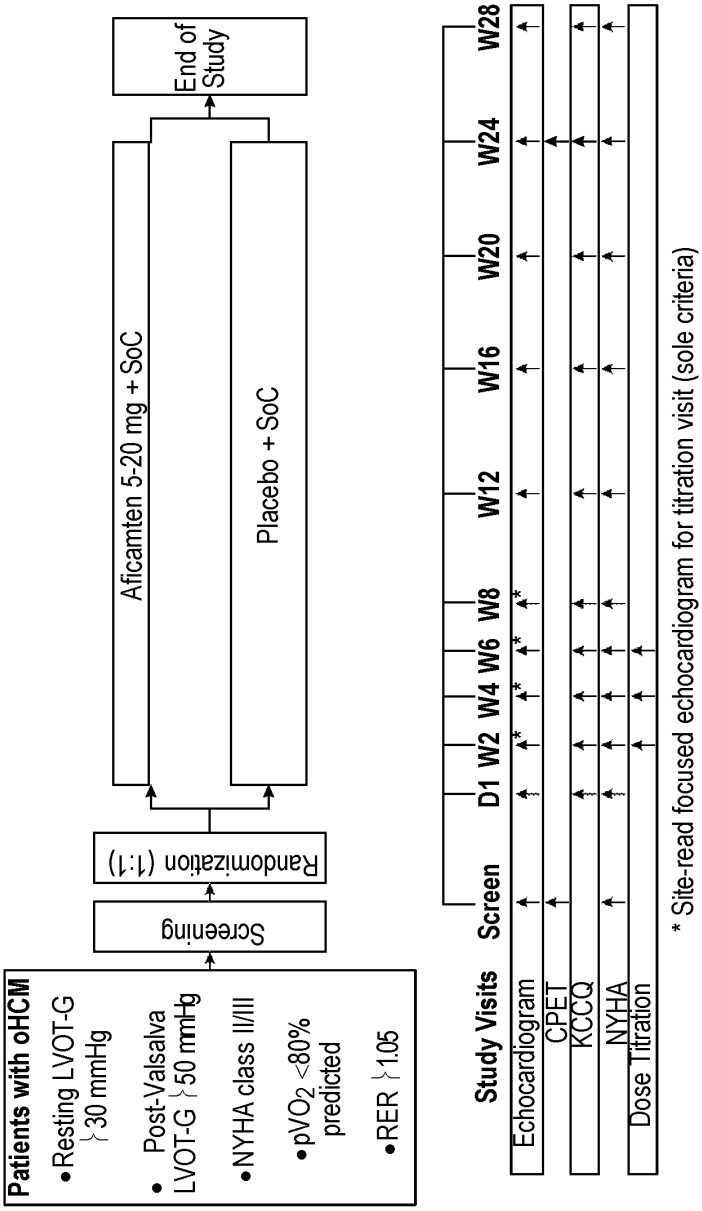

Patients with oHCM
•Resting LVOT-G ≥ 30 mmHg
• Post-Valsalva LVOT-G ≥ 50 mmHg
•NYHA class II/III
•pVO2 <80% predicted
•RER ≥ 1.05
Screening
Randomization (1:1)
Aficamten 5-20 mg + SoC
Placebo + SoC
End of Study
Study Visits
Screen
D1
W2
W4
W6
W8
W12
W16
W20
W24
W28
Echocardiogram
CPET
KCCQ
NYHA
Dose Titration
* Site-read focused echocardiogram for titration visit (sole criteria)

