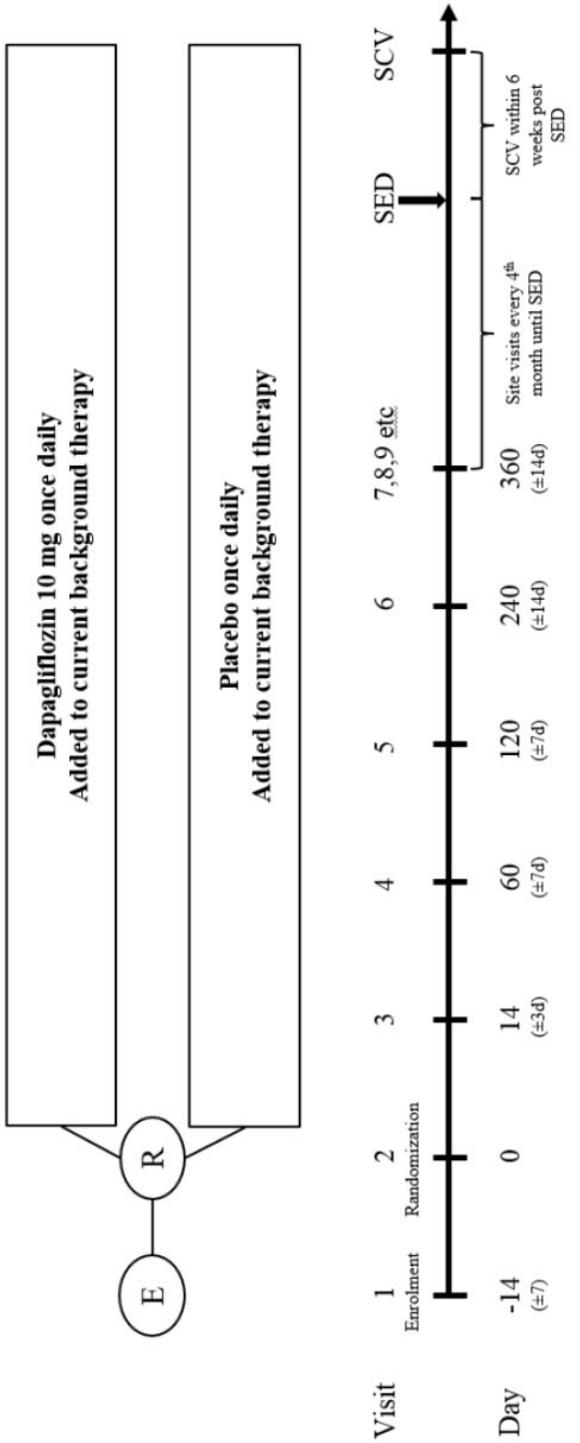

Dapagliflozin 10 mg once daily
Added to current background therapy
Placebo once daily
Added to current background therapy
E
R
Visit
Day
1
Enrolment
-14
(±7)
2
Randomization
0
3
14
(±3d)
4
60
(±7d)
5
120
(±7d)
6
240
(±14d)
7,8,9 etc
360
(±14d)
SED
Site visits every 4th month until SED
SCV
SCV within 6 weeks post SED

Fig. 1

	Number (%) of patients		
	Dapa 10 mg	Placebo	Total
Patients randomised	2152	2152	4304
Patients who discontinued IP	274 (12.7)	309 (14.4)	583 (13.5)
Patient Decision	142 (6.6)	160 (7.4)	302 (7.0)
Adverse Events	118 (5.5)	123 (5.7)	241 (5.6)
Subjects who discontinued study	10 (0.5)	5 (0.2)	15 (0.3)
Withdrew consent	8 (0.4)	3 (0.1)	11 (0.3)
Lost to follow-up	2 (0.1)	2 (0.1)	4 (0.1)
Vital status at end of study			
Dead	107 (5.0)	159 (7.4)	266 (6.2)
Alive	2043 (94.9)	1990 (92.5)	4033 (93.7)
Unknown	2 (0.1)	3 (0.1)	5 (0.1)

Fig. 2

		Dapa 10 mg (N=2152)	Placebo (N=2152)	Total (N=4304)
Age (years)	Mean	61.8	61.9	61.8
Sex n (%)	Female	709 (32.9)	716 (33.3)	1425 (33.1)
Race n (%)	White	1124 (52.2)	1166 (54.2)	2290 (53.2)
	Black or African American	104 (4.8)	87 (4.0)	191 (4.4)
	Asian	749 (34.8)	718 (33.4)	1467 (34.1)
	Hawaiian or other Pacific Islander	1 (0.0)	1 (0.0)	2 (0.0)
	American Indian or Alaska Native	62 (2.9)	74 (3.4)	136 (3.2)
	Other	112 (5.2)	106 (4.9)	218 (5.1)

Fig. 3

	Category / Metric	Dapa 10 mg (N=2152)	Placebo (N=2152)	Total (N=4304)
Diabetes Status n (%)	T2DM	1455 (67.6)	1451 (67.4)	2906 (67.5)
	No diabetes	697 (32.4)	701 (32.6)	1398 (32.5)
eGFR (mL/min/1.73 m^2)	Mean	43.2	43.0	43.1
UACR (mg/g)	Median	964.8	933.8	949.3
Most likely aetiology of CKD n (%)	Diabetic Nephropathy	1271 (59.1)	1239 (57.6)	2510 (58.3)
	Ischemic / Hypertension	324 (15.1)	363 (16.9)	687 (16.0)
	Chronic Glomerulonephritis	343 (15.9)	352 (16.4)	695 (16.1)
	IgA nephropathy	137 (6.4)	133 (6.2)	270 (6.3)

Fig. 4

	Number (%) of patients		
	Dapa 10 mg (N=2152)	Placebo (N=2152)	Total (N=4304)
ACE-I or ARB	2094 (97.3)	2080 (96.7)	4174 (97.0)
ACE-I	673 (31.3)	681 (31.6)	1354 (31.5)
ARB	1444 (67.1)	1426 (66.3)	2870 (66.7)
Antithrombotic agents	1022 (47.5)	1020 (47.4)	2042 (47.4)
Lipid lowering agents	1495 (69.5)	1493 (69.4)	2988 (69.4)
Diuretics	928 (43.1)	954 (44.3)	1882 (43.7)

Fig. 5

Variable	Dapa 10 mg (N=2152) Subjects with events n (%)	Event rate	Placebo (N=2152) Subjects with events n (%)	Event rate	Hazard ratio	95% CI	p-value
Composite of ≥50% eGFR decline, ESRD, and renal or CV death	197 (9.2)	4.6	312 (14.5)	7.5	0.61	(0.51, 0.72)	<0.0001
≥50% decline in eGFR	112 (5.2)	2.6	201 (9.3)	4.8	0.53	(0.42, 0.67)	<0.0001
ESRD	109 (5.1)	2.5	161 (7.5)	3.8	0.64	(0.50, 0.82)	0.0004
eGFR <15ml/min/1.73 m^2	84 (3.9)	1.9	120 (5.6)	2.8	0.67	(0.51, 0.88)	0.0045
Chronic dialysis[a]	68 (3.2)	1.5	99 (4.6)	2.2	0.66	(0.48, 0.90)	0.0080
Receiving renal transplant[a]	3 (0.1)	0.1	8 (0.4)	0.2			
Renal death[a]	2 (<0.1)	0.0	6 (0.3)	0.1			
CV death[a]	65 (3.0)	1.4	80 (3.7)	1.7	0.81	(0.58, 1.12)	0.2029

