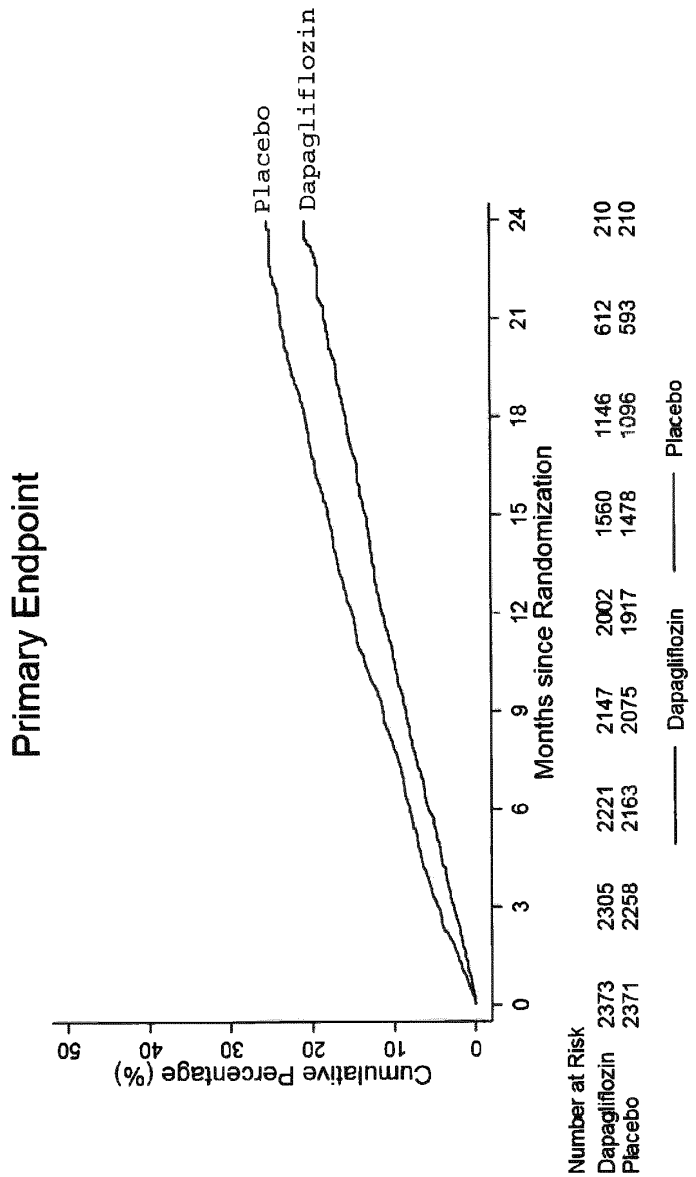
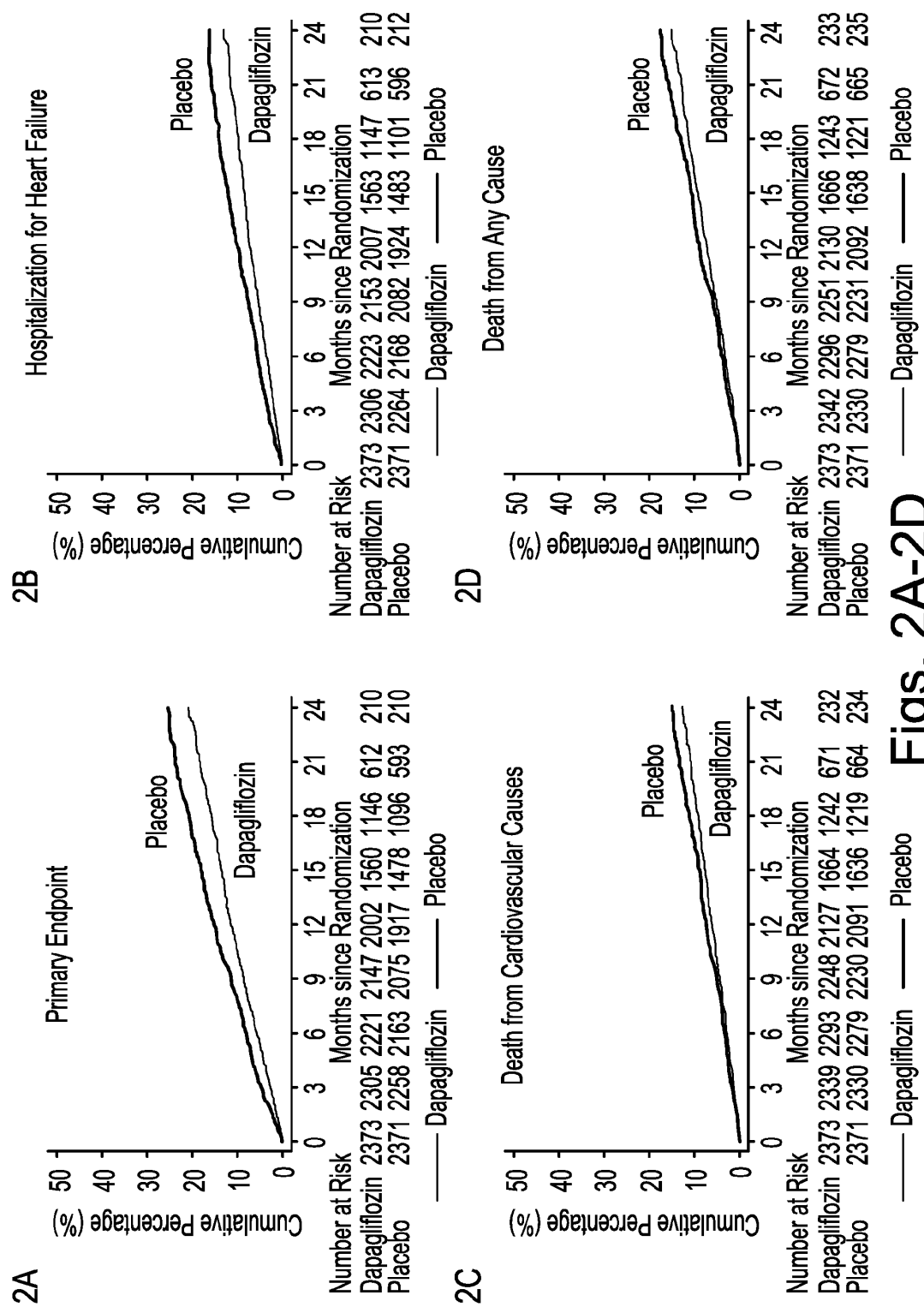

Primary Endpoint
Placebo
Dapagliflozin
Cumulative Percentage (%)
0
10
20
30
40
50
0
3
6
9
12
15
18
21
24
Months since Randomization
Number at Risk
Dapagliflozin 2373 2305 2221 2147 2002 1560 1146 612 210
Placebo 2371 2258 2163 2075 1917 1478 1096 593 210
Dapagliflozin
Placebo

Fig. 1


2A
Primary Endpoint
Cumulative Percentage (%)
50
40
30
20
10
0
Placebo
Dapagliflozin
0 3 6 9 12 15 18 21 24
Months since Randomization
Number at Risk
Dapagliflozin 2373 2305 2221 2147 2002 1560 1146 612 210
Placebo 2371 2258 2163 2075 1917 1478 1096 593 210
Dapagliflozin
Placebo
2B
Hospitalization for Heart Failure
Cumulative Percentage (%)
50
40
30
20
10
0
Placebo
Dapagliflozin
0 3 6 9 12 15 18 21 24
Months since Randomization
Number at Risk
Dapagliflozin 2373 2306 2223 2153 2007 1563 1147 613 210
Placebo 2371 2264 2168 2082 1924 1483 1101 596 212
Dapagliflozin
Placebo
2C
Death from Cardiovascular Causes
Cumulative Percentage (%)
50
40
30
20
10
0
Placebo
Dapagliflozin
0 3 6 9 12 15 18 21 24
Months since Randomization
Number at Risk
Dapagliflozin 2373 2339 2293 2248 2127 1664 1242 671 232
Placebo 2371 2330 2279 2230 2091 1636 1219 664 234
Dapagliflozin
Placebo
2D
Death from Any Cause
Cumulative Percentage (%)
50
40
30
20
10
0
Placebo
Dapagliflozin
0 3 6 9 12 15 18 21 24
Months since Randomization
Number at Risk
Dapagliflozin 2373 2342 2296 2251 2130 1666 1243 672 233
Placebo 2371 2330 2279 2231 2092 1638 1221 665 235
Dapagliflozin
Placebo

Figs. 2A-2D

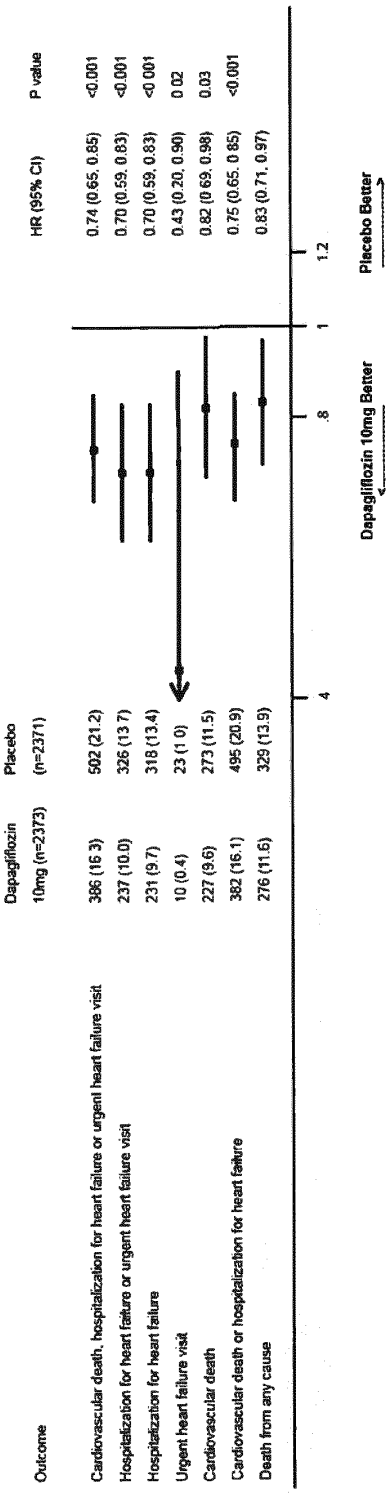

Outcome
Dapagliflozin 10mg (n=2373)
Placebo (n=2371)
HR (95% CI)
P value
Cardiovascular death, hospitalization for heart failure or urgent heart failure visit
386 (16 3)
502 (21.2)
0.74 (0.65, 0.85)
<0.001
Hospitalization for heart failure or urgent heart failure visit
237 (10.0)
326 (13 7)
0.70 (0.59, 0.83)
<0.001
Hospitalization for heart failure
231 (9.7)
318 (13.4)
0.70 (0.59, 0.83)
<0 001
Urgent heart failure visit
10 (0.4)
23 (1 0)
0.43 (0.20, 0.90)
0 02
Cardiovascular death
227 (9.6)
273 (11.5)
0.82 (0 69, 0.98)
0.03
Cardiovascular death or hospitalization for heart failure
382 (16.1)
495 (20.9)
0.75 (0.65, 0 85)
<0.001
Death from any cause
276 (11.6)
329 (13.9)
0.83 (0.71, 0.97)
.4
.8
1
1.2
Dapagliflozin 10mg Better
Placebo Better