FIG. 1

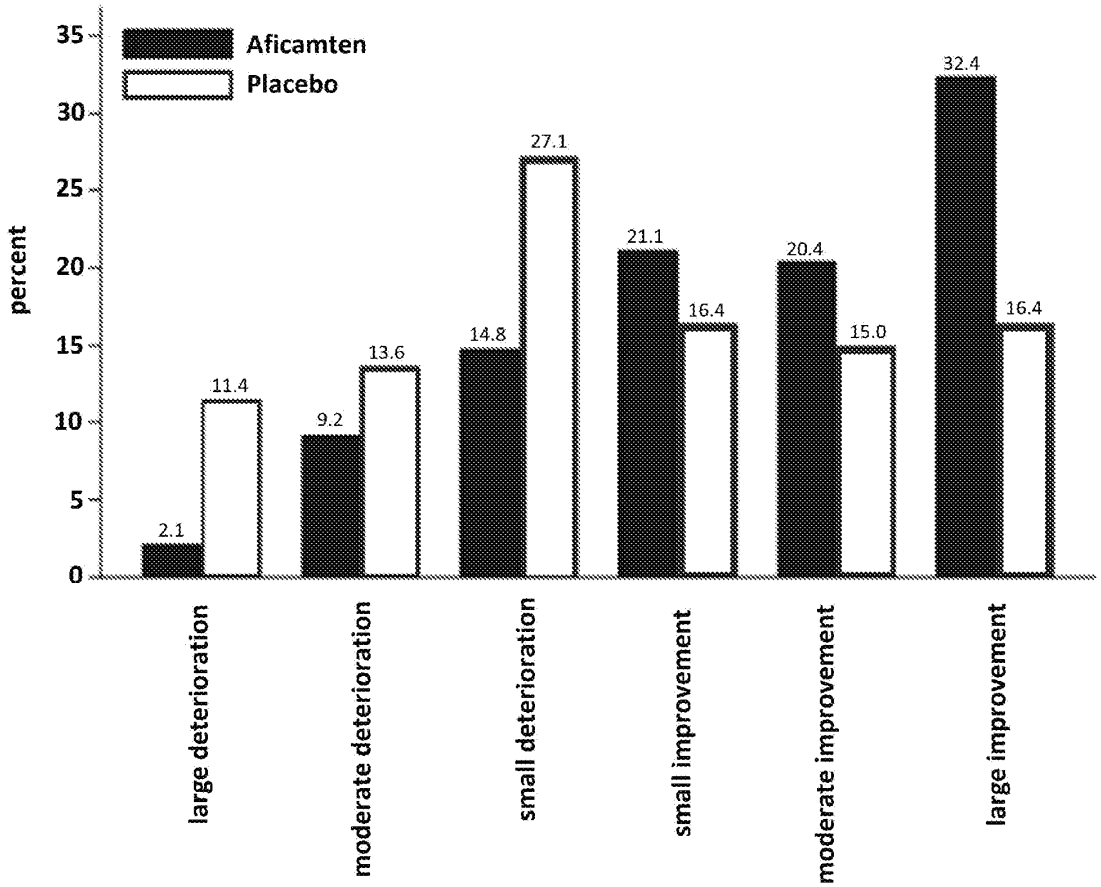

Aficamten
Placebo
percent
35
30
25
20
15
10
5
0
2.1
11.4
9.2
13.6
14.8
27.1
21.1
16.4
20.4
15.0
32.4
16.4
large deterioration
moderate deterioration
small deterioration
small improvement
moderate improvement
large improvement