Fig. 6

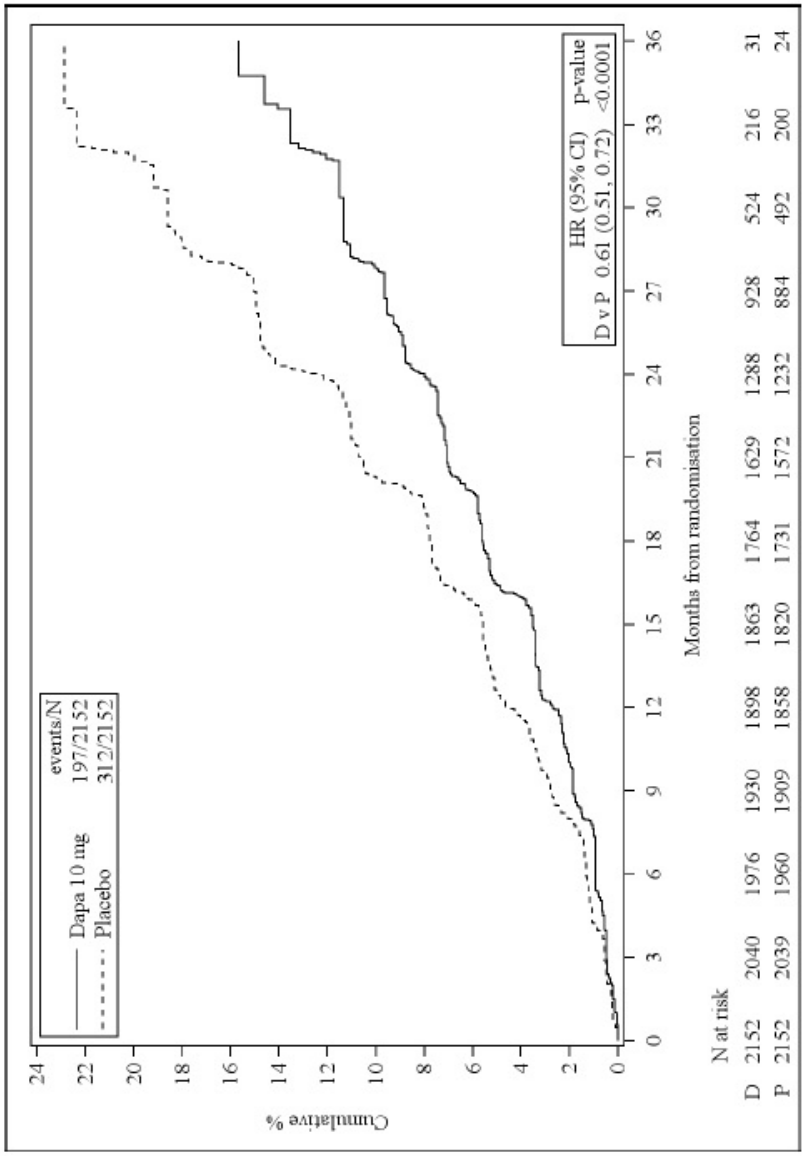

Cumulative %
24
22
20
18
16
14
12
10
8
6
4
2
0
Dapa 10 mg
Placebo
events/N
197/2152
312/2152
HR (95% CI) p-value
D v P 0.61 (0.51, 0.72) <0.0001
0 3 6 9 12 15 18 21 24 27 30 33 36
Months from randomisation
N at risk
D 2152 2040 1976 1930 1898 1863 1764 1629 1288 928 524 216 31
P 2152 2039 1960 1909 1858 1820 1731 1572 1232 884 492 200 24

Fig. 7

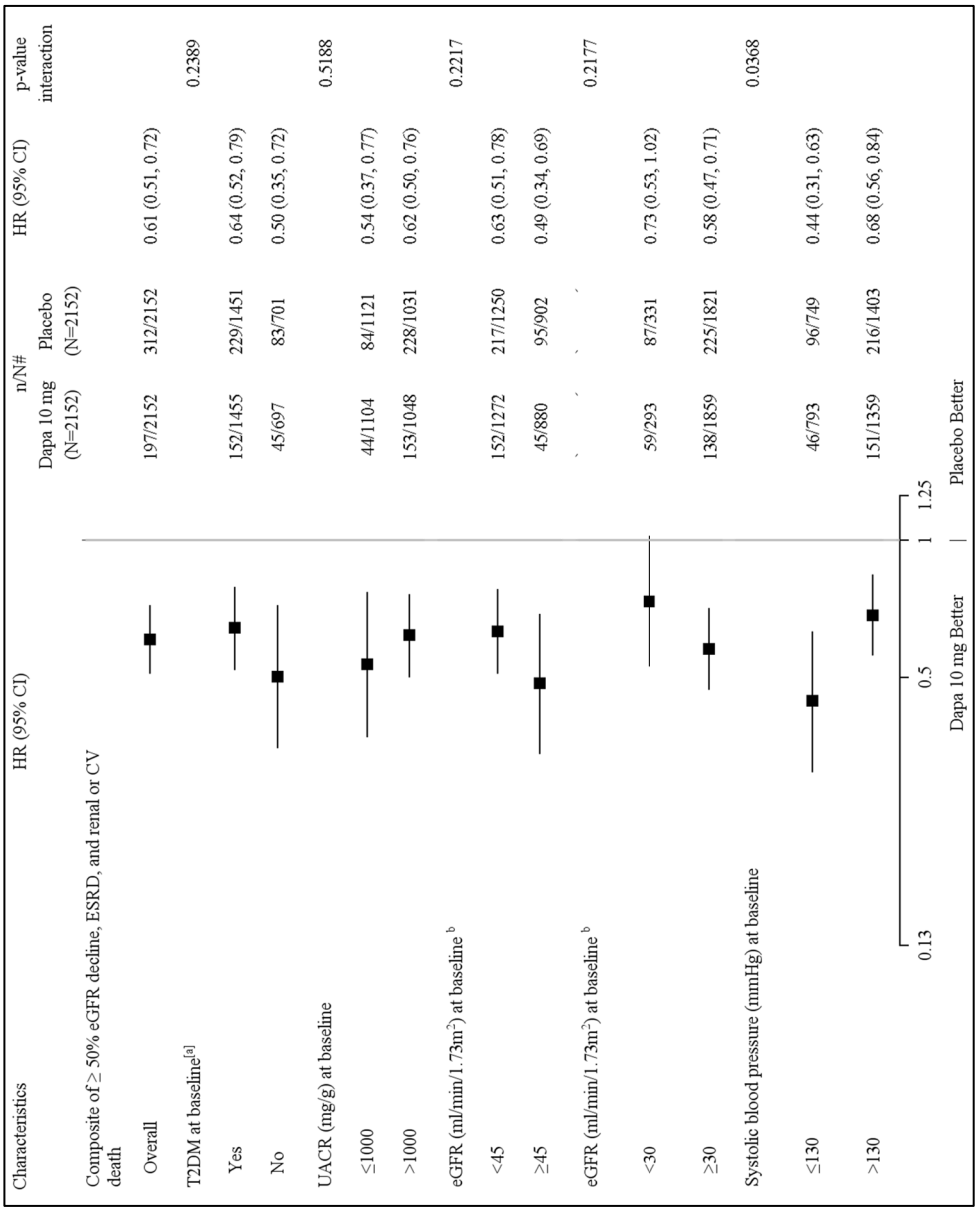

Characteristics
HR (95% CI)
n/N#
Dapa 10 mg (N=2152)
Placebo (N=2152)
HR (95% CI)
p-value interaction
Composite of ≥ 50% eGFR decline, ESRD, and renal or CV death
Overall
197/2152
312/2152
0.61 (0.51, 0.72)
T2DM at baseline[a]
0.2389
Yes
152/1455
229/1451
0.64 (0.52, 0.79)
No
45/697
83/701
0.50 (0.35, 0.72)
UACR (mg/g) at baseline
0.5188
≤1000
44/1104
84/1121
0.54 (0.37, 0.77)
>1000
153/1048
228/1031
0.62 (0.50, 0.76)
eGFR (ml/min/1.73m²) at baseline [b]
0.2217
<45
152/1272
217/1250
0.63 (0.51, 0.78)
≥45
45/880
95/902
0.49 (0.34, 0.69)
eGFR (ml/min/1.73m²) at baseline [b]
0.2177
<30
59/293
87/331
0.73 (0.53, 1.02)
≥30
138/1859
225/1821
0.58 (0.47, 0.71)
Systolic blood pressure (mmHg) at baseline
0.0368
≤130
46/793
96/749
0.44 (0.31, 0.63)
>130
151/1359
216/1403
0.68 (0.56, 0.84)
0.13
0.5
1
1.25
Dapa 10 mg Better
Placebo Better

