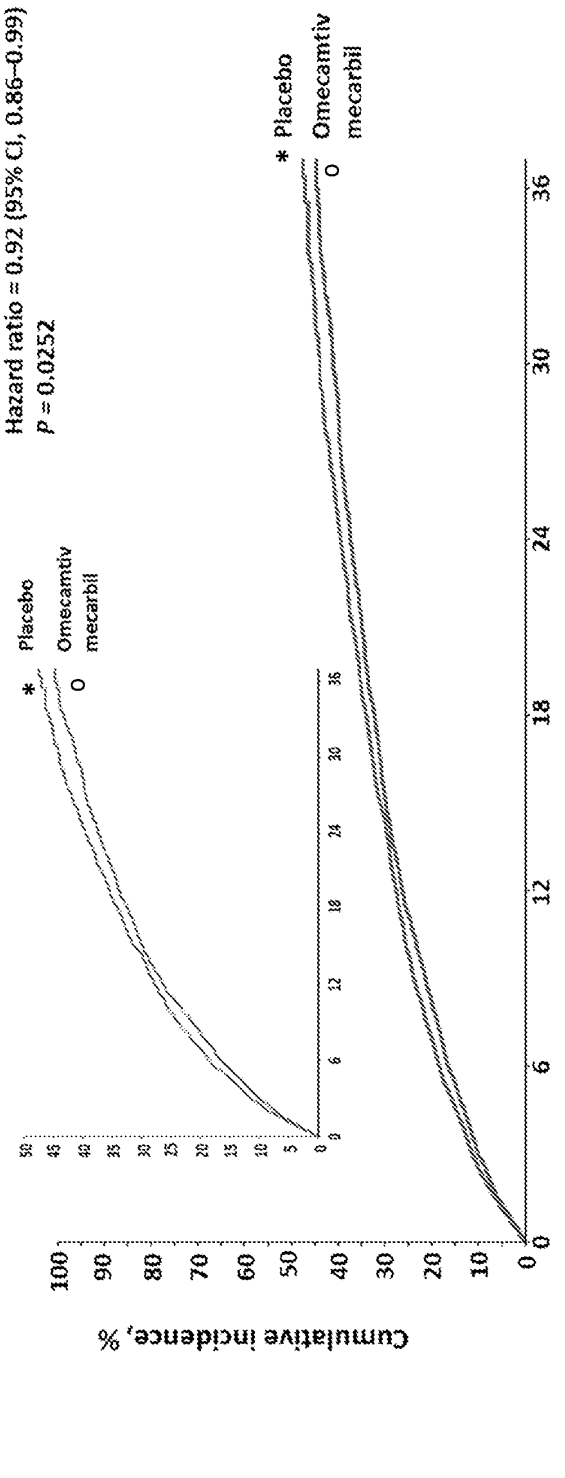

Hazard ratio = 0.92 (95% CI, 0.86–0.99)
P = 0.0252
* Placebo
O Omecamtiv mecarbil
Cumulative incidence, %
Months (30 days) since randomization
Patients at risk, n
* Placebo 4112 3310 2889 2102 1349 647 141
O Omecamtiv mecarbil 4120 3391 2953 2158 1430 700 164

FIGURE 1A

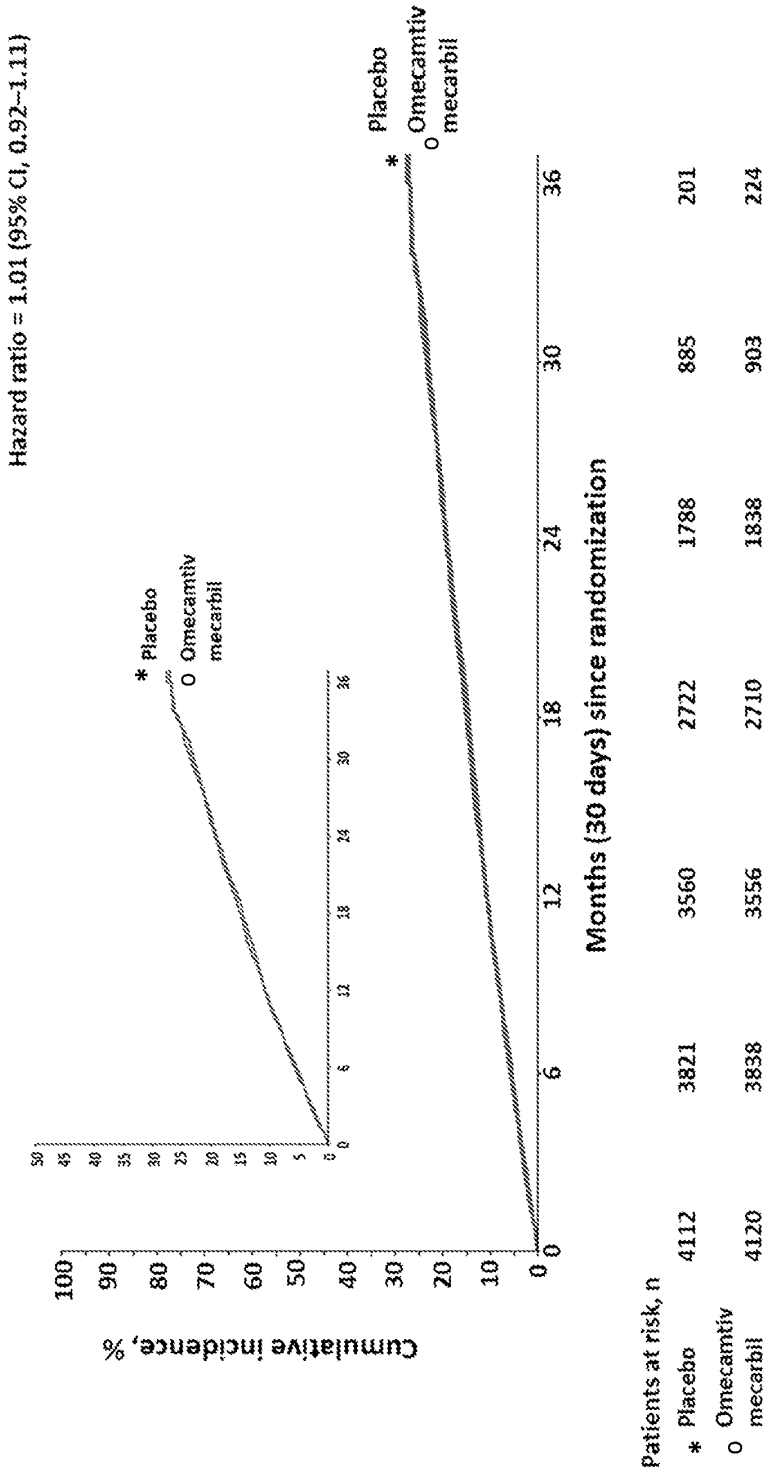

Hazard ratio = 1.01 (95% CI, 0.92–1.11)
* Placebo
O Omecamtiv mecarbil
Cumulative incidence, %
Months (30 days) since randomization
Patients at risk, n
* Placebo 4112 3821 3560 2722 1788 885 201
O Omecamtiv mecarbil 4120 3838 3556 2710 1838 903 224

FIGURE 1B

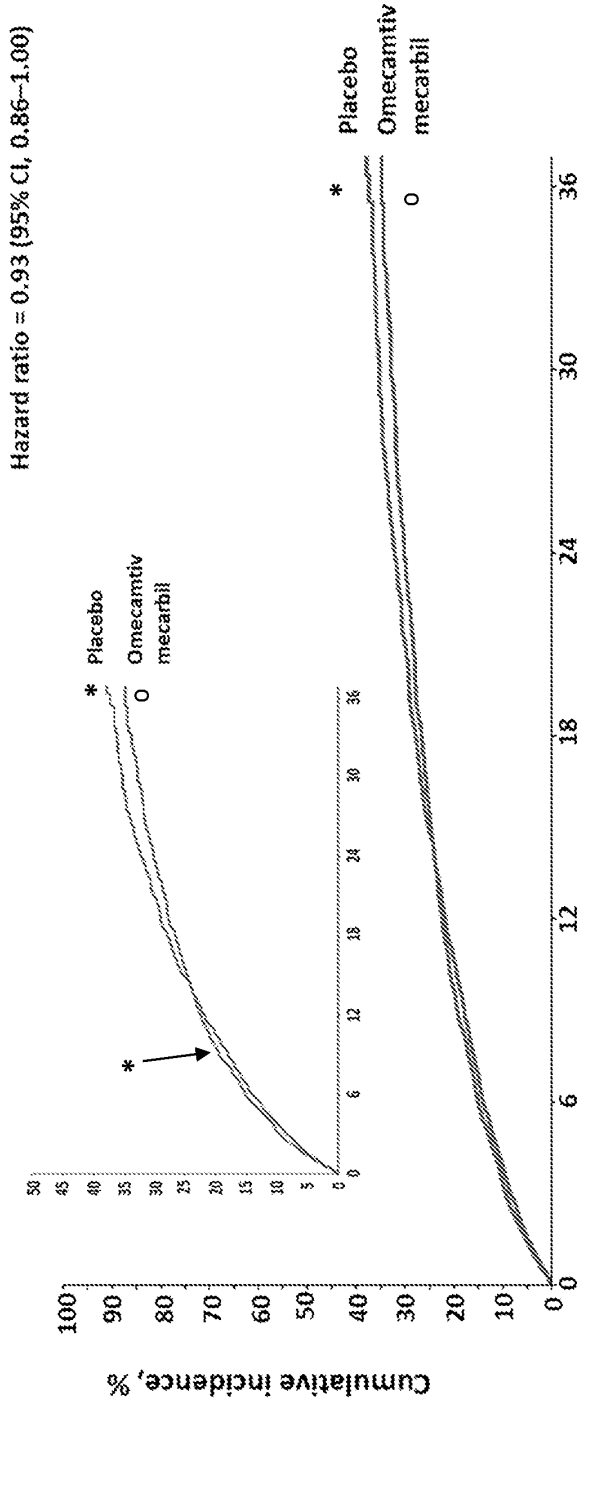

Hazard ratio = 0.93 (95% CI, 0.86–1.00)
* Placebo
o Omecamtiv mecarbil
Cumulative incidence, %
Months (30 days) since randomization
Patients at risk, n
* Placebo 4112 3309 2889 2102 1348 647 141
o Omecamtiv mecarbil 4120 3391 2953 2156 1430 699 164

FIGURE 1C

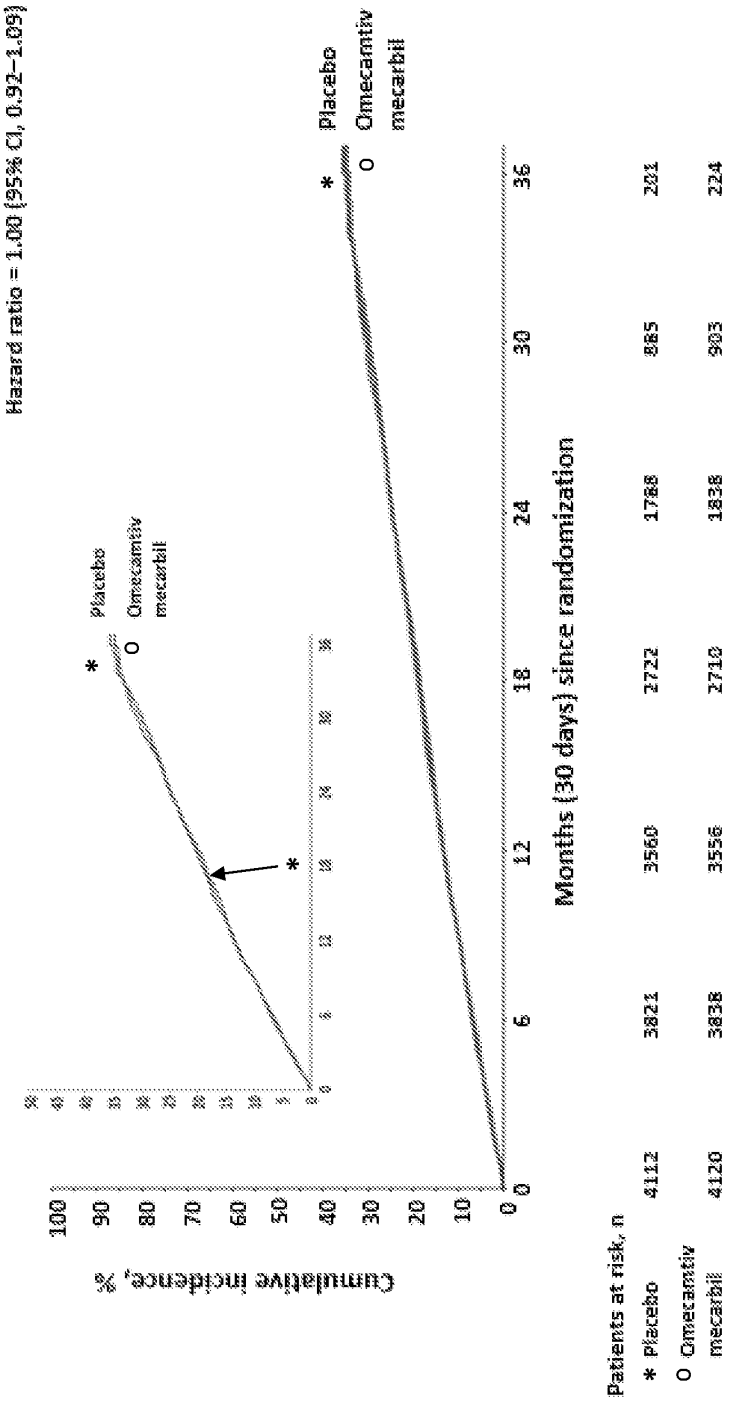

Hazard ratio = 1.00 (95% CI, 0.92–1.09)
Placebo
Omecamtiv mecarbil
Cumulative incidence, %
Months (30 days) since randomization
Patients at risk, n
Placebo 4112 3821 3560 2722 1768 885 201
Omecamtiv mecarbil 4120 3838 3556 2710 1838 903 224

FIGURE 1D

Primary Composite
Subgroup
Omecamtiv mecarbil
Placebo
Hazard Ratio
Overall
1523/4120
1607/4112
0.92 (0.86, 0.99)
Randomization Setting
Inpatient
469/1044
497/1040
0.89 (0.78, 1.01)
Outpatient
1054/3076
1110/3072
0.94 (0.86, 1.02)
Region
Asia
100/336
120/336
0.80 (0.61, 1.05)
EEU with Russia
488/1344
517/1337
0.90 (0.80, 1.02)
Latin America
227/787
246/787
0.90 (0.75, 1.07)
US and Canada
306/693
345/693
0.85 (0.73, 0.99)
WEU, SA, and AUS
402/961
377/960
1.07 (0.93, 1.23)
Age
< 65
616/1874
646/1873
0.91 (0.82, 1.02)
>= 65
907/2246
961/2239
0.94 (0.86, 1.03)
Sex
Female
306/875
307/874
0.95 (0.81, 1.12)
Male
1217/3245
1300/3238
0.92 (0.85, 0.99)
Baseline Weight
Q1: <= 68.4 kg
372/1027
423/1032
0.88 (0.77, 1.02)
Q2: (68.4 kg, 80.0 kg]
380/1030
377/1031
0.99 (0.86, 1.15)
Q3: (80.0 kg, 93.9 kg]
348/1018
396/1033
0.85 (0.74, 0.99)
Q4: > 93.9 kg
422/1042
411/1015
0.98 (0.85, 1.12)
Race
Asian
107/355
129/355
0.79 (0.61, 1.02)
Black or African American
124/265
144/277
0.82 (0.64, 1.04)
White
1196/3196
1233/3201
0.95 (0.88, 1.03)
Other
96/284
101/279
0.91 (0.69, 1.21)
Ethnicity
Hispanic or Latino
264/886
290/885
0.90 (0.76, 1.06)
Not Hispanic or Latino
1259/3234
1317/3227
0.93 (0.86, 1.00)

FIGURE 2A

Baseline NYHA Class
II 676/2195 679/2173 0.97 (0.87, 1.08)
III/IV 847/1925 928/1939 0.88 (0.80, 0.97)
Diabetes at baseline
No 805/2434 858/2421 0.91 (0.83, 1.01)
Yes 718/1686 749/1691 0.93 (0.84, 1.03)
Primary cause of HF
Ischemic 877/2193 961/2222 0.90 (0.82, 0.98)
Non-Ischemic 646/1927 646/1890 0.96 (0.86, 1.07)
History of MI
No 822/2427 838/2370 0.93 (0.85, 1.03)
Yes 701/1693 769/1742 0.91 (0.83, 1.01)
Presence of Atrial fib/flutter
No 981/2974 1103/3013 0.86 (0.79, 0.94)
Yes 542/1146 504/1099 1.05 (0.93, 1.18)
Baseline LVEF
<= median (28%) 850/2213 971/2243 0.84 (0.77, 0.92)
> median (28%) 673/1907 636/1869 1.04 (0.94, 1.16)
Baseline NT-proBNP (excl. Afib)
Inpatient & <= Median 104/344 100/329 0.97 (0.74, 1.28)
Inpatient & > Median 175/334 201/338 0.75 (0.61, 0.92)
Outpatient & <= Median 223/1131 260/1182 0.88 (0.73, 1.05)
Outpatient & > Median 476/1156 539/1157 0.85 (0.75, 0.97)
Baseline HR
<= Median (71 bpm) 723/2109 767/2105 0.91 (0.82, 1.01)
> Median (71 bpm) 800/2011 840/2007 0.93 (0.85, 1.03)
Baseline SBP
<= Median (116 mmHg) 848/2096 889/2038 0.90 (0.82, 0.99)
> Median (116 mmHg) 675/2024 718/2074 0.95 (0.85, 1.05)
Baseline SBP
< 100 mmHg 281/594 282/533 0.89 (0.76, 1.05)
>= 100 mmHg 1242/3526 1325/3579 0.92 (0.86, 1.00)
Baseline eGFR
<= 60 mL/min/1.73m2 973/2156 984/2165 0.98 (0.89, 1.07)
> 60 mL/min/1.73m2 550/1964 623/1947 0.84 (0.75, 0.94)

FIGURE 2B

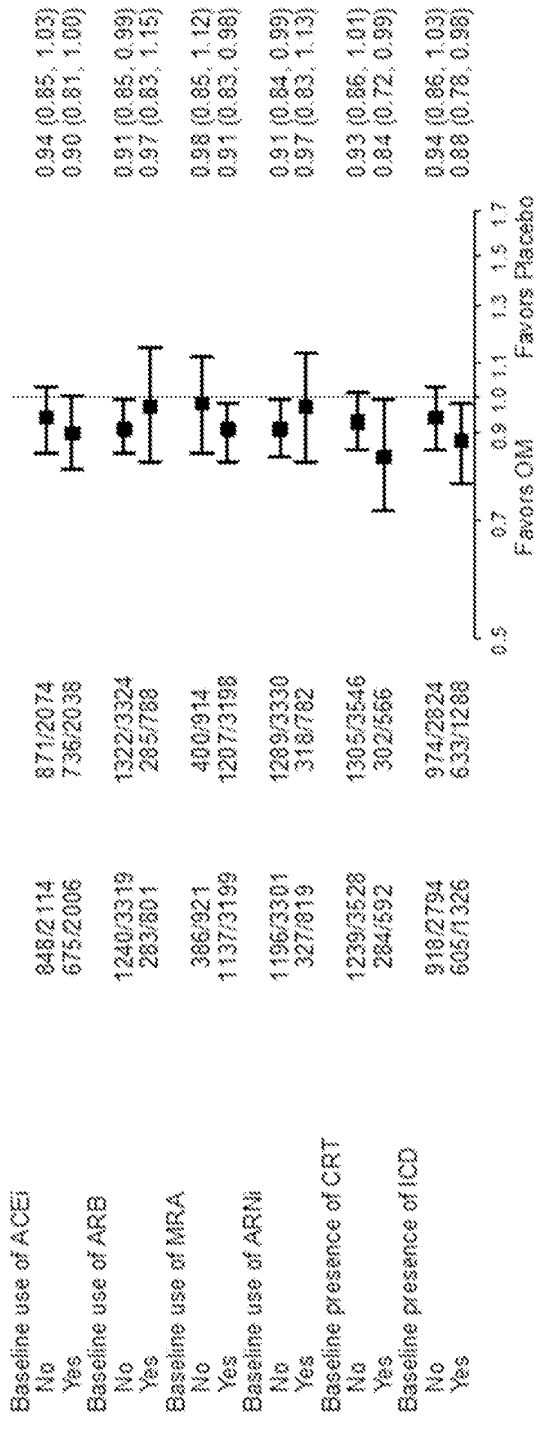
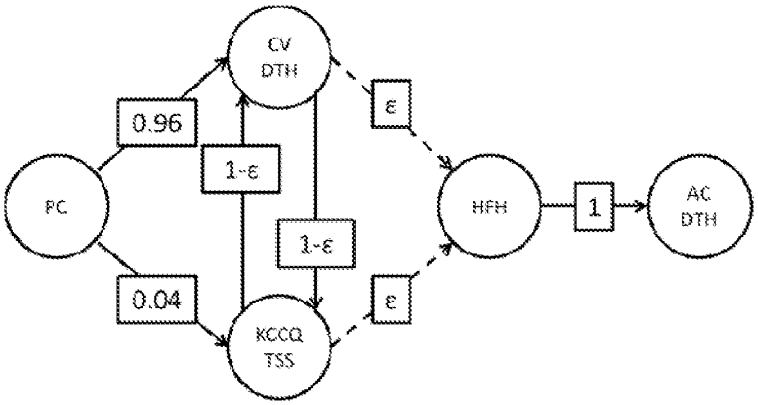

Baseline use of ACEi
No
Yes
Baseline use of ARB
No
Yes
Baseline use of MRA
No
Yes
Baseline use of ARNi
No
Yes
Baseline presence of CRT
No
Yes
Baseline presence of ICD
No
Yes
848/2114
675/2006
1240/3319
283/801
386/921
1137/3199
1196/3301
327/819
1239/3528
284/592
918/2794
605/1326
871/2074
736/2036
1322/3324
285/788
410/914
1207/3199
1289/3330
318/782
1305/3546
302/566
974/2824
633/1288
0.94 (0.85, 1.03)
0.90 (0.81, 1.00)
0.91 (0.85, 0.99)
0.97 (0.83, 1.15)
0.98 (0.85, 1.12)
0.91 (0.83, 0.98)
0.91 (0.84, 0.99)
0.97 (0.83, 1.13)
0.93 (0.86, 1.01)
0.84 (0.72, 0.99)
0.94 (0.86, 1.03)
0.88 (0.78, 0.98)
0.5
0.7
0.9
1.0
1.1
1.3
1.5
1.7
Favors OM
Favors Placebo

FIGURE 2C



PC = primary composite endpoint; CV DTH = time to CV death; KCCQ TSS = Kansas City Cardiomyopathy Questionnaire Total Symptom Score; HFH = time to first heart failure hospitalization; AC DTH = time to all-cause death.

Each circle represents a hypothesis test. The values in boxes on the arrows indicate the fraction of α propagated in the direction of the arrow to the next hypothesis test(s). $\varepsilon = 0.0001$, a small value to complete the graph while prioritizing the CV death and KCCQ TSS endpoints over the time to first heart failure hospitalization and all-cause death endpoints. Dashed arrows used to emphasize this prioritization.

No multiplicity adjustment will be made for exploratory or sensitivity analyses.