FIG. 2

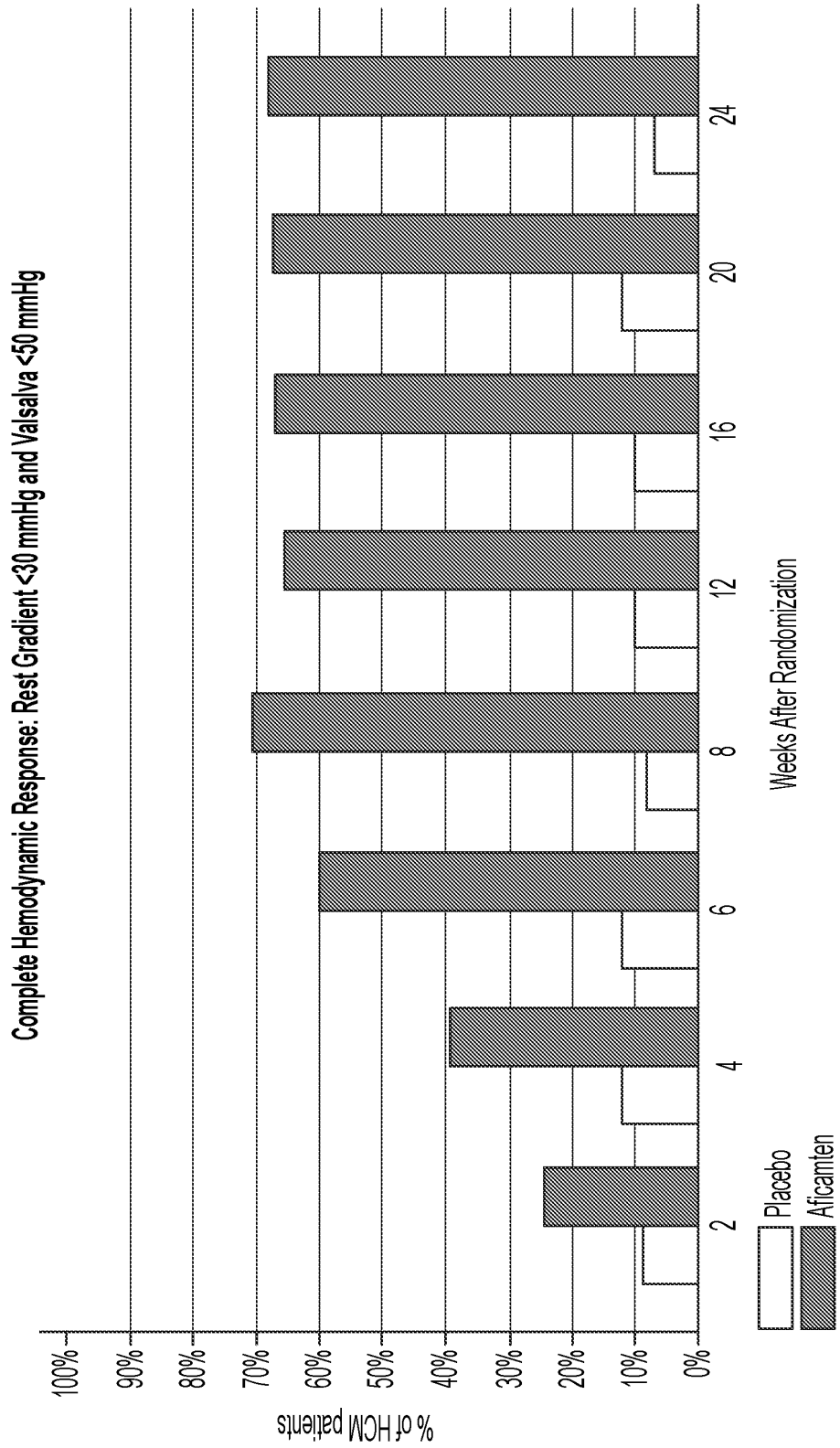

Complete Hemodynamic Response: Rest Gradient <30 mmHg and Valsalva <50 mmHg
% of HCM patients
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2
4
6
8
12
16
20
24
Weeks After Randomization
Placebo
Aficamten

FIG. 3A

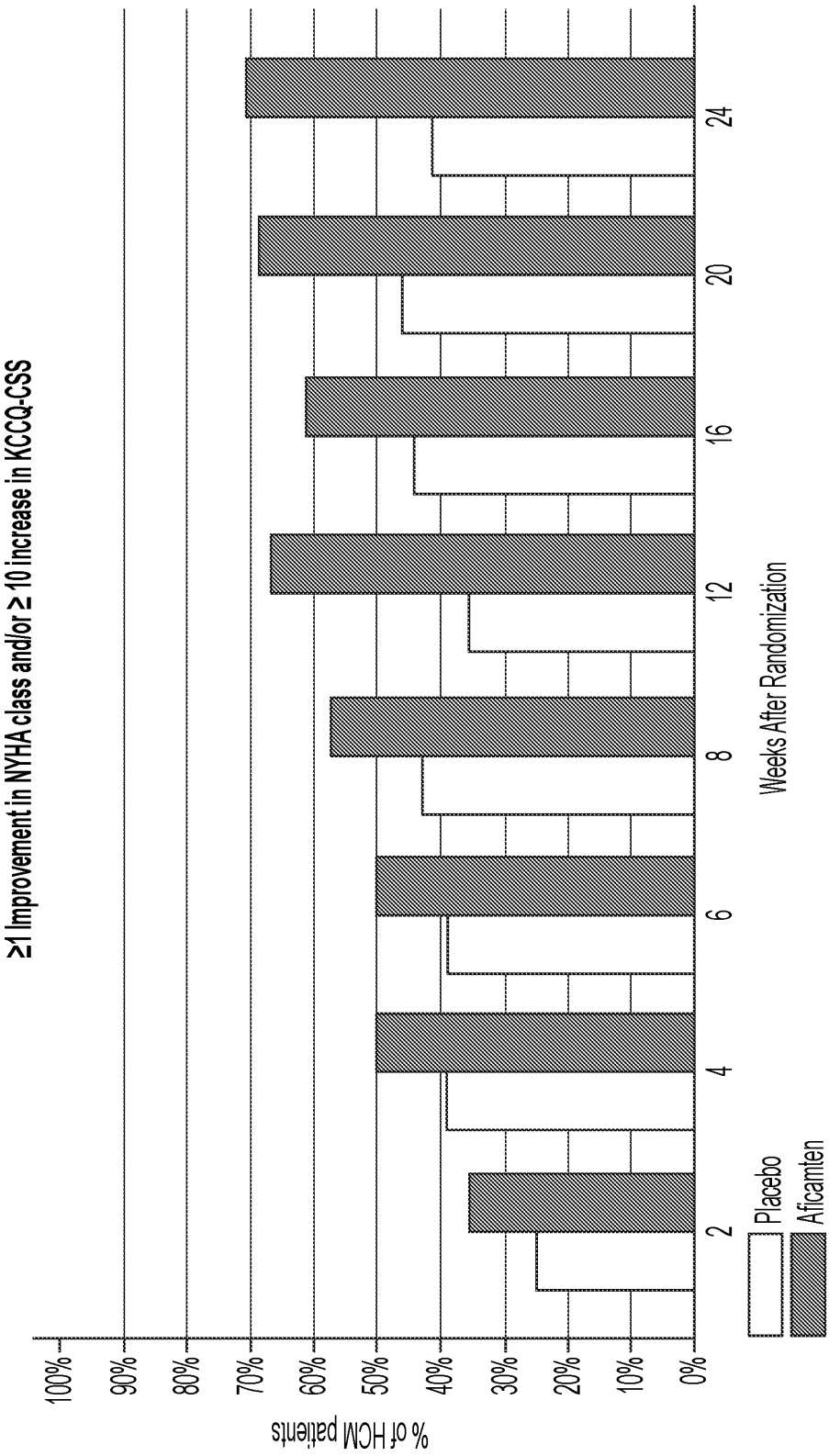

≥1 Improvement in NYHA class and/or ≥ 10 increase in KCCQ-CSS
% of HCM patients
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2
4
6
8
12
16
20
24
Weeks After Randomization
Placebo
Aficamten