Fig. 8

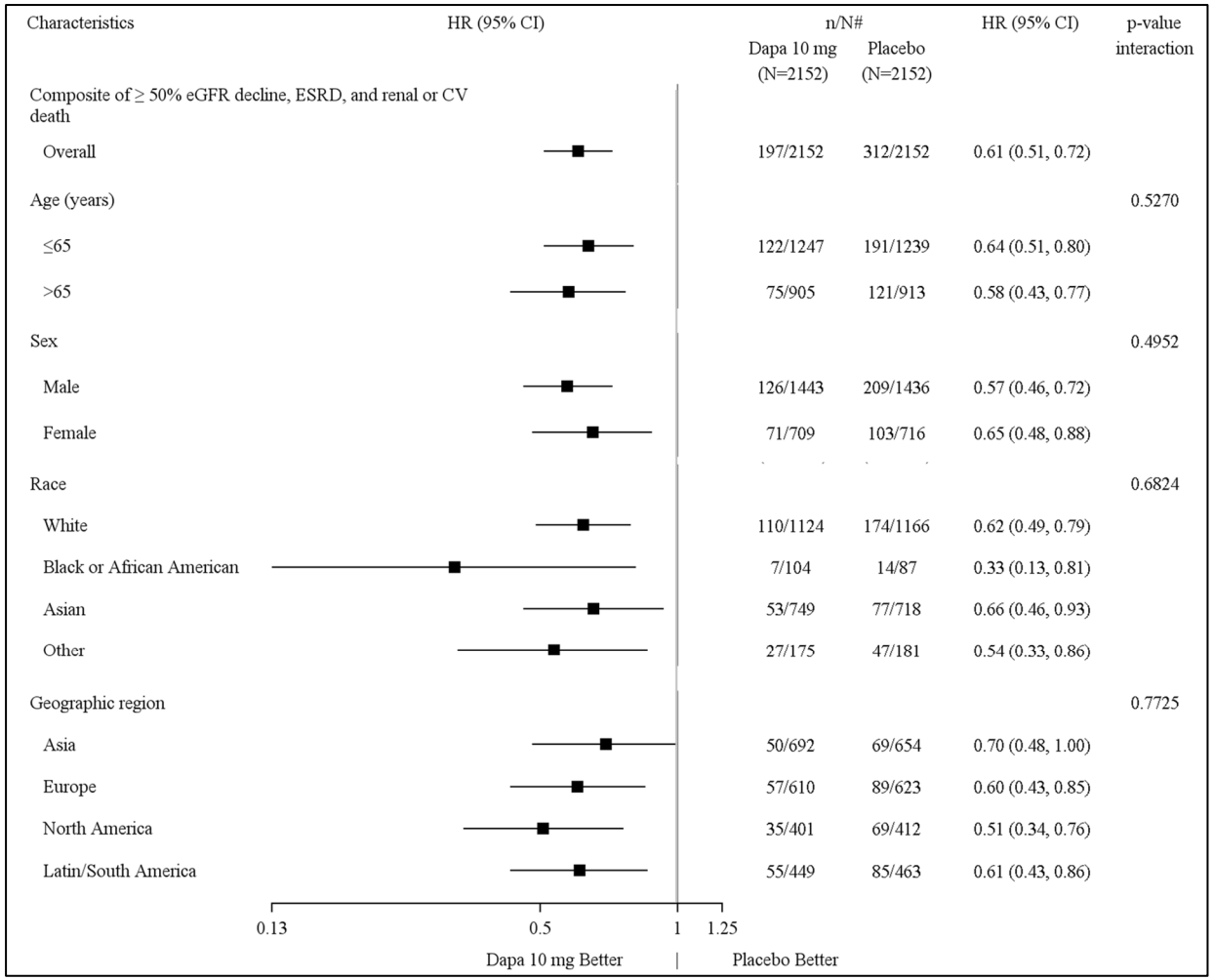

Characteristics
HR (95% CI)
n/N#
Dapa 10 mg (N=2152)
Placebo (N=2152)
HR (95% CI)
p-value interaction
Composite of ≥ 50% eGFR decline, ESRD, and renal or CV death
Overall 197/2152 312/2152 0.61 (0.51, 0.72)
Age (years) 0.5270
≤65 122/1247 191/1239 0.64 (0.51, 0.80)
>65 75/905 121/913 0.58 (0.43, 0.77)
Sex 0.4952
Male 126/1443 209/1436 0.57 (0.46, 0.72)
Female 71/709 103/716 0.65 (0.48, 0.88)
Race 0.6824
White 110/1124 174/1166 0.62 (0.49, 0.79)
Black or African American 7/104 14/87 0.33 (0.13, 0.81)
Asian 53/749 77/718 0.66 (0.46, 0.93)
Other 27/175 47/181 0.54 (0.33, 0.86)
Geographic region 0.7725
Asia 50/692 69/654 0.70 (0.48, 1.00)
Europe 57/610 89/623 0.60 (0.43, 0.85)
North America 35/401 69/412 0.51 (0.34, 0.76)
Latin/South America 55/449 85/463 0.61 (0.43, 0.86)
0.13
0.5
1
1.25
Dapa 10 mg Better
Placebo Better

Fig. 9

Variable	Type of endpoint	Dapa 10 mg (N=2152) Subjects with event n (%)	Placebo (N=2152) Subjects with event n (%)	Hazard ratio	95% CI	p-value
Composite of ≥50% eGFR decline, ESRD and renal or CV death	Primary	197 (9.2)	312 (14.5)	0.61	(0.51, 0.72)	<0.0001[a]
Composite of ≥50% eGFR decline, ESRD and renal death	Secondary	142 (6.6)	243 (11.3)	0.56	(0.45, 0.68)	<0.0001[a]
Composite of CV death and hospitalization for HF	Secondary	100 (4.6)	138 (6.4)	0.71	(0.55, 0.92)	0.0089[a]
Death from any cause	Secondary	101 (4.7)	146 (6.8)	0.69	(0.53, 0.88)	0.0035[a]

Fig. 10

Variable	Dapa 10 mg (N=2152) Subjects with events n (%)	Dapa 10 mg (N=2152) Event rate	Placebo (N=2152) Subjects with events n (%)	Placebo (N=2152) Event rate	Hazard ratio	95% CI	p-value
Composite of CV death and hospitalization for HF	100 (4.6)	2.2	138 (6.4)	3.0	0.71	(0.55, 0.92)	0.0089
Hospitalization for HF	37 (1.7)	0.8	71 (3.3)	1.6	0.51	(0.34, 0.76)	0.0007
CV death	65 (3.0)	1.4	80 (3.7)	1.7	0.81	(0.58, 1.12)	0.2029

Fig. 11

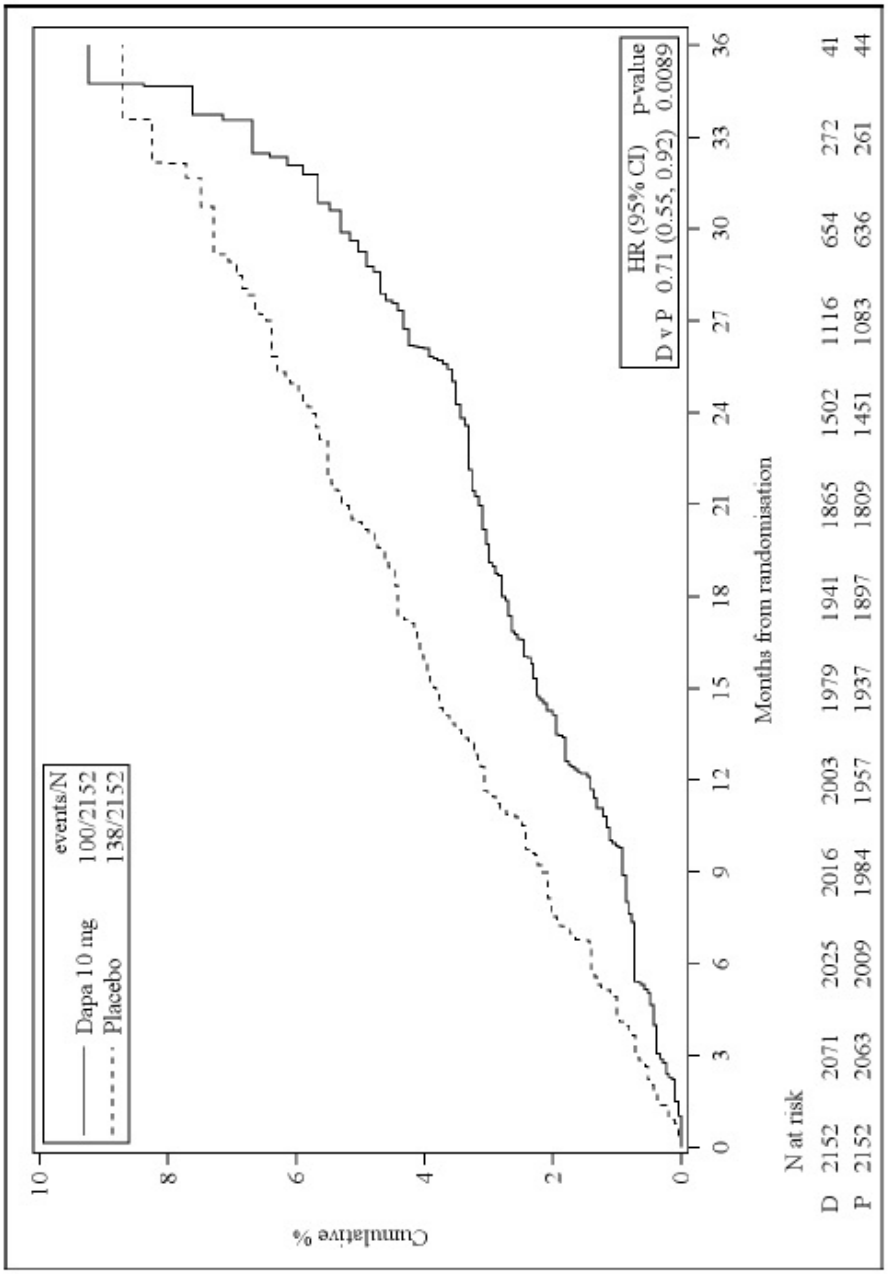

Cumulative %
10
8
6
4
2
0
events/N
Dapa 10 mg 100/2152
Placebo 138/2152
HR (95% CI) p-value
D v P 0.71 (0.55, 0.92) 0.0089
Months from randomisation
0 3 6 9 12 15 18 21 24 27 30 33 36
N at risk
D 2152 2071 2025 2016 2003 1979 1941 1865 1502 1116 654 272 41
P 2152 2063 2009 1984 1957 1937 1897 1809 1451 1083 636 261 44

