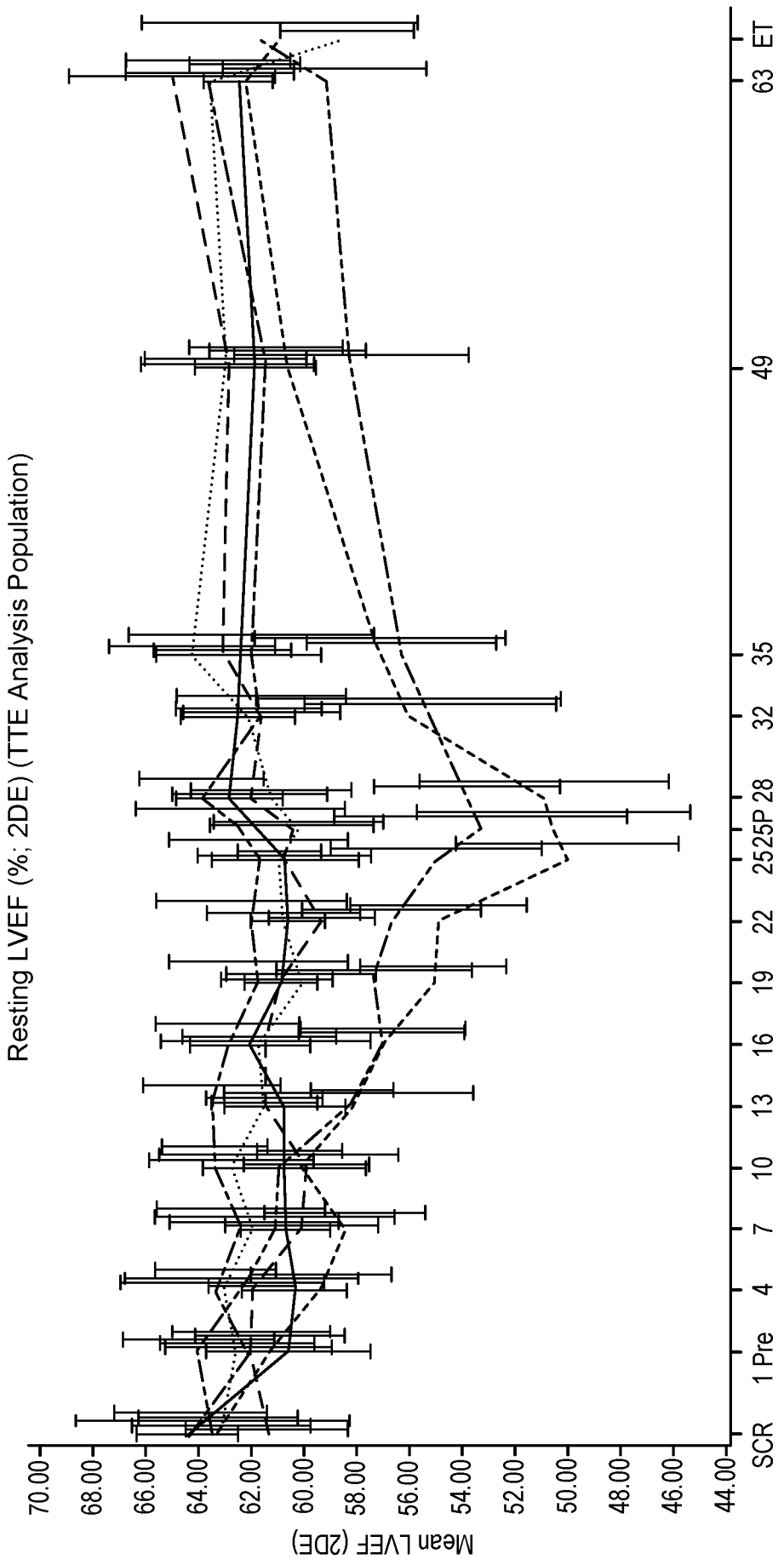

Resting LVEF (%; 2DE) (TTE Analysis Population)
Mean LVEF (2DE)
70.00
68.00
66.00
64.00
62.00
60.00
58.00
56.00
54.00
52.00
50.00
48.00
46.00
44.00
SCR
1 Pre
4
7
10
13
16
19
22
25
25P
28
32
35
49
63
ET
Day
Treatment Group:
MYK-461 1mg BD
MYK-461 3mg BD
MYK-461 12.5mg BD
MYK-461 18.5mg QD
MYK-461 25mg QD
Combined Placebo
Note: SCR = Screening, 1 Pre = Day 1 (Pre-Dose), 25P = Day 25 Post Dose, ET = Early Termination
LVEF = left ventricular ejection fraction, PK = pharmacokinetics

FIG. 1

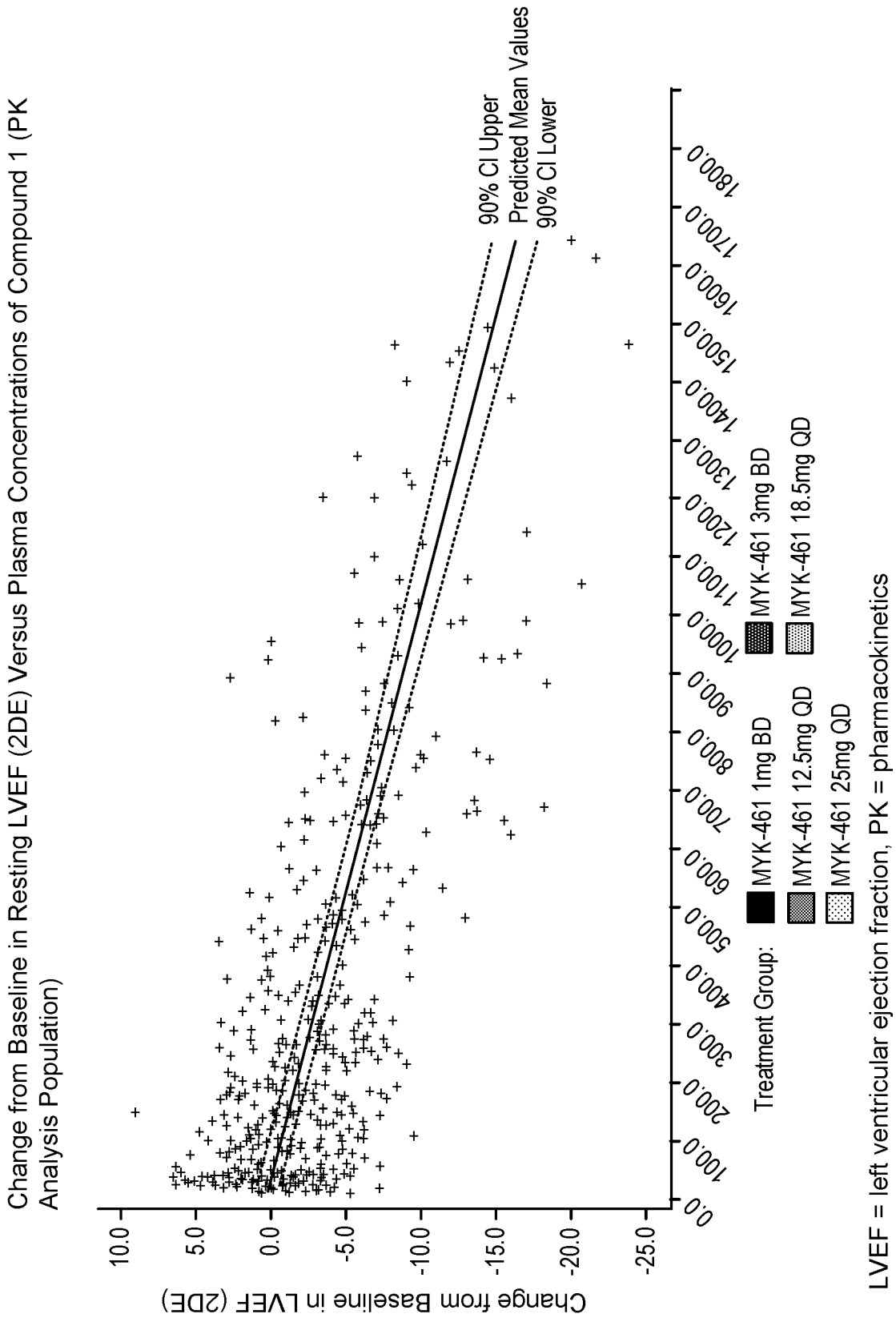

Change from Baseline in Resting LVEF (2DE) Versus Plasma Concentrations of Compound 1 (PK Analysis Population)
Change from Baseline in LVEF (2DE)
10.0
5.0
0.0
-5.0
-10.0
-15.0
-20.0
-25.0
0.0
100.0
200.0
300.0
400.0
500.0
600.0
700.0
800.0
900.0
1000.0
1100.0
1200.0
1300.0
1400.0
1500.0
1600.0
1700.0
1800.0
90% CI Upper
Predicted Mean Values
90% CI Lower
Treatment Group:
MYK-461 1mg BD
MYK-461 3mg BD
MYK-461 12.5mg QD
MYK-461 18.5mg QD
MYK-461 25mg QD
LVEF = left ventricular ejection fraction, PK = pharmacokinetics

FIG. 2A

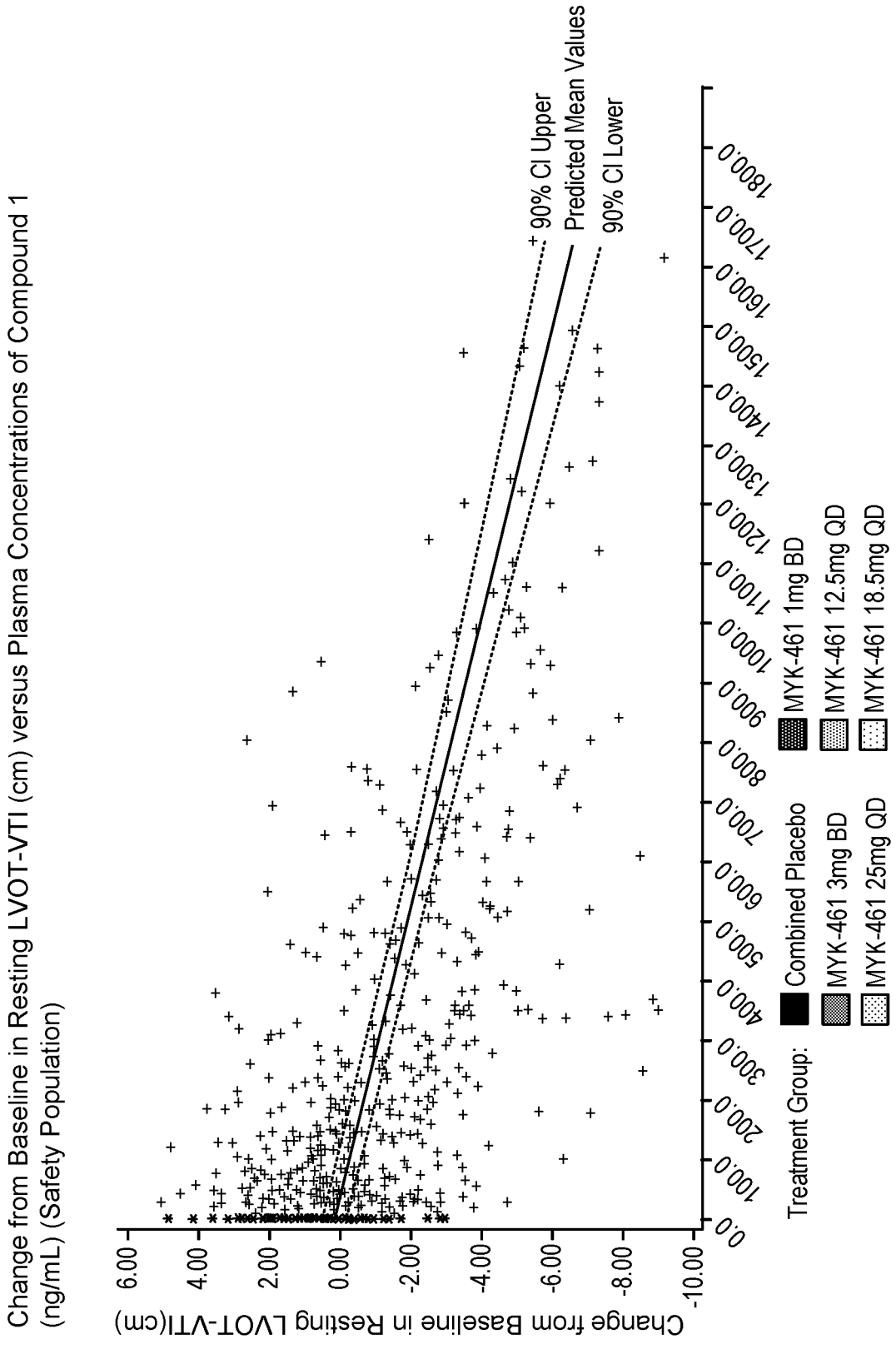

Change from Baseline in Resting LVOT-VTI (cm) versus Plasma Concentrations of Compound 1 (ng/mL) (Safety Population)
Change from Baseline in Resting LVOT-VTI(cm)
6.00
4.00
2.00
0.00
-2.00
-4.00
-6.00
-8.00
-10.00
0.0
100.0
200.0
300.0
400.0
500.0
600.0
700.0
800.0
900.0
1000.0
1100.0
1200.0
1300.0
1400.0
1500.0
1600.0
1700.0
1800.0
90% CI Upper
Predicted Mean Values
90% CI Lower
Treatment Group:
Combined Placebo
MYK-461 1mg BD
MYK-461 3mg BD
MYK-461 12.5mg QD
MYK-461 25mg QD
MYK-461 18.5mg QD