Fig. 3

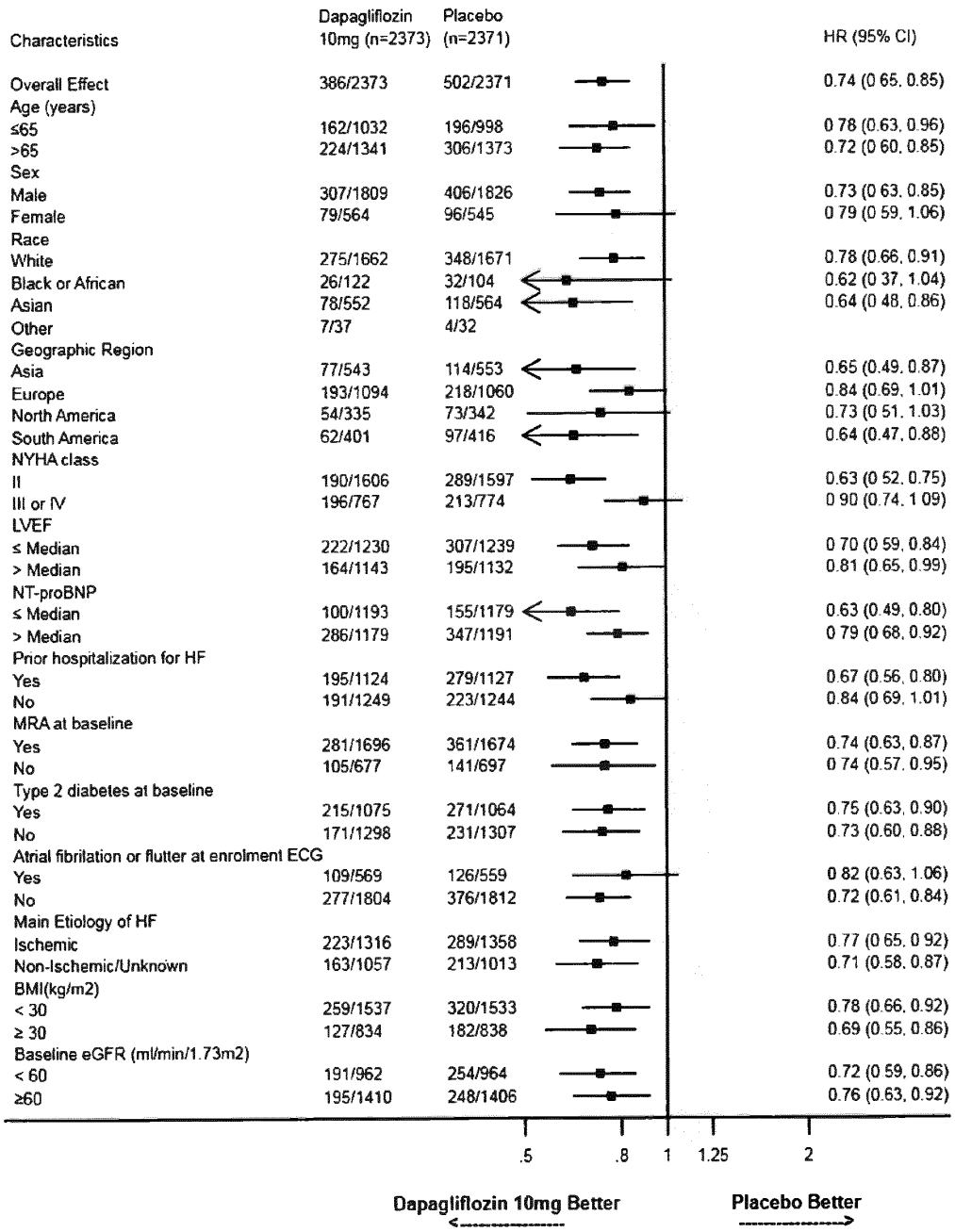

Characteristics
Dapagliflozin 10mg (n=2373)
Placebo (n=2371)
HR (95% CI)
Overall Effect 386/2373 502/2371 0.74 (0.65, 0.85)
Age (years)
≤65 162/1032 196/998 0.78 (0.63, 0.96)
>65 224/1341 306/1373 0.72 (0.60, 0.85)
Sex
Male 307/1809 406/1826 0.73 (0.63, 0.85)
Female 79/564 96/545 0.79 (0.59, 1.06)
Race
White 275/1662 348/1671 0.78 (0.66, 0.91)
Black or African 26/122 32/104 0.62 (0.37, 1.04)
Asian 78/552 118/564 0.64 (0.48, 0.86)
Other 7/37 4/32
Geographic Region
Asia 77/543 114/553 0.65 (0.49, 0.87)
Europe 193/1094 218/1060 0.84 (0.69, 1.01)
North America 54/335 73/342 0.73 (0.51, 1.03)
South America 62/401 97/416 0.64 (0.47, 0.88)
NYHA class
II 190/1606 289/1597 0.63 (0.52, 0.75)
III or IV 196/767 213/774 0.90 (0.74, 1.09)
LVEF
≤ Median 222/1230 307/1239 0.70 (0.59, 0.84)
> Median 164/1143 195/1132 0.81 (0.65, 0.99)
NT-proBNP
≤ Median 100/1193 155/1179 0.63 (0.49, 0.80)
> Median 286/1179 347/1191 0.79 (0.68, 0.92)
Prior hospitalization for HF
Yes 195/1124 279/1127 0.67 (0.56, 0.80)
No 191/1249 223/1244 0.84 (0.69, 1.01)
MRA at baseline
Yes 281/1696 361/1674 0.74 (0.63, 0.87)
No 105/677 141/697 0.74 (0.57, 0.95)
Type 2 diabetes at baseline
Yes 215/1075 271/1064 0.75 (0.63, 0.90)
No 171/1298 231/1307 0.73 (0.60, 0.88)
Atrial fibrilation or flutter at enrolment ECG
Yes 109/569 126/559 0.82 (0.63, 1.06)
No 277/1804 376/1812 0.72 (0.61, 0.84)
Main Etiology of HF
Ischemic 223/1316 289/1358 0.77 (0.65, 0.92)
Non-Ischemic/Unknown 163/1057 213/1013 0.71 (0.58, 0.87)
BMI(kg/m2)
< 30 259/1537 320/1533 0.78 (0.66, 0.92)
≥ 30 127/834 182/838 0.69 (0.55, 0.86)
Baseline eGFR (ml/min/1.73m2)
< 60 191/962 254/964 0.72 (0.59, 0.86)
≥60 195/1410 248/1406 0.76 (0.63, 0.92)
.5
.8
1
1.25
2
Dapagliflozin 10mg Better
Placebo Better

Fig. 4

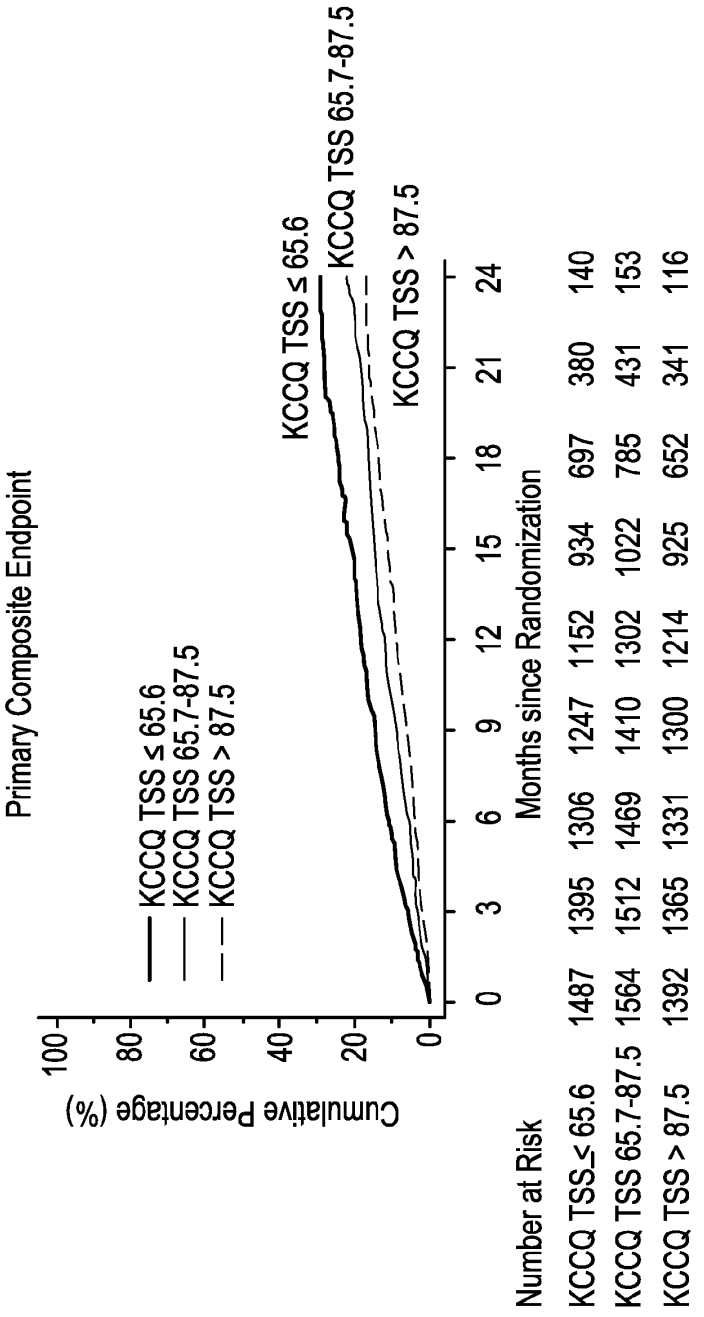

Primary Composite Endpoint
KCCQ TSS ≤ 65.6
KCCQ TSS 65.7-87.5
KCCQ TSS > 87.5
Cumulative Percentage (%)
100
80
60
40
20
0
0
3
6
9
12
15
18
21
24
Months since Randomization
Number at Risk
KCCQ TSS ≤ 65.6 1487 1395 1306 1247 1152 934 697 380 140
KCCQ TSS 65.7-87.5 1564 1512 1469 1410 1302 1022 785 431 153
KCCQ TSS > 87.5 1392 1365 1331 1300 1214 925 652 341 116