Fig. 12

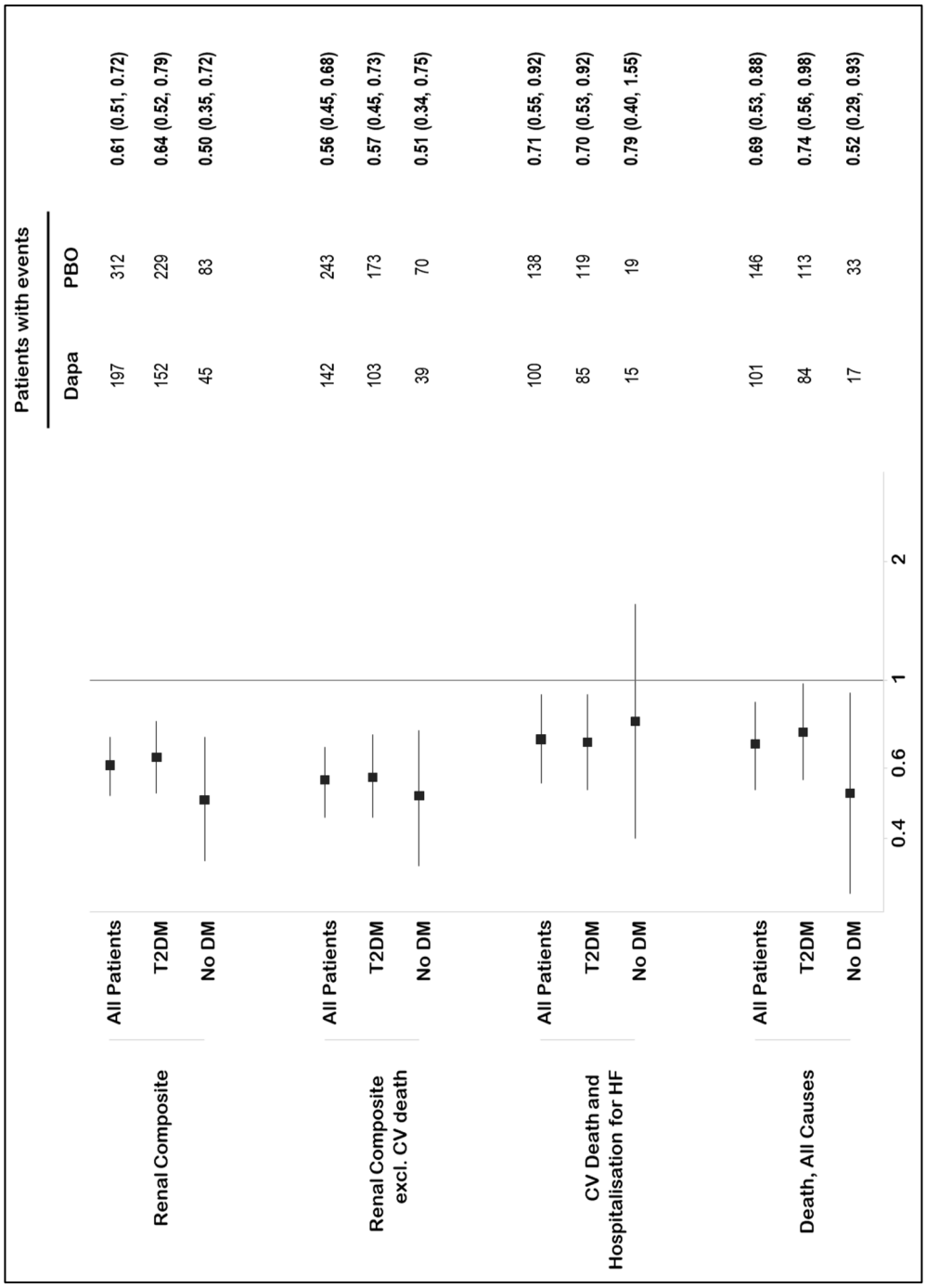

Patients with events
Dapa
PBO
Renal Composite
All Patients 197 312 0.61 (0.51, 0.72)
T2DM 152 229 0.64 (0.52, 0.79)
No DM 45 83 0.50 (0.35, 0.72)
Renal Composite excl. CV death
All Patients 142 243 0.56 (0.45, 0.68)
T2DM 103 173 0.57 (0.45, 0.73)
No DM 39 70 0.51 (0.34, 0.75)
CV Death and Hospitalisation for HF
All Patients 100 138 0.71 (0.55, 0.92)
T2DM 85 119 0.70 (0.53, 0.92)
No DM 15 19 0.79 (0.40, 1.55)
Death, All Causes
All Patients 101 146 0.69 (0.53, 0.88)
T2DM 84 113 0.74 (0.56, 0.98)
No DM 17 33 0.52 (0.29, 0.93)
0.4
0.6
1
2