FIG. 3B

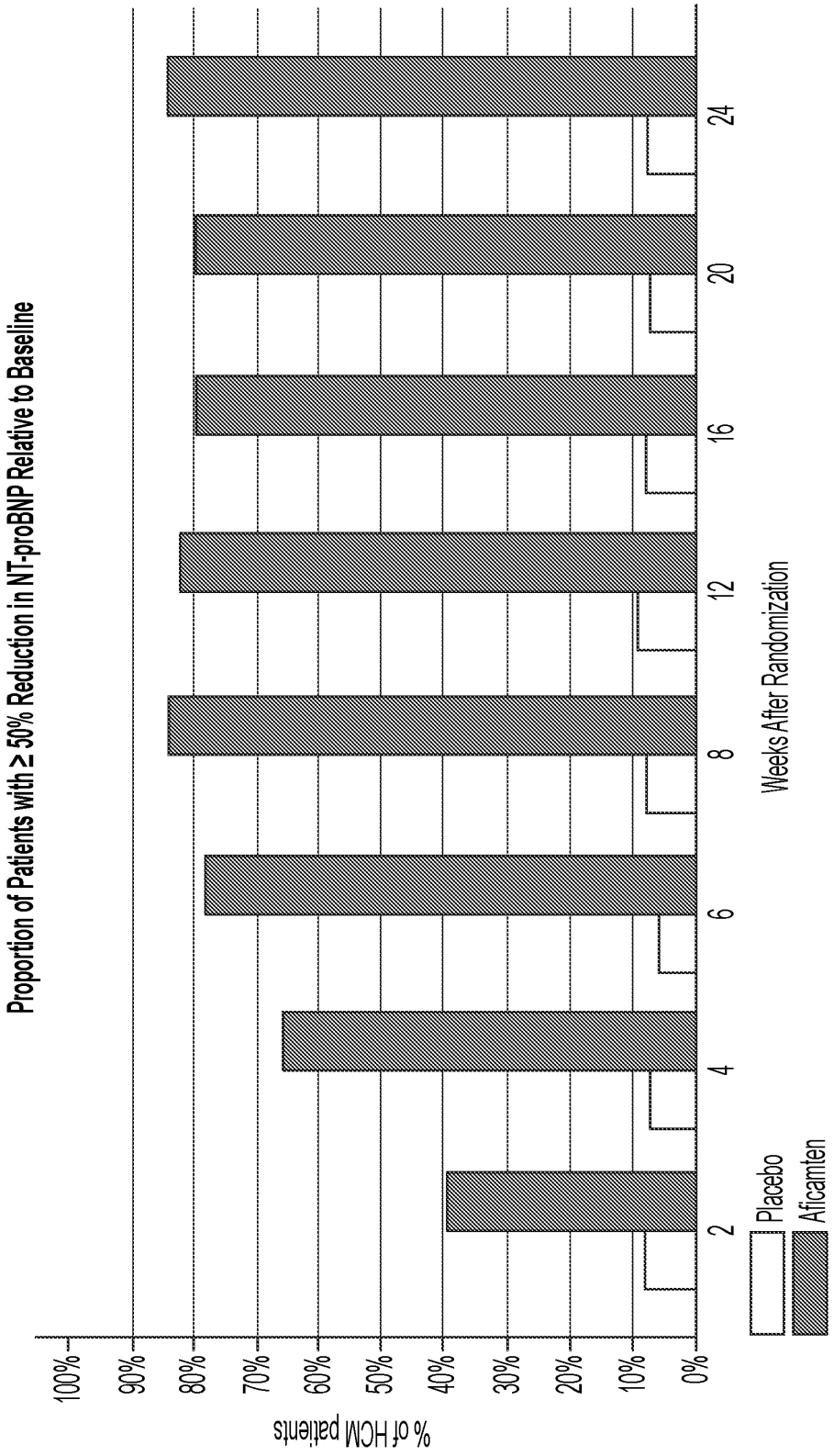

Proportion of Patients with ≥ 50% Reduction in NT-proBNP Relative to Baseline
% of HCM patients
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2
4
6
8
12
16
20
24
Weeks After Randomization
Placebo
Aficamten