FIG. 5

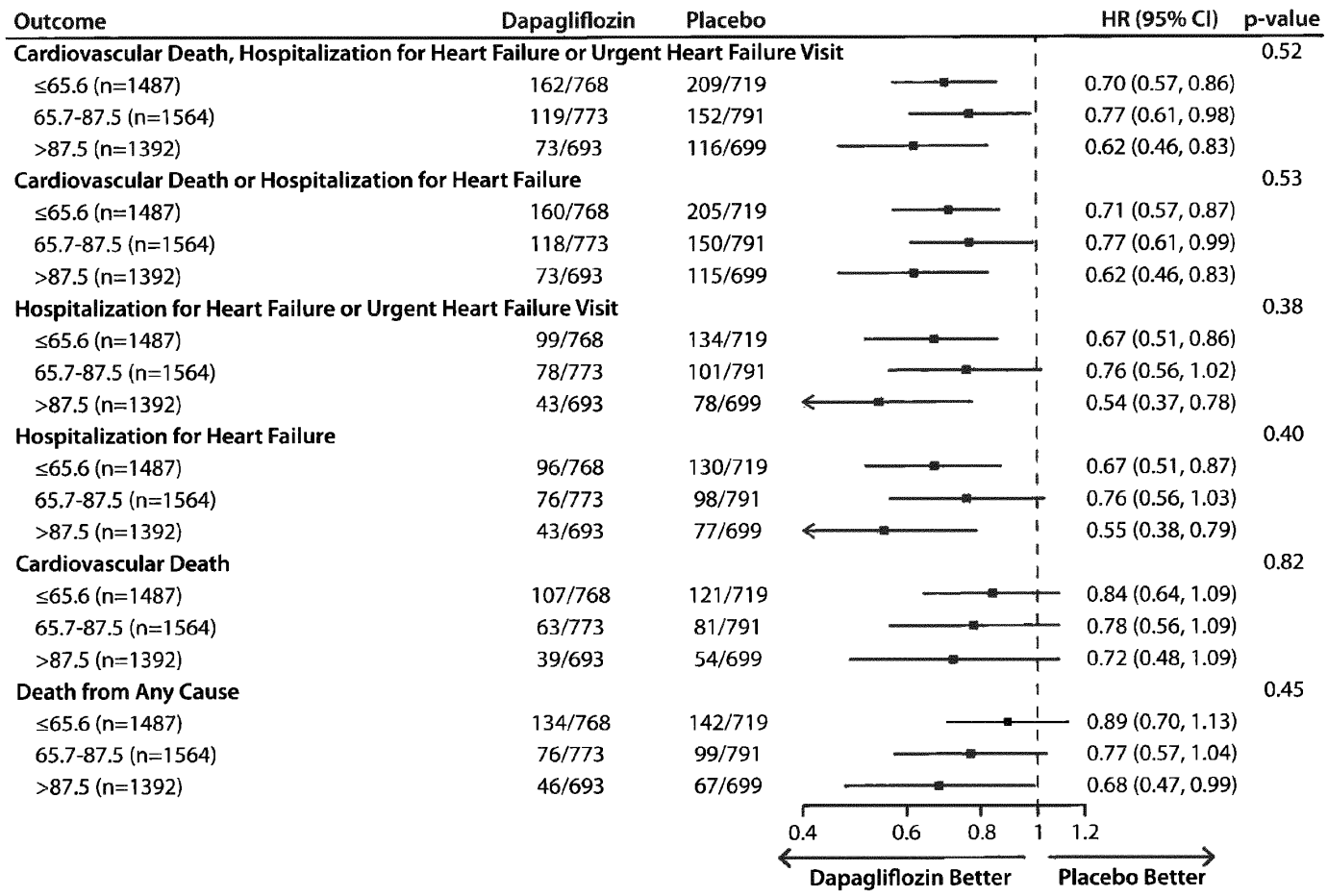

Outcome
Dapagliflozin
Placebo
HR (95% CI)
p-value
Cardiovascular Death, Hospitalization for Heart Failure or Urgent Heart Failure Visit
0.52
≤65.6 (n=1487)
162/768
209/719
0.70 (0.57, 0.86)
65.7-87.5 (n=1564)
119/773
152/791
0.77 (0.61, 0.98)
>87.5 (n=1392)
73/693
116/699
0.62 (0.46, 0.83)
Cardiovascular Death or Hospitalization for Heart Failure
0.53
≤65.6 (n=1487)
160/768
205/719
0.71 (0.57, 0.87)
65.7-87.5 (n=1564)
118/773
150/791
0.77 (0.61, 0.99)
>87.5 (n=1392)
73/693
115/699
0.62 (0.46, 0.83)
Hospitalization for Heart Failure or Urgent Heart Failure Visit
0.38
≤65.6 (n=1487)
99/768
134/719
0.67 (0.51, 0.86)
65.7-87.5 (n=1564)
78/773
101/791
0.76 (0.56, 1.02)
>87.5 (n=1392)
43/693
78/699
0.54 (0.37, 0.78)
Hospitalization for Heart Failure
0.40
≤65.6 (n=1487)
96/768
130/719
0.67 (0.51, 0.87)
65.7-87.5 (n=1564)
76/773
98/791
0.76 (0.56, 1.03)
>87.5 (n=1392)
43/693
77/699
0.55 (0.38, 0.79)
Cardiovascular Death
0.82
≤65.6 (n=1487)
107/768
121/719
0.84 (0.64, 1.09)
65.7-87.5 (n=1564)
63/773
81/791
0.78 (0.56, 1.09)
>87.5 (n=1392)
39/693
54/699
0.72 (0.48, 1.09)
Death from Any Cause
0.45
≤65.6 (n=1487)
134/768
142/719
0.89 (0.70, 1.13)
65.7-87.5 (n=1564)
76/773
99/791
0.77 (0.57, 1.04)
>87.5 (n=1392)
46/693
67/699
0.68 (0.47, 0.99)
0.4
0.6
0.8
1
1.2
Dapagliflozin Better
Placebo Better