Fig. 13

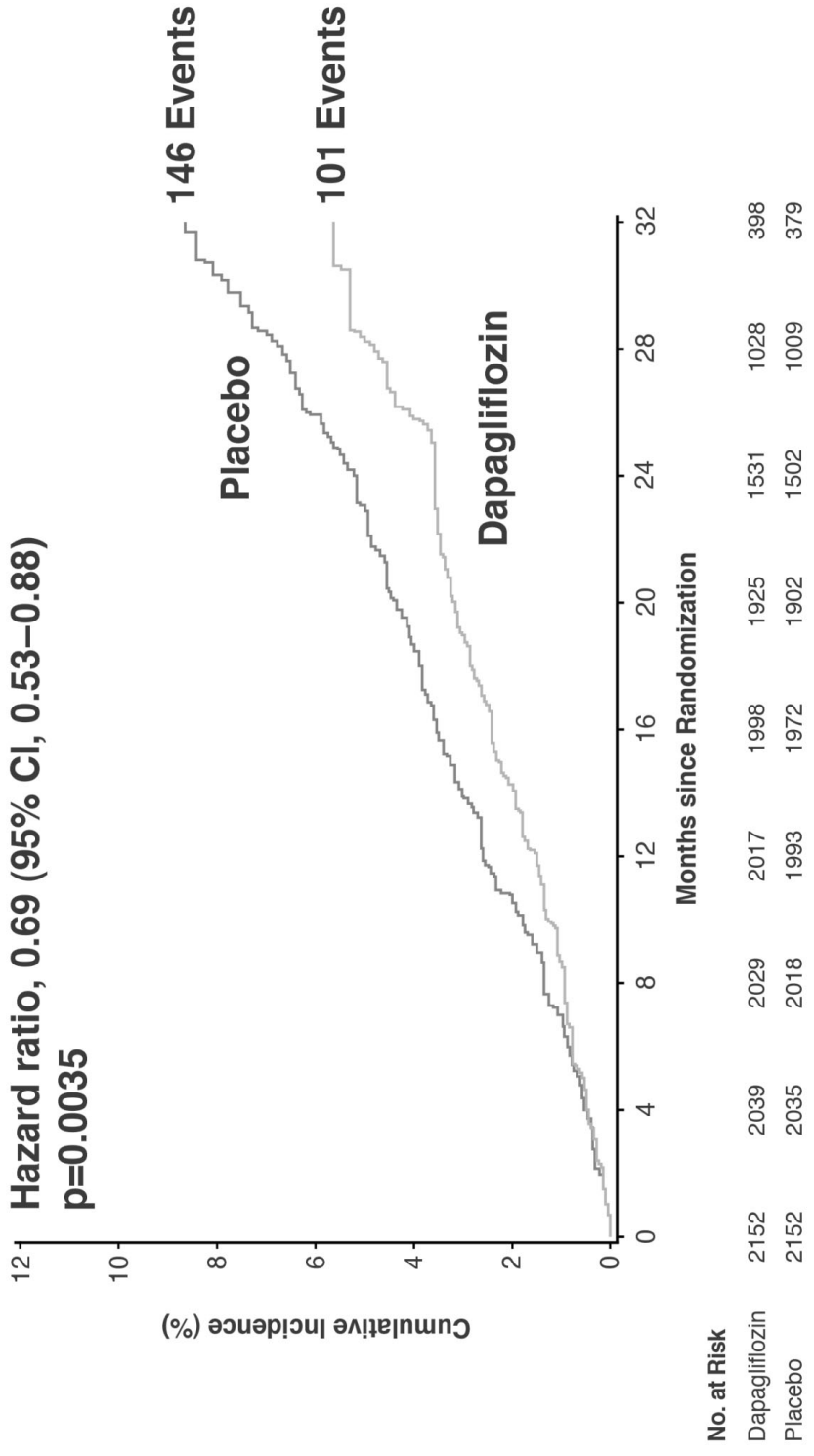

Hazard ratio, 0.69 (95% CI, 0.53–0.88)
p=0.0035
146 Events
101 Events
Placebo
Dapagliflozin
Cumulative Incidence (%)
0
2
4
6
8
10
12
Months since Randomization
0
4
8
12
16
20
24
28
32
No. at Risk
Dapagliflozin 2152 2039 2029 2017 1998 1925 1531 1028 398
Placebo 2152 2035 2018 1993 1972 1902 1502 1009 379

Fig. 14

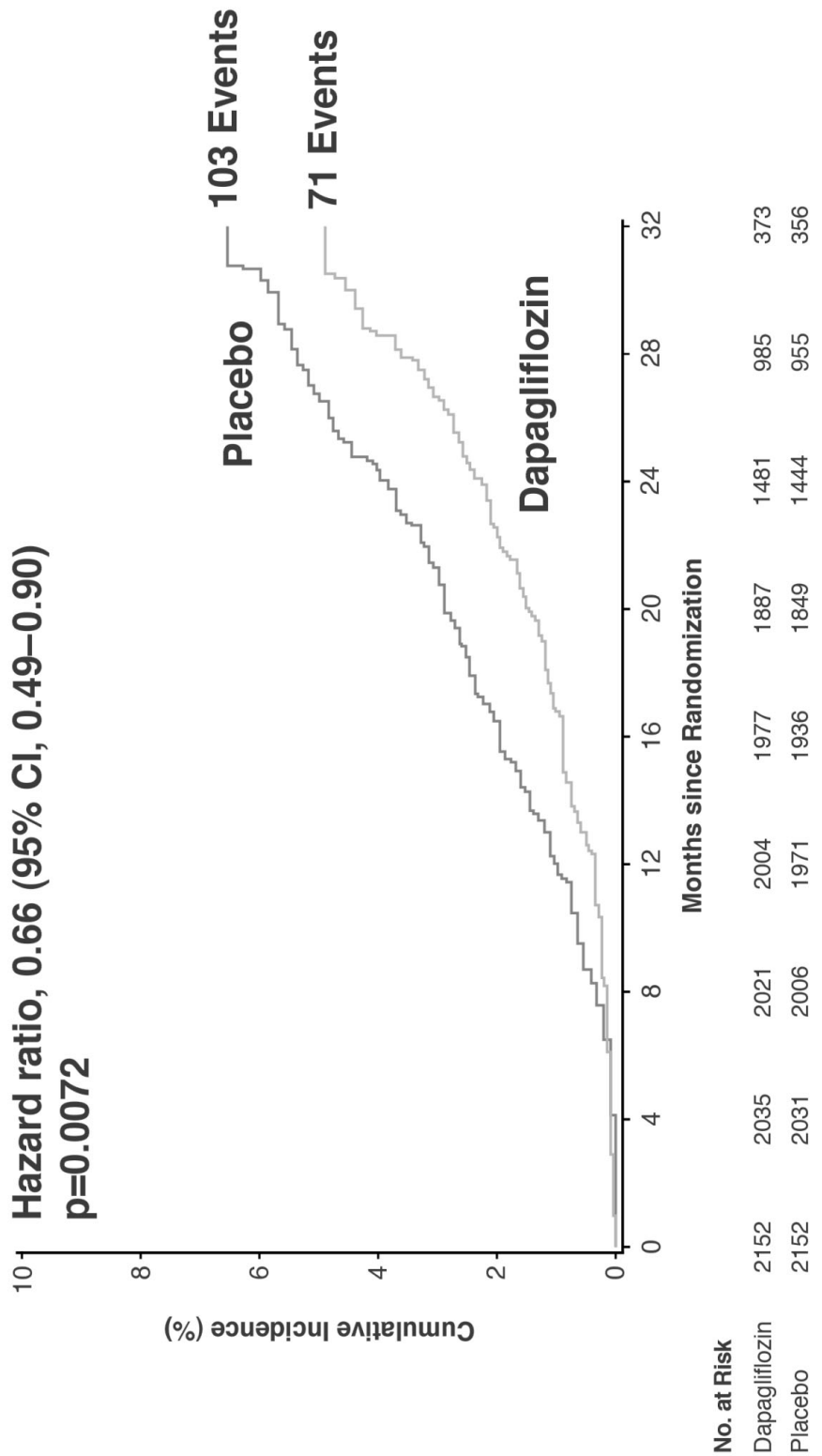

Hazard ratio, 0.66 (95% CI, 0.49–0.90)
p=0.0072
Placebo
103 Events
71 Events
Dapagliflozin
Cumulative Incidence (%)
0
2
4
6
8
10
Months since Randomization
0
4
8
12
16
20
24
28
32
No. at Risk
Dapagliflozin 2152 2035 2021 2004 1977 1887 1481 985 373
Placebo 2152 2031 2006 1971 1936 1849 1444 955 356

Fig. 15

	Dapagliflozin (N=2152)	Placebo (N=2152)	HR/RR* (95%CI)	P-value
Pre-specified exploratory endpoint Time to 1st heart failure hospitalization	37 (1.7%)	71 (3.3%)	0.51 (0.34, 0.76)	0.0007
Post hoc exploratory endpoint** 1 heart failure hospitalization	30	55	0.45* (0.24, 0.87)	
2 heart failure hospitalizations	5	12		
≥3 heart failure hospitalizations	2	4		

Fig. 16

Primary outcome	Dapagliflozin	Placebo	Dapagliflozin	Placebo	Hazard Ratio (95% CI)	P-value for Interaction
	No. of participants/total no.		Events/100 patient-years			
Overall	**197/2152**	**312/2152**	**4.6**	**7.5**	**0.61 (0.51, 0.72)**	
Diabetic nephropathy	139/1271	207/1239	5.4	8.5	0.63 (0.51, 0.78)	0.53
Ischemic/hypertensive nephropathy	24/324	35/363	3.8	4.9	0.75 (0.44, 1.26)	
Glomerulonephritides	22/343	49/352	3.4	7.5	0.43 (0.26, 0.71)	
Other/unknown	12/214	21/198	2.9	5.5	0.58 (0.29, 1.19)	

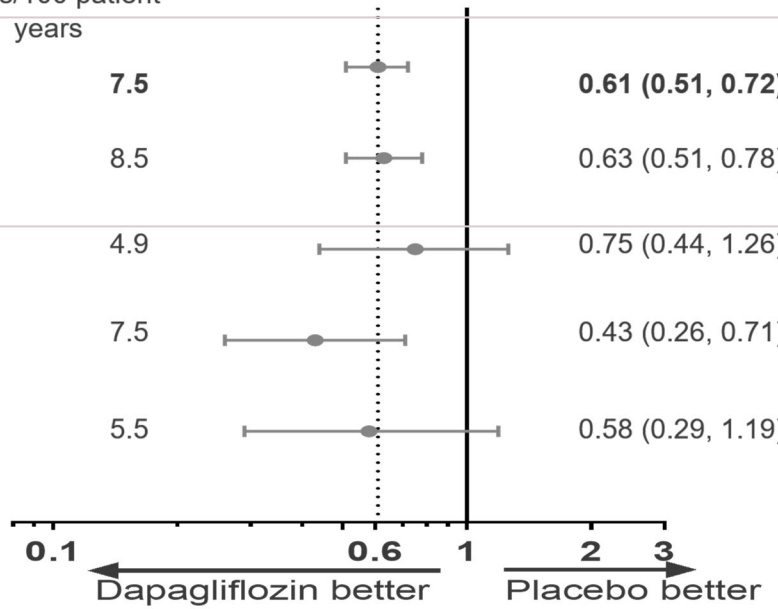


Fig. 17

Renal-specific outcome	Dapagliflozin	Placebo	Dapagliflozin	Placebo	Hazard Ratio (95% CI)	P-value for Interaction
	No. of participants/total no.		Events/100 patient-years			
Overall	**142/2152**	**243/2152**	**3.3**	**5.8**	**0.56 (0.45, 0.68)**	
Diabetic nephropathy	93/1271	157/1239	3.6	6.4	0.55 (0.43, 0.71)	0.67
Ischemic/hypertensive nephropathy	18/324	26/363	2.8	3.7	0.74 (0.40, 1.36)	
Glomerulonephritides	21/343	46/352	3.3	7.0	0.43 (0.26, 0.72)	
Other/unknown	10/214	14/198	2.5	3.7	0.81 (0.35, 1.83)	