FIG. 2B

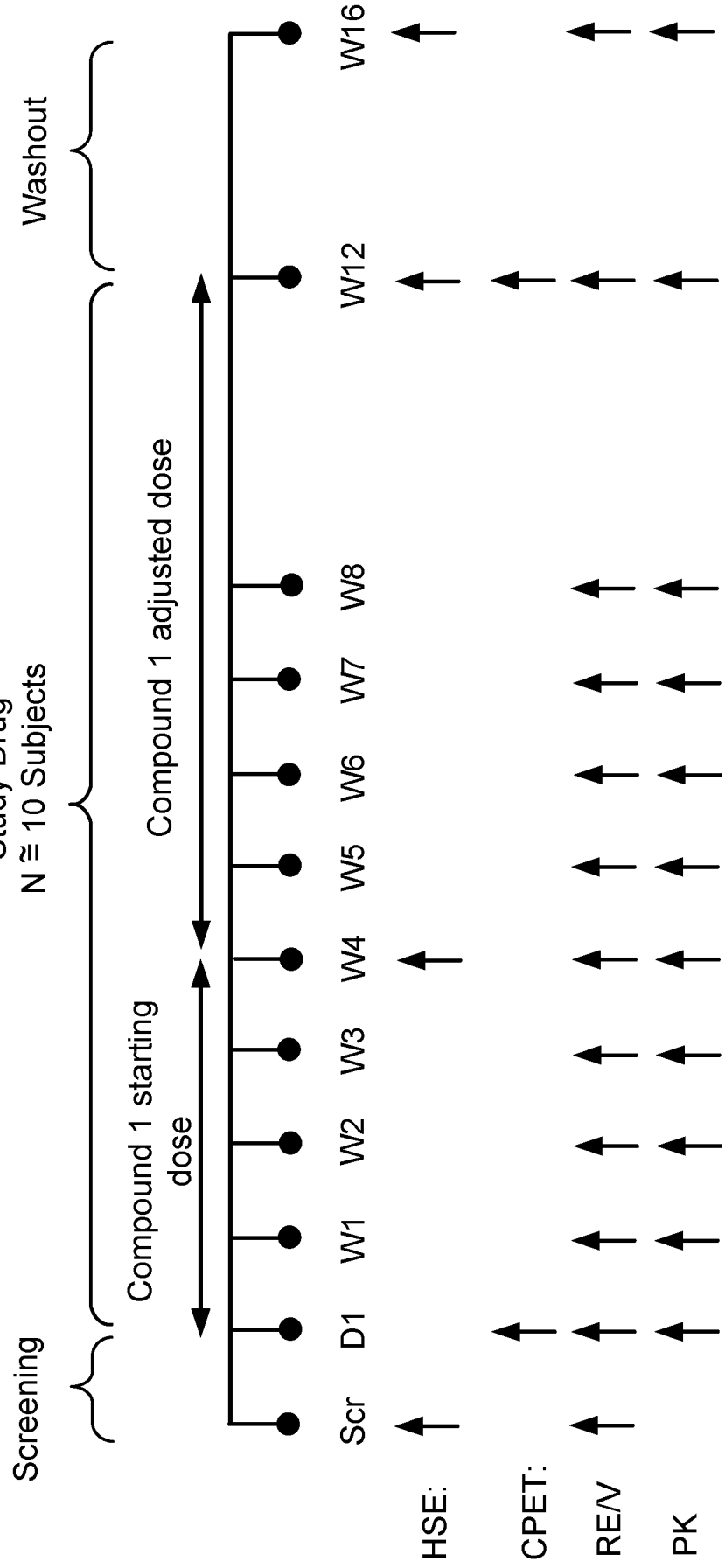

Screening
Study Drug
N ≅ 10 Subjects
Washout
Compound 1 starting dose
Compound 1 adjusted dose
Scr
D1
W1
W2
W3
W4
W5
W6
W7
W8
W12
W16
HSE:
CPET:
RE/V
PK
Dose adjustment
Based on LVEF at W4 and
Compound 1 plasma
Concentration at W2

FIG. 3

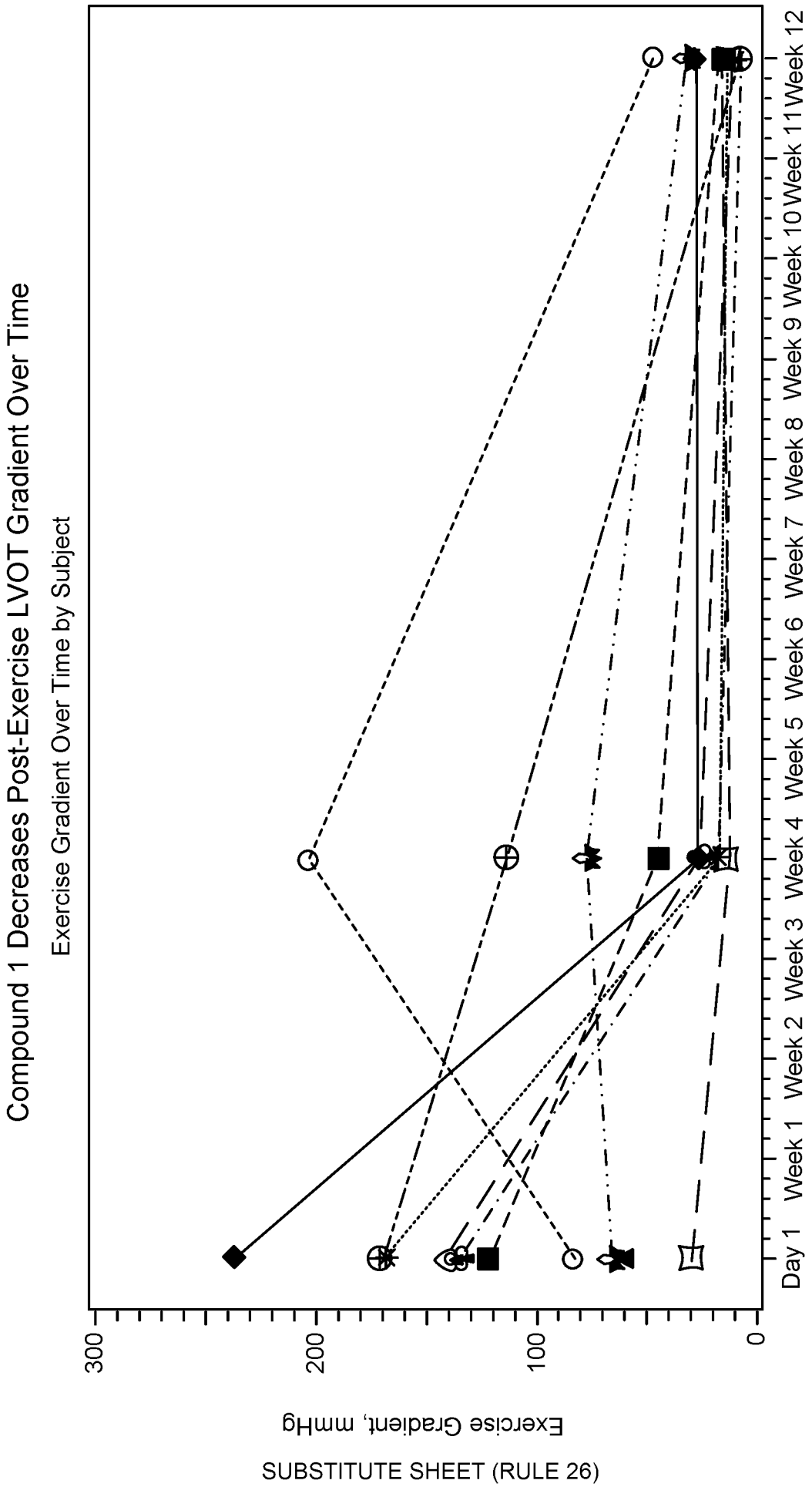

Compound 1 Decreases Post-Exercise LVOT Gradient Over Time
Exercise Gradient Over Time by Subject
Exercise Gradient, mmHg
300
200
100
0
Day 1
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8
Week 9
Week 10
Week 11
Week 12
Timepoint

FIG. 4

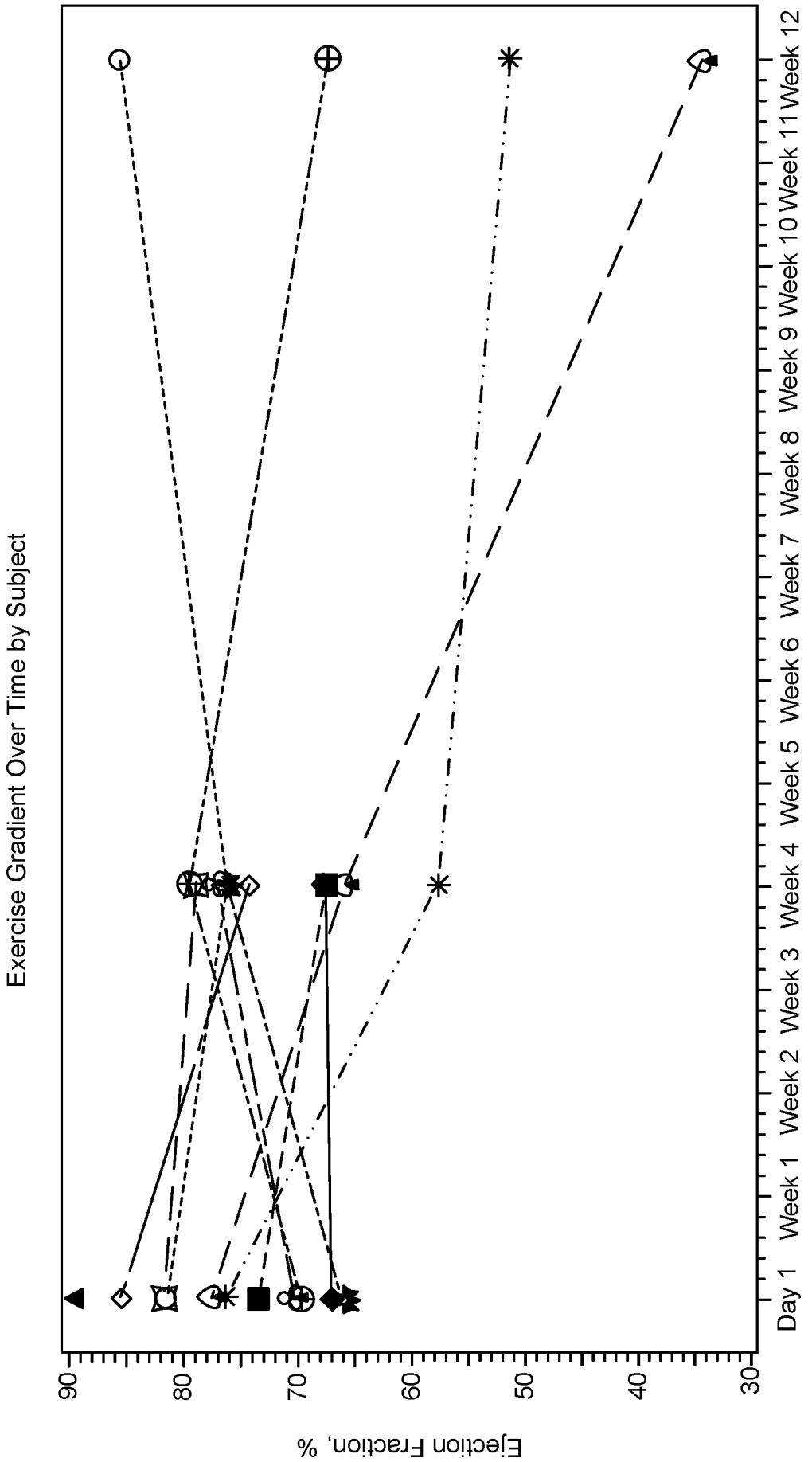

Exercise Gradient Over Time by Subject
Ejection Fraction, %
90
80
70
60
50
40
30
Day 1
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8
Week 9
Week 10
Week 11
Week 12
Weeks