FIG. 6

Fig. 7A KCCQ Total Symptom Score

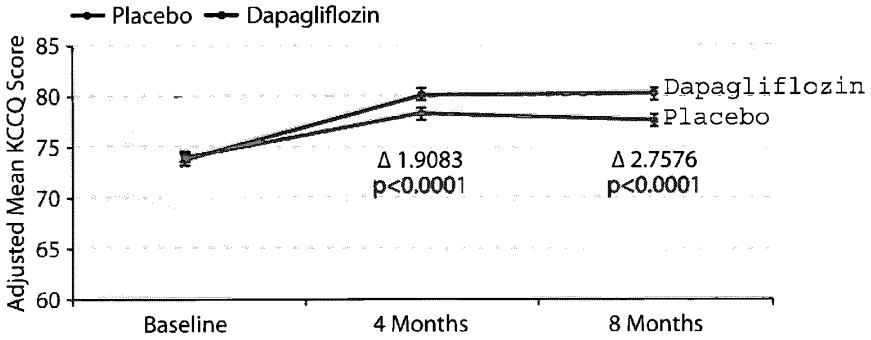


FIG. 7B KCCQ Clinical Summary Score

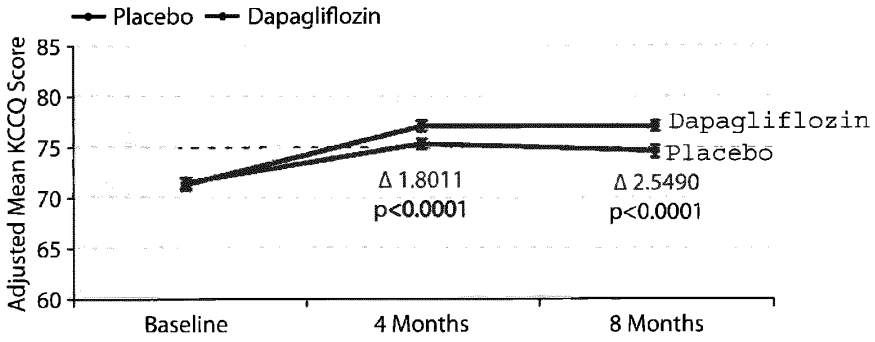


FIG. 7C KCCQ Overall Summary Score

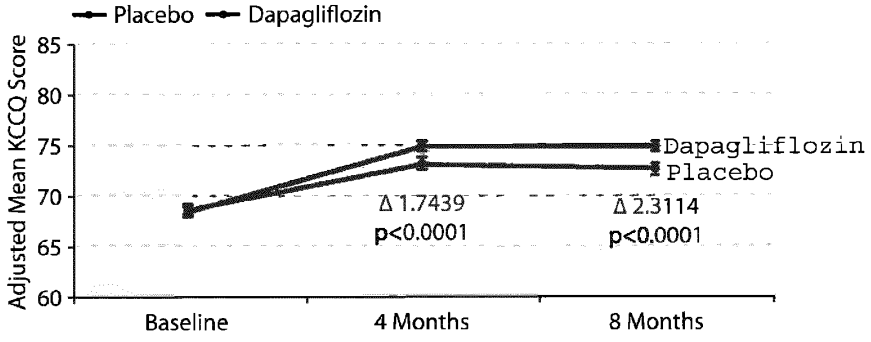


FIG. 8A KCCQ Total Symptom Score

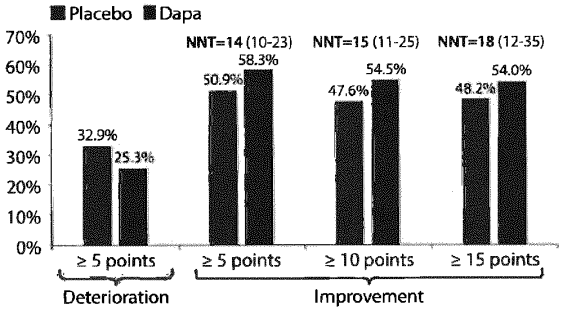


FIG. 8B KCCQ Total Symptom Score

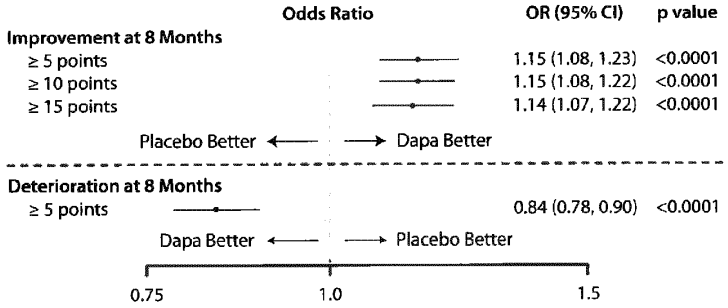


FIG. 8C KCCQ Clinical Summary Score

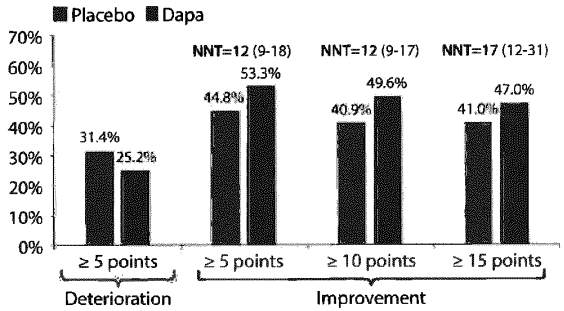


FIG. 8D KCCQ Clinical Summary Score

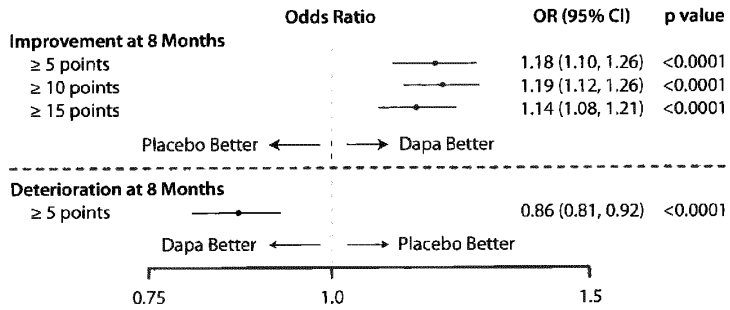


FIG. 8E KCCQ Overall Summary Score

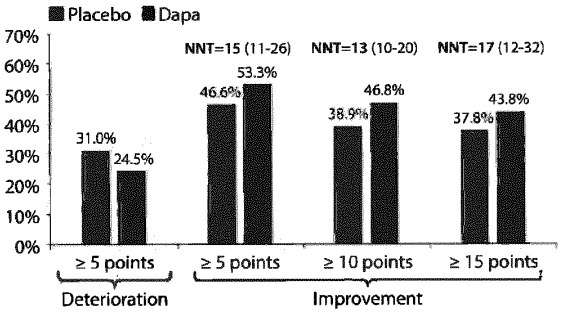


FIG. 8F KCCQ Overall Summary Score

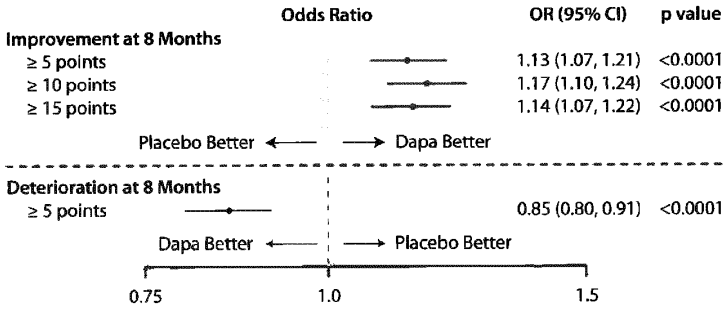
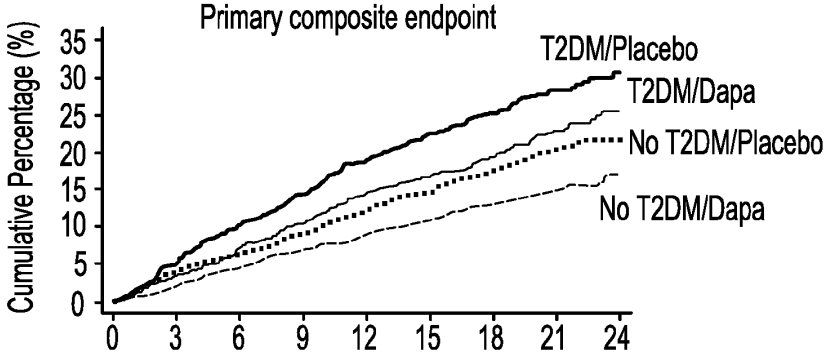


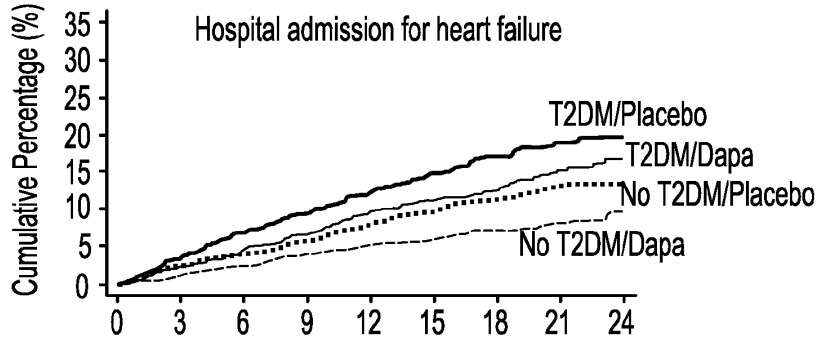
FIG. 9
Primary composite endpoint, hospital admission for worsening heart failure, death from cardiovascular causes and death from all causes, according to diabetes status at baseline



Number at Risk									
No T2DM/Dapagliflozin	1298	1268	1227	1192	1126	882	646	353	122
No T2DM/Placebo	1307	1253	1214	1176	1101	848	627	340	121
T2DM/Dapagliflozin	1075	1037	994	955	876	678	500	259	88
T2DM/Placebo	1064	1005	949	899	816	630	469	253	89

------- No T2DM/Dapagliflozin ····· No T2DM/Placebo
——— T2DM/Dapagliflozin ——— T2DM/Placebo

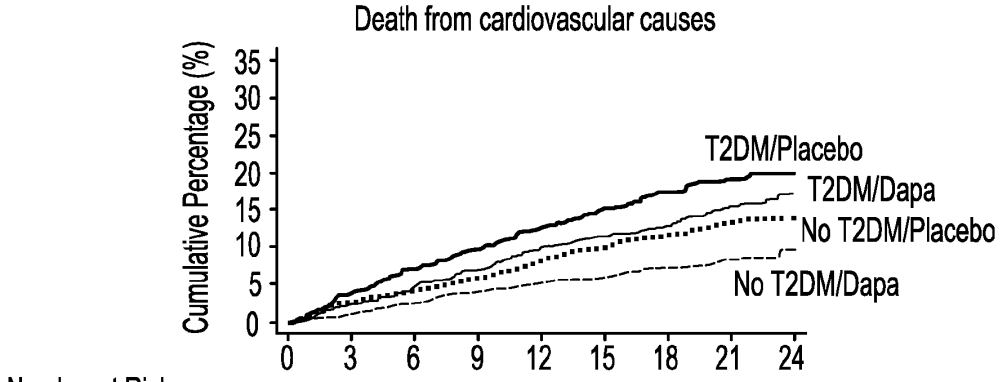
FIG. 9A



Number at Risk									
No T2DM/Dapagliflozin	1298	1268	1227	1194	1128	882	646	353	122
No T2DM/Placebo	1307	1255	1217	1181	1105	851	631	342	122
T2DM/Dapagliflozin	1075	1038	996	959	879	681	501	260	88
T2DM/Placebo	1064	1009	951	901	819	632	470	254	90

------- No T2DM/Dapagliflozin ····· No T2DM/Placebo
——— T2DM/Dapagliflozin ——— T2DM/Placebo

FIG. 9B

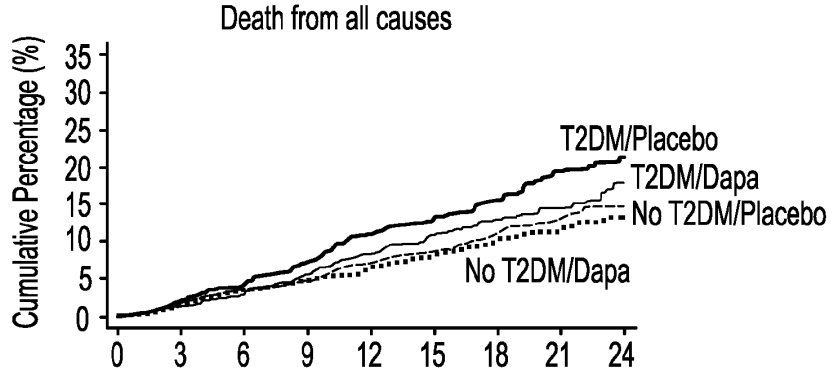


Number at Risk

No T2DM/Dapagliflozin	1298	1268	1227	1192	1126	882	646	353	122
No T2DM/Placebo	1307	1253	1214	1176	1101	848	627	340	121
T2DM/Dapagliflozin	1075	1037	994	955	876	678	500	259	88
T2DM/Placebo	1064	1005	949	899	816	630	469	253	89

------- No T2DM/Dapagliflozin ····· No T2DM/Placebo
——— T2DM/Dapagliflozin —— T2DM/Placebo

FIG. 9C



Number at Risk

No T2DM/Dapagliflozin	1298	1281	1254	1235	1178	926	691	377	129
No T2DM/Placebo	1307	1286	1260	1245	1181	920	686	379	133
T2DM/Dapagliflozin	1075	1061	1042	1016	952	740	552	295	104
T2DM/Placebo	1064	1044	1019	986	911	718	535	286	102

------- No T2DM/Dapagliflozin ····· No T2DM/Placebo
——— T2DM/Dapagliflozin —— T2DM/Placebo

FIG. 9D

FIG. 10A Effect of dapagliflozin on the primary endpoint in patients with and without diabetes and according to glycated haemoglobin level in patients without diabetes.