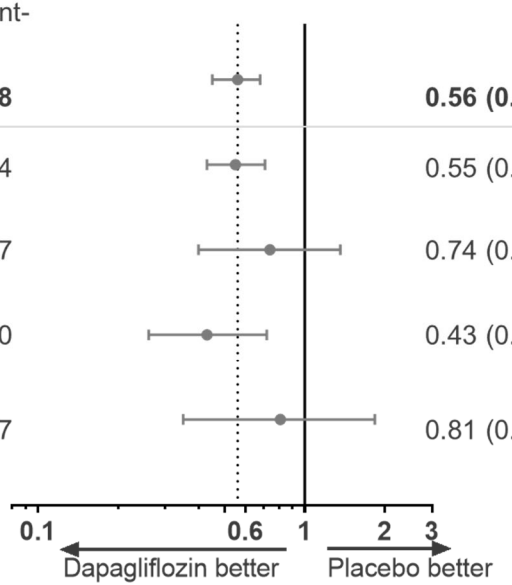


Fig. 18

CV death or heart failure hospitalization	Dapagliflozin	Placebo	Dapagliflozin	Placebo	Hazard Ratio (95% CI)	P-value for Interaction
	No. of participants/total no.		Events/100 patient-years			
Overall	**100/2152**	**138/2152**	**2.2**	**3.0**	**0.71 (0.55, 0.92)**	
Diabetic nephropathy	76/1271	107/1239	2.7	4.0	0.67 (0.50, 0.90)	0.24
Ischemic/hypertensive nephropathy	17/324	15/363	2.5	2.0	1.29 (0.64, 2.60)	
Glomerulonephritides	3/343	7/352	0.4	1.0	0.48 (0.12, 1.84)	
Other/unknown	4/214	9/198	0.9	2.2	0.39 (0.12, 1.28)	

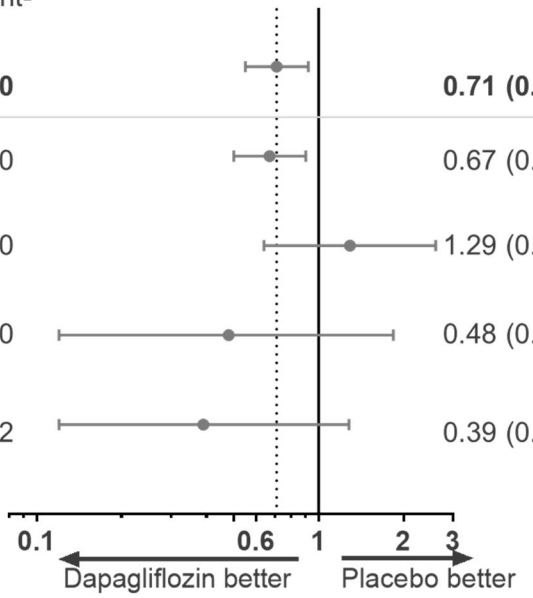


Fig. 19

All-cause mortality	Dapagliflozin	Placebo	Dapagliflozin	Placebo	Hazard Ratio (95% CI)	P-value for Interaction
	No. of participants/total no.		Events/100 patient-years			
Overall	**101/2152**	**146/2152**	**2.2**	**3.2**	**0.69 (0.53, 0.88)**	
Diabetic nephropathy	78/1271	104/1239	2.7	3.8	0.72 (0.54, 0.97)	0.55
Ischemic/hypertensive nephropathy	14/324	22/363	2.0	2.8	0.70 (0.36, 1.37)	
Glomerulonephritides	3/343	11/352	0.4	1.5	0.31 (0.09, 1.13)	
Other/unknown	6/214	9/198	1.3	2.2	0.57 (0.20, 1.61)	

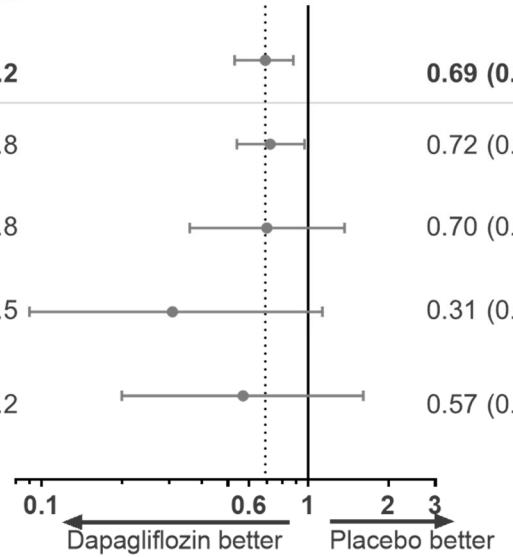


Fig. 20

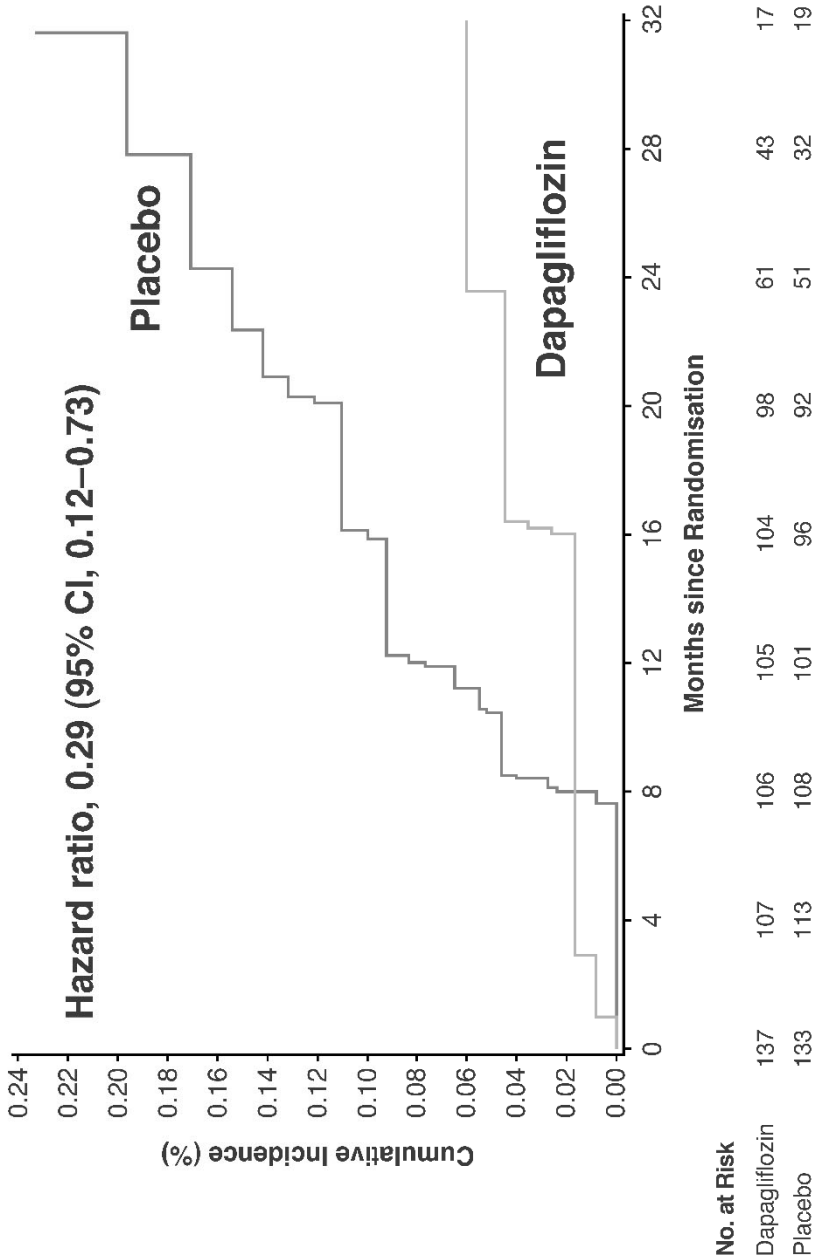

Hazard ratio, 0.29 (95% CI, 0.12–0.73)
Placebo
Dapagliflozin
Cumulative Incidence (%)
0.24
0.22
0.20
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
0
4
8
12
16
20
24
28
32
Months since Randomisation
No. at Risk
Dapagliflozin 137 107 106 105 104 98 61 43 17
Placebo 133 113 108 101 96 92 51 32 19

