0.00, 0.00) 0.9319	
III or IV	3/ 816 (0.4)	7/ 731 (1.0)	0.40 (0.10, 1.52) 0.1779	0.39 (0.10, 1.53) 0.1768	-0.01 (-0.01, 0.00)*0.1580	
LVEF at enrolment						0.8063
<= 49	7/1066 (0.7)	9/1047 (0.9)	0.75 (0.28, 2.00) 0.5627	0.75 (0.28, 2.01) 0.5634	-0.00 (-0.01, 0.01) 0.7422	
50-59	6/1132 (0.5)	6/1121 (0.5)	0.99 (0.32, 3.07) 0.9927	0.99 (0.32, 3.08)*0.9865	-0.00 (-0.01, 0.01)*0.9865	
>= 60	5/ 928 (0.5)	9/ 959 (0.9)	0.59 (0.20, 1.74) 0.3381	0.58 (0.19, 1.75) 0.3375	-0.00 (-0.01, 0.00) 0.3965	
NT-proBNP at enrolment						0.6092
<= median	6/1553 (0.4)	10/1574 (0.6)	0.61 (0.22, 1.66) 0.3321	0.61 (0.22, 1.67) 0.3332	-0.00 (-0.01, 0.00)*0.3284	
> median	12/1573 (0.8)	14/1552 (0.9)	0.84 (0.39, 1.82) 0.6647	0.84 (0.39, 1.83) 0.6626	-0.00 (-0.01, 0.00) 0.4400	
Type 2 Diabetes Medical History						0.9968
Yes	15/1399 (1.1)	20/1402 (1.4)	0.75 (0.39, 1.46)*0.4003	0.75 (0.38, 1.47)*0.4002	-0.00 (-0.01, 0.00)*0.3985	
No	3/1727 (0.2)	4/1725 (0.2)	0.75 (0.17, 3.34)*0.7050	0.75 (0.17, 3.35)*0.7050	-0.00 (-0.00, 0.00)*0.7040	
Atrial fibrillation or flutter at enrolment ECG						0.2200
Yes	3/1325 (0.2)	8/1317 (0.6)	0.38 (0.10, 1.42) 0.1492	0.37 (0.10, 1.42) 0.1484	-0.00 (-0.01, 0.00)*0.1287	
No	15/1800 (0.8)	16/1809 (0.9)	0.93 (0.46, 1.88) 0.8466	0.93 (0.46, 1.90) 0.8484	0.00 (-0.00, 0.01) 0.8126	
BMI (kg/m2) at enrolment						0.2072
< 30	11/1732 (0.6)	10/1733 (0.6)	1.10 (0.47, 2.58) 0.8258	1.10 (0.47, 2.60) 0.8248	0.00 (-0.00, 0.00) 0.6785	
>= 30	7/1392 (0.5)	14/1390 (1.0)	0.50 (0.20, 1.23) 0.1314	0.49 (0.20, 1.23) 0.1304	-0.01 (-0.01, 0.00)*0.1243	
Baseline eGFR (mL/min/1.73m^2)						0.7847
< 60	12/1514 (0.8)	15/1551 (1.0)	0.79 (0.37, 1.69) 0.5504	0.79 (0.37, 1.70) 0.5494	-0.00 (-0.01, 0.00) 0.5174	
>= 60	6/1612 (0.4)	9/1575 (0.6)	0.66 (0.24, 1.86) 0.4358	0.66 (0.24, 1.87) 0.4363	-0.00 (-0.01, 0.00) 0.6462	
SBP at randomisation						0.8052
<= median	4/1567 (0.3)	6/1588 (0.4)	0.66 (0.19, 2.34) 0.5235	0.66 (0.19, 2.35) 0.5232	-0.00 (-0.00, 0.00) 0.5023	
> median	14/1559 (0.9)	18/1539 (1.2)	0.79 (0.39, 1.58) 0.5040	0.79 (0.39, 1.59) 0.5046	-0.00 (-0.01, 0.00) 0.7468	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events of Special Interest: Events leading to Amputation
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.9871
<= 49	7/1066 (0.7)	9/1047 (0.9)	0.75 (0.28, 2.00) 0.5627	0.75 (0.28, 2.01) 0.5634	-0.00 (-0.01, 0.01) 0.7422	
>= 50	11/2060 (0.5)	15/2080 (0.7)	0.75 (0.35, 1.63) 0.4705	0.75 (0.34, 1.64) 0.4698	-0.00 (-0.00, 0.00) 0.4684	
Randomised during hospitalisation for HF or within 30 days of discharge						0.8284
Yes	2/ 328 (0.6)	3/ 326 (0.9)	0.61 (0.10, 3.59) 0.5820	0.66 (0.11, 3.98)*0.6508	-0.00 (-0.02, 0.01)*0.6487	
No	16/2798 (0.6)	21/2801 (0.7)	0.77 (0.40, 1.47) 0.4229	0.77 (0.40, 1.47) 0.4228	-0.00 (-0.00, 0.00) 0.5174	
MRAs at baseline						0.1454
Yes	4/1339 (0.3)	10/1325 (0.8)	0.38 (0.12, 1.22) 0.1046	0.38 (0.12, 1.22) 0.1045	-0.00 (-0.01, 0.00) 0.2667	
No	14/1787 (0.8)	14/1802 (0.8)	1.03 (0.49, 2.15) 0.9351	1.03 (0.49, 2.17) 0.9352	0.00 (-0.00, 0.00) 0.9870	
ACEi+ARB at baseline						0.4738
Yes	15/2259 (0.7)	18/2276 (0.8)	0.84 (0.43, 1.66) 0.6207	0.84 (0.42, 1.67) 0.6224	0.00 (-0.00, 0.00) 0.9160	
No	3/ 867 (0.3)	6/ 851 (0.7)	0.48 (0.12, 1.93) 0.3035	0.48 (0.12, 1.93) 0.3019	-0.00 (-0.01, 0.00)*0.3041	
ARNI at baseline						0.2162
Yes	0/ 165 (0.0)	1/ 136 (0.7)	0.28 (0.01, 6.70)*0.4282	0.27 (0.01, 6.75)*0.4276	-0.01 (-0.02, 0.01)*0.3155	
No	18/2961 (0.6)	23/2991 (0.8)	0.80 (0.43, 1.47) 0.4686	0.80 (0.43, 1.48) 0.4692	-0.00 (-0.00, 0.00) 0.7604	
Beta Blocker at baseline						0.0846
Yes	17/2587 (0.7)	18/2581 (0.7)	0.94 (0.48, 1.81) 0.8456	0.94 (0.48, 1.82) 0.8458	-0.00 (-0.00, 0.00) 0.9326	
No	1/ 539 (0.2)	6/ 546 (1.1)	0.17 (0.02, 1.43) 0.1042	0.17 (0.02, 1.43) 0.1029	-0.01 (-0.02, 0.00)*0.0587	
Diuretics at baseline						0.2898
Yes	18/2789 (0.6)	23/2783 (0.8)	0.78 (0.42, 1.44) 0.4280	0.78 (0.42, 1.45) 0.4286	-0.00 (-0.00, 0.00) 0.7347	
No	0/ 337 (0.0)	1/ 344 (0.3)	0.34 (0.01, 8.32)*0.5087	0.34 (0.01, 8.36)*0.5085	-0.00 (-0.01, 0.00)*0.3166	

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Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Severe Adverse Events of Special Interest: Events leading to Amputation
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	13/3126 (0.4)	14/3127 (0.4)	0.93 (0.44, 1.97) 0.8462	0.93 (0.43, 1.98) 0.8456	-0.00 (-0.00, 0.00) 0.6854	
Age						0.6814
<= median	10/1544 (0.6)	10/1602 (0.6)	1.03 (0.43, 2.47) 0.9393	1.03 (0.43, 2.50) 0.9393	0.00 (-0.00, 0.00) 0.9578	
> median	3/1582 (0.2)	4/1525 (0.3)	0.72 (0.16, 3.22) 0.6699	0.72 (0.16, 3.23) 0.6697	-0.00 (-0.00, 0.00) 0.6044	
Gender						0.5440
Male	8/1765 (0.5)	10/1744 (0.6)	0.78 (0.31, 1.98) 0.6042	0.78 (0.31, 1.98) 0.6013	-0.00 (-0.01, 0.00)*0.6187	
Female	5/1361 (0.4)	4/1383 (0.3)	1.28 (0.35, 4.77) 0.7088	1.29 (0.34, 4.81) 0.7071	0.00 (-0.00, 0.01)*0.7206	
Race						0.3829
White	10/2210 (0.5)	13/2222 (0.6)	0.77 (0.34, 1.76) 0.5401	0.77 (0.34, 1.77) 0.5398	-0.00 (-0.00, 0.00) 0.5438	
Black or African	1/ 81 (1.2)	1/ 78 (1.3)	0.90 (0.06,13.89) 0.9373	0.96 (0.06,15.66)*0.9786	-0.00 (-0.04, 0.03)*0.9786	
Asian	0/ 629 (0.0)	0/ 643 (0.0)	NE	NE	NE	
Other	2/ 206 (1.0)	0/ 184 (0.0)	4.47 (0.22,92.48)*0.3328	4.51 (0.22,94.58)*0.3319	0.01 (-0.00, 0.02)*0.1553	
Geographic region						0.7482
Asia	0/ 606 (0.0)	0/ 619 (0.0)	NE	NE	NE	
Europe and Saudi Arabia	7/1491 (0.5)	10/1508 (0.7)	0.70 (0.27, 1.83) 0.4679	0.70 (0.26, 1.84) 0.4668	-0.00 (-0.01, 0.00) 0.3120	
North America	2/ 427 (0.5)	2/ 422 (0.5)	0.97 (0.14, 6.83) 0.9770	0.99 (0.14, 7.05)*0.9906	-0.00 (-0.01, 0.01)*0.9906	
Latin America	4/ 602 (0.7)	2/ 578 (0.3)	2.04 (0.37,11.06) 0.4107	2.05 (0.37,11.25) 0.4096	0.00 (-0.00, 0.01)*0.4390	
NYHA class at enrolment						0.6035
II	11/2310 (0.5)	11/2395 (0.5)	1.03 (0.45, 2.37) 0.9464	1.03 (0.44, 2.38) 0.9464	0.00 (-0.00, 0.00) 0.9487	
III or IV	2/ 816 (0.2)	3/ 731 (0.4)	0.61 (0.10, 3.64) 0.5887	0.61 (0.10, 3.66) 0.5878	-0.00 (-0.01, 0.00)*0.5727	
LVEF at enrolment						0.9516
<= 49	4/1066 (0.4)	4/1047 (0.4)	0.96 (0.24, 3.84) 0.9585	0.96 (0.24, 3.86) 0.9565	-0.00 (-0.01, 0.01)*0.9797	
50-59	4/1132 (0.4)	5/1121 (0.4)	0.80 (0.21, 2.95) 0.7325	0.79 (0.21, 2.96)*0.7279	-0.00 (-0.01, 0.00)*0.7275	
>= 60	5/ 928 (0.5)	5/ 959 (0.5)	1.05 (0.30, 3.61) 0.9389	1.05 (0.30, 3.64) 0.9378	0.00 (-0.00, 0.01) 0.7260	
NT-proBNP at enrolment						0.8123
<= median	4/1553 (0.3)	5/1574 (0.3)	0.81 (0.22, 3.01) 0.7538	0.81 (0.22, 3.02)*0.7542	-0.00 (-0.00, 0.00)*0.7536	
> median	9/1573 (0.6)	9/1552 (0.6)	0.98 (0.39, 2.47) 0.9738	0.98 (0.39, 2.49) 0.9727	-0.00 (-0.01, 0.00) 0.7763	
Type 2 Diabetes Medical History						0.6846
Yes	11/1399 (0.8)	11/1402 (0.8)	1.00 (0.44, 2.30)*0.9960	1.00 (0.43, 2.32)*0.9960	0.00 (-0.01, 0.01)*0.9960	
No	2/1727 (0.1)	3/1725 (0.2)	0.67 (0.11, 3.98)*0.6558	0.67 (0.11, 3.99)*0.6558	-0.00 (-0.00, 0.00)*0.6536	
Atrial fibrillation or flutter at enrolment ECG						0.7914
Yes	4/1325 (0.3)	5/1317 (0.4)	0.80 (0.22, 2.98) 0.7435	0.80 (0.21, 3.00) 0.7437	-0.00 (-0.00, 0.00) 0.8703	
No	9/1800 (0.5)	9/1809 (0.5)	1.00 (0.40, 2.50) 0.9950	1.00 (0.39, 2.52) 0.9939	-0.00 (-0.00, 0.00) 0.6882	
BMI (kg/m2) at enrolment						0.3026
< 30	9/1732 (0.5)	7/1733 (0.4)	1.29 (0.48, 3.45) 0.6135	1.29 (0.48, 3.47) 0.6152	-0.00 (-0.00, 0.00) 0.7915	
>= 30	4/1392 (0.3)	7/1390 (0.5)	0.57 (0.17, 1.94) 0.3682	0.57 (0.17, 1.95) 0.3685	-0.00 (-0.01, 0.00) 0.5811	
Baseline eGFR (mL/min/1.73m^2)						0.0509
< 60	11/1514 (0.7)	7/1551 (0.5)	1.56 (0.61, 4.01) 0.3551	1.57 (0.60, 4.06) 0.3553	0.00 (-0.00, 0.00) 0.6843	
>= 60	2/1612 (0.1)	7/1575 (0.4)	0.28 (0.06, 1.36) 0.1152	0.28 (0.06, 1.36) 0.1150	-0.00 (-0.01, 0.00) 0.1750	
SBP at randomisation						0.6675
<= median	2/1567 (0.1)	3/1588 (0.2)	0.66 (0.11, 3.93) 0.6459	0.66 (0.11, 3.94) 0.6454	-0.00 (-0.00, 0.00)*0.6648	
> median	11/1559 (0.7)	11/1539 (0.7)	1.01 (0.44, 2.32) 0.9797	1.01 (0.44, 2.34) 0.9799	-0.00 (-0.00, 0.00) 0.9808	

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AstraZeneca
Protocol: D169CC00001
Overall study population
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Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.9600
<= 49	4/1066 (0.4)	4/1047 (0.4)	0.96 (0.24, 3.84) 0.9585	0.96 (0.24, 3.86) 0.9565	-0.00 (-0.01, 0.01)*0.9797	
>= 50	9/2060 (0.4)	10/2080 (0.5)	0.92 (0.38, 2.26) 0.8560	0.92 (0.37, 2.27) 0.8573	0.00 (-0.00, 0.00) 0.7183	
Randomised during hospitalisation for HF or within 30 days of discharge						0.9881
Yes	2/ 328 (0.6)	2/ 326 (0.6)	0.91 (0.13, 6.39) 0.9249	0.99 (0.14, 7.10)*0.9951	-0.00 (-0.01, 0.01)*0.9951	
No	11/2798 (0.4)	12/2801 (0.4)	0.92 (0.41, 2.09) 0.8475	0.92 (0.41, 2.10) 0.8469	-0.00 (-0.00, 0.00) 0.6908	
MRAs at baseline						0.1204
Yes	3/1339 (0.2)	7/1325 (0.5)	0.41 (0.11, 1.59) 0.1971	0.41 (0.11, 1.59) 0.1963	-0.00 (-0.01, 0.00)*0.2000	
No	10/1787 (0.6)	7/1802 (0.4)	1.47 (0.56, 3.85) 0.4335	1.47 (0.56, 3.88) 0.4331	0.00 (-0.00, 0.00) 0.4488	
ACEi+ARB at baseline						0.3787
Yes	11/2259 (0.5)	10/2276 (0.4)	1.11 (0.47, 2.61) 0.8077	1.11 (0.47, 2.63) 0.8078	0.00 (-0.00, 0.00) 0.8984	
No	2/ 867 (0.2)	4/ 851 (0.5)	0.48 (0.09, 2.62) 0.3991	0.48 (0.09, 2.63) 0.3981	-0.00 (-0.01, 0.00)*0.4018	
ARNI at baseline						0.1831
Yes	0/ 165 (0.0)	1/ 136 (0.7)	0.28 (0.01, 6.70)*0.4282	0.27 (0.01, 6.75)*0.4276	-0.01 (-0.02, 0.01)*0.3155	
No	13/2961 (0.4)	13/2991 (0.4)	1.02 (0.47, 2.19) 0.9625	1.02 (0.47, 2.20) 0.9625	0.00 (-0.00, 0.00) 0.9851	
Beta Blocker at baseline						0.9058
Yes	11/2587 (0.4)	12/2581 (0.5)	0.91 (0.40, 2.06) 0.8206	0.91 (0.40, 2.06) 0.8189	-0.00 (-0.00, 0.00) 0.3920	
No	2/ 539 (0.4)	2/ 546 (0.4)	1.03 (0.15, 7.29) 0.9755	1.03 (0.14, 7.37) 0.9739	0.00 (-0.01, 0.01)*0.9897	
Diuretics at baseline						0.2487
Yes	13/2789 (0.5)	13/2783 (0.5)	1.00 (0.46, 2.15) 0.9947	1.00 (0.46, 2.16) 0.9947	-0.00 (-0.00, 0.00) 0.9968	
No	0/ 337 (0.0)	1/ 344 (0.3)	0.34 (0.01, 8.32)*0.5087	0.34 (0.01, 8.36)*0.5085	-0.00 (-0.01, 0.00)*0.3166	

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AstraZeneca
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Analysis of proportion of patients with Non-Severe Adverse Events of Special Interest: Events leading to Amputation
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	6/3126 (0.2)	14/3127 (0.4)	0.43 (0.16, 1.11) 0.0812	0.43 (0.16, 1.11) 0.0814	-0.00 (-0.00, 0.00) 0.7338	
Age						0.0231
<= median	4/1544 (0.3)	14/1602 (0.9)	0.30 (0.10, 0.89) 0.0310	0.29 (0.10, 0.89) 0.0306	-0.01 (-0.01, -0.00)*0.0209	
> median	2/1582 (0.1)	0/1525 (0.0)	4.82 (0.23,100.3)*0.3099	4.83 (0.23,100.6)*0.3097	0.00 (-0.00, 0.00)*0.1570	
Gender						0.0236
Male	6/1765 (0.3)	8/1744 (0.5)	0.73 (0.25, 2.10) 0.5596	0.73 (0.25, 2.11) 0.5619	-0.00 (-0.01, 0.00)*0.5771	
Female	0/1361 (0.0)	6/1383 (0.4)	0.00 (0.00,) 0.9999	0.08 (0.00, 1.38)*0.0820	-0.00 (-0.01, -0.00)*0.0141	
Race						0.9456
White	6/2210 (0.3)	12/2222 (0.5)	0.50 (0.19, 1.33) 0.1671	0.50 (0.19, 1.34) 0.1677	-0.00 (-0.00, 0.00) 0.7958	
Black or African	0/ 81 (0.0)	1/ 78 (1.3)	0.32 (0.01, 7.77)*0.4846	0.32 (0.01, 7.90)*0.4838	-0.01 (-0.04, 0.01)*0.3142	
Asian	0/ 629 (0.0)	1/ 643 (0.2)	0.34 (0.01, 8.35)*0.5095	0.34 (0.01, 8.37)*0.5093	-0.00 (-0.00, 0.00)*0.3169	
Other	0/ 206 (0.0)	0/ 184 (0.0)	NE	NE	NE	
Geographic region						0.6963
Asia	0/ 606 (0.0)	1/ 619 (0.2)	0.34 (0.01, 8.34)*0.5091	0.34 (0.01, 8.36)*0.5090	-0.00 (-0.00, 0.00)*0.3169	
Europe and Saudi Arabia	3/1491 (0.2)	9/1508 (0.6)	0.33 (0.09, 1.22) 0.0972	0.33 (0.09, 1.22) 0.0972	-0.00 (-0.01, 0.00) 0.4399	
North America	2/ 427 (0.5)	3/ 422 (0.7)	0.65 (0.11, 3.86) 0.6355	0.65 (0.11, 3.92) 0.6382	-0.00 (-0.01, 0.01)*0.6446	
Latin America	1/ 602 (0.2)	1/ 578 (0.2)	1.05 (0.07,16.74) 0.9714	0.96 (0.06,15.39)*0.9770	-0.00 (-0.00, 0.00)*0.9770	
NYHA class at enrolment						0.4994
II	5/2310 (0.2)	10/2395 (0.4)	0.51 (0.18, 1.50) 0.2236	0.51 (0.18, 1.50) 0.2242	-0.00 (-0.00, 0.00) 0.8508	
III or IV	1/ 816 (0.1)	4/ 731 (0.5)	0.23 (0.03, 2.07) 0.1915	0.22 (0.02, 2.00)*0.1800	-0.00 (-0.01, 0.00)*0.1556	
LVEF at enrolment						NC
<= 49	3/1066 (0.3)	6/1047 (0.6)	NC	NC	NC	
50-59	2/1132 (0.2)	3/1121 (0.3)	NC	NC	NC	
>= 60	1/ 928 (0.1)	5/ 959 (0.5)	NC	NC	NC	
NT-proBNP at enrolment						0.5069
<= median	2/1553 (0.1)	7/1574 (0.4)	0.29 (0.06, 1.39) 0.1211	0.29 (0.06, 1.39) 0.1213	-0.00 (-0.01, 0.00)*0.0978	
> median	4/1573 (0.3)	7/1552 (0.5)	0.56 (0.16, 1.91) 0.3560	0.56 (0.16, 1.92) 0.3563	-0.00 (-0.00, 0.00) 0.6889	
Type 2 Diabetes Medical History						0.1665
Yes	4/1399 (0.3)	13/1402 (0.9)	0.31 (0.10, 0.94)*0.0392	0.31 (0.10, 0.94)*0.0390	-0.01 (-0.01, -0.00)*0.0287	
No	2/1727 (0.1)	1/1725 (0.1)	2.00 (0.18,22.01)*0.5719	2.00 (0.18,22.06)*0.5719	0.00 (-0.00, 0.00)*0.5641	
Atrial fibrillation or flutter at enrolment ECG						0.0400
Yes	0/1325 (0.0)	5/1317 (0.4)	0.00 (0.00,) 0.9999	0.09 (0.00, 1.63)*0.1032	-0.00 (-0.01, -0.00)*0.0251	
No	6/1800 (0.3)	9/1809 (0.5)	0.66 (0.24, 1.86) 0.4332	0.66 (0.23, 1.87) 0.4352	-0.00 (-0.01, 0.00)*0.4431	
BMI (kg/m2) at enrolment						0.9194
< 30	2/1732 (0.1)	5/1733 (0.3)	0.40 (0.08, 2.06) 0.2724	0.40 (0.08, 2.06) 0.2733	-0.00 (-0.00, 0.00)*0.2565	
>= 30	4/1392 (0.3)	9/1390 (0.6)	0.44 (0.14, 1.43) 0.1745	0.44 (0.14, 1.44) 0.1739	-0.00 (-0.01, 0.00)*0.1637	
Baseline eGFR (mL/min/1.73m^2)						0.1090
< 60	2/1514 (0.1)	10/1551 (0.6)	0.20 (0.04, 0.91) 0.0370	0.20 (0.04, 0.91) 0.0369	-0.00 (-0.01, 0.00) 0.2150	
>= 60	4/1612 (0.2)	4/1575 (0.3)	1.01 (0.25, 4.01) 0.9933	1.01 (0.25, 4.04) 0.9922	-0.00 (-0.00, 0.00)*0.9738	
SBP at randomisation						0.8537
<= median	2/1567 (0.1)	4/1588 (0.3)	0.50 (0.09, 2.72) 0.4207	0.50 (0.09, 2.72) 0.4209	-0.00 (-0.00, 0.00) 0.5992	
> median	4/1559 (0.3)	10/1539 (0.6)	0.41 (0.13, 1.29) 0.1279	0.41 (0.13, 1.30) 0.1281	-0.00 (-0.01, 0.00)*0.1036	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Non-Severe Adverse Events of Special Interest: Events leading to Amputation
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.8267
<= 49	3/1066 (0.3)	6/1047 (0.6)	0.48 (0.12, 1.91) 0.2962	0.48 (0.12, 1.92) 0.2978	-0.00 (-0.01, 0.00)*0.3047	
>= 50	3/2060 (0.1)	8/2080 (0.4)	0.38 (0.10, 1.45) 0.1577	0.38 (0.10, 1.45) 0.1573	-0.00 (-0.01, 0.00)*0.1343	
Randomised during hospitalisation for HF or within 30 days of discharge						0.3759
Yes	0/ 328 (0.0)	1/ 326 (0.3)	0.33 (0.01, 8.10)*0.4982	0.33 (0.01, 8.14)*0.4980	-0.00 (-0.01, 0.00)*0.3166	
No	6/2798 (0.2)	13/2801 (0.5)	0.46 (0.18, 1.22) 0.1196	0.46 (0.18, 1.22) 0.1200	-0.00 (-0.00, 0.00) 0.7905	
MRAs at baseline						0.5181
Yes	1/1339 (0.1)	4/1325 (0.3)	0.24 (0.03, 2.14) 0.2005	0.24 (0.03, 2.14) 0.2008	-0.00 (-0.01, 0.00)*0.1767	
No	5/1787 (0.3)	10/1802 (0.6)	0.52 (0.18, 1.50) 0.2252	0.51 (0.18, 1.51) 0.2253	-0.00 (-0.00, 0.00) 0.6084	
ACEi+ARB at baseline						0.9176
Yes	5/2259 (0.2)	12/2276 (0.5)	0.42 (0.15, 1.19) 0.1030	0.42 (0.15, 1.19) 0.1035	-0.00 (-0.01, 0.00)*0.0913	
No	1/ 867 (0.1)	2/ 851 (0.2)	0.49 (0.04, 5.35) 0.5555	0.49 (0.04, 5.36) 0.5551	-0.00 (-0.01, 0.00)*0.5537	
ARNI at baseline						1.0000
Yes	0/ 165 (0.0)	0/ 136 (0.0)	NE	NE	NE	
No	6/2961 (0.2)	14/2991 (0.5)	0.44 (0.17, 1.13) 0.0883	0.43 (0.17, 1.13) 0.0886	-0.00 (-0.00, 0.00) 0.7407	
Beta Blocker at baseline						0.0757
Yes	6/2587 (0.2)	10/2581 (0.4)	0.59 (0.22, 1.63) 0.3115	0.59 (0.22, 1.64) 0.3128	-0.00 (-0.00, 0.00)*0.3144	
No	0/ 539 (0.0)	4/ 546 (0.7)	0.00 (0.00,) 0.9999	0.11 (0.01, 2.08)*0.1418	-0.01 (-0.01, -0.00)*0.0447	
Diuretics at baseline						1.0000
Yes	6/2789 (0.2)	14/2783 (0.5)	0.43 (0.16, 1.11) 0.0805	0.43 (0.16, 1.11) 0.0807	-0.00 (-0.00, 0.00) 0.7122	
No	0/ 337 (0.0)	0/ 344 (0.0)	NE	NE	NE	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events of Special Interest: Events leading to a risk for Lower Limb Amputations
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	206/3126 (6.6)	218/3127 (7.0)	0.94 (0.79, 1.13) 0.5432	0.94 (0.77, 1.15) 0.5452	-0.00 (-0.02, 0.01) 0.5812	
Age						0.9218
<= median	103/1544 (6.7)	112/1602 (7.0)	0.95 (0.74, 1.23) 0.7105	0.95 (0.72, 1.25) 0.7126	-0.00 (-0.02, 0.01) 0.7611	
> median	103/1582 (6.5)	106/1525 (7.0)	0.94 (0.72, 1.22) 0.6217	0.93 (0.70, 1.23) 0.6222	-0.00 (-0.02, 0.01) 0.6297	
Gender						0.9676
Male	128/1765 (7.3)	134/1744 (7.7)	0.94 (0.74, 1.19) 0.5985	0.93 (0.73, 1.20) 0.5991	-0.00 (-0.02, 0.01) 0.6169	
Female	78/1361 (5.7)	84/1383 (6.1)	0.95 (0.70, 1.28) 0.7180	0.94 (0.69, 1.30) 0.7202	-0.00 (-0.02, 0.01) 0.7578	
Race						0.6990
White	142/2210 (6.4)	157/2222 (7.1)	0.91 (0.73, 1.13) 0.3876	0.90 (0.71, 1.14) 0.3946	-0.00 (-0.02, 0.01) 0.5077	
Black or African	7/ 81 (8.6)	9/ 78 (11.5)	0.74 (0.29, 1.87) 0.5180	0.70 (0.24, 1.99) 0.5008	-0.04 (-0.13, 0.05) 0.3566	
Asian	46/ 629 (7.3)	45/ 643 (7.0)	1.04 (0.70, 1.55) 0.8359	1.04 (0.68, 1.60) 0.8481	0.00 (-0.03, 0.03) 0.9964	
Other	11/ 206 (5.3)	7/ 184 (3.8)	1.46 (0.58, 3.67) 0.4259	1.50 (0.57, 3.98) 0.4141	0.02 (-0.01, 0.06) 0.1920	
Geographic region						0.8374
Asia	45/ 606 (7.4)	44/ 619 (7.1)	1.04 (0.70, 1.56) 0.8355	1.04 (0.68, 1.61) 0.8485	-0.00 (-0.03, 0.03) 0.9979	
Europe and Saudi Arabia	67/1491 (4.5)	75/1508 (5.0)	0.90 (0.65, 1.24) 0.5047	0.89 (0.64, 1.25) 0.5100	-0.00 (-0.02, 0.01) 0.6413	
North America	65/ 427 (15.2)	64/ 422 (15.2)	1.00 (0.73, 1.37) 0.9941	1.00 (0.69, 1.46) 0.9937	0.00 (-0.05, 0.05) 0.9920	
Latin America	29/ 602 (4.8)	35/ 578 (6.1)	0.82 (0.51, 1.33) 0.4236	0.82 (0.49, 1.36) 0.4348	-0.00 (-0.03, 0.02) 0.7364	
NYHA class at enrolment						0.0919
II	143/2310 (6.2)	172/2395 (7.2)	0.86 (0.69, 1.06) 0.1663	0.85 (0.68, 1.07) 0.1659	-0.01 (-0.02, 0.00) 0.1715	
III or IV	63/ 816 (7.7)	46/ 731 (6.3)	1.23 (0.86, 1.78) 0.2595	1.26 (0.85, 1.86) 0.2561	0.02 (-0.01, 0.04) 0.2205	
LVEF at enrolment						0.6523
<= 49	63/1066 (5.9)	61/1047 (5.8)	1.00 (0.71, 1.41) 0.9869	1.00 (0.70, 1.44) 0.9814	0.00 (-0.02, 0.02) 0.8957	
50-59	82/1132 (7.2)	81/1121 (7.2)	1.01 (0.75, 1.35) 0.9708	1.00 (0.73, 1.38) 0.9813	-0.00 (-0.02, 0.02) 0.8907	
>= 60	61/ 928 (6.6)	76/ 959 (7.9)	0.83 (0.60, 1.15) 0.2728	0.82 (0.58, 1.17) 0.2773	-0.01 (-0.03, 0.01) 0.3470	
NT-proBNP at enrolment						0.6003
<= median	87/1553 (5.6)	99/1574 (6.3)	0.89 (0.67, 1.18) 0.4184	0.88 (0.66, 1.19) 0.4160	-0.01 (-0.02, 0.01) 0.3871	
> median	119/1573 (7.6)	119/1552 (7.7)	0.98 (0.77, 1.25) 0.8949	0.98 (0.75, 1.28) 0.9050	0.00 (-0.02, 0.02) 0.9779	
Type 2 Diabetes Medical History						0.8114
Yes	124/1399 (8.9)	129/1402 (9.2)	0.96 (0.76, 1.22)*0.7553	0.96 (0.74, 1.24)*0.7553	-0.00 (-0.02, 0.02)*0.7552	
No	82/1727 (4.7)	89/1725 (5.2)	0.92 (0.69, 1.23)*0.5778	0.92 (0.67, 1.25)*0.5777	-0.00 (-0.02, 0.01)*0.5776	
Atrial fibrillation or flutter at enrolment ECG						0.3444
Yes	83/1325 (6.3)	97/1317 (7.4)	0.85 (0.64, 1.13) 0.2634	0.84 (0.62, 1.14) 0.2658	-0.01 (-0.03, 0.01) 0.2993	
No	123/1800 (6.8)	121/1809 (6.7)	1.02 (0.80, 1.30) 0.8844	1.02 (0.78, 1.32) 0.8914	0.00 (-0.02, 0.02) 0.9981	
BMI (kg/m2) at enrolment						0.6561
< 30	97/1732 (5.6)	98/1733 (5.7)	0.99 (0.76, 1.30) 0.9536	0.99 (0.74, 1.32) 0.9453	-0.00 (-0.02, 0.01) 0.8198	
>= 30	109/1392 (7.8)	119/1390 (8.6)	0.91 (0.71, 1.17) 0.4691	0.91 (0.69, 1.19) 0.4794	-0.01 (-0.03, 0.01) 0.6112	
Baseline eGFR (mL/min/1.73m^2)						0.6685
< 60	131/1514 (8.7)	136/1551 (8.8)	0.98 (0.78, 1.23) 0.8371	0.97 (0.76, 1.25) 0.8380	-0.00 (-0.02, 0.02) 0.8520	
>= 60	75/1612 (4.7)	82/1575 (5.2)	0.90 (0.66, 1.22) 0.4883	0.89 (0.65, 1.23) 0.4904	-0.00 (-0.02, 0.01) 0.5326	
SBP at randomisation						0.5652
<= median	100/1567 (6.4)	112/1588 (7.1)	0.90 (0.69, 1.17) 0.4307	0.89 (0.68, 1.18) 0.4340	-0.01 (-0.02, 0.01) 0.4798	
> median	106/1559 (6.8)	106/1539 (6.9)	1.00 (0.77, 1.30) 0.9843	1.00 (0.76, 1.33) 0.9924	-0.00 (-0.02, 0.02) 0.8922	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Adverse Events of Special Interest: Events leading to a risk for Lower Limb Amputations
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.6872
<= 49	63/1066 (5.9)	61/1047 (5.8)	1.00 (0.71, 1.41) 0.9869	1.00 (0.70, 1.44) 0.9814	0.00 (-0.02, 0.02) 0.8957	
>= 50	143/2060 (6.9)	157/2080 (7.5)	0.92 (0.74, 1.15) 0.4747	0.92 (0.72, 1.16) 0.4737	-0.01 (-0.02, 0.01) 0.4711	
Randomised during hospitalisation for HF or within 30 days of discharge						0.9436
Yes	19/ 328 (5.8)	20/ 326 (6.1)	0.91 (0.50, 1.67) 0.7658	0.90 (0.47, 1.73) 0.7597	-0.01 (-0.04, 0.03) 0.6690	
No	187/2798 (6.7)	198/2801 (7.1)	0.95 (0.78, 1.15) 0.5791	0.94 (0.77, 1.16) 0.5819	-0.00 (-0.02, 0.01) 0.6262	
MRAs at baseline						0.4582
Yes	77/1339 (5.8)	87/1325 (6.6)	0.87 (0.65, 1.17) 0.3568	0.86 (0.63, 1.18) 0.3571	-0.01 (-0.03, 0.01) 0.3671	
No	129/1787 (7.2)	131/1802 (7.3)	1.00 (0.79, 1.26) 0.9929	1.00 (0.78, 1.29) 0.9891	0.00 (-0.02, 0.02) 0.9423	
ACEi+ARB at baseline						0.7948
Yes	147/2259 (6.5)	159/2276 (7.0)	0.93 (0.75, 1.15) 0.5121	0.93 (0.74, 1.17) 0.5271	-0.00 (-0.02, 0.01) 0.7613	
No	59/ 867 (6.8)	59/ 851 (6.9)	0.98 (0.69, 1.39) 0.9191	0.98 (0.67, 1.42) 0.8950	-0.01 (-0.03, 0.02) 0.6097	
ARNI at baseline						0.2317
Yes	7/ 165 (4.2)	10/ 136 (7.4)	0.55 (0.21, 1.42) 0.2189	0.53 (0.19, 1.45) 0.2161	-0.04 (-0.09, 0.02) 0.1764	
No	199/2961 (6.7)	208/2991 (7.0)	0.97 (0.80, 1.17) 0.7377	0.97 (0.79, 1.18) 0.7419	-0.00 (-0.01, 0.01) 0.8037	
Beta Blocker at baseline						0.1953
Yes	165/2587 (6.4)	184/2581 (7.1)	0.89 (0.73, 1.09) 0.2739	0.89 (0.71, 1.10) 0.2722	-0.01 (-0.02, 0.01) 0.2629	
No	41/ 539 (7.6)	34/ 546 (6.2)	1.23 (0.79, 1.90) 0.3615	1.25 (0.78, 2.00) 0.3562	0.02 (-0.01, 0.05) 0.2980	
Diuretics at baseline						0.7055
Yes	194/2789 (7.0)	203/2783 (7.3)	0.95 (0.79, 1.15) 0.6130	0.95 (0.77, 1.17) 0.6219	-0.00 (-0.02, 0.01) 0.7441	
No	12/ 337 (3.6)	15/ 344 (4.4)	0.82 (0.39, 1.73) 0.6087	0.81 (0.37, 1.75) 0.5892	-0.02 (-0.05, 0.01) 0.1826	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events of Special Interest: Events leading to a risk for Lower Limb Amputations
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	103/3126 (3.3)	93/3127 (3.0)	1.11 (0.84, 1.46) 0.4608	1.11 (0.84, 1.48) 0.4683	0.00 (-0.01, 0.01) 0.7640	
Age						0.9025
<= median	61/1544 (4.0)	56/1602 (3.5)	1.13 (0.79, 1.61) 0.4912	1.13 (0.78, 1.64) 0.5048	-0.00 (-0.01, 0.01) 0.9737	
> median	42/1582 (2.7)	37/1525 (2.4)	1.09 (0.71, 1.69) 0.6871	1.10 (0.70, 1.72) 0.6878	0.00 (-0.01, 0.01) 0.7185	
Gender						0.4009
Male	71/1765 (4.0)	58/1744 (3.3)	1.20 (0.86, 1.69) 0.2860	1.21 (0.85, 1.73) 0.2876	0.01 (-0.01, 0.02) 0.3658	
Female	32/1361 (2.4)	35/1383 (2.5)	0.94 (0.58, 1.50) 0.7878	0.93 (0.57, 1.52) 0.7794	-0.00 (-0.02, 0.01) 0.4698	
Race						0.7920
White	75/2210 (3.4)	72/2222 (3.2)	1.05 (0.76, 1.44) 0.7742	1.05 (0.75, 1.46) 0.7755	0.00 (-0.01, 0.01) 0.8253	
Black or African	5/ 81 (6.2)	4/ 78 (5.1)	1.16 (0.33, 4.10) 0.8166	1.15 (0.29, 4.54) 0.8375	0.01 (-0.06, 0.08)*0.7753	
Asian	20/ 629 (3.2)	16/ 643 (2.5)	1.27 (0.67, 2.44) 0.4637	1.28 (0.66, 2.49) 0.4700	0.00 (-0.02, 0.02) 0.7062	
Other	3/ 206 (1.5)	1/ 184 (0.5)	3.03 (0.32,28.62) 0.3328	2.70 (0.28,26.23)*0.3907	0.01 (-0.01, 0.03)*0.3590	
Geographic region						0.5915
Asia	19/ 606 (3.1)	16/ 619 (2.6)	1.21 (0.63, 2.33) 0.5681	1.21 (0.62, 2.38) 0.5748	0.00 (-0.02, 0.02) 0.8130	
Europe and Saudi Arabia	37/1491 (2.5)	41/1508 (2.7)	0.90 (0.58, 1.40) 0.6445	0.90 (0.57, 1.41) 0.6508	-0.00 (-0.01, 0.01) 0.9607	
North America	38/ 427 (8.9)	27/ 422 (6.4)	1.40 (0.87, 2.25) 0.1634	1.43 (0.85, 2.38) 0.1770	0.01 (-0.02, 0.05) 0.4279	
Latin America	9/ 602 (1.5)	9/ 578 (1.6)	1.00 (0.40, 2.49) 0.9918	1.00 (0.39, 2.53) 0.9932	0.00 (-0.01, 0.01) 0.9017	
NYHA class at enrolment						0.9276
II	72/2310 (3.1)	68/2395 (2.8)	1.10 (0.79, 1.52) 0.5816	1.10 (0.78, 1.54) 0.5876	0.00 (-0.01, 0.01) 0.8091	
III or IV	31/ 816 (3.8)	25/ 731 (3.4)	1.13 (0.68, 1.90) 0.6353	1.14 (0.66, 1.95) 0.6411	0.00 (-0.02, 0.02) 0.8667	
LVEF at enrolment						0.8988
<= 49	33/1066 (3.1)	27/1047 (2.6)	1.18 (0.72, 1.95) 0.5083	1.19 (0.71, 2.00) 0.5074	0.00 (-0.01, 0.02) 0.4982	
50-59	37/1132 (3.3)	36/1121 (3.2)	1.02 (0.65, 1.61) 0.9173	1.02 (0.64, 1.63) 0.9327	-0.00 (-0.02, 0.01) 0.5794	
>= 60	33/ 928 (3.6)	30/ 959 (3.1)	1.15 (0.71, 1.87) 0.5761	1.15 (0.70, 1.91) 0.5800	0.00 (-0.01, 0.02) 0.7071	
NT-proBNP at enrolment						0.6748
<= median	45/1553 (2.9)	44/1574 (2.8)	1.04 (0.69, 1.56) 0.8595	1.04 (0.68, 1.58) 0.8636	-0.00 (-0.01, 0.01) 0.9870	
> median	58/1573 (3.7)	49/1552 (3.2)	1.17 (0.80, 1.70) 0.4131	1.17 (0.80, 1.73) 0.4206	0.00 (-0.01, 0.01) 0.7053	
Type 2 Diabetes Medical History						0.1085
Yes	72/1399 (5.1)	55/1402 (3.9)	1.31 (0.93, 1.85)*0.1209	1.33 (0.93, 1.90)*0.1207	0.01 (-0.00, 0.03)*0.1195	
No	31/1727 (1.8)	38/1725 (2.2)	0.81 (0.51, 1.30)*0.3928	0.81 (0.50, 1.31)*0.3927	-0.00 (-0.01, 0.01)*0.3919	
Atrial fibrillation or flutter at enrolment ECG						0.7556
Yes	41/1325 (3.1)	39/1317 (3.0)	1.05 (0.68, 1.62) 0.8248	1.05 (0.67, 1.64) 0.8297	0.00 (-0.01, 0.01) 0.9845	
No	62/1800 (3.4)	54/1809 (3.0)	1.15 (0.80, 1.64) 0.4455	1.15 (0.80, 1.67) 0.4510	0.00 (-0.01, 0.01) 0.7035	
BMI (kg/m2) at enrolment						0.7912
< 30	45/1732 (2.6)	39/1733 (2.3)	1.16 (0.76, 1.77) 0.4992	1.16 (0.75, 1.79) 0.5051	0.00 (-0.01, 0.01) 0.7728	
>= 30	58/1392 (4.2)	54/1390 (3.9)	1.07 (0.75, 1.54) 0.7030	1.08 (0.74, 1.57) 0.7079	0.00 (-0.01, 0.02) 0.8510	
Baseline eGFR (mL/min/1.73m^2)						0.7632
< 60	69/1514 (4.6)	61/1551 (3.9)	1.15 (0.82, 1.60) 0.4262	1.15 (0.81, 1.64) 0.4385	0.00 (-0.01, 0.02) 0.8263	
>= 60	34/1612 (2.1)	32/1575 (2.0)	1.05 (0.65, 1.69) 0.8524	1.05 (0.64, 1.71) 0.8519	0.00 (-0.01, 0.01) 0.8319	
SBP at randomisation						0.8144
<= median	46/1567 (2.9)	43/1588 (2.7)	1.08 (0.72, 1.63) 0.7155	1.08 (0.71, 1.65) 0.7158	0.00 (-0.01, 0.01) 0.7258	
> median	57/1559 (3.7)	50/1539 (3.2)	1.15 (0.79, 1.67) 0.4533	1.15 (0.78, 1.70) 0.4683	-0.00 (-0.01, 0.01) 0.8532	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Serious Adverse Events of Special Interest: Events leading to a risk for Lower Limb Amputations
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.7645
<= 49	33/1066 (3.1)	27/1047 (2.6)	1.18 (0.72, 1.95) 0.5083	1.19 (0.71, 2.00) 0.5074	0.00 (-0.01, 0.02) 0.4982	
>= 50	70/2060 (3.4)	66/2080 (3.2)	1.08 (0.78, 1.50) 0.6458	1.08 (0.77, 1.52) 0.6578	-0.00 (-0.01, 0.01) 0.9359	
Randomised during hospitalisation for HF or within 30 days of discharge						0.9128
Yes	11/ 328 (3.4)	10/ 326 (3.1)	1.04 (0.45, 2.41) 0.9279	1.04 (0.43, 2.50) 0.9271	0.00 (-0.02, 0.02) 0.9085	
No	92/2798 (3.3)	83/2801 (3.0)	1.11 (0.83, 1.49) 0.4652	1.12 (0.83, 1.51) 0.4728	0.00 (-0.01, 0.01) 0.7637	
MRAs at baseline						0.7530
Yes	41/1339 (3.1)	38/1325 (2.9)	1.05 (0.68, 1.63) 0.8094	1.06 (0.67, 1.65) 0.8111	0.00 (-0.01, 0.01) 0.8744	
No	62/1787 (3.5)	55/1802 (3.1)	1.15 (0.81, 1.65) 0.4335	1.16 (0.80, 1.67) 0.4426	0.00 (-0.01, 0.01) 0.8157	
ACEi+ARB at baseline						0.2980
Yes	78/2259 (3.5)	65/2276 (2.9)	1.21 (0.88, 1.68) 0.2415	1.22 (0.87, 1.71) 0.2447	0.00 (-0.01, 0.01) 0.4194	
No	25/ 867 (2.9)	28/ 851 (3.3)	0.87 (0.51, 1.49) 0.6196	0.87 (0.50, 1.50) 0.6162	-0.01 (-0.02, 0.01) 0.5204	
ARNI at baseline						0.5704
Yes	4/ 165 (2.4)	4/ 136 (2.9)	0.87 (0.22, 3.44) 0.8386	0.86 (0.21, 3.57) 0.8398	-0.00 (-0.04, 0.04) 0.8901	
No	99/2961 (3.3)	89/2991 (3.0)	1.13 (0.85, 1.50) 0.3936	1.13 (0.85, 1.52) 0.4006	0.00 (-0.01, 0.01) 0.6943	
Beta Blocker at baseline						0.3339
Yes	79/2587 (3.1)	76/2581 (2.9)	1.04 (0.76, 1.41) 0.8229	1.04 (0.75, 1.43) 0.8328	-0.00 (-0.01, 0.01) 0.8183	
No	24/ 539 (4.5)	17/ 546 (3.1)	1.45 (0.79, 2.66) 0.2354	1.47 (0.78, 2.77) 0.2365	0.01 (-0.01, 0.03) 0.2928	
Diuretics at baseline						0.6600
Yes	97/2789 (3.5)	86/2783 (3.1)	1.13 (0.85, 1.50) 0.4118	1.13 (0.84, 1.52) 0.4171	0.00 (-0.01, 0.01) 0.6301	
No	6/ 337 (1.8)	7/ 344 (2.0)	0.88 (0.30, 2.58) 0.8089	0.87 (0.29, 2.62) 0.8081	-0.00 (-0.03, 0.02) 0.7525	