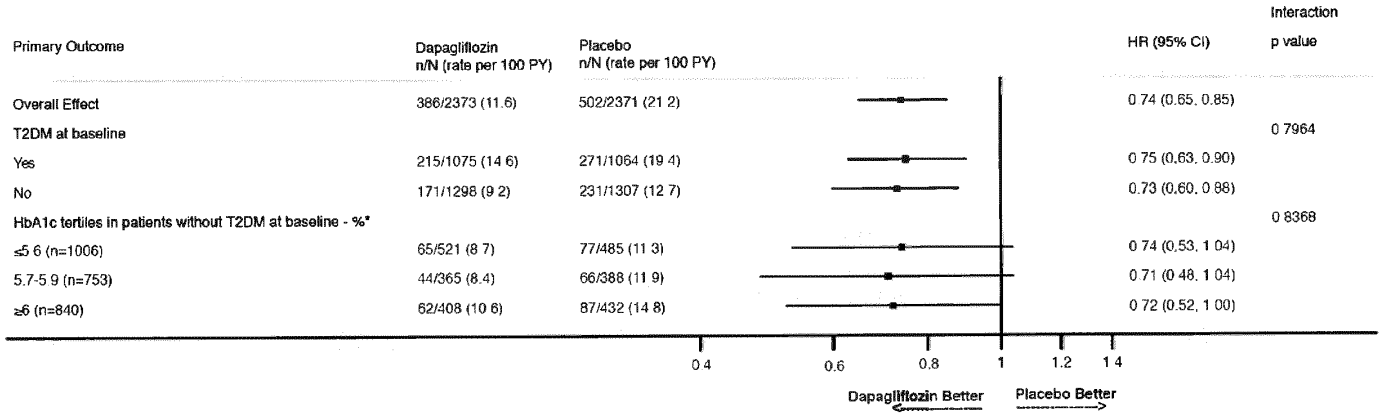


FIG. 10B Effect of dapagliflozin, compared with placebo on the prespecified primary and secondary composite outcomes, their components and all-cause mortality, according to diabetes status at baseline.

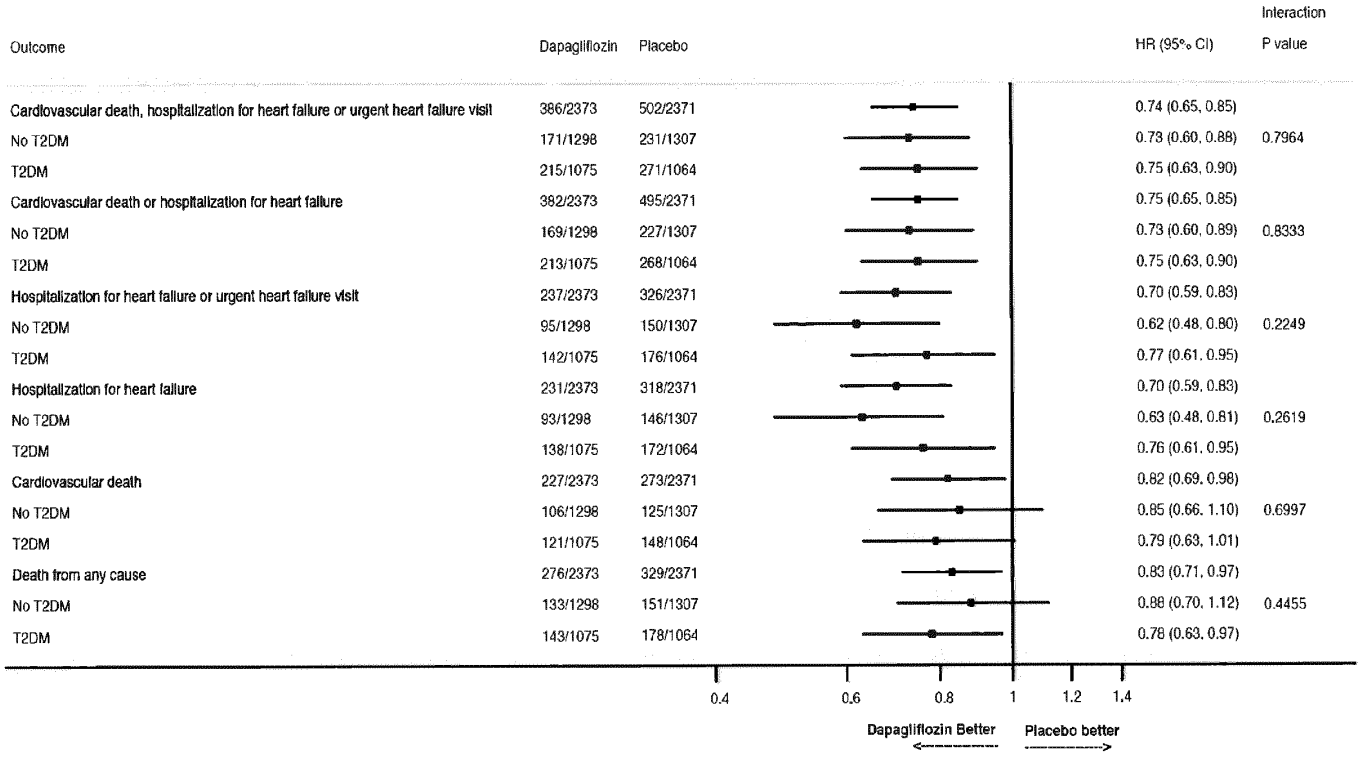


FIG. 11A

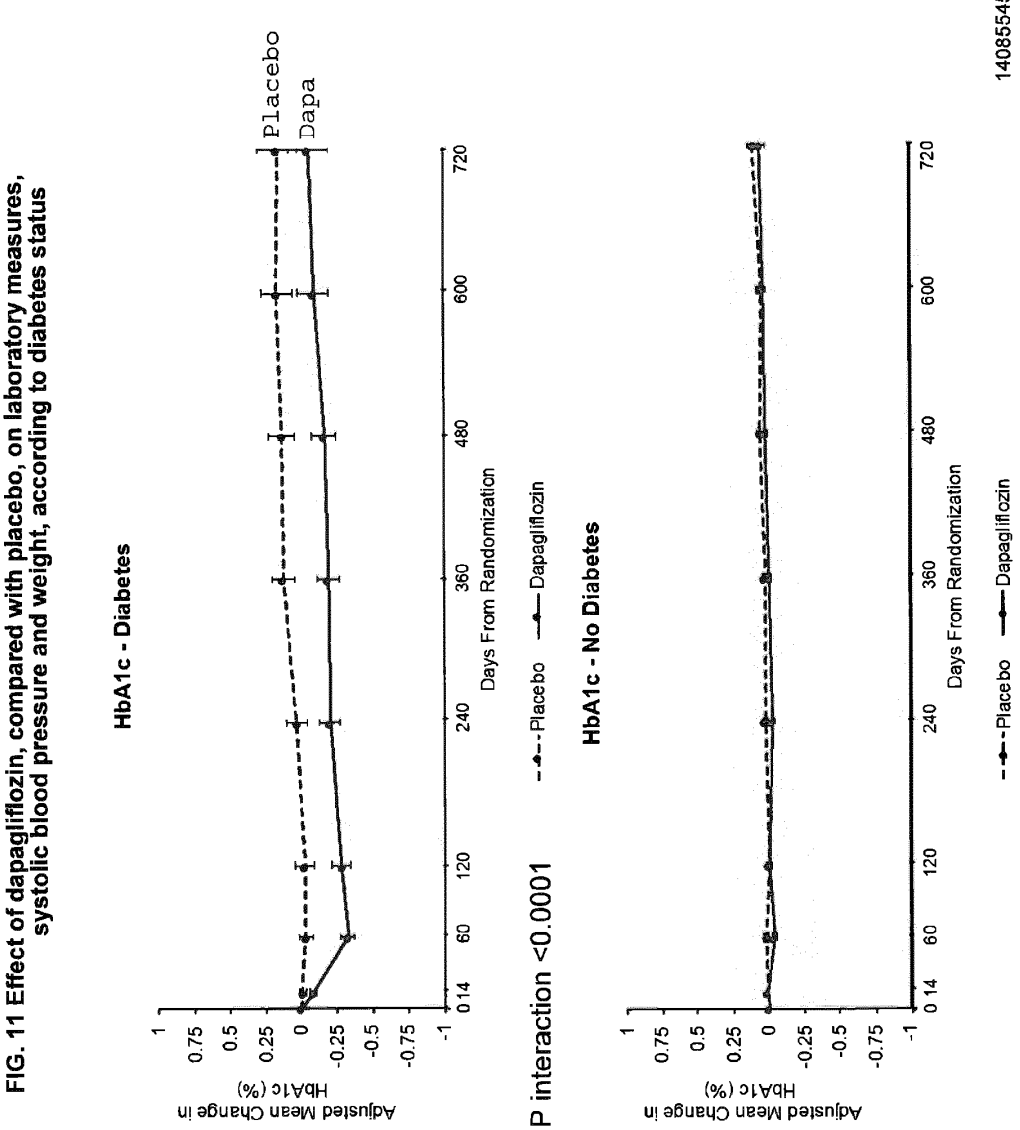
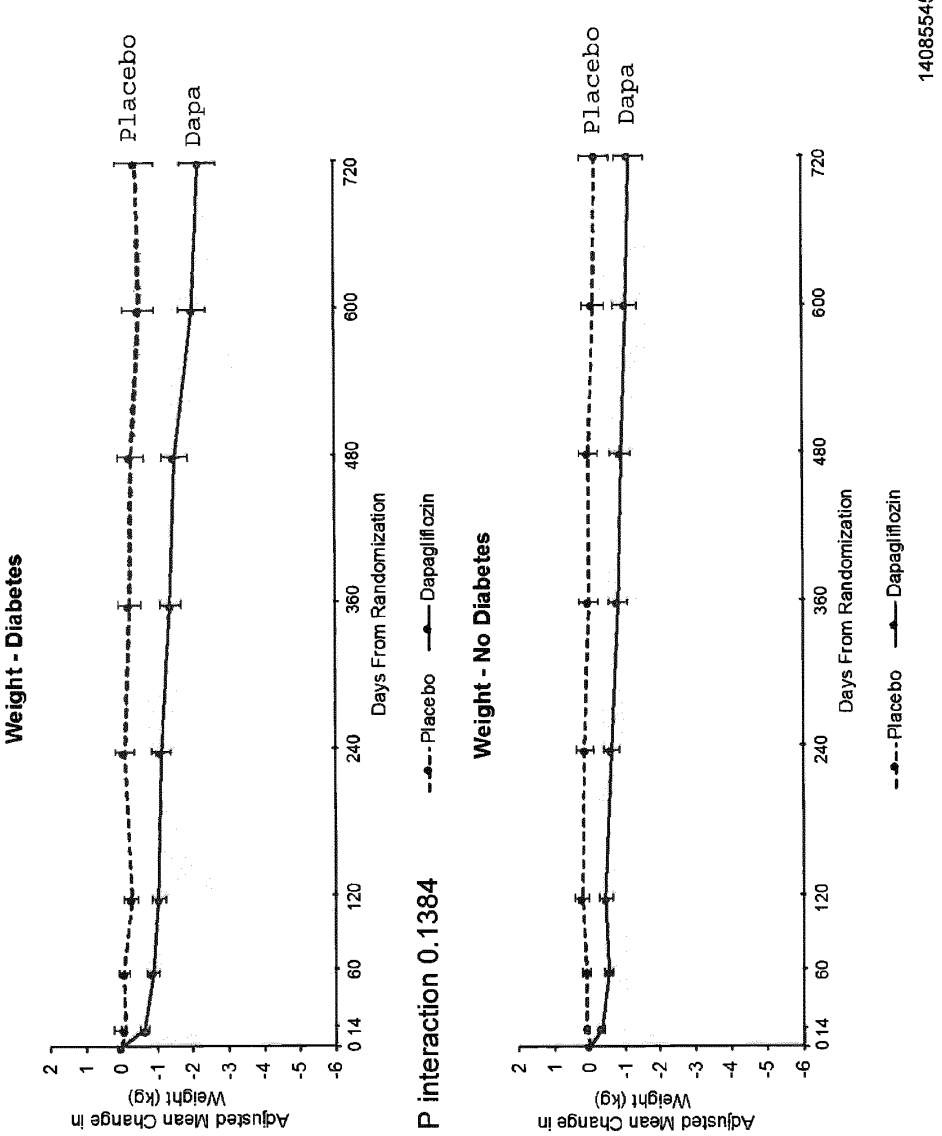