FIGURE 3

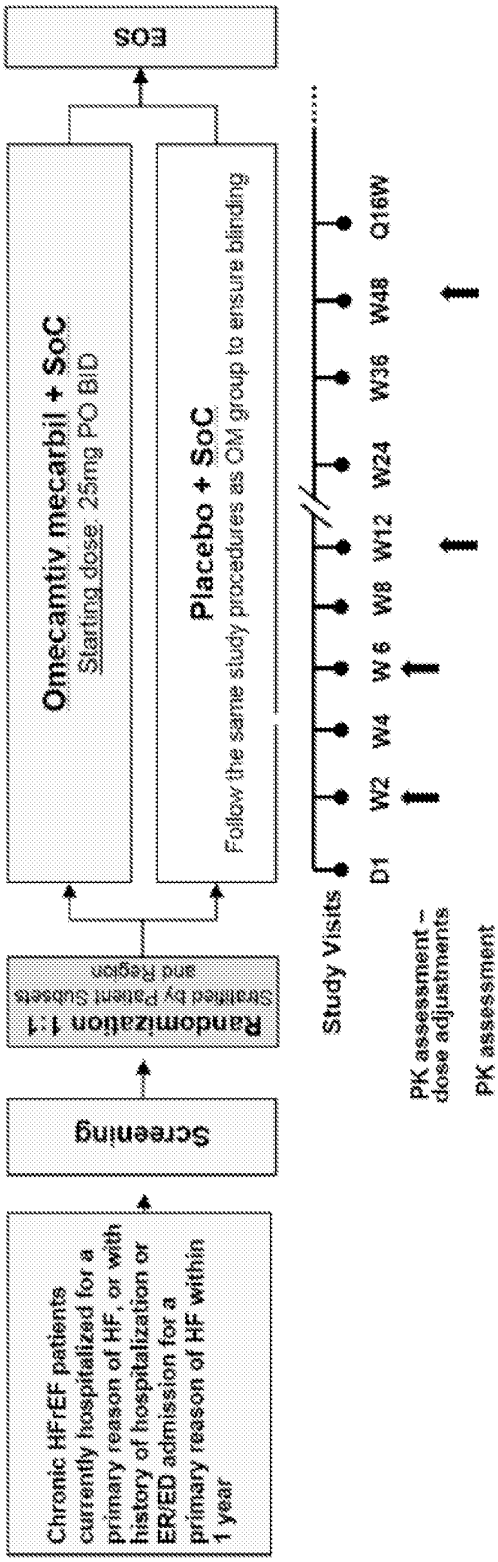


FIGURE 4

BID = twice a day; ED = emergency department; EOS = end of study; ER = emergency room; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; IP = investigational product; PK = pharmacokinetics; PO = by mouth; Q16W = every 16 weeks; SoC = standard of care;

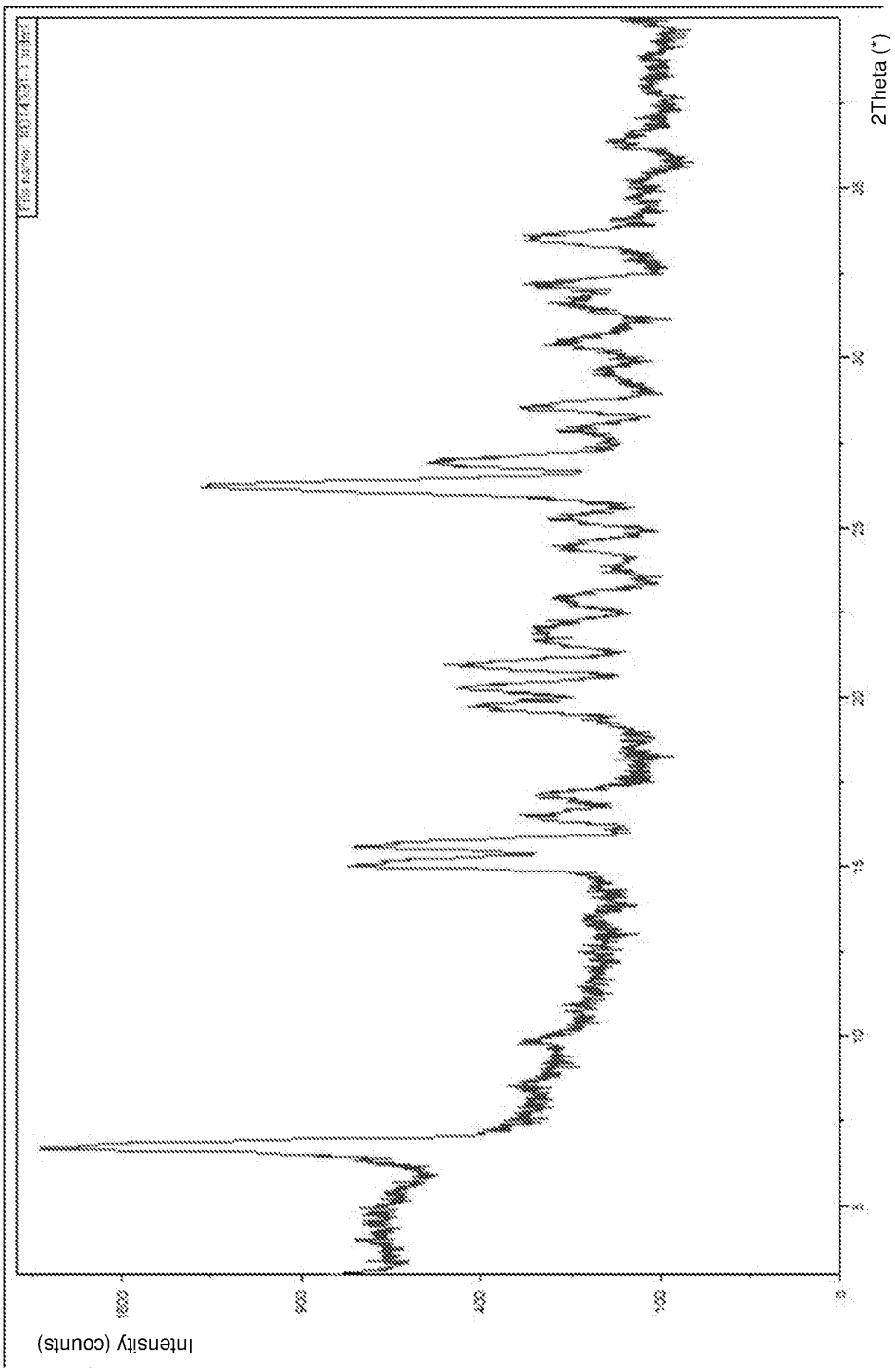


FIGURE 5

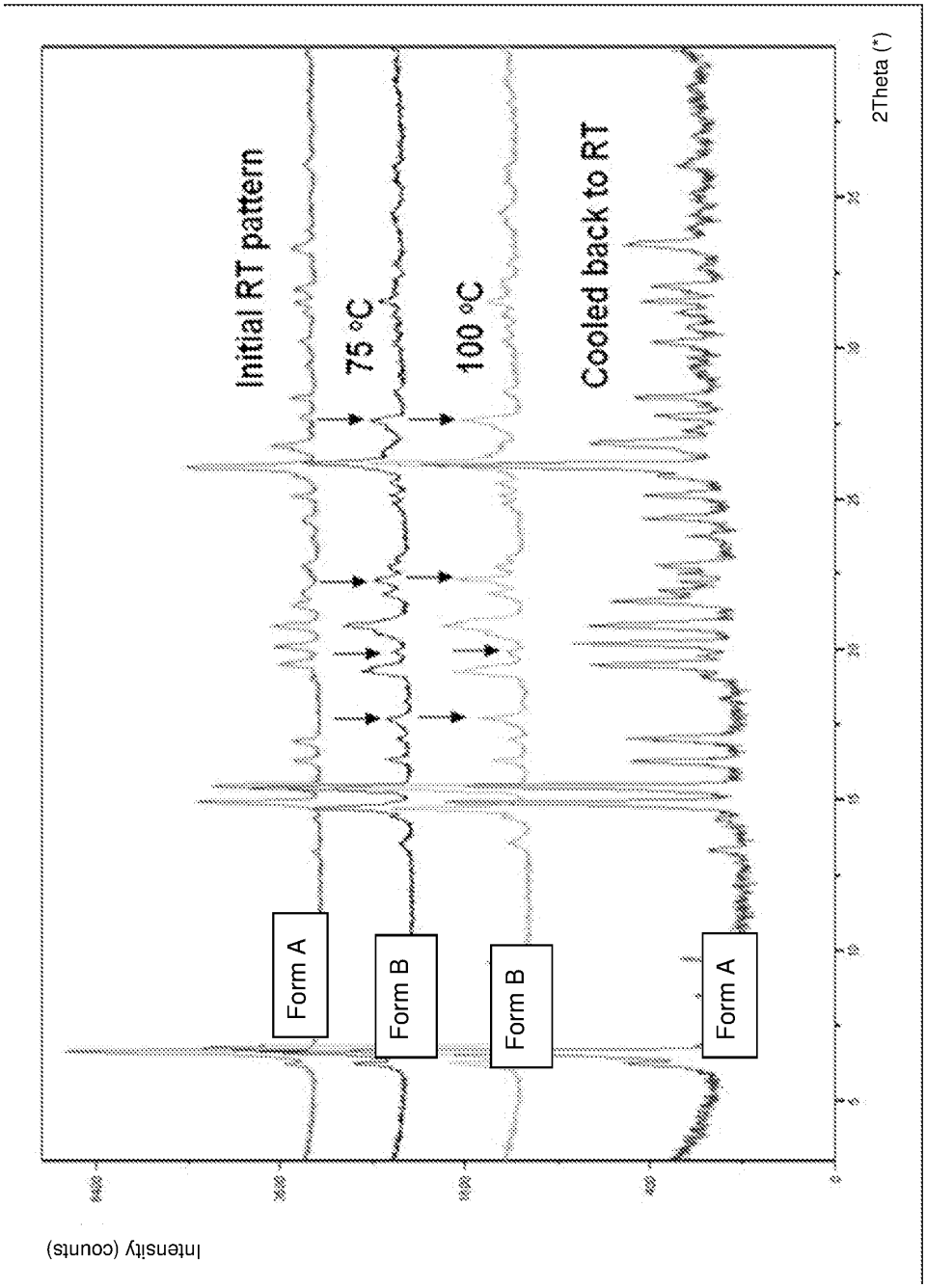

Initial RT pattern
75 °C
100 °C
Cooled back to RT
Form A
Form B
Form B
Form A
Intensity (counts)
2Theta (°)

FIGURE 6

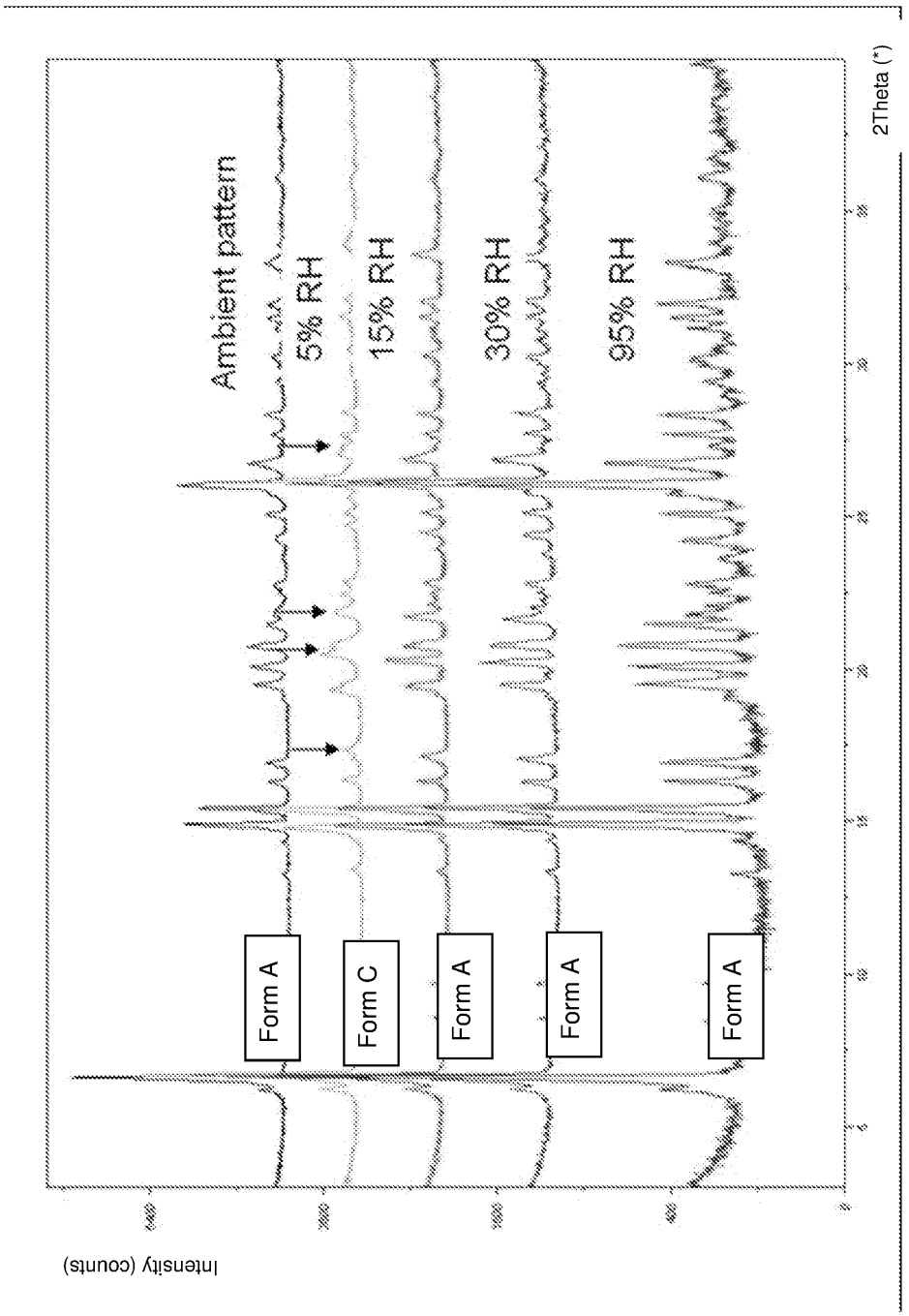

Ambient pattern
5% RH
15% RH
30% RH
95% RH
Form A
Form C
Form A
Form A
Form A
Intensity (counts)
2Theta (°)

FIGURE 7

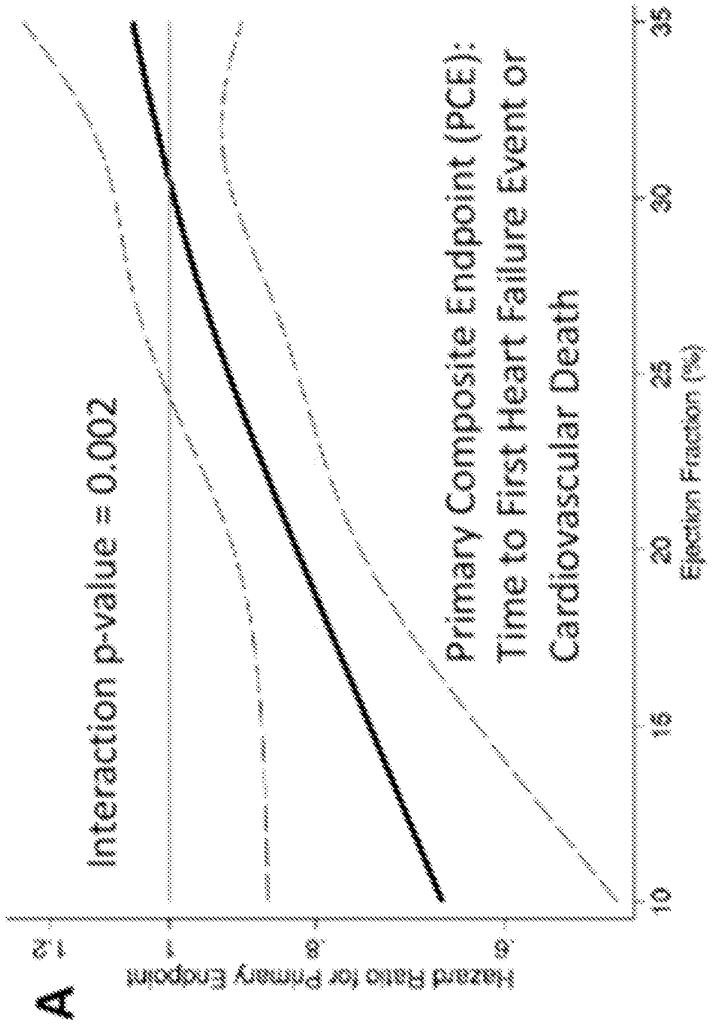

A
Hazard Ratio for Primary Endpoint
1.2
1
.8
.6
Interaction p-value = 0.002
Primary Composite Endpoint (PCE):
Time to First Heart Failure Event or
Cardiovascular Death
10
15
20
25
30
35
Ejection Fraction (%)

FIGURE 8A

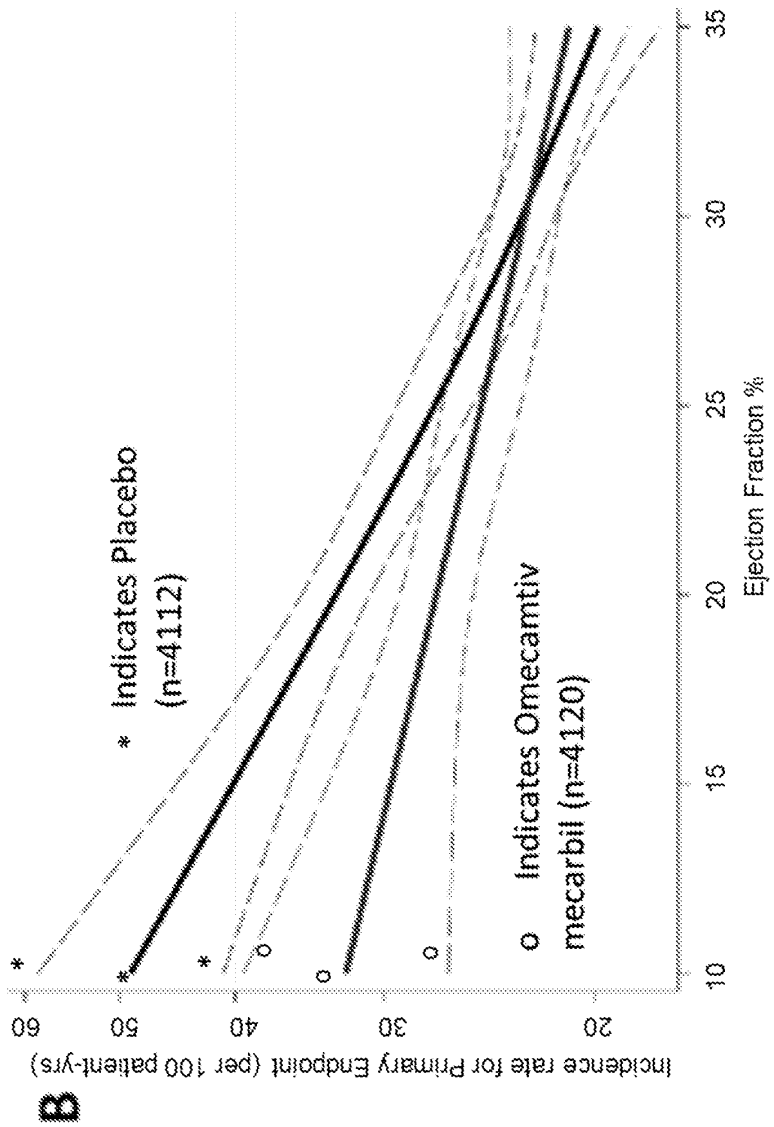

B
Incidence rate for Primary Endpoint (per 100 patient-yrs)
20
30
40
50
60
10
15
20
25
30
35
Ejection Fraction %
* Indicates Placebo
(n=4112)
o Indicates Omecamtiv
mecarbil (n=4120)

FIGURE 8B

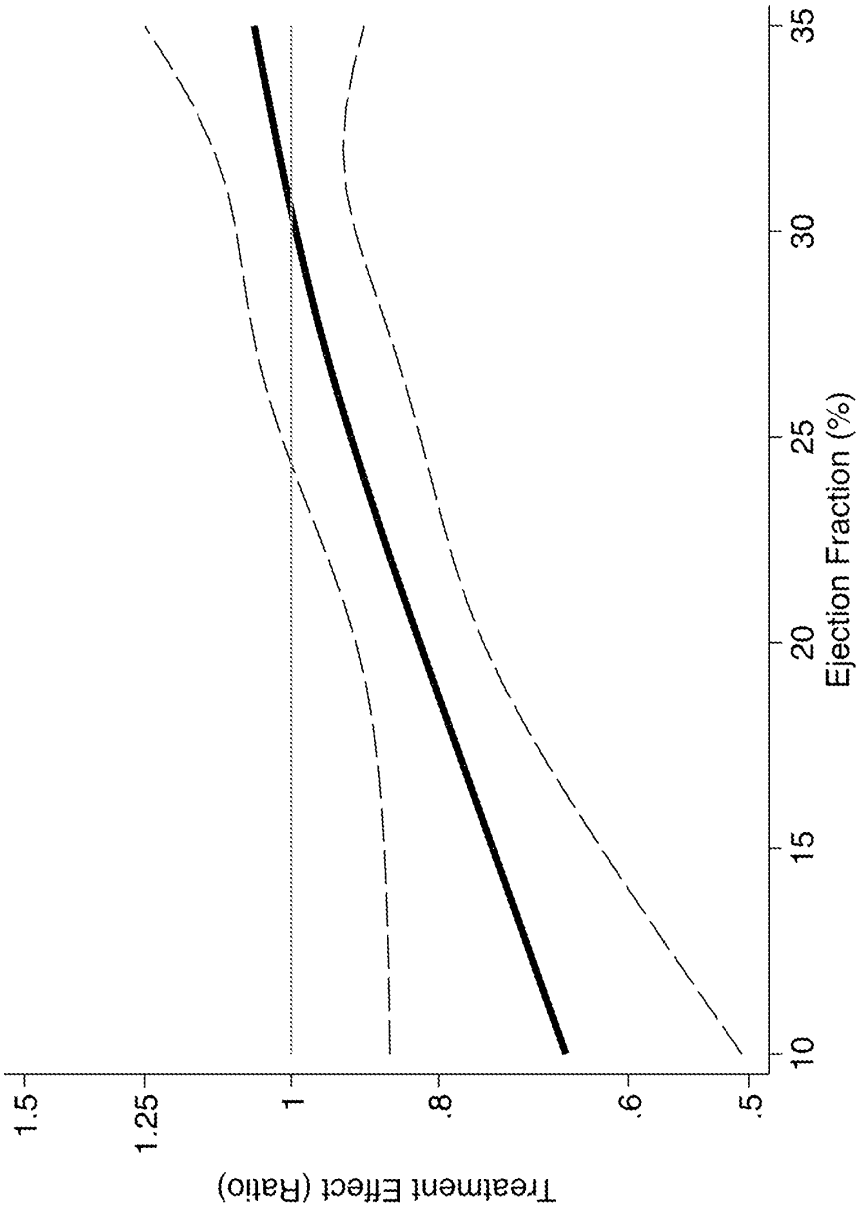

Treatment Effect (Ratio)
1.5
1.25
1
.8
.6
.5
10
15
20
25
30
35
Ejection Fraction (%)

FIGURE 9

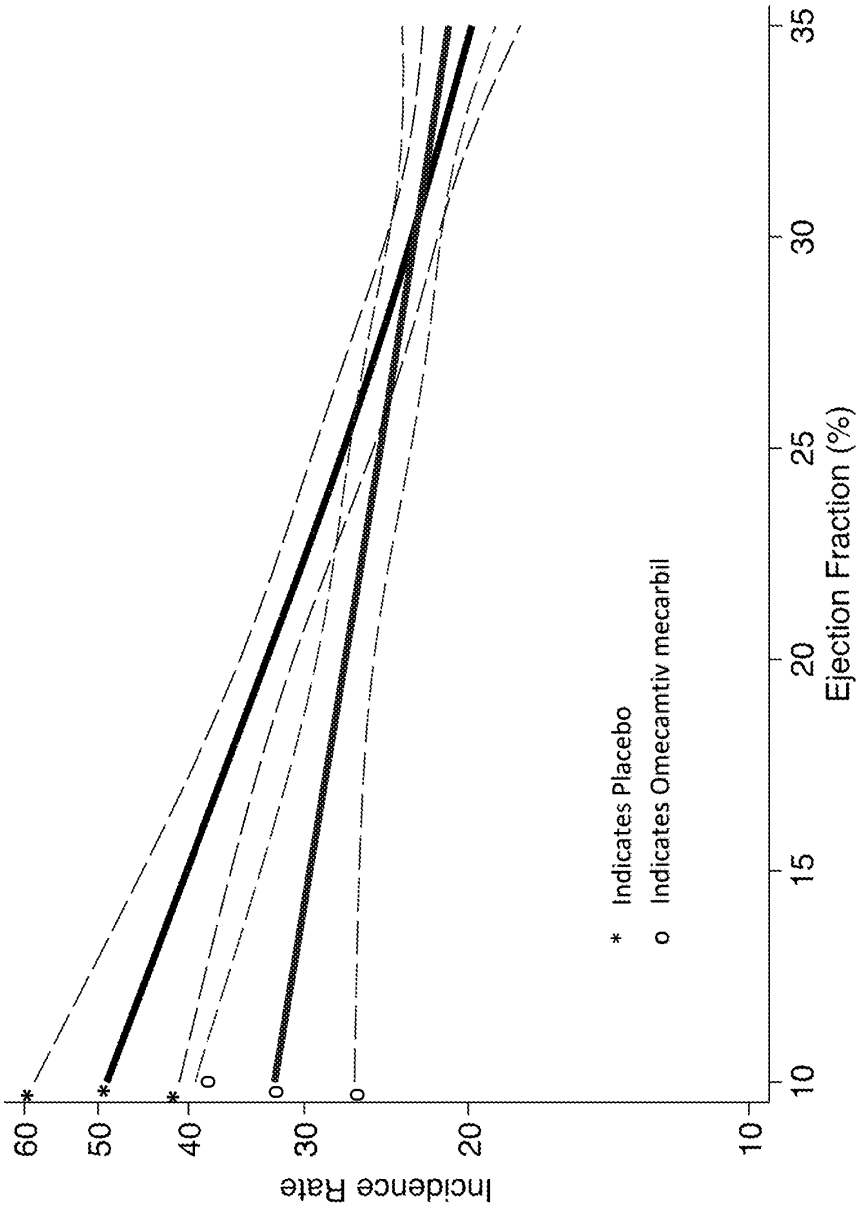

Incidence Rate
60
50
40
30
20
10
10
15
20
25
30
35
Ejection Fraction (%)
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 10A