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AstraZeneca
Protocol: D169CC00001
Overall study population
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Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	50/3126 (1.6)	47/3127 (1.5)	1.07 (0.72, 1.58) 0.7509	1.06 (0.71, 1.59) 0.7596	-0.00 (-0.01, 0.00) 0.6161	
Age						0.9861
<= median	29/1544 (1.9)	28/1602 (1.7)	1.07 (0.64, 1.79) 0.7834	1.07 (0.63, 1.82) 0.7906	-0.00 (-0.01, 0.01) 0.5906	
> median	21/1582 (1.3)	19/1525 (1.2)	1.07 (0.58, 1.97) 0.8406	1.07 (0.57, 1.99) 0.8400	0.00 (-0.01, 0.01) 0.7812	
Gender						0.2636
Male	28/1765 (1.6)	31/1744 (1.8)	0.89 (0.54, 1.47) 0.6465	0.88 (0.53, 1.48) 0.6409	-0.00 (-0.01, 0.00) 0.3378	
Female	22/1361 (1.6)	16/1383 (1.2)	1.41 (0.74, 2.67) 0.2908	1.42 (0.74, 2.71) 0.2944	0.00 (-0.01, 0.01) 0.6945	
Race						0.7418
White	34/2210 (1.5)	36/2222 (1.6)	0.95 (0.60, 1.51) 0.8331	0.95 (0.59, 1.52) 0.8271	-0.00 (-0.01, 0.00) 0.4594	
Black or African	4/ 81 (4.9)	3/ 78 (3.8)	1.19 (0.28, 5.04) 0.8088	1.30 (0.28, 6.00)*0.7378	0.01 (-0.05, 0.07)*0.7365	
Asian	9/ 629 (1.4)	7/ 643 (1.1)	1.31 (0.49, 3.50) 0.5880	1.32 (0.49, 3.55) 0.5890	0.00 (-0.01, 0.02) 0.6524	
Other	3/ 206 (1.5)	1/ 184 (0.5)	3.03 (0.32,28.62) 0.3328	2.70 (0.28,26.23)*0.3907	0.01 (-0.01, 0.03)*0.3590	
Geographic region						0.6254
Asia	8/ 606 (1.3)	7/ 619 (1.1)	1.17 (0.43, 3.20) 0.7648	1.17 (0.42, 3.24) 0.7652	0.00 (-0.01, 0.01) 0.7924	
Europe and Saudi Arabia	20/1491 (1.3)	22/1508 (1.5)	0.91 (0.50, 1.66) 0.7547	0.91 (0.49, 1.67) 0.7573	-0.00 (-0.01, 0.01) 0.9992	
North America	19/ 427 (4.4)	13/ 422 (3.1)	1.46 (0.73, 2.91) 0.2855	1.46 (0.71, 3.00) 0.3038	-0.00 (-0.03, 0.03) 0.9111	
Latin America	3/ 602 (0.5)	5/ 578 (0.9)	0.62 (0.15, 2.57) 0.5063	0.61 (0.15, 2.58) 0.5044	-0.00 (-0.01, 0.01)*0.4452	
NYHA class at enrolment						0.4727
II	35/2310 (1.5)	37/2395 (1.5)	0.98 (0.62, 1.55) 0.9293	0.98 (0.61, 1.56) 0.9242	-0.00 (-0.01, 0.01) 0.6007	
III or IV	15/ 816 (1.8)	10/ 731 (1.4)	1.39 (0.63, 3.06) 0.4177	1.39 (0.62, 3.13) 0.4218	-0.00 (-0.01, 0.01) 0.8391	
LVEF at enrolment						0.3787
<= 49	16/1066 (1.5)	9/1047 (0.9)	1.73 (0.77, 3.91) 0.1839	1.74 (0.77, 3.97) 0.1843	0.01 (-0.00, 0.02) 0.2463	
50-59	17/1132 (1.5)	20/1121 (1.8)	0.85 (0.45, 1.61) 0.6109	0.84 (0.44, 1.62) 0.6026	-0.01 (-0.01, 0.00) 0.1705	
>= 60	17/ 928 (1.8)	18/ 959 (1.9)	0.99 (0.51, 1.91) 0.9801	0.99 (0.51, 1.93) 0.9731	-0.00 (-0.01, 0.01) 0.6001	
NT-proBNP at enrolment						0.4002
<= median	21/1553 (1.4)	24/1574 (1.5)	0.89 (0.50, 1.59) 0.6863	0.89 (0.49, 1.60) 0.6852	-0.00 (-0.01, 0.01) 0.6200	
> median	29/1573 (1.8)	23/1552 (1.5)	1.25 (0.73, 2.14) 0.4244	1.25 (0.72, 2.17) 0.4341	-0.00 (-0.01, 0.01) 0.7382	
Type 2 Diabetes Medical History						0.0521
Yes	38/1399 (2.7)	27/1402 (1.9)	1.41 (0.87, 2.30)*0.1670	1.42 (0.86, 2.34)*0.1668	0.01 (-0.00, 0.02)*0.1647	
No	12/1727 (0.7)	20/1725 (1.2)	0.60 (0.29, 1.22)*0.1591	0.60 (0.29, 1.22)*0.1589	-0.00 (-0.01, 0.00)*0.1544	
Atrial fibrillation or flutter at enrolment ECG						0.1239
Yes	12/1325 (0.9)	18/1317 (1.4)	0.67 (0.32, 1.38) 0.2739	0.66 (0.32, 1.38) 0.2719	-0.01 (-0.01, 0.00) 0.1309	
No	38/1800 (2.1)	29/1809 (1.6)	1.31 (0.81, 2.12) 0.2645	1.32 (0.81, 2.15) 0.2683	0.00 (-0.01, 0.01) 0.6241	
BMI (kg/m2) at enrolment						0.7638
< 30	25/1732 (1.4)	25/1733 (1.4)	1.01 (0.58, 1.74) 0.9836	1.00 (0.57, 1.75) 0.9975	-0.00 (-0.01, 0.00) 0.2012	
>= 30	25/1392 (1.8)	22/1390 (1.6)	1.13 (0.64, 2.00) 0.6635	1.14 (0.64, 2.03) 0.6642	0.00 (-0.01, 0.01) 0.7239	
Baseline eGFR (mL/min/1.73m^2)						0.1135
< 60	37/1514 (2.4)	28/1551 (1.8)	1.34 (0.82, 2.17) 0.2423	1.34 (0.81, 2.20) 0.2514	-0.00 (-0.01, 0.01) 0.8105	
>= 60	13/1612 (0.8)	19/1575 (1.2)	0.67 (0.33, 1.35) 0.2662	0.67 (0.33, 1.36) 0.2664	-0.00 (-0.01, 0.00) 0.2972	
SBP at randomisation						0.2756
<= median	17/1567 (1.1)	21/1588 (1.3)	0.82 (0.43, 1.54) 0.5339	0.81 (0.43, 1.55) 0.5322	-0.00 (-0.01, 0.00) 0.3831	
> median	33/1559 (2.1)	26/1539 (1.7)	1.28 (0.77, 2.13) 0.3386	1.29 (0.76, 2.16) 0.3423	0.00 (-0.01, 0.01) 0.7337	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
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Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.1754
<= 49	16/1066 (1.5)	9/1047 (0.9)	1.73 (0.77, 3.91) 0.1839	1.74 (0.77, 3.97) 0.1843	0.01 (-0.00, 0.02) 0.2463	
>= 50	34/2060 (1.7)	38/2080 (1.8)	0.91 (0.58, 1.44) 0.7000	0.91 (0.57, 1.45) 0.6894	-0.00 (-0.01, 0.00) 0.1909	
Randomised during hospitalisation for HF or within 30 days of discharge						0.4774
Yes	8/ 328 (2.4)	5/ 326 (1.5)	1.50 (0.50, 4.54) 0.4686	1.52 (0.49, 4.71) 0.4694	0.00 (-0.01, 0.02) 0.6757	
No	42/2798 (1.5)	42/2801 (1.5)	1.01 (0.66, 1.54) 0.9768	1.00 (0.65, 1.55) 0.9846	-0.00 (-0.01, 0.00) 0.5014	
MRAs at baseline						0.7013
Yes	20/1339 (1.5)	20/1325 (1.5)	0.98 (0.53, 1.80) 0.9377	0.98 (0.52, 1.82) 0.9371	-0.00 (-0.01, 0.01) 0.8991	
No	30/1787 (1.7)	27/1802 (1.5)	1.14 (0.68, 1.91) 0.6178	1.14 (0.67, 1.92) 0.6292	-0.00 (-0.01, 0.00) 0.4622	
ACEi+ARB at baseline						0.4621
Yes	36/2259 (1.6)	31/2276 (1.4)	1.18 (0.73, 1.89) 0.5045	1.18 (0.72, 1.91) 0.5119	-0.00 (-0.01, 0.01) 0.7715	
No	14/ 867 (1.6)	16/ 851 (1.9)	0.86 (0.42, 1.74) 0.6659	0.85 (0.41, 1.76) 0.6636	-0.00 (-0.02, 0.01) 0.5501	
ARNI at baseline						0.1567
Yes	1/ 165 (0.6)	3/ 136 (2.2)	0.26 (0.03, 2.55) 0.2491	0.26 (0.03, 2.56) 0.2476	-0.02 (-0.04, 0.01)*0.2521	
No	49/2961 (1.7)	44/2991 (1.5)	1.13 (0.76, 1.70) 0.5456	1.13 (0.75, 1.71) 0.5528	-0.00 (-0.01, 0.01) 0.8565	
Beta Blocker at baseline						0.0664
Yes	41/2587 (1.6)	44/2581 (1.7)	0.93 (0.61, 1.42) 0.7318	0.93 (0.60, 1.42) 0.7239	-0.00 (-0.01, 0.00) 0.2986	
No	9/ 539 (1.7)	3/ 546 (0.5)	3.10 (0.85,11.38) 0.0876	3.15 (0.85,11.71) 0.0872	0.01 (-0.00, 0.02) 0.2183	
Diuretics at baseline						0.9489
Yes	46/2789 (1.6)	43/2783 (1.5)	1.07 (0.71, 1.62) 0.7486	1.07 (0.70, 1.63) 0.7570	-0.00 (-0.01, 0.00) 0.6546	
No	4/ 337 (1.2)	4/ 344 (1.2)	1.02 (0.26, 4.04) 0.9769	1.02 (0.25, 4.11) 0.9794	-0.00 (-0.02, 0.01) 0.8122	

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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Non-Severe Adverse Events of Special Interest: Events leading to a risk for Lower Limb Amputations
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	169/3126 (5.4)	188/3127 (6.0)	0.90 (0.73, 1.10) 0.2936	0.89 (0.72, 1.11) 0.3001	-0.00 (-0.02, 0.01) 0.4262	
Age						0.7806
<= median	79/1544 (5.1)	94/1602 (5.9)	0.87 (0.65, 1.16) 0.3418	0.86 (0.63, 1.18) 0.3501	-0.00 (-0.02, 0.01) 0.5528	
> median	90/1582 (5.7)	94/1525 (6.2)	0.92 (0.70, 1.22) 0.5702	0.92 (0.68, 1.24) 0.5729	-0.00 (-0.02, 0.01) 0.6138	
Gender						0.3453
Male	110/1765 (6.2)	112/1744 (6.4)	0.97 (0.75, 1.24) 0.7851	0.96 (0.73, 1.27) 0.7913	-0.00 (-0.02, 0.01) 0.8882	
Female	59/1361 (4.3)	76/1383 (5.5)	0.79 (0.57, 1.10) 0.1630	0.78 (0.55, 1.11) 0.1655	-0.01 (-0.03, 0.01) 0.2239	
Race						0.7588
White	117/2210 (5.3)	135/2222 (6.1)	0.87 (0.68, 1.10) 0.2520	0.86 (0.67, 1.11) 0.2609	-0.01 (-0.02, 0.01) 0.4496	
Black or African	4/ 81 (4.9)	6/ 78 (7.7)	0.64 (0.19, 2.18) 0.4754	0.62 (0.17, 2.29) 0.4729	-0.03 (-0.11, 0.05) 0.4330	
Asian	39/ 629 (6.2)	41/ 643 (6.4)	0.97 (0.63, 1.48) 0.8845	0.97 (0.61, 1.52) 0.8778	-0.00 (-0.03, 0.02) 0.7868	
Other	9/ 206 (4.4)	6/ 184 (3.3)	1.37 (0.50, 3.78) 0.5415	1.40 (0.49, 4.02) 0.5330	0.02 (-0.02, 0.06) 0.3008	
Geographic region						0.9470
Asia	39/ 606 (6.4)	40/ 619 (6.5)	0.99 (0.65, 1.52) 0.9756	0.99 (0.63, 1.56) 0.9668	-0.00 (-0.03, 0.02) 0.8518	
Europe and Saudi Arabia	52/1491 (3.5)	60/1508 (4.0)	0.87 (0.60, 1.25) 0.4533	0.87 (0.59, 1.27) 0.4574	-0.00 (-0.02, 0.01) 0.5885	
North America	52/ 427 (12.2)	57/ 422 (13.5)	0.90 (0.63, 1.27) 0.5430	0.89 (0.59, 1.33) 0.5564	-0.01 (-0.06, 0.03) 0.6370	
Latin America	26/ 602 (4.3)	31/ 578 (5.4)	0.83 (0.50, 1.38) 0.4716	0.83 (0.48, 1.41) 0.4847	-0.00 (-0.03, 0.02) 0.8519	
NYHA class at enrolment						0.0757
II	115/2310 (5.0)	148/2395 (6.2)	0.80 (0.63, 1.02) 0.0680	0.79 (0.62, 1.02) 0.0697	-0.01 (-0.02, 0.00) 0.1139	
III or IV	54/ 816 (6.6)	40/ 731 (5.5)	1.21 (0.82, 1.80) 0.3385	1.23 (0.81, 1.88) 0.3358	0.01 (-0.01, 0.04) 0.2972	
LVEF at enrolment						0.3020
<= 49	49/1066 (4.6)	53/1047 (5.1)	0.90 (0.61, 1.31) 0.5680	0.89 (0.60, 1.33) 0.5779	-0.00 (-0.02, 0.02) 0.7987	
50-59	73/1132 (6.4)	68/1121 (6.1)	1.06 (0.77, 1.47) 0.7010	1.07 (0.76, 1.50) 0.7030	0.00 (-0.02, 0.02) 0.7377	
>= 60	47/ 928 (5.1)	67/ 959 (7.0)	0.73 (0.51, 1.04) 0.0841	0.71 (0.49, 1.05) 0.0858	-0.02 (-0.04, 0.00) 0.1194	
NT-proBNP at enrolment						0.7124
<= median	71/1553 (4.6)	84/1574 (5.3)	0.86 (0.63, 1.17) 0.3259	0.85 (0.61, 1.17) 0.3246	-0.01 (-0.02, 0.01) 0.3067	
> median	98/1573 (6.2)	104/1552 (6.7)	0.92 (0.71, 1.21) 0.5640	0.92 (0.69, 1.23) 0.5853	-0.00 (-0.02, 0.02) 0.9136	
Type 2 Diabetes Medical History						0.5256
Yes	96/1399 (6.9)	113/1402 (8.1)	0.85 (0.66, 1.11)*0.2283	0.84 (0.63, 1.12)*0.2282	-0.01 (-0.03, 0.01)*0.2275	
No	73/1727 (4.2)	75/1725 (4.3)	0.97 (0.71, 1.33)*0.8609	0.97 (0.70, 1.35)*0.8609	-0.00 (-0.01, 0.01)*0.8609	
Atrial fibrillation or flutter at enrolment ECG						0.6848
Yes	75/1325 (5.7)	87/1317 (6.6)	0.86 (0.64, 1.16) 0.3118	0.85 (0.62, 1.17) 0.3151	-0.01 (-0.03, 0.01) 0.3641	
No	94/1800 (5.2)	101/1809 (5.6)	0.93 (0.71, 1.22) 0.6049	0.93 (0.69, 1.24) 0.6082	-0.00 (-0.02, 0.01) 0.6883	
BMI (kg/m2) at enrolment						0.5585
< 30	79/1732 (4.6)	82/1733 (4.7)	0.96 (0.71, 1.30) 0.8097	0.96 (0.70, 1.32) 0.8120	-0.00 (-0.02, 0.01) 0.8582	
>= 30	90/1392 (6.5)	105/1390 (7.6)	0.85 (0.65, 1.12) 0.2523	0.85 (0.63, 1.13) 0.2592	-0.01 (-0.03, 0.01) 0.3754	
Baseline eGFR (mL/min/1.73m^2)						0.9966
< 60	103/1514 (6.8)	116/1551 (7.5)	0.90 (0.70, 1.16) 0.4162	0.89 (0.68, 1.18) 0.4272	-0.00 (-0.02, 0.01) 0.5905	
>= 60	66/1612 (4.1)	72/1575 (4.6)	0.90 (0.65, 1.25) 0.5283	0.90 (0.64, 1.26) 0.5303	-0.00 (-0.02, 0.01) 0.5773	
SBP at randomisation						0.9218
<= median	86/1567 (5.5)	97/1588 (6.1)	0.89 (0.67, 1.18) 0.4352	0.89 (0.66, 1.20) 0.4400	-0.01 (-0.02, 0.01) 0.5165	
> median	83/1559 (5.3)	91/1539 (5.9)	0.91 (0.68, 1.22) 0.5264	0.91 (0.67, 1.23) 0.5301	-0.00 (-0.02, 0.01) 0.6191	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with Non-Severe Adverse Events of Special Interest: Events leading to a risk for Lower Limb Amputations
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.9938
<= 49	49/1066 (4.6)	53/1047 (5.1)	0.90 (0.61, 1.31) 0.5680	0.89 (0.60, 1.33) 0.5779	-0.00 (-0.02, 0.02) 0.7987	
>= 50	120/2060 (5.8)	135/2080 (6.5)	0.90 (0.71, 1.14) 0.3843	0.89 (0.69, 1.15) 0.3883	-0.01 (-0.02, 0.01) 0.4575	
Randomised during hospitalisation for HF or within 30 days of discharge						0.5641
Yes	12/ 328 (3.7)	16/ 326 (4.9)	0.72 (0.35, 1.50) 0.3837	0.71 (0.33, 1.53) 0.3825	-0.01 (-0.04, 0.02) 0.3852	
No	157/2798 (5.6)	172/2801 (6.1)	0.91 (0.74, 1.13) 0.4010	0.91 (0.73, 1.14) 0.4089	-0.00 (-0.02, 0.01) 0.5496	
MRAs at baseline						0.4183
Yes	61/1339 (4.6)	74/1325 (5.6)	0.81 (0.58, 1.13) 0.2156	0.80 (0.57, 1.14) 0.2161	-0.01 (-0.03, 0.01) 0.2285	
No	108/1787 (6.0)	114/1802 (6.3)	0.96 (0.74, 1.24) 0.7563	0.96 (0.73, 1.26) 0.7730	0.00 (-0.01, 0.02) 0.9602	
ACEi+ARB at baseline						0.5116
Yes	120/2259 (5.3)	140/2276 (6.2)	0.86 (0.68, 1.09) 0.2159	0.86 (0.67, 1.10) 0.2275	-0.00 (-0.02, 0.01) 0.4872	
No	49/ 867 (5.7)	48/ 851 (5.6)	1.00 (0.68, 1.47) 0.9907	1.00 (0.66, 1.50) 0.9895	-0.00 (-0.03, 0.02) 0.6876	
ARNI at baseline						0.5757
Yes	6/ 165 (3.6)	7/ 136 (5.1)	0.67 (0.23, 1.98) 0.4725	0.66 (0.21, 2.04) 0.4710	-0.02 (-0.06, 0.03) 0.4436	
No	163/2961 (5.5)	181/2991 (6.1)	0.91 (0.74, 1.12) 0.3700	0.91 (0.73, 1.13) 0.3781	-0.00 (-0.02, 0.01) 0.5295	
Beta Blocker at baseline						0.4690
Yes	135/2587 (5.2)	155/2581 (6.0)	0.87 (0.69, 1.08) 0.2087	0.86 (0.68, 1.09) 0.2123	-0.01 (-0.02, 0.01) 0.2896	
No	34/ 539 (6.3)	33/ 546 (6.0)	1.05 (0.66, 1.66) 0.8482	1.05 (0.64, 1.72) 0.8417	0.00 (-0.02, 0.03) 0.7512	
Diuretics at baseline						0.5701
Yes	160/2789 (5.7)	175/2783 (6.3)	0.91 (0.74, 1.12) 0.3741	0.91 (0.73, 1.13) 0.3857	-0.00 (-0.02, 0.01) 0.5925	
No	9/ 337 (2.7)	13/ 344 (3.8)	0.71 (0.31, 1.64) 0.4257	0.70 (0.29, 1.65) 0.4124	-0.02 (-0.05, 0.00) 0.0724	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with SAE/DAE Renal events
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	84/3126 (2.7)	91/3127 (2.9)	0.92 (0.69, 1.24) 0.5921	0.92 (0.68, 1.24) 0.5913	-0.00 (-0.01, 0.01) 0.5751	
Age						0.6481
<= median	39/1544 (2.5)	47/1602 (2.9)	0.86 (0.57, 1.31) 0.4784	0.86 (0.56, 1.32) 0.4789	-0.00 (-0.01, 0.01) 0.5272	
> median	45/1582 (2.8)	44/1525 (2.9)	0.99 (0.65, 1.48) 0.9452	0.99 (0.65, 1.50) 0.9442	-0.00 (-0.01, 0.01) 0.9105	
Gender						0.5819
Male	49/1765 (2.8)	56/1744 (3.2)	0.86 (0.59, 1.26) 0.4383	0.86 (0.58, 1.26) 0.4343	-0.01 (-0.02, 0.01) 0.3267	
Female	35/1361 (2.6)	35/1383 (2.5)	1.02 (0.64, 1.62) 0.9407	1.02 (0.63, 1.64) 0.9396	0.00 (-0.01, 0.01) 0.8958	
Race						0.8355
White	60/2210 (2.7)	69/2222 (3.1)	0.87 (0.62, 1.23) 0.4398	0.87 (0.61, 1.24) 0.4396	-0.00 (-0.01, 0.01) 0.4393	
Black or African	9/ 81 (11.1)	6/ 78 (7.7)	1.42 (0.53, 3.80) 0.4846	1.48 (0.50, 4.37) 0.4817	0.03 (-0.06, 0.12) 0.4694	
Asian	12/ 629 (1.9)	13/ 643 (2.0)	0.93 (0.43, 2.03) 0.8637	0.93 (0.42, 2.06) 0.8648	-0.00 (-0.02, 0.01) 0.9235	
Other	3/ 206 (1.5)	3/ 184 (1.6)	0.90 (0.18, 4.41) 0.8942	0.90 (0.18, 4.51) 0.8937	-0.00 (-0.03, 0.02) 0.8556	
Geographic region						0.5402
Asia	10/ 606 (1.7)	13/ 619 (2.1)	0.78 (0.34, 1.76) 0.5495	0.78 (0.34, 1.79) 0.5514	-0.00 (-0.02, 0.01) 0.6599	
Europe and Saudi Arabia	33/1491 (2.2)	38/1508 (2.5)	0.87 (0.55, 1.39) 0.5678	0.87 (0.54, 1.40) 0.5680	-0.00 (-0.01, 0.01) 0.5862	
North America	31/ 427 (7.3)	25/ 422 (5.9)	1.22 (0.74, 2.03) 0.4372	1.24 (0.72, 2.14) 0.4437	0.01 (-0.02, 0.04) 0.5640	
Latin America	10/ 602 (1.7)	15/ 578 (2.6)	0.64 (0.29, 1.41) 0.2656	0.63 (0.28, 1.42) 0.2654	-0.01 (-0.03, 0.01) 0.2649	
NYHA class at enrolment						0.3814
II	58/2310 (2.5)	60/2395 (2.5)	1.00 (0.70, 1.43) 0.9986	1.00 (0.69, 1.44) 0.9991	-0.00 (-0.01, 0.01) 0.9793	
III or IV	26/ 816 (3.2)	31/ 731 (4.2)	0.76 (0.45, 1.26) 0.2889	0.75 (0.44, 1.28) 0.2880	-0.01 (-0.03, 0.01) 0.2808	
LVEF at enrolment						0.0214
<= 49	20/1066 (1.9)	38/1047 (3.6)	0.52 (0.30, 0.88) 0.0151	0.51 (0.29, 0.87) 0.0148	-0.02 (-0.03, -0.00) 0.0099	
50-59	32/1132 (2.8)	29/1121 (2.6)	1.09 (0.67, 1.79) 0.7244	1.10 (0.66, 1.82) 0.7240	0.00 (-0.01, 0.02) 0.7093	
>= 60	32/ 928 (3.4)	24/ 959 (2.5)	1.39 (0.83, 2.35) 0.2100	1.41 (0.83, 2.42) 0.2064	0.01 (-0.00, 0.02) 0.1327	
NT-proBNP at enrolment						0.8652
<= median	30/1553 (1.9)	32/1574 (2.0)	0.95 (0.58, 1.56) 0.8413	0.95 (0.57, 1.57) 0.8388	-0.00 (-0.01, 0.01) 0.7163	
> median	54/1573 (3.4)	59/1552 (3.8)	0.90 (0.63, 1.30) 0.5761	0.90 (0.62, 1.31) 0.5773	-0.00 (-0.02, 0.01) 0.6156	
Type 2 Diabetes Medical History						0.6191
Yes	51/1399 (3.6)	52/1402 (3.7)	0.98 (0.67, 1.44)*0.9288	0.98 (0.66, 1.46)*0.9288	-0.00 (-0.01, 0.01)*0.9288	
No	33/1727 (1.9)	39/1725 (2.3)	0.85 (0.53, 1.34)*0.4723	0.84 (0.53, 1.35)*0.4723	-0.00 (-0.01, 0.01)*0.4718	
Atrial fibrillation or flutter at enrolment ECG						0.7970
Yes	29/1325 (2.2)	33/1317 (2.5)	0.87 (0.53, 1.43) 0.5935	0.87 (0.53, 1.44) 0.5930	-0.00 (-0.01, 0.01) 0.5733	
No	55/1800 (3.1)	58/1809 (3.2)	0.95 (0.66, 1.36) 0.7775	0.95 (0.65, 1.38) 0.7792	-0.00 (-0.01, 0.01) 0.8430	
BMI (kg/m2) at enrolment						0.9292
< 30	40/1732 (2.3)	44/1733 (2.5)	0.91 (0.60, 1.39) 0.6613	0.91 (0.59, 1.40) 0.6609	-0.00 (-0.01, 0.01) 0.6461	
>= 30	44/1392 (3.2)	47/1390 (3.4)	0.93 (0.62, 1.40) 0.7414	0.93 (0.61, 1.42) 0.7413	-0.00 (-0.01, 0.01) 0.7467	
Baseline eGFR (mL/min/1.73m^2)						0.8769
< 60	69/1514 (4.6)	76/1551 (4.9)	0.92 (0.67, 1.27) 0.6300	0.92 (0.66, 1.29) 0.6302	-0.00 (-0.02, 0.01) 0.6380	
>= 60	15/1612 (0.9)	15/1575 (1.0)	0.99 (0.48, 2.01) 0.9709	0.99 (0.48, 2.03) 0.9707	-0.00 (-0.01, 0.01) 0.9510	
SBP at randomisation						0.7306
<= median	41/1567 (2.6)	47/1588 (3.0)	0.88 (0.58, 1.33) 0.5460	0.88 (0.57, 1.34) 0.5451	-0.00 (-0.02, 0.01) 0.5149	
> median	43/1559 (2.8)	44/1539 (2.9)	0.98 (0.65, 1.48) 0.9081	0.98 (0.64, 1.50) 0.9104	-0.00 (-0.01, 0.01) 0.9990	

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LVEF at enrolment 2						0.0071
<= 49	20/1066 (1.9)	38/1047 (3.6)	0.52 (0.30, 0.88) 0.0151	0.51 (0.29, 0.87) 0.0148	-0.02 (-0.03, -0.00) 0.0099	
>= 50	64/2060 (3.1)	53/2080 (2.5)	1.22 (0.86, 1.75) 0.2687	1.23 (0.85, 1.78) 0.2666	0.01 (-0.00, 0.02) 0.2155	
Randomised during hospitalisation for HF or within 30 days of discharge						0.5913
Yes	10/ 328 (3.0)	13/ 326 (4.0)	0.75 (0.33, 1.69) 0.4866	0.74 (0.32, 1.72) 0.4855	-0.01 (-0.04, 0.02) 0.4672	
No	74/2798 (2.6)	78/2801 (2.8)	0.95 (0.70, 1.30) 0.7566	0.95 (0.69, 1.31) 0.7561	-0.00 (-0.01, 0.01) 0.7432	
MRAs at baseline						0.2675
Yes	29/1339 (2.2)	38/1325 (2.9)	0.76 (0.47, 1.22) 0.2584	0.75 (0.46, 1.23) 0.2586	-0.01 (-0.02, 0.01) 0.2733	
No	55/1787 (3.1)	53/1802 (2.9)	1.06 (0.73, 1.53) 0.7615	1.06 (0.72, 1.56) 0.7584	0.00 (-0.01, 0.01) 0.6708	
ACEi+ARB at baseline						0.1028
Yes	59/2259 (2.6)	54/2276 (2.4)	1.10 (0.77, 1.59) 0.6029	1.11 (0.76, 1.61) 0.6005	0.00 (-0.01, 0.01) 0.5165	
No	25/ 867 (2.9)	37/ 851 (4.3)	0.66 (0.40, 1.09) 0.1040	0.65 (0.39, 1.09) 0.1026	-0.02 (-0.03, 0.00) 0.0786	
ARNI at baseline						0.0571
Yes	3/ 165 (1.8)	8/ 136 (5.9)	0.32 (0.09, 1.20) 0.0919	0.31 (0.08, 1.20) 0.0896	-0.04 (-0.08, 0.00) 0.0794	
No	81/2961 (2.7)	83/2991 (2.8)	0.99 (0.73, 1.34) 0.9406	0.99 (0.72, 1.35) 0.9400	-0.00 (-0.01, 0.01) 0.9216	
Beta Blocker at baseline						0.4721
Yes	67/2587 (2.6)	76/2581 (2.9)	0.88 (0.63, 1.21) 0.4284	0.87 (0.63, 1.22) 0.4288	-0.00 (-0.01, 0.01) 0.4594	
No	17/ 539 (3.2)	15/ 546 (2.7)	1.15 (0.58, 2.27) 0.6934	1.15 (0.57, 2.33) 0.6932	0.00 (-0.02, 0.02) 0.6836	
Diuretics at baseline						0.4958
Yes	79/2789 (2.8)	83/2783 (3.0)	0.95 (0.70, 1.29) 0.7362	0.95 (0.69, 1.30) 0.7383	-0.00 (-0.01, 0.01) 0.8171	
No	5/ 337 (1.5)	8/ 344 (2.3)	0.64 (0.21, 1.92) 0.4229	0.63 (0.20, 1.96) 0.4275	-0.00 (-0.03, 0.02) 0.7439	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with SAE/DAE Volume depletion
Safety Analysis Set

Subgroup Level	_Dapa 10 mg (N=3126)__ n/ N (%)	___Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
Overall	49/3126 (1.6)	37/3127 (1.2)	1.32 (0.87, 2.02) 0.1939	1.33 (0.87, 2.04) 0.1930	0.00 (-0.00, 0.01) 0.1392	
Age						0.0237
<= median	24/1544 (1.6)	10/1602 (0.6)	2.49 (1.20, 5.19) 0.0148	2.52 (1.20, 5.28) 0.0147	0.01 (0.00, 0.02) 0.0124	
> median	25/1582 (1.6)	27/1525 (1.8)	0.89 (0.52, 1.53) 0.6795	0.89 (0.51, 1.54) 0.6811	-0.00 (-0.01, 0.01) 0.7750	
Gender						0.4406
Male	24/1765 (1.4)	21/1744 (1.2)	1.13 (0.63, 2.03) 0.6756	1.13 (0.63, 2.05) 0.6738	0.00 (-0.01, 0.01) 0.5365	
Female	25/1361 (1.8)	16/1383 (1.2)	1.58 (0.85, 2.95) 0.1486	1.59 (0.85, 3.00) 0.1481	0.01 (-0.00, 0.02) 0.1308	
Race						0.0349
White	41/2210 (1.9)	22/2222 (1.0)	1.87 (1.12, 3.13) 0.0169	1.89 (1.12, 3.19) 0.0166	0.01 (0.00, 0.02) 0.0086	
Black or African	3/ 81 (3.7)	5/ 78 (6.4)	0.59 (0.14, 2.38) 0.4547	0.57 (0.13, 2.47) 0.4501	-0.03 (-0.10, 0.04) 0.3664	
Asian	4/ 629 (0.6)	10/ 643 (1.6)	0.41 (0.13, 1.30) 0.1314	0.41 (0.13, 1.31) 0.1311	-0.01 (-0.02, 0.00) 0.1518	
Other	1/ 206 (0.5)	0/ 184 (0.0)	2.68 (0.11,65.41)*0.5451	2.69 (0.11,66.53)*0.5448	0.00 (-0.00, 0.01)*0.3161	
Geographic region						0.2191
Asia	4/ 606 (0.7)	8/ 619 (1.3)	0.51 (0.16, 1.70) 0.2743	0.51 (0.15, 1.71) 0.2747	-0.01 (-0.02, 0.01) 0.3526	
Europe and Saudi Arabia	15/1491 (1.0)	8/1508 (0.5)	1.91 (0.81, 4.49) 0.1384	1.92 (0.81, 4.55) 0.1373	0.01 (0.00, 0.01) 0.0350	
North America	26/ 427 (6.1)	16/ 422 (3.8)	1.61 (0.87, 2.95) 0.1270	1.64 (0.87, 3.11) 0.1262	0.02 (-0.01, 0.05) 0.1217	
Latin America	4/ 602 (0.7)	5/ 578 (0.9)	0.74 (0.20, 2.74) 0.6497	0.74 (0.20, 2.76) 0.6490	-0.00 (-0.01, 0.01) 0.5778	
NYHA class at enrolment						0.5616
II	33/2310 (1.4)	24/2395 (1.0)	1.43 (0.85, 2.41) 0.1831	1.43 (0.84, 2.43) 0.1827	0.00 (-0.00, 0.01) 0.1433	
III or IV	16/ 816 (2.0)	13/ 731 (1.8)	1.08 (0.53, 2.24) 0.8254	1.09 (0.52, 2.28) 0.8271	0.00 (-0.01, 0.01) 0.9300	
LVEF at enrolment						0.3653
<= 49	14/1066 (1.3)	6/1047 (0.6)	2.32 (0.90, 6.02) 0.0827	2.34 (0.90, 6.12) 0.0824	0.01 (-0.00, 0.01) 0.0937	
50-59	21/1132 (1.9)	20/1121 (1.8)	1.04 (0.57, 1.91) 0.9025	1.04 (0.56, 1.93) 0.9007	0.00 (-0.01, 0.01) 0.8003	
>= 60	14/ 928 (1.5)	11/ 959 (1.1)	1.31 (0.60, 2.86) 0.5044	1.31 (0.59, 2.90) 0.5038	0.00 (-0.01, 0.01) 0.4637	
NT-proBNP at enrolment						0.8640
<= median	20/1553 (1.3)	16/1574 (1.0)	1.27 (0.66, 2.43) 0.4789	1.27 (0.66, 2.46) 0.4780	0.00 (-0.00, 0.01) 0.3789	
> median	29/1573 (1.8)	21/1552 (1.4)	1.36 (0.78, 2.38) 0.2741	1.37 (0.78, 2.42) 0.2744	0.00 (-0.00, 0.01) 0.3150	
Type 2 Diabetes Medical History						0.2376
Yes	22/1399 (1.6)	12/1402 (0.9)	1.84 (0.91, 3.70)*0.0883	1.85 (0.91, 3.75)*0.0881	0.01 (-0.00, 0.02)*0.0832	
No	27/1727 (1.6)	25/1725 (1.4)	1.08 (0.63, 1.85)*0.7832	1.08 (0.62, 1.87)*0.7832	0.00 (-0.01, 0.01)*0.7831	
Atrial fibrillation or flutter at enrolment ECG						0.5657
Yes	21/1325 (1.6)	18/1317 (1.4)	1.15 (0.62, 2.15) 0.6577	1.16 (0.61, 2.18) 0.6549	0.00 (-0.01, 0.01) 0.4711	
No	28/1800 (1.6)	19/1809 (1.1)	1.48 (0.83, 2.64) 0.1836	1.49 (0.83, 2.68) 0.1835	0.01 (-0.00, 0.01) 0.1786	
BMI (kg/m2) at enrolment						0.5091
< 30	27/1732 (1.6)	23/1733 (1.3)	1.17 (0.68, 2.04) 0.5690	1.18 (0.67, 2.06) 0.5680	0.00 (-0.01, 0.01) 0.4922	
>= 30	22/1392 (1.6)	14/1390 (1.0)	1.57 (0.81, 3.05) 0.1845	1.58 (0.80, 3.10) 0.1839	0.01 (-0.00, 0.01) 0.1621	
Baseline eGFR (mL/min/1.73m^2)						0.4131
< 60	34/1514 (2.2)	29/1551 (1.9)	1.21 (0.74, 1.97) 0.4469	1.22 (0.74, 2.01) 0.4438	0.01 (-0.00, 0.02) 0.3143	
>= 60	15/1612 (0.9)	8/1575 (0.5)	1.82 (0.77, 4.27) 0.1713	1.82 (0.77, 4.32) 0.1712	0.00 (-0.00, 0.01) 0.1879	
SBP at randomisation						0.7025
<= median	28/1567 (1.8)	20/1588 (1.3)	1.43 (0.81, 2.52) 0.2220	1.43 (0.80, 2.56) 0.2223	0.01 (-0.00, 0.01) 0.2467	
> median	21/1559 (1.3)	17/1539 (1.1)	1.21 (0.64, 2.28) 0.5627	1.21 (0.64, 2.31) 0.5587	0.00 (-0.00, 0.01) 0.2600	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of proportion of patients with SAE/DAE Volume depletion
Safety Analysis Set

Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
LVEF at enrolment 2						0.1812
<= 49	14/1066 (1.3)	6/1047 (0.6)	2.32 (0.90, 6.02) 0.0827	2.34 (0.90, 6.12) 0.0824	0.01 (-0.00, 0.01) 0.0937	
>= 50	35/2060 (1.7)	31/2080 (1.5)	1.14 (0.70, 1.84) 0.6004	1.14 (0.70, 1.86) 0.5986	0.00 (-0.00, 0.01) 0.4897	
Randomised during hospitalisation for HF or within 30 days of discharge						0.6850
Yes	4/ 328 (1.2)	4/ 326 (1.2)	0.98 (0.25, 3.89) 0.9782	0.98 (0.24, 3.96) 0.9774	-0.00 (-0.02, 0.02) 0.9068	
No	45/2798 (1.6)	33/2801 (1.2)	1.36 (0.87, 2.13) 0.1749	1.37 (0.87, 2.15) 0.1739	0.00 (-0.00, 0.01) 0.1211	
MRAs at baseline						0.1739
Yes	23/1339 (1.7)	12/1325 (0.9)	1.91 (0.95, 3.81) 0.0685	1.92 (0.95, 3.88) 0.0681	0.01 (-0.00, 0.02) 0.0522	
No	26/1787 (1.5)	25/1802 (1.4)	1.04 (0.60, 1.79) 0.8857	1.04 (0.60, 1.81) 0.8836	0.00 (-0.01, 0.01) 0.7472	
ACEi+ARB at baseline						0.1000
Yes	37/2259 (1.6)	22/2276 (1.0)	1.69 (1.00, 2.86) 0.0490	1.71 (1.00, 2.90) 0.0488	0.01 (0.00, 0.01) 0.0448	
No	12/ 867 (1.4)	15/ 851 (1.8)	0.79 (0.37, 1.68) 0.5375	0.79 (0.37, 1.69) 0.5409	-0.00 (-0.01, 0.01) 0.8214	
ARNI at baseline						0.1605
Yes	2/ 165 (1.2)	4/ 136 (2.9)	0.40 (0.07, 2.17) 0.2859	0.39 (0.07, 2.20) 0.2857	-0.02 (-0.05, 0.02) 0.3047	
No	47/2961 (1.6)	33/2991 (1.1)	1.43 (0.92, 2.23) 0.1096	1.44 (0.92, 2.26) 0.1089	0.01 (-0.00, 0.01) 0.0675	
Beta Blocker at baseline						0.5087
Yes	40/2587 (1.5)	28/2581 (1.1)	1.43 (0.88, 2.30) 0.1470	1.43 (0.88, 2.33) 0.1466	0.00 (-0.00, 0.01) 0.1221	
No	9/ 539 (1.7)	9/ 546 (1.6)	1.00 (0.40, 2.49) 0.9951	1.00 (0.39, 2.54) 0.9980	0.00 (-0.01, 0.02) 0.8120	
Diuretics at baseline						0.0363
Yes	48/2789 (1.7)	32/2783 (1.1)	1.50 (0.96, 2.33) 0.0753	1.51 (0.96, 2.36) 0.0749	0.01 (-0.00, 0.01) 0.0579	
No	1/ 337 (0.3)	5/ 344 (1.5)	0.20 (0.02, 1.74) 0.1458	0.20 (0.02, 1.74) 0.1452	-0.01 (-0.03, 0.00)*0.1033	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Blood and lymphatic system disorders	Overall	114/3126 (3.6)	142/3127 (4.5)	0.80 (0.63, 1.02) 0.0747	0.80 (0.62, 1.02) 0.0748	-0.01 (-0.02, 0.00) 0.0791	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Blood and lymphatic system disorders, PT: Anaemia	Overall	52/3126 (1.7)	66/3127 (2.1)	0.79 (0.55, 1.13) 0.1947	0.78 (0.54, 1.13) 0.1946	-0.00 (-0.01, 0.00) 0.1927	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders	Overall	880/3126 (28.2)	984/3127 (31.5)	0.89 (0.83, 0.96) 0.0036	0.85 (0.76, 0.95) 0.0040	-0.03 (-0.06, -0.01) 0.0048	
	Age						0.3742
	<= median	411/1544 (26.6)	492/1602 (30.7)	0.86 (0.77, 0.96) 0.0067	0.82 (0.70, 0.95) 0.0106	-0.04 (-0.07, -0.01) 0.0218	
	> median	469/1582 (29.6)	492/1525 (32.3)	0.92 (0.83, 1.02) 0.1235	0.88 (0.76, 1.03) 0.1133	-0.03 (-0.06, 0.01) 0.1020	
	Gender						0.4188
	Male	510/1765 (28.9)	578/1744 (33.1)	0.87 (0.79, 0.96) 0.0054	0.82 (0.71, 0.94) 0.0058	-0.04 (-0.07, -0.01) 0.0065	
	Female	370/1361 (27.2)	406/1383 (29.4)	0.93 (0.82, 1.04) 0.2090	0.90 (0.76, 1.06) 0.2187	-0.02 (-0.05, 0.01) 0.2359	
	Race						0.6496
	White	646/2210 (29.2)	732/2222 (32.9)	0.89 (0.81, 0.97) 0.0067	0.84 (0.74, 0.95) 0.0075	-0.04 (-0.06, -0.01) 0.0088	
	Black or African	29/ 81 (35.8)	37/ 78 (47.4)	0.75 (0.52, 1.09) 0.1298	0.61 (0.32, 1.15) 0.1250	-0.12 (-0.27, 0.03) 0.1202	
	Asian	173/ 629 (27.5)	187/ 643 (29.1)	0.94 (0.79, 1.12) 0.5162	0.92 (0.72, 1.17) 0.4969	-0.02 (-0.07, 0.03) 0.4708	
	Other	32/ 206 (15.5)	28/ 184 (15.2)	1.05 (0.66, 1.67) 0.8213	1.08 (0.62, 1.88) 0.7948	0.01 (-0.05, 0.08) 0.6792	
	Geographic region						0.5042
	Asia	163/ 606 (26.9)	176/ 619 (28.4)	0.94 (0.79, 1.13) 0.5345	0.92 (0.72, 1.18) 0.5231	-0.02 (-0.07, 0.03) 0.5070	
	Europe and Saudi Arabia	418/1491 (28.0)	467/1508 (31.0)	0.90 (0.81, 1.01) 0.0713	0.87 (0.74, 1.01) 0.0721	-0.03 (-0.06, 0.00) 0.0740	
	North America	170/ 427 (39.8)	181/ 422 (42.9)	0.92 (0.79, 1.08) 0.3174	0.88 (0.67, 1.15) 0.3528	-0.03 (-0.10, 0.04) 0.3684	
	Latin America	129/ 602 (21.4)	160/ 578 (27.7)	0.78 (0.64, 0.95) 0.0160	0.72 (0.55, 0.95) 0.0182	-0.06 (-0.10, -0.01) 0.0257	
	NYHA class at enrolment						0.9877
	II	612/2310 (26.5)	712/2395 (29.7)	0.89 (0.81, 0.97) 0.0115	0.85 (0.75, 0.97) 0.0127	-0.03 (-0.06, -0.01) 0.0152	
	III or IV	268/ 816 (32.8)	271/ 731 (37.1)	0.89 (0.78, 1.02) 0.0925	0.83 (0.68, 1.03) 0.0917	-0.04 (-0.09, 0.01) 0.0916	
	LVEF at enrolment						0.6462
	<= 49	306/1066 (28.7)	332/1047 (31.7)	0.90 (0.79, 1.03) 0.1144	0.86 (0.72, 1.04) 0.1188	-0.03 (-0.07, 0.01) 0.1257	
	50-59	308/1132 (27.2)	357/1121 (31.8)	0.85 (0.75, 0.97) 0.0155	0.80 (0.67, 0.96) 0.0160	-0.05 (-0.08, -0.01) 0.0171	
	>= 60	266/ 928 (28.7)	295/ 959 (30.8)	0.93 (0.81, 1.07) 0.3282	0.91 (0.75, 1.11) 0.3423	-0.02 (-0.06, 0.02) 0.3634	
	NT-proBNP at enrolment						0.4161
	<= median	387/1553 (24.9)	423/1574 (26.9)	0.93 (0.82, 1.04) 0.1977	0.90 (0.77, 1.06) 0.2115	-0.02 (-0.05, 0.01) 0.2412	
	> median	493/1573 (31.3)	560/1552 (36.1)	0.87 (0.79, 0.96) 0.0046	0.81 (0.70, 0.94) 0.0048	-0.05 (-0.08, -0.01) 0.0050	
	Type 2 Diabetes Medical History						0.2974
	Yes	434/1399 (31.0)	506/1402 (36.1)	0.86 (0.77, 0.95)*0.0046	0.80 (0.68, 0.93)*0.0045	-0.05 (-0.09, -0.02)*0.0044	
	No	446/1727 (25.8)	478/1725 (27.7)	0.93 (0.83, 1.04)*0.2112	0.91 (0.78, 1.06)*0.2111	-0.02 (-0.05, 0.01)*0.2109	
	Atrial fibrillation or flutter at enrolment ECG						0.4510
	Yes	375/1325 (28.3)	403/1317 (30.6)	0.93 (0.82, 1.04) 0.1988	0.90 (0.76, 1.06) 0.2036	-0.02 (-0.06, 0.01) 0.2116	
	No	505/1800 (28.1)	580/1809 (32.1)	0.87 (0.79, 0.96) 0.0072	0.82 (0.71, 0.95) 0.0079	-0.04 (-0.07, -0.01) 0.0092	
	BMI (kg/m2) at enrolment						0.3737
	< 30	466/1732 (26.9)	505/1733 (29.1)	0.92 (0.83, 1.03) 0.1453	0.89 (0.77, 1.04) 0.1425	-0.02 (-0.05, 0.01) 0.1398	
	>= 30	414/1392 (29.7)	478/1390 (34.4)	0.86 (0.77, 0.96) 0.0077	0.81 (0.69, 0.95) 0.0086	-0.05 (-0.08, -0.01) 0.0097	
	Baseline eGFR (mL/min/1.73m^2)						0.8716
	< 60	482/1514 (31.8)	546/1551 (35.2)	0.90 (0.81, 0.99) 0.0381	0.85 (0.73, 0.99) 0.0394	-0.03 (-0.07, -0.00) 0.0412	
	>= 60	398/1612 (24.7)	438/1575 (27.8)	0.89 (0.79, 1.00) 0.0471	0.85 (0.73, 1.00) 0.0509	-0.03 (-0.06, 0.00) 0.0588	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders	SBP at randomisation						0.0225
	<= median	461/1567 (29.4)	477/1588 (30.0)	0.98 (0.88, 1.09) 0.6667	0.97 (0.83, 1.13) 0.6680	-0.01 (-0.04, 0.02) 0.6700	
	> median	419/1559 (26.9)	507/1539 (32.9)	0.82 (0.73, 0.91) 0.0003	0.75 (0.64, 0.88) 0.0003	-0.06 (-0.09, -0.03) 0.0004	
	LVEF at enrolment 2						0.8801
	<= 49	306/1066 (28.7)	332/1047 (31.7)	0.90 (0.79, 1.03) 0.1144	0.86 (0.72, 1.04) 0.1188	-0.03 (-0.07, 0.01) 0.1257	
	>= 50	574/2060 (27.9)	652/2080 (31.3)	0.89 (0.81, 0.98) 0.0144	0.85 (0.74, 0.97) 0.0157	-0.03 (-0.06, -0.01) 0.0180	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.7982
	Yes	117/ 328 (35.7)	133/ 326 (40.8)	0.87 (0.72, 1.06) 0.1738	0.80 (0.58, 1.10) 0.1664	-0.05 (-0.13, 0.02) 0.1611	
	No	763/2798 (27.3)	851/2801 (30.4)	0.90 (0.83, 0.97) 0.0091	0.86 (0.77, 0.97) 0.0107	-0.03 (-0.05, -0.01) 0.0139	
	MRAs at baseline						0.5686
	Yes	362/1339 (27.0)	409/1325 (30.9)	0.87 (0.77, 0.98) 0.0241	0.83 (0.70, 0.98) 0.0255	-0.04 (-0.07, -0.00) 0.0277	
	No	518/1787 (29.0)	575/1802 (31.9)	0.91 (0.83, 1.01) 0.0635	0.88 (0.76, 1.01) 0.0671	-0.03 (-0.06, 0.00) 0.0735	
	ACEi+ARB at baseline						0.8152
	Yes	626/2259 (27.7)	709/2276 (31.2)	0.89 (0.81, 0.97) 0.0097	0.85 (0.75, 0.96) 0.0113	-0.03 (-0.06, -0.01) 0.0141	
	No	254/ 867 (29.3)	275/ 851 (32.3)	0.91 (0.79, 1.04) 0.1704	0.86 (0.70, 1.06) 0.1638	-0.03 (-0.07, 0.01) 0.1572	
	ARNI at baseline						0.8425
	Yes	45/ 165 (27.3)	42/ 136 (30.9)	0.84 (0.59, 1.20) 0.3434	0.77 (0.46, 1.28) 0.3141	-0.06 (-0.16, 0.05) 0.2763	
	No	835/2961 (28.2)	942/2991 (31.5)	0.89 (0.83, 0.97) 0.0052	0.86 (0.77, 0.96) 0.0059	-0.03 (-0.05, -0.01) 0.0072	
	Beta Blocker at baseline						0.6731
	Yes	717/2587 (27.7)	805/2581 (31.2)	0.89 (0.81, 0.96) 0.0050	0.84 (0.75, 0.95) 0.0056	-0.03 (-0.06, -0.01) 0.0068	
	No	163/ 539 (30.2)	179/ 546 (32.8)	0.92 (0.77, 1.10) 0.3688	0.89 (0.69, 1.15) 0.3695	-0.03 (-0.08, 0.03) 0.3703	
	Diuretics at baseline						0.8981
	Yes	803/2789 (28.8)	895/2783 (32.2)	0.89 (0.83, 0.97) 0.0058	0.85 (0.76, 0.96) 0.0062	-0.03 (-0.06, -0.01) 0.0069	
	No	77/ 337 (22.8)	89/ 344 (25.9)	0.88 (0.68, 1.15) 0.3465	0.85 (0.60, 1.20) 0.3569	-0.03 (-0.09, 0.04) 0.3789	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Acute myocardial infarction	Overall	64/3126 (2.0)	65/3127 (2.1)	0.98 (0.70, 1.38) 0.9242	0.98 (0.69, 1.40) 0.9285	0.00 (-0.01, 0.01) 0.8581	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	_Dapa 10 mg (N=3126)_ n/ N (%)	__Placebo (N=3127)___ n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Angina pectoris	Overall	34/3126 (1.1)	41/3127 (1.3)	0.83 (0.53, 1.30) 0.4149	0.83 (0.52, 1.31) 0.4161	-0.00 (-0.01, 0.00) 0.5517	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Angina unstable	Overall	57/3126 (1.8)	71/3127 (2.3)	0.80 (0.57, 1.13) 0.2106	0.80 (0.56, 1.14) 0.2122	-0.00 (-0.01, 0.00) 0.3058	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Atrial fibrillation	Overall	148/3126 (4.7)	115/3127 (3.7)	1.29 (1.01, 1.63) 0.0378	1.30 (1.01, 1.67) 0.0378	0.01 (0.00, 0.02) 0.0379	
	Age						0.3465
	<= median	66/1544 (4.3)	60/1602 (3.7)	1.14 (0.81, 1.61) 0.4511	1.15 (0.80, 1.64) 0.4499	0.01 (-0.01, 0.02) 0.4207	
	> median	82/1582 (5.2)	55/1525 (3.6)	1.44 (1.03, 2.01) 0.0338	1.46 (1.03, 2.07) 0.0329	0.02 (0.00, 0.03) 0.0197	
	Gender						0.4565
	Male	81/1765 (4.6)	57/1744 (3.3)	1.40 (1.01, 1.96) 0.0457	1.42 (1.01, 2.01) 0.0455	0.01 (0.00, 0.03) 0.0416	
	Female	67/1361 (4.9)	58/1383 (4.2)	1.17 (0.83, 1.65) 0.3706	1.18 (0.82, 1.69) 0.3687	0.01 (-0.01, 0.02) 0.3361	
	Race						0.1280
	White	113/2210 (5.1)	97/2222 (4.4)	1.17 (0.90, 1.53) 0.2416	1.18 (0.89, 1.56) 0.2418	0.01 (-0.01, 0.02) 0.2491	
	Black or African	5/ 81 (6.2)	3/ 78 (3.8)	1.60 (0.40, 6.46) 0.5106	1.63 (0.38, 7.08) 0.5136	0.02 (-0.05, 0.10) 0.5464	
	Asian	21/ 629 (3.3)	14/ 643 (2.2)	1.54 (0.79, 2.99) 0.2071	1.56 (0.78, 3.09) 0.2068	0.01 (-0.01, 0.03) 0.2071	
	Other	9/ 206 (4.4)	1/ 184 (0.5)	8.11 (1.04,63.47) 0.0461	8.45 (1.06,67.44) 0.0440	0.04 (0.01, 0.07)*0.0121	
	Geographic region						0.6424
	Asia	20/ 606 (3.3)	13/ 619 (2.1)	1.58 (0.79, 3.14) 0.1955	1.60 (0.79, 3.24) 0.1951	0.01 (-0.01, 0.03) 0.1947	
	Europe and Saudi Arabia	77/1491 (5.2)	69/1508 (4.6)	1.13 (0.82, 1.55) 0.4486	1.14 (0.81, 1.59) 0.4495	0.01 (-0.01, 0.02) 0.4685	
	North America	37/ 427 (8.7)	23/ 422 (5.5)	1.59 (0.96, 2.63) 0.0699	1.65 (0.96, 2.83) 0.0686	0.03 (-0.00, 0.07) 0.0594	
	Latin America	14/ 602 (2.3)	10/ 578 (1.7)	1.37 (0.61, 3.06) 0.4429	1.38 (0.61, 3.13) 0.4437	0.01 (-0.01, 0.02) 0.4985	
	NYHA class at enrolment						0.6640
	II	107/2310 (4.6)	89/2395 (3.7)	1.25 (0.95, 1.64) 0.1151	1.26 (0.95, 1.68) 0.1150	0.01 (-0.00, 0.02) 0.1150	
	III or IV	41/ 816 (5.0)	26/ 731 (3.6)	1.42 (0.87, 2.29) 0.1572	1.44 (0.87, 2.37) 0.1564	0.02 (-0.01, 0.04) 0.1436	
	LVEF at enrolment						0.4581
	<= 49	48/1066 (4.5)	32/1047 (3.1)	1.49 (0.96, 2.30) 0.0774	1.51 (0.95, 2.38) 0.0785	0.01 (-0.00, 0.03) 0.1202	
	50-59	54/1132 (4.8)	50/1121 (4.5)	1.07 (0.74, 1.56) 0.7226	1.07 (0.72, 1.59) 0.7240	0.00 (-0.01, 0.02) 0.7534	
	>= 60	46/ 928 (5.0)	33/ 959 (3.4)	1.43 (0.92, 2.21) 0.1099	1.45 (0.92, 2.30) 0.1077	0.02 (-0.00, 0.03) 0.0706	
	NT-proBNP at enrolment						0.1539
	<= median	89/1553 (5.7)	60/1574 (3.8)	1.50 (1.09, 2.07) 0.0125	1.53 (1.10, 2.15) 0.0123	0.02 (0.00, 0.03) 0.0114	
	> median	59/1573 (3.8)	55/1552 (3.5)	1.06 (0.74, 1.52) 0.7558	1.06 (0.73, 1.54) 0.7566	0.00 (-0.01, 0.02) 0.7773	
	Type 2 Diabetes Medical History						0.9311
	Yes	65/1399 (4.6)	50/1402 (3.6)	1.30 (0.91, 1.87)*0.1512	1.32 (0.90, 1.92)*0.1510	0.01 (-0.00, 0.03)*0.1497	
	No	83/1727 (4.8)	65/1725 (3.8)	1.28 (0.93, 1.75)*0.1334	1.29 (0.93, 1.80)*0.1332	0.01 (-0.00, 0.02)*0.1321	
	Atrial fibrillation or flutter at enrolment ECG						0.7106
	Yes	45/1325 (3.4)	32/1317 (2.4)	1.40 (0.89, 2.19) 0.1415	1.41 (0.89, 2.24) 0.1412	0.01 (-0.00, 0.02) 0.1365	
	No	103/1800 (5.7)	82/1809 (4.5)	1.26 (0.95, 1.68) 0.1039	1.28 (0.95, 1.72) 0.1037	0.01 (-0.00, 0.03) 0.1040	
	BMI (kg/m2) at enrolment						0.9071
	< 30	73/1732 (4.2)	56/1733 (3.2)	1.31 (0.93, 1.84) 0.1262	1.32 (0.92, 1.88) 0.1274	0.01 (-0.00, 0.02) 0.1665	
	>= 30	75/1392 (5.4)	59/1390 (4.2)	1.27 (0.91, 1.77) 0.1607	1.28 (0.91, 1.82) 0.1598	0.01 (-0.00, 0.03) 0.1444	
	Baseline eGFR (mL/min/1.73m^2)						0.7549
	< 60	73/1514 (4.8)	56/1551 (3.6)	1.34 (0.95, 1.88) 0.0947	1.35 (0.95, 1.93) 0.0943	0.01 (-0.00, 0.03) 0.0867	
	>= 60	75/1612 (4.7)	59/1575 (3.7)	1.24 (0.89, 1.73) 0.2074	1.25 (0.88, 1.77) 0.2082	0.01 (-0.01, 0.02) 0.2304	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Atrial fibrillation	SBP at randomisation						0.2606
	<= median	72/1567 (4.6)	49/1588 (3.1)	1.50 (1.05, 2.14) 0.0269	1.52 (1.05, 2.20) 0.0269	0.01 (0.00, 0.03) 0.0301	
	> median	76/1559 (4.9)	66/1539 (4.3)	1.14 (0.82, 1.57) 0.4405	1.14 (0.81, 1.60) 0.4400	0.01 (-0.01, 0.02) 0.4297	
	LVEF at enrolment 2						0.4622
	<= 49	48/1066 (4.5)	32/1047 (3.1)	1.49 (0.96, 2.30) 0.0774	1.51 (0.95, 2.38) 0.0785	0.01 (-0.00, 0.03) 0.1202	
	>= 50	100/2060 (4.9)	83/2080 (4.0)	1.22 (0.91, 1.62) 0.1776	1.23 (0.91, 1.65) 0.1774	0.01 (-0.00, 0.02) 0.1729	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6261
	Yes	21/ 328 (6.4)	14/ 326 (4.3)	1.48 (0.76, 2.86) 0.2446	1.51 (0.75, 3.03) 0.2439	0.02 (-0.01, 0.05) 0.2424	
	No	127/2798 (4.5)	101/2801 (3.6)	1.26 (0.97, 1.62) 0.0789	1.27 (0.97, 1.66) 0.0789	0.01 (-0.00, 0.02) 0.0814	
	MRAs at baseline						0.9013
	Yes	53/1339 (4.0)	40/1325 (3.0)	1.31 (0.88, 1.97) 0.1849	1.33 (0.87, 2.01) 0.1852	0.01 (-0.00, 0.02) 0.1953	
	No	95/1787 (5.3)	75/1802 (4.2)	1.27 (0.95, 1.71) 0.1085	1.29 (0.95, 1.76) 0.1077	0.01 (-0.00, 0.03) 0.0948	
	ACEi+ARB at baseline						0.7459
	Yes	110/2259 (4.9)	84/2276 (3.7)	1.32 (1.00, 1.74) 0.0511	1.34 (1.00, 1.78) 0.0508	0.01 (0.00, 0.02) 0.0456	
	No	38/ 867 (4.4)	31/ 851 (3.6)	1.21 (0.76, 1.92) 0.4301	1.21 (0.75, 1.97) 0.4321	0.01 (-0.01, 0.03) 0.4762	
	ARNI at baseline						0.7582
	Yes	4/ 165 (2.4)	2/ 136 (1.5)	1.63 (0.30, 8.93) 0.5707	1.65 (0.29, 9.30) 0.5701	0.01 (-0.02, 0.04) 0.5475	
	No	144/2961 (4.9)	113/2991 (3.8)	1.29 (1.01, 1.64) 0.0406	1.30 (1.01, 1.67) 0.0405	0.01 (0.00, 0.02) 0.0403	
	Beta Blocker at baseline						0.4977
	Yes	126/2587 (4.9)	101/2581 (3.9)	1.25 (0.96, 1.61) 0.0928	1.26 (0.96, 1.64) 0.0929	0.01 (-0.00, 0.02) 0.0965	
	No	22/ 539 (4.1)	14/ 546 (2.6)	1.59 (0.82, 3.08) 0.1671	1.62 (0.82, 3.19) 0.1667	0.02 (-0.01, 0.04) 0.1614	
	Diuretics at baseline						0.0362
	Yes	138/2789 (4.9)	113/2783 (4.1)	1.22 (0.96, 1.55) 0.1107	1.23 (0.95, 1.59) 0.1106	0.01 (-0.00, 0.02) 0.1125	
	No	10/ 337 (3.0)	2/ 344 (0.6)	5.10 (1.13,23.10) 0.0345	5.23 (1.14,24.04) 0.0336	0.02 (0.00, 0.04) 0.0195	

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SOC: Cardiac disorders, PT: Bradycardia	Overall	28/3126 (0.9)	36/3127 (1.2)	0.78 (0.48, 1.27) 0.3163	0.78 (0.47, 1.27) 0.3165	-0.00 (-0.01, 0.00) 0.3414	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure	Overall	436/3126 (13.9)	526/3127 (16.8)	0.83 (0.74, 0.93) 0.0016	0.80 (0.70, 0.92) 0.0016	-0.03 (-0.05, -0.01) 0.0018	
	Age						0.6072
	<= median	200/1544 (13.0)	242/1602 (15.1)	0.85 (0.72, 1.01) 0.0719	0.83 (0.68, 1.02) 0.0799	-0.02 (-0.04, 0.01) 0.1479	
	> median	236/1582 (14.9)	284/1525 (18.6)	0.80 (0.69, 0.94) 0.0061	0.77 (0.63, 0.92) 0.0056	-0.04 (-0.06, -0.01) 0.0042	
	Gender						0.7496
	Male	258/1765 (14.6)	312/1744 (17.9)	0.82 (0.70, 0.95) 0.0079	0.78 (0.65, 0.94) 0.0078	-0.03 (-0.06, -0.01) 0.0080	
	Female	178/1361 (13.1)	214/1383 (15.5)	0.85 (0.71, 1.02) 0.0774	0.82 (0.66, 1.02) 0.0781	-0.02 (-0.05, 0.00) 0.0851	
	Race						0.3689
	White	324/2210 (14.7)	402/2222 (18.1)	0.81 (0.71, 0.93) 0.0021	0.78 (0.66, 0.91) 0.0020	-0.03 (-0.06, -0.01) 0.0020	
	Black or African	9/ 81 (11.1)	15/ 78 (19.2)	0.57 (0.26, 1.22) 0.1480	0.52 (0.21, 1.27) 0.1498	-0.08 (-0.19, 0.03) 0.1673	
	Asian	91/ 629 (14.5)	93/ 643 (14.5)	0.99 (0.76, 1.30) 0.9646	0.99 (0.73, 1.36) 0.9726	0.00 (-0.04, 0.04) 0.9885	
	Other	12/ 206 (5.8)	16/ 184 (8.7)	0.70 (0.34, 1.44) 0.3362	0.68 (0.31, 1.49) 0.3330	-0.02 (-0.07, 0.03) 0.3438	
	Geographic region						0.5842
	Asia	86/ 606 (14.2)	92/ 619 (14.9)	0.95 (0.72, 1.24) 0.7039	0.94 (0.69, 1.30) 0.7163	-0.01 (-0.04, 0.03) 0.7784	
	Europe and Saudi Arabia	241/1491 (16.2)	309/1508 (20.5)	0.79 (0.68, 0.92) 0.0020	0.74 (0.62, 0.90) 0.0019	-0.04 (-0.07, -0.02) 0.0019	
	North America	47/ 427 (11.0)	49/ 422 (11.6)	0.94 (0.65, 1.38) 0.7660	0.94 (0.61, 1.44) 0.7670	-0.01 (-0.05, 0.04) 0.7775	
	Latin America	62/ 602 (10.3)	76/ 578 (13.1)	0.80 (0.58, 1.09) 0.1554	0.77 (0.54, 1.10) 0.1541	-0.03 (-0.06, 0.01) 0.1533	
	NYHA class at enrolment						0.7865
	II	288/2310 (12.5)	359/2395 (15.0)	0.83 (0.72, 0.96) 0.0114	0.81 (0.68, 0.95) 0.0112	-0.03 (-0.04, -0.01) 0.0115	
	III or IV	148/ 816 (18.1)	166/ 731 (22.7)	0.80 (0.66, 0.98) 0.0284	0.76 (0.59, 0.97) 0.0287	-0.04 (-0.08, -0.00) 0.0305	
	LVEF at enrolment						0.3736
	<= 49	166/1066 (15.6)	175/1047 (16.7)	0.93 (0.76, 1.12) 0.4324	0.91 (0.72, 1.15) 0.4403	-0.01 (-0.04, 0.02) 0.4785	
	50-59	152/1132 (13.4)	196/1121 (17.5)	0.77 (0.63, 0.93) 0.0081	0.73 (0.58, 0.92) 0.0079	-0.04 (-0.07, -0.01) 0.0081	
	>= 60	118/ 928 (12.7)	155/ 959 (16.2)	0.79 (0.63, 0.99) 0.0382	0.76 (0.59, 0.98) 0.0374	-0.03 (-0.07, -0.00) 0.0355	
	NT-proBNP at enrolment						0.5310
	<= median	164/1553 (10.6)	192/1574 (12.2)	0.87 (0.71, 1.05) 0.1521	0.85 (0.68, 1.06) 0.1487	-0.02 (-0.04, 0.01) 0.1324	
	> median	272/1573 (17.3)	334/1552 (21.5)	0.80 (0.69, 0.93) 0.0025	0.76 (0.64, 0.91) 0.0027	-0.04 (-0.07, -0.01) 0.0035	
	Type 2 Diabetes Medical History						0.8025
	Yes	226/1399 (16.2)	277/1402 (19.8)	0.82 (0.70, 0.96)*0.0132	0.78 (0.64, 0.95)*0.0131	-0.04 (-0.06, -0.01)*0.0129	
	No	210/1727 (12.2)	249/1725 (14.4)	0.84 (0.71, 1.00)*0.0494	0.82 (0.67, 1.00)*0.0493	-0.02 (-0.05, -0.00)*0.0489	
	Atrial fibrillation or flutter at enrolment ECG						0.5956
	Yes	213/1325 (16.1)	248/1317 (18.8)	0.86 (0.72, 1.01) 0.0660	0.83 (0.68, 1.01) 0.0651	-0.03 (-0.06, 0.00) 0.0639	
	No	223/1800 (12.4)	278/1809 (15.4)	0.80 (0.68, 0.95) 0.0087	0.78 (0.64, 0.94) 0.0088	-0.03 (-0.05, -0.01) 0.0104	
	BMI (kg/m2) at enrolment						0.5416
	< 30	220/1732 (12.7)	256/1733 (14.8)	0.86 (0.73, 1.02) 0.0792	0.84 (0.69, 1.02) 0.0767	-0.02 (-0.04, 0.00) 0.0674	
	>= 30	216/1392 (15.5)	269/1390 (19.4)	0.80 (0.68, 0.94) 0.0074	0.76 (0.63, 0.93) 0.0076	-0.04 (-0.07, -0.01) 0.0093	
	Baseline eGFR (mL/min/1.73m^2)						0.9960
	< 60	248/1514 (16.4)	304/1551 (19.6)	0.83 (0.71, 0.97) 0.0166	0.80 (0.66, 0.96) 0.0167	-0.03 (-0.06, -0.01) 0.0178	
	>= 60	188/1612 (11.7)	222/1575 (14.1)	0.83 (0.69, 1.00) 0.0457	0.81 (0.66, 1.00) 0.0458	-0.02 (-0.05, -0.00) 0.0491	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure	SBP at randomisation						0.0701
	<= median	226/1567 (14.4)	246/1588 (15.5)	0.93 (0.78, 1.09) 0.3590	0.91 (0.75, 1.11) 0.3641	-0.01 (-0.04, 0.01) 0.3922	
	> median	210/1559 (13.5)	280/1539 (18.2)	0.75 (0.63, 0.88) 0.0005	0.70 (0.58, 0.86) 0.0004	-0.05 (-0.07, -0.02) 0.0004	
	LVEF at enrolment 2						0.1668
	<= 49	166/1066 (15.6)	175/1047 (16.7)	0.93 (0.76, 1.12) 0.4324	0.91 (0.72, 1.15) 0.4403	-0.01 (-0.04, 0.02) 0.4785	
	>= 50	270/2060 (13.1)	351/2080 (16.9)	0.78 (0.67, 0.90) 0.0008	0.74 (0.63, 0.88) 0.0008	-0.04 (-0.06, -0.02) 0.0008	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2088
	Yes	68/ 328 (20.7)	95/ 326 (29.1)	0.71 (0.54, 0.93) 0.0138	0.64 (0.44, 0.91) 0.0133	-0.08 (-0.15, -0.02) 0.0125	
	No	368/2798 (13.2)	431/2801 (15.4)	0.86 (0.75, 0.97) 0.0173	0.83 (0.72, 0.97) 0.0178	-0.02 (-0.04, -0.00) 0.0226	
	MRAs at baseline						0.2225
	Yes	188/1339 (14.0)	242/1325 (18.3)	0.76 (0.64, 0.91) 0.0026	0.73 (0.59, 0.89) 0.0026	-0.04 (-0.07, -0.02) 0.0025	
	No	248/1787 (13.9)	284/1802 (15.8)	0.88 (0.76, 1.03) 0.1260	0.87 (0.72, 1.04) 0.1289	-0.02 (-0.04, 0.01) 0.1500	
	ACEi+ARB at baseline						0.8656
	Yes	314/2259 (13.9)	384/2276 (16.9)	0.82 (0.72, 0.94) 0.0055	0.80 (0.68, 0.94) 0.0057	-0.03 (-0.05, -0.01) 0.0074	
	No	122/ 867 (14.1)	142/ 851 (16.7)	0.84 (0.67, 1.05) 0.1306	0.81 (0.63, 1.06) 0.1253	-0.03 (-0.06, 0.01) 0.1068	
	ARNI at baseline						0.5119
	Yes	26/ 165 (15.8)	21/ 136 (15.4)	0.98 (0.57, 1.66) 0.9296	0.97 (0.51, 1.82) 0.9141	-0.01 (-0.09, 0.07) 0.8471	
	No	410/2961 (13.8)	505/2991 (16.9)	0.82 (0.73, 0.93) 0.0013	0.79 (0.69, 0.91) 0.0013	-0.03 (-0.05, -0.01) 0.0015	
	Beta Blocker at baseline						0.6449
	Yes	354/2587 (13.7)	431/2581 (16.7)	0.82 (0.72, 0.93) 0.0024	0.79 (0.68, 0.92) 0.0023	-0.03 (-0.05, -0.01) 0.0025	
	No	82/ 539 (15.2)	95/ 546 (17.4)	0.88 (0.67, 1.15) 0.3370	0.85 (0.62, 1.18) 0.3387	-0.02 (-0.06, 0.02) 0.3472	
	Diuretics at baseline						0.2200
	Yes	405/2789 (14.5)	477/2783 (17.1)	0.85 (0.75, 0.96) 0.0073	0.82 (0.71, 0.95) 0.0073	-0.03 (-0.04, -0.01) 0.0079	
	No	31/ 337 (9.2)	49/ 344 (14.2)	0.65 (0.42, 0.99) 0.0431	0.61 (0.38, 0.98) 0.0423	-0.05 (-0.10, -0.00) 0.0403	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure acute	Overall	61/3126 (2.0)	67/3127 (2.1)	0.91 (0.65, 1.28) 0.5916	0.91 (0.64, 1.29) 0.5923	-0.00 (-0.01, 0.01) 0.6301	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure chronic	Overall	26/3126 (0.8)	39/3127 (1.2)	0.67 (0.41, 1.09) 0.1080	0.66 (0.40, 1.09) 0.1076	-0.00 (-0.01, 0.00) 0.0661	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure congestive	Overall	93/3126 (3.0)	122/3127 (3.9)	0.76 (0.58, 0.99) 0.0451	0.75 (0.57, 0.99) 0.0448	-0.01 (-0.02, -0.00) 0.0408	
	Age						0.0876
	<= median	32/1544 (2.1)	58/1602 (3.6)	0.57 (0.37, 0.88) 0.0101	0.56 (0.36, 0.87) 0.0098	-0.02 (-0.03, -0.00) 0.0067	
	> median	61/1582 (3.9)	64/1525 (4.2)	0.92 (0.65, 1.30) 0.6286	0.92 (0.64, 1.31) 0.6280	-0.00 (-0.02, 0.01) 0.6139	
	Gender						0.3115
	Male	54/1765 (3.1)	78/1744 (4.5)	0.68 (0.49, 0.96) 0.0275	0.67 (0.47, 0.96) 0.0272	-0.01 (-0.03, -0.00) 0.0247	
	Female	39/1361 (2.9)	44/1383 (3.2)	0.90 (0.59, 1.38) 0.6359	0.90 (0.58, 1.39) 0.6354	-0.00 (-0.02, 0.01) 0.6212	
	Race						0.1666
	White	75/2210 (3.4)	98/2222 (4.4)	0.77 (0.57, 1.03) 0.0816	0.76 (0.56, 1.03) 0.0813	-0.01 (-0.02, 0.00) 0.0785	
	Black or African	12/ 81 (14.8)	8/ 78 (10.3)	1.44 (0.62, 3.33) 0.3935	1.51 (0.58, 3.94) 0.3942	0.04 (-0.06, 0.15) 0.4014	
	Asian	5/ 629 (0.8)	15/ 643 (2.3)	0.34 (0.12, 0.93) 0.0349	0.33 (0.12, 0.92) 0.0344	-0.02 (-0.03, -0.00) 0.0269	
	Other	1/ 206 (0.5)	1/ 184 (0.5)	0.90 (0.06,14.30) 0.9386	0.90 (0.06,14.51) 0.9388	-0.00 (-0.01, 0.01)*0.9364	
	Geographic region						0.8261
	Asia	4/ 606 (0.7)	9/ 619 (1.5)	0.46 (0.14, 1.47) 0.1885	0.45 (0.14, 1.48) 0.1883	-0.01 (-0.02, 0.00) 0.1939	
	Europe and Saudi Arabia	17/1491 (1.1)	23/1508 (1.5)	0.74 (0.40, 1.38) 0.3439	0.74 (0.39, 1.39) 0.3428	-0.00 (-0.01, 0.00) 0.2992	
	North America	54/ 427 (12.6)	69/ 422 (16.4)	0.77 (0.55, 1.07) 0.1226	0.74 (0.50, 1.09) 0.1232	-0.04 (-0.08, 0.01) 0.1298	
	Latin America	18/ 602 (3.0)	21/ 578 (3.6)	0.83 (0.45, 1.55) 0.5606	0.83 (0.44, 1.57) 0.5592	-0.01 (-0.03, 0.01) 0.5225	
	NYHA class at enrolment						0.1901
	II	58/2310 (2.5)	89/2395 (3.7)	0.67 (0.49, 0.93) 0.0179	0.67 (0.48, 0.93) 0.0178	-0.01 (-0.02, -0.00) 0.0189	
	III or IV	35/ 816 (4.3)	32/ 731 (4.4)	0.99 (0.62, 1.58) 0.9693	0.99 (0.61, 1.62) 0.9638	-0.00 (-0.02, 0.02) 0.8421	
	LVEF at enrolment						0.0486
	<= 49	19/1066 (1.8)	40/1047 (3.8)	0.46 (0.27, 0.80) 0.0053	0.45 (0.26, 0.79) 0.0051	-0.02 (-0.03, -0.01) 0.0038	
	50-59	35/1132 (3.1)	45/1121 (4.0)	0.77 (0.50, 1.19) 0.2388	0.76 (0.49, 1.20) 0.2388	-0.01 (-0.02, 0.01) 0.2427	
	>= 60	39/ 928 (4.2)	37/ 959 (3.9)	1.10 (0.71, 1.71) 0.6710	1.10 (0.70, 1.75) 0.6735	0.00 (-0.01, 0.02) 0.7426	
	NT-proBNP at enrolment						0.6582
	<= median	38/1553 (2.4)	47/1574 (3.0)	0.82 (0.54, 1.25) 0.3521	0.81 (0.53, 1.26) 0.3545	-0.00 (-0.02, 0.01) 0.4538	
	> median	55/1573 (3.5)	75/1552 (4.8)	0.72 (0.52, 1.02) 0.0634	0.71 (0.50, 1.02) 0.0616	-0.01 (-0.03, -0.00) 0.0344	
	Type 2 Diabetes Medical History						0.5187
	Yes	52/1399 (3.7)	63/1402 (4.5)	0.83 (0.58, 1.19)*0.3011	0.82 (0.56, 1.19)*0.3010	-0.01 (-0.02, 0.01)*0.3002	
	No	41/1727 (2.4)	59/1725 (3.4)	0.69 (0.47, 1.03)*0.0685	0.69 (0.46, 1.03)*0.0684	-0.01 (-0.02, 0.00)*0.0668	
	Atrial fibrillation or flutter at enrolment ECG						0.2139
	Yes	46/1325 (3.5)	50/1317 (3.8)	0.92 (0.62, 1.36) 0.6661	0.91 (0.61, 1.37) 0.6629	-0.00 (-0.02, 0.01) 0.5851	
	No	47/1800 (2.6)	72/1809 (4.0)	0.65 (0.46, 0.94) 0.0214	0.64 (0.44, 0.94) 0.0214	-0.01 (-0.02, -0.00) 0.0246	
	BMI (kg/m2) at enrolment						0.8566
	< 30	43/1732 (2.5)	55/1733 (3.2)	0.78 (0.53, 1.16) 0.2219	0.78 (0.52, 1.16) 0.2211	-0.01 (-0.02, 0.00) 0.2009	
	>= 30	50/1392 (3.6)	67/1390 (4.8)	0.75 (0.52, 1.07) 0.1078	0.74 (0.51, 1.07) 0.1074	-0.01 (-0.03, 0.00) 0.1051	
	Baseline eGFR (mL/min/1.73m^2)						0.8249
	< 60	60/1514 (4.0)	78/1551 (5.0)	0.78 (0.56, 1.09) 0.1466	0.77 (0.55, 1.09) 0.1457	-0.01 (-0.03, 0.00) 0.1326	
	>= 60	33/1612 (2.0)	44/1575 (2.8)	0.74 (0.47, 1.15) 0.1784	0.73 (0.46, 1.15) 0.1784	-0.01 (-0.02, 0.00) 0.1857	