FIG. 11 Effect of dapagliflozin, compared with placebo, on laboratory measures, systolic blood pressure and weight, according to diabetes status
HbA1c - Diabetes
Placebo
Dapa
Adjusted Mean Change in HbA1c (%)
1
0.75
0.5
0.25
0
-0.25
-0.5
-0.75
-1
0 14
60
120
240
360
480
600
720
Days From Randomization
Placebo
Dapagliflozin
P interaction <0.0001
HbA1c - No Diabetes
Adjusted Mean Change in HbA1c (%)
Days From Randomization
Placebo
Dapagliflozin
14085545_1 / 10

FIG. 11B



14085545_1 / 11

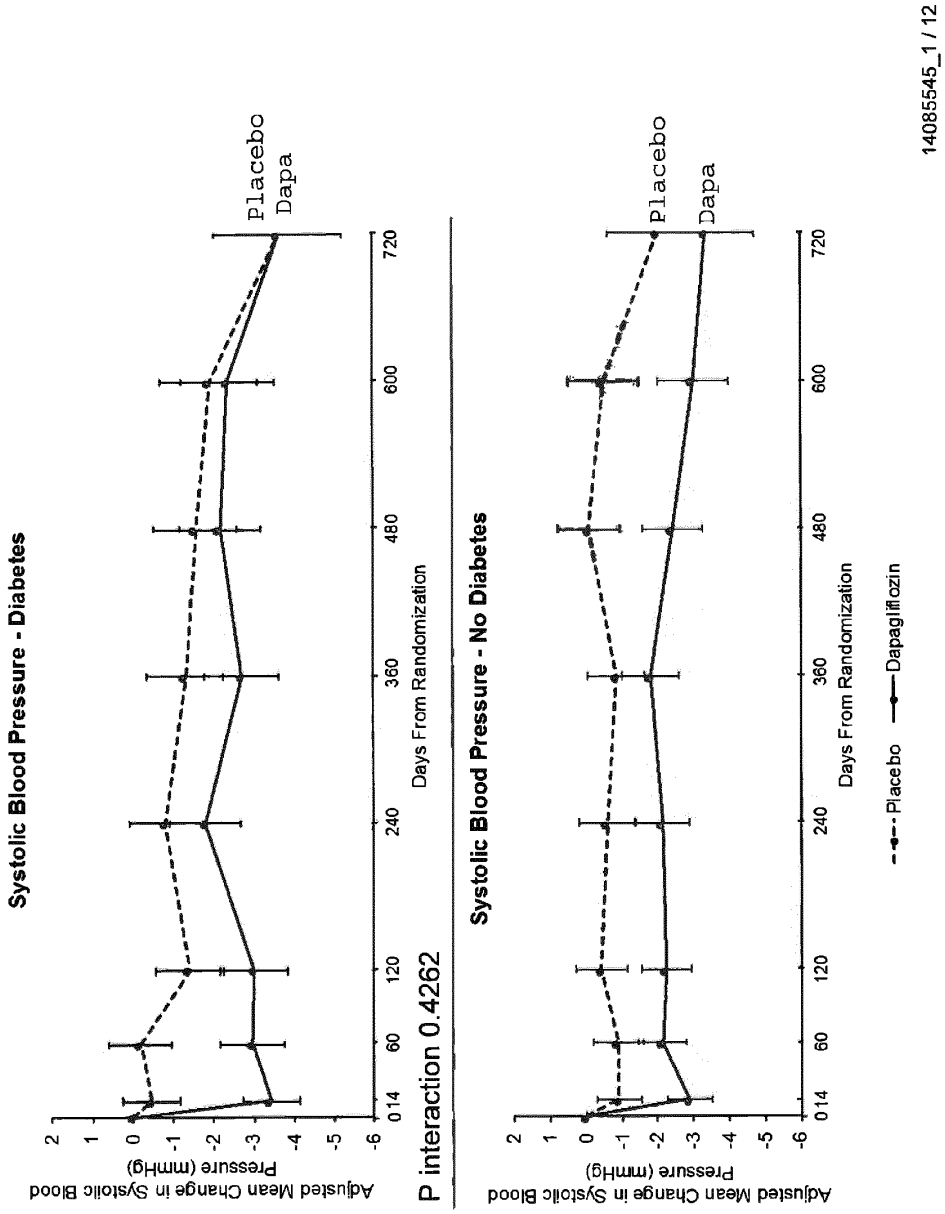

Systolic Blood Pressure - Diabetes
Adjusted Mean Change in Systolic Blood Pressure (mmHg)
2
1
0
-1
-2
-3
-4
-5
-6
0 14 60 120 240 360 480 600 720
Days From Randomization
Placebo
Dapa
P interaction 0.4262
Systolic Blood Pressure - No Diabetes
Adjusted Mean Change in Systolic Blood Pressure (mmHg)
2
1
0
-1
-2
-3
-4
-5
-6
0 14 60 120 240 360 480 600 720
Days From Randomization
Placebo
Dapa
Placebo
Dapagliflozin
14085545_1 / 12

FIG. 11C

FIG. 11D

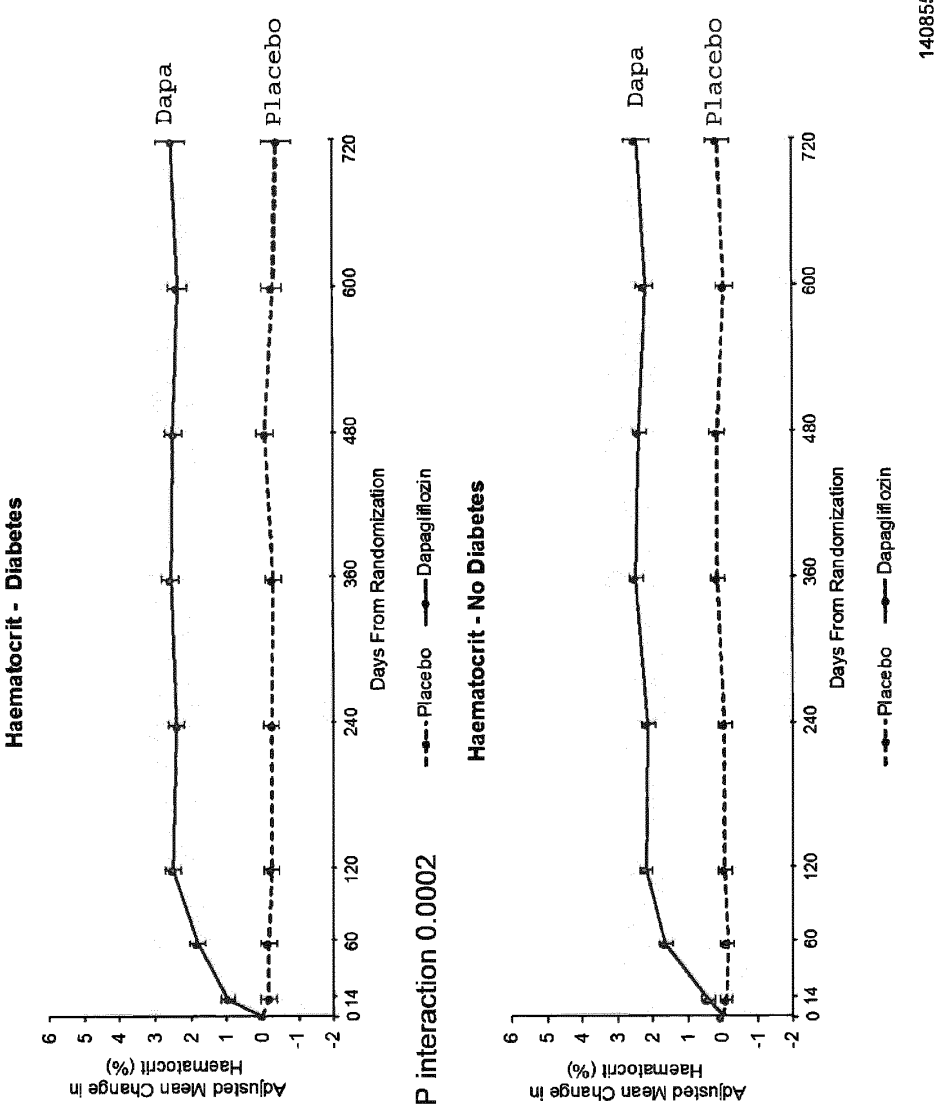

Haematocrit - Diabetes
Adjusted Mean Change in Haematocrit (%)
6
5
4
3
2
1
0
-1
-2
0 14 60 120 240 360 480 600 720
Days From Randomization
Dapa
Placebo
Placebo
Dapagliflozin
P interaction 0.0002
Haematocrit - No Diabetes
Adjusted Mean Change in Haematocrit (%)
Dapa
Placebo
Placebo
Dapagliflozin
14085545_1 / 13