FIG. 3C

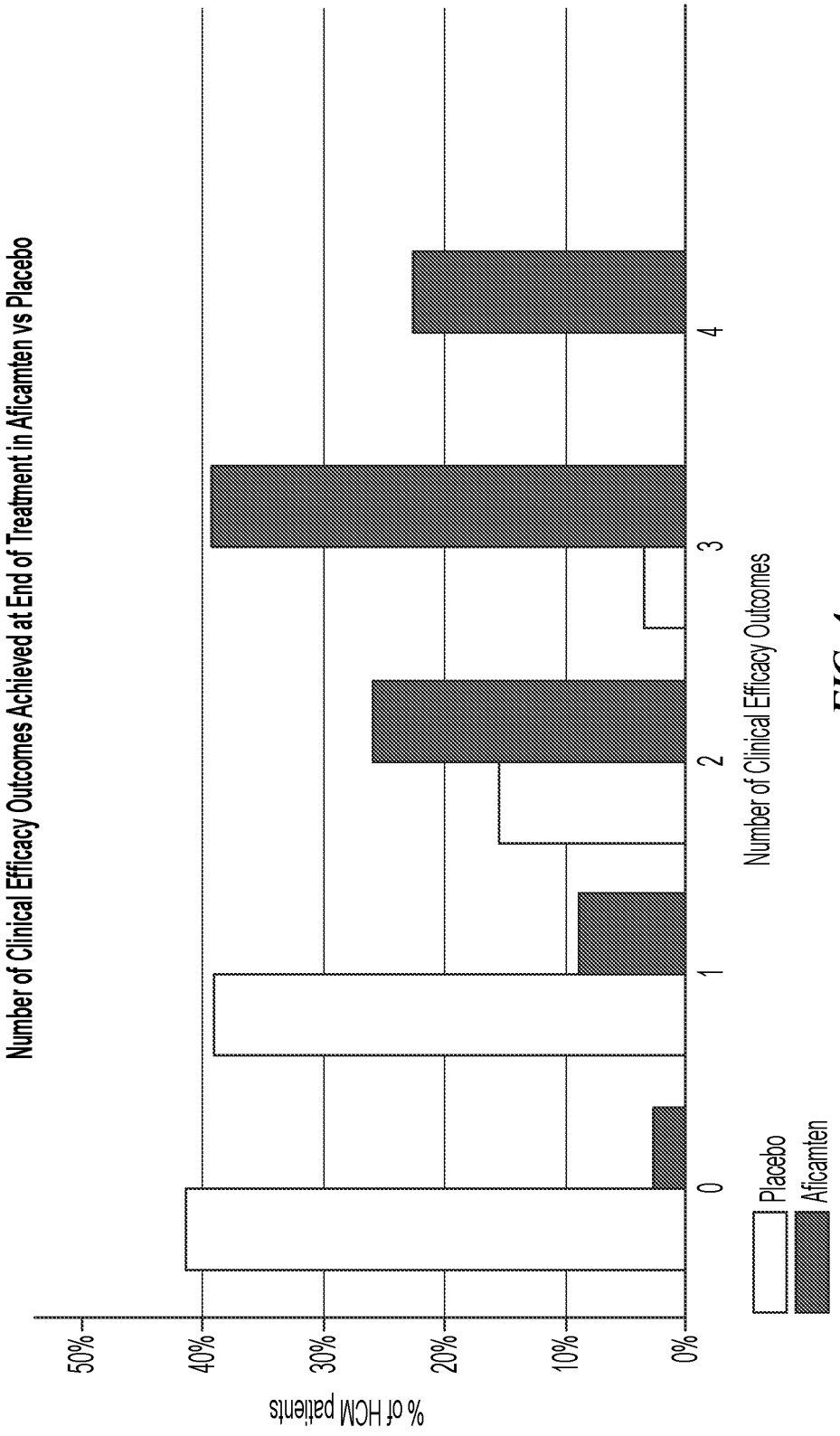

Number of Clinical Efficacy Outcomes Achieved at End of Treatment in Aficamten vs Placebo
% of HCM patients
50%
40%
30%
20%
10%
0%
0
1
2
3
4
Number of Clinical Efficacy Outcomes
Placebo
Aficamten