FIG. 5

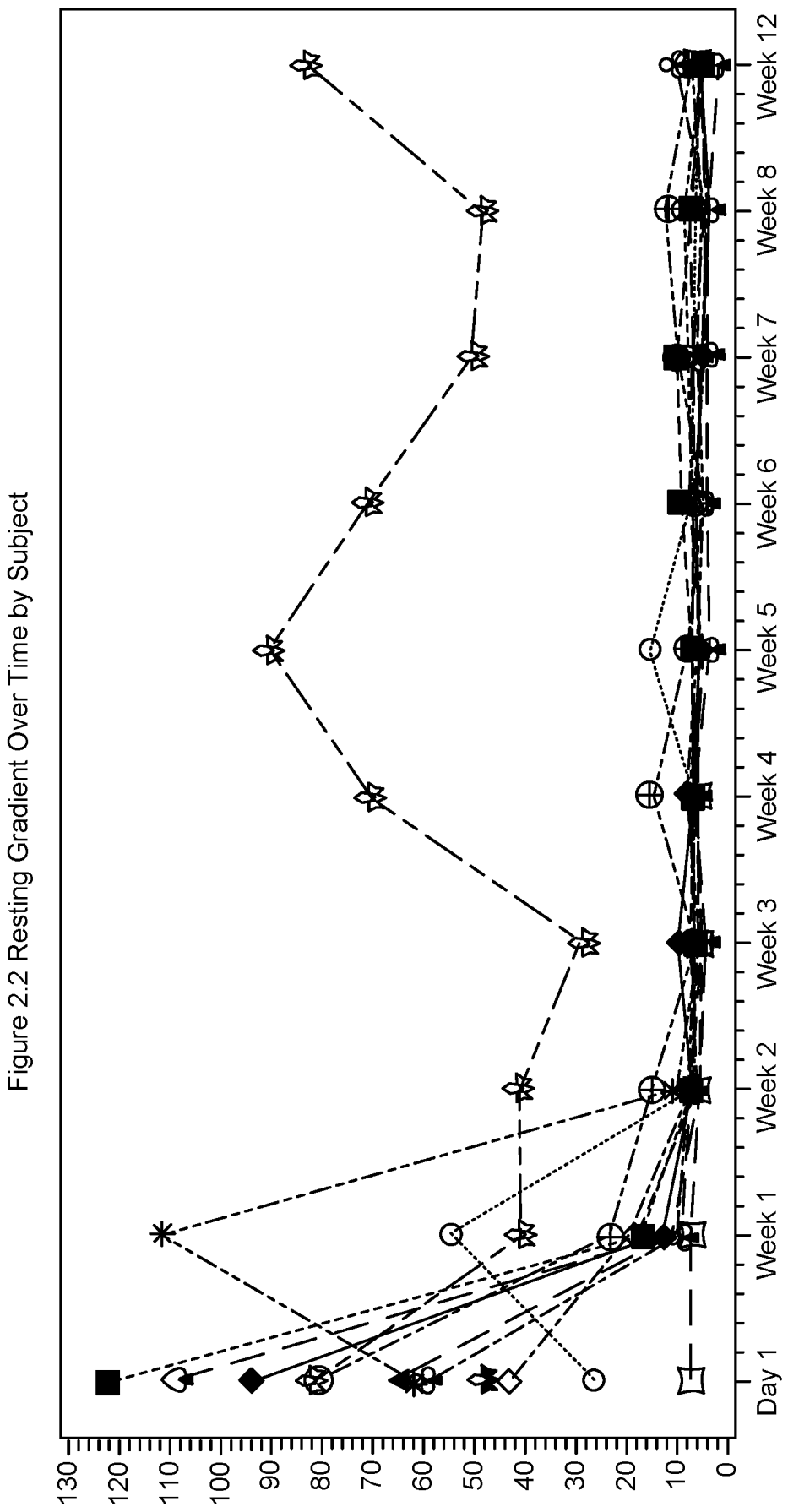
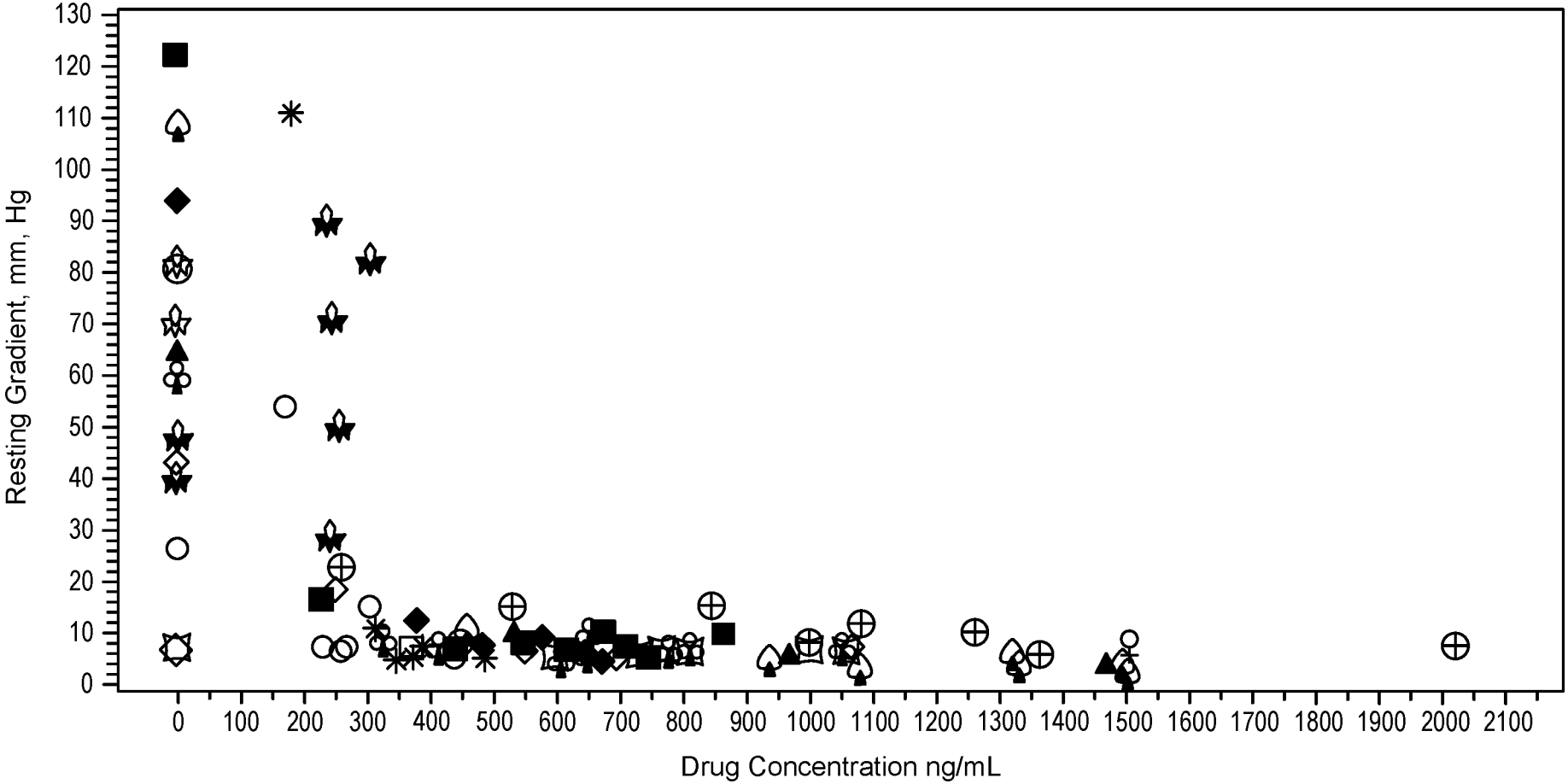

Figure 2.2 Resting Gradient Over Time by Subject
Resting Gradient, mm, Hg
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Day 1
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8
Week 12
Timepoint

FIG. 6

SUBSTITUTE SHEET (RULE 26)

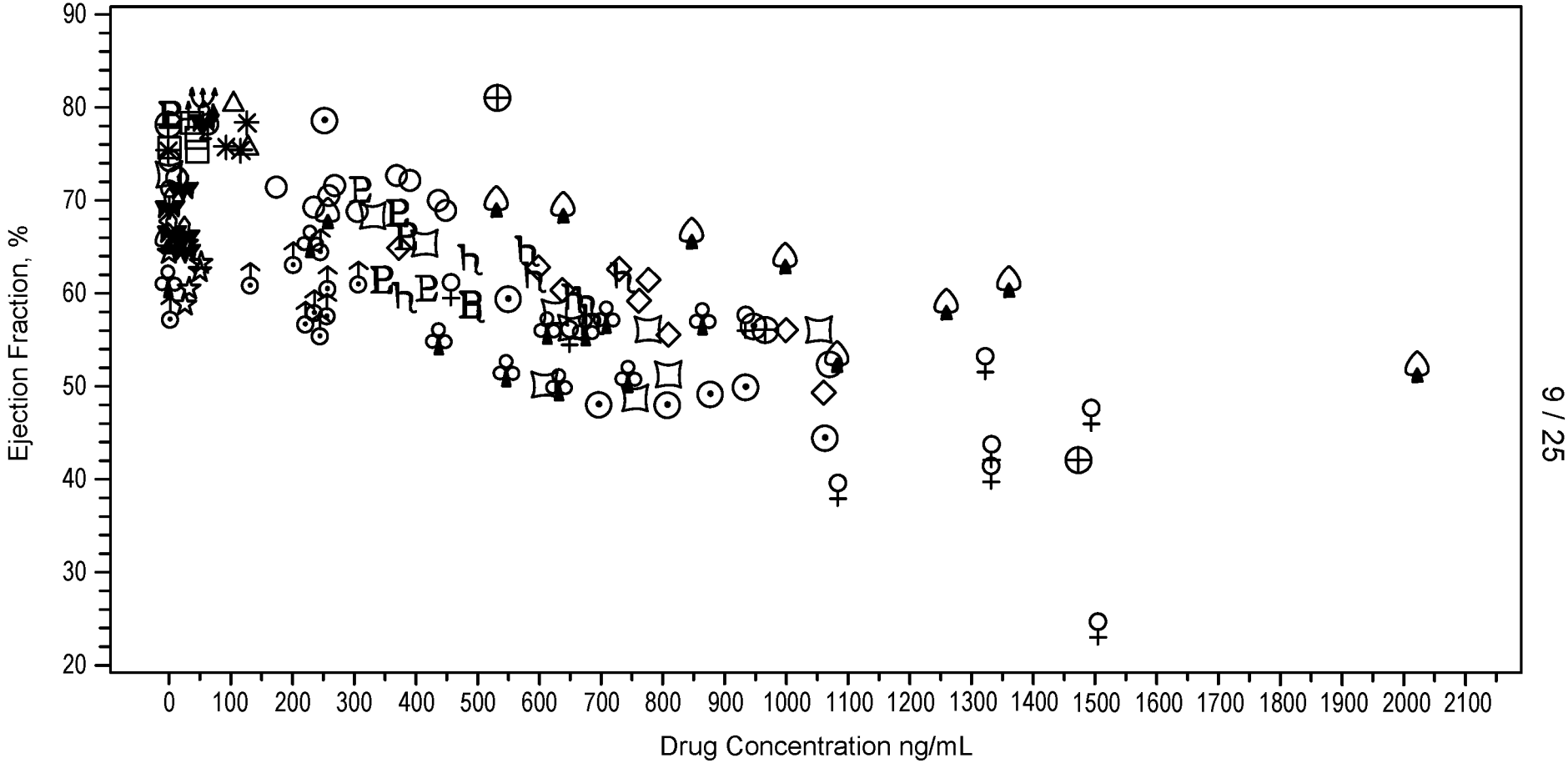
Figure 2.1 Resting Gradient vs Drug Concentration – All Visits