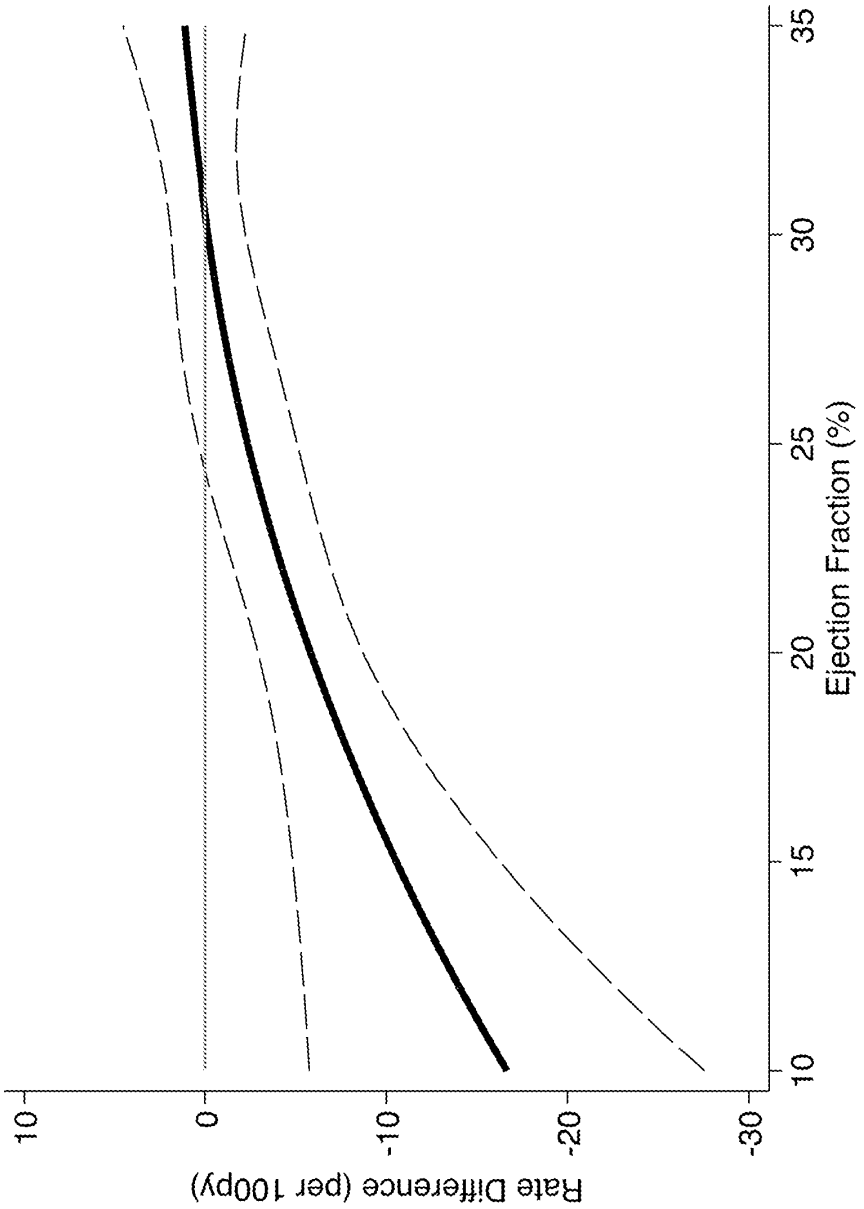

Rate Difference (per 100py)
10
0
-10
-20
-30
10
15
20
25
30
35
Ejection Fraction (%)

FIGURE 10B

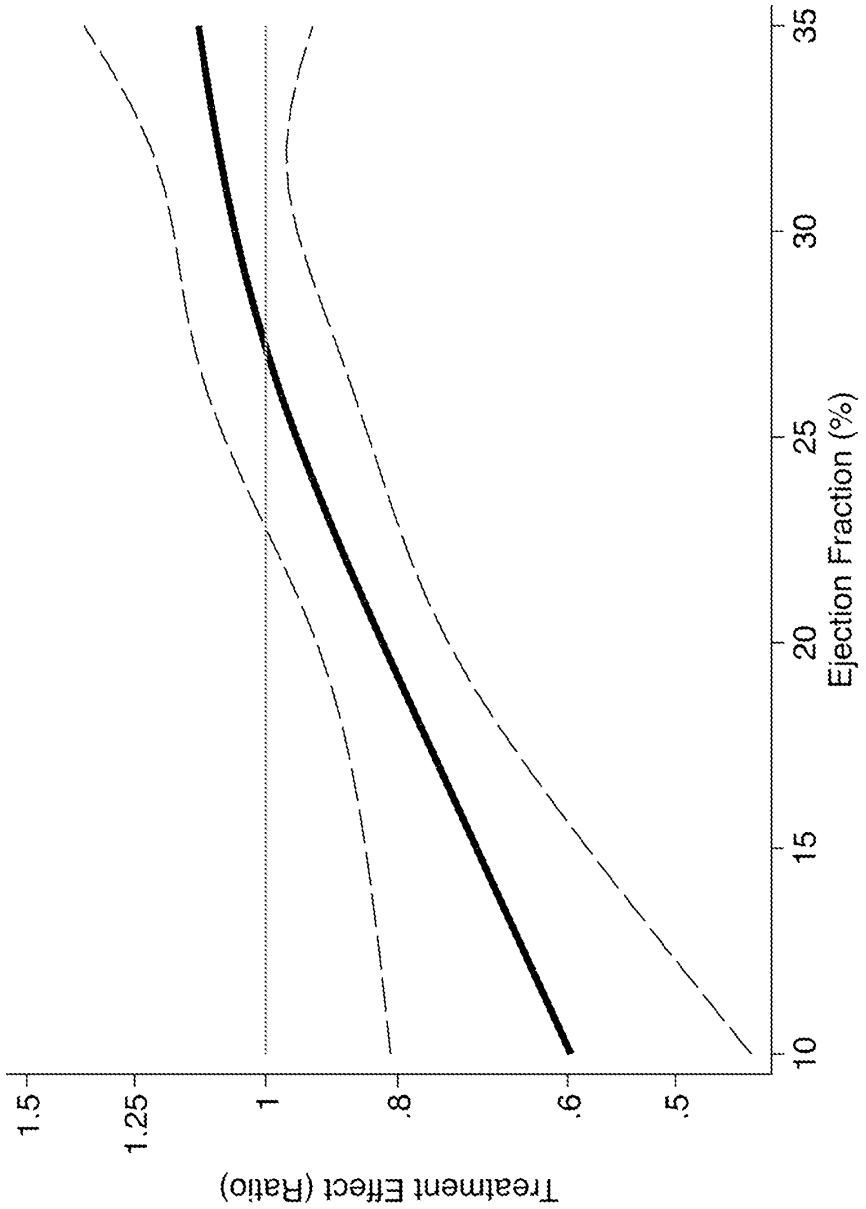

Treatment Effect (Ratio)
1.5
1.25
1
.8
.6
.5
10
15
20
25
30
35
Ejection Fraction (%)

FIGURE 11A

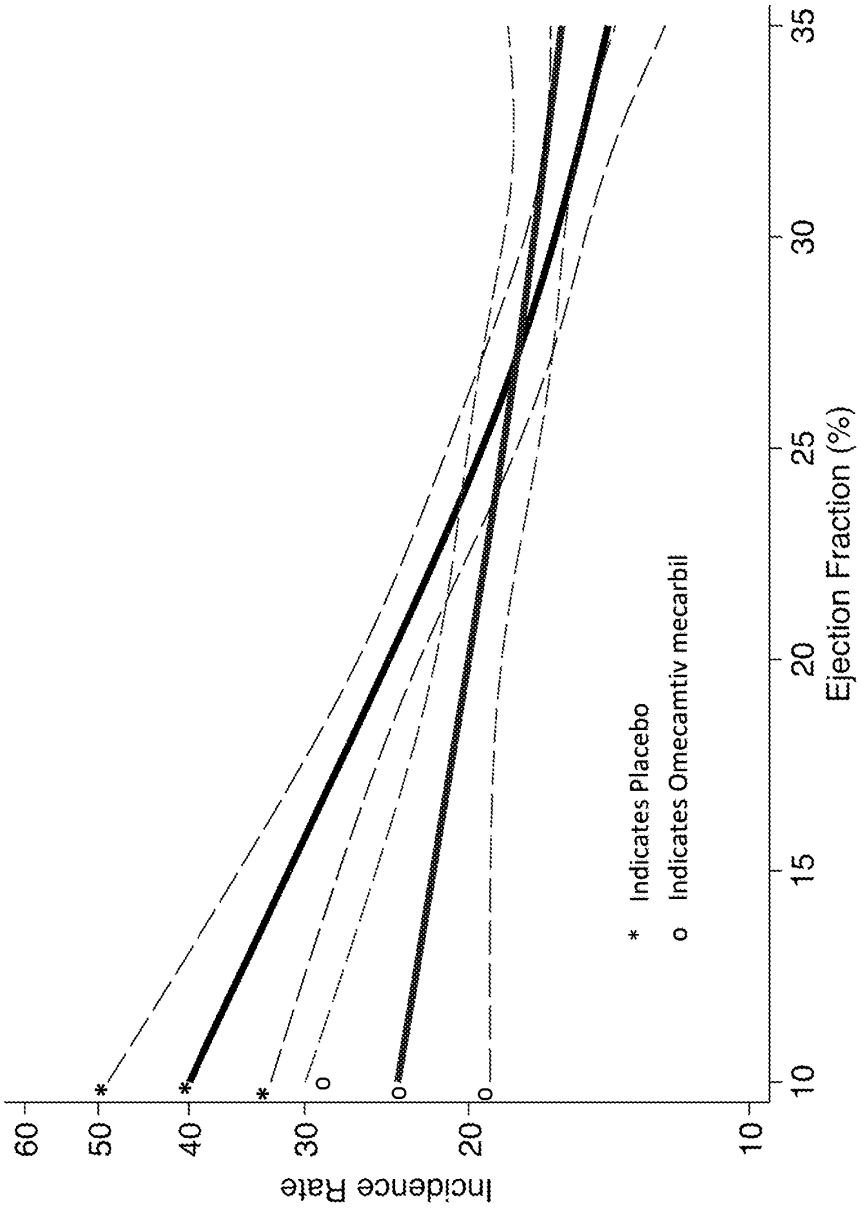

Incidence Rate
60
50
40
30
20
10
10
15
20
25
30
35
Ejection Fraction (%)
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 11B

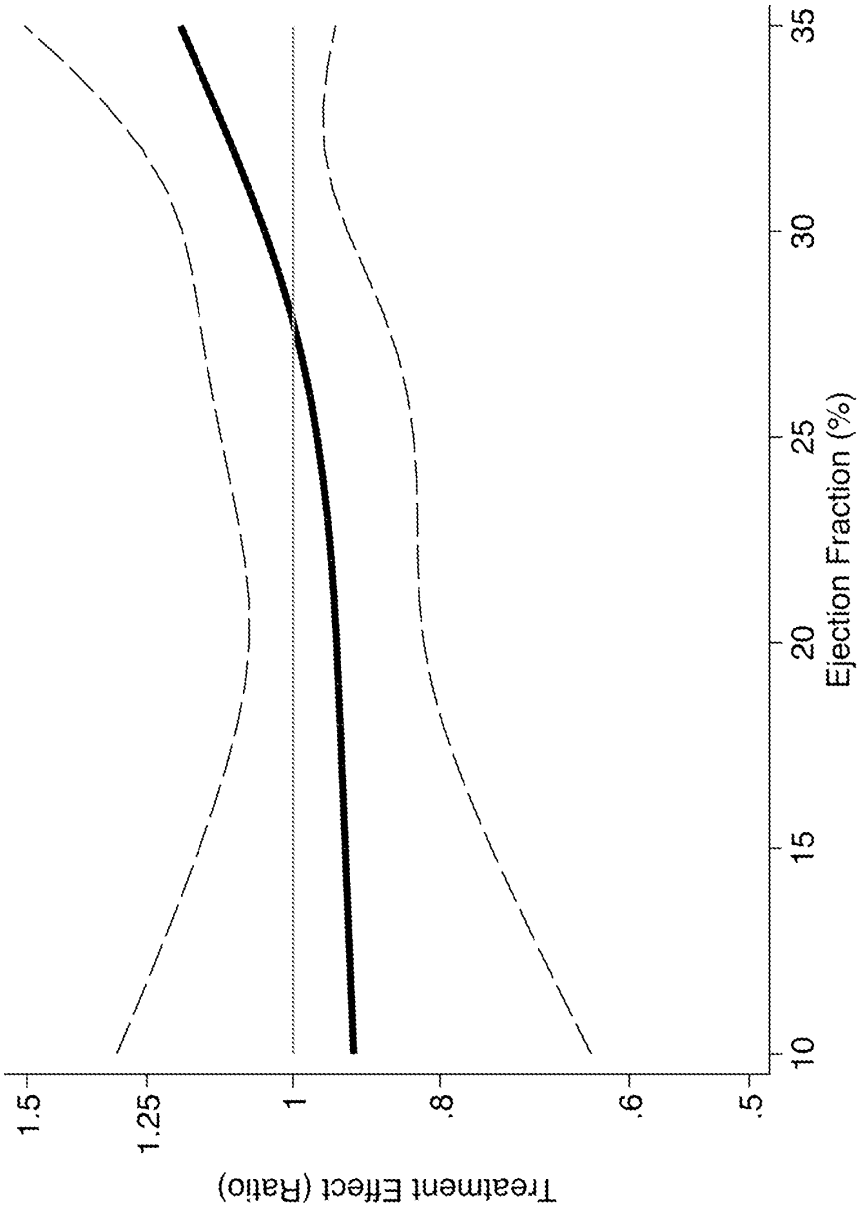

Treatment Effect (Ratio)
1.5
1.25
1
.8
.6
.5
10
15
20
25
30
35
Ejection Fraction (%)

FIGURE 12A

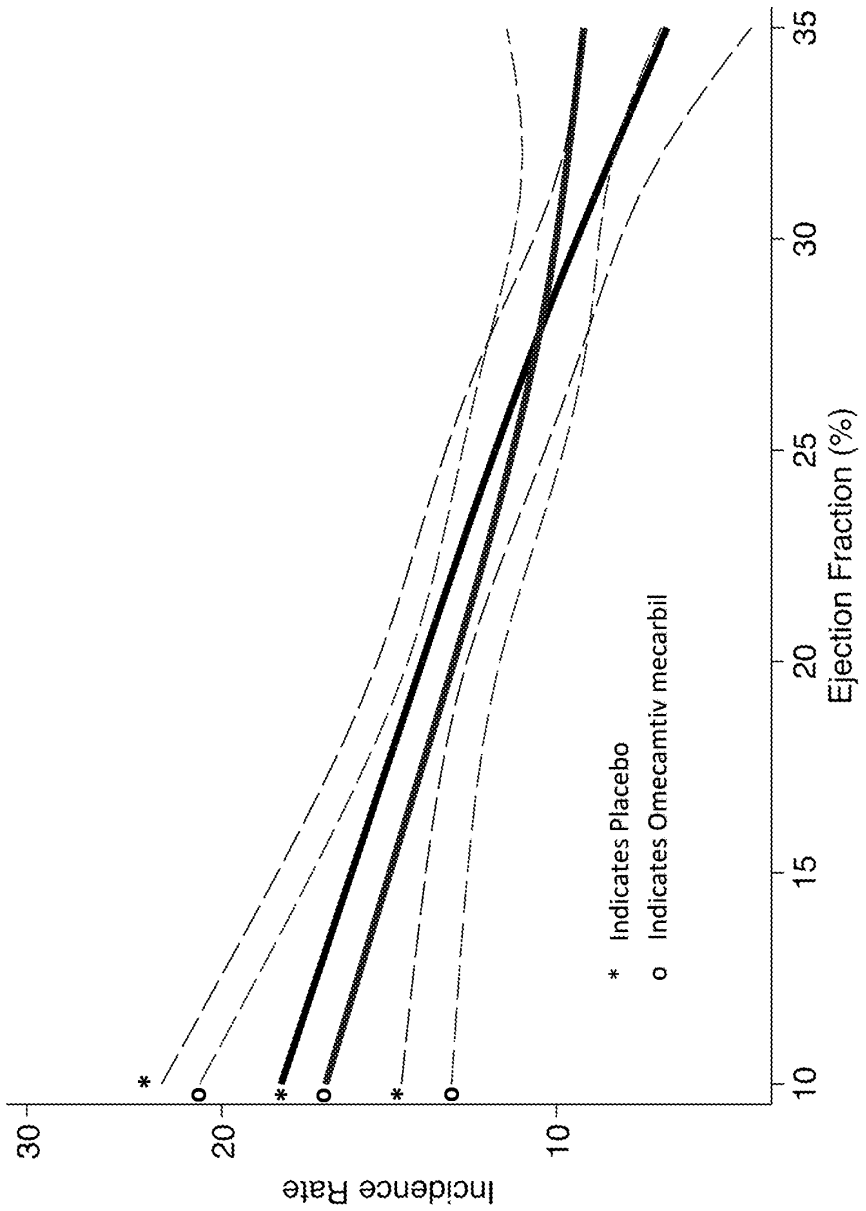

Incidence Rate
30
20
10
10
15
20
25
30
35
Ejection Fraction (%)
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 12B

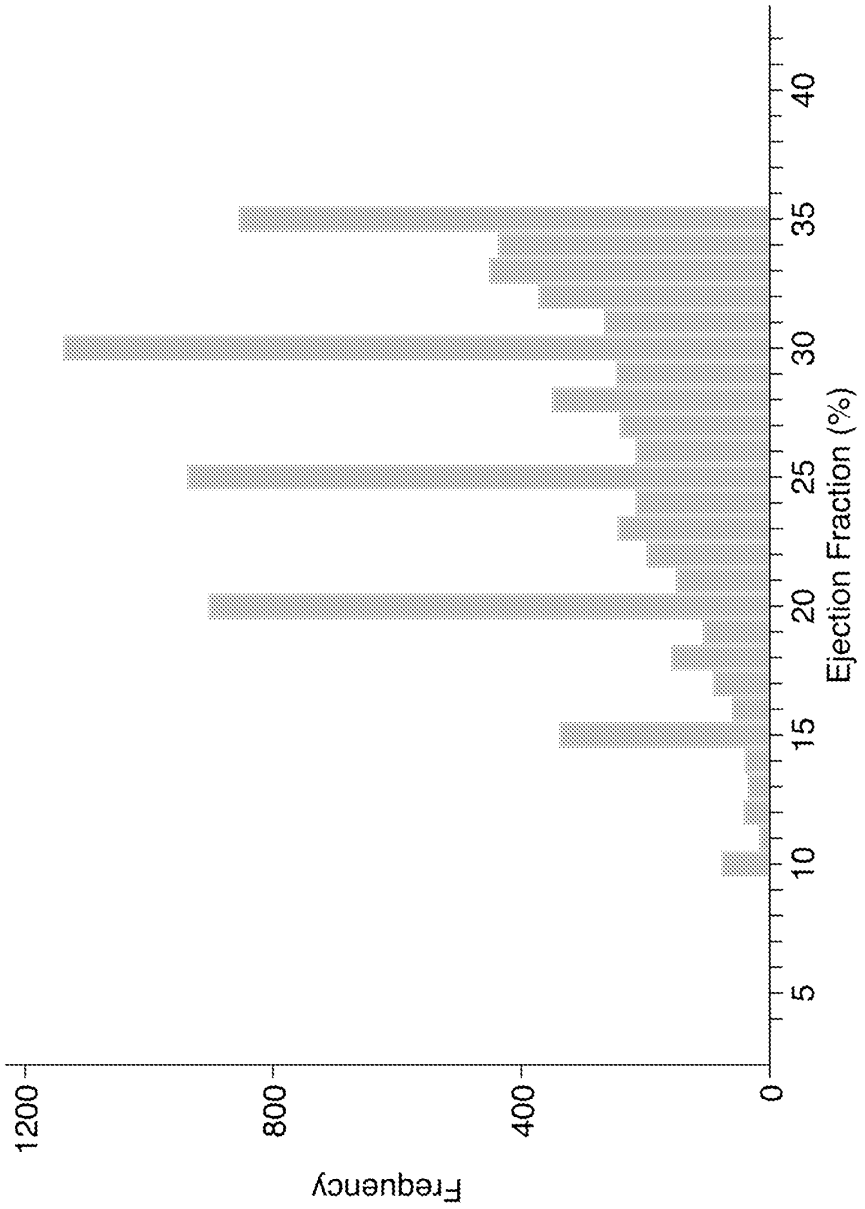

Frequency
0
400
800
1200
5
10
15
20
25
30
35
40
Ejection Fraction (%)

FIGURE 13A

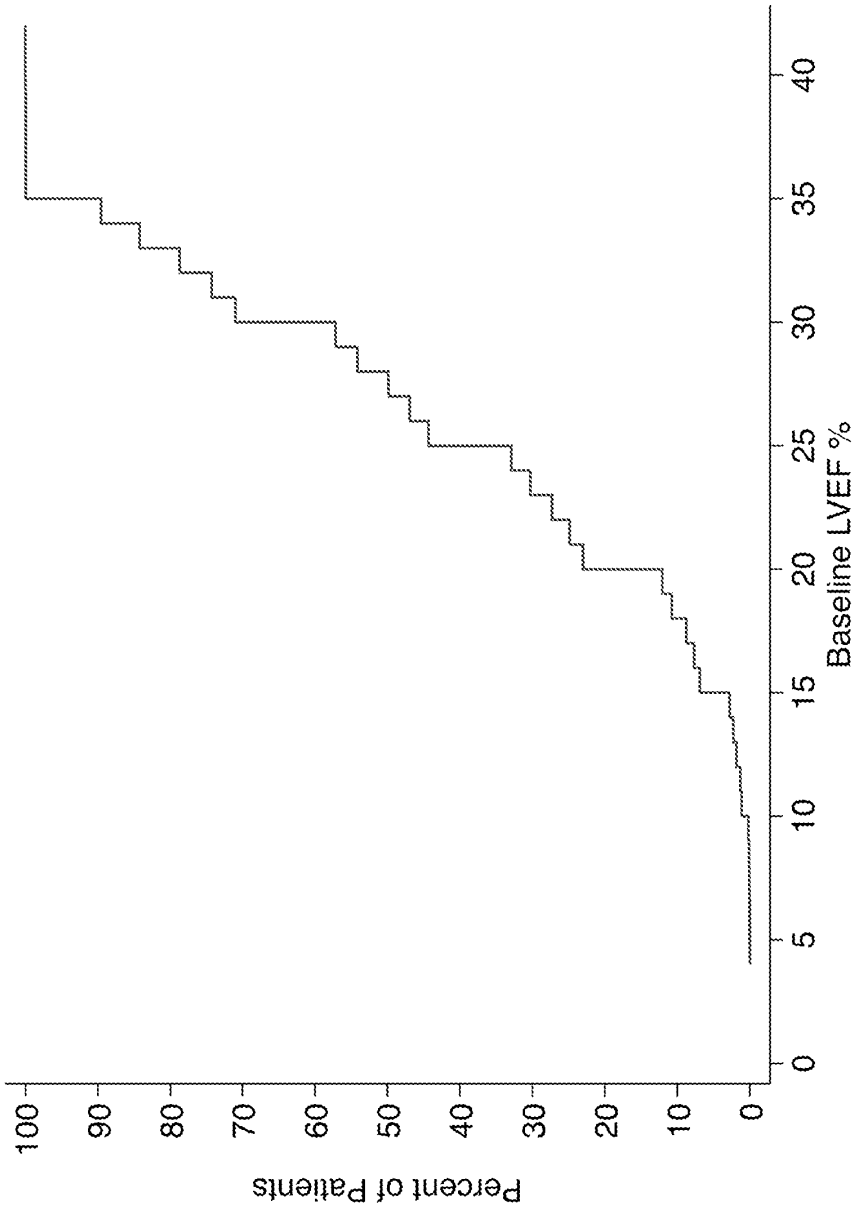

Percent of Patients
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
40
Baseline LVEF %

FIGURE 13B

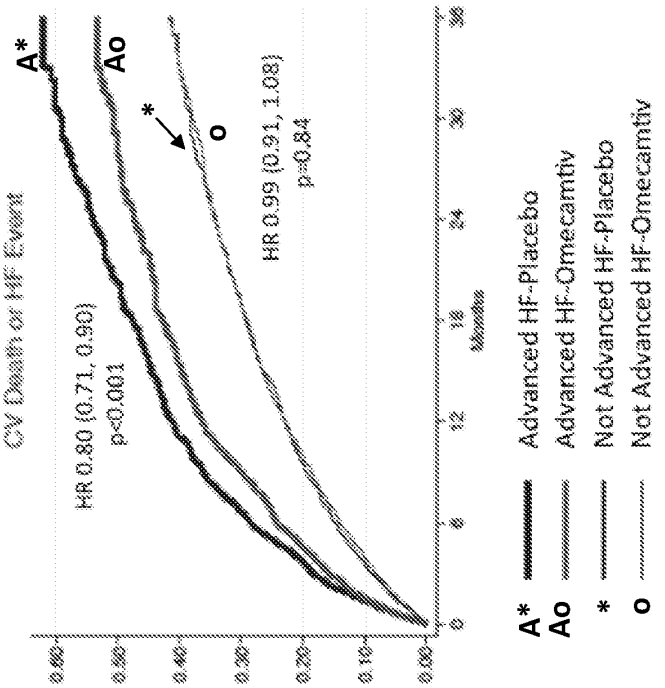

CV Death or HF Event
A*
Ao
*
o
HR 0.80 (0.71, 0.90)
p<0.001
HR 0.99 (0.91, 1.08)
p=0.84
0.60
0.50
0.40
0.30
0.20
0.10
0.00
0
6
12
18
24
30
36
Months
A* Advanced HF-Placebo
Ao Advanced HF-Omecamtiv
* Not Advanced HF-Placebo
o Not Advanced HF-Omecamtiv