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Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure congestive	SBP at randomisation						0.1564
	<= median	52/1567 (3.3)	57/1588 (3.6)	0.92 (0.64, 1.33) 0.6658	0.92 (0.63, 1.35) 0.6635	-0.00 (-0.02, 0.01) 0.6020	
	> median	41/1559 (2.6)	65/1539 (4.2)	0.63 (0.43, 0.92) 0.0176	0.62 (0.41, 0.92) 0.0176	-0.01 (-0.03, -0.00) 0.0245	
	LVEF at enrolment 2						0.0290
	<= 49	19/1066 (1.8)	40/1047 (3.8)	0.46 (0.27, 0.80) 0.0053	0.45 (0.26, 0.79) 0.0051	-0.02 (-0.03, -0.01) 0.0038	
	>= 50	74/2060 (3.6)	82/2080 (3.9)	0.91 (0.67, 1.24) 0.5684	0.91 (0.66, 1.25) 0.5674	-0.00 (-0.01, 0.01) 0.5491	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2927
	Yes	8/ 328 (2.4)	6/ 326 (1.8)	1.29 (0.45, 3.68) 0.6328	1.29 (0.44, 3.78) 0.6388	-0.00 (-0.02, 0.02) 0.9977	
	No	85/2798 (3.0)	116/2801 (4.1)	0.73 (0.56, 0.97) 0.0278	0.73 (0.55, 0.97) 0.0277	-0.01 (-0.02, -0.00) 0.0287	
	MRAs at baseline						0.2285
	Yes	22/1339 (1.6)	37/1325 (2.8)	0.59 (0.35, 0.99) 0.0447	0.58 (0.34, 0.99) 0.0444	-0.01 (-0.02, -0.00) 0.0366	
	No	71/1787 (4.0)	85/1802 (4.7)	0.85 (0.62, 1.15) 0.2898	0.84 (0.61, 1.16) 0.2894	-0.01 (-0.02, 0.01) 0.2883	
	ACEi+ARB at baseline						0.7250
	Yes	64/2259 (2.8)	82/2276 (3.6)	0.79 (0.57, 1.09) 0.1438	0.78 (0.56, 1.09) 0.1445	-0.01 (-0.02, 0.00) 0.1777	
	No	29/ 867 (3.3)	40/ 851 (4.7)	0.71 (0.44, 1.14) 0.1535	0.70 (0.43, 1.14) 0.1518	-0.01 (-0.03, 0.00) 0.1185	
	ARNI at baseline						0.7638
	Yes	4/ 165 (2.4)	5/ 136 (3.7)	0.54 (0.15, 1.98) 0.3542	0.53 (0.14, 2.06) 0.3596	-0.01 (-0.04, 0.03) 0.6876	
	No	89/2961 (3.0)	117/2991 (3.9)	0.77 (0.59, 1.01) 0.0584	0.76 (0.58, 1.01) 0.0580	-0.01 (-0.02, 0.00) 0.0511	
	Beta Blocker at baseline						0.7192
	Yes	74/2587 (2.9)	99/2581 (3.8)	0.74 (0.55, 1.00) 0.0509	0.74 (0.54, 1.00) 0.0504	-0.01 (-0.02, -0.00) 0.0438	
	No	19/ 539 (3.5)	23/ 546 (4.2)	0.83 (0.46, 1.51) 0.5504	0.83 (0.45, 1.54) 0.5504	-0.01 (-0.03, 0.02) 0.5529	
	Diuretics at baseline						0.2841
	Yes	91/2789 (3.3)	116/2783 (4.2)	0.78 (0.60, 1.02) 0.0749	0.78 (0.59, 1.03) 0.0745	-0.01 (-0.02, 0.00) 0.0689	
	No	2/ 337 (0.6)	6/ 344 (1.7)	0.34 (0.07, 1.67) 0.1844	0.34 (0.07, 1.68) 0.1836	-0.01 (-0.03, 0.00) 0.1648	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Ear and labyrinth disorders	Overall	44/3126 (1.4)	47/3127 (1.5)	0.94 (0.62, 1.41) 0.7547	0.94 (0.62, 1.42) 0.7534	-0.00 (-0.01, 0.00) 0.6697	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC: Endocrine disorders	Overall	23/3126 (0.7)	34/3127 (1.1)	0.68 (0.40, 1.15) 0.1462	0.67 (0.40, 1.15) 0.1461	-0.00 (-0.01, 0.00) 0.1365	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Eye disorders	Overall	81/3126 (2.6)	78/3127 (2.5)	1.04 (0.76, 1.41) 0.8080	1.04 (0.76, 1.42) 0.8090	0.00 (-0.01, 0.01) 0.8464	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders	Overall	306/3126 (9.8)	384/3127 (12.3)	0.80 (0.69, 0.92) 0.0017	0.78 (0.66, 0.91) 0.0017	-0.02 (-0.04, -0.01) 0.0017	
	Age						0.1650
	<= median	138/1544 (8.9)	161/1602 (10.0)	0.89 (0.72, 1.10) 0.2870	0.88 (0.69, 1.12) 0.2875	-0.01 (-0.03, 0.01) 0.2923	
	> median	168/1582 (10.6)	223/1525 (14.6)	0.73 (0.60, 0.88) 0.0008	0.69 (0.56, 0.86) 0.0008	-0.04 (-0.06, -0.02) 0.0008	
	Gender						0.7167
	Male	175/1765 (9.9)	212/1744 (12.2)	0.82 (0.68, 0.99) 0.0347	0.80 (0.64, 0.98) 0.0347	-0.02 (-0.04, -0.00) 0.0355	
	Female	131/1361 (9.6)	172/1383 (12.4)	0.77 (0.62, 0.96) 0.0191	0.75 (0.59, 0.95) 0.0188	-0.03 (-0.05, -0.00) 0.0174	
	Race						0.2706
	White	192/2210 (8.7)	234/2222 (10.5)	0.82 (0.69, 0.99) 0.0378	0.81 (0.66, 0.99) 0.0376	-0.02 (-0.04, -0.00) 0.0373	
	Black or African	4/ 81 (4.9)	11/ 78 (14.1)	0.33 (0.11, 1.00) 0.0495	0.30 (0.09, 1.00) 0.0503	-0.08 (-0.18, 0.02) 0.1117	
	Asian	89/ 629 (14.1)	122/ 643 (19.0)	0.75 (0.58, 0.96) 0.0223	0.71 (0.52, 0.95) 0.0222	-0.05 (-0.09, -0.01) 0.0231	
	Other	21/ 206 (10.2)	17/ 184 (9.2)	1.09 (0.59, 2.01) 0.7734	1.11 (0.56, 2.17) 0.7693	0.01 (-0.05, 0.07) 0.7340	
	Geographic region						0.9495
	Asia	88/ 606 (14.5)	120/ 619 (19.4)	0.75 (0.58, 0.96) 0.0248	0.71 (0.52, 0.96) 0.0247	-0.05 (-0.09, -0.01) 0.0250	
	Europe and Saudi Arabia	105/1491 (7.0)	130/1508 (8.6)	0.82 (0.64, 1.05) 0.1082	0.80 (0.61, 1.05) 0.1077	-0.02 (-0.04, 0.00) 0.1029	
	North America	70/ 427 (16.4)	84/ 422 (19.9)	0.82 (0.62, 1.09) 0.1770	0.79 (0.55, 1.12) 0.1821	-0.03 (-0.09, 0.02) 0.2017	
	Latin America	43/ 602 (7.1)	50/ 578 (8.7)	0.82 (0.56, 1.22) 0.3332	0.81 (0.53, 1.24) 0.3324	-0.02 (-0.05, 0.02) 0.3248	
	NYHA class at enrolment						0.2565
	II	227/2310 (9.8)	308/2395 (12.9)	0.76 (0.65, 0.90) 0.0011	0.74 (0.62, 0.89) 0.0011	-0.03 (-0.05, -0.01) 0.0010	
	III or IV	79/ 816 (9.7)	76/ 731 (10.4)	0.93 (0.69, 1.26) 0.6562	0.93 (0.66, 1.29) 0.6544	-0.01 (-0.04, 0.02) 0.6408	
	LVEF at enrolment						0.1046
	<= 49	83/1066 (7.8)	120/1047 (11.5)	0.68 (0.52, 0.89) 0.0050	0.66 (0.49, 0.88) 0.0050	-0.04 (-0.06, -0.01) 0.0062	
	50-59	104/1132 (9.2)	138/1121 (12.3)	0.75 (0.59, 0.95) 0.0171	0.72 (0.55, 0.94) 0.0171	-0.03 (-0.06, -0.01) 0.0181	
	>= 60	119/ 928 (12.8)	126/ 959 (13.1)	0.98 (0.77, 1.23) 0.8383	0.97 (0.74, 1.27) 0.8384	-0.00 (-0.03, 0.03) 0.8385	
	NT-proBNP at enrolment						0.4059
	<= median	137/1553 (8.8)	163/1574 (10.4)	0.85 (0.69, 1.06) 0.1464	0.84 (0.66, 1.06) 0.1456	-0.02 (-0.04, 0.01) 0.1407	
	> median	169/1573 (10.7)	221/1552 (14.2)	0.75 (0.63, 0.91) 0.0032	0.72 (0.59, 0.90) 0.0032	-0.04 (-0.06, -0.01) 0.0030	
	Type 2 Diabetes Medical History						0.5870
	Yes	142/1399 (10.2)	171/1402 (12.2)	0.83 (0.67, 1.03)*0.0862	0.81 (0.64, 1.03)*0.0860	-0.02 (-0.04, 0.00)*0.0854	
	No	164/1727 (9.5)	213/1725 (12.3)	0.77 (0.63, 0.93)*0.0075	0.74 (0.60, 0.92)*0.0074	-0.03 (-0.05, -0.01)*0.0072	
	Atrial fibrillation or flutter at enrolment ECG						0.6115
	Yes	130/1325 (9.8)	169/1317 (12.8)	0.76 (0.62, 0.95) 0.0141	0.74 (0.58, 0.94) 0.0141	-0.03 (-0.05, -0.01) 0.0150	
	No	176/1800 (9.8)	215/1809 (11.9)	0.82 (0.68, 0.99) 0.0420	0.80 (0.65, 0.99) 0.0418	-0.02 (-0.04, -0.00) 0.0416	
	BMI (kg/m2) at enrolment						0.5355
	< 30	193/1732 (11.1)	234/1733 (13.5)	0.83 (0.69, 0.99) 0.0350	0.80 (0.66, 0.98) 0.0349	-0.02 (-0.05, -0.00) 0.0346	
	>= 30	113/1392 (8.1)	150/1390 (10.8)	0.75 (0.60, 0.95) 0.0164	0.73 (0.57, 0.94) 0.0163	-0.03 (-0.05, -0.01) 0.0158	
	Baseline eGFR (mL/min/1.73m^2)						0.0168
	< 60	150/1514 (9.9)	226/1551 (14.6)	0.68 (0.56, 0.83) <.0001	0.65 (0.52, 0.80) <.0001	-0.05 (-0.07, -0.02) <.0001	
	>= 60	156/1612 (9.7)	158/1575 (10.0)	0.96 (0.78, 1.19) 0.7293	0.96 (0.76, 1.21) 0.7282	-0.00 (-0.02, 0.02) 0.7193	

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SOC: Gastrointestinal disorders	SBP at randomisation						0.4719
	<= median	170/1567 (10.8)	206/1588 (13.0)	0.84 (0.69, 1.01) 0.0675	0.82 (0.66, 1.01) 0.0675	-0.02 (-0.04, 0.00) 0.0682	
	> median	136/1559 (8.7)	178/1539 (11.6)	0.75 (0.61, 0.93) 0.0090	0.73 (0.58, 0.92) 0.0089	-0.03 (-0.05, -0.01) 0.0086	
	LVEF at enrolment 2						0.1569
	<= 49	83/1066 (7.8)	120/1047 (11.5)	0.68 (0.52, 0.89) 0.0050	0.66 (0.49, 0.88) 0.0050	-0.04 (-0.06, -0.01) 0.0062	
	>= 50	223/2060 (10.8)	264/2080 (12.7)	0.85 (0.72, 1.01) 0.0635	0.84 (0.69, 1.01) 0.0634	-0.02 (-0.04, 0.00) 0.0636	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0607
	Yes	17/ 328 (5.2)	35/ 326 (10.7)	0.48 (0.28, 0.84) 0.0105	0.45 (0.25, 0.83) 0.0100	-0.06 (-0.10, -0.01) 0.0083	
	No	289/2798 (10.3)	349/2801 (12.5)	0.83 (0.72, 0.96) 0.0122	0.81 (0.69, 0.95) 0.0121	-0.02 (-0.04, -0.00) 0.0122	
	MRAs at baseline						0.5686
	Yes	135/1339 (10.1)	160/1325 (12.1)	0.84 (0.67, 1.04) 0.1054	0.82 (0.64, 1.04) 0.1047	-0.02 (-0.04, 0.00) 0.1013	
	No	171/1787 (9.6)	224/1802 (12.4)	0.77 (0.64, 0.93) 0.0063	0.75 (0.60, 0.92) 0.0062	-0.03 (-0.05, -0.01) 0.0061	
	ACEi+ARB at baseline						0.0153
	Yes	208/2259 (9.2)	293/2276 (12.9)	0.71 (0.60, 0.85) <.0001	0.69 (0.57, 0.83) <.0001	-0.04 (-0.05, -0.02) <.0001	
	No	98/ 867 (11.3)	91/ 851 (10.7)	1.05 (0.81, 1.38) 0.6969	1.06 (0.79, 1.44) 0.6907	0.01 (-0.02, 0.04) 0.6450	
	ARNI at baseline						0.5360
	Yes	15/ 165 (9.1)	19/ 136 (14.0)	0.64 (0.34, 1.23) 0.1791	0.61 (0.29, 1.26) 0.1804	-0.05 (-0.12, 0.02) 0.1896	
	No	291/2961 (9.8)	365/2991 (12.2)	0.81 (0.70, 0.93) 0.0035	0.78 (0.67, 0.92) 0.0034	-0.02 (-0.04, -0.01) 0.0034	
	Beta Blocker at baseline						0.7195
	Yes	251/2587 (9.7)	318/2581 (12.3)	0.79 (0.67, 0.92) 0.0027	0.76 (0.64, 0.91) 0.0027	-0.03 (-0.04, -0.01) 0.0026	
	No	55/ 539 (10.2)	66/ 546 (12.1)	0.84 (0.60, 1.18) 0.3106	0.82 (0.56, 1.20) 0.3137	-0.02 (-0.06, 0.02) 0.3399	
	Diuretics at baseline						0.1117
	Yes	282/2789 (10.1)	340/2783 (12.2)	0.83 (0.71, 0.96) 0.0128	0.81 (0.68, 0.96) 0.0127	-0.02 (-0.04, -0.00) 0.0124	
	No	24/ 337 (7.1)	44/ 344 (12.8)	0.56 (0.35, 0.90) 0.0156	0.52 (0.31, 0.88) 0.0148	-0.06 (-0.10, -0.01) 0.0111	

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SOC: Gastrointestinal disorders, PT: Constipation	Overall	46/3126 (1.5)	52/3127 (1.7)	0.88 (0.60, 1.31) 0.5427	0.88 (0.59, 1.32) 0.5427	-0.00 (-0.01, 0.00) 0.5451	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders, PT: Diarrhoea	Overall	55/3126 (1.8)	66/3127 (2.1)	0.83 (0.58, 1.19) 0.3137	0.83 (0.58, 1.19) 0.3138	-0.00 (-0.01, 0.00) 0.3246	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions	Overall	256/3126 (8.2)	293/3127 (9.4)	0.87 (0.74, 1.03) 0.0983	0.86 (0.72, 1.03) 0.0992	-0.01 (-0.03, 0.00) 0.1070	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Death	Overall	54/3126 (1.7)	52/3127 (1.7)	1.04 (0.71, 1.52) 0.8433	1.04 (0.71, 1.53) 0.8432	0.00 (-0.01, 0.01) 0.8402	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Oedema peripheral	Overall	17/3126 (0.5)	33/3127 (1.1)	0.52 (0.29, 0.92) 0.0257	0.51 (0.28, 0.92) 0.0257	-0.00 (-0.01, -0.00) 0.0328	
	Age						0.8268
	<= median	9/1544 (0.6)	17/1602 (1.1)	0.55 (0.25, 1.23) 0.1431	0.55 (0.24, 1.23) 0.1437	-0.00 (-0.01, 0.00) 0.2576	
	> median	8/1582 (0.5)	16/1525 (1.0)	0.48 (0.21, 1.12) 0.0908	0.48 (0.20, 1.12) 0.0906	-0.01 (-0.01, 0.00) 0.0818	
	Gender						0.6996
	Male	10/1765 (0.6)	21/1744 (1.2)	0.47 (0.22, 0.99) 0.0476	0.47 (0.22, 0.99) 0.0476	-0.01 (-0.01, 0.00) 0.0686	
	Female	7/1361 (0.5)	12/1383 (0.9)	0.59 (0.23, 1.50) 0.2696	0.59 (0.23, 1.50) 0.2694	-0.00 (-0.01, 0.00) 0.2272	
	Race						0.1663
	White	5/2210 (0.2)	19/2222 (0.9)	0.26 (0.10, 0.71) 0.0080	0.26 (0.10, 0.71) 0.0080	-0.01 (-0.01, -0.00) 0.0026	
	Black or African	1/ 81 (1.2)	1/ 78 (1.3)	0.90 (0.06,13.89) 0.9373	0.96 (0.06,15.66)*0.9786	-0.00 (-0.04, 0.03)*0.9786	
	Asian	9/ 629 (1.4)	8/ 643 (1.2)	1.14 (0.44, 2.95) 0.7793	1.15 (0.44, 2.99) 0.7795	0.00 (-0.01, 0.01) 0.7991	
	Other	2/ 206 (1.0)	5/ 184 (2.7)	0.35 (0.07, 1.80) 0.2099	0.35 (0.07, 1.81) 0.2079	-0.02 (-0.04, 0.01)*0.2055	
	Geographic region						0.0558
	Asia	9/ 606 (1.5)	8/ 619 (1.3)	1.14 (0.44, 2.94) 0.7806	1.15 (0.44, 2.99) 0.7809	0.00 (-0.01, 0.01) 0.8047	
	Europe and Saudi Arabia	1/1491 (0.1)	9/1508 (0.6)	0.11 (0.01, 0.89) 0.0380	0.11 (0.01, 0.88) 0.0378	-0.01 (-0.01, -0.00)*0.0114	
	North America	5/ 427 (1.2)	7/ 422 (1.7)	0.70 (0.22, 2.20) 0.5438	0.70 (0.22, 2.22) 0.5456	-0.00 (-0.02, 0.01) 0.6764	
	Latin America	2/ 602 (0.3)	9/ 578 (1.6)	0.22 (0.05, 1.00) 0.0499	0.21 (0.05, 1.00) 0.0496	-0.01 (-0.02, -0.00)*0.0304	
	NYHA class at enrolment						0.1608
	II	11/2310 (0.5)	28/2395 (1.2)	0.41 (0.20, 0.82) 0.0112	0.40 (0.20, 0.81) 0.0112	-0.01 (-0.01, -0.00) 0.0064	
	III or IV	6/ 816 (0.7)	5/ 731 (0.7)	1.09 (0.33, 3.56) 0.8849	1.09 (0.33, 3.60) 0.8841	0.00 (-0.01, 0.01) 0.7590	
	LVEF at enrolment						0.7115
	<= 49	3/1066 (0.3)	9/1047 (0.9)	0.33 (0.09, 1.21) 0.0934	0.33 (0.09, 1.21) 0.0931	-0.01 (-0.01, 0.00) 0.0714	
	50-59	7/1132 (0.6)	12/1121 (1.1)	0.58 (0.23, 1.46) 0.2463	0.58 (0.23, 1.47) 0.2470	-0.00 (-0.01, 0.00) 0.3195	
	>= 60	7/ 928 (0.8)	12/ 959 (1.3)	0.61 (0.24, 1.53) 0.2909	0.60 (0.24, 1.54) 0.2914	-0.00 (-0.01, 0.01) 0.3664	
	NT-proBNP at enrolment						0.8673
	<= median	7/1553 (0.5)	13/1574 (0.8)	0.55 (0.22, 1.36) 0.1943	0.54 (0.22, 1.37) 0.1948	-0.00 (-0.01, 0.00) 0.3299	
	> median	10/1573 (0.6)	20/1552 (1.3)	0.49 (0.23, 1.05) 0.0667	0.49 (0.23, 1.05) 0.0666	-0.01 (-0.01, 0.00) 0.0650	
	Type 2 Diabetes Medical History						0.1402
	Yes	6/1399 (0.4)	19/1402 (1.4)	0.32 (0.13, 0.79)*0.0137	0.31 (0.12, 0.79)*0.0136	-0.01 (-0.02, -0.00)*0.0090	
	No	11/1727 (0.6)	14/1725 (0.8)	0.78 (0.36, 1.72)*0.5461	0.78 (0.35, 1.73)*0.5461	-0.00 (-0.01, 0.00)*0.5451	
	Atrial fibrillation or flutter at enrolment ECG						0.4934
	Yes	11/1325 (0.8)	18/1317 (1.4)	0.61 (0.29, 1.28) 0.1901	0.60 (0.28, 1.28) 0.1899	-0.01 (-0.01, 0.00) 0.1766	
	No	6/1800 (0.3)	15/1809 (0.8)	0.40 (0.16, 1.03) 0.0568	0.40 (0.15, 1.03) 0.0569	-0.00 (-0.01, 0.00) 0.1621	
	BMI (kg/m2) at enrolment						0.7610
	< 30	9/1732 (0.5)	16/1733 (0.9)	0.56 (0.25, 1.27) 0.1663	0.56 (0.25, 1.27) 0.1662	-0.00 (-0.01, 0.00) 0.1571	
	>= 30	8/1392 (0.6)	17/1390 (1.2)	0.47 (0.20, 1.08) 0.0764	0.47 (0.20, 1.08) 0.0765	-0.01 (-0.01, 0.00) 0.1113	
	Baseline eGFR (mL/min/1.73m^2)						0.9543
	< 60	10/1514 (0.7)	20/1551 (1.3)	0.51 (0.24, 1.08) 0.0801	0.51 (0.24, 1.08) 0.0799	-0.01 (-0.01, 0.00) 0.0788	
	>= 60	7/1612 (0.4)	13/1575 (0.8)	0.53 (0.21, 1.32) 0.1708	0.53 (0.21, 1.32) 0.1709	-0.00 (-0.01, 0.00) 0.1262	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Oedema peripheral	SBP at randomisation						0.7941
	<= median	7/1567 (0.4)	15/1588 (0.9)	0.47 (0.19, 1.14) 0.0962	0.47 (0.19, 1.15) 0.0960	-0.00 (-0.01, 0.00) 0.1105	
	> median	10/1559 (0.6)	18/1539 (1.2)	0.55 (0.25, 1.18) 0.1264	0.55 (0.25, 1.19) 0.1262	-0.01 (-0.01, 0.00) 0.0972	
	LVEF at enrolment 2						0.4127
	<= 49	3/1066 (0.3)	9/1047 (0.9)	0.33 (0.09, 1.21) 0.0934	0.33 (0.09, 1.21) 0.0931	-0.01 (-0.01, 0.00) 0.0714	
	>= 50	14/2060 (0.7)	24/2080 (1.2)	0.59 (0.31, 1.14) 0.1154	0.59 (0.30, 1.14) 0.1159	-0.00 (-0.01, 0.00) 0.1862	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6133
	Yes	3/ 328 (0.9)	4/ 326 (1.2)	0.76 (0.17, 3.39) 0.7241	0.76 (0.17, 3.44) 0.7229	-0.00 (-0.02, 0.01) 0.6227	
	No	14/2798 (0.5)	29/2801 (1.0)	0.48 (0.26, 0.91) 0.0252	0.48 (0.25, 0.91) 0.0252	-0.00 (-0.01, -0.00) 0.0385	
	MRAs at baseline						0.4365
	Yes	6/1339 (0.4)	8/1325 (0.6)	0.75 (0.26, 2.14) 0.5858	0.74 (0.26, 2.15) 0.5859	-0.00 (-0.01, 0.00) 0.6105	
	No	11/1787 (0.6)	25/1802 (1.4)	0.45 (0.22, 0.90) 0.0250	0.44 (0.22, 0.90) 0.0250	-0.01 (-0.01, -0.00) 0.0396	
	ACEi+ARB at baseline						0.9015
	Yes	11/2259 (0.5)	21/2276 (0.9)	0.53 (0.26, 1.09) 0.0851	0.53 (0.25, 1.09) 0.0852	-0.00 (-0.01, 0.00) 0.1085	
	No	6/ 867 (0.7)	12/ 851 (1.4)	0.49 (0.18, 1.30) 0.1509	0.49 (0.18, 1.30) 0.1509	-0.01 (-0.02, 0.00) 0.1639	
	ARNI at baseline						0.8263
	Yes	1/ 165 (0.6)	2/ 136 (1.5)	0.44 (0.04, 4.91) 0.5042	0.44 (0.04, 4.95) 0.5025	-0.01 (-0.03, 0.01)*0.4698	
	No	16/2961 (0.5)	31/2991 (1.0)	0.52 (0.29, 0.95) 0.0341	0.52 (0.28, 0.95) 0.0341	-0.00 (-0.01, -0.00) 0.0465	
	Beta Blocker at baseline						0.5368
	Yes	11/2587 (0.4)	24/2581 (0.9)	0.46 (0.22, 0.93) 0.0306	0.45 (0.22, 0.93) 0.0306	-0.00 (-0.01, -0.00) 0.0459	
	No	6/ 539 (1.1)	9/ 546 (1.6)	0.67 (0.24, 1.88) 0.4527	0.67 (0.24, 1.90) 0.4525	-0.01 (-0.02, 0.01) 0.4292	
	Diuretics at baseline						0.4815
	Yes	16/2789 (0.6)	29/2783 (1.0)	0.55 (0.30, 1.01) 0.0539	0.55 (0.30, 1.01) 0.0542	-0.00 (-0.01, 0.00) 0.1080	
	No	1/ 337 (0.3)	4/ 344 (1.2)	0.25 (0.03, 2.27) 0.2200	0.25 (0.03, 2.28) 0.2207	-0.01 (-0.02, 0.00)*0.1824	

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Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Sudden cardiac death	Overall	26/3126 (0.8)	37/3127 (1.2)	0.70 (0.43, 1.16) 0.1664	0.70 (0.42, 1.16) 0.1663	-0.00 (-0.01, 0.00) 0.1615	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Hepatobiliary disorders	Overall	61/3126 (2.0)	61/3127 (2.0)	1.00 (0.70, 1.42) 0.9964	1.00 (0.70, 1.43) 0.9977	-0.00 (-0.01, 0.01) 0.9343	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations	Overall	915/3126 (29.3)	893/3127 (28.6)	1.02 (0.95, 1.11) 0.5474	1.04 (0.93, 1.15) 0.5350	0.01 (-0.02, 0.03) 0.5173	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Bronchitis	Overall	39/3126 (1.2)	37/3127 (1.2)	1.05 (0.67, 1.65) 0.8160	1.06 (0.67, 1.66) 0.8158	0.00 (-0.00, 0.01) 0.7963	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19	Overall	183/3126 (5.9)	144/3127 (4.6)	1.27 (1.03, 1.57) 0.0268	1.29 (1.03, 1.61) 0.0269	0.01 (0.00, 0.02) 0.0325	
	Age						0.9246
	<= median	98/1544 (6.3)	79/1602 (4.9)	1.29 (0.96, 1.72) 0.0861	1.31 (0.96, 1.77) 0.0862	0.01 (-0.00, 0.03) 0.0941	
	> median	85/1582 (5.4)	65/1525 (4.3)	1.26 (0.92, 1.73) 0.1497	1.27 (0.92, 1.78) 0.1503	0.01 (-0.00, 0.03) 0.1649	
	Gender						0.0626
	Male	86/1765 (4.9)	81/1744 (4.6)	1.05 (0.78, 1.41) 0.7587	1.05 (0.77, 1.43) 0.7602	0.00 (-0.01, 0.02) 0.7889	
	Female	97/1361 (7.1)	63/1383 (4.6)	1.57 (1.15, 2.14) 0.0041	1.61 (1.16, 2.24) 0.0041	0.02 (0.01, 0.04) 0.0052	
	Race						0.3755
	White	157/2210 (7.1)	129/2222 (5.8)	1.22 (0.98, 1.53) 0.0785	1.24 (0.98, 1.58) 0.0790	0.01 (-0.00, 0.03) 0.0881	
	Black or African	11/ 81 (13.6)	4/ 78 (5.1)	2.64 (0.88, 7.95) 0.0841	2.90 (0.88, 9.53) 0.0800	0.08 (-0.01, 0.17) 0.0651	
	Asian	6/ 629 (1.0)	7/ 643 (1.1)	0.88 (0.30, 2.62) 0.8248	0.88 (0.30, 2.65) 0.8251	-0.00 (-0.01, 0.01) 0.8646	
	Other	9/ 206 (4.4)	4/ 184 (2.2)	2.13 (0.67, 6.78) 0.1983	2.23 (0.67, 7.44) 0.1907	0.02 (-0.01, 0.06)*0.2186	
	Geographic region						0.1483
	Asia	5/ 606 (0.8)	7/ 619 (1.1)	0.74 (0.24, 2.31) 0.6027	0.74 (0.23, 2.33) 0.6017	-0.00 (-0.01, 0.01) 0.5241	
	Europe and Saudi Arabia	105/1491 (7.0)	96/1508 (6.4)	1.11 (0.85, 1.44) 0.4631	1.11 (0.84, 1.48) 0.4666	0.01 (-0.01, 0.02) 0.5143	
	North America	28/ 427 (6.6)	13/ 422 (3.1)	2.12 (1.11, 4.04) 0.0221	2.20 (1.12, 4.32) 0.0213	0.03 (0.01, 0.06) 0.0176	
	Latin America	45/ 602 (7.5)	28/ 578 (4.8)	1.57 (0.99, 2.48) 0.0533	1.62 (1.00, 2.64) 0.0517	0.03 (0.00, 0.06) 0.0354	
	NYHA class at enrolment						0.9468
	II	137/2310 (5.9)	111/2395 (4.6)	1.28 (1.00, 1.63) 0.0484	1.30 (1.00, 1.68) 0.0484	0.01 (-0.00, 0.03) 0.0519	
	III or IV	46/ 816 (5.6)	33/ 731 (4.5)	1.26 (0.81, 1.94) 0.3058	1.27 (0.80, 2.01) 0.3080	0.01 (-0.01, 0.03) 0.3524	
	LVEF at enrolment						0.9955
	<= 49	66/1066 (6.2)	50/1047 (4.8)	1.29 (0.90, 1.85) 0.1618	1.31 (0.90, 1.91) 0.1611	0.01 (-0.01, 0.03) 0.1553	
	50-59	61/1132 (5.4)	48/1121 (4.3)	1.26 (0.87, 1.82) 0.2195	1.27 (0.86, 1.88) 0.2205	0.01 (-0.01, 0.03) 0.2480	
	>= 60	56/ 928 (6.0)	46/ 959 (4.8)	1.27 (0.87, 1.85) 0.2237	1.28 (0.86, 1.91) 0.2256	0.01 (-0.01, 0.03) 0.2630	
	NT-proBNP at enrolment						0.0168
	<= median	115/1553 (7.4)	73/1574 (4.6)	1.60 (1.20, 2.12) 0.0013	1.64 (1.22, 2.22) 0.0012	0.03 (0.01, 0.04) 0.0013	
	> median	68/1573 (4.3)	71/1552 (4.6)	0.94 (0.68, 1.31) 0.7293	0.94 (0.67, 1.32) 0.7288	-0.00 (-0.02, 0.01) 0.7225	
	Type 2 Diabetes Medical History						0.4246
	Yes	98/1399 (7.0)	71/1402 (5.1)	1.38 (1.03, 1.86)*0.0319	1.41 (1.03, 1.93)*0.0317	0.02 (0.00, 0.04)*0.0309	
	No	85/1727 (4.9)	73/1725 (4.2)	1.16 (0.86, 1.58)*0.3327	1.17 (0.85, 1.61)*0.3326	0.01 (-0.01, 0.02)*0.3320	
	Atrial fibrillation or flutter at enrolment ECG						0.2025
	Yes	57/1325 (4.3)	54/1317 (4.1)	1.05 (0.73, 1.51) 0.7946	1.05 (0.72, 1.54) 0.7936	0.00 (-0.01, 0.02) 0.7713	
	No	126/1800 (7.0)	90/1809 (5.0)	1.41 (1.08, 1.83) 0.0109	1.44 (1.09, 1.90) 0.0111	0.02 (0.00, 0.03) 0.0171	
	BMI (kg/m2) at enrolment						0.1312
	< 30	69/1732 (4.0)	66/1733 (3.8)	1.05 (0.75, 1.46) 0.7877	1.05 (0.74, 1.48) 0.7892	0.00 (-0.01, 0.01) 0.8274	
	>= 30	114/1392 (8.2)	78/1390 (5.6)	1.46 (1.10, 1.93) 0.0077	1.50 (1.11, 2.02) 0.0077	0.03 (0.01, 0.04) 0.0075	
	Baseline eGFR (mL/min/1.73m^2)						0.6134
	< 60	91/1514 (6.0)	77/1551 (5.0)	1.20 (0.90, 1.61) 0.2197	1.21 (0.89, 1.66) 0.2264	0.01 (-0.01, 0.02) 0.3811	
	>= 60	92/1612 (5.7)	67/1575 (4.3)	1.34 (0.99, 1.82) 0.0603	1.36 (0.99, 1.88) 0.0601	0.01 (-0.00, 0.03) 0.0575	

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Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19	SBP at randomisation						0.8804
	<= median	83/1567 (5.3)	67/1588 (4.2)	1.26 (0.92, 1.72) 0.1560	1.27 (0.91, 1.77) 0.1559	0.01 (-0.00, 0.03) 0.1548	
	> median	100/1559 (6.4)	77/1539 (5.0)	1.30 (0.97, 1.73) 0.0776	1.31 (0.97, 1.79) 0.0805	0.01 (-0.00, 0.03) 0.1533	
	LVEF at enrolment 2						0.9197
	<= 49	66/1066 (6.2)	50/1047 (4.8)	1.29 (0.90, 1.85) 0.1618	1.31 (0.90, 1.91) 0.1611	0.01 (-0.01, 0.03) 0.1553	
	>= 50	117/2060 (5.7)	94/2080 (4.5)	1.26 (0.97, 1.64) 0.0859	1.28 (0.97, 1.69) 0.0868	0.01 (-0.00, 0.02) 0.1096	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5930
	Yes	15/ 328 (4.6)	14/ 326 (4.3)	1.06 (0.52, 2.15) 0.8818	1.05 (0.50, 2.22) 0.8904	-0.00 (-0.04, 0.03) 0.9143	
	No	168/2798 (6.0)	130/2801 (4.6)	1.30 (1.04, 1.62) 0.0228	1.31 (1.04, 1.66) 0.0228	0.01 (0.00, 0.03) 0.0239	
	MRAs at baseline						0.5959
	Yes	66/1339 (4.9)	55/1325 (4.2)	1.18 (0.83, 1.67) 0.3566	1.19 (0.82, 1.71) 0.3583	0.01 (-0.01, 0.02) 0.4022	
	No	117/1787 (6.5)	89/1802 (4.9)	1.33 (1.02, 1.74) 0.0370	1.35 (1.02, 1.80) 0.0371	0.02 (0.00, 0.03) 0.0403	
	ACEi+ARB at baseline						0.7528
	Yes	140/2259 (6.2)	113/2276 (5.0)	1.25 (0.98, 1.59) 0.0687	1.27 (0.98, 1.63) 0.0699	0.01 (-0.00, 0.02) 0.0972	
	No	43/ 867 (5.0)	31/ 851 (3.6)	1.36 (0.87, 2.14) 0.1797	1.38 (0.86, 2.21) 0.1795	0.01 (-0.01, 0.03) 0.1808	
	ARNI at baseline						0.0373
	Yes	9/ 165 (5.5)	1/ 136 (0.7)	8.79 (1.13,68.40) 0.0378	9.52 (1.18,76.95) 0.0345	0.05 (0.01, 0.08)*0.0137	
	No	174/2961 (5.9)	143/2991 (4.8)	1.23 (0.99, 1.53) 0.0573	1.25 (0.99, 1.56) 0.0582	0.01 (-0.00, 0.02) 0.0791	
	Beta Blocker at baseline						0.4936
	Yes	152/2587 (5.9)	115/2581 (4.5)	1.32 (1.04, 1.67) 0.0219	1.34 (1.04, 1.72) 0.0219	0.01 (0.00, 0.03) 0.0241	
	No	31/ 539 (5.8)	29/ 546 (5.3)	1.09 (0.67, 1.79) 0.7214	1.10 (0.65, 1.85) 0.7275	0.00 (-0.02, 0.03) 0.8322	
	Diuretics at baseline						0.1511
	Yes	172/2789 (6.2)	129/2783 (4.6)	1.33 (1.07, 1.66) 0.0116	1.35 (1.07, 1.71) 0.0117	0.01 (0.00, 0.03) 0.0149	
	No	11/ 337 (3.3)	15/ 344 (4.4)	0.75 (0.35, 1.60) 0.4514	0.74 (0.33, 1.63) 0.4546	-0.01 (-0.04, 0.02) 0.5452	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19 pneumonia	Overall	86/3126 (2.8)	89/3127 (2.8)	0.97 (0.72, 1.29) 0.8115	0.97 (0.71, 1.30) 0.8181	0.00 (-0.01, 0.01) 0.9473	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Cellulitis	Overall	57/3126 (1.8)	53/3127 (1.7)	1.08 (0.74, 1.56) 0.6991	1.08 (0.74, 1.57) 0.7002	0.00 (-0.01, 0.01) 0.7724	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Nasopharyngitis	Overall	59/3126 (1.9)	60/3127 (1.9)	0.98 (0.69, 1.40) 0.9295	0.98 (0.68, 1.41) 0.9288	-0.00 (-0.01, 0.01) 0.8914	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Pneumonia	Overall	145/3126 (4.6)	146/3127 (4.7)	0.99 (0.79, 1.24) 0.9537	0.99 (0.78, 1.26) 0.9538	-0.00 (-0.01, 0.01) 0.9565	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Urinary tract infection	Overall	146/3126 (4.7)	140/3127 (4.5)	1.04 (0.83, 1.31) 0.7170	1.05 (0.82, 1.33) 0.7147	0.00 (-0.01, 0.01) 0.6669	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Injury, poisoning and procedural complications	Overall	238/3126 (7.6)	260/3127 (8.3)	0.92 (0.77, 1.08) 0.3057	0.91 (0.76, 1.09) 0.3064	-0.01 (-0.02, 0.01) 0.3147	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Injury, poisoning and procedural complications, PT: Contusion	Overall	23/3126 (0.7)	34/3127 (1.1)	0.68 (0.40, 1.15) 0.1465	0.67 (0.40, 1.15) 0.1464	-0.00 (-0.01, 0.00) 0.1602	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Injury, poisoning and procedural complications, PT: Fall	Overall	34/3126 (1.1)	35/3127 (1.1)	0.97 (0.61, 1.55) 0.9061	0.97 (0.60, 1.56) 0.9040	-0.00 (-0.01, 0.00) 0.7163	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Investigations	Overall	95/3126 (3.0)	112/3127 (3.6)	0.85 (0.65, 1.11) 0.2331	0.84 (0.64, 1.11) 0.2312	-0.01 (-0.02, 0.00) 0.1787	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders	Overall	303/3126 (9.7)	351/3127 (11.2)	0.86 (0.75, 1.00) 0.0463	0.85 (0.72, 1.00) 0.0467	-0.01 (-0.03, 0.00) 0.0564	
	Age						0.9189
	<= median	153/1544 (9.9)	182/1602 (11.4)	0.87 (0.71, 1.06) 0.1724	0.86 (0.68, 1.08) 0.1807	-0.01 (-0.03, 0.01) 0.2922	
	> median	150/1582 (9.5)	169/1525 (11.1)	0.86 (0.70, 1.05) 0.1426	0.84 (0.67, 1.06) 0.1399	-0.02 (-0.04, 0.00) 0.1248	
	Gender						0.4879
	Male	170/1765 (9.6)	203/1744 (11.6)	0.83 (0.68, 1.00) 0.0501	0.80 (0.65, 1.00) 0.0484	-0.02 (-0.04, -0.00) 0.0416	
	Female	133/1361 (9.8)	148/1383 (10.7)	0.92 (0.73, 1.14) 0.4340	0.91 (0.71, 1.16) 0.4477	-0.01 (-0.03, 0.02) 0.5798	
	Race						0.3546
	White	190/2210 (8.6)	217/2222 (9.8)	0.88 (0.73, 1.06) 0.1729	0.87 (0.71, 1.07) 0.1768	-0.01 (-0.03, 0.01) 0.2323	
	Black or African	13/ 81 (16.0)	20/ 78 (25.6)	0.62 (0.33, 1.15) 0.1289	0.53 (0.24, 1.17) 0.1186	-0.10 (-0.22, 0.02) 0.0984	
	Asian	84/ 629 (13.4)	104/ 643 (16.2)	0.82 (0.63, 1.07) 0.1443	0.79 (0.58, 1.08) 0.1435	-0.03 (-0.07, 0.01) 0.1457	
	Other	16/ 206 (7.8)	10/ 184 (5.4)	1.51 (0.71, 3.23) 0.2853	1.58 (0.69, 3.60) 0.2791	0.02 (-0.02, 0.07) 0.2549	
	Geographic region						0.3151
	Asia	81/ 606 (13.4)	103/ 619 (16.6)	0.80 (0.61, 1.04) 0.0999	0.77 (0.56, 1.05) 0.1001	-0.03 (-0.07, 0.01) 0.1069	
	Europe and Saudi Arabia	89/1491 (6.0)	113/1508 (7.5)	0.79 (0.61, 1.04) 0.0892	0.78 (0.58, 1.04) 0.0858	-0.02 (-0.03, 0.00) 0.0579	
	North America	86/ 427 (20.1)	77/ 422 (18.2)	1.09 (0.83, 1.43) 0.5473	1.13 (0.80, 1.59) 0.4962	0.02 (-0.03, 0.08) 0.3497	
	Latin America	47/ 602 (7.8)	58/ 578 (10.0)	0.81 (0.56, 1.17) 0.2545	0.79 (0.52, 1.18) 0.2457	-0.02 (-0.05, 0.01) 0.1933	
	NYHA class at enrolment						0.2583
	II	221/2310 (9.6)	277/2395 (11.6)	0.82 (0.70, 0.97) 0.0231	0.81 (0.67, 0.97) 0.0235	-0.02 (-0.04, -0.00) 0.0327	
	III or IV	82/ 816 (10.0)	74/ 731 (10.1)	1.00 (0.74, 1.35) 0.9884	1.00 (0.72, 1.40) 0.9925	-0.00 (-0.03, 0.03) 0.9720	
	LVEF at enrolment						0.8229
	<= 49	81/1066 (7.6)	98/1047 (9.4)	0.81 (0.61, 1.07) 0.1313	0.79 (0.58, 1.07) 0.1291	-0.02 (-0.04, 0.00) 0.1164	
	50-59	115/1132 (10.2)	129/1121 (11.5)	0.88 (0.69, 1.11) 0.2882	0.87 (0.67, 1.14) 0.3060	-0.01 (-0.03, 0.02) 0.4862	
	>= 60	107/ 928 (11.5)	124/ 959 (12.9)	0.90 (0.71, 1.15) 0.3996	0.89 (0.67, 1.17) 0.3876	-0.01 (-0.04, 0.01) 0.3255	
	NT-proBNP at enrolment						0.0574
	<= median	126/1553 (8.1)	173/1574 (11.0)	0.74 (0.59, 0.92) 0.0063	0.71 (0.56, 0.91) 0.0062	-0.03 (-0.05, -0.01) 0.0073	
	> median	177/1573 (11.3)	178/1552 (11.5)	0.98 (0.81, 1.19) 0.8380	0.98 (0.78, 1.22) 0.8401	-0.00 (-0.02, 0.02) 0.8567	
	Type 2 Diabetes Medical History						0.8998
	Yes	171/1399 (12.2)	200/1402 (14.3)	0.86 (0.71, 1.04)*0.1114	0.84 (0.67, 1.04)*0.1112	-0.02 (-0.05, 0.00)*0.1107	
	No	132/1727 (7.6)	151/1725 (8.8)	0.87 (0.70, 1.09)*0.2349	0.86 (0.68, 1.10)*0.2348	-0.01 (-0.03, 0.01)*0.2344	
	Atrial fibrillation or flutter at enrolment ECG						0.4094
	Yes	135/1325 (10.2)	145/1317 (11.0)	0.93 (0.74, 1.16) 0.4935	0.92 (0.72, 1.18) 0.5023	-0.01 (-0.03, 0.02) 0.5709	
	No	168/1800 (9.3)	206/1809 (11.4)	0.82 (0.68, 0.99) 0.0410	0.79 (0.64, 0.99) 0.0374	-0.02 (-0.04, -0.00) 0.0213	
	BMI (kg/m2) at enrolment						0.7201
	< 30	163/1732 (9.4)	194/1733 (11.2)	0.84 (0.69, 1.03) 0.0924	0.82 (0.66, 1.03) 0.0836	-0.02 (-0.04, -0.00) 0.0420	
	>= 30	140/1392 (10.1)	156/1390 (11.2)	0.89 (0.72, 1.11) 0.2943	0.88 (0.69, 1.13) 0.3158	-0.01 (-0.03, 0.02) 0.5386	
	Baseline eGFR (mL/min/1.73m^2)						0.9071
	< 60	178/1514 (11.8)	210/1551 (13.5)	0.86 (0.71, 1.03) 0.1094	0.84 (0.68, 1.04) 0.1133	-0.02 (-0.04, 0.01) 0.1499	
	>= 60	125/1612 (7.8)	141/1575 (9.0)	0.87 (0.69, 1.10) 0.2525	0.86 (0.67, 1.11) 0.2495	-0.01 (-0.03, 0.01) 0.2324	