[Compound 1] (ng/mL)

FIG. 7

Figure 2.6 Ejection Fraction vs Drug Concentration – All Visits
Part A & B



[Compound 1] (ng/mL)

FIG. 8

SUBSTITUTE SHEET (RULE 26)

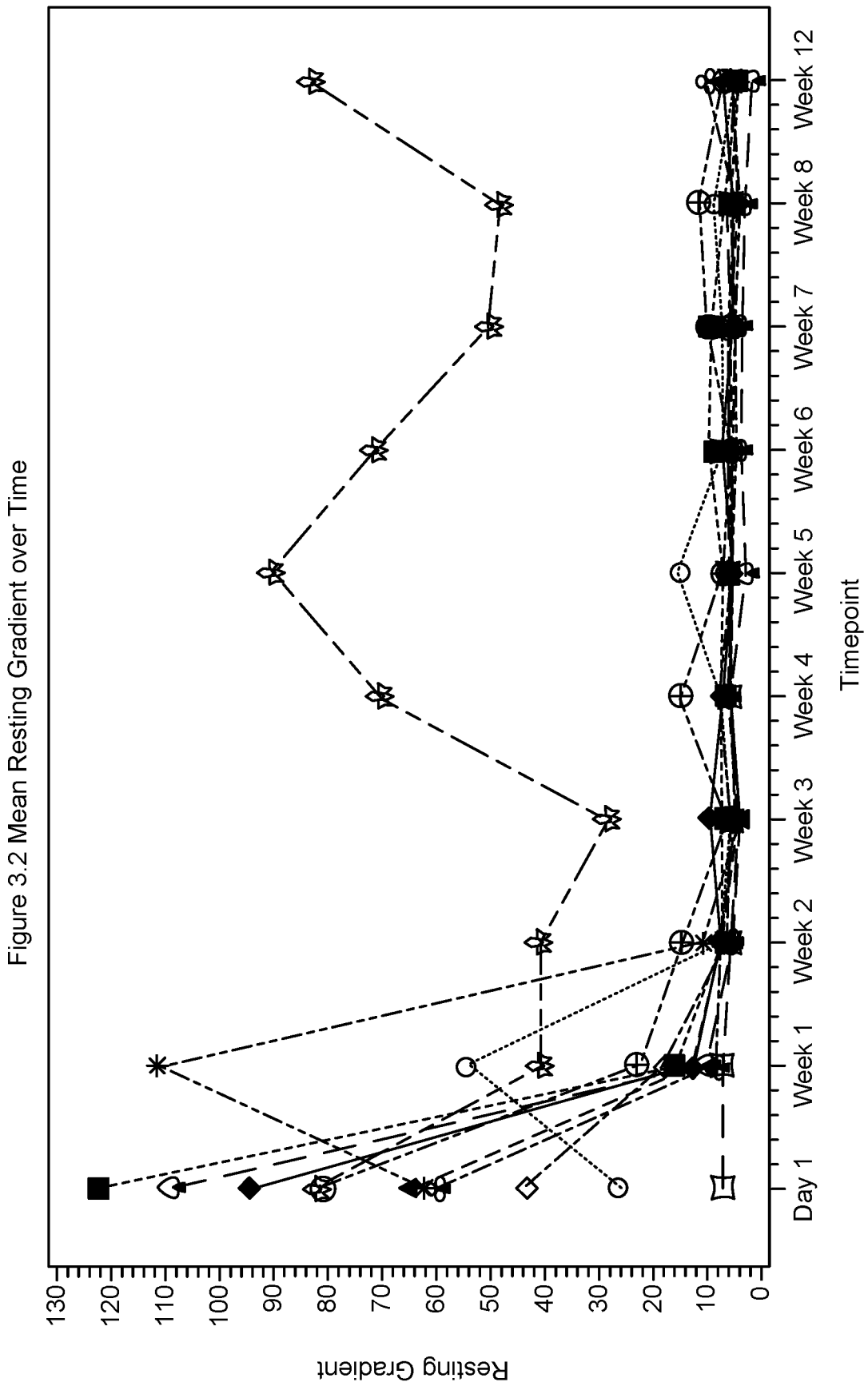

Figure 3.2 Mean Resting Gradient over Time
Resting Gradient
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Day 1
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8
Week 12
Timepoint

FIG. 9

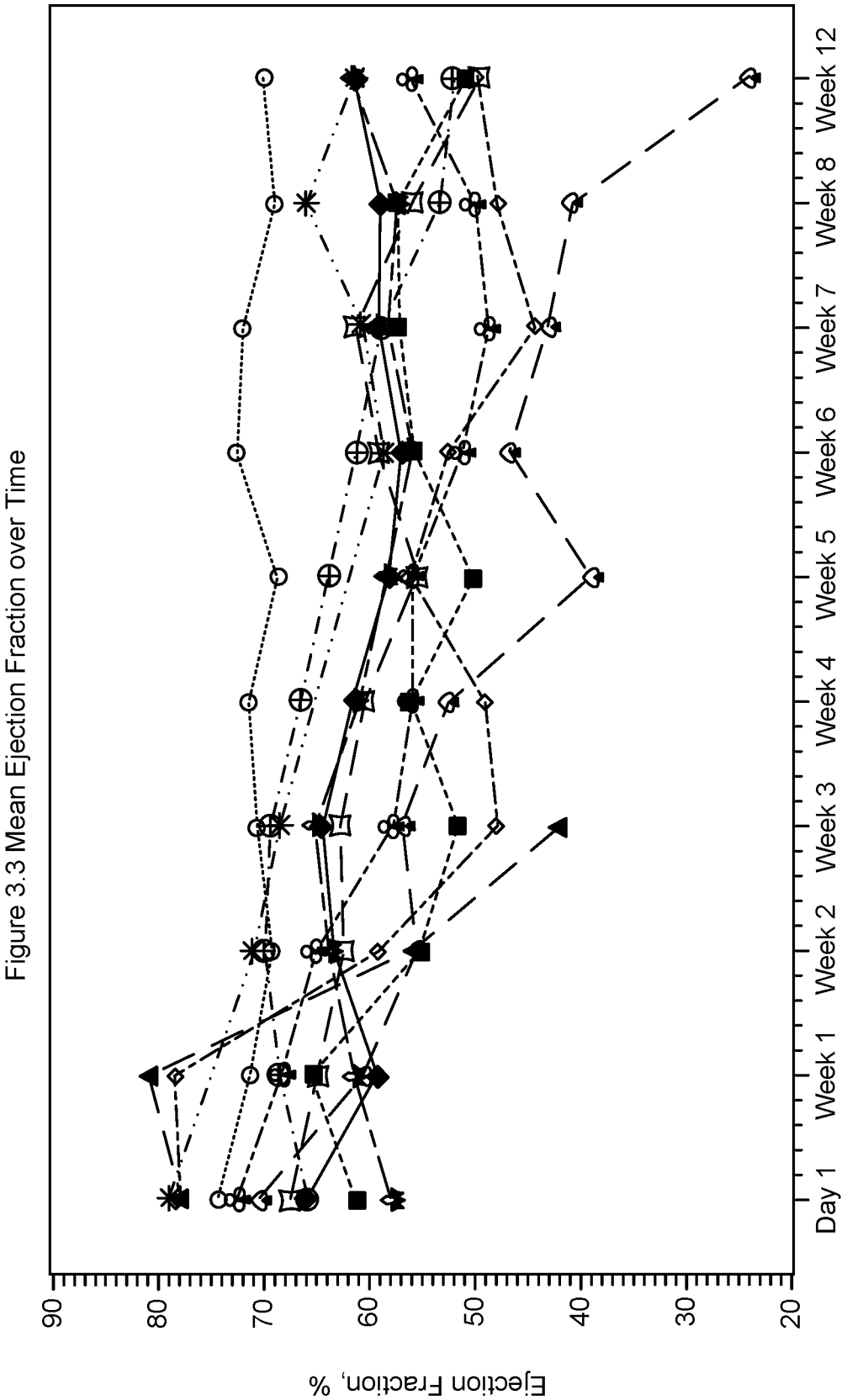

Figure 3.3 Mean Ejection Fraction over Time
Ejection Fraction, %
90
80
70
60
50
40
30
20
Day 1
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8
Week 12

FIG. 10

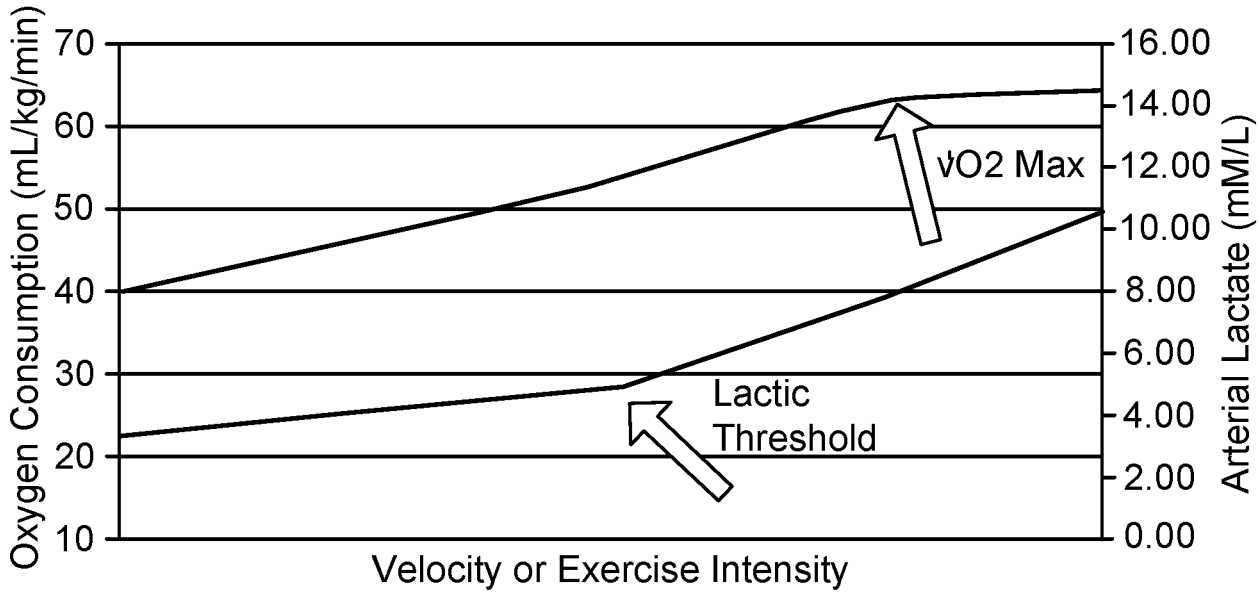

Oxygen Consumption (mL/kg/min)
70
60
50
40
30
20
10
16.00
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
Arterial Lactate (mM/L)
V̇O2 Max
Lactic
Threshold
Velocity or Exercise Intensity