FIG. 4

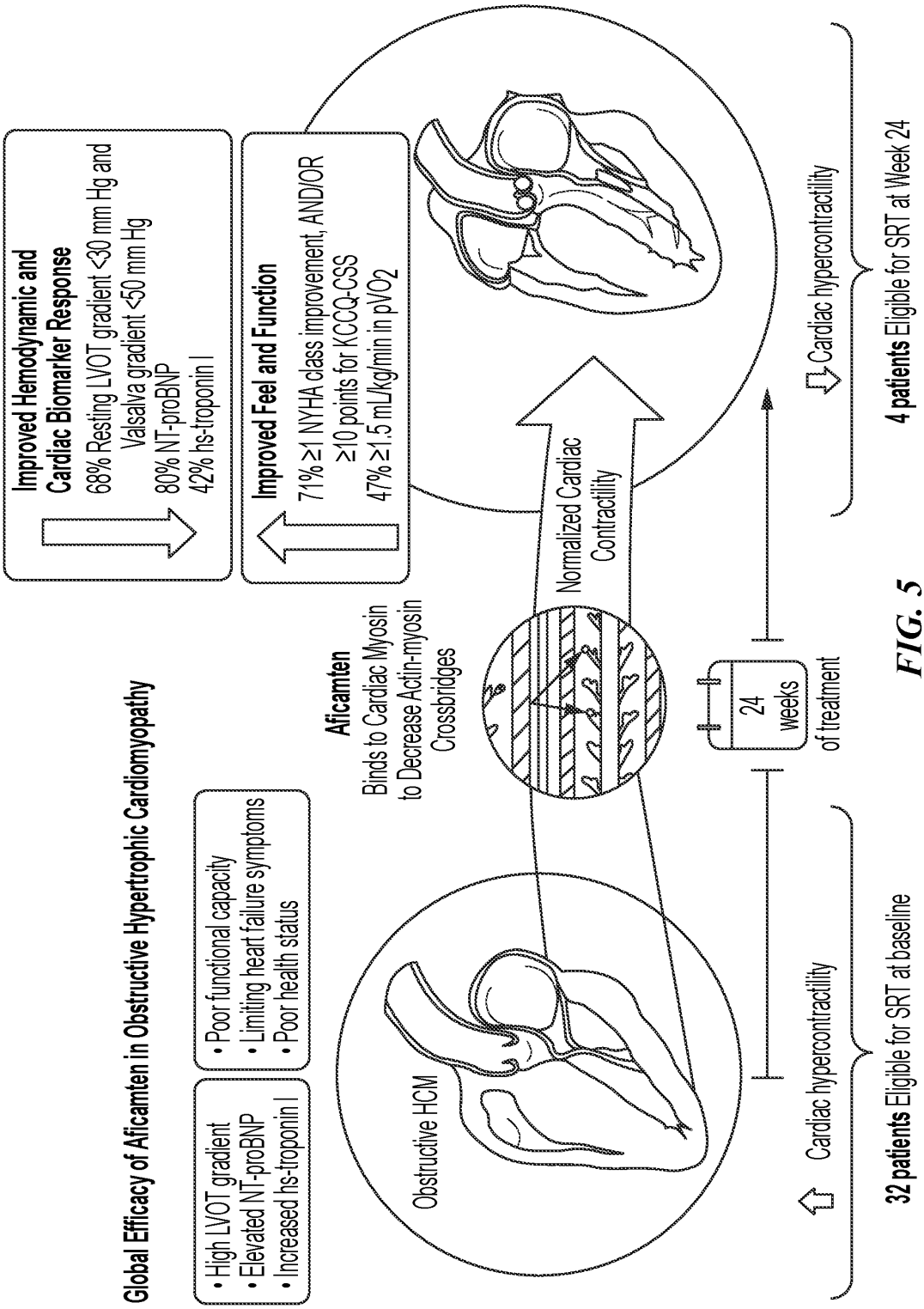

Global Efficacy of Aficamten in Obstructive Hypertrophic Cardiomyopathy
• High LVOT gradient
• Elevated NT-proBNP
• Increased hs-troponin I
• Poor functional capacity
• Limiting heart failure symptoms
• Poor health status
Aficamten
Binds to Cardiac Myosin to Decrease Actin-myosin Crossbridges
Obstructive HCM
Normalized Cardiac Contractility
24 weeks of treatment
Improved Hemodynamic and Cardiac Biomarker Response
68% Resting LVOT gradient <30 mm Hg and Valsalva gradient <50 mm Hg
80% NT-proBNP
42% hs-troponin I
Improved Feel and Function
71% ≥1 NYHA class improvement, AND/OR ≥10 points for KCCQ-CSS
47% ≥1.5 mL/kg/min in pVO2
Cardiac hypercontractility
32 patients Eligible for SRT at baseline
Cardiac hypercontractility
4 patients Eligible for SRT at Week 24