Fig. 21

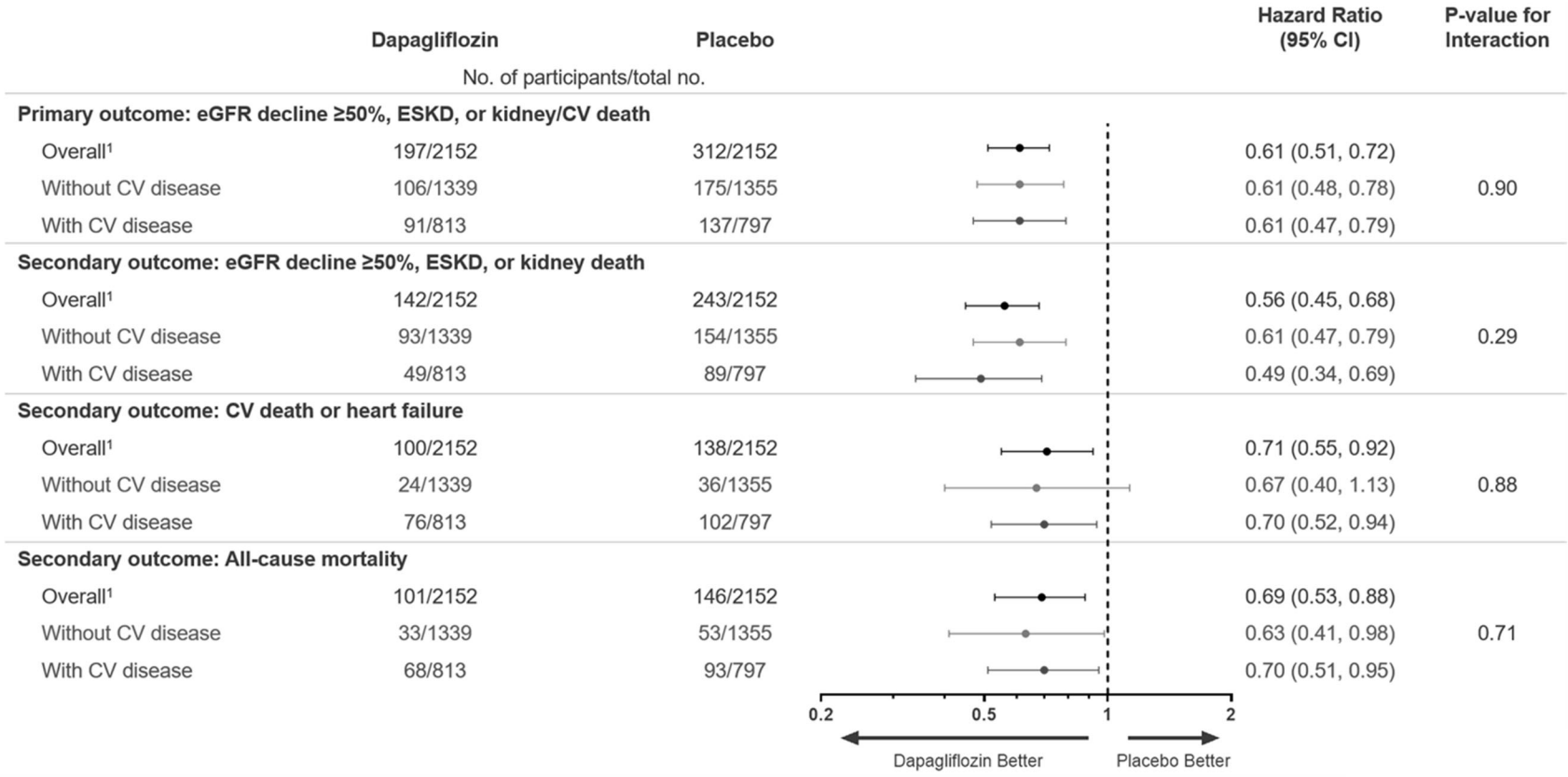

Dapagliflozin
Placebo
Hazard Ratio (95% CI)
P-value for Interaction
No. of participants/total no.
Primary outcome: eGFR decline ≥50%, ESKD, or kidney/CV death
Overall[1] 197/2152 312/2152 0.61 (0.51, 0.72)
Without CV disease 106/1339 175/1355 0.61 (0.48, 0.78) 0.90
With CV disease 91/813 137/797 0.61 (0.47, 0.79)
Secondary outcome: eGFR decline ≥50%, ESKD, or kidney death
Overall[1] 142/2152 243/2152 0.56 (0.45, 0.68)
Without CV disease 93/1339 154/1355 0.61 (0.47, 0.79) 0.29
With CV disease 49/813 89/797 0.49 (0.34, 0.69)
Secondary outcome: CV death or heart failure
Overall[1] 100/2152 138/2152 0.71 (0.55, 0.92)
Without CV disease 24/1339 36/1355 0.67 (0.40, 1.13) 0.88
With CV disease 76/813 102/797 0.70 (0.52, 0.94)
Secondary outcome: All-cause mortality
Overall[1] 101/2152 146/2152 0.69 (0.53, 0.88)
Without CV disease 33/1339 53/1355 0.63 (0.41, 0.98) 0.71
With CV disease 68/813 93/797 0.70 (0.51, 0.95)
0.2
0.5
1
2
Dapagliflozin Better
Placebo Better