FIG. 11

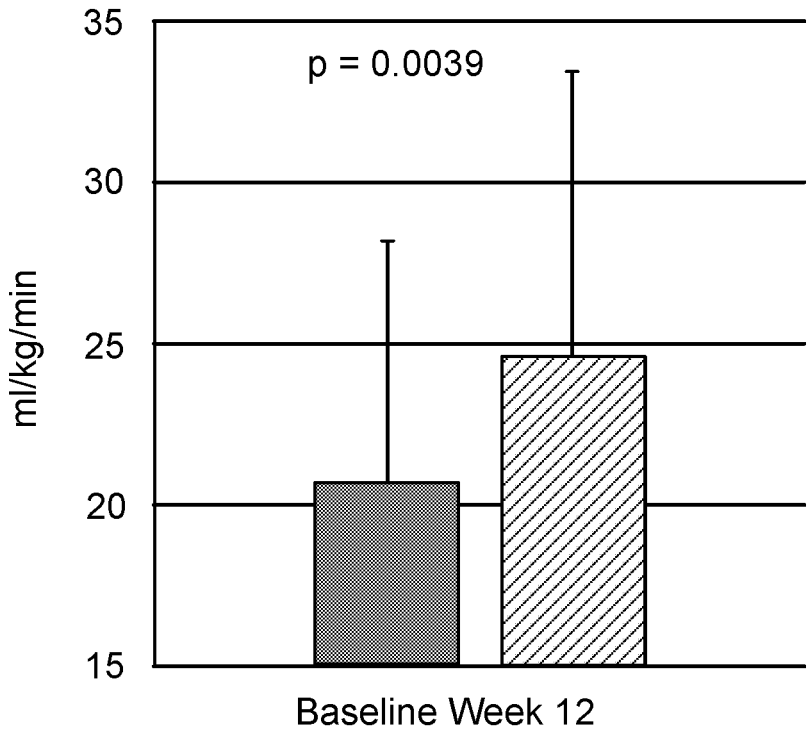

35
30
25
20
15
p = 0.0039
ml/kg/min
Baseline Week 12

FIG. 12

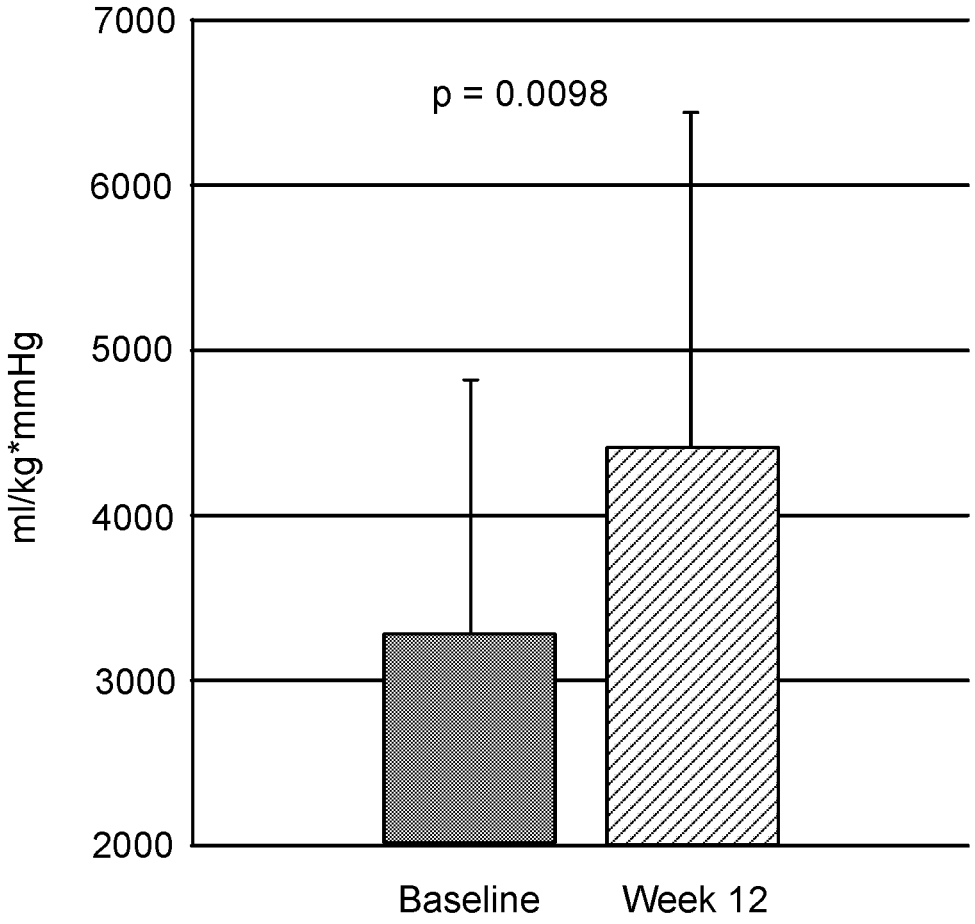

7000
6000
5000
4000
3000
2000
p = 0.0098
ml/kg*mmHg
Baseline
Week 12

FIG. 13

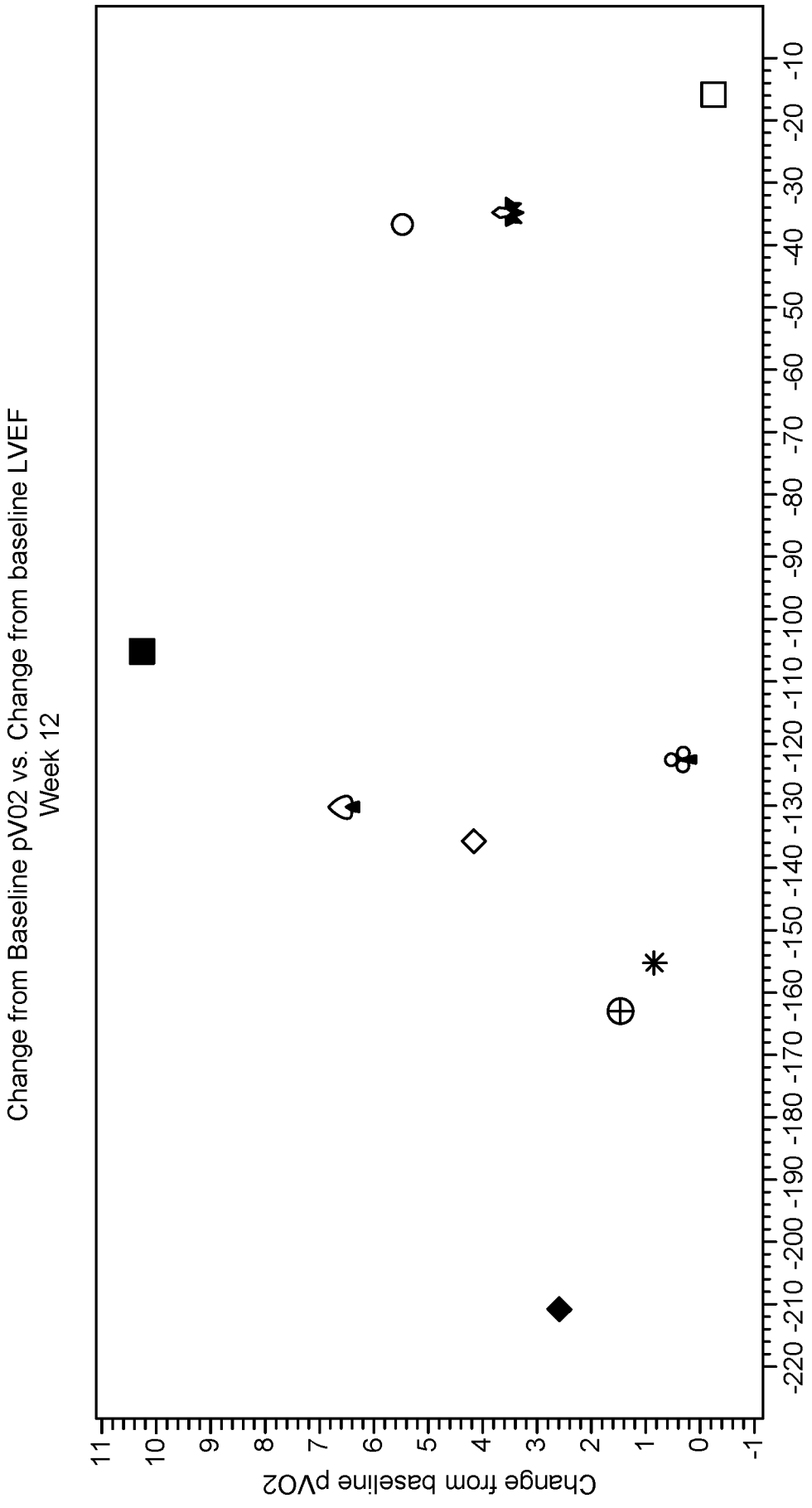

Change from Baseline pV02 vs. Change from baseline LVEF
Week 12
Change from pVO2 baseline
11
10
9
8
7
6
5
4
3
2
1
0
-1
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
Change from baseline LVEF

FIG. 14

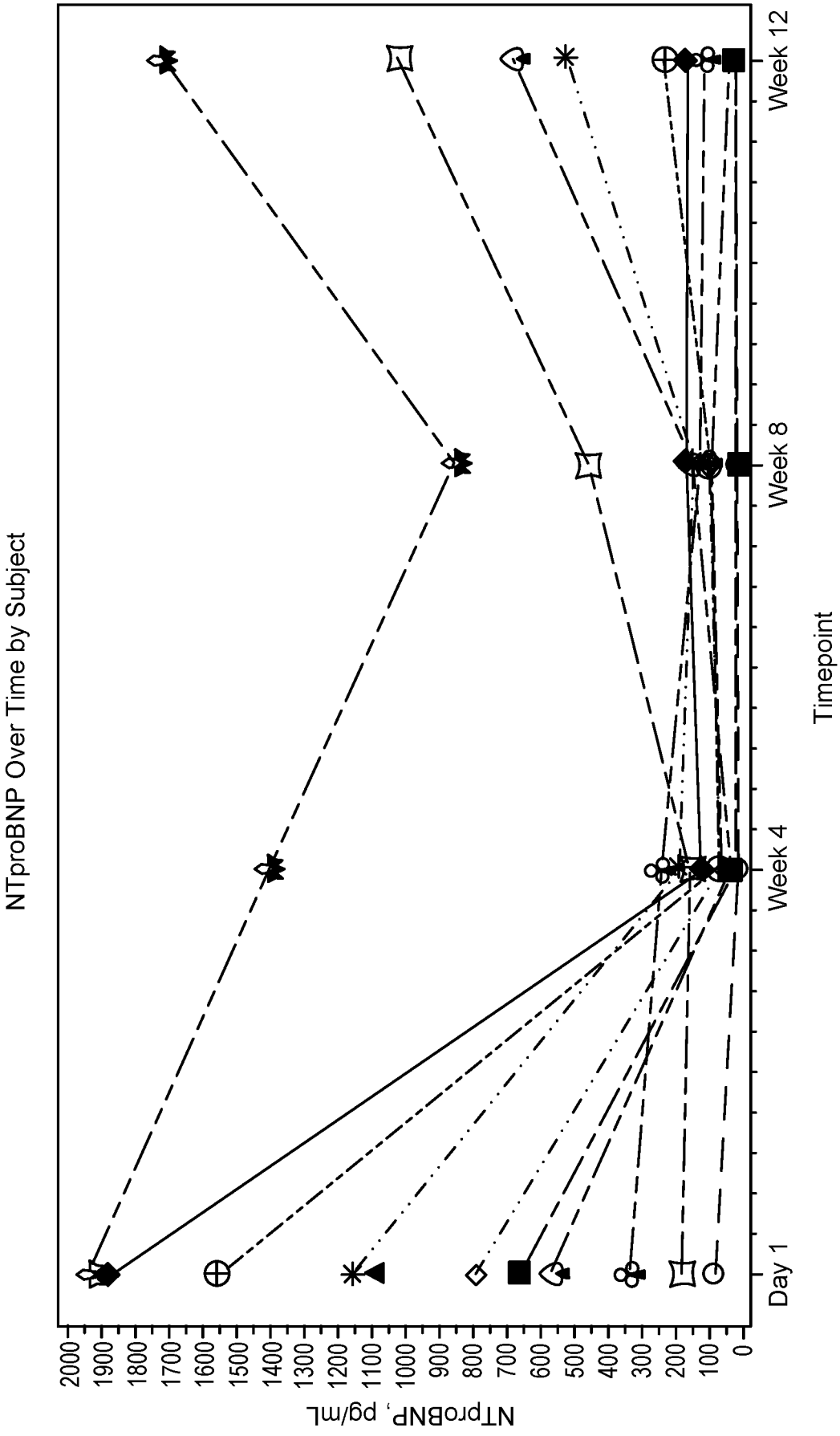

NTproBNP Over Time by Subject
NTproBNP, pg/mL
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
Day 1
Week 4
Week 8
Week 12
Timepoint