FIG. 11E

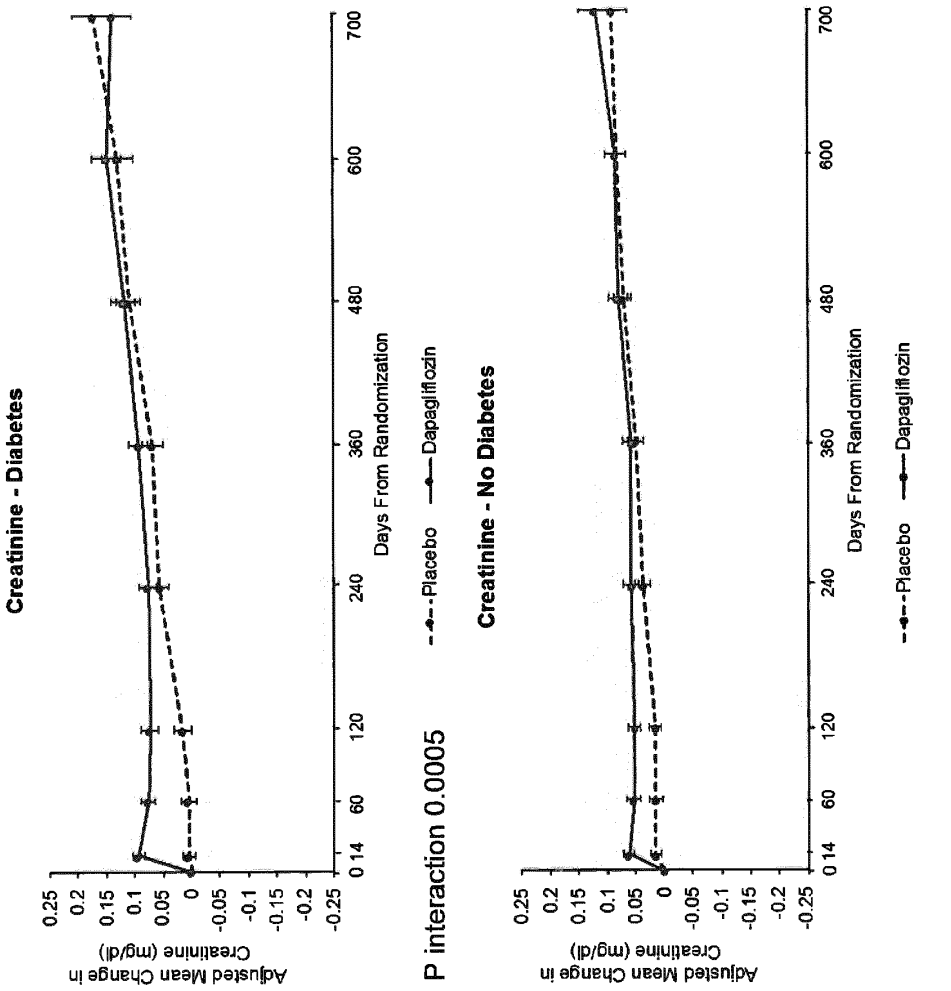

Creatinine - Diabetes
Adjusted Mean Change in Creatinine (mg/dl)
0.25
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
-0.25
0 14 60 120 240 360 480 600 700
Days From Randomization
Placebo
Dapagliflozin
P interaction 0.0005
Creatinine - No Diabetes
Adjusted Mean Change in Creatinine (mg/dl)
0.25
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
-0.25
0 14 60 120 240 360 480 600 700
Days From Randomization
Placebo
Dapagliflozin

FIG. 12 Outcomes according to baseline flycated haemoglobin level (as a continuous variable)

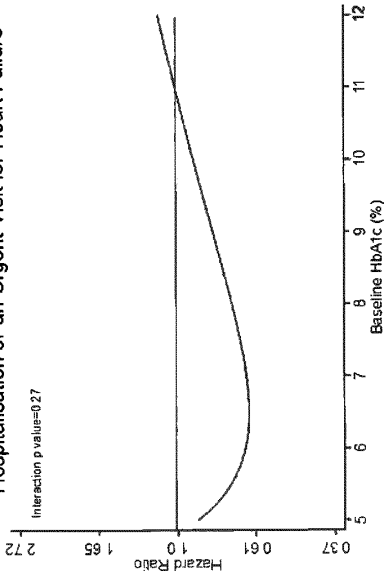


FIG. 12A

FIG. 12B

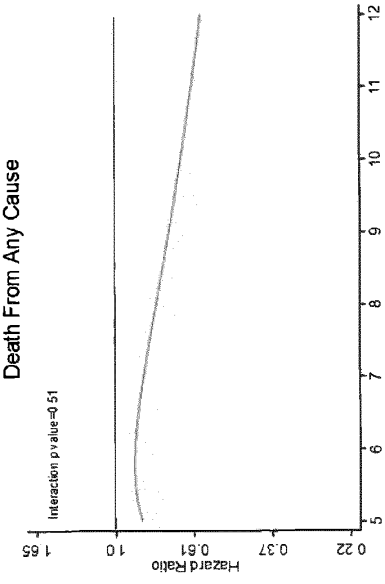


FIG. 12C

FIG. 12D

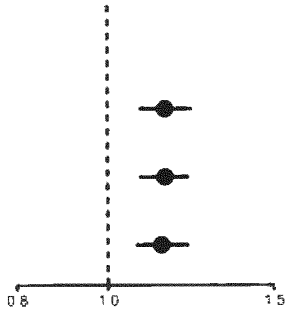
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Consistent symptom benefit irrespective of threshold on KCCQ-TSS, 8 months

Responder analysis

KCCQ-TSS Win Ratio = 1.18 (CI 1.11, 1.26), P<0.0001

	Dapa 10 mg (N=2086)	Placebo (N=2062)	OR (95%CI)
Improvement			
5 or more points	1198 (57.4%)	1030 (50.0%)	1.15 (1.08, 1.23)
10 or more points	1124 (53.9%)	968 (46.9%)	1.15 (1.08, 1.22)
15 or more points	1120 (53.7%)	984 (47.7%)	1.14 (1.07, 1.22)



	Dapa 10 mg (N=2086)	Placebo (N=2062)	OR (95%CI)
Deterioration			
5 or more points	524 (25.1%)	682 (33.1%)	0.84 (0.78, 0.90)
10 or more points	385 (18.5%)	495 (24.0%)	0.85 (0.79, 0.92)

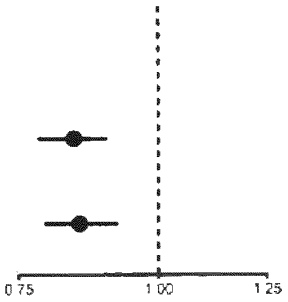


FIG. 13

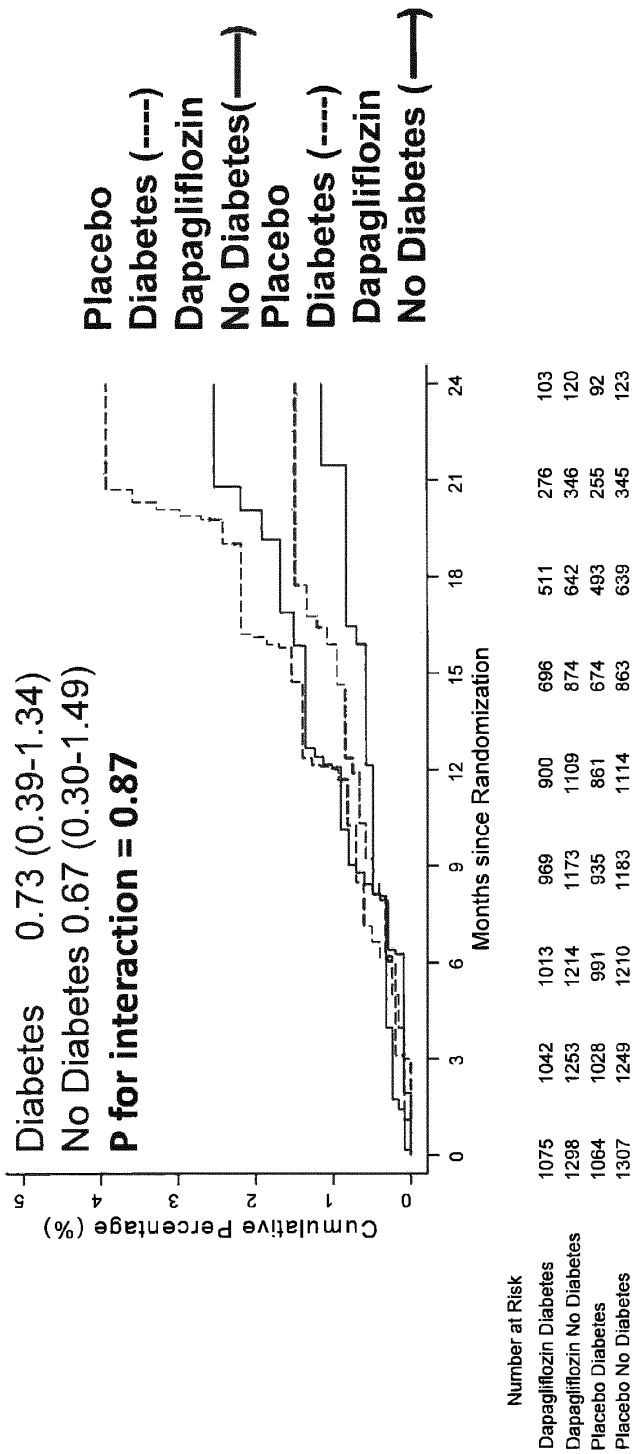

Placebo
Diabetes (----)
Dapagliflozin
No Diabetes(——)
Placebo
Diabetes (----)
Dapagliflozin
No Diabetes (——)
Diabetes 0.73 (0.39-1.34)
No Diabetes 0.67 (0.30-1.49)
P for interaction = 0.87
Cumulative Percentage (%)
0
1
2
3
4
5
0
3
6
9
12
15
18
21
24
Months since Randomization
Number at Risk
Dapagliflozin Diabetes 1075 1042 1013 969 900 696 511 276 103
Dapagliflozin No Diabetes 1298 1253 1214 1173 1109 874 642 346 120
Placebo Diabetes 1064 1028 991 935 861 674 493 255 92
Placebo No Diabetes 1307 1249 1210 1183 1114 863 639 345 123