Fig. 22

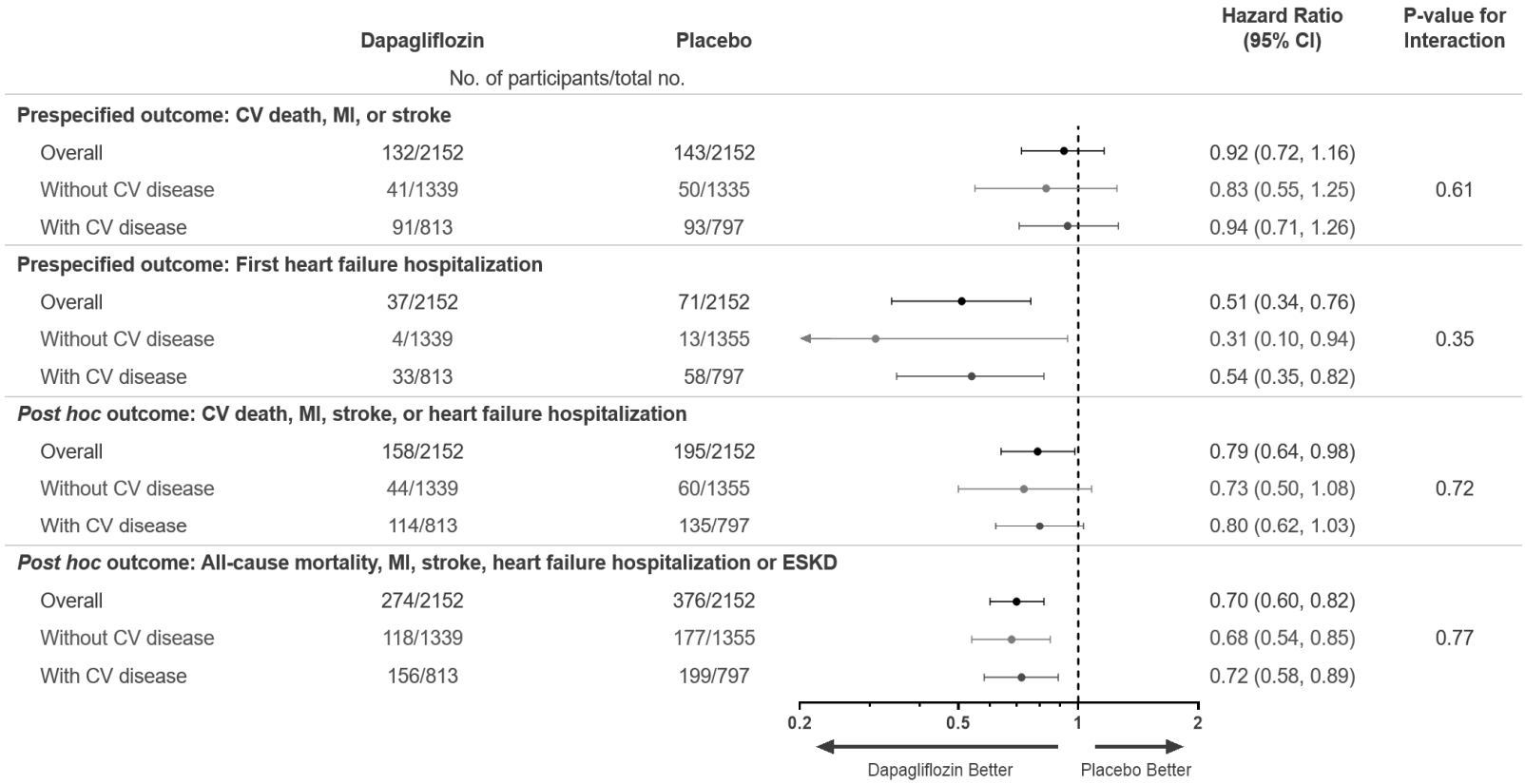
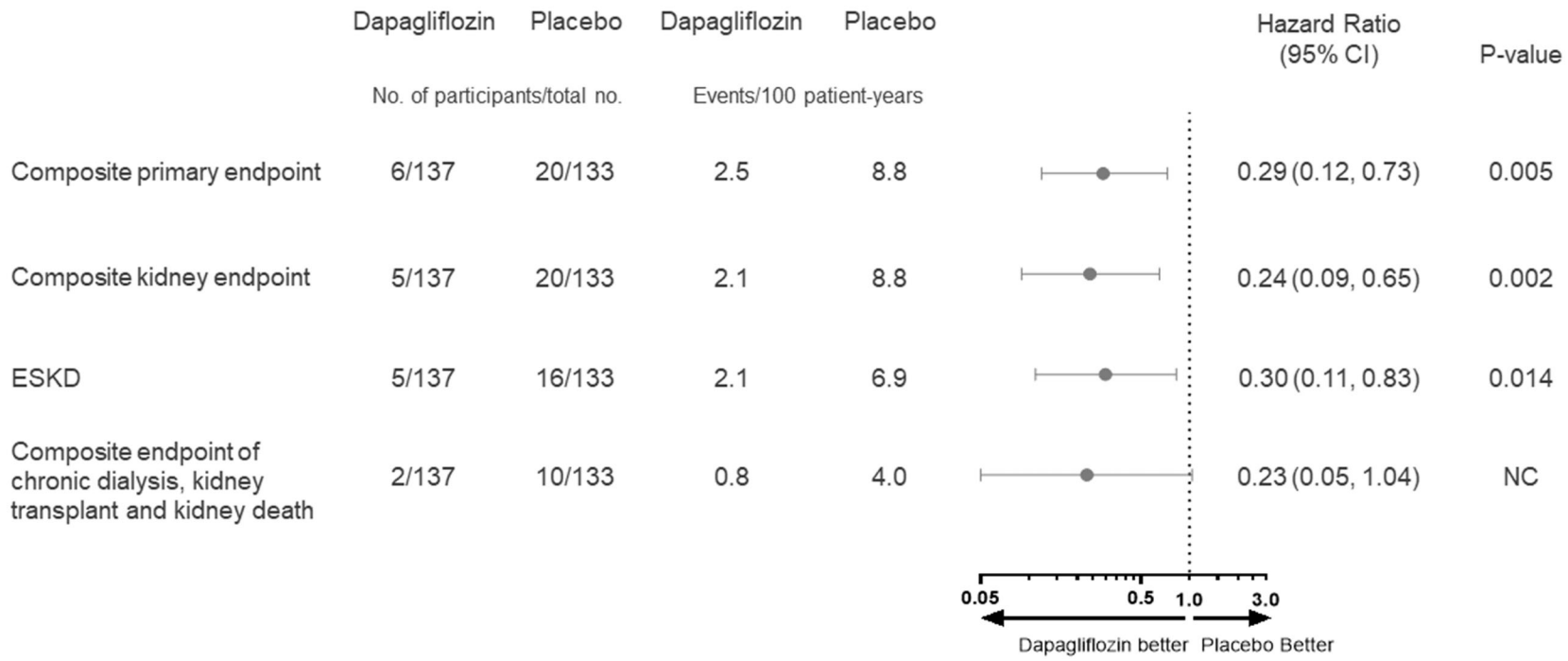

Dapagliflozin
Placebo
Hazard Ratio (95% CI)
P-value for Interaction
No. of participants/total no.
Prespecified outcome: CV death, MI, or stroke
Overall 132/2152 143/2152 0.92 (0.72, 1.16)
Without CV disease 41/1339 50/1335 0.83 (0.55, 1.25) 0.61
With CV disease 91/813 93/797 0.94 (0.71, 1.26)
Prespecified outcome: First heart failure hospitalization
Overall 37/2152 71/2152 0.51 (0.34, 0.76)
Without CV disease 4/1339 13/1355 0.31 (0.10, 0.94) 0.35
With CV disease 33/813 58/797 0.54 (0.35, 0.82)
Post hoc outcome: CV death, MI, stroke, or heart failure hospitalization
Overall 158/2152 195/2152 0.79 (0.64, 0.98)
Without CV disease 44/1339 60/1355 0.73 (0.50, 1.08) 0.72
With CV disease 114/813 135/797 0.80 (0.62, 1.03)
Post hoc outcome: All-cause mortality, MI, stroke, heart failure hospitalization or ESKD
Overall 274/2152 376/2152 0.70 (0.60, 0.82)
Without CV disease 118/1339 177/1355 0.68 (0.54, 0.85) 0.77
With CV disease 156/813 199/797 0.72 (0.58, 0.89)
0.2
0.5
1
2
Dapagliflozin Better
Placebo Better

Fig. 23



Composite primary endpoint: Composite of sustained ≥50% decline in eGFR, onset of ESKD, or death from a kidney or cardiovascular cause.
Composite renal endpoint: Composite of sustained ≥50% decline in eGFR, onset of ESKD, or death from a kidney cause.
ESKD: sustained eGFR <15/chronic dialysis/renal transplant
ESKD, end-stage kidney disease

Fig. 24

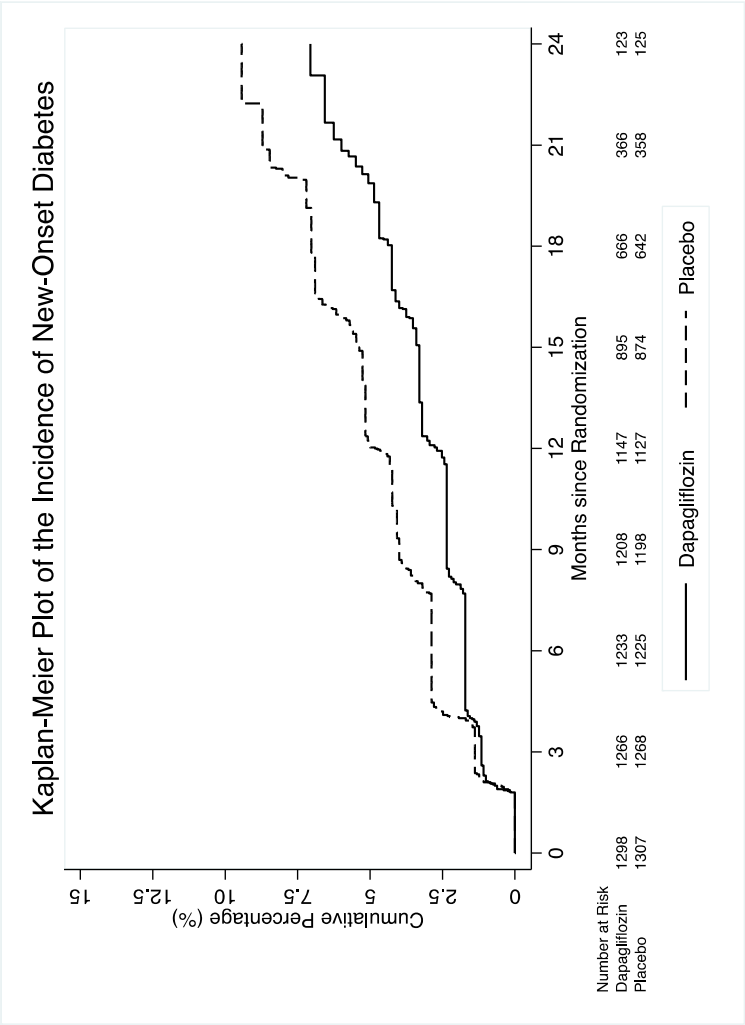

Kaplan-Meier Plot of the Incidence of New-Onset Diabetes
Cumulative Percentage (%)
0
2.5
5
7.5
10
12.5
15
0
3
6
9
12
15
18
21
24
Months since Randomization
Number at Risk
Dapagliflozin 1298 1266 1233 1208 1147 895 666 366 123
Placebo 1307 1268 1225 1198 1127 874 642 358 125
Dapagliflozin
Placebo

Fig. 25