FIG. 15

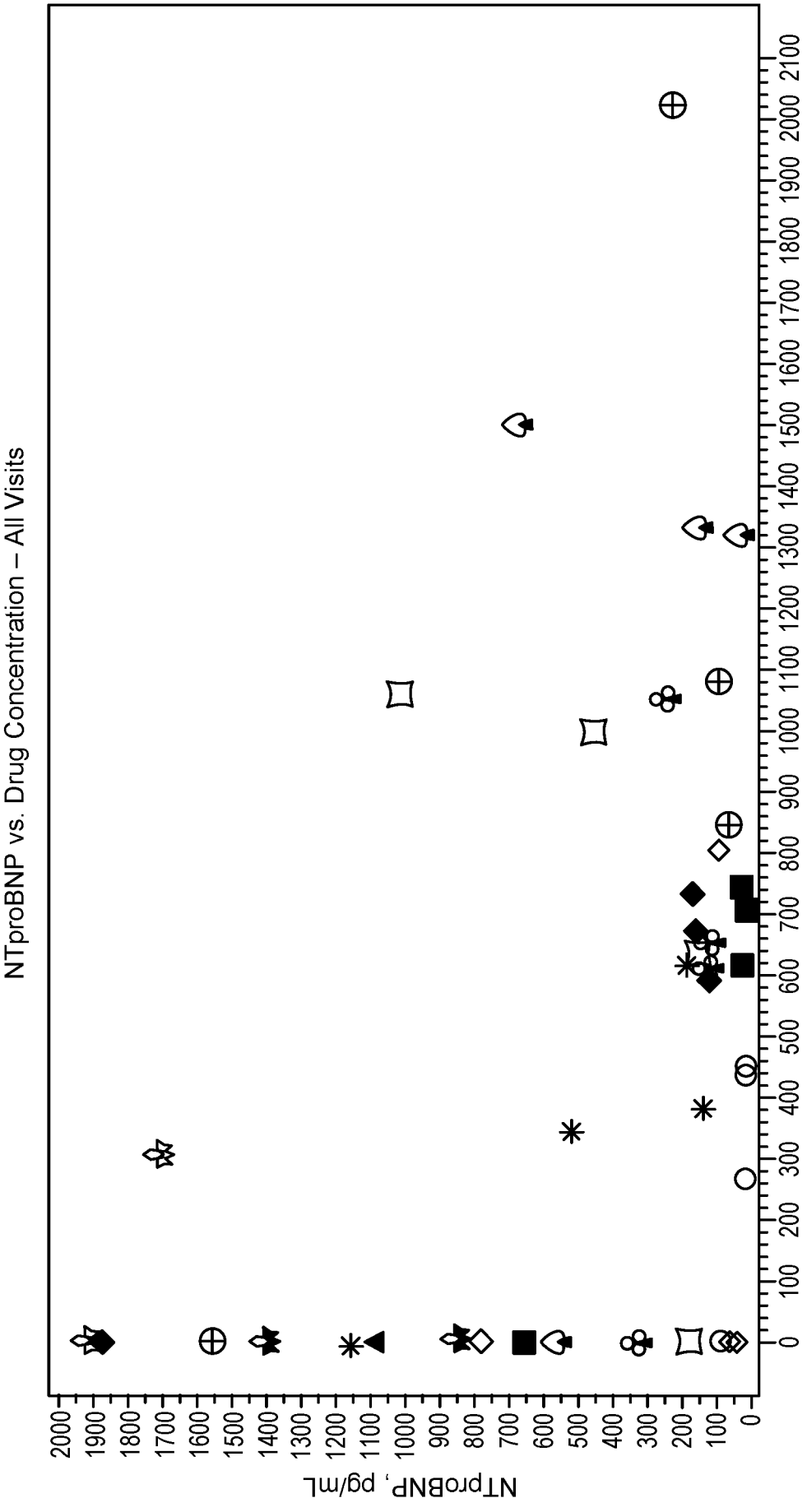
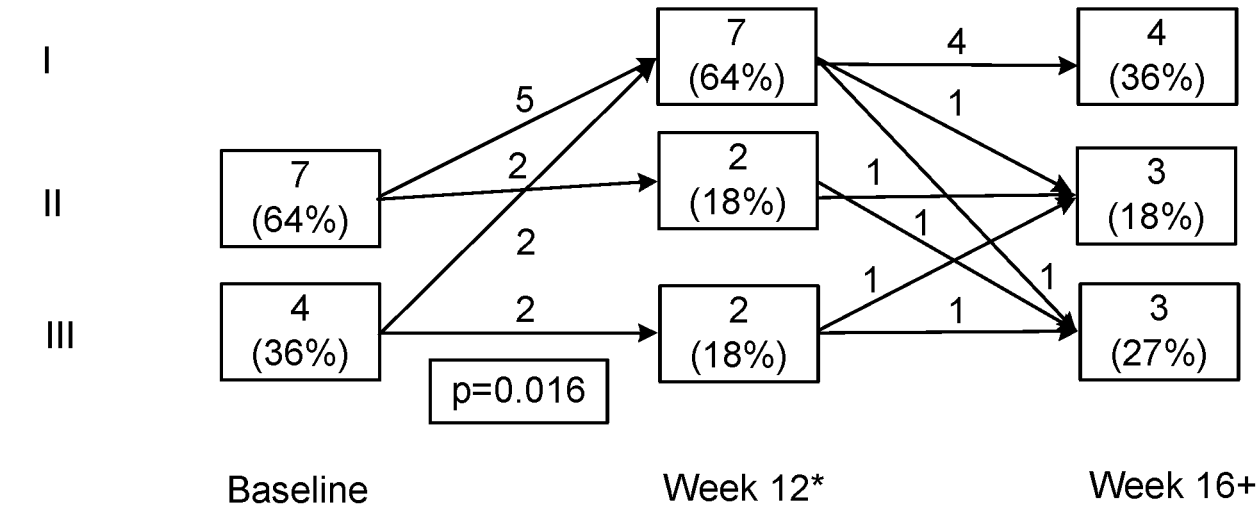

NTproBNP vs. Drug Concentration – All Visits
NTproBNP, pg/mL
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Drug Concentration ng/mL
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
2100
[Compound 1] (ng/mL)

FIG. 16

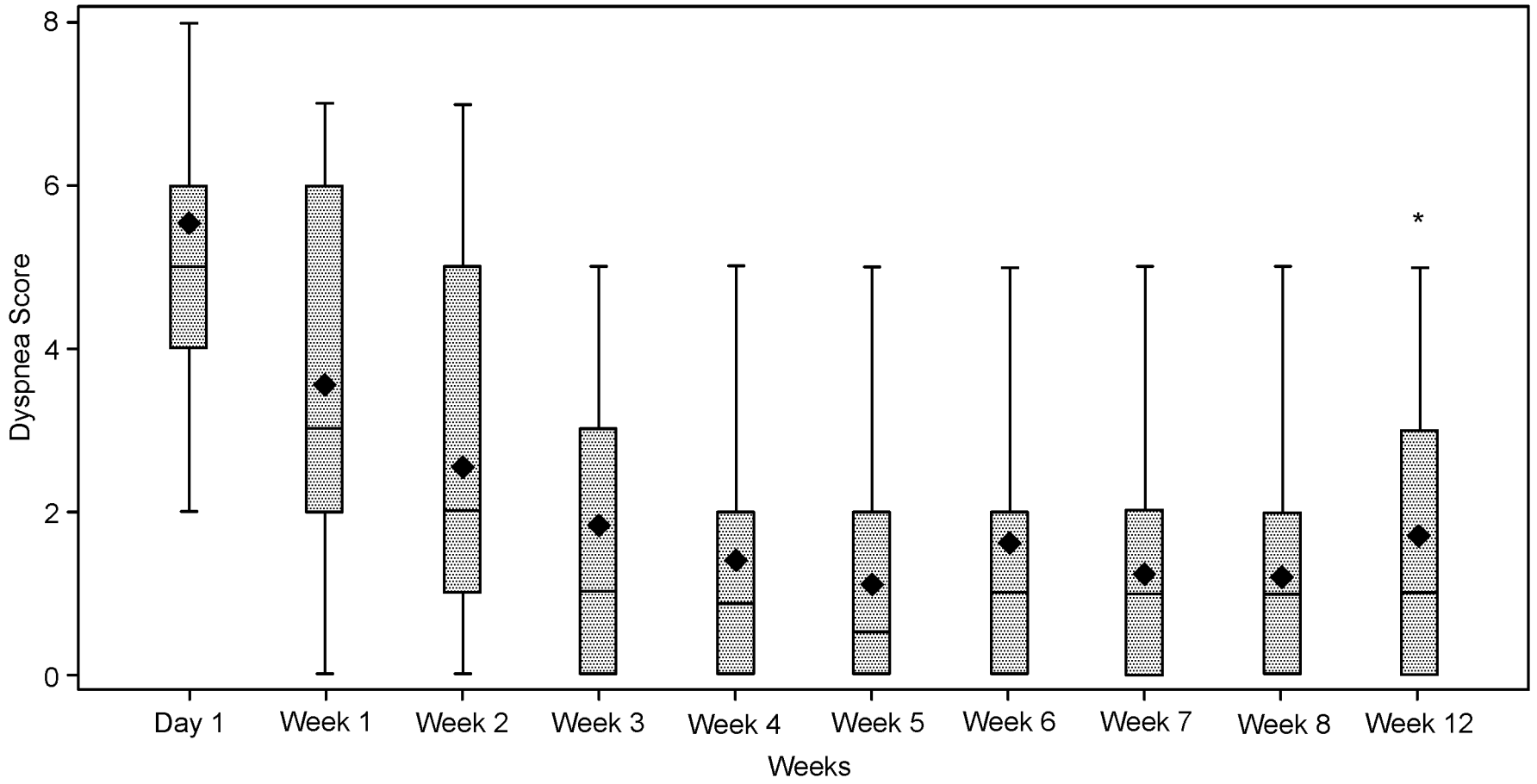


* One subject remained unchanged in Class 3 having stopped MYK-461 during Week 4 (AE)

+ n=10

FIG. 17

SUBSTITUTE SHEET (RULE 26)



The length of the box represents the interquartile range (the distance between the 25th and 75th percentiles).
The symbol in the box interior represents the group mean.
The horizontal line in the box interior represents the group median.
The vertical lines (called whiskers) issuing from the box extend to the group minimum and maximum values.

FIG. 18

SUBSTITUTE SHEET (RULE 26)