FIG. 14

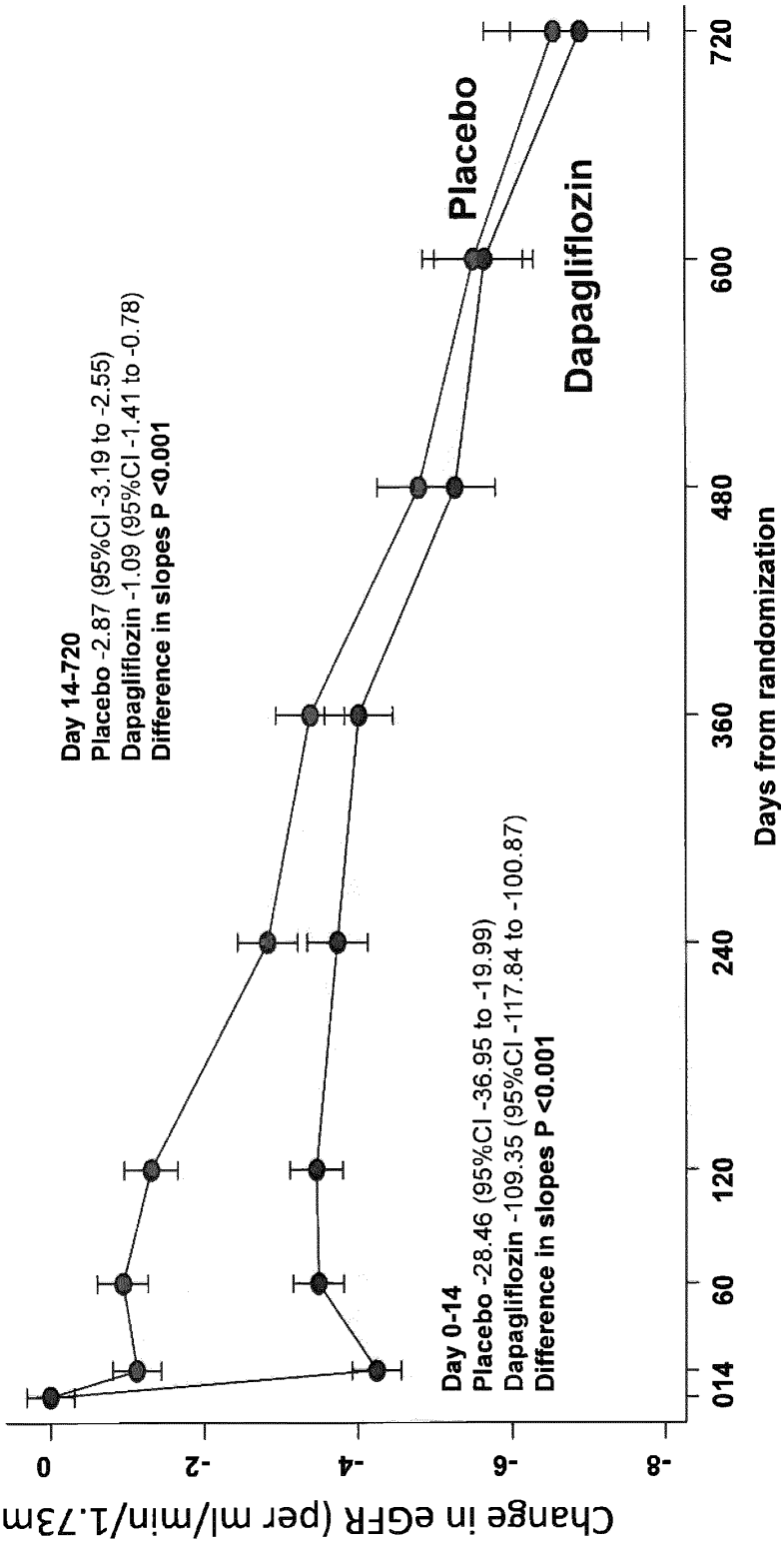

Change in eGFR (per ml/min/1.73m)
0
-2
-4
-6
-8
014
60
120
240
360
480
600
720
Days from randomization
Placebo
Dapagliflozin
Day 0-14
Placebo -28.46 (95%CI -36.95 to -19.99)
Dapagliflozin -109.35 (95%CI -117.84 to -100.87)
Difference in slopes P <0.001
Day 14-720
Placebo -2.87 (95%CI -3.19 to -2.55)
Dapagliflozin -1.09 (95%CI -1.41 to -0.78)
Difference in slopes P <0.001

FIG. 15

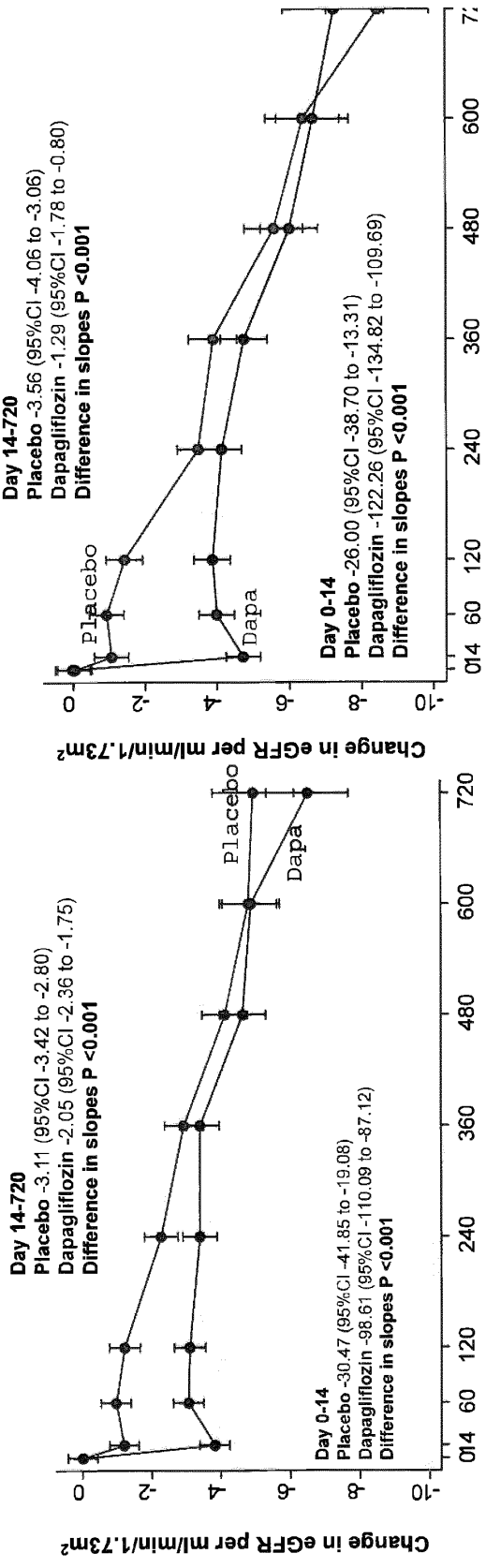

Change in eGFR per ml/min/1.73m²
Day 14-720
Placebo -3.11 (95%CI -3.42 to -2.80)
Dapagliflozin -2.05 (95%CI -2.36 to -1.75)
Difference in slopes P <0.001
Day 0-14
Placebo -30.47 (95%CI -41.85 to -19.08)
Dapagliflozin -98.61 (95%CI -110.09 to -87.12)
Difference in slopes P <0.001
Placebo
Dapa
Days from randomization
No Diabetes at Baseline
Change in eGFR per ml/min/1.73m²
Day 14-720
Placebo -3.56 (95%CI -4.06 to -3.06)
Dapagliflozin -1.29 (95%CI -1.78 to -0.80)
Difference in slopes P <0.001
Day 0-14
Placebo -26.00 (95%CI -38.70 to -13.31)
Dapagliflozin -122.26 (95%CI -134.82 to -109.69)
Difference in slopes P <0.001
Placebo
Dapa
Days from randomization
Diabetes at Baseline

FIG. 16

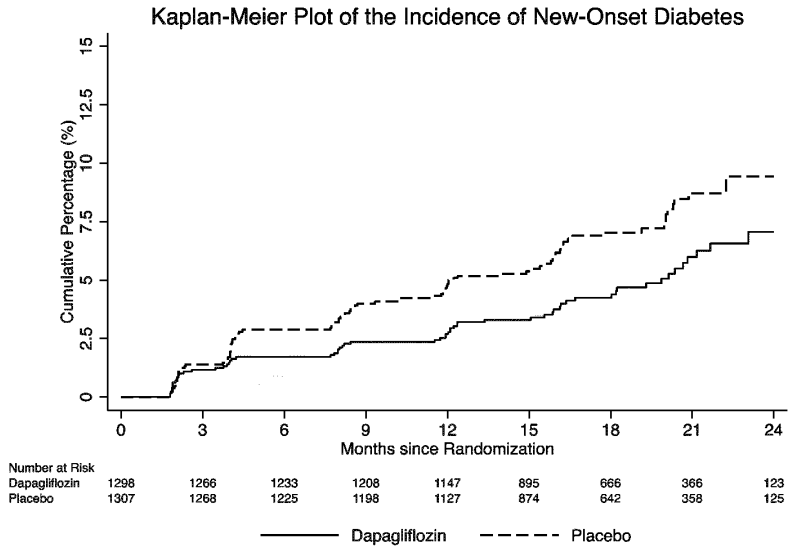

Kaplan-Meier Plot of the Incidence of New-Onset Diabetes
Cumulative Percentage (%)
0
2.5
5
7.5
10
12.5
15
0
3
6
9
12
15
18
21
24
Months since Randomization
Number at Risk
Dapagliflozin 1298 1266 1233 1208 1147 895 666 366 123
Placebo 1307 1268 1225 1198 1127 874 642 358 125
Dapagliflozin
Placebo

FIG. 17

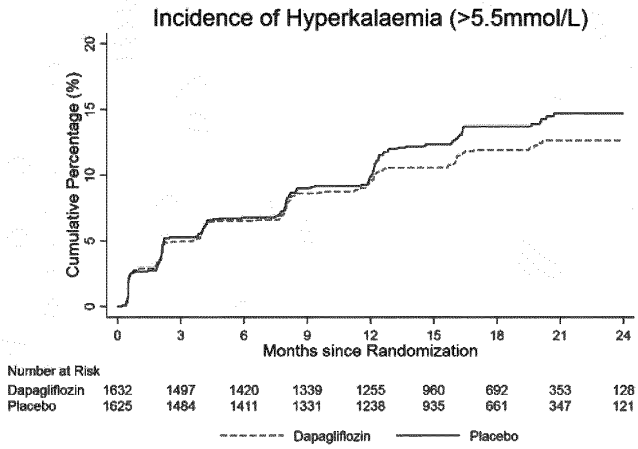


Fig. 18A

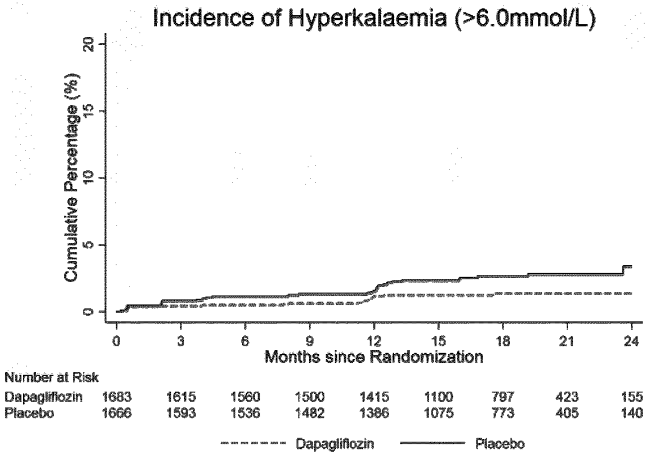


Fig. 18B