FIGURE 14A

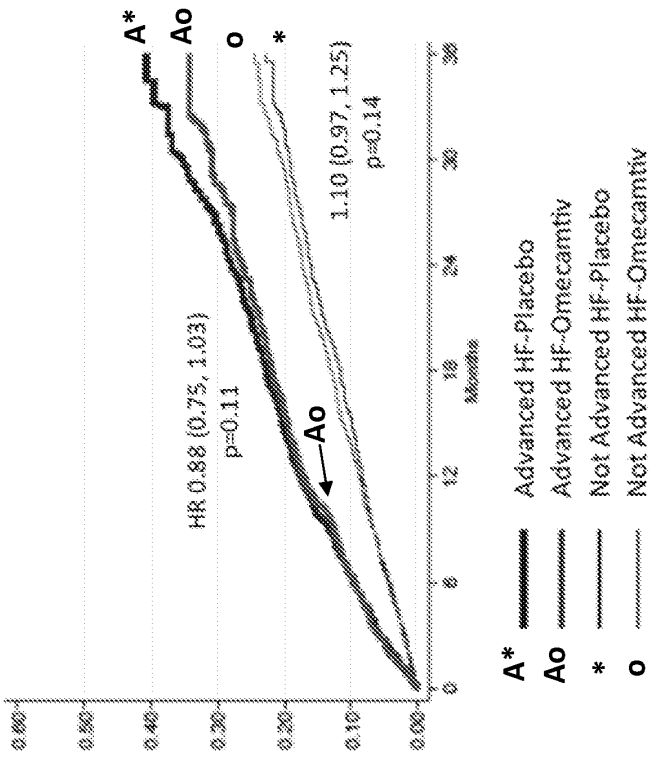

CV Death
HR 0.88 (0.75, 1.03)
p=0.11
1.10 (0.97, 1.25)
p=0.14
A*
Ao
o
*
Ao
0.60
0.50
0.40
0.30
0.20
0.10
0.00
0
6
12
18
24
30
36
Months
A* Advanced HF-Placebo
Ao Advanced HF-Omecamtiv
* Not Advanced HF-Placebo
o Not Advanced HF-Omecamtiv

FIGURE 14B

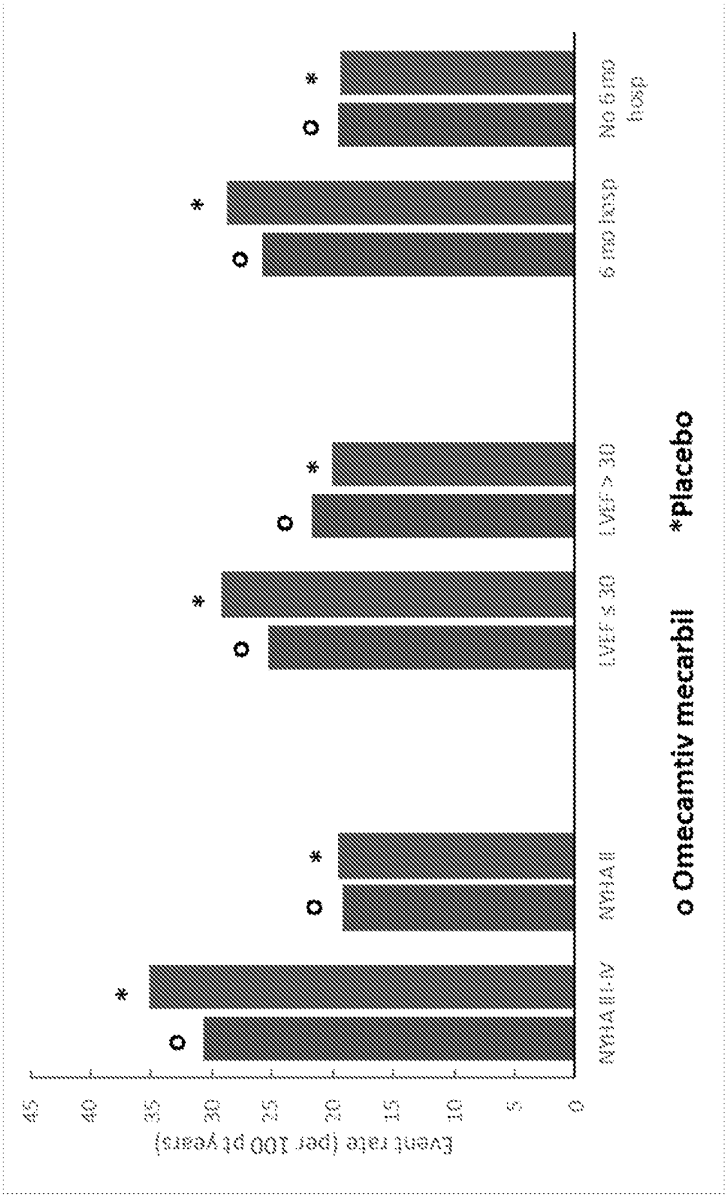

Event rate (per 100 pt years)
45
40
35
30
25
20
15
10
5
0
NYHA III-IV
NYHA II
LVEF ≤ 30
LVEF > 30
6 mo hosp
No 6 mo hosp
o Omecamtiv mecarbil
*Placebo

FIGURE 15A

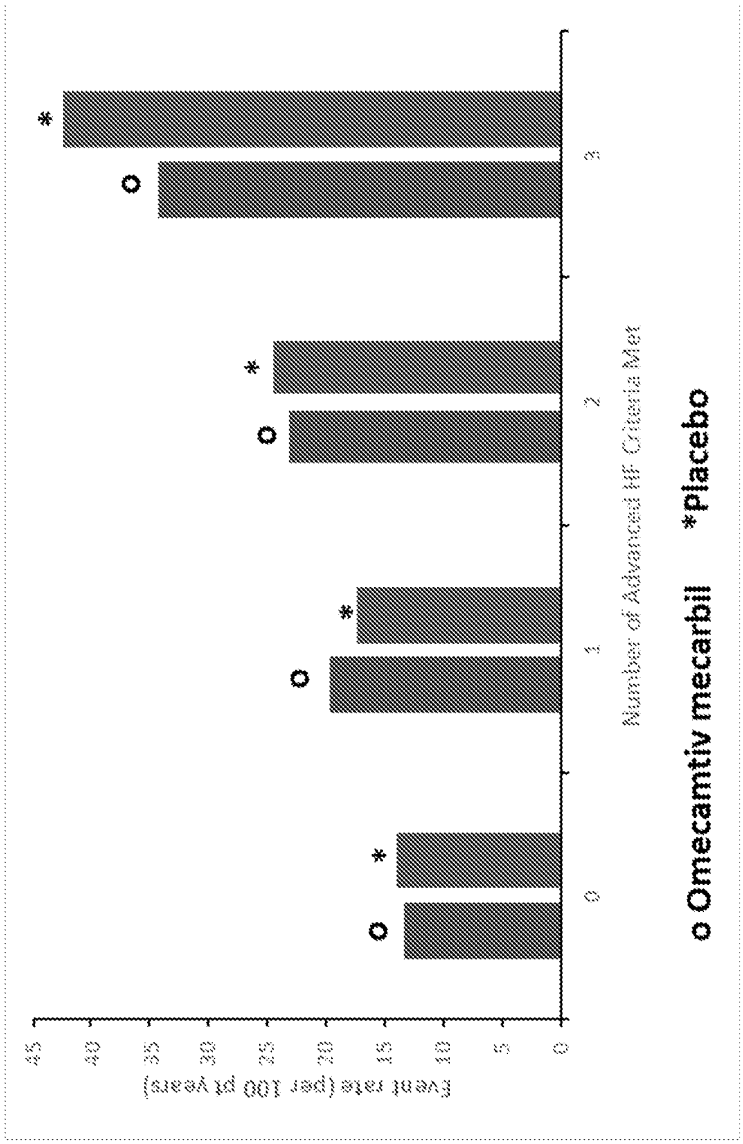

Event rate (per 100 pt years)
0
5
10
15
20
25
30
35
40
45
0
1
2
3
Number of Advanced HF Criteria Met
o Omecamtiv mecarbil
*Placebo

FIGURE 15B

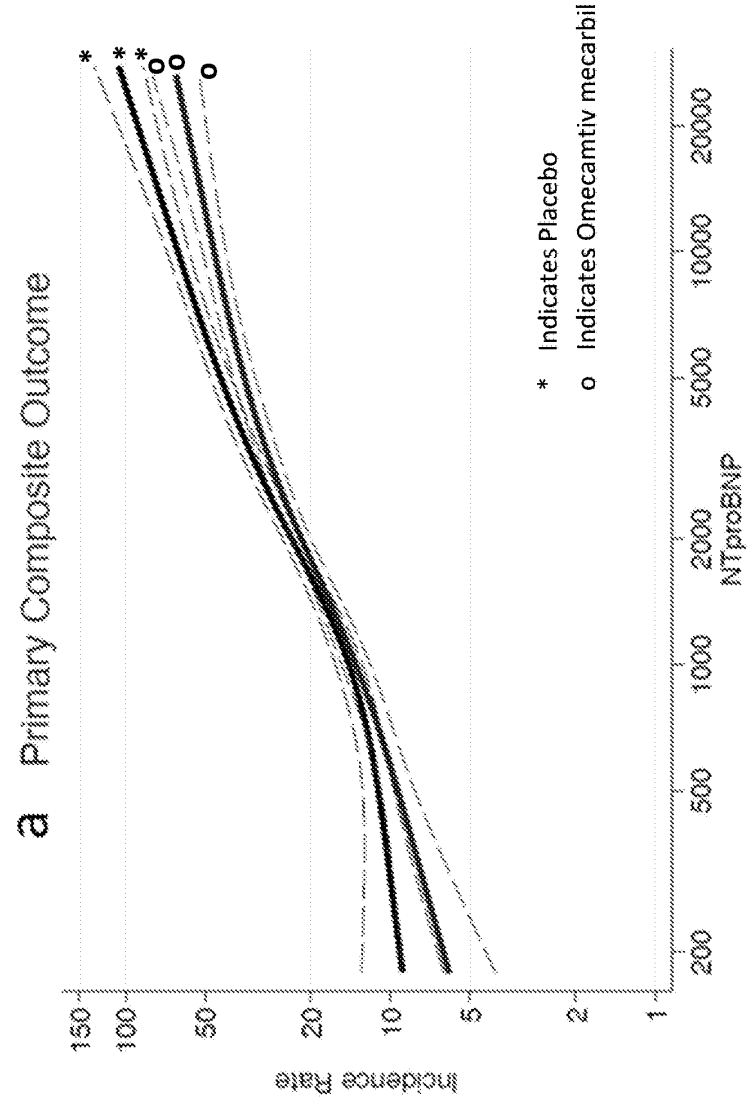

a Primary Composite Outcome
Incidence Rate
150
100
50
20
10
5
2
1
200
500
1000
2000
5000
10000
20000
NTproBNP
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 16A

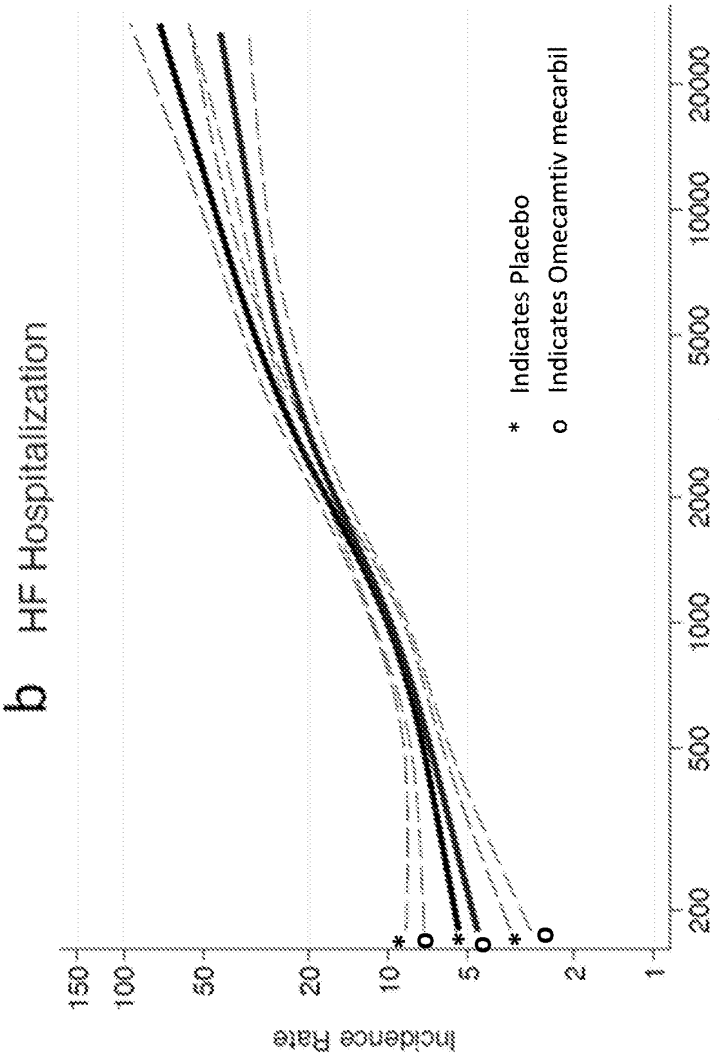

b HF Hospitalization
Incidence Rate
150
100
50
20
10
5
2
1
200
500
1000
2000
5000
10000
20000
NTproBNP
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 16B

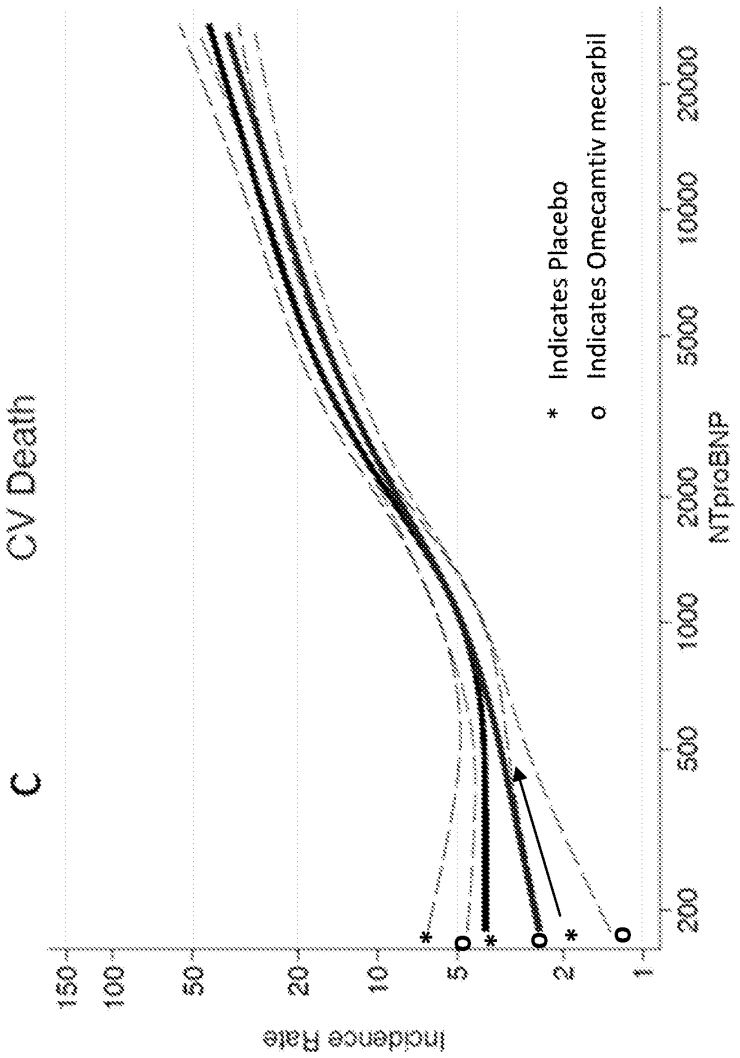

C
CV Death
Incidence Rate
150
100
50
20
10
5
2
1
200
500
1000
2000
5000
10000
20000
NTproBNP
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 16C

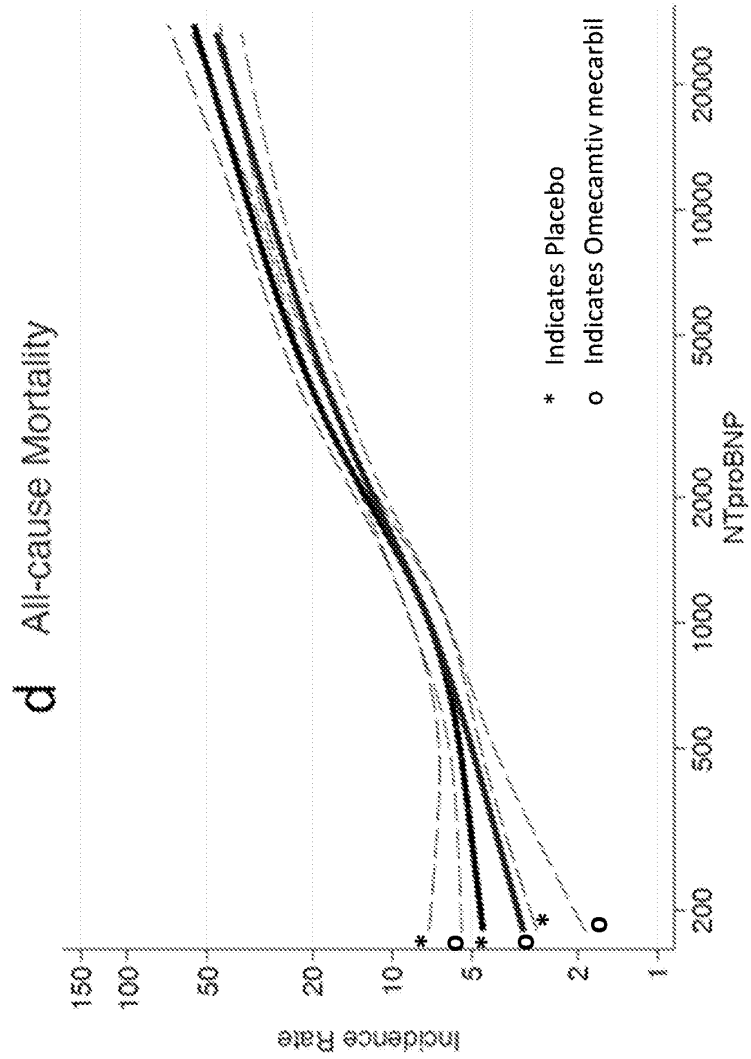

d All-cause Mortality
Incidence Rate
150
100
50
20
10
5
2
1
200
500
1000
2000
5000
10000
20000
NTproBNP
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 16D

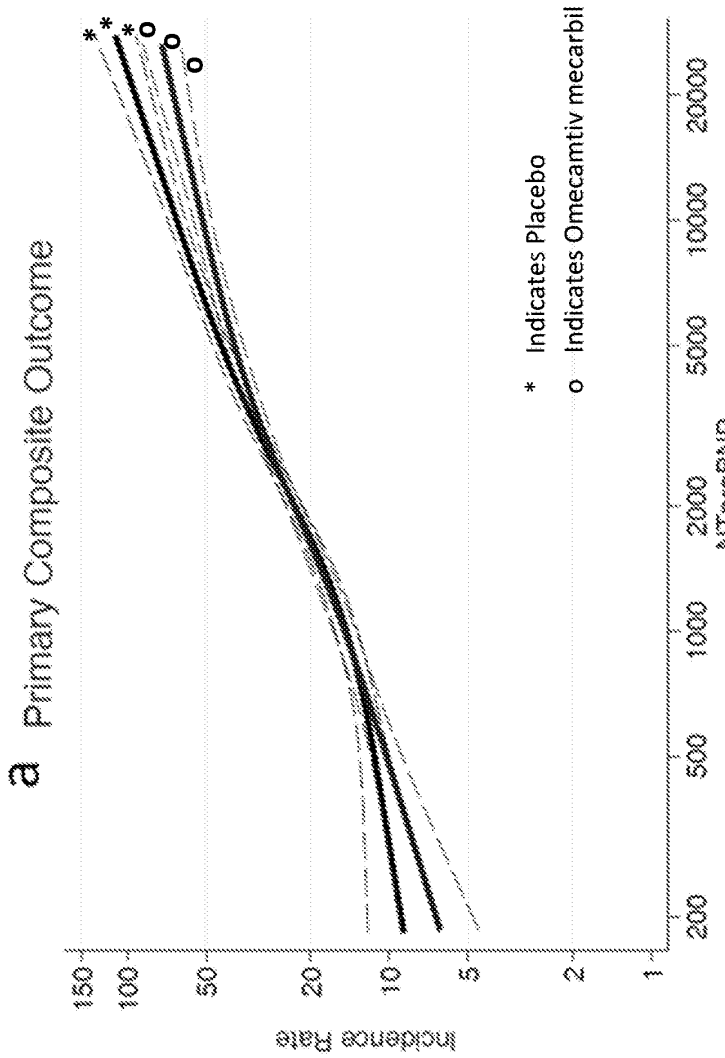

a Primary Composite Outcome
Incidence Rate
150
100
50
20
10
5
2
1
200
500
1000
2000
5000
10000
20000
NTproBNP
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 17A

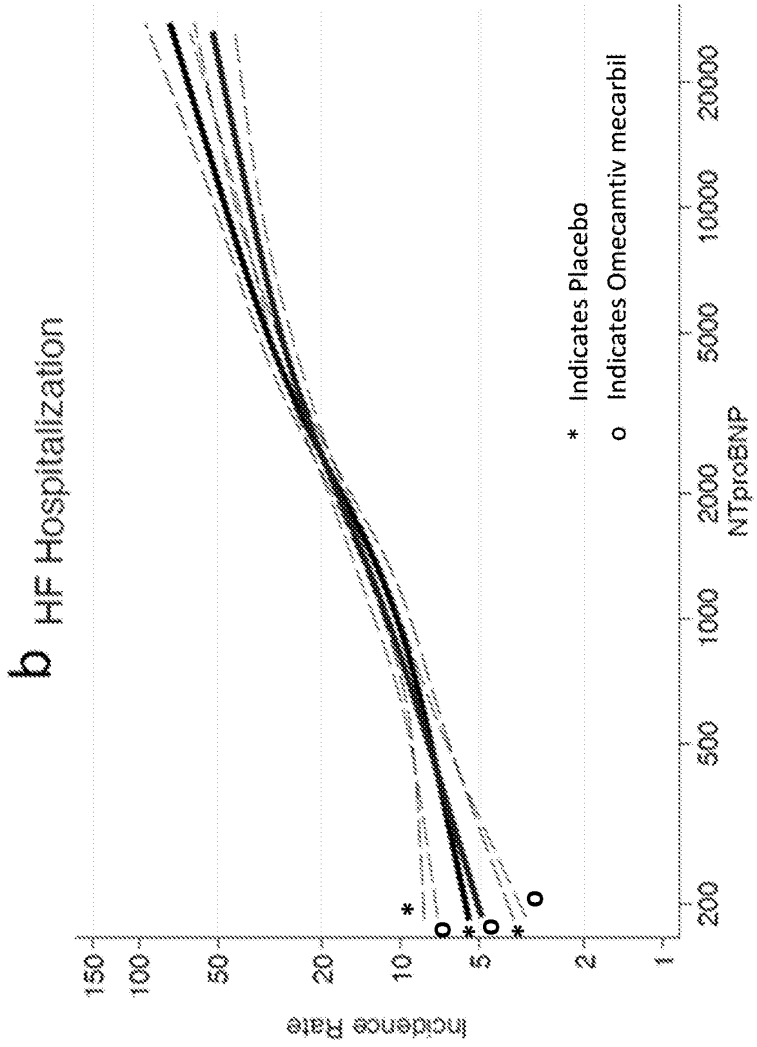

b HF Hospitalization
Incidence Rate
150
100
50
20
10
5
2
1
200
500
1000
2000
5000
10000
20000
NTproBNP
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 17B