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Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders	SBP at randomisation						0.1982
	<= median	166/1567 (10.6)	176/1588 (11.1)	0.95 (0.78, 1.16) 0.5914	0.94 (0.75, 1.18) 0.6006	-0.00 (-0.03, 0.02) 0.6751	
	> median	137/1559 (8.8)	175/1539 (11.4)	0.78 (0.63, 0.97) 0.0231	0.76 (0.60, 0.96) 0.0221	-0.02 (-0.04, -0.00) 0.0197	
	LVEF at enrolment 2						0.5519
	<= 49	81/1066 (7.6)	98/1047 (9.4)	0.81 (0.61, 1.07) 0.1313	0.79 (0.58, 1.07) 0.1291	-0.02 (-0.04, 0.00) 0.1164	
	>= 50	222/2060 (10.8)	253/2080 (12.2)	0.89 (0.75, 1.05) 0.1733	0.88 (0.72, 1.06) 0.1768	-0.01 (-0.03, 0.01) 0.2168	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9573
	Yes	27/ 328 (8.2)	31/ 326 (9.5)	0.85 (0.52, 1.39) 0.5220	0.83 (0.48, 1.43) 0.5038	-0.02 (-0.06, 0.02) 0.3356	
	No	276/2798 (9.9)	320/2801 (11.4)	0.86 (0.74, 1.01) 0.0598	0.85 (0.72, 1.01) 0.0617	-0.01 (-0.03, 0.00) 0.0864	
	MRAs at baseline						0.3408
	Yes	130/1339 (9.7)	135/1325 (10.2)	0.94 (0.75, 1.18) 0.5980	0.94 (0.73, 1.21) 0.6099	-0.00 (-0.03, 0.02) 0.7184	
	No	173/1787 (9.7)	216/1802 (12.0)	0.81 (0.67, 0.98) 0.0329	0.79 (0.64, 0.98) 0.0318	-0.02 (-0.04, -0.00) 0.0287	
	ACEi+ARB at baseline						0.1255
	Yes	202/2259 (8.9)	255/2276 (11.2)	0.80 (0.67, 0.95) 0.0123	0.78 (0.64, 0.95) 0.0118	-0.02 (-0.04, -0.01) 0.0103	
	No	101/ 867 (11.6)	96/ 851 (11.3)	1.02 (0.79, 1.33) 0.8696	1.03 (0.76, 1.39) 0.8452	0.01 (-0.02, 0.04) 0.6922	
	ARNI at baseline						0.5273
	Yes	24/ 165 (14.5)	18/ 136 (13.2)	0.97 (0.55, 1.71) 0.9298	0.98 (0.50, 1.91) 0.9417	0.00 (-0.07, 0.07) 0.9910	
	No	279/2961 (9.4)	333/2991 (11.1)	0.85 (0.73, 0.99) 0.0319	0.83 (0.70, 0.98) 0.0322	-0.02 (-0.03, -0.00) 0.0399	
	Beta Blocker at baseline						0.5784
	Yes	250/2587 (9.7)	294/2581 (11.4)	0.85 (0.72, 0.99) 0.0407	0.83 (0.69, 0.99) 0.0397	-0.02 (-0.03, -0.00) 0.0385	
	No	53/ 539 (9.8)	57/ 546 (10.4)	0.94 (0.66, 1.35) 0.7498	0.94 (0.63, 1.40) 0.7617	-0.00 (-0.04, 0.03) 0.8581	
	Diuretics at baseline						0.5712
	Yes	281/2789 (10.1)	321/2783 (11.5)	0.87 (0.75, 1.02) 0.0782	0.86 (0.72, 1.02) 0.0784	-0.01 (-0.03, 0.00) 0.0870	
	No	22/ 337 (6.5)	30/ 344 (8.7)	0.75 (0.44, 1.26) 0.2749	0.73 (0.41, 1.29) 0.2786	-0.02 (-0.06, 0.02) 0.3439	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Diabetes mellitus inadequate control	Overall	49/3126 (1.6)	52/3127 (1.7)	0.94 (0.64, 1.38) 0.7592	0.94 (0.63, 1.40) 0.7568	-0.00 (-0.01, 0.01)*0.7647	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hyperkalaemia	Overall	45/3126 (1.4)	43/3127 (1.4)	1.05 (0.69, 1.58) 0.8309	1.05 (0.69, 1.60) 0.8293	0.00 (-0.00, 0.01) 0.7229	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hyperuricaemia	Overall	20/3126 (0.6)	36/3127 (1.2)	0.56 (0.32, 0.96) 0.0344	0.55 (0.32, 0.96) 0.0342	-0.01 (-0.01, -0.00) 0.0300	
	Age						0.2911
	<= median	12/1544 (0.8)	17/1602 (1.1)	0.73 (0.35, 1.53) 0.4060	0.73 (0.35, 1.53) 0.4055	-0.00 (-0.01, 0.00) 0.3686	
	> median	8/1582 (0.5)	19/1525 (1.2)	0.41 (0.18, 0.92) 0.0317	0.40 (0.18, 0.92) 0.0315	-0.01 (-0.01, -0.00) 0.0295	
	Gender						0.2173
	Male	16/1765 (0.9)	23/1744 (1.3)	0.69 (0.36, 1.29) 0.2448	0.68 (0.36, 1.30) 0.2445	-0.00 (-0.01, 0.00) 0.2189	
	Female	4/1361 (0.3)	13/1383 (0.9)	0.31 (0.10, 0.96) 0.0423	0.31 (0.10, 0.96) 0.0421	-0.01 (-0.01, -0.00) 0.0414	
	Race						0.5262
	White	7/2210 (0.3)	15/2222 (0.7)	0.47 (0.19, 1.15) 0.0973	0.47 (0.19, 1.15) 0.0973	-0.00 (-0.01, 0.00) 0.1783	
	Black or African	1/ 81 (1.2)	1/ 78 (1.3)	1.06 (0.07,16.27) 0.9663	0.96 (0.06,15.66)*0.9786	-0.00 (-0.04, 0.03)*0.9786	
	Asian	11/ 629 (1.7)	20/ 643 (3.1)	0.56 (0.27, 1.16) 0.1182	0.55 (0.26, 1.16) 0.1163	-0.02 (-0.03, 0.00) 0.0567	
	Other	1/ 206 (0.5)	0/ 184 (0.0)	2.68 (0.11,65.41)*0.5451	2.69 (0.11,66.53)*0.5448	0.00 (-0.00, 0.01)*0.3161	
	Geographic region						0.9558
	Asia	11/ 606 (1.8)	20/ 619 (3.2)	0.56 (0.27, 1.16) 0.1178	0.55 (0.26, 1.16) 0.1156	-0.02 (-0.03, 0.00) 0.0534	
	Europe and Saudi Arabia	6/1491 (0.4)	9/1508 (0.6)	0.67 (0.24, 1.87) 0.4440	0.67 (0.24, 1.88) 0.4450	-0.00 (-0.01, 0.00) 0.6961	
	North America	1/ 427 (0.2)	2/ 422 (0.5)	0.50 (0.05, 5.50) 0.5728	0.49 (0.04, 5.46)*0.5642	-0.00 (-0.01, 0.01)*0.5568	
	Latin America	2/ 602 (0.3)	5/ 578 (0.9)	0.40 (0.08, 2.04) 0.2683	0.39 (0.08, 2.05) 0.2684	-0.00 (-0.01, 0.01) 0.3828	
	NYHA class at enrolment						0.5019
	II	15/2310 (0.6)	25/2395 (1.0)	0.62 (0.33, 1.17) 0.1425	0.62 (0.32, 1.18) 0.1421	-0.00 (-0.01, 0.00) 0.1096	
	III or IV	5/ 816 (0.6)	11/ 731 (1.5)	0.41 (0.14, 1.16) 0.0929	0.40 (0.14, 1.16) 0.0925	-0.01 (-0.02, 0.00) 0.0804	
	LVEF at enrolment						0.4990
	<= 49	5/1066 (0.5)	14/1047 (1.3)	0.35 (0.13, 0.96) 0.0414	0.34 (0.12, 0.96) 0.0412	-0.01 (-0.02, -0.00) 0.0479	
	50-59	5/1132 (0.4)	8/1121 (0.7)	0.62 (0.20, 1.89) 0.3989	0.62 (0.20, 1.89) 0.3966	-0.00 (-0.01, 0.00)*0.3946	
	>= 60	10/ 928 (1.1)	14/ 959 (1.5)	0.75 (0.34, 1.68) 0.4864	0.75 (0.33, 1.69) 0.4806	-0.01 (-0.02, 0.00) 0.0913	
	NT-proBNP at enrolment						0.1055
	<= median	6/1553 (0.4)	19/1574 (1.2)	0.32 (0.13, 0.80) 0.0147	0.32 (0.13, 0.80) 0.0145	-0.01 (-0.01, -0.00) 0.0069	
	> median	14/1573 (0.9)	17/1552 (1.1)	0.81 (0.40, 1.64) 0.5630	0.81 (0.40, 1.65) 0.5630	-0.00 (-0.01, 0.00) 0.5602	
	Type 2 Diabetes Medical History						0.8130
	Yes	11/1399 (0.8)	21/1402 (1.5)	0.52 (0.25, 1.08)*0.0818	0.52 (0.25, 1.09)*0.0815	-0.01 (-0.01, 0.00)*0.0762	
	No	9/1727 (0.5)	15/1725 (0.9)	0.60 (0.26, 1.37)*0.2231	0.60 (0.26, 1.37)*0.2230	-0.00 (-0.01, 0.00)*0.2180	
	Atrial fibrillation or flutter at enrolment ECG						0.6076
	Yes	12/1325 (0.9)	19/1317 (1.4)	0.63 (0.31, 1.29) 0.2029	0.62 (0.30, 1.29) 0.2027	-0.01 (-0.01, 0.00) 0.2010	
	No	8/1800 (0.4)	17/1809 (0.9)	0.47 (0.20, 1.09) 0.0774	0.47 (0.20, 1.09) 0.0768	-0.00 (-0.01, -0.00) 0.0479	
	BMI (kg/m2) at enrolment						0.4985
	< 30	14/1732 (0.8)	22/1733 (1.3)	0.64 (0.33, 1.24) 0.1851	0.63 (0.32, 1.24) 0.1844	-0.00 (-0.01, 0.00) 0.1470	
	>= 30	6/1392 (0.4)	14/1390 (1.0)	0.43 (0.16, 1.11) 0.0811	0.43 (0.16, 1.11) 0.0809	-0.01 (-0.01, 0.00) 0.0690	
	Baseline eGFR (mL/min/1.73m^2)						0.1202
	< 60	13/1514 (0.9)	16/1551 (1.0)	0.83 (0.40, 1.72) 0.6127	0.83 (0.40, 1.73) 0.6131	-0.00 (-0.01, 0.01) 0.6544	
	>= 60	7/1612 (0.4)	20/1575 (1.3)	0.34 (0.15, 0.81) 0.0149	0.34 (0.14, 0.81) 0.0147	-0.01 (-0.01, -0.00) 0.0065	

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RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hyperuricaemia	SBP at randomisation						0.4623
	<= median	9/1567 (0.6)	20/1588 (1.3)	0.46 (0.21, 1.00) 0.0501	0.45 (0.21, 1.00) 0.0499	-0.01 (-0.01, -0.00) 0.0433	
	> median	11/1559 (0.7)	16/1539 (1.0)	0.69 (0.32, 1.48) 0.3385	0.69 (0.32, 1.48) 0.3380	-0.00 (-0.01, 0.00) 0.3139	
	LVEF at enrolment 2						0.2575
	<= 49	5/1066 (0.5)	14/1047 (1.3)	0.35 (0.13, 0.96) 0.0414	0.34 (0.12, 0.96) 0.0412	-0.01 (-0.02, -0.00) 0.0479	
	>= 50	15/2060 (0.7)	22/2080 (1.1)	0.69 (0.36, 1.33) 0.2651	0.69 (0.36, 1.33) 0.2649	-0.00 (-0.01, 0.00) 0.2372	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4613
	Yes	3/ 328 (0.9)	3/ 326 (0.9)	0.97 (0.20, 4.79) 0.9722	0.97 (0.19, 4.86) 0.9724	-0.00 (-0.01, 0.01) 0.9940	
	No	17/2798 (0.6)	33/2801 (1.2)	0.52 (0.29, 0.92) 0.0262	0.51 (0.29, 0.92) 0.0261	-0.01 (-0.01, -0.00) 0.0222	
	MRAs at baseline						0.1081
	Yes	10/1339 (0.7)	10/1325 (0.8)	0.98 (0.41, 2.34) 0.9599	0.98 (0.41, 2.36) 0.9600	-0.00 (-0.01, 0.01) 0.9816	
	No	10/1787 (0.6)	26/1802 (1.4)	0.39 (0.19, 0.80) 0.0108	0.39 (0.19, 0.80) 0.0107	-0.01 (-0.02, -0.00) 0.0073	
	ACEi+ARB at baseline						0.5816
	Yes	16/2259 (0.7)	31/2276 (1.4)	0.52 (0.29, 0.95) 0.0330	0.52 (0.28, 0.95) 0.0328	-0.01 (-0.01, -0.00) 0.0262	
	No	4/ 867 (0.5)	5/ 851 (0.6)	0.78 (0.21, 2.90) 0.7119	0.78 (0.21, 2.92) 0.7122	-0.00 (-0.01, 0.01) 0.7707	
	ARNI at baseline						0.1803
	Yes	1/ 165 (0.6)	0/ 136 (0.0)	2.48 (0.10,60.29)*0.5778	2.49 (0.10,61.60)*0.5775	0.01 (-0.01, 0.02)*0.3158	
	No	19/2961 (0.6)	36/2991 (1.2)	0.53 (0.31, 0.93) 0.0264	0.53 (0.30, 0.93) 0.0263	-0.01 (-0.01, -0.00) 0.0199	
	Beta Blocker at baseline						0.6907
	Yes	16/2587 (0.6)	27/2581 (1.0)	0.59 (0.32, 1.09) 0.0936	0.59 (0.32, 1.09) 0.0934	-0.00 (-0.01, 0.00) 0.0815	
	No	4/ 539 (0.7)	9/ 546 (1.6)	0.45 (0.14, 1.46) 0.1843	0.45 (0.14, 1.46) 0.1838	-0.01 (-0.02, 0.00) 0.1801	
	Diuretics at baseline						0.0999
	Yes	20/2789 (0.7)	33/2783 (1.2)	0.60 (0.35, 1.05) 0.0746	0.60 (0.34, 1.05) 0.0745	-0.00 (-0.01, 0.00) 0.0663	
	No	0/ 337 (0.0)	3/ 344 (0.9)	0.00 (0.00,) 0.9999	0.14 (0.01, 2.81)*0.2014	-0.01 (-0.02, 0.00)*0.0819	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hypoglycaemia	Overall	38/3126 (1.2)	31/3127 (1.0)	1.22 (0.76, 1.96) 0.3999	1.23 (0.76, 1.98) 0.3981	0.00 (-0.00, 0.00) 0.3384	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hypokalaemia	Overall	41/3126 (1.3)	29/3127 (0.9)	1.41 (0.88, 2.27) 0.1508	1.42 (0.88, 2.29) 0.1508	0.00 (-0.00, 0.01) 0.1521	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Type 2 diabetes mellitus	Overall	22/3126 (0.7)	32/3127 (1.0)	0.69 (0.40, 1.18) 0.1747	0.69 (0.40, 1.18) 0.1748	-0.00 (-0.01, 0.00) 0.1944	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Musculoskeletal and connective tissue disorders	Overall	251/3126 (8.0)	266/3127 (8.5)	0.94 (0.80, 1.11) 0.4939	0.94 (0.78, 1.12) 0.4937	-0.00 (-0.02, 0.01) 0.4925	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Musculoskeletal and connective tissue disorders, PT: Arthralgia	Overall	43/3126 (1.4)	60/3127 (1.9)	0.72 (0.49, 1.06) 0.0934	0.71 (0.48, 1.06) 0.0932	-0.01 (-0.01, 0.00) 0.0833	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Musculoskeletal and connective tissue disorders, PT: Back pain	Overall	58/3126 (1.9)	58/3127 (1.9)	1.00 (0.70, 1.43) 0.9986	1.00 (0.69, 1.44) 0.9985	0.00 (-0.01, 0.01) 0.9902	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Overall	143/3126 (4.6)	158/3127 (5.1)	0.91 (0.73, 1.13) 0.3774	0.90 (0.71, 1.14) 0.3773	-0.00 (-0.02, 0.01) 0.3754	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders	Overall	384/3126 (12.3)	397/3127 (12.7)	0.97 (0.85, 1.10) 0.6224	0.96 (0.83, 1.12) 0.6224	-0.00 (-0.02, 0.01) 0.6224	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders, PT: Dizziness	Overall	66/3126 (2.1)	58/3127 (1.9)	1.14 (0.80, 1.61) 0.4650	1.14 (0.80, 1.63) 0.4662	0.00 (-0.00, 0.01) 0.5353	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders, PT: Headache	Overall	62/3126 (2.0)	61/3127 (2.0)	1.02 (0.72, 1.44) 0.9262	1.02 (0.71, 1.45) 0.9256	0.00 (-0.01, 0.01) 0.8966	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders, PT: Ischaemic stroke	Overall	71/3126 (2.3)	68/3127 (2.2)	1.04 (0.75, 1.45) 0.7959	1.05 (0.75, 1.46) 0.7959	0.00 (-0.01, 0.01) 0.7991	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders, PT: Syncope	Overall	35/3126 (1.1)	36/3127 (1.2)	0.97 (0.61, 1.54) 0.9052	0.97 (0.61, 1.55) 0.9067	0.00 (-0.01, 0.01) 0.9603	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Psychiatric disorders	Overall	84/3126 (2.7)	87/3127 (2.8)	0.97 (0.72, 1.30) 0.8184	0.96 (0.71, 1.31) 0.8182	-0.00 (-0.01, 0.01) 0.8135	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders	Overall	276/3126 (8.8)	300/3127 (9.6)	0.92 (0.79, 1.08) 0.2963	0.91 (0.77, 1.08) 0.2950	-0.01 (-0.02, 0.01) 0.2848	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Acute kidney injury	Overall	90/3126 (2.9)	99/3127 (3.2)	0.91 (0.69, 1.21) 0.5123	0.91 (0.68, 1.21) 0.5062	-0.00 (-0.01, 0.00) 0.3354	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Chronic kidney disease	Overall	50/3126 (1.6)	39/3127 (1.2)	1.28 (0.85, 1.94) 0.2426	1.29 (0.84, 1.96) 0.2413	0.00 (-0.00, 0.01) 0.1693	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Renal failure	Overall	31/3126 (1.0)	34/3127 (1.1)	0.91 (0.56, 1.48) 0.7085	0.91 (0.56, 1.49) 0.7081	-0.00 (-0.01, 0.00) 0.6747	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Renal impairment	Overall	62/3126 (2.0)	61/3127 (2.0)	1.02 (0.72, 1.44) 0.9266	1.02 (0.71, 1.45) 0.9263	0.00 (-0.01, 0.01) 0.9121	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Reproductive system and breast disorders	Overall	62/3126 (2.0)	55/3127 (1.8)	1.13 (0.79, 1.62) 0.5135	1.13 (0.78, 1.63) 0.5118	0.00 (-0.00, 0.01) 0.4307	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders	Overall	282/3126 (9.0)	303/3127 (9.7)	0.93 (0.80, 1.09) 0.3648	0.92 (0.78, 1.10) 0.3639	-0.01 (-0.02, 0.01) 0.3559	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders, PT: Chronic obstructive pulmonary disease	Overall	30/3126 (1.0)	38/3127 (1.2)	0.79 (0.49, 1.27) 0.3314	0.79 (0.49, 1.27) 0.3303	-0.00 (-0.01, 0.00) 0.2472	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders, PT: Cough	Overall	32/3126 (1.0)	35/3127 (1.1)	0.91 (0.57, 1.47) 0.7125	0.91 (0.56, 1.48) 0.7142	-0.00 (-0.01, 0.00) 0.8757	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders, PT: Dyspnoea	Overall	40/3126 (1.3)	32/3127 (1.0)	1.25 (0.79, 1.98) 0.3434	1.25 (0.79, 2.00) 0.3436	0.00 (-0.00, 0.01) 0.3659	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Skin and subcutaneous tissue disorders	Overall	169/3126 (5.4)	172/3127 (5.5)	0.98 (0.80, 1.21) 0.8646	0.98 (0.79, 1.22) 0.8683	-0.00 (-0.01, 0.01) 0.9300	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders	Overall	318/3126 (10.2)	288/3127 (9.2)	1.10 (0.95, 1.29) 0.1988	1.12 (0.94, 1.32) 0.1985	0.01 (-0.01, 0.02) 0.1972	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders, PT: Hypertension	Overall	95/3126 (3.0)	111/3127 (3.5)	0.86 (0.65, 1.12) 0.2580	0.85 (0.64, 1.13) 0.2583	-0.01 (-0.01, 0.00) 0.2666	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Analysis of frequent Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders, PT: Hypotension	Overall	79/3126 (2.5)	67/3127 (2.1)	1.18 (0.86, 1.63) 0.3139	1.18 (0.85, 1.65) 0.3139	0.00 (-0.00, 0.01) 0.3200	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders, PT: Peripheral arterial occlusive disease	Overall	40/3126 (1.3)	30/3127 (1.0)	1.33 (0.83, 2.13) 0.2309	1.34 (0.83, 2.15) 0.2310	0.00 (-0.00, 0.01) 0.2665	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Blood and lymphatic system disorders	Overall	34/3126 (1.1)	47/3127 (1.5)	0.72 (0.47, 1.12) 0.1478	0.72 (0.46, 1.12) 0.1478	-0.00 (-0.01, 0.00) 0.1556	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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AstraZeneca
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Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders	Overall	651/3126 (20.8)	717/3127 (22.9)	0.91 (0.83, 1.00) 0.0453	0.88 (0.78, 1.00) 0.0434	-0.02 (-0.04, -0.00) 0.0399	
	Age						0.9674
	<= median	327/1544 (21.2)	371/1602 (23.2)	0.91 (0.80, 1.04) 0.1549	0.89 (0.75, 1.05) 0.1766	-0.02 (-0.05, 0.01) 0.2511	
	> median	324/1582 (20.5)	346/1525 (22.7)	0.91 (0.79, 1.04) 0.1461	0.88 (0.74, 1.04) 0.1331	-0.02 (-0.05, 0.00) 0.1033	
	Gender						0.9900
	Male	389/1765 (22.0)	423/1744 (24.3)	0.91 (0.81, 1.02) 0.1182	0.88 (0.75, 1.03) 0.1126	-0.02 (-0.05, 0.00) 0.1011	
	Female	262/1361 (19.3)	294/1383 (21.3)	0.91 (0.78, 1.05) 0.2017	0.89 (0.73, 1.07) 0.2047	-0.02 (-0.05, 0.01) 0.2184	
	Race						0.6961
	White	470/2210 (21.3)	531/2222 (23.9)	0.89 (0.80, 0.99) 0.0350	0.86 (0.75, 0.99) 0.0360	-0.03 (-0.05, -0.00) 0.0395	
	Black or African	21/ 81 (25.9)	25/ 78 (32.1)	0.80 (0.49, 1.31) 0.3779	0.73 (0.37, 1.46) 0.3719	-0.06 (-0.20, 0.08) 0.3641	
	Asian	140/ 629 (22.3)	142/ 643 (22.1)	1.01 (0.82, 1.24) 0.9168	1.00 (0.77, 1.31) 0.9813	-0.00 (-0.05, 0.04) 0.8593	
	Other	20/ 206 (9.7)	19/ 184 (10.3)	0.97 (0.54, 1.76) 0.9330	0.97 (0.50, 1.90) 0.9386	-0.00 (-0.06, 0.06) 0.9880	
	Geographic region						0.3050
	Asia	131/ 606 (21.6)	134/ 619 (21.6)	1.00 (0.81, 1.24) 0.9908	0.99 (0.76, 1.30) 0.9611	-0.00 (-0.05, 0.04) 0.8388	
	Europe and Saudi Arabia	320/1491 (21.5)	344/1508 (22.8)	0.94 (0.82, 1.07) 0.3605	0.92 (0.78, 1.10) 0.3546	-0.01 (-0.04, 0.02) 0.3414	
	North America	119/ 427 (27.9)	132/ 422 (31.3)	0.89 (0.72, 1.09) 0.2531	0.84 (0.63, 1.14) 0.2610	-0.03 (-0.09, 0.03) 0.2771	
	Latin America	81/ 602 (13.5)	107/ 578 (18.5)	0.73 (0.56, 0.96) 0.0223	0.70 (0.51, 0.95) 0.0238	-0.05 (-0.09, -0.00) 0.0349	
	NYHA class at enrolment						0.7001
	II	436/2310 (18.9)	495/2395 (20.7)	0.91 (0.81, 1.02) 0.1185	0.89 (0.77, 1.03) 0.1167	-0.02 (-0.04, 0.00) 0.1132	
	III or IV	215/ 816 (26.3)	221/ 731 (30.2)	0.88 (0.75, 1.03) 0.1071	0.83 (0.66, 1.04) 0.1011	-0.04 (-0.08, 0.01) 0.0934	
	LVEF at enrolment						0.9396
	<= 49	242/1066 (22.7)	266/1047 (25.4)	0.89 (0.76, 1.04) 0.1300	0.86 (0.70, 1.05) 0.1329	-0.03 (-0.06, 0.01) 0.1406	
	50-59	232/1132 (20.5)	252/1121 (22.5)	0.92 (0.78, 1.07) 0.2754	0.89 (0.73, 1.09) 0.2535	-0.02 (-0.06, 0.01) 0.2032	
	>= 60	177/ 928 (19.1)	199/ 959 (20.8)	0.92 (0.77, 1.11) 0.3899	0.91 (0.72, 1.14) 0.3906	-0.02 (-0.05, 0.02) 0.3962	
	NT-proBNP at enrolment						0.5404
	<= median	272/1553 (17.5)	294/1574 (18.7)	0.94 (0.81, 1.09) 0.4040	0.92 (0.77, 1.11) 0.3966	-0.01 (-0.04, 0.01) 0.3744	
	> median	379/1573 (24.1)	423/1552 (27.3)	0.88 (0.78, 1.00) 0.0428	0.85 (0.72, 0.99) 0.0416	-0.03 (-0.06, -0.00) 0.0406	
	Type 2 Diabetes Medical History						0.7631
	Yes	341/1399 (24.4)	371/1402 (26.5)	0.92 (0.81, 1.05)*0.2048	0.90 (0.76, 1.06)*0.2046	-0.02 (-0.05, 0.01)*0.2044	
	No	310/1727 (18.0)	346/1725 (20.1)	0.89 (0.78, 1.03)*0.1148	0.87 (0.74, 1.03)*0.1147	-0.02 (-0.05, 0.01)*0.1144	
	Atrial fibrillation or flutter at enrolment ECG						0.4982
	Yes	276/1325 (20.8)	291/1317 (22.1)	0.94 (0.82, 1.09) 0.4437	0.93 (0.77, 1.12) 0.4437	-0.01 (-0.04, 0.02) 0.4463	
	No	375/1800 (20.8)	426/1809 (23.5)	0.88 (0.78, 1.00) 0.0491	0.85 (0.73, 1.00) 0.0462	-0.03 (-0.06, -0.00) 0.0404	
	BMI (kg/m2) at enrolment						0.9920
	< 30	339/1732 (19.6)	374/1733 (21.6)	0.91 (0.80, 1.04) 0.1510	0.88 (0.75, 1.04) 0.1434	-0.02 (-0.05, 0.01) 0.1258	
	>= 30	312/1392 (22.4)	343/1390 (24.7)	0.91 (0.79, 1.04) 0.1563	0.88 (0.74, 1.05) 0.1577	-0.02 (-0.05, 0.01) 0.1633	
	Baseline eGFR (mL/min/1.73m^2)						0.6888
	< 60	357/1514 (23.6)	407/1551 (26.2)	0.90 (0.79, 1.01) 0.0770	0.86 (0.73, 1.01) 0.0726	-0.03 (-0.06, 0.00) 0.0652	
	>= 60	294/1612 (18.2)	310/1575 (19.7)	0.93 (0.81, 1.07) 0.3216	0.91 (0.77, 1.09) 0.3218	-0.01 (-0.04, 0.01) 0.3248	

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SOC: Cardiac disorders	SBP at randomisation						0.1130
	<= median	334/1567 (21.3)	344/1588 (21.7)	0.98 (0.86, 1.12) 0.7814	0.97 (0.82, 1.15) 0.7619	-0.01 (-0.03, 0.02) 0.7123	
	> median	317/1559 (20.3)	373/1539 (24.2)	0.84 (0.74, 0.96) 0.0115	0.80 (0.68, 0.95) 0.0114	-0.04 (-0.07, -0.01) 0.0120	
	LVEF at enrolment 2						0.7234
	<= 49	242/1066 (22.7)	266/1047 (25.4)	0.89 (0.76, 1.04) 0.1300	0.86 (0.70, 1.05) 0.1329	-0.03 (-0.06, 0.01) 0.1406	
	>= 50	409/2060 (19.9)	451/2080 (21.7)	0.92 (0.82, 1.04) 0.1698	0.90 (0.77, 1.04) 0.1594	-0.02 (-0.04, 0.01) 0.1351	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.8336
	Yes	103/ 328 (31.4)	115/ 326 (35.3)	0.89 (0.72, 1.10) 0.2895	0.83 (0.60, 1.15) 0.2708	-0.04 (-0.11, 0.03) 0.2514	
	No	548/2798 (19.6)	602/2801 (21.5)	0.91 (0.82, 1.01) 0.0800	0.89 (0.78, 1.01) 0.0809	-0.02 (-0.04, 0.00) 0.0855	
	MRAs at baseline						0.7588
	Yes	271/1339 (20.2)	298/1325 (22.5)	0.90 (0.77, 1.04) 0.1411	0.87 (0.72, 1.05) 0.1439	-0.02 (-0.05, 0.01) 0.1523	
	No	380/1787 (21.3)	419/1802 (23.3)	0.92 (0.82, 1.04) 0.1949	0.90 (0.77, 1.05) 0.1770	-0.02 (-0.05, 0.01) 0.1398	
	ACEi+ARB at baseline						0.8163
	Yes	459/2259 (20.3)	513/2276 (22.5)	0.90 (0.81, 1.01) 0.0697	0.88 (0.76, 1.01) 0.0698	-0.02 (-0.05, 0.00) 0.0718	
	No	192/ 867 (22.1)	204/ 851 (24.0)	0.92 (0.78, 1.10) 0.3706	0.90 (0.72, 1.12) 0.3497	-0.02 (-0.06, 0.02) 0.3072	
	ARNI at baseline						0.8118
	Yes	38/ 165 (23.0)	32/ 136 (23.5)	0.93 (0.62, 1.40) 0.7333	0.89 (0.51, 1.53) 0.6653	-0.03 (-0.13, 0.06) 0.5215	
	No	613/2961 (20.7)	685/2991 (22.9)	0.91 (0.82, 1.00) 0.0432	0.88 (0.78, 1.00) 0.0425	-0.02 (-0.04, -0.00) 0.0418	
	Beta Blocker at baseline						0.7227
	Yes	522/2587 (20.2)	577/2581 (22.4)	0.90 (0.81, 1.00) 0.0533	0.88 (0.77, 1.00) 0.0519	-0.02 (-0.04, 0.00) 0.0501	
	No	129/ 539 (23.9)	140/ 546 (25.6)	0.93 (0.76, 1.15) 0.5237	0.91 (0.69, 1.20) 0.5202	-0.02 (-0.07, 0.03) 0.5130	
	Diuretics at baseline						0.7391
	Yes	594/2789 (21.3)	650/2783 (23.4)	0.91 (0.83, 1.01) 0.0694	0.89 (0.78, 1.01) 0.0643	-0.02 (-0.04, 0.00) 0.0542	
	No	57/ 337 (16.9)	67/ 344 (19.5)	0.87 (0.63, 1.19) 0.3750	0.84 (0.57, 1.24) 0.3849	-0.02 (-0.08, 0.03) 0.4201	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Acute myocardial infarction	Overall	63/3126 (2.0)	63/3127 (2.0)	1.00 (0.71, 1.41) 0.9959	1.00 (0.70, 1.42) 0.9996	0.00 (-0.01, 0.01) 0.8160	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Angina unstable	Overall	49/3126 (1.6)	62/3127 (2.0)	0.79 (0.54, 1.14) 0.2122	0.79 (0.54, 1.15) 0.2141	-0.00 (-0.01, 0.00) 0.3505	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Atrial fibrillation	Overall	69/3126 (2.2)	57/3127 (1.8)	1.21 (0.86, 1.71) 0.2805	1.22 (0.85, 1.73) 0.2805	0.00 (-0.00, 0.01) 0.2855	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure	Overall	308/3126 (9.9)	377/3127 (12.1)	0.82 (0.71, 0.94) 0.0055	0.80 (0.68, 0.93) 0.0053	-0.02 (-0.04, -0.01) 0.0041	
	Age						0.2265
	<= median	152/1544 (9.8)	176/1602 (11.0)	0.89 (0.73, 1.10) 0.2815	0.88 (0.70, 1.11) 0.2908	-0.01 (-0.03, 0.01) 0.3819	
	> median	156/1582 (9.9)	201/1525 (13.2)	0.75 (0.62, 0.91) 0.0041	0.72 (0.58, 0.90) 0.0038	-0.03 (-0.06, -0.01) 0.0024	
	Gender						0.8201
	Male	191/1765 (10.8)	228/1744 (13.1)	0.83 (0.69, 0.99) 0.0395	0.80 (0.66, 0.99) 0.0377	-0.02 (-0.05, -0.00) 0.0290	
	Female	117/1361 (8.6)	149/1383 (10.8)	0.80 (0.64, 1.01) 0.0575	0.78 (0.61, 1.01) 0.0575	-0.02 (-0.04, 0.00) 0.0612	
	Race						0.3116
	White	228/2210 (10.3)	294/2222 (13.2)	0.78 (0.66, 0.92) 0.0028	0.75 (0.63, 0.91) 0.0027	-0.03 (-0.05, -0.01) 0.0023	
	Black or African	4/ 81 (4.9)	7/ 78 (9.0)	0.54 (0.16, 1.75) 0.3016	0.51 (0.14, 1.82) 0.2998	-0.04 (-0.11, 0.04) 0.3268	
	Asian	67/ 629 (10.7)	64/ 643 (10.0)	1.07 (0.77, 1.48) 0.6948	1.07 (0.75, 1.54) 0.7064	0.00 (-0.03, 0.04) 0.7994	
	Other	9/ 206 (4.4)	12/ 184 (6.5)	0.70 (0.30, 1.62) 0.4070	0.68 (0.28, 1.67) 0.4036	-0.02 (-0.06, 0.02) 0.3909	
	Geographic region						0.6054
	Asia	63/ 606 (10.4)	64/ 619 (10.3)	1.00 (0.72, 1.39) 0.9890	1.00 (0.69, 1.45) 0.9964	-0.00 (-0.03, 0.03) 0.9482	
	Europe and Saudi Arabia	178/1491 (11.9)	226/1508 (15.0)	0.80 (0.66, 0.95) 0.0140	0.77 (0.62, 0.95) 0.0137	-0.03 (-0.06, -0.01) 0.0123	
	North America	26/ 427 (6.1)	34/ 422 (8.1)	0.75 (0.46, 1.23) 0.2563	0.73 (0.43, 1.25) 0.2527	-0.02 (-0.05, 0.01) 0.2390	
	Latin America	41/ 602 (6.8)	53/ 578 (9.2)	0.75 (0.50, 1.10) 0.1438	0.73 (0.48, 1.11) 0.1429	-0.02 (-0.05, 0.01) 0.1373	
	NYHA class at enrolment						0.4668
	II	198/2310 (8.6)	245/2395 (10.2)	0.84 (0.70, 1.00) 0.0511	0.82 (0.67, 1.00) 0.0498	-0.02 (-0.03, -0.00) 0.0415	
	III or IV	110/ 816 (13.5)	132/ 731 (18.1)	0.75 (0.59, 0.95) 0.0154	0.71 (0.54, 0.94) 0.0149	-0.05 (-0.08, -0.01) 0.0135	
	LVEF at enrolment						0.4781
	<= 49	128/1066 (12.0)	138/1047 (13.2)	0.90 (0.72, 1.13) 0.3825	0.89 (0.69, 1.16) 0.3881	-0.01 (-0.04, 0.02) 0.4270	
	50-59	106/1132 (9.4)	134/1121 (12.0)	0.79 (0.62, 1.00) 0.0492	0.76 (0.58, 1.00) 0.0471	-0.03 (-0.05, -0.00) 0.0347	
	>= 60	74/ 928 (8.0)	105/ 959 (10.9)	0.73 (0.55, 0.97) 0.0315	0.71 (0.52, 0.97) 0.0305	-0.03 (-0.06, -0.00) 0.0256	
	NT-proBNP at enrolment						0.3086
	<= median	115/1553 (7.4)	130/1574 (8.3)	0.90 (0.71, 1.14) 0.3855	0.89 (0.68, 1.15) 0.3738	-0.01 (-0.03, 0.01) 0.2596	
	> median	193/1573 (12.3)	247/1552 (15.9)	0.77 (0.65, 0.92) 0.0033	0.74 (0.60, 0.90) 0.0033	-0.04 (-0.06, -0.01) 0.0039	
	Type 2 Diabetes Medical History						0.6287
	Yes	162/1399 (11.6)	192/1402 (13.7)	0.85 (0.70, 1.03)*0.0927	0.83 (0.66, 1.03)*0.0924	-0.02 (-0.05, 0.00)*0.0919	
	No	146/1727 (8.5)	185/1725 (10.7)	0.79 (0.64, 0.97)*0.0239	0.77 (0.61, 0.97)*0.0238	-0.02 (-0.04, -0.00)*0.0234	
	Atrial fibrillation or flutter at enrolment ECG						0.6706
	Yes	150/1325 (11.3)	177/1317 (13.4)	0.84 (0.69, 1.03) 0.1019	0.82 (0.65, 1.04) 0.1017	-0.02 (-0.05, 0.00) 0.1029	
	No	158/1800 (8.8)	200/1809 (11.1)	0.79 (0.65, 0.97) 0.0223	0.77 (0.62, 0.96) 0.0209	-0.02 (-0.04, -0.01) 0.0130	
	BMI (kg/m2) at enrolment						0.8118
	< 30	150/1732 (8.7)	187/1733 (10.8)	0.80 (0.65, 0.98) 0.0352	0.78 (0.63, 0.98) 0.0346	-0.02 (-0.04, -0.00) 0.0322	
	>= 30	158/1392 (11.4)	190/1390 (13.7)	0.83 (0.68, 1.01) 0.0662	0.81 (0.64, 1.01) 0.0643	-0.02 (-0.05, 0.00) 0.0548	
	Baseline eGFR (mL/min/1.73m^2)						0.5302
	< 60	169/1514 (11.2)	219/1551 (14.1)	0.79 (0.65, 0.95) 0.0126	0.76 (0.61, 0.94) 0.0119	-0.03 (-0.05, -0.01) 0.0090	
	>= 60	139/1612 (8.6)	158/1575 (10.0)	0.86 (0.69, 1.07) 0.1841	0.85 (0.67, 1.08) 0.1833	-0.01 (-0.03, 0.01) 0.1793	