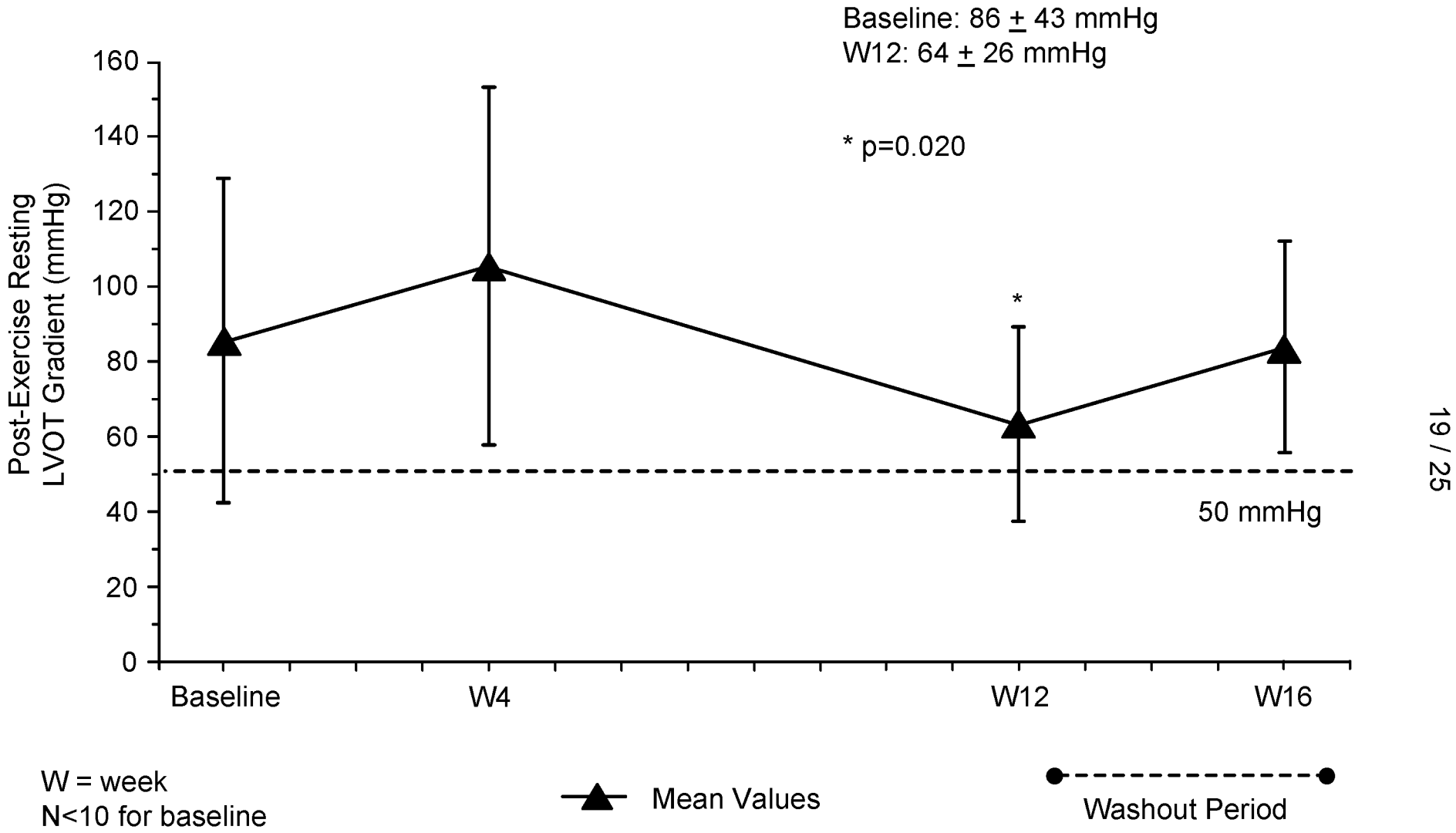


FIG. 19

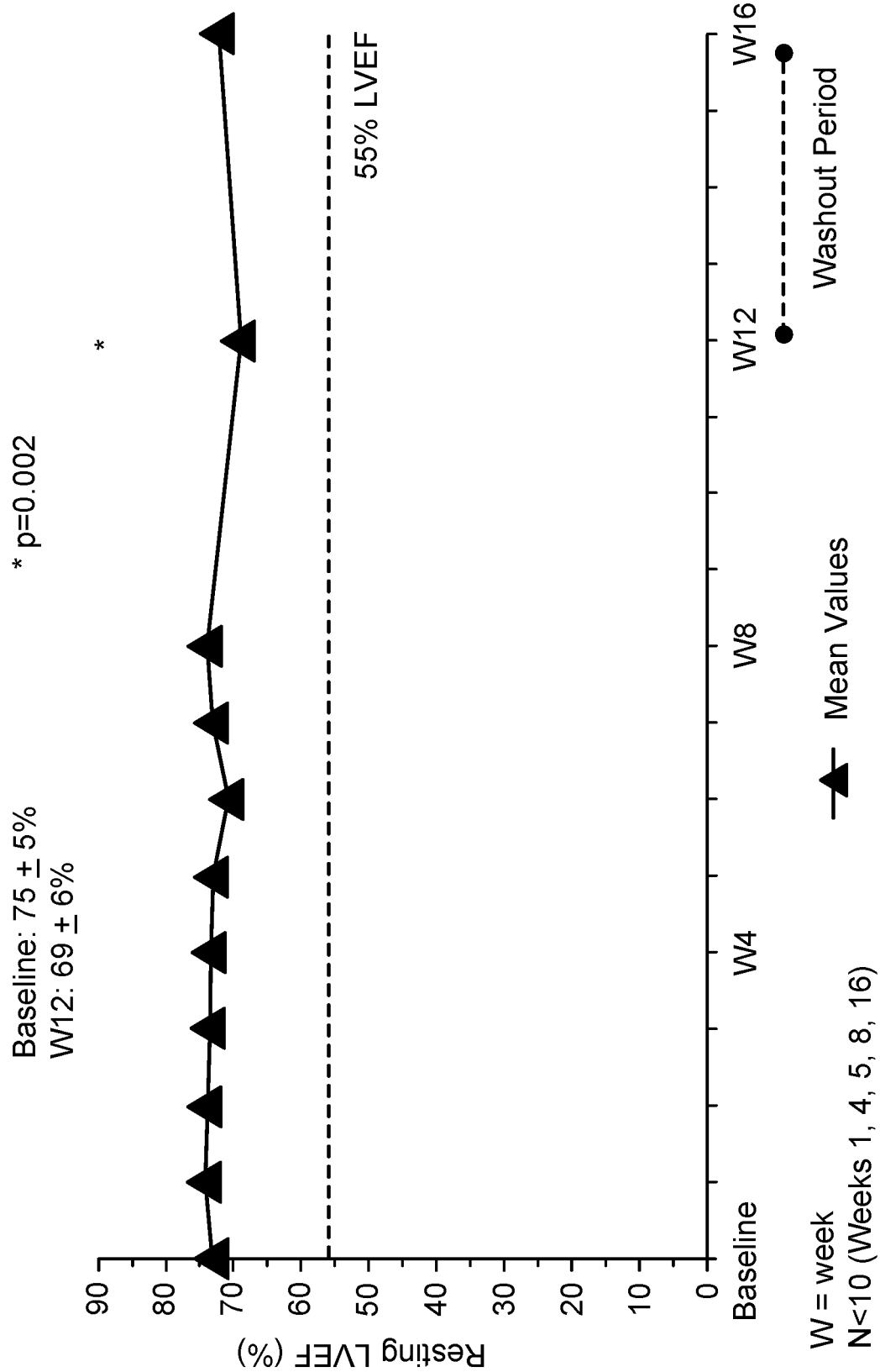

Baseline: 75 ± 5%
W12: 69 ± 6%
* p=0.002
*
55% LVEF
Resting LVEF (%)
90
80
70
60
50
40
30
20
10
0
Baseline
W4
W8
W12
W16
Washout Period
Mean Values
W = week
N<10 (Weeks 1, 4, 5, 8, 16)

FIG. 20

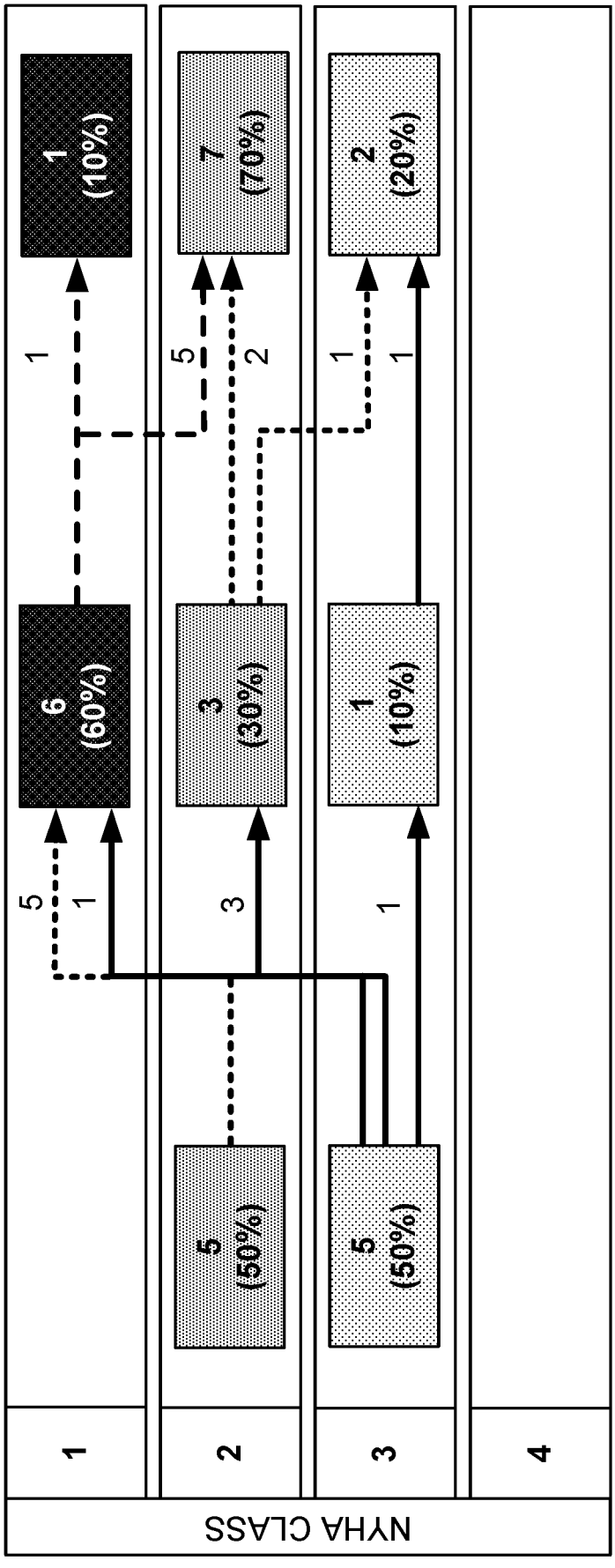

NYHA CLASS
1
2
3
4
1 (10%)
6 (60%)
7 (70%)
3 (30%)
2 (20%)
1 (10%)
5 (50%)
5 (50%)
5
1
3
1
1
5
2
1
1
Baseline
W12
W16
Washout Period
Mean change -1.0 for W12 vs baseline; p=0.004
• 8 subjects with 1 class improvement
• 1 subject with 2 class improvement
• 1 subject with no change
W = week