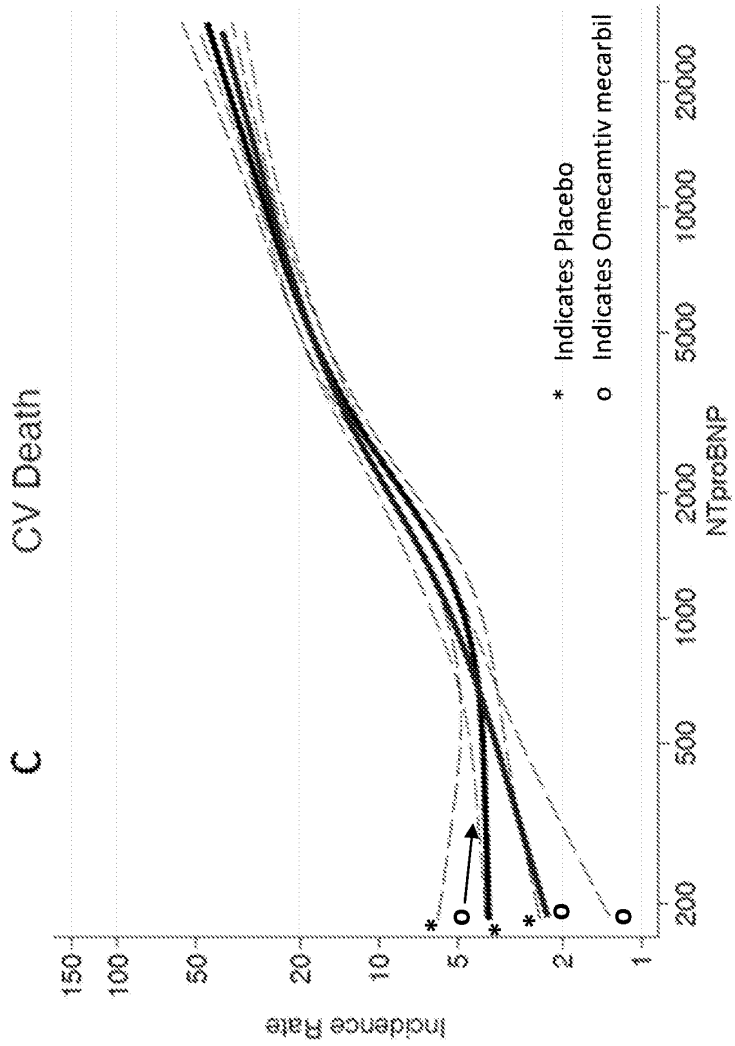

C
CV Death
Incidence Rate
150
100
50
20
10
5
2
1
200
500
1000
2000
5000
10000
20000
NTproBNP
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 17C

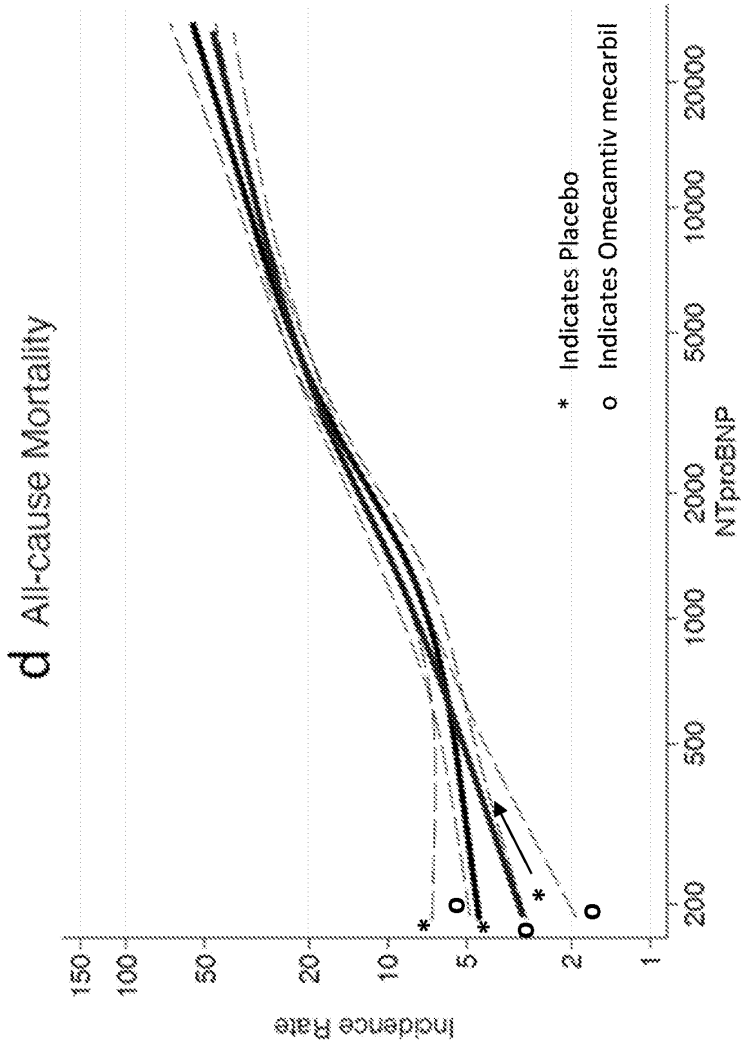

d All-cause Mortality
Incidence Rate
150
100
50
20
10
5
2
1
200
500
1000
2000
5000
10000
20000
NTproBNP
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 17D

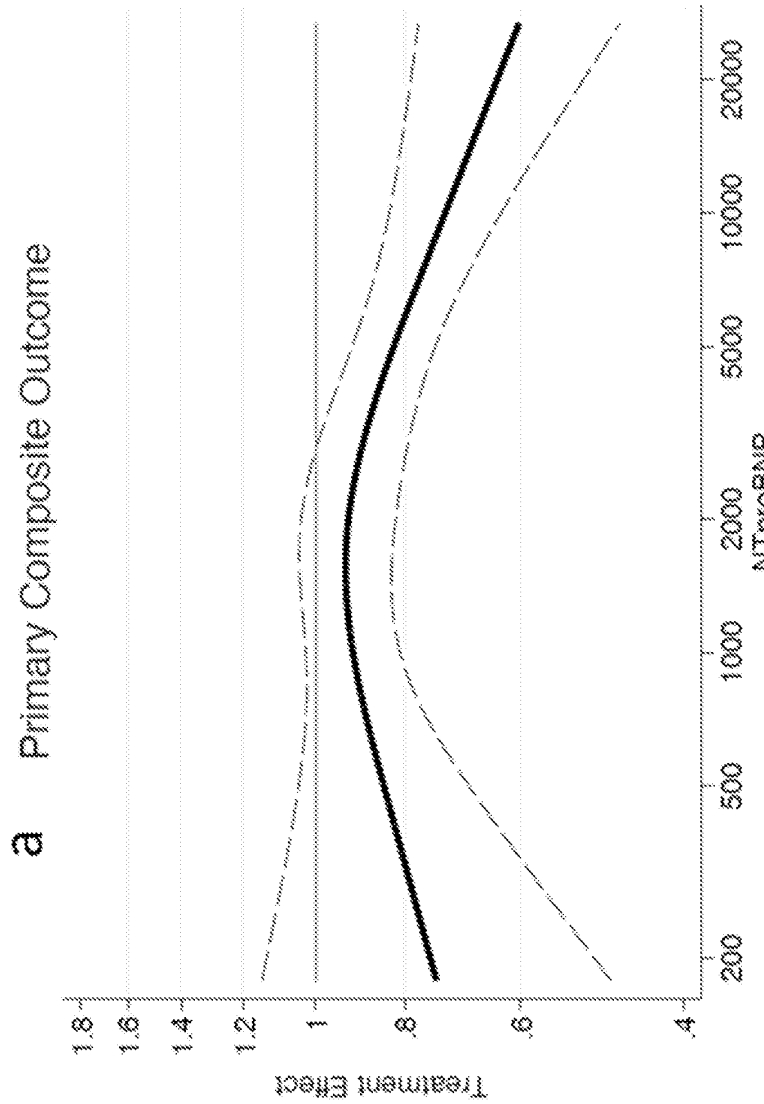

a Primary Composite Outcome
Treatment Effect
1.8
1.6
1.4
1.2
1
.8
.6
.4
200
500
1000
2000
5000
10000
20000
NTproBNP

FIGURE 18A

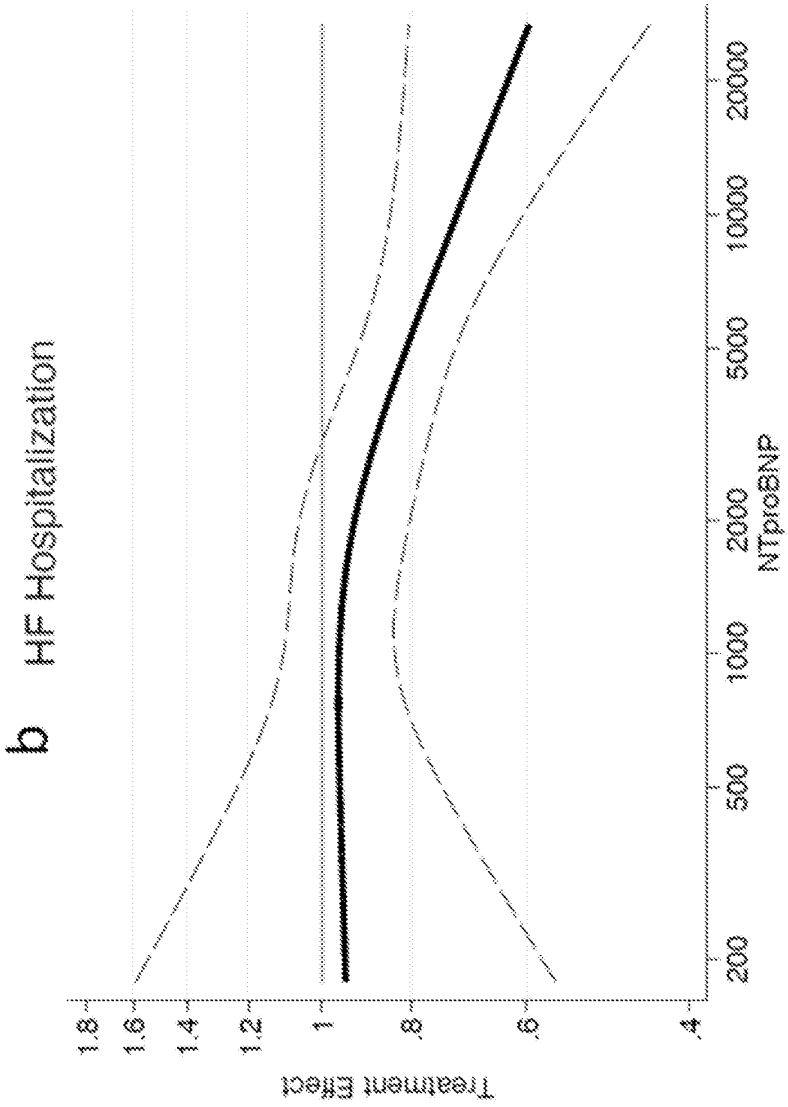

b HF Hospitalization
Treatment Effect
1.8
1.6
1.4
1.2
1
.8
.6
.4
200
500
1000
2000
5000
10000
20000
NTproBNP

FIGURE 18B

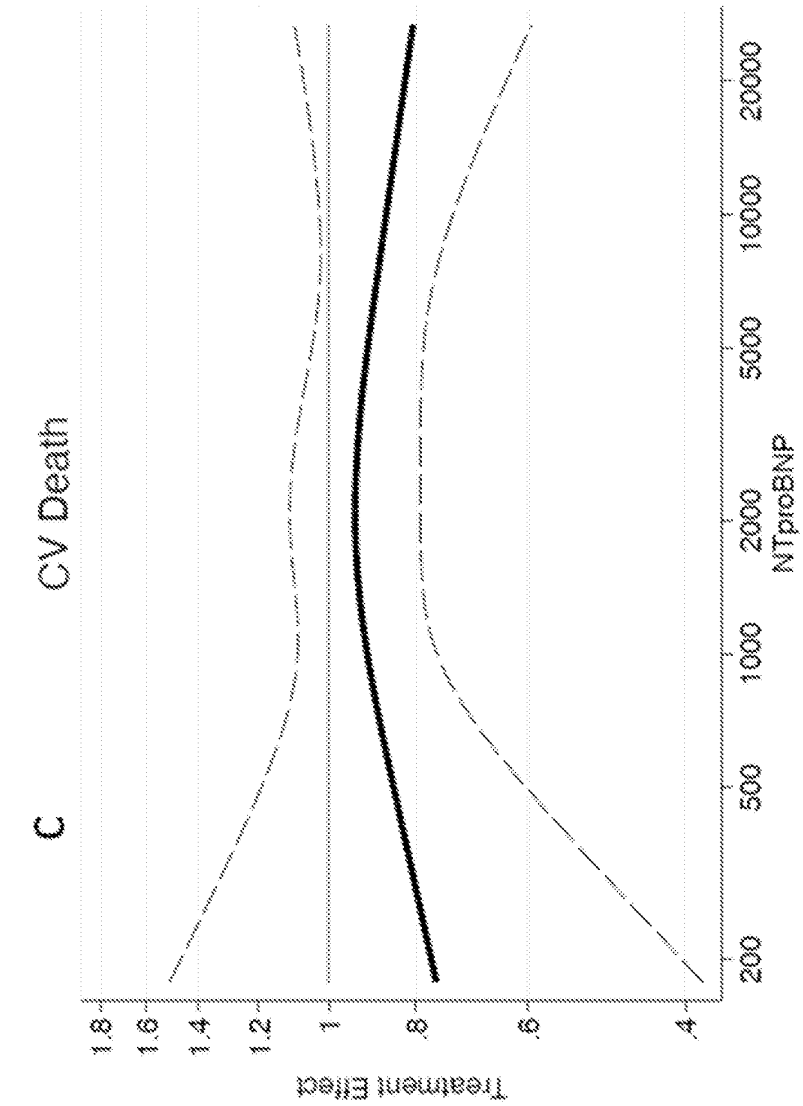

C
CV Death
Treatment Effect
1.8
1.6
1.4
1.2
1
.8
.6
.4
200
500
1000
2000
5000
10000
20000
NTproBNP

FIGURE 18C

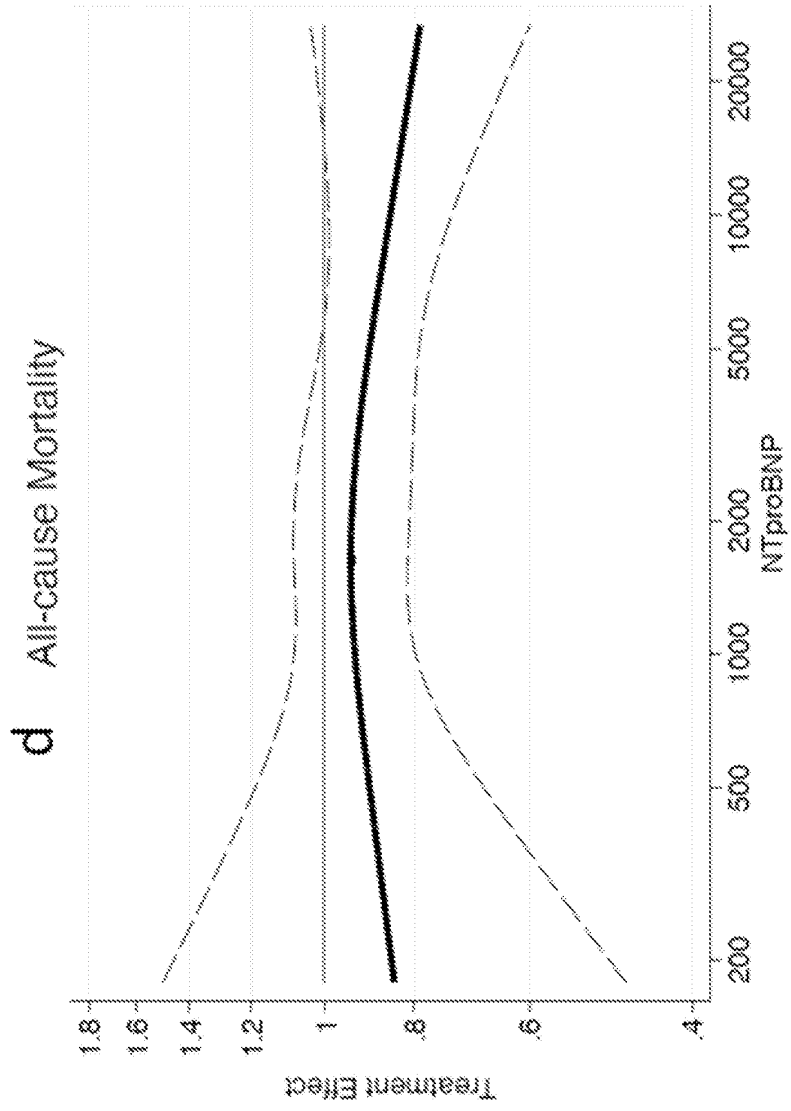

d All-cause Mortality
Treatment Effect
1.8
1.6
1.4
1.2
1
.8
.6
.4
200
500
1000
2000
5000
10000
20000
NTproBNP

FIGURE 18D

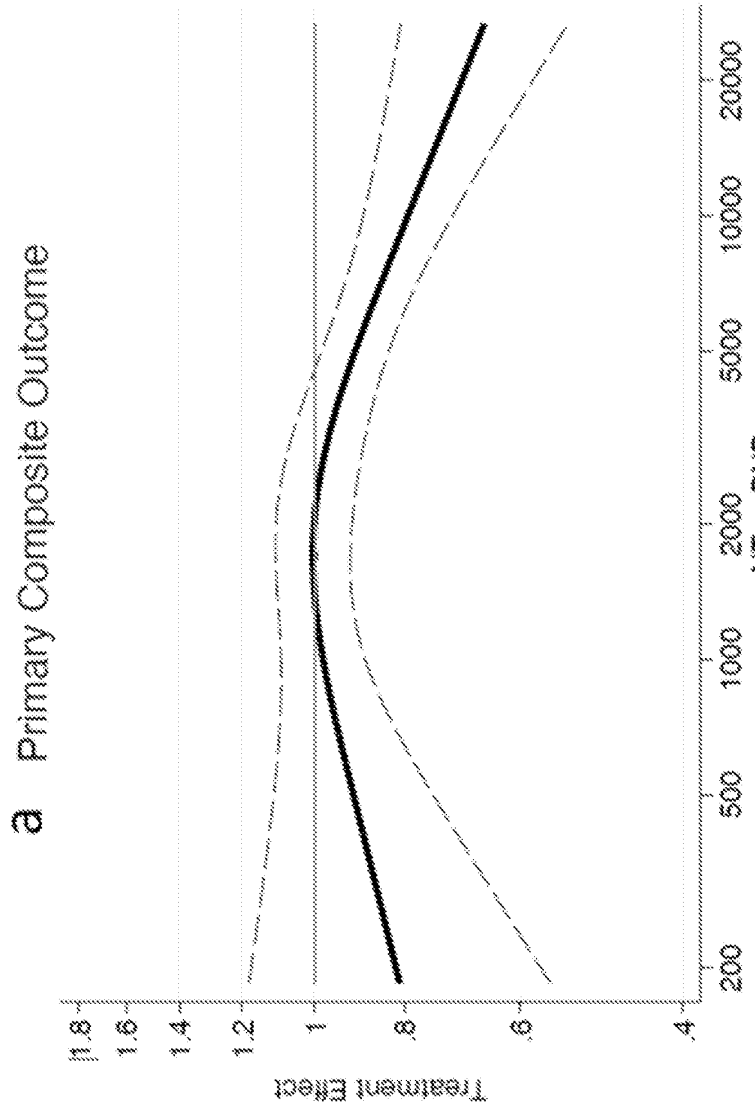

a Primary Composite Outcome
Treatment Effect
1.8
1.6
1.4
1.2
1
.8
.6
.4
200
500
1000
2000
5000
10000
20000
NTproBNP

FIGURE 19A

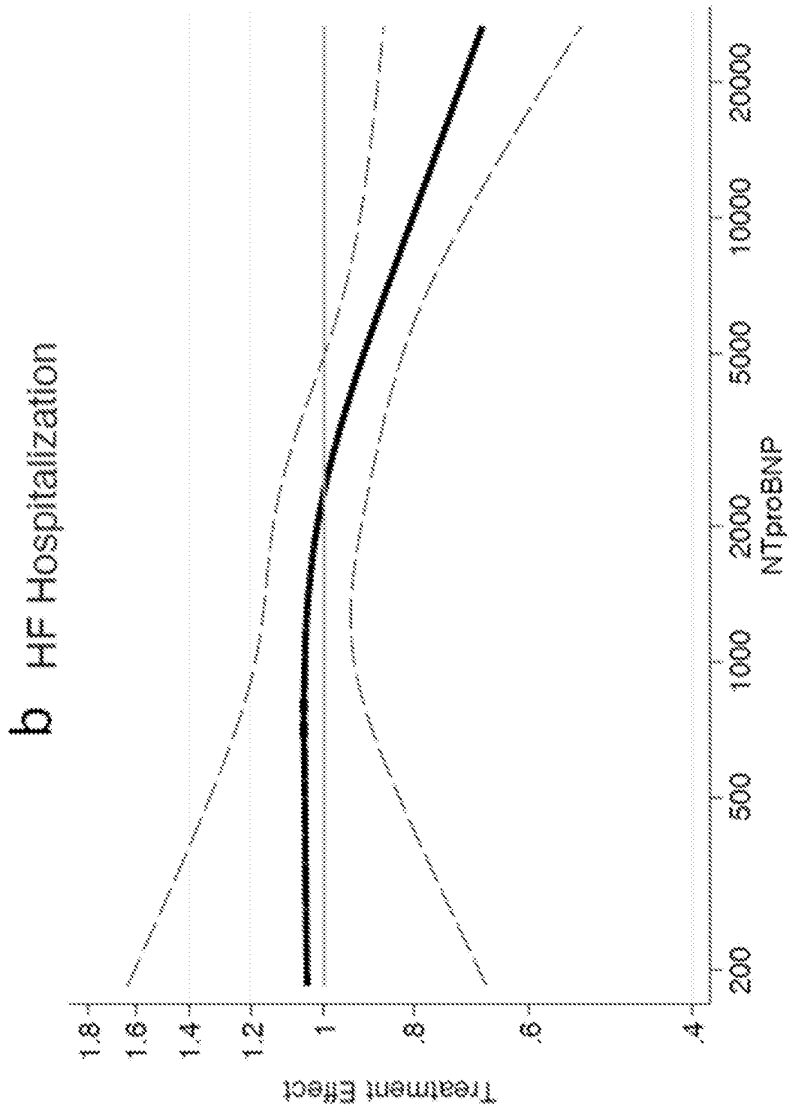

b HF Hospitalization
Treatment Effect
1.8
1.6
1.4
1.2
1
.8
.6
.4
200
500
1000
2000
5000
10000
20000
NTproBNP

FIGURE 19B

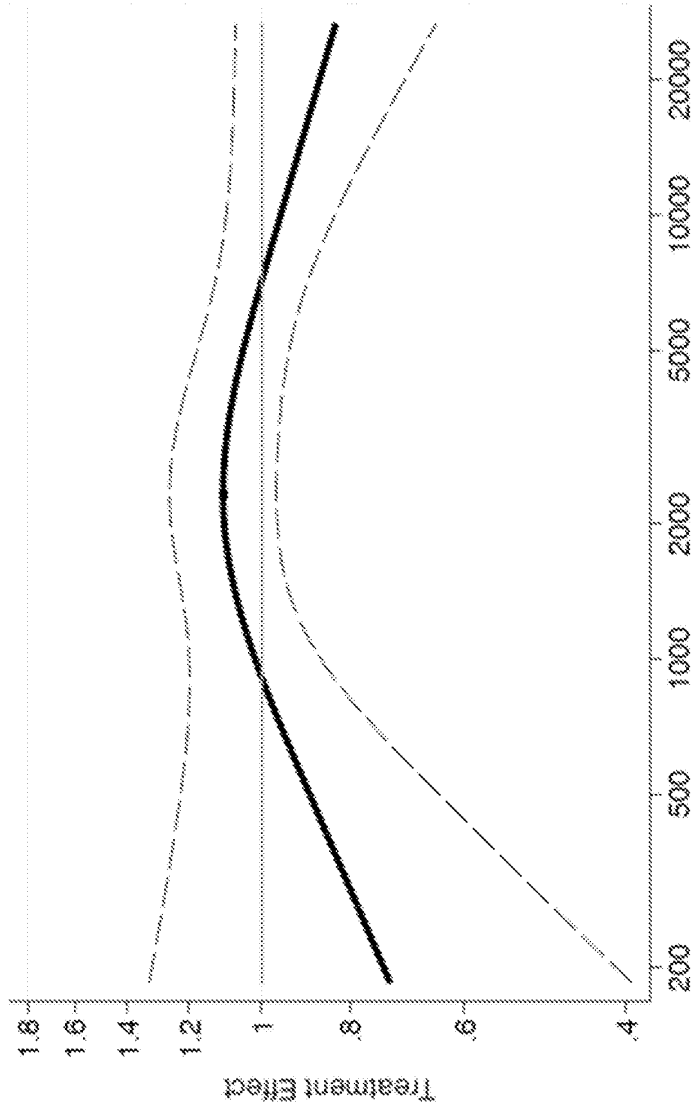

C
CV Death
Treatment Effect
1.8
1.6
1.4
1.2
1
.8
.6
.4
200
500
1000
2000
5000
10000
20000
NTproBNP