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Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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AstraZeneca
Protocol: D169CC00001
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure	SBP at randomisation						0.2990
	<= median	150/1567 (9.6)	171/1588 (10.8)	0.89 (0.72, 1.09) 0.2511	0.87 (0.69, 1.10) 0.2465	-0.01 (-0.03, 0.01) 0.2148	
	> median	158/1559 (10.1)	206/1539 (13.4)	0.76 (0.63, 0.93) 0.0061	0.73 (0.59, 0.91) 0.0059	-0.03 (-0.05, -0.01) 0.0051	
	LVEF at enrolment 2						0.2504
	<= 49	128/1066 (12.0)	138/1047 (13.2)	0.90 (0.72, 1.13) 0.3825	0.89 (0.69, 1.16) 0.3881	-0.01 (-0.04, 0.02) 0.4270	
	>= 50	180/2060 (8.7)	239/2080 (11.5)	0.76 (0.64, 0.92) 0.0039	0.74 (0.60, 0.91) 0.0037	-0.03 (-0.05, -0.01) 0.0023	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.2325
	Yes	59/ 328 (18.0)	84/ 326 (25.8)	0.70 (0.52, 0.94) 0.0167	0.63 (0.43, 0.92) 0.0158	-0.08 (-0.14, -0.02) 0.0136	
	No	249/2798 (8.9)	293/2801 (10.5)	0.85 (0.73, 1.00) 0.0506	0.84 (0.70, 1.00) 0.0501	-0.02 (-0.03, -0.00) 0.0480	
	MRAs at baseline						0.3377
	Yes	132/1339 (9.9)	172/1325 (13.0)	0.76 (0.61, 0.94) 0.0111	0.73 (0.57, 0.93) 0.0108	-0.03 (-0.06, -0.01) 0.0096	
	No	176/1787 (9.8)	205/1802 (11.4)	0.87 (0.72, 1.05) 0.1570	0.86 (0.69, 1.06) 0.1549	-0.01 (-0.03, 0.01) 0.1472	
	ACEi+ARB at baseline						0.9972
	Yes	218/2259 (9.7)	269/2276 (11.8)	0.82 (0.69, 0.97) 0.0191	0.80 (0.66, 0.96) 0.0188	-0.02 (-0.04, -0.00) 0.0182	
	No	90/ 867 (10.4)	108/ 851 (12.7)	0.82 (0.63, 1.06) 0.1337	0.79 (0.59, 1.07) 0.1279	-0.03 (-0.06, 0.00) 0.0966	
	ARNI at baseline						0.4018
	Yes	21/ 165 (12.7)	16/ 136 (11.8)	1.03 (0.56, 1.90) 0.9167	1.03 (0.51, 2.07) 0.9447	-0.01 (-0.08, 0.07) 0.8775	
	No	287/2961 (9.7)	361/2991 (12.1)	0.80 (0.70, 0.93) 0.0036	0.78 (0.66, 0.92) 0.0035	-0.02 (-0.04, -0.01) 0.0030	
	Beta Blocker at baseline						0.7107
	Yes	247/2587 (9.5)	305/2581 (11.8)	0.81 (0.69, 0.95) 0.0082	0.79 (0.66, 0.94) 0.0079	-0.02 (-0.04, -0.01) 0.0064	
	No	61/ 539 (11.3)	72/ 546 (13.2)	0.86 (0.62, 1.18) 0.3528	0.84 (0.58, 1.21) 0.3513	-0.02 (-0.06, 0.02) 0.3423	
	Diuretics at baseline						0.5737
	Yes	285/2789 (10.2)	344/2783 (12.4)	0.83 (0.71, 0.96) 0.0121	0.81 (0.68, 0.95) 0.0115	-0.02 (-0.04, -0.01) 0.0088	
	No	23/ 337 (6.8)	33/ 344 (9.6)	0.71 (0.43, 1.19) 0.1913	0.69 (0.40, 1.20) 0.1906	-0.03 (-0.07, 0.01) 0.1876	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure acute	Overall	57/3126 (1.8)	63/3127 (2.0)	0.90 (0.63, 1.29) 0.5806	0.90 (0.63, 1.30) 0.5804	-0.00 (-0.01, 0.00) 0.5750	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure congestive	Overall	63/3126 (2.0)	82/3127 (2.6)	0.77 (0.56, 1.06) 0.1123	0.76 (0.55, 1.06) 0.1109	-0.01 (-0.01, 0.00) 0.0737	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders	Overall	86/3126 (2.8)	147/3127 (4.7)	0.59 (0.45, 0.76) <.0001	0.57 (0.44, 0.75) <.0001	-0.02 (-0.03, -0.01) <.0001	
	Age						0.6146
	<= median	37/1544 (2.4)	61/1602 (3.8)	0.63 (0.42, 0.94) 0.0241	0.62 (0.41, 0.94) 0.0238	-0.01 (-0.03, -0.00) 0.0191	
	> median	49/1582 (3.1)	86/1525 (5.6)	0.55 (0.39, 0.77) 0.0006	0.53 (0.37, 0.77) 0.0006	-0.03 (-0.04, -0.01) 0.0005	
	Gender						0.1093
	Male	53/1765 (3.0)	74/1744 (4.2)	0.71 (0.50, 1.00) 0.0509	0.70 (0.49, 1.00) 0.0520	-0.01 (-0.02, 0.00) 0.0930	
	Female	33/1361 (2.4)	73/1383 (5.3)	0.46 (0.31, 0.69) 0.0002	0.45 (0.29, 0.68) 0.0002	-0.03 (-0.04, -0.01) 0.0002	
	Race						0.1611
	White	59/2210 (2.7)	92/2222 (4.1)	0.64 (0.47, 0.89) 0.0075	0.64 (0.46, 0.89) 0.0074	-0.01 (-0.03, -0.00) 0.0068	
	Black or African	2/ 81 (2.5)	5/ 78 (6.4)	0.38 (0.08, 1.93) 0.2450	0.37 (0.07, 1.96) 0.2425	-0.04 (-0.10, 0.02) 0.2249	
	Asian	19/ 629 (3.0)	47/ 643 (7.3)	0.42 (0.25, 0.70) 0.0009	0.40 (0.23, 0.68) 0.0009	-0.04 (-0.07, -0.02) 0.0005	
	Other	6/ 206 (2.9)	3/ 184 (1.6)	1.72 (0.43, 6.78) 0.4401	1.75 (0.43, 7.13) 0.4339	0.01 (-0.02, 0.04)*0.3921	
	Geographic region						0.2856
	Asia	19/ 606 (3.1)	46/ 619 (7.4)	0.42 (0.25, 0.71) 0.0013	0.40 (0.23, 0.70) 0.0012	-0.04 (-0.07, -0.02) 0.0008	
	Europe and Saudi Arabia	36/1491 (2.4)	54/1508 (3.6)	0.67 (0.44, 1.02) 0.0619	0.66 (0.43, 1.02) 0.0614	-0.01 (-0.02, 0.00) 0.0509	
	North America	18/ 427 (4.2)	34/ 422 (8.1)	0.52 (0.30, 0.91) 0.0213	0.50 (0.28, 0.90) 0.0213	-0.04 (-0.07, -0.00) 0.0249	
	Latin America	13/ 602 (2.2)	13/ 578 (2.2)	0.94 (0.44, 2.00) 0.8653	0.94 (0.43, 2.04) 0.8711	0.00 (-0.02, 0.02) 0.8707	
	NYHA class at enrolment						0.1213
	II	59/2310 (2.6)	118/2395 (4.9)	0.52 (0.38, 0.71) <.0001	0.51 (0.37, 0.70) <.0001	-0.02 (-0.03, -0.01) <.0001	
	III or IV	27/ 816 (3.3)	29/ 731 (4.0)	0.83 (0.50, 1.40) 0.4909	0.83 (0.49, 1.41) 0.4912	-0.01 (-0.03, 0.01) 0.4990	
	LVEF at enrolment						0.4510
	<= 49	20/1066 (1.9)	44/1047 (4.2)	0.45 (0.27, 0.76) 0.0026	0.44 (0.26, 0.75) 0.0026	-0.02 (-0.04, -0.01) 0.0052	
	50-59	35/1132 (3.1)	51/1121 (4.5)	0.68 (0.45, 1.04) 0.0730	0.67 (0.43, 1.04) 0.0727	-0.01 (-0.03, 0.00) 0.0691	
	>= 60	31/ 928 (3.3)	52/ 959 (5.4)	0.62 (0.40, 0.96) 0.0306	0.61 (0.38, 0.95) 0.0303	-0.02 (-0.04, -0.00) 0.0308	
	NT-proBNP at enrolment						0.3202
	<= median	39/1553 (2.5)	58/1574 (3.7)	0.68 (0.46, 1.02) 0.0601	0.67 (0.45, 1.02) 0.0600	-0.01 (-0.02, 0.00) 0.0577	
	> median	47/1573 (3.0)	89/1552 (5.7)	0.52 (0.37, 0.74) 0.0002	0.51 (0.35, 0.73) 0.0002	-0.03 (-0.04, -0.01) 0.0002	
	Type 2 Diabetes Medical History						0.3097
	Yes	42/1399 (3.0)	62/1402 (4.4)	0.68 (0.46, 1.00)*0.0484	0.67 (0.45, 1.00)*0.0482	-0.01 (-0.03, -0.00)*0.0467	
	No	44/1727 (2.5)	85/1725 (4.9)	0.52 (0.36, 0.74)*0.0003	0.50 (0.35, 0.73)*0.0003	-0.02 (-0.04, -0.01)*0.0002	
	Atrial fibrillation or flutter at enrolment ECG						0.5954
	Yes	37/1325 (2.8)	68/1317 (5.2)	0.54 (0.36, 0.80) 0.0021	0.53 (0.35, 0.79) 0.0020	-0.02 (-0.04, -0.01) 0.0015	
	No	49/1800 (2.7)	79/1809 (4.4)	0.62 (0.44, 0.88) 0.0081	0.61 (0.43, 0.88) 0.0080	-0.02 (-0.03, -0.00) 0.0063	
	BMI (kg/m2) at enrolment						0.3211
	< 30	47/1732 (2.7)	90/1733 (5.2)	0.52 (0.37, 0.74) 0.0002	0.51 (0.36, 0.73) 0.0002	-0.02 (-0.04, -0.01) 0.0002	
	>= 30	39/1392 (2.8)	57/1390 (4.1)	0.68 (0.46, 1.02) 0.0623	0.67 (0.45, 1.02) 0.0621	-0.01 (-0.03, 0.00) 0.0600	
	Baseline eGFR (mL/min/1.73m^2)						0.1434
	< 60	58/1514 (3.8)	87/1551 (5.6)	0.68 (0.49, 0.95) 0.0222	0.67 (0.48, 0.94) 0.0222	-0.02 (-0.03, -0.00) 0.0236	
	>= 60	28/1612 (1.7)	60/1575 (3.8)	0.46 (0.29, 0.71) 0.0005	0.45 (0.28, 0.70) 0.0005	-0.02 (-0.03, -0.01) 0.0003	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders	SBP at randomisation						0.5432
	<= median	45/1567 (2.9)	72/1588 (4.5)	0.63 (0.44, 0.91) 0.0140	0.62 (0.43, 0.91) 0.0139	-0.02 (-0.03, -0.00) 0.0129	
	> median	41/1559 (2.6)	75/1539 (4.9)	0.54 (0.37, 0.78) 0.0011	0.52 (0.36, 0.77) 0.0011	-0.02 (-0.04, -0.01) 0.0011	
	LVEF at enrolment 2						0.2238
	<= 49	20/1066 (1.9)	44/1047 (4.2)	0.45 (0.27, 0.76) 0.0026	0.44 (0.26, 0.75) 0.0026	-0.02 (-0.04, -0.01) 0.0052	
	>= 50	66/2060 (3.2)	103/2080 (5.0)	0.65 (0.48, 0.88) 0.0049	0.64 (0.46, 0.87) 0.0049	-0.02 (-0.03, -0.01) 0.0049	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3065
	Yes	7/ 328 (2.1)	18/ 326 (5.5)	0.38 (0.16, 0.90) 0.0283	0.37 (0.15, 0.90) 0.0277	-0.03 (-0.06, -0.00) 0.0252	
	No	79/2798 (2.8)	129/2801 (4.6)	0.61 (0.47, 0.81) 0.0005	0.60 (0.45, 0.80) 0.0005	-0.02 (-0.03, -0.01) 0.0004	
	MRAs at baseline						0.1089
	Yes	41/1339 (3.1)	54/1325 (4.1)	0.75 (0.51, 1.12) 0.1636	0.75 (0.49, 1.13) 0.1634	-0.01 (-0.02, 0.00) 0.1620	
	No	45/1787 (2.5)	93/1802 (5.2)	0.49 (0.34, 0.69) <.0001	0.47 (0.33, 0.68) <.0001	-0.03 (-0.04, -0.01) <.0001	
	ACEi+ARB at baseline						0.1177
	Yes	59/2259 (2.6)	115/2276 (5.1)	0.52 (0.38, 0.70) <.0001	0.50 (0.37, 0.69) <.0001	-0.02 (-0.04, -0.01) <.0001	
	No	27/ 867 (3.1)	32/ 851 (3.8)	0.82 (0.50, 1.36) 0.4534	0.82 (0.49, 1.38) 0.4579	-0.01 (-0.02, 0.01) 0.5737	
	ARNI at baseline						0.1363
	Yes	2/ 165 (1.2)	8/ 136 (5.9)	0.18 (0.04, 0.86) 0.0313	0.17 (0.04, 0.85) 0.0304	-0.05 (-0.09, -0.00) 0.0447	
	No	84/2961 (2.8)	139/2991 (4.6)	0.61 (0.47, 0.80) 0.0003	0.60 (0.45, 0.79) 0.0003	-0.02 (-0.03, -0.01) 0.0002	
	Beta Blocker at baseline						0.2126
	Yes	62/2587 (2.4)	116/2581 (4.5)	0.53 (0.39, 0.72) <.0001	0.52 (0.38, 0.71) <.0001	-0.02 (-0.03, -0.01) <.0001	
	No	24/ 539 (4.5)	31/ 546 (5.7)	0.78 (0.46, 1.30) 0.3366	0.77 (0.44, 1.32) 0.3399	-0.01 (-0.04, 0.02) 0.4307	
	Diuretics at baseline						0.3373
	Yes	79/2789 (2.8)	129/2783 (4.6)	0.61 (0.46, 0.80) 0.0004	0.60 (0.45, 0.80) 0.0004	-0.02 (-0.03, -0.01) 0.0004	
	No	7/ 337 (2.1)	18/ 344 (5.2)	0.40 (0.17, 0.94) 0.0353	0.38 (0.16, 0.93) 0.0344	-0.03 (-0.06, -0.00) 0.0273	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions	Overall	140/3126 (4.5)	151/3127 (4.8)	0.93 (0.74, 1.16) 0.5094	0.92 (0.73, 1.17) 0.5104	-0.00 (-0.01, 0.01) 0.5303	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Death	Overall	54/3126 (1.7)	52/3127 (1.7)	1.04 (0.71, 1.52) 0.8433	1.04 (0.71, 1.53) 0.8432	0.00 (-0.01, 0.01) 0.8402	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Sudden cardiac death	Overall	26/3126 (0.8)	37/3127 (1.2)	0.70 (0.43, 1.16) 0.1664	0.70 (0.42, 1.16) 0.1663	-0.00 (-0.01, 0.00) 0.1615	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Hepatobiliary disorders	Overall	34/3126 (1.1)	33/3127 (1.1)	1.03 (0.64, 1.66) 0.9001	1.03 (0.64, 1.67) 0.9005	0.00 (-0.00, 0.01) 0.9400	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations	Overall	585/3126 (18.7)	559/3127 (17.9)	1.05 (0.94, 1.16) 0.3931	1.06 (0.93, 1.20) 0.3931	0.01 (-0.01, 0.03) 0.3962	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19	Overall	183/3126 (5.9)	144/3127 (4.6)	1.27 (1.03, 1.57) 0.0268	1.29 (1.03, 1.61) 0.0269	0.01 (0.00, 0.02) 0.0325	
	Age						0.9246
	<= median	98/1544 (6.3)	79/1602 (4.9)	1.29 (0.96, 1.72) 0.0861	1.31 (0.96, 1.77) 0.0862	0.01 (-0.00, 0.03) 0.0941	
	> median	85/1582 (5.4)	65/1525 (4.3)	1.26 (0.92, 1.73) 0.1497	1.27 (0.92, 1.78) 0.1503	0.01 (-0.00, 0.03) 0.1649	
	Gender						0.0626
	Male	86/1765 (4.9)	81/1744 (4.6)	1.05 (0.78, 1.41) 0.7587	1.05 (0.77, 1.43) 0.7602	0.00 (-0.01, 0.02) 0.7889	
	Female	97/1361 (7.1)	63/1383 (4.6)	1.57 (1.15, 2.14) 0.0041	1.61 (1.16, 2.24) 0.0041	0.02 (0.01, 0.04) 0.0052	
	Race						0.3755
	White	157/2210 (7.1)	129/2222 (5.8)	1.22 (0.98, 1.53) 0.0785	1.24 (0.98, 1.58) 0.0790	0.01 (-0.00, 0.03) 0.0881	
	Black or African	11/ 81 (13.6)	4/ 78 (5.1)	2.64 (0.88, 7.95) 0.0841	2.90 (0.88, 9.53) 0.0800	0.08 (-0.01, 0.17) 0.0651	
	Asian	6/ 629 (1.0)	7/ 643 (1.1)	0.88 (0.30, 2.62) 0.8248	0.88 (0.30, 2.65) 0.8251	-0.00 (-0.01, 0.01) 0.8646	
	Other	9/ 206 (4.4)	4/ 184 (2.2)	2.13 (0.67, 6.78) 0.1983	2.23 (0.67, 7.44) 0.1907	0.02 (-0.01, 0.06)*0.2186	
	Geographic region						0.1483
	Asia	5/ 606 (0.8)	7/ 619 (1.1)	0.74 (0.24, 2.31) 0.6027	0.74 (0.23, 2.33) 0.6017	-0.00 (-0.01, 0.01) 0.5241	
	Europe and Saudi Arabia	105/1491 (7.0)	96/1508 (6.4)	1.11 (0.85, 1.44) 0.4631	1.11 (0.84, 1.48) 0.4666	0.01 (-0.01, 0.02) 0.5143	
	North America	28/ 427 (6.6)	13/ 422 (3.1)	2.12 (1.11, 4.04) 0.0221	2.20 (1.12, 4.32) 0.0213	0.03 (0.01, 0.06) 0.0176	
	Latin America	45/ 602 (7.5)	28/ 578 (4.8)	1.57 (0.99, 2.48) 0.0533	1.62 (1.00, 2.64) 0.0517	0.03 (0.00, 0.06) 0.0354	
	NYHA class at enrolment						0.9468
	II	137/2310 (5.9)	111/2395 (4.6)	1.28 (1.00, 1.63) 0.0484	1.30 (1.00, 1.68) 0.0484	0.01 (-0.00, 0.03) 0.0519	
	III or IV	46/ 816 (5.6)	33/ 731 (4.5)	1.26 (0.81, 1.94) 0.3058	1.27 (0.80, 2.01) 0.3080	0.01 (-0.01, 0.03) 0.3524	
	LVEF at enrolment						0.9955
	<= 49	66/1066 (6.2)	50/1047 (4.8)	1.29 (0.90, 1.85) 0.1618	1.31 (0.90, 1.91) 0.1611	0.01 (-0.01, 0.03) 0.1553	
	50-59	61/1132 (5.4)	48/1121 (4.3)	1.26 (0.87, 1.82) 0.2195	1.27 (0.86, 1.88) 0.2205	0.01 (-0.01, 0.03) 0.2480	
	>= 60	56/ 928 (6.0)	46/ 959 (4.8)	1.27 (0.87, 1.85) 0.2237	1.28 (0.86, 1.91) 0.2256	0.01 (-0.01, 0.03) 0.2630	
	NT-proBNP at enrolment						0.0168
	<= median	115/1553 (7.4)	73/1574 (4.6)	1.60 (1.20, 2.12) 0.0013	1.64 (1.22, 2.22) 0.0012	0.03 (0.01, 0.04) 0.0013	
	> median	68/1573 (4.3)	71/1552 (4.6)	0.94 (0.68, 1.31) 0.7293	0.94 (0.67, 1.32) 0.7288	-0.00 (-0.02, 0.01) 0.7225	
	Type 2 Diabetes Medical History						0.4246
	Yes	98/1399 (7.0)	71/1402 (5.1)	1.38 (1.03, 1.86)*0.0319	1.41 (1.03, 1.93)*0.0317	0.02 (0.00, 0.04)*0.0309	
	No	85/1727 (4.9)	73/1725 (4.2)	1.16 (0.86, 1.58)*0.3327	1.17 (0.85, 1.61)*0.3326	0.01 (-0.01, 0.02)*0.3320	
	Atrial fibrillation or flutter at enrolment ECG						0.2025
	Yes	57/1325 (4.3)	54/1317 (4.1)	1.05 (0.73, 1.51) 0.7946	1.05 (0.72, 1.54) 0.7936	0.00 (-0.01, 0.02) 0.7713	
	No	126/1800 (7.0)	90/1809 (5.0)	1.41 (1.08, 1.83) 0.0109	1.44 (1.09, 1.90) 0.0111	0.02 (0.00, 0.03) 0.0171	
	BMI (kg/m2) at enrolment						0.1312
	< 30	69/1732 (4.0)	66/1733 (3.8)	1.05 (0.75, 1.46) 0.7877	1.05 (0.74, 1.48) 0.7892	0.00 (-0.01, 0.01) 0.8274	
	>= 30	114/1392 (8.2)	78/1390 (5.6)	1.46 (1.10, 1.93) 0.0077	1.50 (1.11, 2.02) 0.0077	0.03 (0.01, 0.04) 0.0075	
	Baseline eGFR (mL/min/1.73m^2)						0.6134
	< 60	91/1514 (6.0)	77/1551 (5.0)	1.20 (0.90, 1.61) 0.2197	1.21 (0.89, 1.66) 0.2264	0.01 (-0.01, 0.02) 0.3811	
	>= 60	92/1612 (5.7)	67/1575 (4.3)	1.34 (0.99, 1.82) 0.0603	1.36 (0.99, 1.88) 0.0601	0.01 (-0.00, 0.03) 0.0575	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19	SBP at randomisation						0.8804
	<= median	83/1567 (5.3)	67/1588 (4.2)	1.26 (0.92, 1.72) 0.1560	1.27 (0.91, 1.77) 0.1559	0.01 (-0.00, 0.03) 0.1548	
	> median	100/1559 (6.4)	77/1539 (5.0)	1.30 (0.97, 1.73) 0.0776	1.31 (0.97, 1.79) 0.0805	0.01 (-0.00, 0.03) 0.1533	
	LVEF at enrolment 2						0.9197
	<= 49	66/1066 (6.2)	50/1047 (4.8)	1.29 (0.90, 1.85) 0.1618	1.31 (0.90, 1.91) 0.1611	0.01 (-0.01, 0.03) 0.1553	
	>= 50	117/2060 (5.7)	94/2080 (4.5)	1.26 (0.97, 1.64) 0.0859	1.28 (0.97, 1.69) 0.0868	0.01 (-0.00, 0.02) 0.1096	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5930
	Yes	15/ 328 (4.6)	14/ 326 (4.3)	1.06 (0.52, 2.15) 0.8818	1.05 (0.50, 2.22) 0.8904	-0.00 (-0.04, 0.03) 0.9143	
	No	168/2798 (6.0)	130/2801 (4.6)	1.30 (1.04, 1.62) 0.0228	1.31 (1.04, 1.66) 0.0228	0.01 (0.00, 0.03) 0.0239	
	MRAs at baseline						0.5959
	Yes	66/1339 (4.9)	55/1325 (4.2)	1.18 (0.83, 1.67) 0.3566	1.19 (0.82, 1.71) 0.3583	0.01 (-0.01, 0.02) 0.4022	
	No	117/1787 (6.5)	89/1802 (4.9)	1.33 (1.02, 1.74) 0.0370	1.35 (1.02, 1.80) 0.0371	0.02 (0.00, 0.03) 0.0403	
	ACEi+ARB at baseline						0.7528
	Yes	140/2259 (6.2)	113/2276 (5.0)	1.25 (0.98, 1.59) 0.0687	1.27 (0.98, 1.63) 0.0699	0.01 (-0.00, 0.02) 0.0972	
	No	43/ 867 (5.0)	31/ 851 (3.6)	1.36 (0.87, 2.14) 0.1797	1.38 (0.86, 2.21) 0.1795	0.01 (-0.01, 0.03) 0.1808	
	ARNI at baseline						0.0373
	Yes	9/ 165 (5.5)	1/ 136 (0.7)	8.79 (1.13,68.40) 0.0378	9.52 (1.18,76.95) 0.0345	0.05 (0.01, 0.08)*0.0137	
	No	174/2961 (5.9)	143/2991 (4.8)	1.23 (0.99, 1.53) 0.0573	1.25 (0.99, 1.56) 0.0582	0.01 (-0.00, 0.02) 0.0791	
	Beta Blocker at baseline						0.4936
	Yes	152/2587 (5.9)	115/2581 (4.5)	1.32 (1.04, 1.67) 0.0219	1.34 (1.04, 1.72) 0.0219	0.01 (0.00, 0.03) 0.0241	
	No	31/ 539 (5.8)	29/ 546 (5.3)	1.09 (0.67, 1.79) 0.7214	1.10 (0.65, 1.85) 0.7275	0.00 (-0.02, 0.03) 0.8322	
	Diuretics at baseline						0.1511
	Yes	172/2789 (6.2)	129/2783 (4.6)	1.33 (1.07, 1.66) 0.0116	1.35 (1.07, 1.71) 0.0117	0.01 (0.00, 0.03) 0.0149	
	No	11/ 337 (3.3)	15/ 344 (4.4)	0.75 (0.35, 1.60) 0.4514	0.74 (0.33, 1.63) 0.4546	-0.01 (-0.04, 0.02) 0.5452	

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SOC: Infections and infestations, PT: COVID-19 pneumonia	Overall	86/3126 (2.8)	89/3127 (2.8)	0.97 (0.72, 1.29) 0.8115	0.97 (0.71, 1.30) 0.8181	0.00 (-0.01, 0.01) 0.9473	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Cellulitis	Overall	35/3126 (1.1)	22/3127 (0.7)	1.59 (0.94, 2.70) 0.0863	1.60 (0.94, 2.73) 0.0864	0.00 (-0.00, 0.01) 0.1342	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Pneumonia	Overall	113/3126 (3.6)	106/3127 (3.4)	1.07 (0.82, 1.38) 0.6301	1.07 (0.82, 1.40) 0.6292	0.00 (-0.01, 0.01) 0.6072	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Urinary tract infection	Overall	40/3126 (1.3)	33/3127 (1.1)	1.21 (0.77, 1.92) 0.4096	1.21 (0.76, 1.93) 0.4107	0.00 (-0.00, 0.01) 0.5363	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Injury, poisoning and procedural complications	Overall	97/3126 (3.1)	103/3127 (3.3)	0.94 (0.72, 1.24) 0.6700	0.94 (0.71, 1.25) 0.6688	-0.00 (-0.01, 0.01) 0.6355	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders	Overall	74/3126 (2.4)	84/3127 (2.7)	0.88 (0.65, 1.20) 0.4178	0.88 (0.64, 1.20) 0.4189	-0.00 (-0.01, 0.00) 0.4984	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Musculoskeletal and connective tissue disorders	Overall	39/3126 (1.2)	51/3127 (1.6)	0.76 (0.51, 1.16) 0.2044	0.76 (0.50, 1.16) 0.2044	-0.00 (-0.01, 0.00) 0.2058	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Overall	123/3126 (3.9)	125/3127 (4.0)	0.98 (0.77, 1.26) 0.8990	0.98 (0.76, 1.27) 0.8990	-0.00 (-0.01, 0.01) 0.8989	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders	Overall	172/3126 (5.5)	169/3127 (5.4)	1.02 (0.83, 1.25) 0.8623	1.02 (0.82, 1.27) 0.8657	0.00 (-0.01, 0.01) 0.9219	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders, PT: Ischaemic stroke	Overall	70/3126 (2.2)	65/3127 (2.1)	1.08 (0.77, 1.50) 0.6625	1.08 (0.77, 1.52) 0.6626	0.00 (-0.01, 0.01) 0.6649	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders	Overall	104/3126 (3.3)	107/3127 (3.4)	0.97 (0.75, 1.27) 0.8348	0.97 (0.74, 1.28) 0.8335	-0.00 (-0.01, 0.01) 0.8013	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Acute kidney injury	Overall	54/3126 (1.7)	63/3127 (2.0)	0.86 (0.60, 1.23) 0.4017	0.85 (0.59, 1.23) 0.4010	-0.00 (-0.01, 0.00) 0.3772	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders	Overall	101/3126 (3.2)	111/3127 (3.5)	0.91 (0.70, 1.19) 0.4902	0.91 (0.69, 1.19) 0.4850	-0.00 (-0.01, 0.00) 0.3534	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Serious Adverses Event by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders	Overall	93/3126 (3.0)	76/3127 (2.4)	1.22 (0.91, 1.65) 0.1853	1.23 (0.91, 1.67) 0.1853	0.01 (-0.00, 0.01) 0.1900	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders	Overall	374/3126 (12.0)	404/3127 (12.9)	0.93 (0.81, 1.06) 0.2523	0.92 (0.79, 1.06) 0.2496	-0.01 (-0.03, 0.01) 0.2400	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Acute myocardial infarction	Overall	44/3126 (1.4)	41/3127 (1.3)	1.07 (0.70, 1.63) 0.7480	1.07 (0.70, 1.65) 0.7437	0.00 (-0.00, 0.01) 0.4512	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure	Overall	171/3126 (5.5)	196/3127 (6.3)	0.87 (0.72, 1.07) 0.1810	0.86 (0.70, 1.07) 0.1788	-0.01 (-0.02, 0.00) 0.1528	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure congestive	Overall	28/3126 (0.9)	39/3127 (1.2)	0.72 (0.44, 1.16) 0.1792	0.72 (0.44, 1.17) 0.1785	-0.00 (-0.01, 0.00) 0.1240	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders	Overall	50/3126 (1.6)	71/3127 (2.3)	0.70 (0.49, 1.01) 0.0552	0.70 (0.49, 1.01) 0.0552	-0.01 (-0.01, 0.00) 0.0608	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions	Overall	124/3126 (4.0)	132/3127 (4.2)	0.94 (0.74, 1.19) 0.6106	0.94 (0.73, 1.20) 0.6113	-0.00 (-0.01, 0.01) 0.6268	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Death	Overall	54/3126 (1.7)	51/3127 (1.6)	1.06 (0.72, 1.55) 0.7665	1.06 (0.72, 1.56) 0.7665	0.00 (-0.01, 0.01) 0.7657	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Sudden cardiac death	Overall	26/3126 (0.8)	37/3127 (1.2)	0.70 (0.43, 1.16) 0.1664	0.70 (0.42, 1.16) 0.1663	-0.00 (-0.01, 0.00) 0.1615	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations	Overall	273/3126 (8.7)	264/3127 (8.4)	1.03 (0.88, 1.22) 0.6840	1.04 (0.87, 1.24) 0.6836	0.00 (-0.01, 0.02) 0.6833	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19	Overall	40/3126 (1.3)	43/3127 (1.4)	0.93 (0.61, 1.43) 0.7415	0.93 (0.60, 1.43) 0.7404	-0.00 (-0.01, 0.00) 0.6628	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19 pneumonia	Overall	57/3126 (1.8)	66/3127 (2.1)	0.86 (0.61, 1.23) 0.4095	0.86 (0.60, 1.23) 0.4123	-0.00 (-0.01, 0.00) 0.5851	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Pneumonia	Overall	69/3126 (2.2)	49/3127 (1.6)	1.41 (0.98, 2.02) 0.0645	1.42 (0.98, 2.05) 0.0642	0.01 (-0.00, 0.01) 0.0618	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Injury, poisoning and procedural complications	Overall	46/3126 (1.5)	49/3127 (1.6)	0.94 (0.63, 1.40) 0.7581	0.94 (0.63, 1.41) 0.7579	-0.00 (-0.01, 0.01) 0.7443	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders	Overall	31/3126 (1.0)	40/3127 (1.3)	0.77 (0.49, 1.23) 0.2822	0.77 (0.48, 1.24) 0.2834	-0.00 (-0.01, 0.00) 0.4402	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Overall	68/3126 (2.2)	78/3127 (2.5)	0.87 (0.63, 1.20) 0.4056	0.87 (0.63, 1.21) 0.4030	-0.00 (-0.01, 0.00) 0.3027	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders	Overall	106/3126 (3.4)	101/3127 (3.2)	1.05 (0.80, 1.37) 0.7216	1.05 (0.80, 1.39) 0.7222	0.00 (-0.01, 0.01) 0.7386	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders, PT: Ischaemic stroke	Overall	52/3126 (1.7)	39/3127 (1.2)	1.33 (0.88, 2.01) 0.1709	1.34 (0.88, 2.03) 0.1707	0.00 (-0.00, 0.01) 0.1597	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders	Overall	56/3126 (1.8)	69/3127 (2.2)	0.81 (0.57, 1.15) 0.2429	0.81 (0.57, 1.15) 0.2408	-0.00 (-0.01, 0.00) 0.1598	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Acute kidney injury	Overall	35/3126 (1.1)	36/3127 (1.2)	0.97 (0.61, 1.55) 0.9084	0.97 (0.61, 1.55) 0.9051	-0.00 (-0.01, 0.00) 0.6117	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders	Overall	60/3126 (1.9)	69/3127 (2.2)	0.87 (0.62, 1.22) 0.4243	0.87 (0.61, 1.23) 0.4241	-0.00 (-0.01, 0.00) 0.4154	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Severe Adverse Events by SOC and PT (incidence in either arm >= 5% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders	Overall	43/3126 (1.4)	42/3127 (1.3)	1.02 (0.67, 1.56) 0.9119	1.02 (0.67, 1.57) 0.9133	-0.00 (-0.01, 0.01) 0.9821	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Blood and lymphatic system disorders	Overall	94/3126 (3.0)	126/3127 (4.0)	0.75 (0.57, 0.97) 0.0288	0.74 (0.56, 0.97) 0.0288	-0.01 (-0.02, -0.00) 0.0287	
	Age						0.7490
	<= median	33/1544 (2.1)	49/1602 (3.1)	0.70 (0.45, 1.08) 0.1059	0.69 (0.44, 1.08) 0.1062	-0.01 (-0.02, 0.00) 0.1269	
	> median	61/1582 (3.9)	77/1525 (5.0)	0.76 (0.55, 1.06) 0.1078	0.75 (0.53, 1.06) 0.1076	-0.01 (-0.03, 0.00) 0.1074	
	Gender						0.8194
	Male	58/1765 (3.3)	75/1744 (4.3)	0.76 (0.55, 1.07) 0.1148	0.76 (0.53, 1.07) 0.1149	-0.01 (-0.02, 0.00) 0.1214	
	Female	36/1361 (2.6)	51/1383 (3.7)	0.72 (0.47, 1.09) 0.1195	0.71 (0.46, 1.09) 0.1191	-0.01 (-0.02, 0.00) 0.1106	
	Race						0.4837
	White	60/2210 (2.7)	78/2222 (3.5)	0.77 (0.56, 1.08) 0.1288	0.77 (0.54, 1.08) 0.1284	-0.01 (-0.02, 0.00) 0.1196	
	Black or African	4/ 81 (4.9)	2/ 78 (2.6)	1.89 (0.35,10.02) 0.4567	1.95 (0.35,10.96) 0.4507	0.02 (-0.04, 0.08)*0.4287	
	Asian	25/ 629 (4.0)	42/ 643 (6.5)	0.61 (0.37, 0.98) 0.0425	0.59 (0.35, 0.98) 0.0418	-0.03 (-0.05, -0.00) 0.0346	
	Other	5/ 206 (2.4)	4/ 184 (2.2)	1.14 (0.31, 4.19) 0.8449	1.14 (0.30, 4.33) 0.8463	0.00 (-0.03, 0.03) 0.9036	
	Geographic region						0.1113
	Asia	25/ 606 (4.1)	41/ 619 (6.6)	0.62 (0.38, 1.01) 0.0543	0.60 (0.36, 1.01) 0.0533	-0.03 (-0.05, -0.00) 0.0431	
	Europe and Saudi Arabia	28/1491 (1.9)	49/1508 (3.2)	0.58 (0.37, 0.92) 0.0194	0.57 (0.36, 0.91) 0.0192	-0.01 (-0.03, -0.00) 0.0122	
	North America	31/ 427 (7.3)	24/ 422 (5.7)	1.28 (0.76, 2.14) 0.3532	1.30 (0.75, 2.25) 0.3529	0.02 (-0.02, 0.05) 0.3515	
	Latin America	10/ 602 (1.7)	12/ 578 (2.1)	0.82 (0.36, 1.88) 0.6335	0.81 (0.35, 1.90) 0.6314	-0.00 (-0.02, 0.01) 0.5260	
	NYHA class at enrolment						0.5751
	II	65/2310 (2.8)	95/2395 (4.0)	0.71 (0.52, 0.97) 0.0298	0.70 (0.51, 0.97) 0.0298	-0.01 (-0.02, -0.00) 0.0304	
	III or IV	29/ 816 (3.6)	31/ 731 (4.2)	0.84 (0.51, 1.37) 0.4792	0.83 (0.50, 1.39) 0.4795	-0.01 (-0.03, 0.01) 0.4875	
	LVEF at enrolment						0.0644
	<= 49	11/1066 (1.0)	29/1047 (2.8)	0.37 (0.19, 0.74) 0.0046	0.36 (0.18, 0.73) 0.0045	-0.02 (-0.03, -0.01) 0.0037	
	50-59	42/1132 (3.7)	51/1121 (4.5)	0.82 (0.55, 1.22) 0.3176	0.81 (0.53, 1.23) 0.3177	-0.01 (-0.02, 0.01) 0.3222	
	>= 60	41/ 928 (4.4)	46/ 959 (4.8)	0.92 (0.61, 1.39) 0.6876	0.92 (0.59, 1.41) 0.6880	-0.00 (-0.02, 0.02) 0.6973	
	NT-proBNP at enrolment						0.0470
	<= median	34/1553 (2.2)	63/1574 (4.0)	0.55 (0.36, 0.83) 0.0040	0.54 (0.35, 0.82) 0.0040	-0.02 (-0.03, -0.01) 0.0031	
	> median	60/1573 (3.8)	63/1552 (4.1)	0.94 (0.66, 1.33) 0.7223	0.94 (0.65, 1.34) 0.7230	-0.00 (-0.02, 0.01) 0.7410	
	Type 2 Diabetes Medical History						0.0837
	Yes	39/1399 (2.8)	67/1402 (4.8)	0.58 (0.40, 0.86)*0.0064	0.57 (0.38, 0.85)*0.0063	-0.02 (-0.03, -0.01)*0.0057	
	No	55/1727 (3.2)	59/1725 (3.4)	0.93 (0.65, 1.34)*0.6986	0.93 (0.64, 1.35)*0.6986	-0.00 (-0.01, 0.01)*0.6986	
	Atrial fibrillation or flutter at enrolment ECG						0.2027
	Yes	53/1325 (4.0)	60/1317 (4.6)	0.88 (0.61, 1.26) 0.4860	0.87 (0.60, 1.28) 0.4855	-0.01 (-0.02, 0.01) 0.4767	
	No	41/1800 (2.3)	66/1809 (3.6)	0.62 (0.43, 0.92) 0.0164	0.62 (0.41, 0.91) 0.0163	-0.01 (-0.02, -0.00) 0.0136	
	BMI (kg/m2) at enrolment						0.0213
	< 30	50/1732 (2.9)	86/1733 (5.0)	0.58 (0.41, 0.82) 0.0019	0.57 (0.40, 0.81) 0.0019	-0.02 (-0.03, -0.01) 0.0017	
	>= 30	44/1392 (3.2)	40/1390 (2.9)	1.10 (0.72, 1.67) 0.6632	1.10 (0.71, 1.70) 0.6628	0.00 (-0.01, 0.02) 0.6470	
	Baseline eGFR (mL/min/1.73m^2)						0.0737
	< 60	65/1514 (4.3)	74/1551 (4.8)	0.90 (0.65, 1.25) 0.5267	0.90 (0.64, 1.26) 0.5267	-0.00 (-0.02, 0.01) 0.5273	
	>= 60	29/1612 (1.8)	52/1575 (3.3)	0.54 (0.35, 0.85) 0.0080	0.54 (0.34, 0.85) 0.0079	-0.02 (-0.03, -0.00) 0.0062	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Blood and lymphatic system disorders	SBP at randomisation						0.4532
	<= median	53/1567 (3.4)	78/1588 (4.9)	0.69 (0.49, 0.97) 0.0326	0.68 (0.47, 0.97) 0.0325	-0.02 (-0.03, -0.00) 0.0314	
	> median	41/1559 (2.6)	48/1539 (3.1)	0.85 (0.56, 1.28) 0.4236	0.84 (0.55, 1.29) 0.4254	-0.00 (-0.02, 0.01) 0.4900	
	LVEF at enrolment 2						0.0214
	<= 49	11/1066 (1.0)	29/1047 (2.8)	0.37 (0.19, 0.74) 0.0046	0.36 (0.18, 0.73) 0.0045	-0.02 (-0.03, -0.01) 0.0037	
	>= 50	83/2060 (4.0)	97/2080 (4.7)	0.86 (0.65, 1.15) 0.3165	0.86 (0.64, 1.16) 0.3163	-0.01 (-0.02, 0.01) 0.3128	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.3480
	Yes	4/ 328 (1.2)	9/ 326 (2.8)	0.46 (0.14, 1.46) 0.1868	0.45 (0.14, 1.47) 0.1866	-0.01 (-0.03, 0.01) 0.2512	
	No	90/2798 (3.2)	117/2801 (4.2)	0.77 (0.59, 1.01) 0.0579	0.76 (0.58, 1.01) 0.0579	-0.01 (-0.02, 0.00) 0.0609	
	MRAs at baseline						0.9990
	Yes	40/1339 (3.0)	53/1325 (4.0)	0.75 (0.50, 1.12) 0.1551	0.74 (0.49, 1.12) 0.1551	-0.01 (-0.02, 0.00) 0.1555	
	No	54/1787 (3.0)	73/1802 (4.1)	0.75 (0.53, 1.05) 0.0973	0.74 (0.52, 1.06) 0.0971	-0.01 (-0.02, 0.00) 0.0942	
	ACEi+ARB at baseline						0.7852
	Yes	62/2259 (2.7)	86/2276 (3.8)	0.73 (0.53, 1.00) 0.0512	0.72 (0.52, 1.00) 0.0509	-0.01 (-0.02, -0.00) 0.0453	
	No	32/ 867 (3.7)	40/ 851 (4.7)	0.78 (0.50, 1.23) 0.2932	0.77 (0.48, 1.25) 0.2913	-0.01 (-0.03, 0.01) 0.2567	
	ARNI at baseline						0.2882
	Yes	2/ 165 (1.2)	5/ 136 (3.7)	0.36 (0.07, 1.84) 0.2199	0.35 (0.07, 1.86) 0.2191	-0.02 (-0.06, 0.02) 0.2864	
	No	92/2961 (3.1)	121/2991 (4.0)	0.77 (0.59, 1.00) 0.0523	0.76 (0.58, 1.00) 0.0523	-0.01 (-0.02, 0.00) 0.0533	
	Beta Blocker at baseline						0.1265
	Yes	70/2587 (2.7)	104/2581 (4.0)	0.67 (0.50, 0.90) 0.0087	0.66 (0.49, 0.90) 0.0086	-0.01 (-0.02, -0.00) 0.0076	
	No	24/ 539 (4.5)	22/ 546 (4.0)	1.10 (0.62, 1.94) 0.7417	1.10 (0.61, 1.99) 0.7528	-0.00 (-0.02, 0.02) 0.9735	
	Diuretics at baseline						0.2707
	Yes	90/2789 (3.2)	116/2783 (4.2)	0.77 (0.59, 1.01) 0.0635	0.77 (0.58, 1.01) 0.0633	-0.01 (-0.02, 0.00) 0.0625	
	No	4/ 337 (1.2)	10/ 344 (2.9)	0.41 (0.13, 1.28) 0.1241	0.40 (0.12, 1.29) 0.1249	-0.02 (-0.04, 0.01) 0.1997	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Blood and lymphatic system disorders, PT: Anaemia	Overall	44/3126 (1.4)	56/3127 (1.8)	0.79 (0.53, 1.16) 0.2282	0.78 (0.53, 1.17) 0.2280	-0.00 (-0.01, 0.00) 0.2202	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders	Overall	670/3126 (21.4)	749/3127 (24.0)	0.89 (0.81, 0.98) 0.0154	0.87 (0.77, 0.97) 0.0172	-0.02 (-0.04, -0.00) 0.0226	
	Age						0.3626
	<= median	302/1544 (19.6)	366/1602 (22.8)	0.85 (0.74, 0.97) 0.0173	0.82 (0.69, 0.97) 0.0234	-0.03 (-0.06, 0.00) 0.0538	
	> median	368/1582 (23.3)	383/1525 (25.1)	0.93 (0.82, 1.05) 0.2306	0.90 (0.77, 1.06) 0.2266	-0.02 (-0.05, 0.01) 0.2185	
	Gender						0.0473
	Male	367/1765 (20.8)	439/1744 (25.2)	0.82 (0.73, 0.93) 0.0017	0.78 (0.66, 0.91) 0.0019	-0.04 (-0.07, -0.02) 0.0023	
	Female	303/1361 (22.3)	310/1383 (22.4)	0.99 (0.86, 1.14) 0.9204	0.99 (0.83, 1.19) 0.9429	-0.00 (-0.03, 0.03) 0.9991	
	Race						0.2105
	White	491/2210 (22.2)	571/2222 (25.7)	0.86 (0.78, 0.96) 0.0062	0.83 (0.72, 0.95) 0.0067	-0.03 (-0.06, -0.01) 0.0077	
	Black or African	25/ 81 (30.9)	29/ 78 (37.2)	0.80 (0.52, 1.24) 0.3171	0.74 (0.38, 1.43) 0.3663	-0.06 (-0.21, 0.09) 0.4230	
	Asian	131/ 629 (20.8)	136/ 643 (21.2)	0.98 (0.79, 1.21) 0.8343	0.97 (0.74, 1.28) 0.8531	-0.00 (-0.05, 0.04) 0.9054	
	Other	23/ 206 (11.2)	13/ 184 (7.1)	1.63 (0.85, 3.11) 0.1413	1.72 (0.84, 3.52) 0.1367	0.04 (-0.01, 0.10) 0.1129	
	Geographic region						0.4813
	Asia	128/ 606 (21.1)	125/ 619 (20.2)	1.04 (0.84, 1.30) 0.7202	1.05 (0.80, 1.39) 0.7120	0.01 (-0.04, 0.05) 0.6910	
	Europe and Saudi Arabia	320/1491 (21.5)	375/1508 (24.9)	0.86 (0.75, 0.98) 0.0230	0.82 (0.69, 0.98) 0.0247	-0.03 (-0.06, -0.00) 0.0298	
	North America	131/ 427 (30.7)	144/ 422 (34.1)	0.89 (0.74, 1.09) 0.2596	0.85 (0.64, 1.14) 0.2793	-0.03 (-0.10, 0.03) 0.3012	
	Latin America	91/ 602 (15.1)	105/ 578 (18.2)	0.83 (0.65, 1.08) 0.1681	0.81 (0.59, 1.10) 0.1687	-0.03 (-0.07, 0.01) 0.1723	
	NYHA class at enrolment						0.5888
	II	476/2310 (20.6)	560/2395 (23.4)	0.88 (0.79, 0.98) 0.0181	0.85 (0.74, 0.98) 0.0207	-0.03 (-0.05, -0.00) 0.0288	
	III or IV	194/ 816 (23.8)	188/ 731 (25.7)	0.93 (0.78, 1.11) 0.4090	0.91 (0.72, 1.14) 0.4003	-0.02 (-0.06, 0.02) 0.3841	
	LVEF at enrolment						0.3290
	<= 49	226/1066 (21.2)	235/1047 (22.4)	0.94 (0.80, 1.10) 0.4379	0.92 (0.75, 1.14) 0.4568	-0.01 (-0.05, 0.02) 0.5098	
	50-59	227/1132 (20.1)	276/1121 (24.6)	0.81 (0.70, 0.95) 0.0089	0.77 (0.63, 0.94) 0.0094	-0.04 (-0.08, -0.01) 0.0110	
	>= 60	217/ 928 (23.4)	238/ 959 (24.8)	0.94 (0.80, 1.11) 0.4739	0.93 (0.75, 1.15) 0.4839	-0.01 (-0.05, 0.03) 0.5064	
	NT-proBNP at enrolment						0.0879
	<= median	310/1553 (20.0)	321/1574 (20.4)	0.98 (0.85, 1.12) 0.7319	0.97 (0.82, 1.16) 0.7629	-0.00 (-0.03, 0.03) 0.8582	
	> median	360/1573 (22.9)	427/1552 (27.5)	0.83 (0.74, 0.94) 0.0027	0.78 (0.66, 0.92) 0.0028	-0.05 (-0.08, -0.02) 0.0031	
	Type 2 Diabetes Medical History						0.1482
	Yes	323/1399 (23.1)	387/1402 (27.6)	0.84 (0.74, 0.95)*0.0062	0.79 (0.66, 0.93)*0.0061	-0.05 (-0.08, -0.01)*0.0059	
	No	347/1727 (20.1)	362/1725 (21.0)	0.96 (0.84, 1.09)*0.5162	0.95 (0.80, 1.12)*0.5162	-0.01 (-0.04, 0.02)*0.5161	
	Atrial fibrillation or flutter at enrolment ECG						0.9944
	Yes	283/1325 (21.4)	315/1317 (23.9)	0.89 (0.78, 1.03) 0.1191	0.87 (0.72, 1.04) 0.1205	-0.02 (-0.06, 0.01) 0.1251	
	No	387/1800 (21.5)	433/1809 (23.9)	0.89 (0.79, 1.01) 0.0698	0.87 (0.74, 1.02) 0.0773	-0.02 (-0.05, 0.00) 0.0995	
	BMI (kg/m2) at enrolment						0.1424
	< 30	350/1732 (20.2)	366/1733 (21.1)	0.96 (0.84, 1.09) 0.5027	0.95 (0.80, 1.12) 0.5076	-0.01 (-0.04, 0.02) 0.5232	
	>= 30	320/1392 (23.0)	382/1390 (27.5)	0.84 (0.73, 0.95) 0.0061	0.79 (0.66, 0.94) 0.0064	-0.04 (-0.08, -0.01) 0.0071	
	Baseline eGFR (mL/min/1.73m^2)						0.7043
	< 60	372/1514 (24.6)	417/1551 (26.9)	0.91 (0.81, 1.03) 0.1220	0.88 (0.75, 1.04) 0.1278	-0.02 (-0.05, 0.01) 0.1403	
	>= 60	298/1612 (18.5)	332/1575 (21.1)	0.88 (0.76, 1.01) 0.0675	0.85 (0.72, 1.01) 0.0718	-0.02 (-0.05, 0.00) 0.0873	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders	SBP at randomisation						0.0786
	<= median	348/1567 (22.2)	362/1588 (22.8)	0.97 (0.85, 1.11) 0.6656	0.96 (0.82, 1.14) 0.6735	-0.01 (-0.03, 0.02) 0.6928	
	> median	322/1559 (20.7)	387/1539 (25.1)	0.82 (0.72, 0.94) 0.0033	0.78 (0.66, 0.92) 0.0037	-0.04 (-0.07, -0.01) 0.0055	
	LVEF at enrolment 2						0.4602
	<= 49	226/1066 (21.2)	235/1047 (22.4)	0.94 (0.80, 1.10) 0.4379	0.92 (0.75, 1.14) 0.4568	-0.01 (-0.05, 0.02) 0.5098	
	>= 50	444/2060 (21.6)	514/2080 (24.7)	0.87 (0.78, 0.97) 0.0160	0.84 (0.73, 0.97) 0.0172	-0.03 (-0.06, -0.00) 0.0206	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4367
	Yes	87/ 328 (26.5)	105/ 326 (32.2)	0.82 (0.64, 1.04) 0.0941	0.75 (0.53, 1.05) 0.0932	-0.06 (-0.13, 0.01) 0.0926	
	No	583/2798 (20.8)	644/2801 (23.0)	0.91 (0.82, 1.00) 0.0483	0.88 (0.78, 1.00) 0.0529	-0.02 (-0.04, 0.00) 0.0670	
	MRAs at baseline						0.8449
	Yes	268/1339 (20.0)	292/1325 (22.0)	0.91 (0.78, 1.05) 0.1851	0.88 (0.73, 1.06) 0.1873	-0.02 (-0.05, 0.01) 0.1941	
	No	402/1787 (22.5)	457/1802 (25.4)	0.89 (0.79, 1.00) 0.0445	0.86 (0.74, 1.00) 0.0501	-0.03 (-0.05, 0.00) 0.0656	
	ACEi+ARB at baseline						0.3158
	Yes	480/2259 (21.2)	556/2276 (24.4)	0.87 (0.78, 0.97) 0.0098	0.83 (0.73, 0.96) 0.0110	-0.03 (-0.05, -0.01) 0.0143	
	No	190/ 867 (21.9)	193/ 851 (22.7)	0.96 (0.81, 1.15) 0.6824	0.95 (0.76, 1.20) 0.6784	-0.01 (-0.05, 0.03) 0.6705	
	ARNI at baseline						0.7043
	Yes	35/ 165 (21.2)	29/ 136 (21.3)	0.92 (0.60, 1.43) 0.7210	0.90 (0.51, 1.59) 0.7223	-0.02 (-0.11, 0.08) 0.7307	
	No	635/2961 (21.4)	720/2991 (24.1)	0.89 (0.81, 0.98) 0.0149	0.86 (0.76, 0.97) 0.0165	-0.02 (-0.05, -0.00) 0.0212	
	Beta Blocker at baseline						0.3824
	Yes	543/2587 (21.0)	617/2581 (23.9)	0.88 (0.79, 0.97) 0.0104	0.84 (0.74, 0.96) 0.0113	-0.03 (-0.05, -0.01) 0.0143	
	No	127/ 539 (23.6)	132/ 546 (24.2)	0.97 (0.79, 1.21) 0.8136	0.97 (0.73, 1.28) 0.8107	-0.01 (-0.06, 0.04) 0.8039	
	Diuretics at baseline						0.9973
	Yes	620/2789 (22.2)	692/2783 (24.9)	0.89 (0.81, 0.98) 0.0185	0.86 (0.76, 0.98) 0.0203	-0.03 (-0.05, -0.00) 0.0255	
	No	50/ 337 (14.8)	57/ 344 (16.6)	0.89 (0.63, 1.27) 0.5263	0.88 (0.58, 1.33) 0.5328	-0.02 (-0.07, 0.04) 0.5618	