FIG. 5

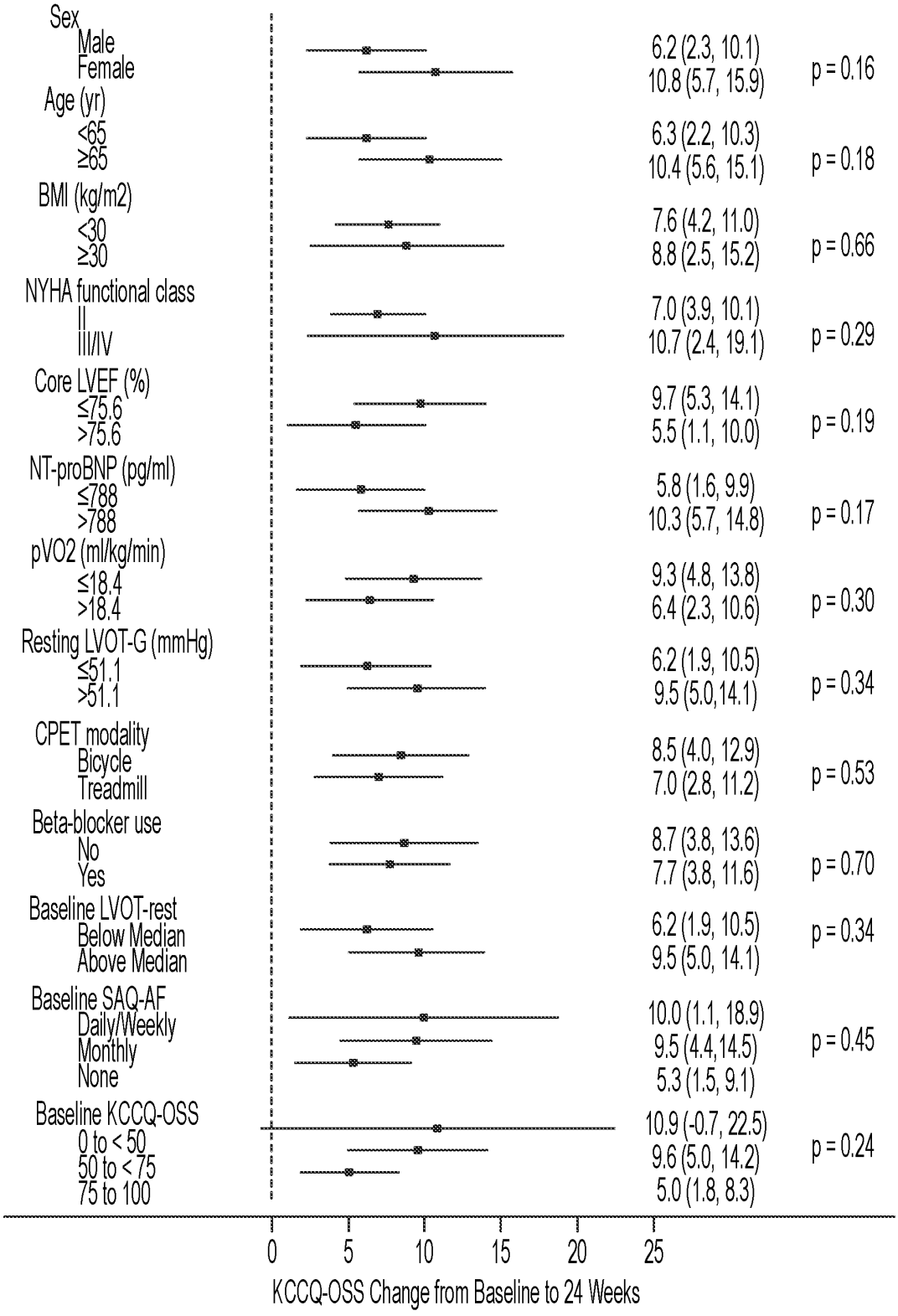

Sex
Male
Female
6.2 (2.3, 10.1)
10.8 (5.7, 15.9)
p = 0.16
Age (yr)
<65
≥65
6.3 (2.2, 10.3)
10.4 (5.6, 15.1)
p = 0.18
BMI (kg/m2)
<30
≥30
7.6 (4.2, 11.0)
8.8 (2.5, 15.2)
p = 0.66
NYHA functional class
II
III/IV
7.0 (3.9, 10.1)
10.7 (2.4, 19.1)
p = 0.29
Core LVEF (%)
≤75.6
>75.6
9.7 (5.3, 14.1)
5.5 (1.1, 10.0)
p = 0.19
NT-proBNP (pg/ml)
≤788
>788
5.8 (1.6, 9.9)
10.3 (5.7, 14.8)
p = 0.17
pVO2 (ml/kg/min)
≤18.4
>18.4
9.3 (4.8, 13.8)
6.4 (2.3, 10.6)
p = 0.30
Resting LVOT-G (mmHg)
≤51.1
>51.1
6.2 (1.9, 10.5)
9.5 (5.0,14.1)
p = 0.34
CPET modality
Bicycle
Treadmill
8.5 (4.0, 12.9)
7.0 (2.8, 11.2)
p = 0.53
Beta-blocker use
No
Yes
8.7 (3.8, 13.6)
7.7 (3.8, 11.6)
p = 0.70
Baseline LVOT-rest
Below Median
Above Median
6.2 (1.9, 10.5)
9.5 (5.0, 14.1)
p = 0.34
Baseline SAQ-AF
Daily/Weekly
Monthly
None
10.0 (1.1, 18.9)
9.5 (4.4,14.5)
5.3 (1.5, 9.1)
p = 0.45
Baseline KCCQ-OSS
0 to < 50
50 to < 75
75 to 100
10.9 (-0.7, 22.5)
9.6 (5.0, 14.2)
5.0 (1.8, 8.3)
p = 0.24
0
5
10
15
20
25
KCCQ-OSS Change from Baseline to 24 Weeks