FIGURE 19C

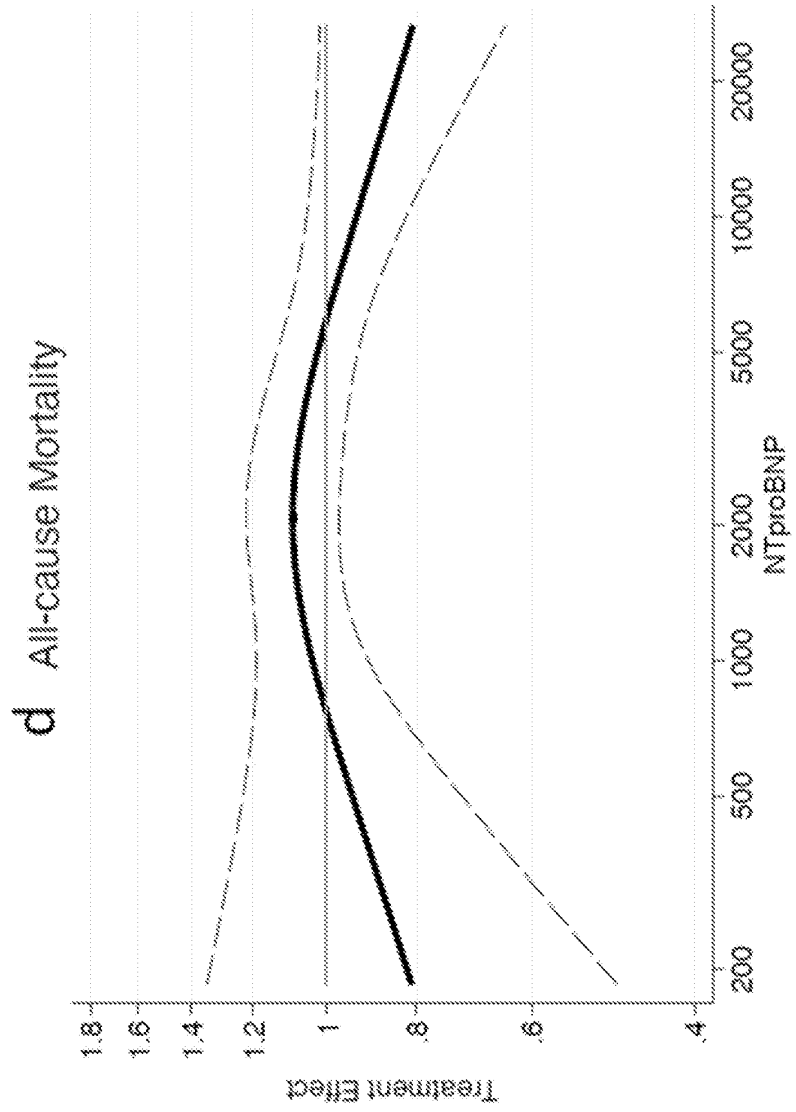

d All-cause Mortality
Treatment Effect
1.8
1.6
1.4
1.2
1
.8
.6
.4
200
500
1000
2000
5000
10000
20000
NTproBNP

FIGURE 19D

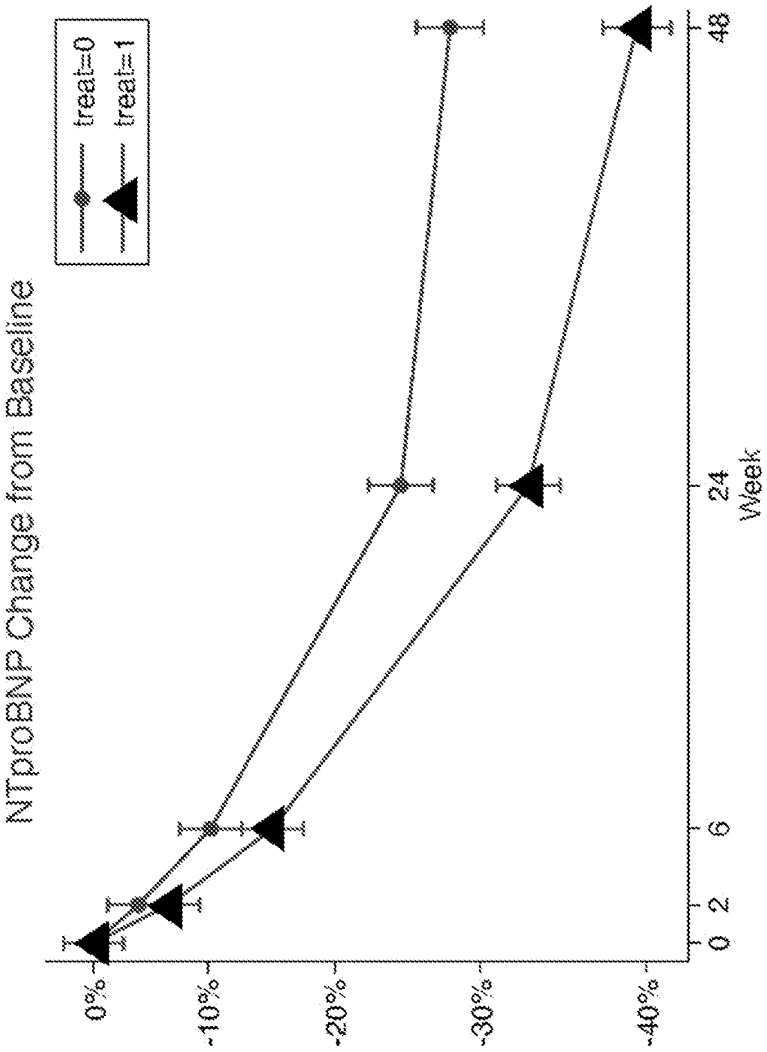

NTproBNP Change from Baseline
treat=0
treat=1
0%
-10%
-20%
-30%
-40%
0
2
6
24
48
Week

FIGURE 20A

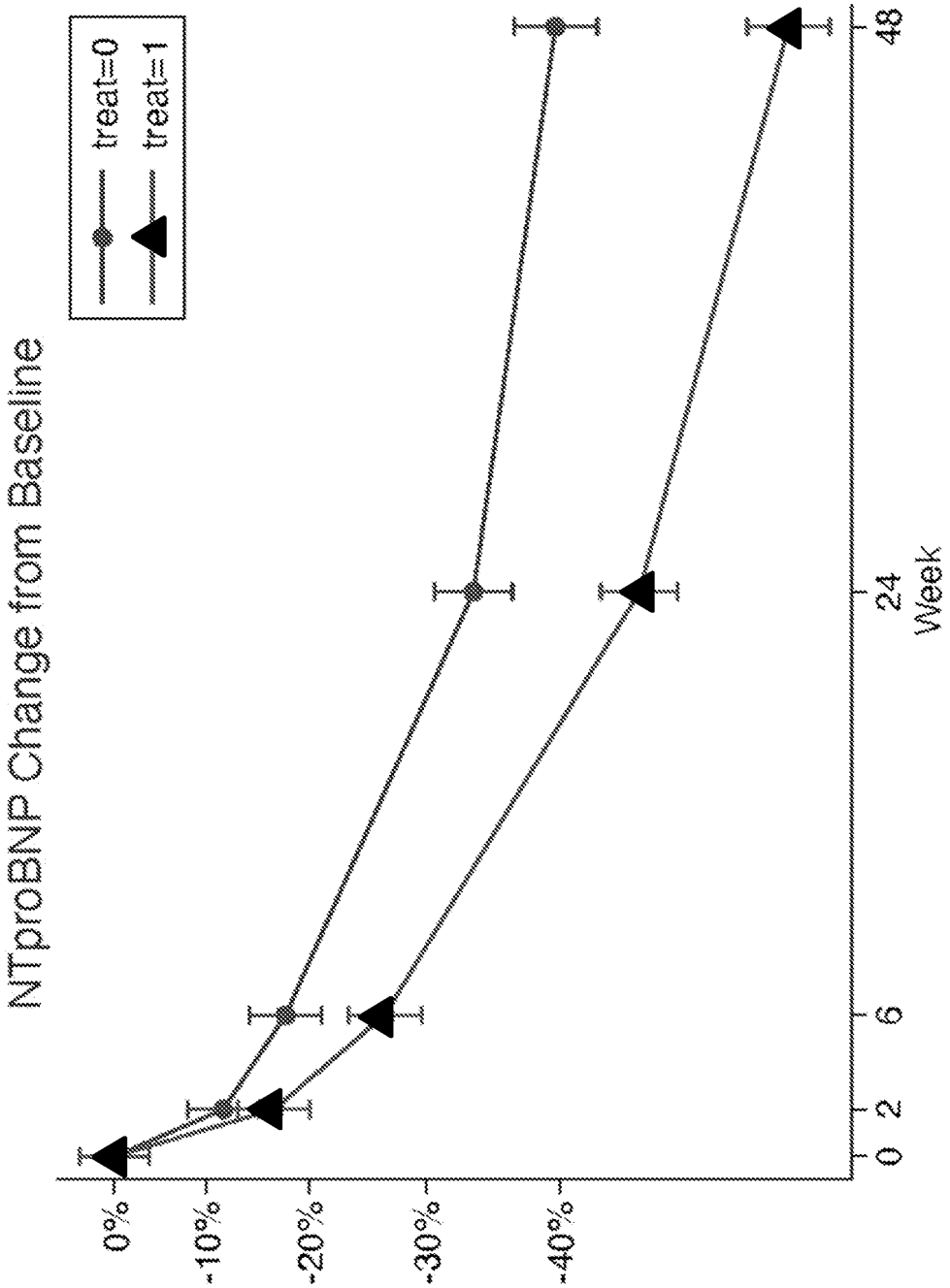

NTproBNP Change from Baseline
treat=0
treat=1
0%
-10%
-20%
-30%
-40%
0
2
6
24
48
Week

FIGURE 20B

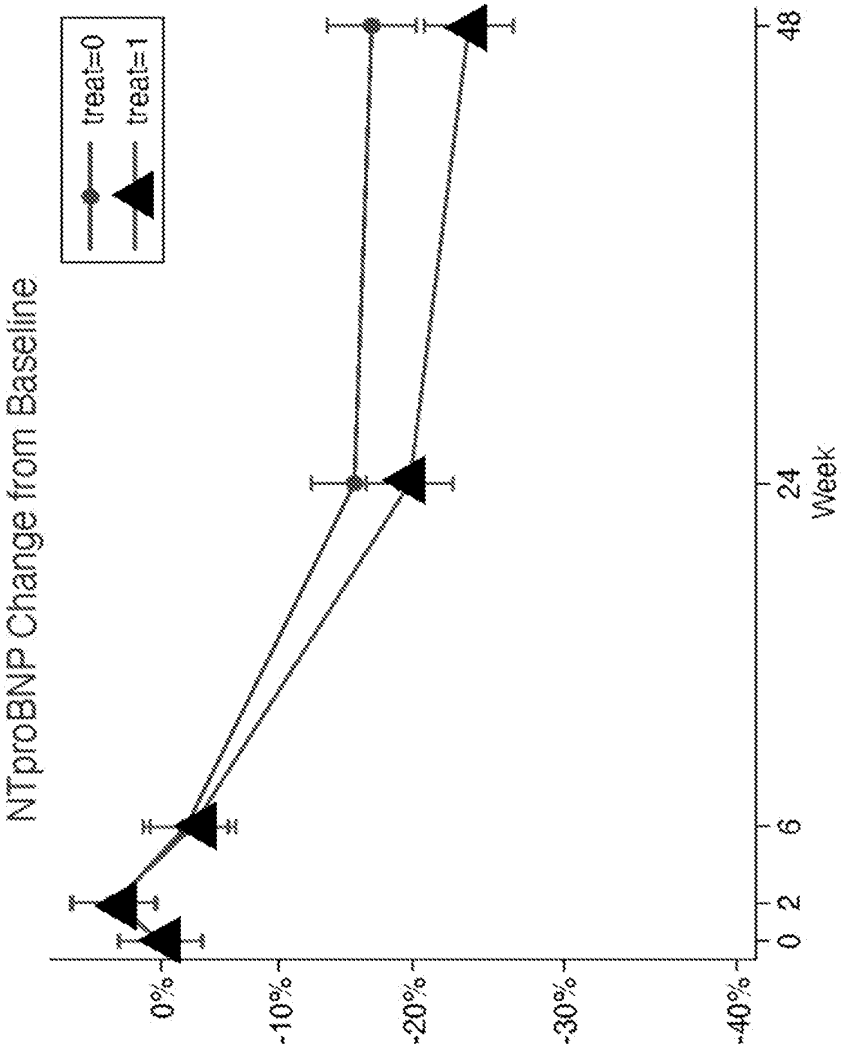

NTproBNP Change from Baseline
treat=0
treat=1
0%
-10%
-20%
-30%
-40%
0
2
6
24
48
Week

FIGURE 20C

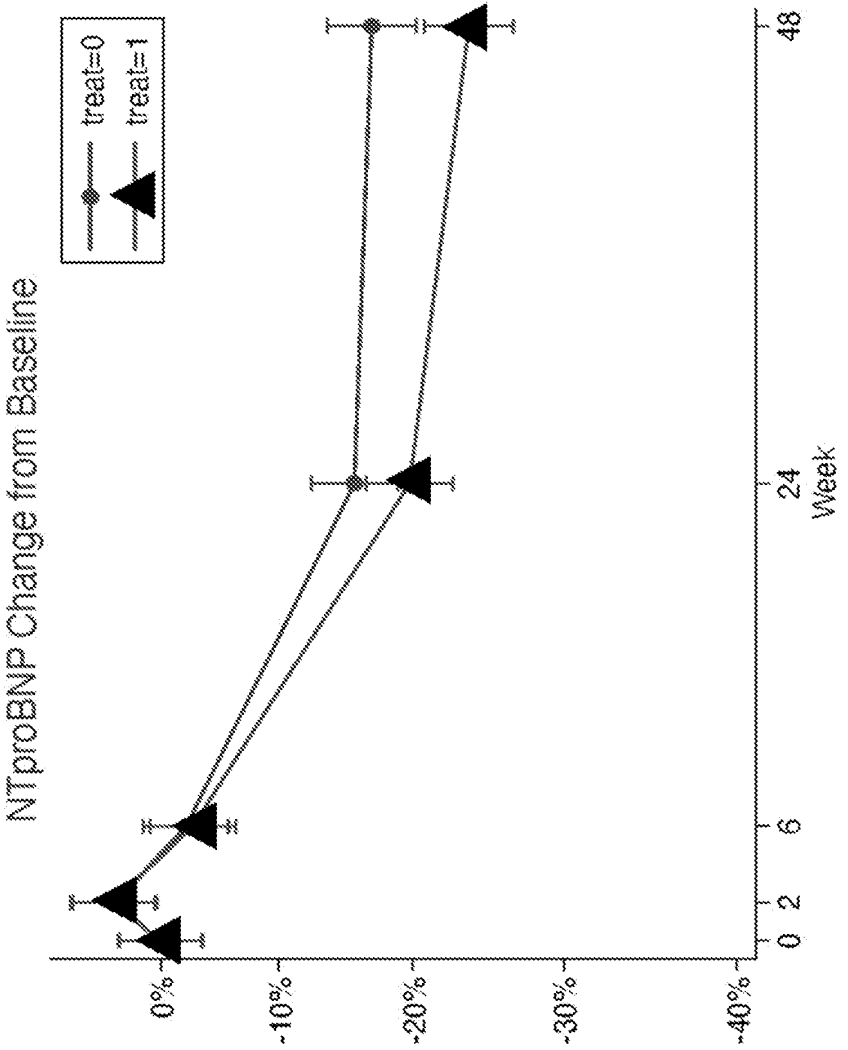

NTproBNP Change from Baseline
treat=0
treat=1
0%
-10%
-20%
-30%
-40%
0
2
6
24
48
Week

FIGURE 20D

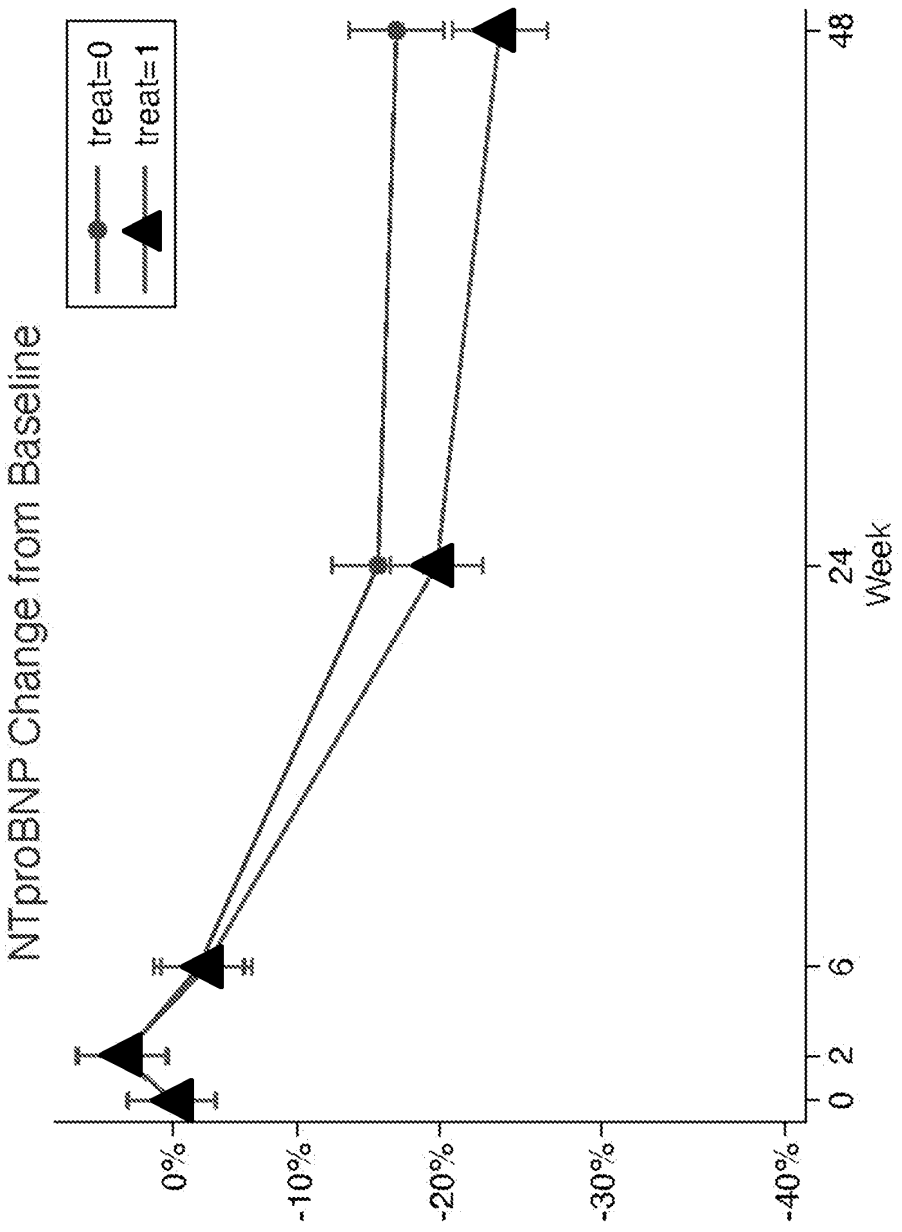

NTproBNP Change from Baseline
treat=0
treat=1
0%
-10%
-20%
-30%
-40%
0
2
6
24
48
Week

FIGURE 20E

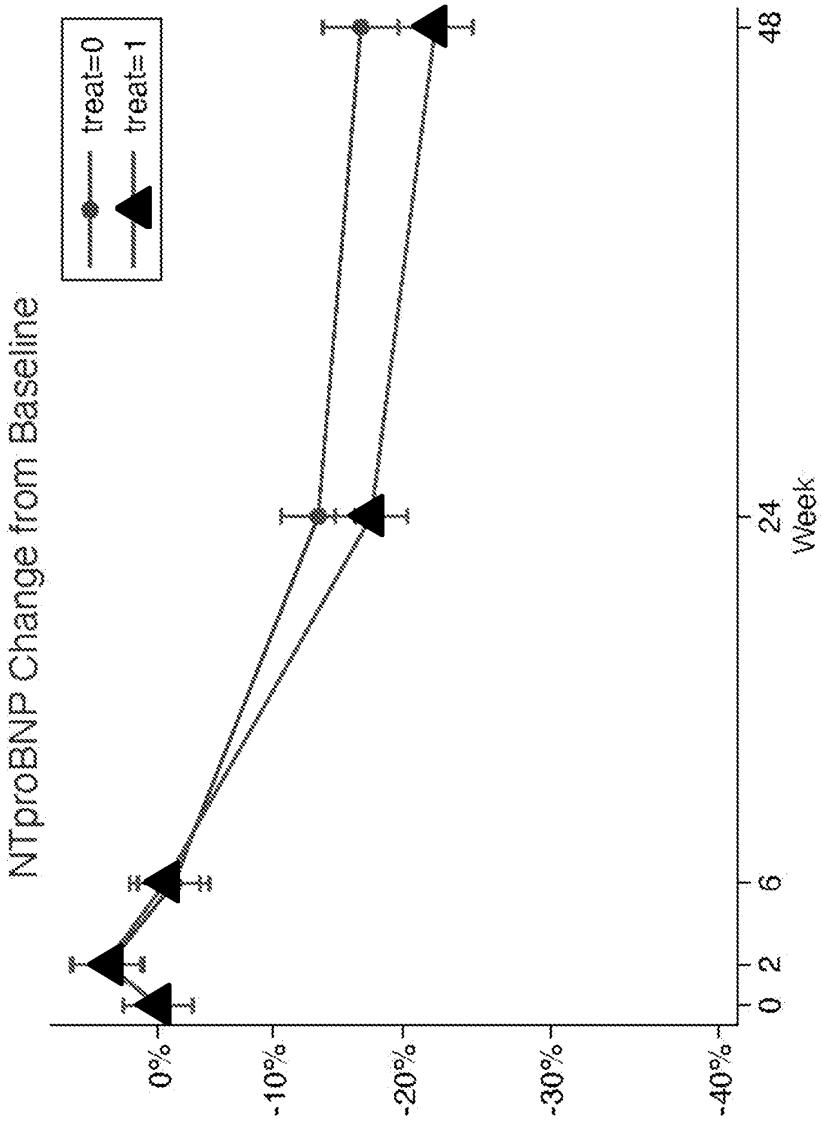

NTproBNP Change from Baseline
treat=0
treat=1
0%
-10%
-20%
-30%
-40%
0
2
6
24
48
Week

FIGURE 20F

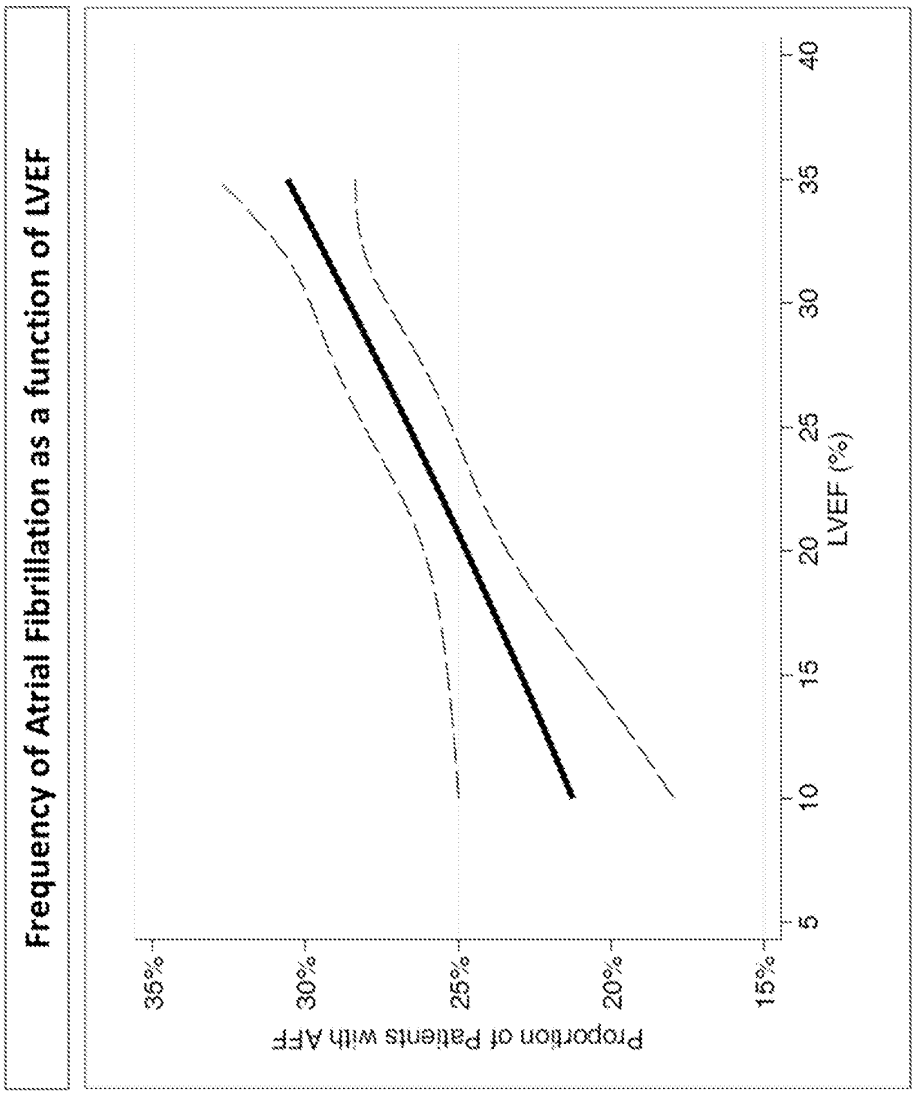

Frequency of Atrial Fibrillation as a function of LVEF
Proportion of Patients with AFF
35%
30%
25%
20%
15%
5
10
15
20
25
30
35
40
LVEF (%)