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SOC: Cardiac disorders, PT: Angina pectoris	Overall	30/3126 (1.0)	35/3127 (1.1)	0.86 (0.53, 1.39) 0.5315	0.86 (0.52, 1.40) 0.5328	-0.00 (-0.01, 0.00) 0.6974	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Angina unstable	Overall	33/3126 (1.1)	47/3127 (1.5)	0.70 (0.45, 1.09) 0.1175	0.70 (0.45, 1.09) 0.1174	-0.00 (-0.01, 0.00) 0.1044	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Atrial fibrillation	Overall	127/3126 (4.1)	99/3127 (3.2)	1.28 (0.99, 1.66) 0.0577	1.30 (0.99, 1.69) 0.0579	0.01 (-0.00, 0.02) 0.0659	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure	Overall	323/3126 (10.3)	395/3127 (12.6)	0.82 (0.71, 0.94) 0.0043	0.80 (0.68, 0.93) 0.0043	-0.02 (-0.04, -0.01) 0.0051	
	Age						0.3699
	<= median	146/1544 (9.5)	173/1602 (10.8)	0.87 (0.71, 1.07) 0.1995	0.86 (0.68, 1.09) 0.2078	-0.01 (-0.03, 0.01) 0.3054	
	> median	177/1582 (11.2)	222/1525 (14.6)	0.77 (0.64, 0.92) 0.0052	0.74 (0.60, 0.91) 0.0050	-0.03 (-0.06, -0.01) 0.0046	
	Gender						0.6163
	Male	185/1765 (10.5)	230/1744 (13.2)	0.79 (0.66, 0.95) 0.0123	0.77 (0.62, 0.94) 0.0122	-0.03 (-0.05, -0.01) 0.0122	
	Female	138/1361 (10.1)	165/1383 (11.9)	0.85 (0.69, 1.05) 0.1403	0.84 (0.66, 1.06) 0.1430	-0.02 (-0.04, 0.01) 0.1706	
	Race						0.6544
	White	247/2210 (11.2)	307/2222 (13.8)	0.81 (0.69, 0.95) 0.0079	0.78 (0.66, 0.94) 0.0079	-0.03 (-0.05, -0.01) 0.0084	
	Black or African	8/ 81 (9.9)	14/ 78 (17.9)	0.54 (0.24, 1.22) 0.1390	0.49 (0.19, 1.25) 0.1377	-0.08 (-0.19, 0.03) 0.1450	
	Asian	61/ 629 (9.7)	67/ 643 (10.4)	0.93 (0.67, 1.29) 0.6438	0.92 (0.64, 1.32) 0.6497	-0.01 (-0.04, 0.03) 0.6984	
	Other	7/ 206 (3.4)	7/ 184 (3.8)	0.95 (0.34, 2.64) 0.9154	0.94 (0.32, 2.75) 0.9128	-0.00 (-0.04, 0.03) 0.8512	
	Geographic region						0.7787
	Asia	59/ 606 (9.7)	66/ 619 (10.7)	0.91 (0.65, 1.27) 0.5701	0.90 (0.62, 1.30) 0.5766	-0.01 (-0.04, 0.03) 0.6299	
	Europe and Saudi Arabia	187/1491 (12.5)	243/1508 (16.1)	0.77 (0.65, 0.92) 0.0044	0.74 (0.60, 0.91) 0.0046	-0.03 (-0.06, -0.01) 0.0061	
	North America	35/ 427 (8.2)	37/ 422 (8.8)	0.93 (0.60, 1.45) 0.7622	0.93 (0.57, 1.50) 0.7612	-0.01 (-0.04, 0.03) 0.7526	
	Latin America	42/ 602 (7.0)	49/ 578 (8.5)	0.84 (0.56, 1.24) 0.3730	0.82 (0.53, 1.26) 0.3685	-0.02 (-0.05, 0.02) 0.3242	
	NYHA class at enrolment						0.7909
	II	219/2310 (9.5)	282/2395 (11.8)	0.80 (0.68, 0.95) 0.0102	0.78 (0.65, 0.94) 0.0102	-0.02 (-0.04, -0.01) 0.0116	
	III or IV	104/ 816 (12.7)	112/ 731 (15.3)	0.84 (0.65, 1.07) 0.1561	0.81 (0.61, 1.08) 0.1570	-0.02 (-0.06, 0.01) 0.1666	
	LVEF at enrolment						0.4356
	<= 49	116/1066 (10.9)	123/1047 (11.7)	0.92 (0.72, 1.17) 0.4905	0.91 (0.70, 1.19) 0.5021	-0.01 (-0.03, 0.02) 0.5883	
	50-59	111/1132 (9.8)	149/1121 (13.3)	0.74 (0.59, 0.93) 0.0100	0.71 (0.55, 0.92) 0.0099	-0.03 (-0.06, -0.01) 0.0110	
	>= 60	96/ 928 (10.3)	123/ 959 (12.8)	0.81 (0.63, 1.04) 0.1041	0.79 (0.59, 1.05) 0.1006	-0.03 (-0.05, 0.00) 0.0827	
	NT-proBNP at enrolment						0.4025
	<= median	129/1553 (8.3)	149/1574 (9.5)	0.88 (0.70, 1.10) 0.2534	0.87 (0.68, 1.11) 0.2537	-0.01 (-0.03, 0.01) 0.2677	
	> median	194/1573 (12.3)	246/1552 (15.9)	0.78 (0.65, 0.92) 0.0046	0.75 (0.61, 0.91) 0.0046	-0.03 (-0.06, -0.01) 0.0055	
	Type 2 Diabetes Medical History						0.6147
	Yes	169/1399 (12.1)	214/1402 (15.3)	0.79 (0.66, 0.95)*0.0145	0.76 (0.61, 0.95)*0.0144	-0.03 (-0.06, -0.01)*0.0141	
	No	154/1727 (8.9)	181/1725 (10.5)	0.85 (0.69, 1.04)*0.1185	0.84 (0.67, 1.05)*0.1183	-0.02 (-0.04, 0.00)*0.1178	
	Atrial fibrillation or flutter at enrolment ECG						0.4338
	Yes	150/1325 (11.3)	194/1317 (14.7)	0.77 (0.63, 0.94) 0.0102	0.74 (0.59, 0.93) 0.0099	-0.03 (-0.06, -0.01) 0.0088	
	No	173/1800 (9.6)	201/1809 (11.1)	0.86 (0.71, 1.04) 0.1265	0.85 (0.68, 1.05) 0.1312	-0.01 (-0.03, 0.01) 0.1843	
	BMI (kg/m2) at enrolment						0.2138
	< 30	163/1732 (9.4)	182/1733 (10.5)	0.90 (0.73, 1.10) 0.2884	0.89 (0.71, 1.11) 0.2835	-0.01 (-0.03, 0.01) 0.2533	
	>= 30	160/1392 (11.5)	212/1390 (15.3)	0.75 (0.62, 0.91) 0.0036	0.72 (0.58, 0.90) 0.0036	-0.04 (-0.06, -0.01) 0.0044	
	Baseline eGFR (mL/min/1.73m^2)						0.7647
	< 60	188/1514 (12.4)	229/1551 (14.8)	0.83 (0.70, 1.00) 0.0481	0.81 (0.66, 1.00) 0.0501	-0.02 (-0.05, 0.00) 0.0655	
	>= 60	135/1612 (8.4)	166/1575 (10.5)	0.80 (0.64, 0.99) 0.0426	0.78 (0.61, 0.99) 0.0416	-0.02 (-0.04, -0.00) 0.0365	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure	SBP at randomisation						0.2585
	<= median	164/1567 (10.5)	186/1588 (11.7)	0.89 (0.73, 1.08) 0.2448	0.88 (0.70, 1.10) 0.2482	-0.01 (-0.03, 0.01) 0.2748	
	> median	159/1559 (10.2)	209/1539 (13.6)	0.76 (0.62, 0.92) 0.0050	0.73 (0.58, 0.91) 0.0047	-0.03 (-0.06, -0.01) 0.0040	
	LVEF at enrolment 2						0.2445
	<= 49	116/1066 (10.9)	123/1047 (11.7)	0.92 (0.72, 1.17) 0.4905	0.91 (0.70, 1.19) 0.5021	-0.01 (-0.03, 0.02) 0.5883	
	>= 50	207/2060 (10.0)	272/2080 (13.1)	0.77 (0.65, 0.91) 0.0028	0.74 (0.61, 0.90) 0.0026	-0.03 (-0.05, -0.01) 0.0022	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.5106
	Yes	52/ 328 (15.9)	69/ 326 (21.2)	0.74 (0.54, 1.03) 0.0729	0.69 (0.47, 1.03) 0.0727	-0.05 (-0.11, 0.01) 0.0737	
	No	271/2798 (9.7)	326/2801 (11.6)	0.83 (0.72, 0.97) 0.0186	0.82 (0.69, 0.97) 0.0188	-0.02 (-0.03, -0.00) 0.0222	
	MRAs at baseline						0.3460
	Yes	134/1339 (10.0)	174/1325 (13.1)	0.76 (0.61, 0.94) 0.0098	0.73 (0.57, 0.93) 0.0095	-0.03 (-0.06, -0.01) 0.0089	
	No	189/1787 (10.6)	221/1802 (12.3)	0.87 (0.72, 1.04) 0.1211	0.85 (0.69, 1.05) 0.1237	-0.02 (-0.04, 0.01) 0.1485	
	ACEi+ARB at baseline						0.6915
	Yes	238/2259 (10.5)	298/2276 (13.1)	0.80 (0.69, 0.94) 0.0077	0.78 (0.65, 0.94) 0.0079	-0.02 (-0.04, -0.01) 0.0101	
	No	85/ 867 (9.8)	97/ 851 (11.4)	0.86 (0.65, 1.13) 0.2743	0.84 (0.62, 1.14) 0.2692	-0.02 (-0.05, 0.01) 0.2403	
	ARNI at baseline						0.4143
	Yes	20/ 165 (12.1)	15/ 136 (11.0)	1.04 (0.55, 1.96) 0.9071	1.04 (0.51, 2.14) 0.9126	0.00 (-0.07, 0.07) 0.9506	
	No	303/2961 (10.2)	380/2991 (12.7)	0.81 (0.70, 0.93) 0.0030	0.78 (0.67, 0.92) 0.0030	-0.02 (-0.04, -0.01) 0.0037	
	Beta Blocker at baseline						0.9167
	Yes	265/2587 (10.2)	324/2581 (12.6)	0.81 (0.70, 0.95) 0.0085	0.79 (0.67, 0.94) 0.0084	-0.02 (-0.04, -0.01) 0.0091	
	No	58/ 539 (10.8)	71/ 546 (13.0)	0.83 (0.60, 1.15) 0.2562	0.81 (0.56, 1.17) 0.2567	-0.02 (-0.06, 0.02) 0.2615	
	Diuretics at baseline						0.1453
	Yes	303/2789 (10.9)	359/2783 (12.9)	0.84 (0.73, 0.97) 0.0187	0.82 (0.70, 0.97) 0.0187	-0.02 (-0.04, -0.00) 0.0209	
	No	20/ 337 (5.9)	36/ 344 (10.5)	0.57 (0.33, 0.96) 0.0341	0.54 (0.31, 0.95) 0.0335	-0.05 (-0.09, -0.00) 0.0321	

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Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure acute	Overall	37/3126 (1.2)	42/3127 (1.3)	0.88 (0.57, 1.37) 0.5708	0.88 (0.56, 1.37) 0.5715	-0.00 (-0.01, 0.00) 0.6396	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Cardiac disorders, PT: Cardiac failure congestive	Overall	74/3126 (2.4)	94/3127 (3.0)	0.79 (0.58, 1.06) 0.1188	0.78 (0.57, 1.07) 0.1187	-0.01 (-0.01, 0.00) 0.1199	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Ear and labyrinth disorders	Overall	39/3126 (1.2)	44/3127 (1.4)	0.89 (0.58, 1.36) 0.5835	0.89 (0.57, 1.37) 0.5826	-0.00 (-0.01, 0.00) 0.5174	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Endocrine disorders	Overall	23/3126 (0.7)	33/3127 (1.1)	0.70 (0.41, 1.18) 0.1823	0.69 (0.41, 1.19) 0.1822	-0.00 (-0.01, 0.00) 0.1721	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Eye disorders	Overall	71/3126 (2.3)	73/3127 (2.3)	0.97 (0.70, 1.34) 0.8675	0.97 (0.70, 1.35) 0.8669	-0.00 (-0.01, 0.01) 0.8421	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders	Overall	273/3126 (8.7)	328/3127 (10.5)	0.83 (0.71, 0.97) 0.0186	0.82 (0.69, 0.97) 0.0187	-0.02 (-0.03, -0.00) 0.0200	
	Age						0.0917
	<= median	121/1544 (7.8)	130/1602 (8.1)	0.97 (0.76, 1.22) 0.7732	0.96 (0.74, 1.25) 0.7734	-0.00 (-0.02, 0.02) 0.7754	
	> median	152/1582 (9.6)	198/1525 (13.0)	0.74 (0.61, 0.90) 0.0030	0.71 (0.57, 0.89) 0.0030	-0.03 (-0.06, -0.01) 0.0036	
	Gender						0.7488
	Male	155/1765 (8.8)	180/1744 (10.3)	0.85 (0.69, 1.04) 0.1221	0.84 (0.67, 1.05) 0.1230	-0.01 (-0.03, 0.00) 0.1310	
	Female	118/1361 (8.7)	148/1383 (10.7)	0.81 (0.64, 1.02) 0.0717	0.79 (0.61, 1.02) 0.0716	-0.02 (-0.04, 0.00) 0.0718	
	Race						0.5792
	White	170/2210 (7.7)	199/2222 (9.0)	0.86 (0.71, 1.04) 0.1283	0.85 (0.68, 1.05) 0.1282	-0.01 (-0.03, 0.00) 0.1286	
	Black or African	3/ 81 (3.7)	6/ 78 (7.7)	0.47 (0.12, 1.80) 0.2696	0.45 (0.11, 1.88) 0.2754	-0.04 (-0.12, 0.04) 0.3528	
	Asian	81/ 629 (12.9)	108/ 643 (16.8)	0.77 (0.59, 1.00) 0.0520	0.73 (0.54, 1.00) 0.0522	-0.04 (-0.08, 0.00) 0.0553	
	Other	19/ 206 (9.2)	15/ 184 (8.2)	1.13 (0.59, 2.16) 0.7132	1.14 (0.56, 2.32) 0.7126	0.01 (-0.05, 0.07) 0.7072	
	Geographic region						0.7761
	Asia	80/ 606 (13.2)	107/ 619 (17.3)	0.76 (0.59, 1.00) 0.0489	0.73 (0.53, 1.00) 0.0488	-0.04 (-0.08, -0.00) 0.0497	
	Europe and Saudi Arabia	93/1491 (6.2)	115/1508 (7.6)	0.82 (0.63, 1.07) 0.1359	0.81 (0.61, 1.07) 0.1362	-0.01 (-0.03, 0.00) 0.1406	
	North America	64/ 427 (15.0)	67/ 422 (15.9)	0.94 (0.69, 1.29) 0.7151	0.93 (0.64, 1.35) 0.7171	-0.01 (-0.06, 0.04) 0.7262	
	Latin America	36/ 602 (6.0)	39/ 578 (6.7)	0.89 (0.57, 1.37) 0.5876	0.88 (0.55, 1.40) 0.5875	-0.01 (-0.04, 0.02) 0.5870	
	NYHA class at enrolment						0.3817
	II	205/2310 (8.9)	264/2395 (11.0)	0.81 (0.68, 0.96) 0.0145	0.79 (0.65, 0.95) 0.0144	-0.02 (-0.04, -0.00) 0.0146	
	III or IV	68/ 816 (8.3)	64/ 731 (8.8)	0.96 (0.69, 1.33) 0.7882	0.95 (0.67, 1.36) 0.7820	-0.01 (-0.03, 0.02) 0.7220	
	LVEF at enrolment						0.0629
	<= 49	76/1066 (7.1)	108/1047 (10.3)	0.70 (0.53, 0.92) 0.0110	0.67 (0.49, 0.91) 0.0112	-0.03 (-0.05, -0.01) 0.0153	
	50-59	90/1132 (8.0)	116/1121 (10.3)	0.77 (0.59, 1.00) 0.0494	0.75 (0.56, 1.00) 0.0492	-0.02 (-0.05, 0.00) 0.0501	
	>= 60	107/ 928 (11.5)	104/ 959 (10.8)	1.06 (0.82, 1.37) 0.6493	1.07 (0.80, 1.42) 0.6456	0.01 (-0.02, 0.04) 0.6199	
	NT-proBNP at enrolment						0.6284
	<= median	119/1553 (7.7)	139/1574 (8.8)	0.87 (0.69, 1.10) 0.2344	0.86 (0.66, 1.11) 0.2353	-0.01 (-0.03, 0.01) 0.2479	
	> median	154/1573 (9.8)	189/1552 (12.2)	0.80 (0.66, 0.98) 0.0333	0.78 (0.62, 0.98) 0.0330	-0.02 (-0.05, -0.00) 0.0320	
	Type 2 Diabetes Medical History						0.3431
	Yes	128/1399 (9.1)	142/1402 (10.1)	0.90 (0.72, 1.13)*0.3803	0.89 (0.70, 1.15)*0.3802	-0.01 (-0.03, 0.01)*0.3800	
	No	145/1727 (8.4)	186/1725 (10.8)	0.78 (0.63, 0.96)*0.0176	0.76 (0.60, 0.95)*0.0175	-0.02 (-0.04, -0.00)*0.0172	
	Atrial fibrillation or flutter at enrolment ECG						0.9734
	Yes	122/1325 (9.2)	146/1317 (11.1)	0.83 (0.66, 1.04) 0.1065	0.81 (0.63, 1.05) 0.1077	-0.02 (-0.04, 0.00) 0.1193	
	No	151/1800 (8.4)	182/1809 (10.1)	0.83 (0.68, 1.02) 0.0833	0.82 (0.65, 1.03) 0.0831	-0.02 (-0.04, 0.00) 0.0825	
	BMI (kg/m2) at enrolment						0.5197
	< 30	173/1732 (10.0)	200/1733 (11.5)	0.87 (0.71, 1.05) 0.1403	0.85 (0.69, 1.05) 0.1407	-0.02 (-0.04, 0.01) 0.1445	
	>= 30	100/1392 (7.2)	128/1390 (9.2)	0.78 (0.61, 1.00) 0.0523	0.76 (0.58, 1.00) 0.0522	-0.02 (-0.04, 0.00) 0.0522	
	Baseline eGFR (mL/min/1.73m^2)						0.0028
	< 60	128/1514 (8.5)	196/1551 (12.6)	0.67 (0.54, 0.83) 0.0002	0.64 (0.51, 0.81) 0.0002	-0.04 (-0.06, -0.02) 0.0002	
	>= 60	145/1612 (9.0)	132/1575 (8.4)	1.07 (0.86, 1.34) 0.5497	1.08 (0.84, 1.38) 0.5494	0.01 (-0.01, 0.03) 0.5466	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders	SBP at randomisation						0.2527
	<= median	155/1567 (9.9)	174/1588 (11.0)	0.90 (0.74, 1.11) 0.3328	0.89 (0.71, 1.12) 0.3354	-0.01 (-0.03, 0.01) 0.3555	
	> median	118/1559 (7.6)	154/1539 (10.0)	0.76 (0.60, 0.95) 0.0165	0.74 (0.57, 0.95) 0.0164	-0.02 (-0.04, -0.00) 0.0159	
	LVEF at enrolment 2						0.1173
	<= 49	76/1066 (7.1)	108/1047 (10.3)	0.70 (0.53, 0.92) 0.0110	0.67 (0.49, 0.91) 0.0112	-0.03 (-0.05, -0.01) 0.0153	
	>= 50	197/2060 (9.6)	220/2080 (10.6)	0.90 (0.75, 1.09) 0.2808	0.89 (0.73, 1.10) 0.2803	-0.01 (-0.03, 0.01) 0.2766	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.0983
	Yes	15/ 328 (4.6)	29/ 326 (8.9)	0.52 (0.28, 0.95) 0.0322	0.49 (0.26, 0.94) 0.0315	-0.04 (-0.08, -0.00) 0.0297	
	No	258/2798 (9.2)	299/2801 (10.7)	0.86 (0.74, 1.01) 0.0684	0.85 (0.71, 1.01) 0.0687	-0.01 (-0.03, 0.00) 0.0723	
	MRAs at baseline						0.9129
	Yes	117/1339 (8.7)	138/1325 (10.4)	0.84 (0.67, 1.06) 0.1484	0.83 (0.64, 1.07) 0.1477	-0.02 (-0.04, 0.01) 0.1433	
	No	156/1787 (8.7)	190/1802 (10.5)	0.83 (0.68, 1.01) 0.0641	0.81 (0.65, 1.01) 0.0646	-0.02 (-0.04, 0.00) 0.0691	
	ACEi+ARB at baseline						0.0077
	Yes	184/2259 (8.1)	253/2276 (11.1)	0.73 (0.61, 0.88) 0.0007	0.71 (0.58, 0.87) 0.0007	-0.03 (-0.05, -0.01) 0.0009	
	No	89/ 867 (10.3)	75/ 851 (8.8)	1.17 (0.87, 1.56) 0.3057	1.18 (0.86, 1.64) 0.3058	0.01 (-0.01, 0.04) 0.3064	
	ARNI at baseline						0.9937
	Yes	15/ 165 (9.1)	15/ 136 (11.0)	0.84 (0.42, 1.67) 0.6156	0.82 (0.38, 1.76) 0.6136	-0.02 (-0.09, 0.05) 0.6001	
	No	258/2961 (8.7)	313/2991 (10.5)	0.83 (0.71, 0.97) 0.0215	0.82 (0.69, 0.97) 0.0216	-0.02 (-0.03, -0.00) 0.0232	
	Beta Blocker at baseline						0.9956
	Yes	226/2587 (8.7)	271/2581 (10.5)	0.83 (0.70, 0.98) 0.0319	0.82 (0.68, 0.98) 0.0319	-0.02 (-0.03, -0.00) 0.0319	
	No	47/ 539 (8.7)	57/ 546 (10.4)	0.83 (0.57, 1.19) 0.3109	0.81 (0.54, 1.22) 0.3207	-0.01 (-0.05, 0.02) 0.4209	
	Diuretics at baseline						0.0760
	Yes	253/2789 (9.1)	290/2783 (10.4)	0.87 (0.74, 1.02) 0.0894	0.86 (0.72, 1.02) 0.0898	-0.01 (-0.03, 0.00) 0.0945	
	No	20/ 337 (5.9)	38/ 344 (11.0)	0.54 (0.32, 0.90) 0.0194	0.51 (0.29, 0.89) 0.0185	-0.05 (-0.09, -0.01) 0.0137	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders, PT: Constipation	Overall	46/3126 (1.5)	51/3127 (1.6)	0.90 (0.61, 1.34) 0.6102	0.90 (0.60, 1.35) 0.6102	-0.00 (-0.01, 0.00) 0.6108	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Gastrointestinal disorders, PT: Diarrhoea	Overall	52/3126 (1.7)	66/3127 (2.1)	0.79 (0.55, 1.13) 0.1946	0.78 (0.54, 1.13) 0.1946	-0.00 (-0.01, 0.00) 0.2011	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions	Overall	140/3126 (4.5)	168/3127 (5.4)	0.83 (0.67, 1.04) 0.1022	0.83 (0.66, 1.04) 0.1027	-0.01 (-0.02, 0.00) 0.1130	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Oedema peripheral	Overall	17/3126 (0.5)	32/3127 (1.0)	0.53 (0.30, 0.95) 0.0344	0.53 (0.29, 0.95) 0.0344	-0.00 (-0.01, -0.00) 0.0407	
	Age						0.7496
	<= median	9/1544 (0.6)	16/1602 (1.0)	0.58 (0.26, 1.31) 0.1931	0.58 (0.26, 1.32) 0.1936	-0.00 (-0.01, 0.00) 0.3028	
	> median	8/1582 (0.5)	16/1525 (1.0)	0.48 (0.21, 1.12) 0.0908	0.48 (0.20, 1.12) 0.0906	-0.01 (-0.01, 0.00) 0.0818	
	Gender						0.6018
	Male	10/1765 (0.6)	21/1744 (1.2)	0.47 (0.22, 0.99) 0.0476	0.47 (0.22, 0.99) 0.0476	-0.01 (-0.01, 0.00) 0.0686	
	Female	7/1361 (0.5)	11/1383 (0.8)	0.65 (0.25, 1.66) 0.3641	0.64 (0.25, 1.67) 0.3638	-0.00 (-0.01, 0.00) 0.2985	
	Race						0.1786
	White	5/2210 (0.2)	19/2222 (0.9)	0.26 (0.10, 0.71) 0.0080	0.26 (0.10, 0.71) 0.0080	-0.01 (-0.01, -0.00) 0.0026	
	Black or African	1/ 81 (1.2)	1/ 78 (1.3)	0.90 (0.06,13.89) 0.9373	0.96 (0.06,15.66)*0.9786	-0.00 (-0.04, 0.03)*0.9786	
	Asian	9/ 629 (1.4)	8/ 643 (1.2)	1.14 (0.44, 2.95) 0.7793	1.15 (0.44, 2.99) 0.7795	0.00 (-0.01, 0.01) 0.7991	
	Other	2/ 206 (1.0)	4/ 184 (2.2)	0.43 (0.08, 2.33) 0.3293	0.42 (0.08, 2.35) 0.3265	-0.01 (-0.04, 0.01)*0.3449	
	Geographic region						0.0678
	Asia	9/ 606 (1.5)	8/ 619 (1.3)	1.14 (0.44, 2.94) 0.7806	1.15 (0.44, 2.99) 0.7809	0.00 (-0.01, 0.01) 0.8047	
	Europe and Saudi Arabia	1/1491 (0.1)	9/1508 (0.6)	0.11 (0.01, 0.89) 0.0380	0.11 (0.01, 0.88) 0.0378	-0.01 (-0.01, -0.00)*0.0114	
	North America	5/ 427 (1.2)	7/ 422 (1.7)	0.70 (0.22, 2.20) 0.5438	0.70 (0.22, 2.22) 0.5456	-0.00 (-0.02, 0.01) 0.6764	
	Latin America	2/ 602 (0.3)	8/ 578 (1.4)	0.24 (0.05, 1.14) 0.0723	0.24 (0.05, 1.14) 0.0719	-0.01 (-0.02, 0.00)*0.0512	
	NYHA class at enrolment						0.0975
	II	11/2310 (0.5)	28/2395 (1.2)	0.41 (0.20, 0.82) 0.0112	0.40 (0.20, 0.81) 0.0112	-0.01 (-0.01, -0.00) 0.0064	
	III or IV	6/ 816 (0.7)	4/ 731 (0.5)	1.36 (0.39, 4.80) 0.6315	1.36 (0.38, 4.86) 0.6312	0.00 (-0.01, 0.01) 0.5932	
	LVEF at enrolment						0.8099
	<= 49	3/1066 (0.3)	8/1047 (0.8)	0.37 (0.10, 1.39) 0.1409	0.37 (0.10, 1.39) 0.1407	-0.00 (-0.01, 0.00) 0.1301	
	50-59	7/1132 (0.6)	12/1121 (1.1)	0.58 (0.23, 1.46) 0.2463	0.58 (0.23, 1.47) 0.2470	-0.00 (-0.01, 0.00) 0.3195	
	>= 60	7/ 928 (0.8)	12/ 959 (1.3)	0.61 (0.24, 1.53) 0.2909	0.60 (0.24, 1.54) 0.2914	-0.00 (-0.01, 0.01) 0.3664	
	NT-proBNP at enrolment						0.9346
	<= median	7/1553 (0.5)	13/1574 (0.8)	0.55 (0.22, 1.36) 0.1943	0.54 (0.22, 1.37) 0.1948	-0.00 (-0.01, 0.00) 0.3299	
	> median	10/1573 (0.6)	19/1552 (1.2)	0.52 (0.24, 1.11) 0.0920	0.52 (0.24, 1.11) 0.0919	-0.01 (-0.01, 0.00) 0.0865	
	Type 2 Diabetes Medical History						0.1670
	Yes	6/1399 (0.4)	18/1402 (1.3)	0.33 (0.13, 0.84)*0.0196	0.33 (0.13, 0.84)*0.0195	-0.01 (-0.02, -0.00)*0.0139	
	No	11/1727 (0.6)	14/1725 (0.8)	0.78 (0.36, 1.72)*0.5461	0.78 (0.35, 1.73)*0.5461	-0.00 (-0.01, 0.00)*0.5451	
	Atrial fibrillation or flutter at enrolment ECG						0.5712
	Yes	11/1325 (0.8)	18/1317 (1.4)	0.61 (0.29, 1.28) 0.1901	0.60 (0.28, 1.28) 0.1899	-0.01 (-0.01, 0.00) 0.1766	
	No	6/1800 (0.3)	14/1809 (0.8)	0.43 (0.16, 1.11) 0.0814	0.43 (0.16, 1.11) 0.0816	-0.00 (-0.01, 0.00) 0.1903	
	BMI (kg/m2) at enrolment						0.8407
	< 30	9/1732 (0.5)	16/1733 (0.9)	0.56 (0.25, 1.27) 0.1663	0.56 (0.25, 1.27) 0.1662	-0.00 (-0.01, 0.00) 0.1571	
	>= 30	8/1392 (0.6)	16/1390 (1.2)	0.50 (0.21, 1.16) 0.1068	0.50 (0.21, 1.16) 0.1069	-0.01 (-0.01, 0.00) 0.1404	
	Baseline eGFR (mL/min/1.73m^2)						0.9765
	< 60	10/1514 (0.7)	19/1551 (1.2)	0.54 (0.25, 1.15) 0.1097	0.53 (0.25, 1.15) 0.1095	-0.01 (-0.01, 0.00) 0.1048	
	>= 60	7/1612 (0.4)	13/1575 (0.8)	0.53 (0.21, 1.32) 0.1708	0.53 (0.21, 1.32) 0.1709	-0.00 (-0.01, 0.00) 0.1262	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: General disorders and administration site conditions, PT: Oedema peripheral	SBP at randomisation						0.8867
	<= median	7/1567 (0.4)	14/1588 (0.9)	0.50 (0.20, 1.24) 0.1358	0.50 (0.20, 1.24) 0.1357	-0.00 (-0.01, 0.00) 0.1418	
	> median	10/1559 (0.6)	18/1539 (1.2)	0.55 (0.25, 1.18) 0.1264	0.55 (0.25, 1.19) 0.1262	-0.01 (-0.01, 0.00) 0.0972	
	LVEF at enrolment 2						0.5204
	<= 49	3/1066 (0.3)	8/1047 (0.8)	0.37 (0.10, 1.39) 0.1409	0.37 (0.10, 1.39) 0.1407	-0.00 (-0.01, 0.00) 0.1301	
	>= 50	14/2060 (0.7)	24/2080 (1.2)	0.59 (0.31, 1.14) 0.1154	0.59 (0.30, 1.14) 0.1159	-0.00 (-0.01, 0.00) 0.1862	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.6415
	Yes	3/ 328 (0.9)	4/ 326 (1.2)	0.76 (0.17, 3.39) 0.7241	0.76 (0.17, 3.44) 0.7229	-0.00 (-0.02, 0.01) 0.6227	
	No	14/2798 (0.5)	28/2801 (1.0)	0.50 (0.26, 0.95) 0.0341	0.50 (0.26, 0.95) 0.0342	-0.00 (-0.01, -0.00) 0.0473	
	MRAs at baseline						0.3340
	Yes	6/1339 (0.4)	7/1325 (0.5)	0.86 (0.29, 2.54) 0.7787	0.86 (0.29, 2.55) 0.7792	-0.00 (-0.01, 0.00) 0.8841	
	No	11/1787 (0.6)	25/1802 (1.4)	0.45 (0.22, 0.90) 0.0250	0.44 (0.22, 0.90) 0.0250	-0.01 (-0.01, -0.00) 0.0396	
	ACEi+ARB at baseline						0.8405
	Yes	11/2259 (0.5)	20/2276 (0.9)	0.55 (0.27, 1.15) 0.1149	0.55 (0.26, 1.16) 0.1149	-0.00 (-0.01, 0.00) 0.1349	
	No	6/ 867 (0.7)	12/ 851 (1.4)	0.49 (0.18, 1.30) 0.1509	0.49 (0.18, 1.30) 0.1509	-0.01 (-0.02, 0.00) 0.1639	
	ARNI at baseline						0.8091
	Yes	1/ 165 (0.6)	2/ 136 (1.5)	0.44 (0.04, 4.91) 0.5042	0.44 (0.04, 4.95) 0.5025	-0.01 (-0.03, 0.01)*0.4698	
	No	16/2961 (0.5)	30/2991 (1.0)	0.54 (0.29, 0.99) 0.0454	0.54 (0.29, 0.99) 0.0454	-0.00 (-0.01, 0.00) 0.0571	
	Beta Blocker at baseline						0.5830
	Yes	11/2587 (0.4)	23/2581 (0.9)	0.48 (0.23, 0.97) 0.0424	0.47 (0.23, 0.97) 0.0424	-0.00 (-0.01, 0.00) 0.0571	
	No	6/ 539 (1.1)	9/ 546 (1.6)	0.67 (0.24, 1.88) 0.4527	0.67 (0.24, 1.90) 0.4525	-0.01 (-0.02, 0.01) 0.4292	
	Diuretics at baseline						0.4607
	Yes	16/2789 (0.6)	28/2783 (1.0)	0.57 (0.31, 1.05) 0.0715	0.57 (0.31, 1.05) 0.0718	-0.00 (-0.01, 0.00) 0.1262	
	No	1/ 337 (0.3)	4/ 344 (1.2)	0.25 (0.03, 2.27) 0.2200	0.25 (0.03, 2.28) 0.2207	-0.01 (-0.02, 0.00)*0.1824	