FIG. 21

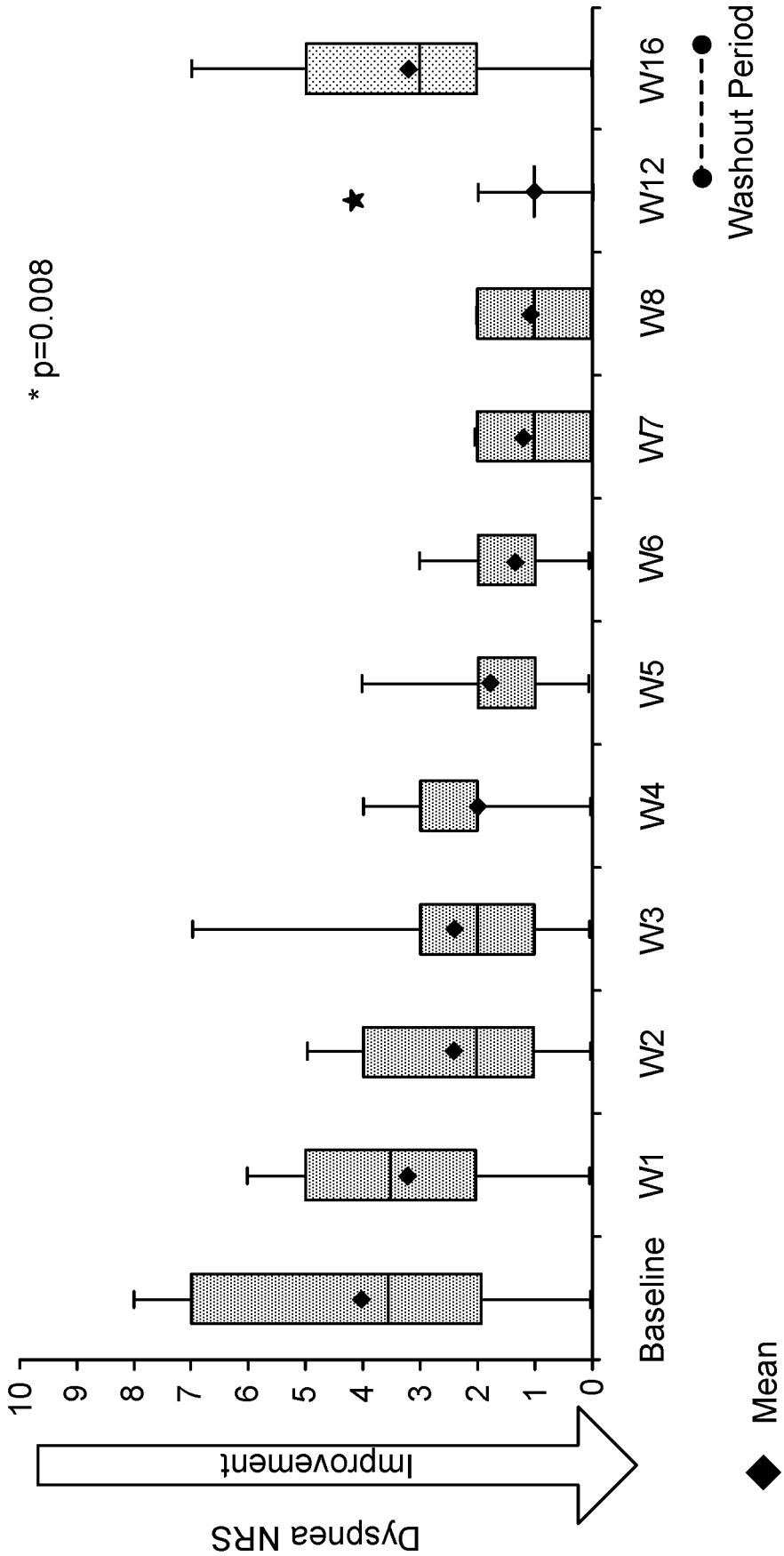
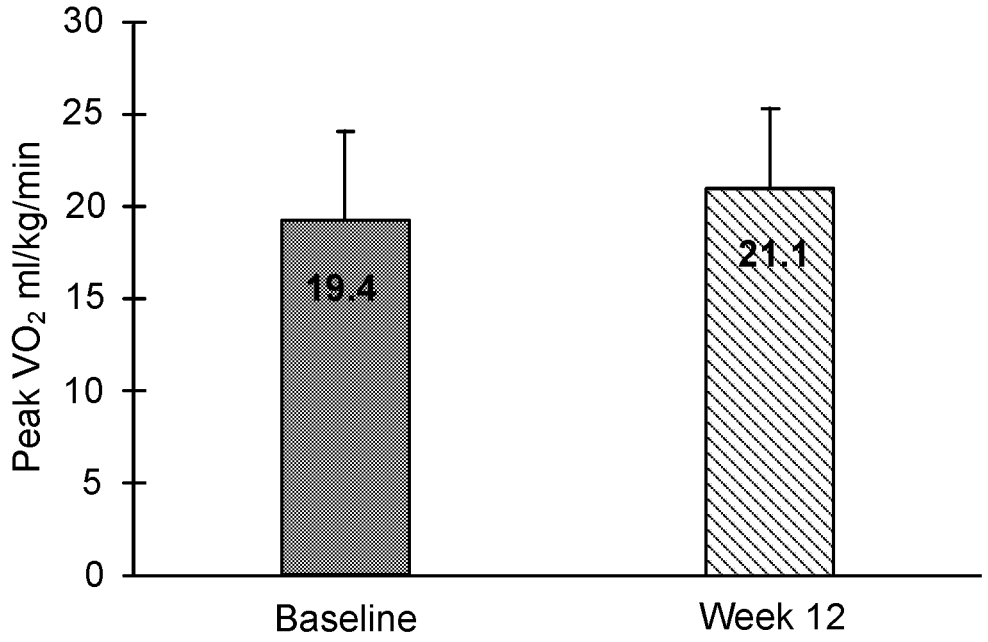

* p=0.008
Dyspnea NRS
Improvement
10
9
8
7
6
5
4
3
2
1
0
Baseline
W1
W2
W3
W4
W5
W6
W7
W8
W12
W16
Washout Period
Mean
Median
W = week

FIG. 22

Mean D = 1.67 ml/kg/min
SD + 2.30

p=0.121



Additional CPET Parameters	Baseline	Week 12	Change	*p*-value
VE/VCO_2	23.3 ± 4.4	29.8 ± 4.9	-2.47 ± 2.53	0.0137
Circulatory Power (mm Hg-mLO2-kg-1·min-1)	2944 ± 14220	3445 ± 1659	501 ± 680	0.0645

FIG. 23

SUBSTITUTE SHEET (RULE 26)

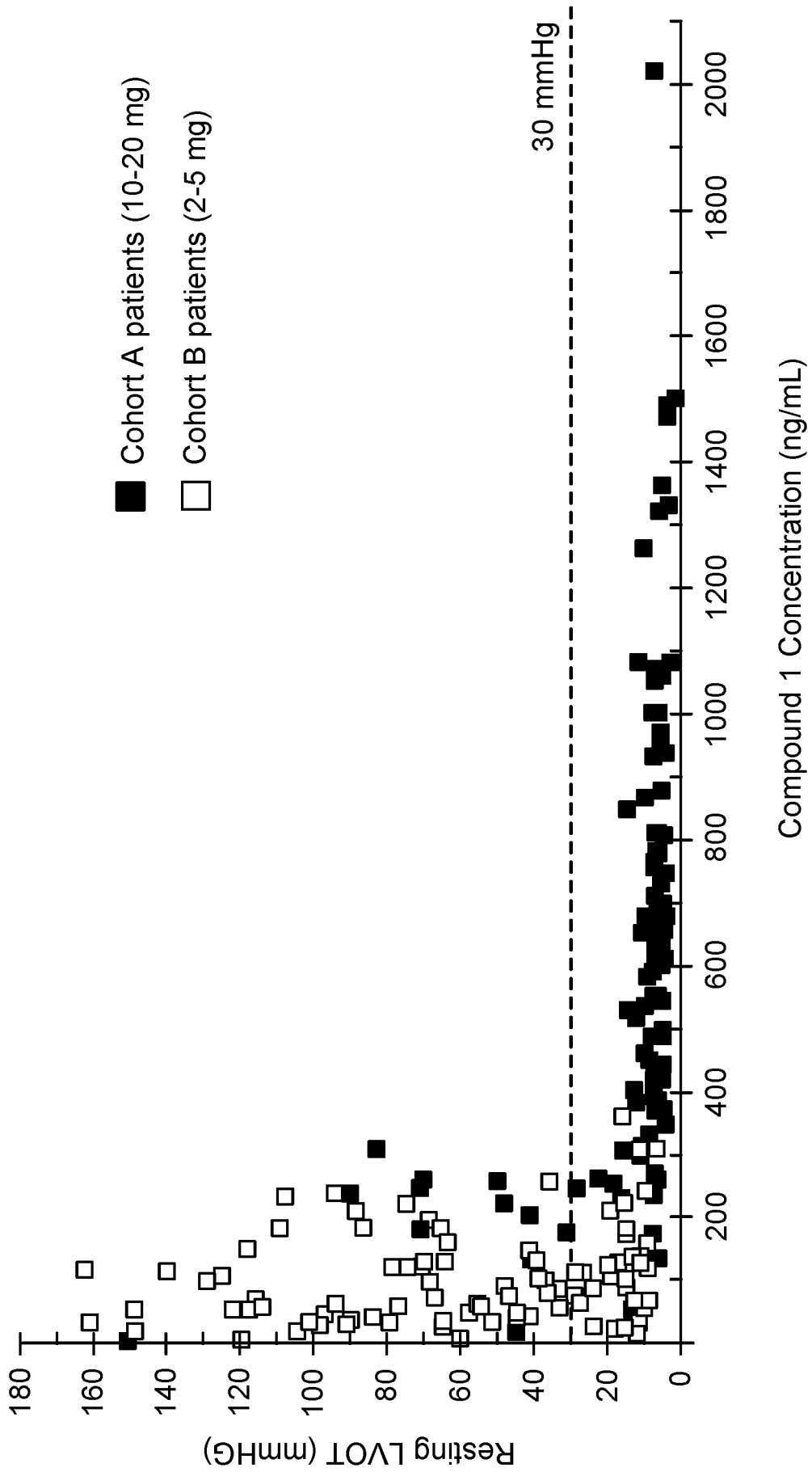

Cohort A patients (10-20 mg)
Cohort B patients (2-5 mg)
30 mmHg
Resting LVOT (mmHG)
Compound 1 Concentration (ng/mL)
0
20
40
60
80
100
120
140
160
180
200
400
600
800
1000
1200
1400
1600
1800
2000

FIG. 24

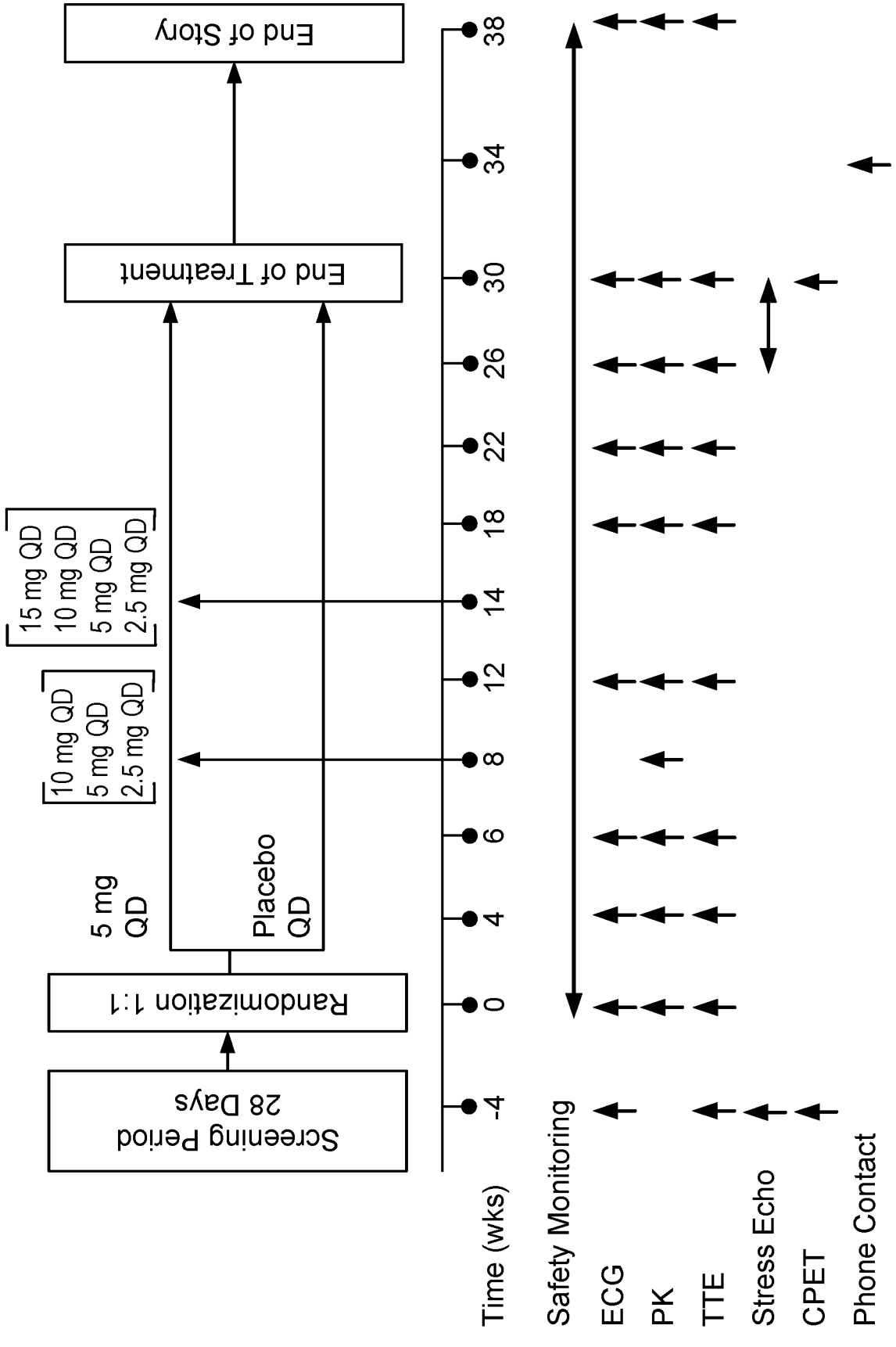

Screening Period
28 Days
Randomization 1:1
5 mg
QD
Placebo
QD
10 mg QD
5 mg QD
2.5 mg QD
15 mg QD
10 mg QD
5 mg QD
2.5 mg QD
End of Treatment
End of Story
Time (wks)
-4
0
4
6
8
12
14
18
22
26
30
34
38
Safety Monitoring
ECG
PK
TTE
Stress Echo
CPET
Phone Contact

FIG. 25