FIGURE 21A

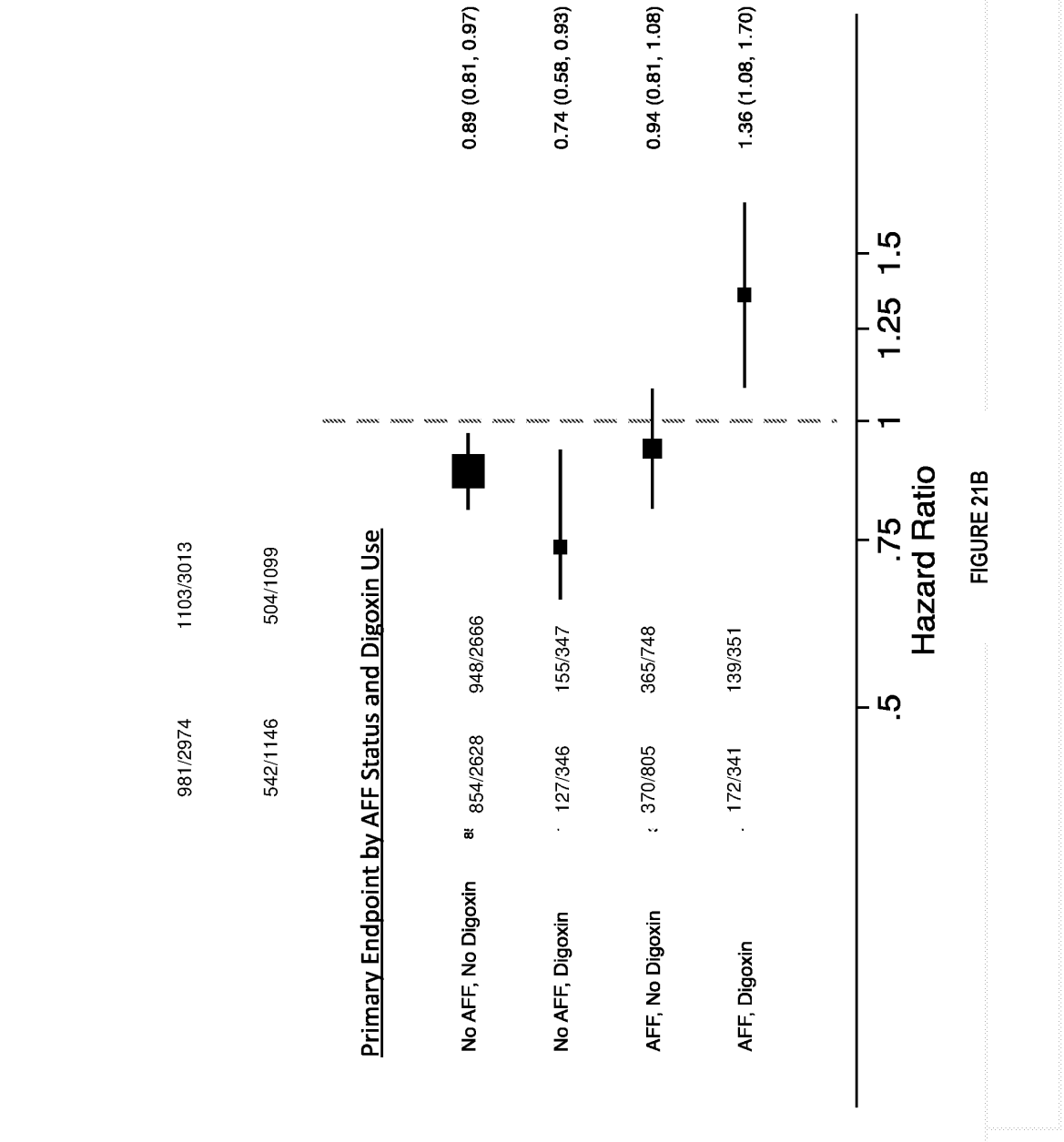

Primary Endpoint by AFF Status and Digoxin Use
No AFF, No Digoxin
854/2628
948/2666
0.89 (0.81, 0.97)
No AFF, Digoxin
127/346
155/347
0.74 (0.58, 0.93)
AFF, No Digoxin
370/805
365/748
0.94 (0.81, 1.08)
AFF, Digoxin
172/341
139/351
1.36 (1.08, 1.70)
981/2974
1103/3013
542/1146
504/1099
.5
.75
1
1.25
1.5
Hazard Ratio

FIGURE 21B

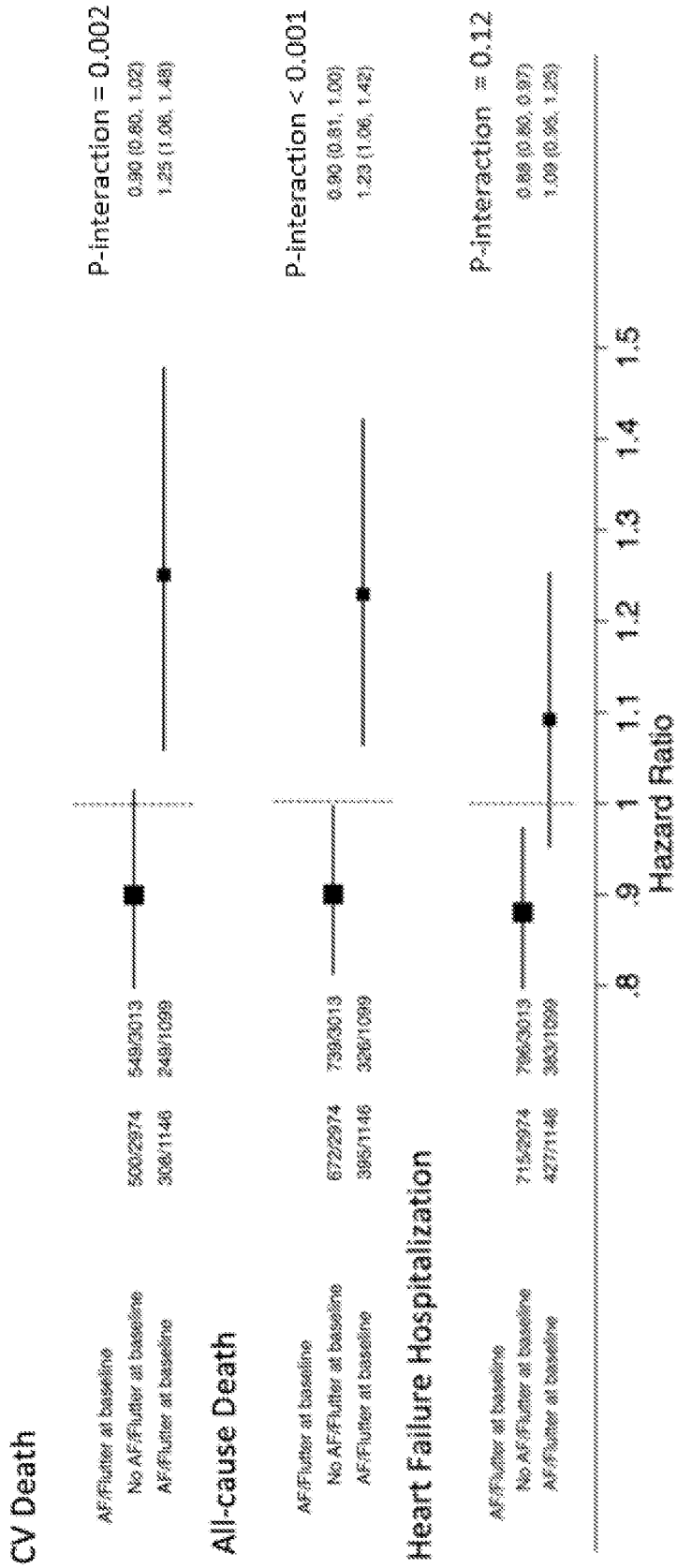

CV Death
AF/Flutter at baseline
No AF/Flutter at baseline 500/2874 548/3013 0.90 (0.80, 1.02)
AF/Flutter at baseline 308/1146 248/1099 1.25 (1.06, 1.48)
P-interaction = 0.002
All-cause Death
AF/Flutter at baseline
No AF/Flutter at baseline 672/2874 739/3013 0.90 (0.81, 1.00)
AF/Flutter at baseline 396/1146 326/1099 1.23 (1.06, 1.42)
P-interaction < 0.001
Heart Failure Hospitalization
AF/Flutter at baseline
No AF/Flutter at baseline 715/2874 796/3013 0.88 (0.80, 0.97)
AF/Flutter at baseline 427/1146 363/1099 1.09 (0.94, 1.25)
P-interaction = 0.12
.8 .9 1 1.1 1.2 1.3 1.4 1.5
Hazard Ratio

FIGURE 21C

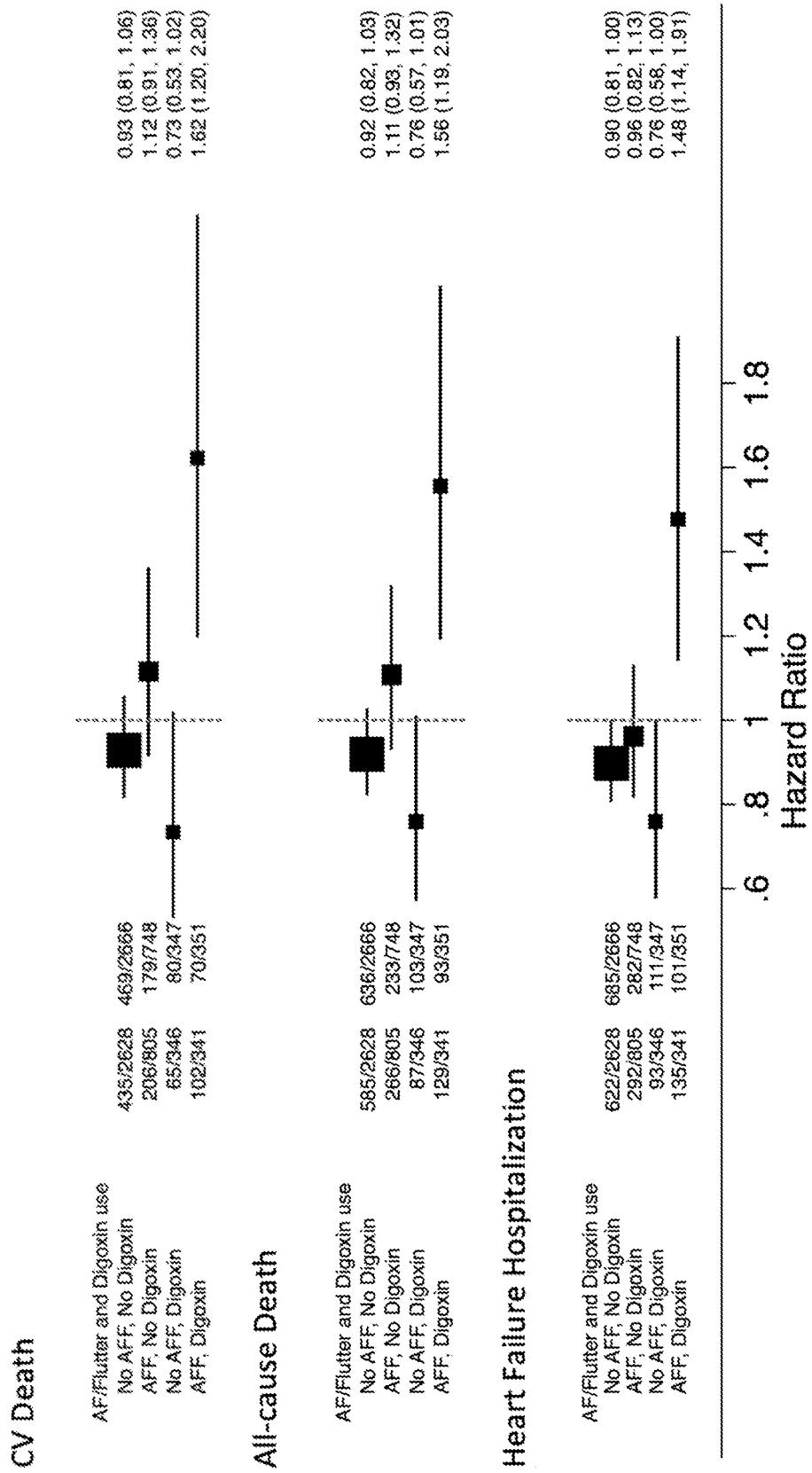

CV Death
AF/Flutter and Digoxin use
No AFF, No Digoxin 435/2628 469/2666 0.93 (0.81, 1.06)
AFF, No Digoxin 206/805 179/748 1.12 (0.91, 1.36)
No AFF, Digoxin 65/346 80/347 0.73 (0.53, 1.02)
AFF, Digoxin 102/341 70/351 1.62 (1.20, 2.20)
All-cause Death
AF/Flutter and Digoxin use
No AFF, No Digoxin 585/2628 636/2666 0.92 (0.82, 1.03)
AFF, No Digoxin 266/805 233/748 1.11 (0.93, 1.32)
No AFF, Digoxin 87/346 103/347 0.76 (0.57, 1.01)
AFF, Digoxin 129/341 93/351 1.56 (1.19, 2.03)
Heart Failure Hospitalization
AF/Flutter and Digoxin use
No AFF, No Digoxin 622/2628 685/2666 0.90 (0.81, 1.00)
AFF, No Digoxin 292/805 282/748 0.96 (0.82, 1.13)
No AFF, Digoxin 93/346 111/347 0.76 (0.58, 1.00)
AFF, Digoxin 135/341 101/351 1.48 (1.14, 1.91)
.6
.8
1
1.2
1.4
1.6
1.8
Hazard Ratio

FIGURE 21D

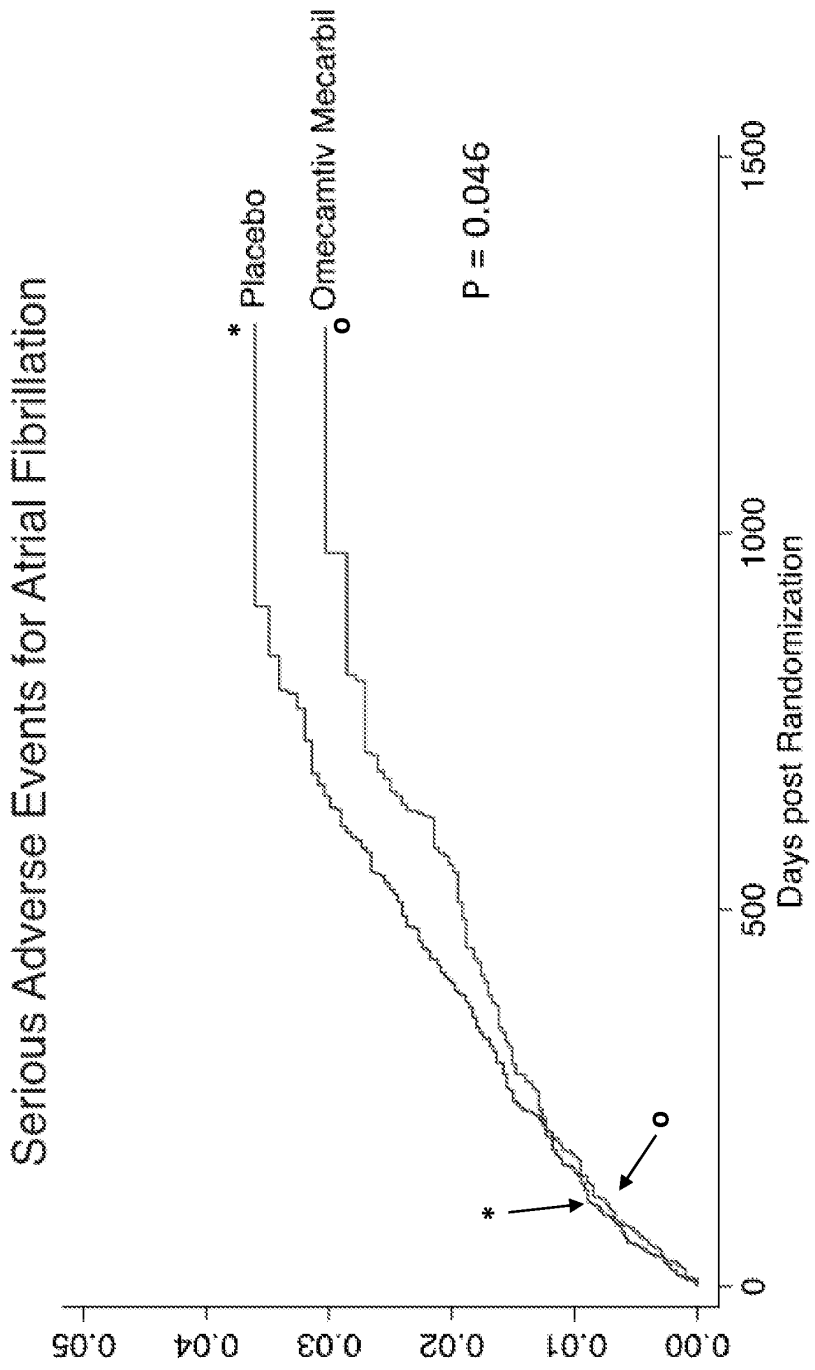

Serious Adverse Events for Atrial Fibrillation
* Placebo
o Omecamtiv Mecarbil
P = 0.046
0.00
0.01
0.02
0.03
0.04
0.05
0
500
1000
1500
Days post Randomization

FIGURE 21E

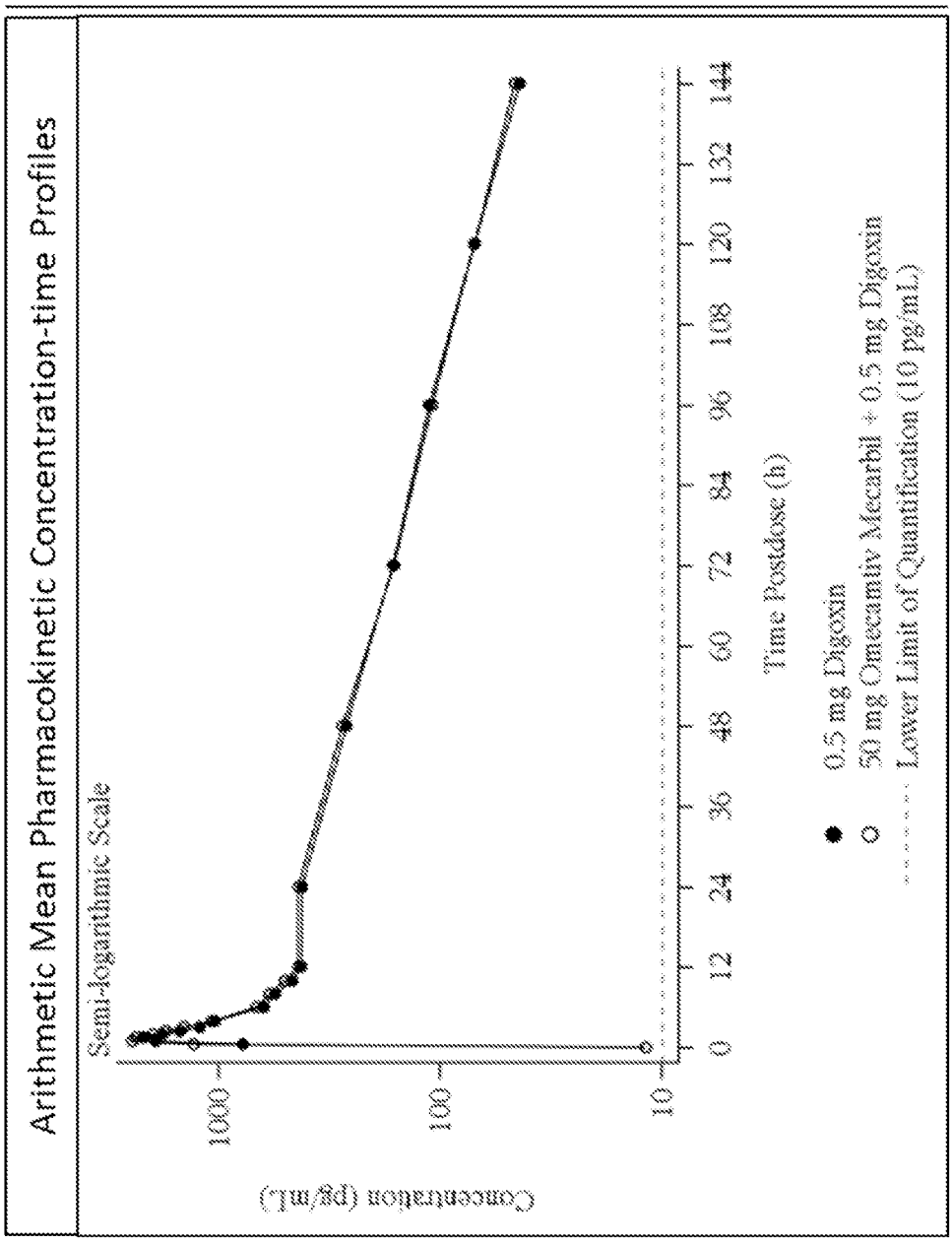

Arithmetic Mean Pharmacokinetic Concentration-time Profiles
Semi-logarithmic Scale
Concentration (pg/mL)
1000
100
10
0
12
24
36
48
60
72
84
96
108
120
132
144
Time Postdose (h)
0.5 mg Digoxin
50 mg Omecamtiv Mecarbil + 0.5 mg Digoxin
Lower Limit of Quantification (10 pg/mL)

FIGURE 21F

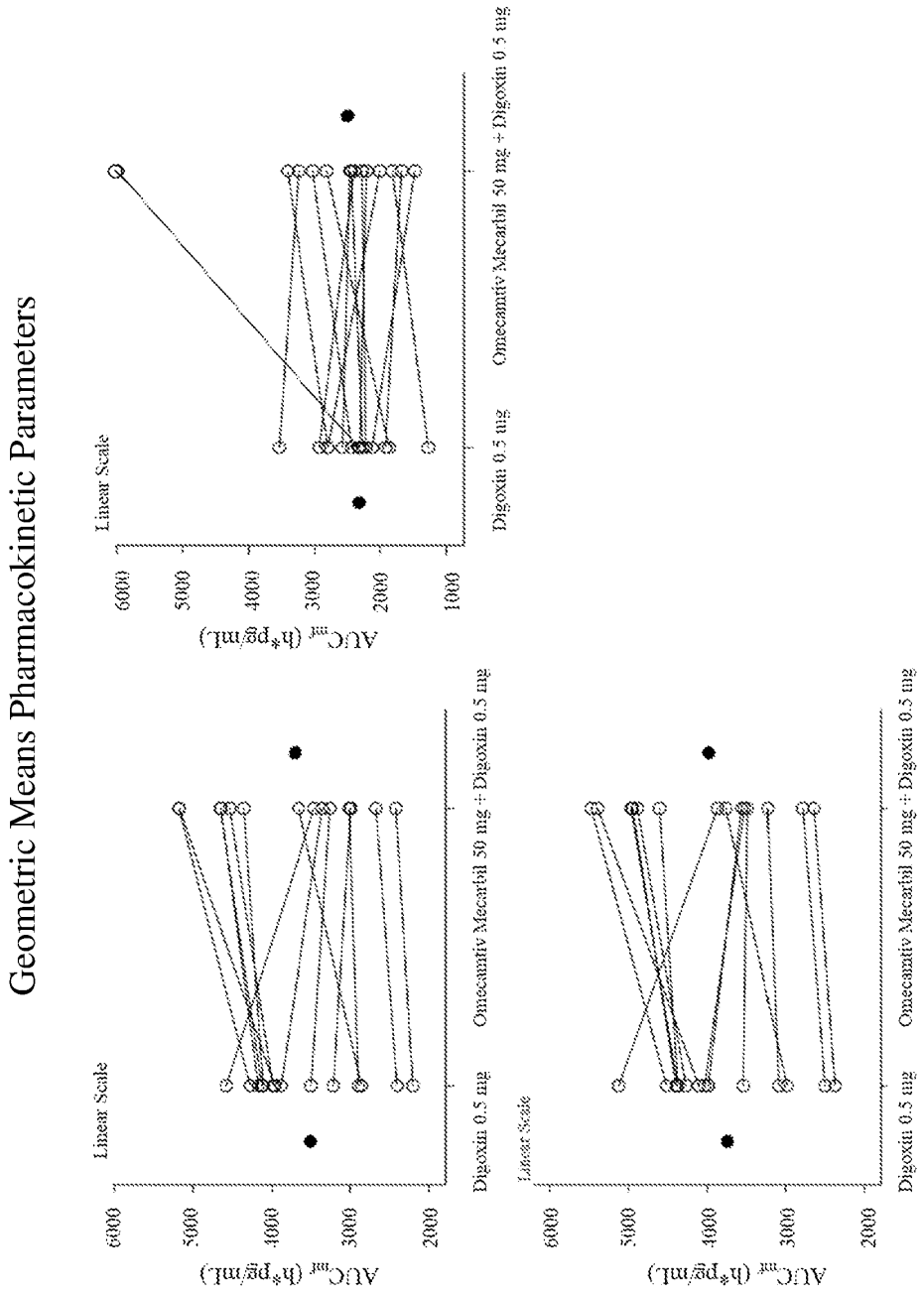

Geometric Means Pharmacokinetic Parameters
Linear Scale
AUC_{inf} (h*pg/mL)
6000
5000
4000
3000
2000
1000
Digoxin 0.5 mg
Omecamtiv Mecarbil 50 mg + Digoxin 0.5 mg
Linear Scale
AUC_{inf} (h*pg/mL)
6000
5000
4000
3000
2000
Digoxin 0.5 mg
Omecamtiv Mecarbil 50 mg + Digoxin 0.5 mg
Geometric Mean
Individual Value