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SOC: Hepatobiliary disorders	Overall	51/3126 (1.6)	46/3127 (1.5)	1.11 (0.75, 1.65) 0.6071	1.11 (0.74, 1.66) 0.6071	0.00 (-0.00, 0.01) 0.6143	

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p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations	Overall	713/3126 (22.8)	705/3127 (22.5)	1.01 (0.92, 1.11) 0.8041	1.02 (0.90, 1.14) 0.8038	0.00 (-0.02, 0.02) 0.8032	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Bronchitis	Overall	35/3126 (1.1)	35/3127 (1.1)	1.00 (0.63, 1.59) 0.9985	1.00 (0.62, 1.60) 0.9985	0.00 (-0.01, 0.01) 0.9989	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19	Overall	143/3126 (4.6)	103/3127 (3.3)	1.39 (1.08, 1.78) 0.0095	1.41 (1.09, 1.82) 0.0095	0.01 (0.00, 0.02) 0.0106	
	Age						0.5441
	<= median	82/1544 (5.3)	57/1602 (3.6)	1.49 (1.07, 2.08) 0.0176	1.52 (1.08, 2.15) 0.0176	0.02 (0.00, 0.03) 0.0184	
	> median	61/1582 (3.9)	46/1525 (3.0)	1.28 (0.88, 1.86) 0.2013	1.29 (0.87, 1.90) 0.2015	0.01 (-0.00, 0.02) 0.2098	
	Gender						0.1885
	Male	67/1765 (3.8)	56/1744 (3.2)	1.18 (0.83, 1.67) 0.3499	1.19 (0.83, 1.70) 0.3499	0.01 (-0.01, 0.02) 0.3526	
	Female	76/1361 (5.6)	47/1383 (3.4)	1.65 (1.16, 2.35) 0.0059	1.69 (1.16, 2.45) 0.0058	0.02 (0.01, 0.04) 0.0072	
	Race						0.5952
	White	120/2210 (5.4)	93/2222 (4.2)	1.30 (1.00, 1.69) 0.0533	1.31 (1.00, 1.73) 0.0534	0.01 (-0.00, 0.02) 0.0571	
	Black or African	9/ 81 (11.1)	4/ 78 (5.1)	2.18 (0.70, 6.80) 0.1785	2.33 (0.69, 7.92) 0.1749	0.06 (-0.02, 0.14) 0.1599	
	Asian	6/ 629 (1.0)	3/ 643 (0.5)	2.05 (0.51, 8.15) 0.3096	2.06 (0.51, 8.26) 0.3094	0.01 (-0.00, 0.01) 0.2805	
	Other	8/ 206 (3.9)	3/ 184 (1.6)	2.57 (0.70, 9.47) 0.1567	2.69 (0.70,10.39) 0.1516	0.02 (-0.01, 0.05)*0.1690	
	Geographic region						0.5382
	Asia	5/ 606 (0.8)	3/ 619 (0.5)	1.71 (0.41, 7.13) 0.4606	1.72 (0.41, 7.21) 0.4612	0.00 (-0.01, 0.01) 0.5331	
	Europe and Saudi Arabia	79/1491 (5.3)	66/1508 (4.4)	1.21 (0.88, 1.67) 0.2400	1.22 (0.87, 1.71) 0.2398	0.01 (-0.01, 0.02) 0.2357	
	North America	23/ 427 (5.4)	11/ 422 (2.6)	2.06 (1.02, 4.17) 0.0448	2.12 (1.02, 4.41) 0.0437	0.03 (0.00, 0.05) 0.0316	
	Latin America	36/ 602 (6.0)	23/ 578 (4.0)	1.54 (0.93, 2.57) 0.0965	1.58 (0.92, 2.70) 0.0958	0.02 (-0.00, 0.04) 0.0987	
	NYHA class at enrolment						0.6950
	II	112/2310 (4.8)	81/2395 (3.4)	1.43 (1.08, 1.89) 0.0120	1.45 (1.09, 1.95) 0.0119	0.01 (0.00, 0.03) 0.0126	
	III or IV	31/ 816 (3.8)	22/ 731 (3.0)	1.27 (0.74, 2.17) 0.3872	1.28 (0.73, 2.23) 0.3880	0.01 (-0.01, 0.03) 0.4141	
	LVEF at enrolment						0.8175
	<= 49	57/1066 (5.3)	38/1047 (3.6)	1.47 (0.98, 2.19) 0.0613	1.49 (0.98, 2.27) 0.0609	0.02 (-0.00, 0.03) 0.0587	
	50-59	47/1132 (4.2)	32/1121 (2.9)	1.46 (0.94, 2.26) 0.0959	1.47 (0.93, 2.33) 0.0959	0.01 (-0.00, 0.03) 0.0983	
	>= 60	39/ 928 (4.2)	33/ 959 (3.4)	1.23 (0.78, 1.94) 0.3752	1.24 (0.77, 1.99) 0.3760	0.01 (-0.01, 0.02) 0.4047	
	NT-proBNP at enrolment						0.1192
	<= median	92/1553 (5.9)	57/1574 (3.6)	1.64 (1.19, 2.26) 0.0028	1.68 (1.20, 2.35) 0.0028	0.02 (0.01, 0.04) 0.0029	
	> median	51/1573 (3.2)	46/1552 (3.0)	1.09 (0.74, 1.62) 0.6579	1.10 (0.73, 1.64) 0.6562	0.00 (-0.01, 0.02) 0.6072	
	Type 2 Diabetes Medical History						0.4596
	Yes	76/1399 (5.4)	50/1402 (3.6)	1.52 (1.07, 2.16)*0.0181	1.55 (1.08, 2.24)*0.0180	0.02 (0.00, 0.03)*0.0171	
	No	67/1727 (3.9)	53/1725 (3.1)	1.26 (0.89, 1.80)*0.1967	1.27 (0.88, 1.84)*0.1965	0.01 (-0.00, 0.02)*0.1954	
	Atrial fibrillation or flutter at enrolment ECG						0.8619
	Yes	49/1325 (3.7)	34/1317 (2.6)	1.43 (0.93, 2.20) 0.1020	1.45 (0.93, 2.26) 0.1018	0.01 (-0.00, 0.02) 0.0989	
	No	94/1800 (5.2)	69/1809 (3.8)	1.37 (1.01, 1.85) 0.0432	1.39 (1.01, 1.91) 0.0436	0.01 (-0.00, 0.03) 0.0573	
	BMI (kg/m2) at enrolment						0.4992
	< 30	55/1732 (3.2)	44/1733 (2.5)	1.25 (0.85, 1.85) 0.2614	1.26 (0.84, 1.88) 0.2615	0.01 (-0.00, 0.02) 0.2691	
	>= 30	88/1392 (6.3)	59/1390 (4.2)	1.49 (1.08, 2.05) 0.0151	1.52 (1.09, 2.14) 0.0150	0.02 (0.00, 0.04) 0.0144	
	Baseline eGFR (mL/min/1.73m^2)						0.2728
	< 60	65/1514 (4.3)	55/1551 (3.5)	1.20 (0.85, 1.71) 0.3047	1.21 (0.84, 1.75) 0.3068	0.01 (-0.01, 0.02) 0.3721	
	>= 60	78/1612 (4.8)	48/1575 (3.0)	1.59 (1.12, 2.26) 0.0101	1.62 (1.12, 2.34) 0.0100	0.02 (0.00, 0.03) 0.0092	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: COVID-19	SBP at randomisation						0.3439
	<= median	69/1567 (4.4)	44/1588 (2.8)	1.59 (1.10, 2.31) 0.0143	1.62 (1.10, 2.38) 0.0142	0.02 (0.00, 0.03) 0.0136	
	> median	74/1559 (4.7)	59/1539 (3.8)	1.25 (0.89, 1.75) 0.1920	1.26 (0.89, 1.79) 0.1944	0.01 (-0.01, 0.02) 0.2659	
	LVEF at enrolment 2						0.7250
	<= 49	57/1066 (5.3)	38/1047 (3.6)	1.47 (0.98, 2.19) 0.0613	1.49 (0.98, 2.27) 0.0609	0.02 (-0.00, 0.03) 0.0587	
	>= 50	86/2060 (4.2)	65/2080 (3.1)	1.34 (0.98, 1.84) 0.0706	1.35 (0.97, 1.88) 0.0708	0.01 (-0.00, 0.02) 0.0791	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.9568
	Yes	11/ 328 (3.4)	8/ 326 (2.5)	1.37 (0.56, 3.37) 0.4892	1.39 (0.55, 3.50) 0.4868	0.01 (-0.01, 0.04) 0.3595	
	No	132/2798 (4.7)	95/2801 (3.4)	1.39 (1.08, 1.80) 0.0120	1.41 (1.08, 1.85) 0.0120	0.01 (0.00, 0.02) 0.0117	
	MRAs at baseline						0.8727
	Yes	55/1339 (4.1)	40/1325 (3.0)	1.35 (0.90, 2.01) 0.1441	1.36 (0.90, 2.06) 0.1448	0.01 (-0.00, 0.02) 0.1817	
	No	88/1787 (4.9)	63/1802 (3.5)	1.41 (1.03, 1.93) 0.0338	1.43 (1.03, 1.99) 0.0337	0.01 (0.00, 0.03) 0.0331	
	ACEi+ARB at baseline						0.7752
	Yes	111/2259 (4.9)	82/2276 (3.6)	1.37 (1.03, 1.81) 0.0287	1.38 (1.03, 1.85) 0.0289	0.01 (0.00, 0.02) 0.0386	
	No	32/ 867 (3.7)	21/ 851 (2.5)	1.50 (0.87, 2.58) 0.1427	1.52 (0.87, 2.66) 0.1428	0.01 (-0.00, 0.03) 0.1549	
	ARNI at baseline						0.0752
	Yes	8/ 165 (4.8)	1/ 136 (0.7)	7.72 (0.98,60.95) 0.0525	8.25 (1.01,67.54) 0.0491	0.04 (0.01, 0.08)*0.0243	
	No	135/2961 (4.6)	102/2991 (3.4)	1.34 (1.04, 1.72) 0.0230	1.36 (1.04, 1.76) 0.0232	0.01 (0.00, 0.02) 0.0290	
	Beta Blocker at baseline						0.9951
	Yes	117/2587 (4.5)	84/2581 (3.3)	1.39 (1.06, 1.83) 0.0192	1.41 (1.06, 1.87) 0.0191	0.01 (0.00, 0.02) 0.0202	
	No	26/ 539 (4.8)	19/ 546 (3.5)	1.40 (0.78, 2.49) 0.2577	1.42 (0.77, 2.60) 0.2578	0.01 (-0.01, 0.04) 0.2760	
	Diuretics at baseline						0.7986
	Yes	132/2789 (4.7)	94/2783 (3.4)	1.40 (1.08, 1.82) 0.0107	1.42 (1.08, 1.86) 0.0107	0.01 (0.00, 0.02) 0.0123	
	No	11/ 337 (3.3)	9/ 344 (2.6)	1.24 (0.52, 2.96) 0.6238	1.25 (0.51, 3.07) 0.6193	0.01 (-0.02, 0.03) 0.4827	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Cellulitis	Overall	47/3126 (1.5)	51/3127 (1.6)	0.92 (0.62, 1.37) 0.6858	0.92 (0.62, 1.37) 0.6839	-0.00 (-0.01, 0.00) 0.5728	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Nasopharyngitis	Overall	59/3126 (1.9)	60/3127 (1.9)	0.98 (0.69, 1.40) 0.9295	0.98 (0.68, 1.41) 0.9288	-0.00 (-0.01, 0.01) 0.8914	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Pneumonia	Overall	82/3126 (2.6)	102/3127 (3.3)	0.80 (0.60, 1.07) 0.1363	0.80 (0.59, 1.07) 0.1359	-0.01 (-0.01, 0.00) 0.1274	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Infections and infestations, PT: Urinary tract infection	Overall	140/3126 (4.5)	131/3127 (4.2)	1.07 (0.85, 1.35) 0.5759	1.07 (0.84, 1.37) 0.5746	0.00 (-0.01, 0.01) 0.5426	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Injury, poisoning and procedural complications	Overall	205/3126 (6.6)	220/3127 (7.0)	0.93 (0.78, 1.12) 0.4521	0.93 (0.76, 1.13) 0.4538	-0.00 (-0.02, 0.01) 0.4763	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Injury, poisoning and procedural complications, PT: Contusion	Overall	22/3126 (0.7)	34/3127 (1.1)	0.65 (0.38, 1.10) 0.1105	0.64 (0.38, 1.11) 0.1105	-0.00 (-0.01, 0.00) 0.1273	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Injury, poisoning and procedural complications, PT: Fall	Overall	33/3126 (1.1)	35/3127 (1.1)	0.94 (0.59, 1.51) 0.8101	0.94 (0.58, 1.52) 0.8076	-0.00 (-0.01, 0.00) 0.5847	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Investigations	Overall	91/3126 (2.9)	109/3127 (3.5)	0.84 (0.64, 1.10) 0.1992	0.83 (0.63, 1.10) 0.1974	-0.01 (-0.02, 0.00) 0.1467	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
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Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders	Overall	284/3126 (9.1)	325/3127 (10.4)	0.87 (0.75, 1.02) 0.0793	0.86 (0.73, 1.02) 0.0796	-0.01 (-0.03, 0.00) 0.0910	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Diabetes mellitus inadequate control	Overall	46/3126 (1.5)	44/3127 (1.4)	1.04 (0.70, 1.57) 0.8329	1.05 (0.69, 1.59) 0.8353	0.00 (-0.01, 0.01)*0.8306	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hyperkalaemia	Overall	42/3126 (1.3)	40/3127 (1.3)	1.05 (0.68, 1.61) 0.8242	1.05 (0.68, 1.63) 0.8233	0.00 (-0.00, 0.01) 0.7601	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hyperuricaemia	Overall	20/3126 (0.6)	36/3127 (1.2)	0.56 (0.32, 0.96) 0.0344	0.55 (0.32, 0.96) 0.0342	-0.01 (-0.01, -0.00) 0.0300	
	Age						0.2911
	<= median	12/1544 (0.8)	17/1602 (1.1)	0.73 (0.35, 1.53) 0.4060	0.73 (0.35, 1.53) 0.4055	-0.00 (-0.01, 0.00) 0.3686	
	> median	8/1582 (0.5)	19/1525 (1.2)	0.41 (0.18, 0.92) 0.0317	0.40 (0.18, 0.92) 0.0315	-0.01 (-0.01, -0.00) 0.0295	
	Gender						0.2173
	Male	16/1765 (0.9)	23/1744 (1.3)	0.69 (0.36, 1.29) 0.2448	0.68 (0.36, 1.30) 0.2445	-0.00 (-0.01, 0.00) 0.2189	
	Female	4/1361 (0.3)	13/1383 (0.9)	0.31 (0.10, 0.96) 0.0423	0.31 (0.10, 0.96) 0.0421	-0.01 (-0.01, -0.00) 0.0414	
	Race						0.5262
	White	7/2210 (0.3)	15/2222 (0.7)	0.47 (0.19, 1.15) 0.0973	0.47 (0.19, 1.15) 0.0973	-0.00 (-0.01, 0.00) 0.1783	
	Black or African	1/ 81 (1.2)	1/ 78 (1.3)	1.06 (0.07,16.27) 0.9663	0.96 (0.06,15.66)*0.9786	-0.00 (-0.04, 0.03)*0.9786	
	Asian	11/ 629 (1.7)	20/ 643 (3.1)	0.56 (0.27, 1.16) 0.1182	0.55 (0.26, 1.16) 0.1163	-0.02 (-0.03, 0.00) 0.0567	
	Other	1/ 206 (0.5)	0/ 184 (0.0)	2.68 (0.11,65.41)*0.5451	2.69 (0.11,66.53)*0.5448	0.00 (-0.00, 0.01)*0.3161	
	Geographic region						0.9558
	Asia	11/ 606 (1.8)	20/ 619 (3.2)	0.56 (0.27, 1.16) 0.1178	0.55 (0.26, 1.16) 0.1156	-0.02 (-0.03, 0.00) 0.0534	
	Europe and Saudi Arabia	6/1491 (0.4)	9/1508 (0.6)	0.67 (0.24, 1.87) 0.4440	0.67 (0.24, 1.88) 0.4450	-0.00 (-0.01, 0.00) 0.6961	
	North America	1/ 427 (0.2)	2/ 422 (0.5)	0.50 (0.05, 5.50) 0.5728	0.49 (0.04, 5.46)*0.5642	-0.00 (-0.01, 0.01)*0.5568	
	Latin America	2/ 602 (0.3)	5/ 578 (0.9)	0.40 (0.08, 2.04) 0.2683	0.39 (0.08, 2.05) 0.2684	-0.00 (-0.01, 0.01) 0.3828	
	NYHA class at enrolment						0.5019
	II	15/2310 (0.6)	25/2395 (1.0)	0.62 (0.33, 1.17) 0.1425	0.62 (0.32, 1.18) 0.1421	-0.00 (-0.01, 0.00) 0.1096	
	III or IV	5/ 816 (0.6)	11/ 731 (1.5)	0.41 (0.14, 1.16) 0.0929	0.40 (0.14, 1.16) 0.0925	-0.01 (-0.02, 0.00) 0.0804	
	LVEF at enrolment						0.4990
	<= 49	5/1066 (0.5)	14/1047 (1.3)	0.35 (0.13, 0.96) 0.0414	0.34 (0.12, 0.96) 0.0412	-0.01 (-0.02, -0.00) 0.0479	
	50-59	5/1132 (0.4)	8/1121 (0.7)	0.62 (0.20, 1.89) 0.3989	0.62 (0.20, 1.89) 0.3966	-0.00 (-0.01, 0.00)*0.3946	
	>= 60	10/ 928 (1.1)	14/ 959 (1.5)	0.75 (0.34, 1.68) 0.4864	0.75 (0.33, 1.69) 0.4806	-0.01 (-0.02, 0.00) 0.0913	
	NT-proBNP at enrolment						0.1055
	<= median	6/1553 (0.4)	19/1574 (1.2)	0.32 (0.13, 0.80) 0.0147	0.32 (0.13, 0.80) 0.0145	-0.01 (-0.01, -0.00) 0.0069	
	> median	14/1573 (0.9)	17/1552 (1.1)	0.81 (0.40, 1.64) 0.5630	0.81 (0.40, 1.65) 0.5630	-0.00 (-0.01, 0.00) 0.5602	
	Type 2 Diabetes Medical History						0.8130
	Yes	11/1399 (0.8)	21/1402 (1.5)	0.52 (0.25, 1.08)*0.0818	0.52 (0.25, 1.09)*0.0815	-0.01 (-0.01, 0.00)*0.0762	
	No	9/1727 (0.5)	15/1725 (0.9)	0.60 (0.26, 1.37)*0.2231	0.60 (0.26, 1.37)*0.2230	-0.00 (-0.01, 0.00)*0.2180	
	Atrial fibrillation or flutter at enrolment ECG						0.6076
	Yes	12/1325 (0.9)	19/1317 (1.4)	0.63 (0.31, 1.29) 0.2029	0.62 (0.30, 1.29) 0.2027	-0.01 (-0.01, 0.00) 0.2010	
	No	8/1800 (0.4)	17/1809 (0.9)	0.47 (0.20, 1.09) 0.0774	0.47 (0.20, 1.09) 0.0768	-0.00 (-0.01, -0.00) 0.0479	
	BMI (kg/m2) at enrolment						0.4985
	< 30	14/1732 (0.8)	22/1733 (1.3)	0.64 (0.33, 1.24) 0.1851	0.63 (0.32, 1.24) 0.1844	-0.00 (-0.01, 0.00) 0.1470	
	>= 30	6/1392 (0.4)	14/1390 (1.0)	0.43 (0.16, 1.11) 0.0811	0.43 (0.16, 1.11) 0.0809	-0.01 (-0.01, 0.00) 0.0690	
	Baseline eGFR (mL/min/1.73m^2)						0.1202
	< 60	13/1514 (0.9)	16/1551 (1.0)	0.83 (0.40, 1.72) 0.6127	0.83 (0.40, 1.73) 0.6131	-0.00 (-0.01, 0.01) 0.6544	
	>= 60	7/1612 (0.4)	20/1575 (1.3)	0.34 (0.15, 0.81) 0.0149	0.34 (0.14, 0.81) 0.0147	-0.01 (-0.01, -0.00) 0.0065	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hyperuricaemia	SBP at randomisation						0.4623
	<= median	9/1567 (0.6)	20/1588 (1.3)	0.46 (0.21, 1.00) 0.0501	0.45 (0.21, 1.00) 0.0499	-0.01 (-0.01, -0.00) 0.0433	
	> median	11/1559 (0.7)	16/1539 (1.0)	0.69 (0.32, 1.48) 0.3385	0.69 (0.32, 1.48) 0.3380	-0.00 (-0.01, 0.00) 0.3139	
	LVEF at enrolment 2						0.2575
	<= 49	5/1066 (0.5)	14/1047 (1.3)	0.35 (0.13, 0.96) 0.0414	0.34 (0.12, 0.96) 0.0412	-0.01 (-0.02, -0.00) 0.0479	
	>= 50	15/2060 (0.7)	22/2080 (1.1)	0.69 (0.36, 1.33) 0.2651	0.69 (0.36, 1.33) 0.2649	-0.00 (-0.01, 0.00) 0.2372	
	Randomised during hospitalisation for HF or within 30 days of discharge						0.4613
	Yes	3/ 328 (0.9)	3/ 326 (0.9)	0.97 (0.20, 4.79) 0.9722	0.97 (0.19, 4.86) 0.9724	-0.00 (-0.01, 0.01) 0.9940	
	No	17/2798 (0.6)	33/2801 (1.2)	0.52 (0.29, 0.92) 0.0262	0.51 (0.29, 0.92) 0.0261	-0.01 (-0.01, -0.00) 0.0222	
	MRAs at baseline						0.1081
	Yes	10/1339 (0.7)	10/1325 (0.8)	0.98 (0.41, 2.34) 0.9599	0.98 (0.41, 2.36) 0.9600	-0.00 (-0.01, 0.01) 0.9816	
	No	10/1787 (0.6)	26/1802 (1.4)	0.39 (0.19, 0.80) 0.0108	0.39 (0.19, 0.80) 0.0107	-0.01 (-0.02, -0.00) 0.0073	
	ACEi+ARB at baseline						0.5816
	Yes	16/2259 (0.7)	31/2276 (1.4)	0.52 (0.29, 0.95) 0.0330	0.52 (0.28, 0.95) 0.0328	-0.01 (-0.01, -0.00) 0.0262	
	No	4/ 867 (0.5)	5/ 851 (0.6)	0.78 (0.21, 2.90) 0.7119	0.78 (0.21, 2.92) 0.7122	-0.00 (-0.01, 0.01) 0.7707	
	ARNI at baseline						0.1803
	Yes	1/ 165 (0.6)	0/ 136 (0.0)	2.48 (0.10,60.29)*0.5778	2.49 (0.10,61.60)*0.5775	0.01 (-0.01, 0.02)*0.3158	
	No	19/2961 (0.6)	36/2991 (1.2)	0.53 (0.31, 0.93) 0.0264	0.53 (0.30, 0.93) 0.0263	-0.01 (-0.01, -0.00) 0.0199	
	Beta Blocker at baseline						0.6907
	Yes	16/2587 (0.6)	27/2581 (1.0)	0.59 (0.32, 1.09) 0.0936	0.59 (0.32, 1.09) 0.0934	-0.00 (-0.01, 0.00) 0.0815	
	No	4/ 539 (0.7)	9/ 546 (1.6)	0.45 (0.14, 1.46) 0.1843	0.45 (0.14, 1.46) 0.1838	-0.01 (-0.02, 0.00) 0.1801	
	Diuretics at baseline						0.0999
	Yes	20/2789 (0.7)	33/2783 (1.2)	0.60 (0.35, 1.05) 0.0746	0.60 (0.34, 1.05) 0.0745	-0.00 (-0.01, 0.00) 0.0663	
	No	0/ 337 (0.0)	3/ 344 (0.9)	0.00 (0.00,) 0.9999	0.14 (0.01, 2.81)*0.2014	-0.01 (-0.02, 0.00)*0.0819	

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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hypoglycaemia	Overall	34/3126 (1.1)	30/3127 (1.0)	1.13 (0.70, 1.84) 0.6182	1.13 (0.69, 1.86) 0.6171	0.00 (-0.00, 0.00) 0.5905	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Hypokalaemia	Overall	38/3126 (1.2)	27/3127 (0.9)	1.41 (0.86, 2.30) 0.1718	1.41 (0.86, 2.32) 0.1718	0.00 (-0.00, 0.01) 0.1712	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Metabolism and nutrition disorders, PT: Type 2 diabetes mellitus	Overall	22/3126 (0.7)	32/3127 (1.0)	0.69 (0.40, 1.18) 0.1747	0.69 (0.40, 1.18) 0.1748	-0.00 (-0.01, 0.00) 0.1944	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
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SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Musculoskeletal and connective tissue disorders	Overall	244/3126 (7.8)	249/3127 (8.0)	0.98 (0.83, 1.16) 0.8184	0.98 (0.81, 1.18) 0.8178	-0.00 (-0.01, 0.01) 0.8120	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Musculoskeletal and connective tissue disorders, PT: Arthralgia	Overall	43/3126 (1.4)	58/3127 (1.9)	0.74 (0.50, 1.10) 0.1347	0.74 (0.50, 1.10) 0.1345	-0.00 (-0.01, 0.00) 0.1261	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
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Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Musculoskeletal and connective tissue disorders, PT: Back pain	Overall	57/3126 (1.8)	55/3127 (1.8)	1.04 (0.72, 1.50) 0.8477	1.04 (0.71, 1.51) 0.8471	0.00 (-0.01, 0.01) 0.8144	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

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Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Overall	81/3126 (2.6)	83/3127 (2.7)	0.98 (0.72, 1.32) 0.8836	0.98 (0.72, 1.33) 0.8771	-0.00 (-0.01, 0.01) 0.6427	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders	Overall	304/3126 (9.7)	307/3127 (9.8)	0.99 (0.85, 1.15) 0.9021	0.99 (0.84, 1.17) 0.9017	-0.00 (-0.02, 0.01) 0.8990	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders, PT: Dizziness	Overall	64/3126 (2.0)	58/3127 (1.9)	1.10 (0.78, 1.57) 0.5796	1.11 (0.77, 1.58) 0.5811	0.00 (-0.01, 0.01) 0.6615	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Nervous system disorders, PT: Headache	Overall	62/3126 (2.0)	61/3127 (2.0)	1.02 (0.72, 1.44) 0.9262	1.02 (0.71, 1.45) 0.9256	0.00 (-0.01, 0.01) 0.8966	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Psychiatric disorders	Overall	81/3126 (2.6)	80/3127 (2.6)	1.01 (0.75, 1.37) 0.9345	1.01 (0.74, 1.39) 0.9343	0.00 (-0.01, 0.01) 0.9239	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders	Overall	241/3126 (7.7)	249/3127 (8.0)	0.97 (0.82, 1.15) 0.7087	0.97 (0.80, 1.16) 0.7082	-0.00 (-0.02, 0.01) 0.7032	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Acute kidney injury	Overall	61/3126 (2.0)	70/3127 (2.2)	0.87 (0.62, 1.22) 0.4295	0.87 (0.61, 1.23) 0.4268	-0.00 (-0.01, 0.00) 0.3207	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Chronic kidney disease	Overall	45/3126 (1.4)	33/3127 (1.1)	1.36 (0.87, 2.13) 0.1740	1.37 (0.87, 2.15) 0.1731	0.00 (-0.00, 0.01) 0.1206	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Renal and urinary disorders, PT: Renal impairment	Overall	61/3126 (2.0)	54/3127 (1.7)	1.13 (0.79, 1.62) 0.5094	1.13 (0.78, 1.64) 0.5093	0.00 (-0.00, 0.01) 0.5011	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Reproductive system and breast disorders	Overall	62/3126 (2.0)	54/3127 (1.7)	1.15 (0.80, 1.65) 0.4537	1.15 (0.80, 1.66) 0.4518	0.00 (-0.00, 0.01) 0.3617	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders	Overall	238/3126 (7.6)	251/3127 (8.0)	0.95 (0.80, 1.12) 0.5419	0.94 (0.79, 1.14) 0.5430	-0.00 (-0.02, 0.01) 0.5547	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders, PT: Cough	Overall	32/3126 (1.0)	35/3127 (1.1)	0.91 (0.57, 1.47) 0.7125	0.91 (0.56, 1.48) 0.7142	-0.00 (-0.01, 0.00) 0.8757	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Respiratory, thoracic and mediastinal disorders, PT: Dyspnoea	Overall	39/3126 (1.2)	31/3127 (1.0)	1.26 (0.79, 2.01) 0.3368	1.26 (0.79, 2.03) 0.3371	0.00 (-0.00, 0.01) 0.3655	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Skin and subcutaneous tissue disorders	Overall	161/3126 (5.2)	168/3127 (5.4)	0.96 (0.78, 1.18) 0.6889	0.96 (0.77, 1.19) 0.6926	-0.00 (-0.01, 0.01) 0.7590	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders	Overall	283/3126 (9.1)	254/3127 (8.1)	1.11 (0.95, 1.31) 0.1895	1.13 (0.94, 1.34) 0.1894	0.01 (-0.00, 0.02) 0.1896	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders, PT: Hypertension	Overall	93/3126 (3.0)	107/3127 (3.4)	0.87 (0.66, 1.14) 0.3157	0.87 (0.65, 1.15) 0.3158	-0.00 (-0.01, 0.00) 0.3179	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Analysis of frequent Non-Severe Adverse Events by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm)
Safety Analysis Set

SOC/PT	Subgroup Level	Dapa 10 mg (N=3126) n/ N (%)	Placebo (N=3127) n/ N (%)	RR (95% CI) p-Value	OR (95% CI) p-Value	ARR (95% CI) p-Value	p-Value for interaction
SOC: Vascular disorders, PT: Hypotension	Overall	77/3126 (2.5)	65/3127 (2.1)	1.19 (0.86, 1.64) 0.3074	1.19 (0.85, 1.66) 0.3074	0.00 (-0.00, 0.01) 0.3136	

Odds ratios, Relative Risk and Risk Reduction are obtained from logistic regression (RR: log-link, OR: logit-link, ARR: identity-link) with treatment group and T2DM stratum as covariates.
Subgroup analysis only performed for SOC/PT with significant (alpha=0.05) Relative Risk for overall population.
p-Value for interaction from logistic regression (log-link function) with factors for T2DM stratum, the relevant subgroup variable, treatment group and the interaction between treatment group and the subgroup variable.
Effects and interaction for subgroups only calculated if both >=10 events in at least one subgroup level and >=10 patients in all subgroup levels are observed. Else results were not calculated (NC).
RR: Relative Risk, OR: Odds Ratio, ARR: Absolute Risk Reduction

AstraZeneca
Protocol: D169CC00001
Overall study population
Incidences of Adverse Events leading to discontinuation of study drug by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	Dapa 10 mg (N=3126) n (%)	Placebo (N=3127) n (%)
Subjects with events	183 (5.9)	181 (5.8)
Infections and infestations	35 (1.1)	28 (0.9)
Urinary tract infection	11 (0.4)	6 (0.2)
COVID-19	5 (0.2)	2 (0.1)
Pneumonia	3 (0.1)	3 (0.1)
Cellulitis	2 (0.1)	2 (0.1)
Cystitis	1 (0.0)	3 (0.1)
Septic shock	2 (0.1)	1 (0.0)
Urosepsis	1 (0.0)	2 (0.1)
COVID-19 pneumonia	0	2 (0.1)
Respiratory tract infection	1 (0.0)	1 (0.0)
Sepsis	2 (0.1)	0
Bullous erysipelas	1 (0.0)	0
Candida infection	1 (0.0)	0
Endocarditis	0	1 (0.0)
Fungal skin infection	1 (0.0)	0
Gastroenteritis viral	0	1 (0.0)
Gastrointestinal viral infection	0	1 (0.0)
Genital infection fungal	1 (0.0)	0
Implant site infection	1 (0.0)	0
Necrotising fasciitis	0	1 (0.0)
Pneumonia bacterial	0	1 (0.0)
Pyelonephritis	1 (0.0)	0
Tinea cruris	0	1 (0.0)
Tooth abscess	1 (0.0)	0
Upper respiratory tract infection	1 (0.0)	0
Wound infection	0	1 (0.0)
Renal and urinary disorders	34 (1.1)	26 (0.8)
Renal impairment	10 (0.3)	7 (0.2)
Acute kidney injury	7 (0.2)	8 (0.3)
Chronic kidney disease	6 (0.2)	8 (0.3)
Renal failure	5 (0.2)	3 (0.1)
Dysuria	2 (0.1)	0
End stage renal disease	1 (0.0)	0
Prerenal failure	1 (0.0)	0
Stress urinary incontinence	1 (0.0)	0
Tubulointerstitial nephritis	1 (0.0)	0
Urinary incontinence	1 (0.0)	0
Cardiac disorders	14 (0.4)	36 (1.2)
Cardiac failure	9 (0.3)	20 (0.6)
Acute myocardial infarction	0	4 (0.1)
Cardiac failure acute	0	3 (0.1)
Cardiac failure congestive	1 (0.0)	2 (0.1)
Atrial fibrillation	1 (0.0)	1 (0.0)
Acute coronary syndrome	0	1 (0.0)
Atrial flutter	0	1 (0.0)
Cardiac arrest	0	1 (0.0)
Cardiac failure chronic	0	1 (0.0)
Congestive cardiomyopathy	1 (0.0)	0
Myocardial infarction	1 (0.0)	0
Palpitations	0	1 (0.0)
Right ventricular failure	0	1 (0.0)
Sinus node dysfunction	1 (0.0)	0
Ventricular fibrillation	0	1 (0.0)
Nervous system disorders	16 (0.5)	20 (0.6)

MedDRA version 22.0.

AstraZeneca
Protocol: D169CC00001
Overall study population
Incidences of Adverse Events leading to discontinuation of study drug by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	Dapa 10 mg (N=3126) n (%)	Placebo (N=3127) n (%)
Ischaemic stroke	4 (0.1)	5 (0.2)
Haemorrhagic stroke	4 (0.1)	2 (0.1)
Dizziness	1 (0.0)	4 (0.1)
Cognitive disorder	1 (0.0)	1 (0.0)
Dementia	1 (0.0)	1 (0.0)
Cerebral haemorrhage	0	1 (0.0)
Cerebrovascular disorder	0	1 (0.0)
Dementia Alzheimer's type	0	1 (0.0)
Dizziness postural	0	1 (0.0)
Embolic stroke	1 (0.0)	0
Headache	1 (0.0)	0
Hypoaesthesia	1 (0.0)	0
Polyneuropathy alcoholic	0	1 (0.0)
Presyncope	0	1 (0.0)
Senile dementia	1 (0.0)	0
Syncope	0	1 (0.0)
Transient ischaemic attack	1 (0.0)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	15 (0.5)	16 (0.5)
Lung neoplasm malignant	1 (0.0)	3 (0.1)
Adenocarcinoma of colon	2 (0.1)	1 (0.0)
Diffuse large B-cell lymphoma	1 (0.0)	1 (0.0)
Pancreatic carcinoma	2 (0.1)	0
Plasma cell myeloma	1 (0.0)	1 (0.0)
Adult T-cell lymphoma/leukaemia	0	1 (0.0)
Bladder transitional cell carcinoma	1 (0.0)	0
Brain neoplasm	1 (0.0)	0
Cervix carcinoma	0	1 (0.0)
Colon cancer	1 (0.0)	0
Fallopian tube cancer	1 (0.0)	0
Hepatic cancer	0	1 (0.0)
Invasive ductal breast carcinoma	0	1 (0.0)
Lung cancer metastatic	0	1 (0.0)
Lung squamous cell carcinoma stage IV	0	1 (0.0)
Lymphoproliferative disorder	0	1 (0.0)
Non-small cell lung cancer	0	1 (0.0)
Oesophageal carcinoma	0	1 (0.0)
Prostate cancer metastatic	1 (0.0)	0
Prostatic adenoma	1 (0.0)	0
Small cell lung cancer	1 (0.0)	0
Triple negative breast cancer	0	1 (0.0)
Uterine cancer	1 (0.0)	0
Gastrointestinal disorders	11 (0.4)	19 (0.6)
Nausea	2 (0.1)	3 (0.1)
Abdominal discomfort	2 (0.1)	1 (0.0)
Constipation	1 (0.0)	2 (0.1)
Gastrointestinal haemorrhage	1 (0.0)	2 (0.1)
Abdominal distension	1 (0.0)	1 (0.0)
Diarrhoea	1 (0.0)	1 (0.0)
Abdominal pain	0	1 (0.0)
Abdominal pain upper	0	1 (0.0)
Abdominal rigidity	0	1 (0.0)
Colitis	0	1 (0.0)
Diverticular perforation	0	1 (0.0)
Dyspepsia	0	1 (0.0)
Dysphagia	0	1 (0.0)
Erosive duodenitis	0	1 (0.0)
Gastrointestinal disorder	1 (0.0)	0
Gastrointestinal necrosis	0	1 (0.0)

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AstraZeneca
Protocol: D169CC00001
Overall study population
Incidences of Adverse Events leading to discontinuation of study drug by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	Dapa 10 mg (N=3126) n (%)	Placebo (N=3127) n (%)
Gastrointestinal perforation	0	1 (0.0)
Pancreatitis	0	1 (0.0)
Pancreatitis chronic	1 (0.0)	0
Rectal haemorrhage	1 (0.0)	0
Skin and subcutaneous tissue disorders	12 (0.4)	8 (0.3)
Pruritus	3 (0.1)	1 (0.0)
Rash	3 (0.1)	1 (0.0)
Alopecia	1 (0.0)	1 (0.0)
Diabetic foot	1 (0.0)	1 (0.0)
Dermal cyst	0	1 (0.0)
Eczema	0	1 (0.0)
Pemphigoid	1 (0.0)	0
Pruritus allergic	1 (0.0)	0
Psoriasis	1 (0.0)	0
Rash pruritic	1 (0.0)	0
Skin ulcer	0	1 (0.0)
Urticaria	0	1 (0.0)
Metabolism and nutrition disorders	10 (0.3)	4 (0.1)
Diabetes mellitus inadequate control	3 (0.1)	1 (0.0)
Decreased appetite	1 (0.0)	1 (0.0)
Dehydration	2 (0.1)	0
Diabetic ketoacidosis	1 (0.0)	1 (0.0)
Gout	1 (0.0)	0
Hyperuricaemia	1 (0.0)	0
Hypoglycaemia	1 (0.0)	0
Hypovolaemia	1 (0.0)	0
Latent autoimmune diabetes in adults	0	1 (0.0)
General disorders and administration site conditions	9 (0.3)	4 (0.1)
Asthenia	4 (0.1)	1 (0.0)
Fatigue	3 (0.1)	1 (0.0)
Chest pain	0	1 (0.0)
Death	1 (0.0)	0
General physical health deterioration	1 (0.0)	0
Non-cardiac chest pain	0	1 (0.0)
Vascular disorders	7 (0.2)	5 (0.2)
Hypotension	6 (0.2)	1 (0.0)
Aortic dissection	0	1 (0.0)
Extremity necrosis	0	1 (0.0)
Hypertension	0	1 (0.0)
Hypovolaemic shock	0	1 (0.0)
Peripheral ischaemia	1 (0.0)	0
Investigations	2 (0.1)	9 (0.3)
Glomerular filtration rate decreased	0	3 (0.1)
Blood creatinine increased	0	2 (0.1)
Blood lactic acid increased	0	1 (0.0)
Blood urine present	1 (0.0)	0
Body temperature increased	1 (0.0)	0
Ejection fraction decreased	0	1 (0.0)
Renal function test	0	1 (0.0)
Weight decreased	0	1 (0.0)
Injury, poisoning and procedural complications	4 (0.1)	4 (0.1)
Ankle fracture	0	1 (0.0)
Compression fracture	1 (0.0)	0
Ligament sprain	1 (0.0)	0

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AstraZeneca
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Overall study population
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System Organ Class (SOC) Preferred Term (PT)	Dapa 10 mg (N=3126) n (%)	Placebo (N=3127) n (%)
Patella fracture	1 (0.0)	0
Spinal cord injury	0	1 (0.0)
Subdural haematoma	0	1 (0.0)
Toxicity to various agents	0	1 (0.0)
Traumatic haematoma	1 (0.0)	0
Respiratory, thoracic and mediastinal disorders	5 (0.2)	3 (0.1)
Acute respiratory failure	1 (0.0)	2 (0.1)
Acute pulmonary oedema	1 (0.0)	0
Cough	0	1 (0.0)
Dyspnoea	1 (0.0)	0
Respiratory failure	1 (0.0)	0
Sputum retention	1 (0.0)	0
Reproductive system and breast disorders	6 (0.2)	1 (0.0)
Balanoposthitis	2 (0.1)	0
Atrophic vulvovaginitis	1 (0.0)	0
Penile swelling	1 (0.0)	0
Pruritus genital	0	1 (0.0)
Vulvovaginal discomfort	1 (0.0)	0
Vulvovaginal pruritus	1 (0.0)	0
Musculoskeletal and connective tissue disorders	4 (0.1)	1 (0.0)
Back pain	1 (0.0)	0
Flank pain	1 (0.0)	0
Musculoskeletal chest pain	1 (0.0)	0
Nuchal rigidity	0	1 (0.0)
Spinal pain	1 (0.0)	0
Psychiatric disorders	3 (0.1)	2 (0.1)
Affective disorder	1 (0.0)	0
Delusion	1 (0.0)	0
Depression	1 (0.0)	0
Insomnia	0	1 (0.0)
Mental status changes	0	1 (0.0)
Hepatobiliary disorders	0	3 (0.1)
Bile duct stone	0	1 (0.0)
Hepatic cirrhosis	0	1 (0.0)
Liver disorder	0	1 (0.0)
Ear and labyrinth disorders	1 (0.0)	1 (0.0)
Vertigo	0	1 (0.0)
Vestibular disorder	1 (0.0)	0
Immune system disorders	2 (0.1)	0
Primary amyloidosis	2 (0.1)	0
Blood and lymphatic system disorders	0	1 (0.0)
Anaemia	0	1 (0.0)
Eye disorders	1 (0.0)	0
Eyelid oedema	1 (0.0)	0

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