FIG. 6A

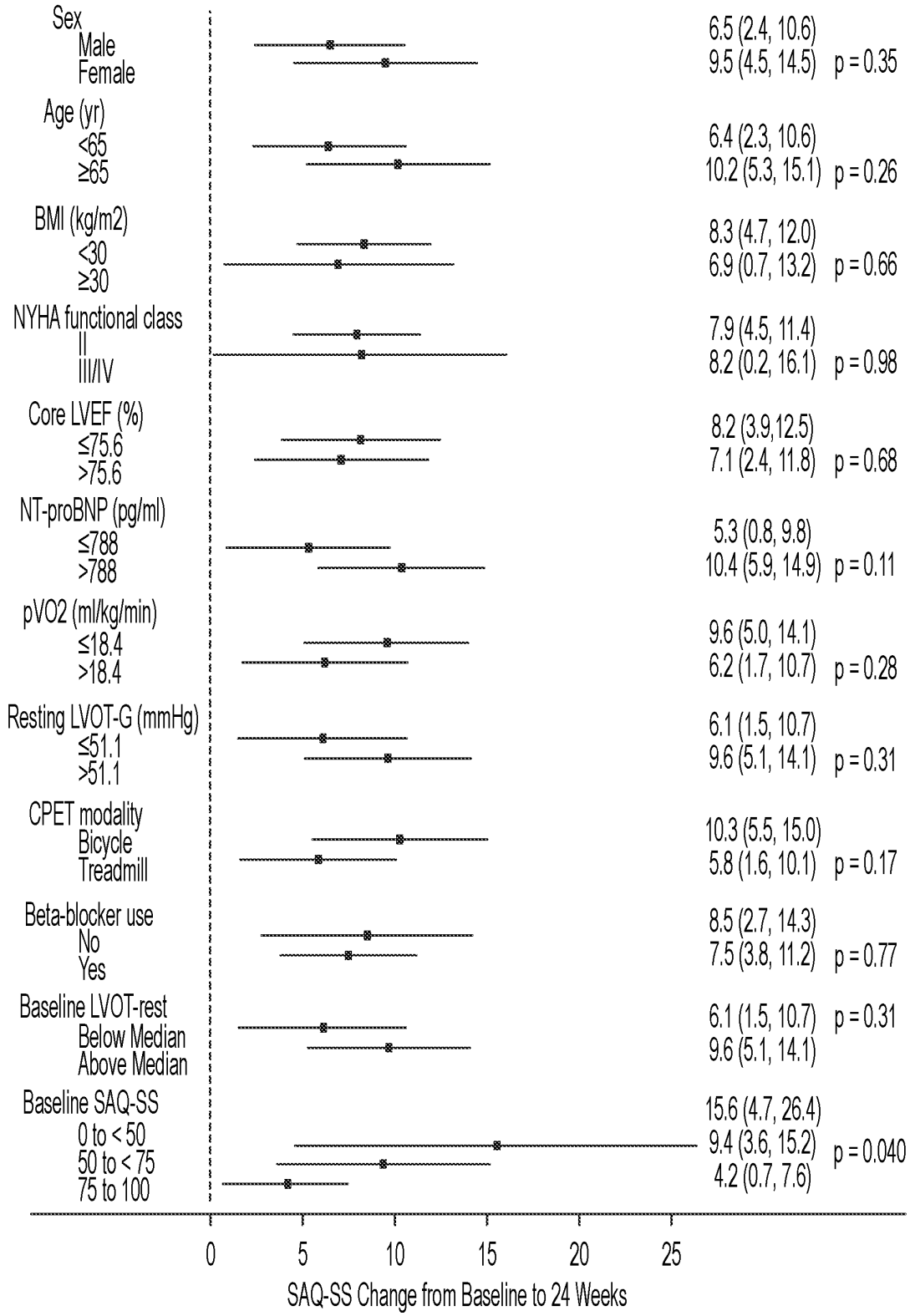

Sex
Male
Female
6.5 (2.4, 10.6)
9.5 (4.5, 14.5) p = 0.35
Age (yr)
<65
≥65
6.4 (2.3, 10.6)
10.2 (5.3, 15.1) p = 0.26
BMI (kg/m2)
<30
≥30
8.3 (4.7, 12.0)
6.9 (0.7, 13.2) p = 0.66
NYHA functional class
II
III/IV
7.9 (4.5, 11.4)
8.2 (0.2, 16.1) p = 0.98
Core LVEF (%)
≤75.6
>75.6
8.2 (3.9,12.5)
7.1 (2.4, 11.8) p = 0.68
NT-proBNP (pg/ml)
≤788
>788
5.3 (0.8, 9.8)
10.4 (5.9, 14.9) p = 0.11
pVO2 (ml/kg/min)
≤18.4
>18.4
9.6 (5.0, 14.1)
6.2 (1.7, 10.7) p = 0.28
Resting LVOT-G (mmHg)
≤51.1
>51.1
6.1 (1.5, 10.7)
9.6 (5.1, 14.1) p = 0.31
CPET modality
Bicycle
Treadmill
10.3 (5.5, 15.0)
5.8 (1.6, 10.1) p = 0.17
Beta-blocker use
No
Yes
8.5 (2.7, 14.3)
7.5 (3.8, 11.2) p = 0.77
Baseline LVOT-rest
Below Median
Above Median
6.1 (1.5, 10.7) p = 0.31
9.6 (5.1, 14.1)
Baseline SAQ-SS
0 to < 50
50 to < 75
75 to 100
15.6 (4.7, 26.4)
9.4 (3.6, 15.2) p = 0.040
4.2 (0.7, 7.6)
0
5
10
15
20
25
SAQ-SS Change from Baseline to 24 Weeks

FIG. 6B