FIGURE 21G

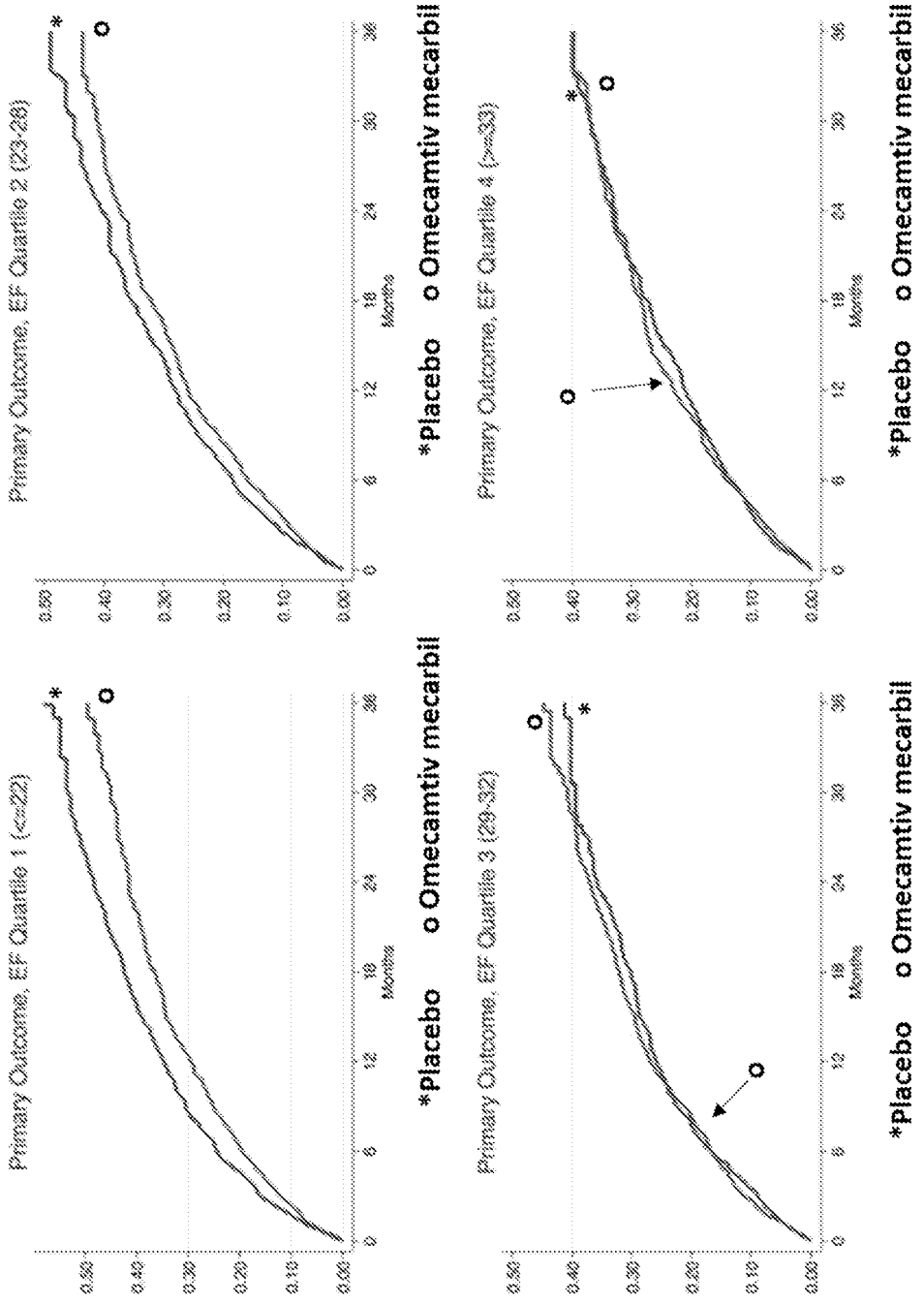

Primary Outcome, EF Quartile 1 (<=22)
Primary Outcome, EF Quartile 2 (23-28)
Primary Outcome, EF Quartile 3 (29-32)
Primary Outcome, EF Quartile 4 (>=33)
0.50
0.40
0.30
0.20
0.10
0.00
0
6
12
18
24
30
36
Months
*Placebo
o Omecamtiv mecarbil

FIGURE 22

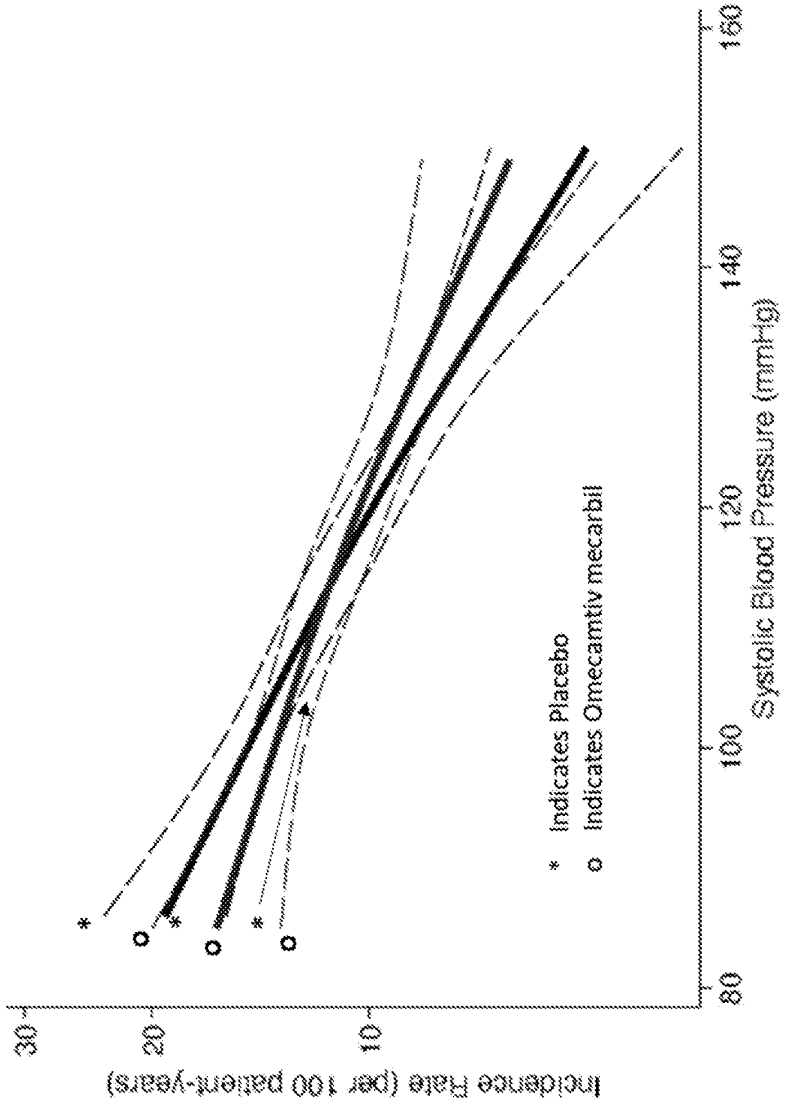

Incidence Rate (per 100 patient-years)
30
20
10
80
100
120
140
160
Systolic Blood Pressure (mmHg)
* Indicates Placebo
o Indicates Omecamtiv mecarbil

FIGURE 23A

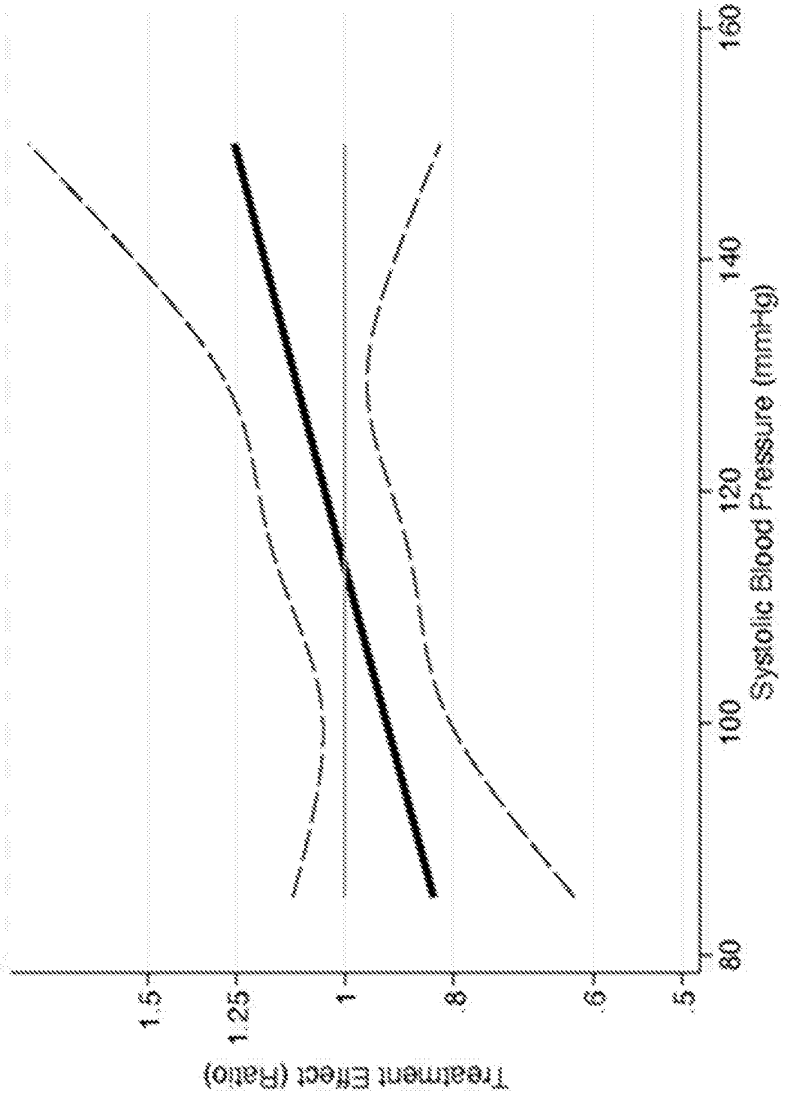

Treatment Effect (Ratio)
1.5
1.25
1
.8
.6
.5
80
100
120
140
160
Systolic Blood Pressure (mmHg)

FIGURE 23B

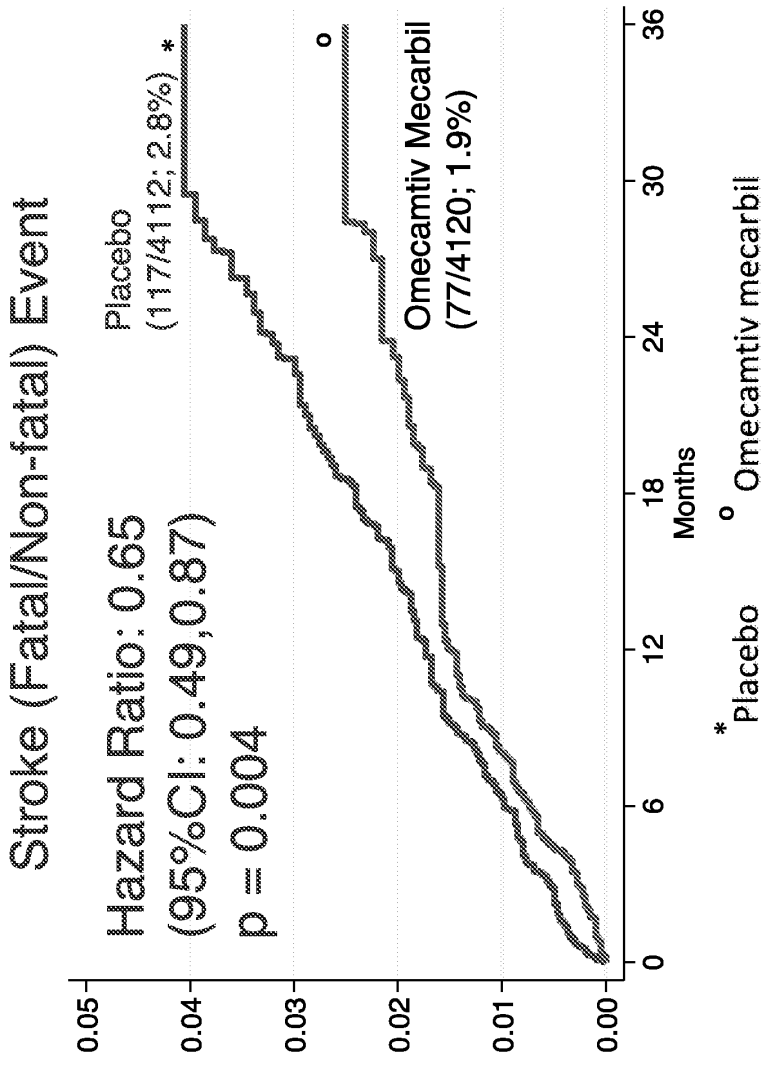

Stroke (Fatal/Non-fatal) Event
Hazard Ratio: 0.65
(95%CI: 0.49,0.87)
p = 0.004
Placebo
(117/4112; 2.8%) *
Omecamtiv Mecarbil
(77/4120; 1.9%)
0.05
0.04
0.03
0.02
0.01
0.00
0
6
12
18
24
30
36
Months
* Placebo
o Omecamtiv mecarbil

FIGURE 24

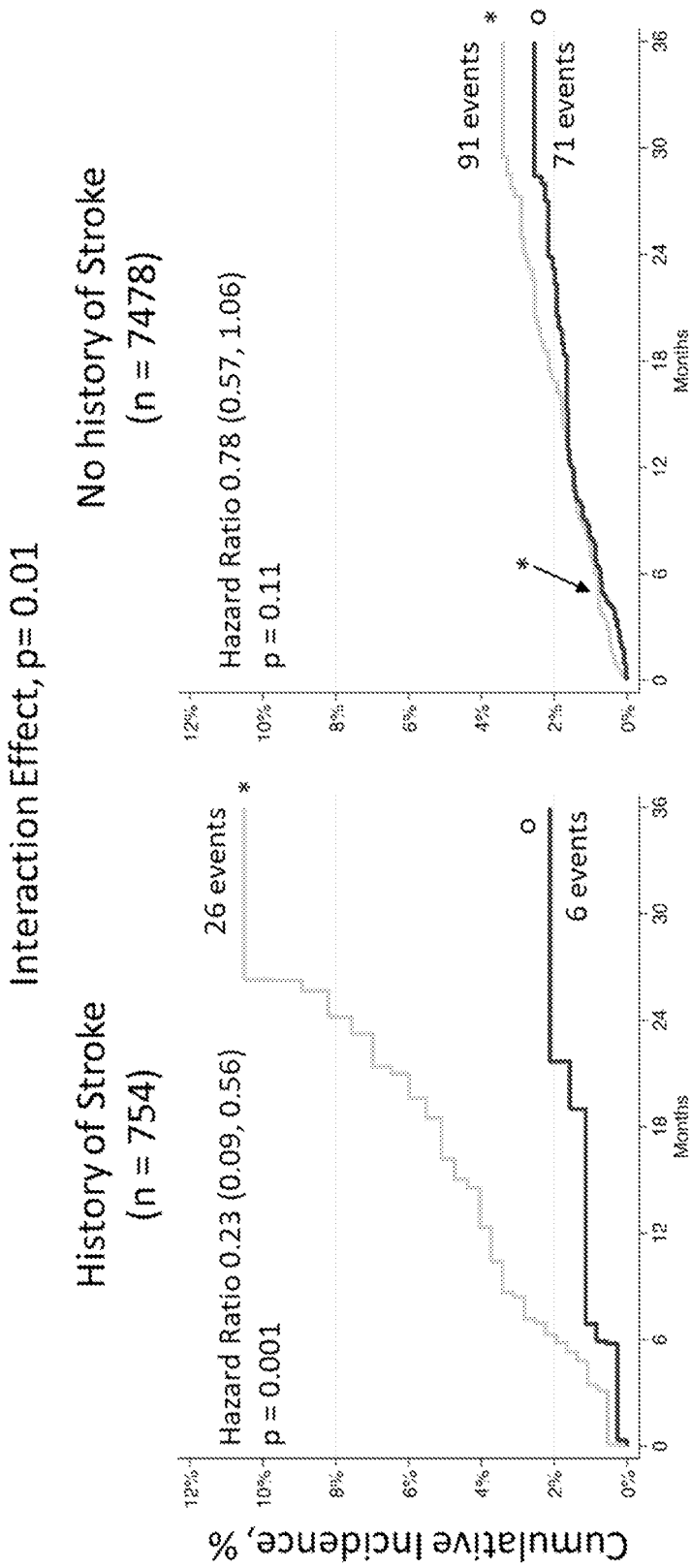

Interaction Effect, p= 0.01
History of Stroke
(n = 754)
No history of Stroke
(n = 7478)
Hazard Ratio 0.23 (0.09, 0.56)
p = 0.001
Hazard Ratio 0.78 (0.57, 1.06)
p = 0.11
26 events
6 events
91 events
71 events
Cumulative Incidence, %
Months
* Placebo o Omecamtiv mecarbil

FIGURE 25

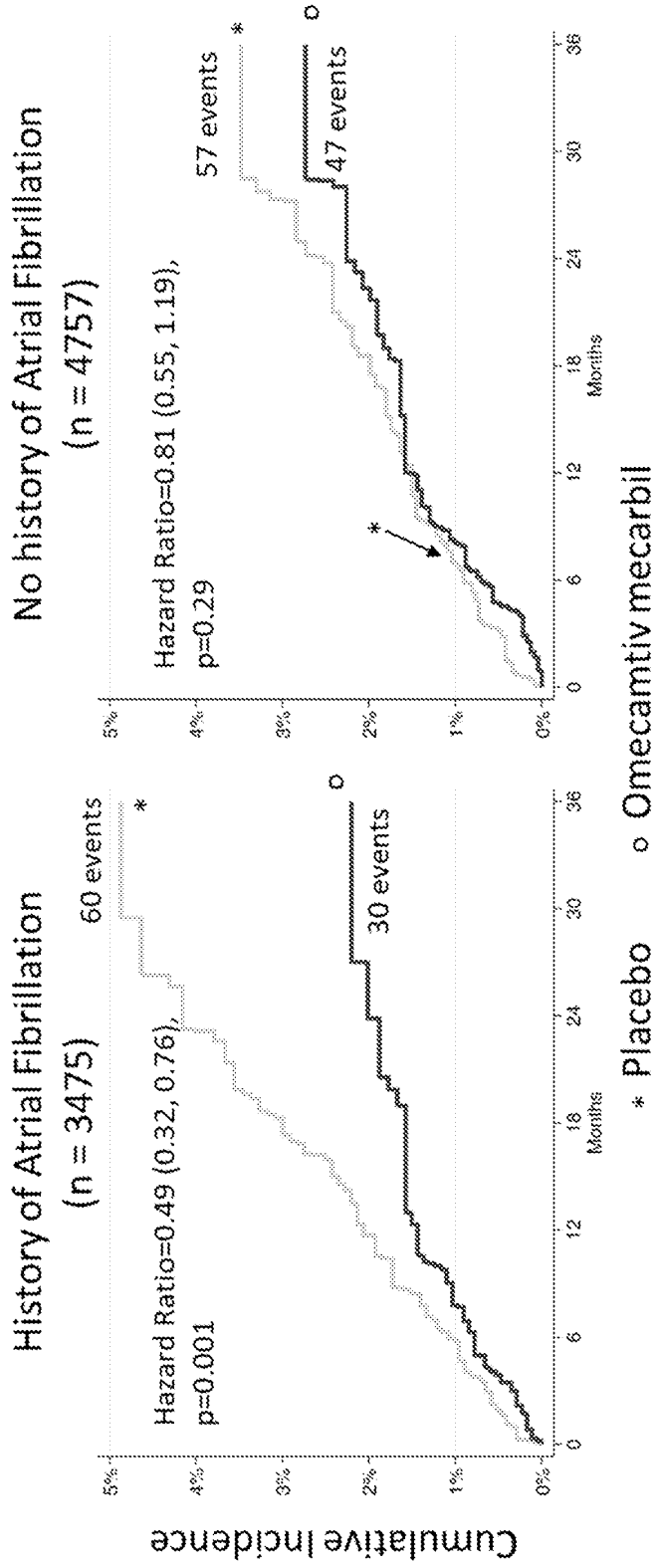

History of Atrial Fibrillation
(n = 3475)
Hazard Ratio=0.49 (0.32, 0.76),
p=0.001
60 events
30 events
No history of Atrial Fibrillation
(n = 4757)
Hazard Ratio=0.81 (0.55, 1.19),
p=0.29
57 events
47 events
Cumulative Incidence
5%
4%
3%
2%
1%
0%
0
6
12
18
24
30
36
Months
* Placebo
o Omecamtiv mecarbil

FIGURE 26

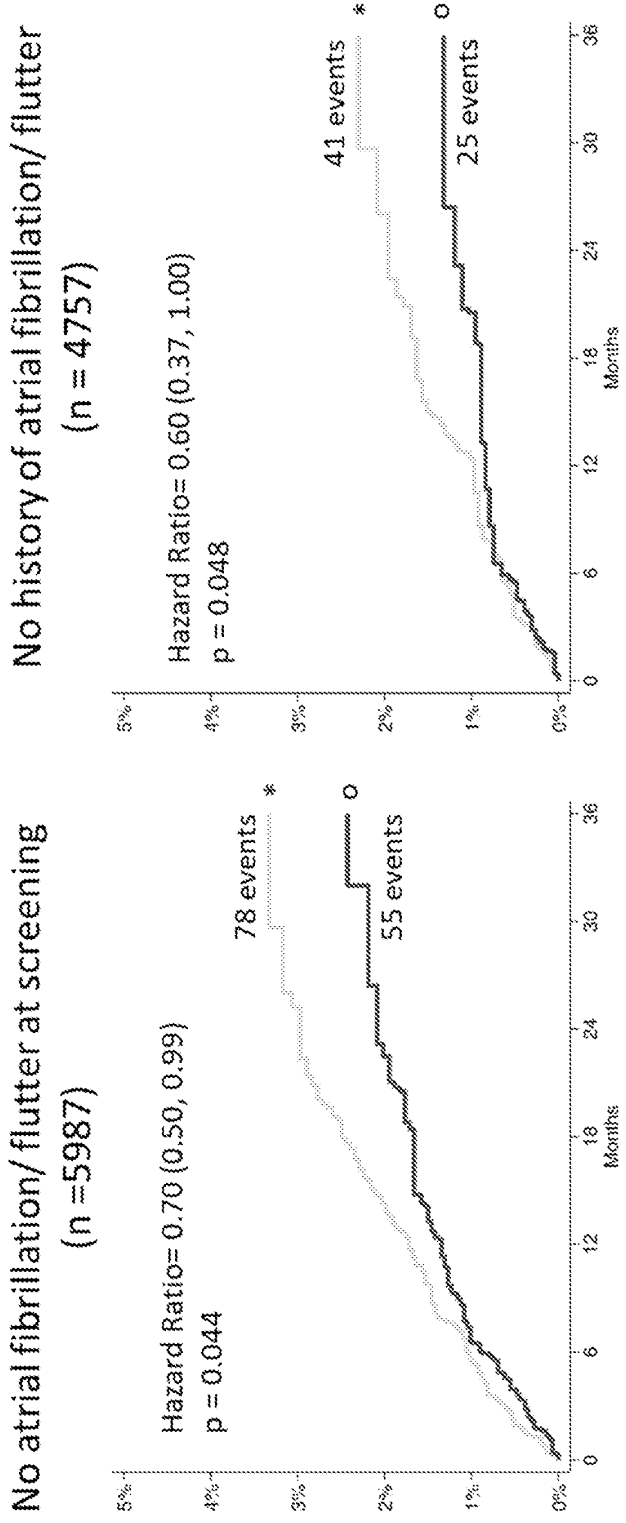

No atrial fibrillation/ flutter at screening
(n =5987)
Hazard Ratio= 0.70 (0.50, 0.99)
p = 0.044
78 events
55 events
No history of atrial fibrillation/ flutter
(n = 4757)
Hazard Ratio= 0.60 (0.37, 1.00)
p = 0.048
41 events
25 events
5%
4%
3%
2%
1%
0%
0
6
12
18
24
30
36
Months
* Placebo
o Omecamtiv mecarbil

FIGURE 27