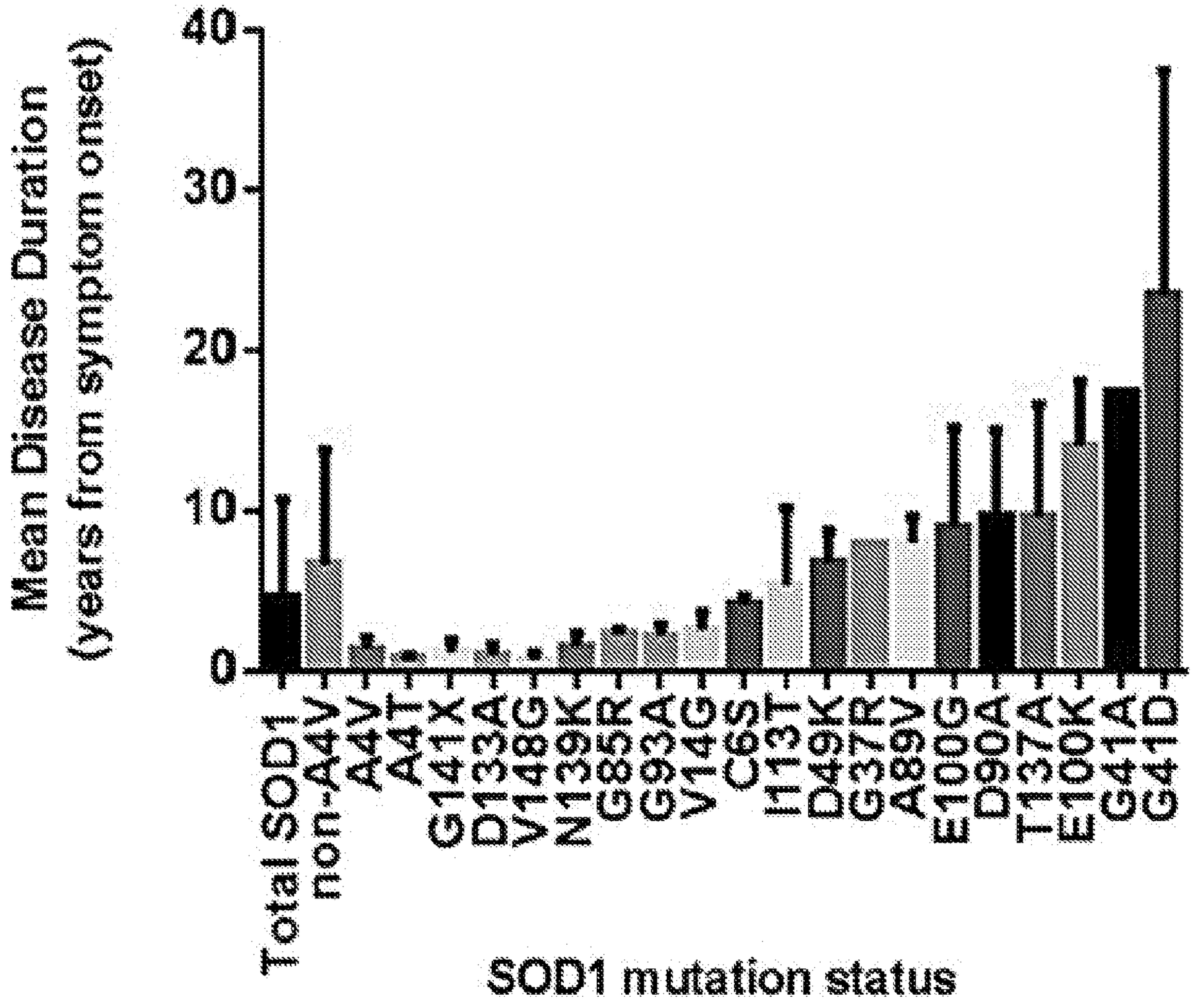
FIGURE 1


Mean Disease Duration
(years from symptom onset)
40
30
20
10
0
Total SOD1
non-A4V
A4V
A4T
G141X
D134A
V148G
N139K
G85R
G93A
V14G
C6S
I113T
D49K
G37R
A89V
E100G
D90A
T137A
-E30K
G41A
G41D
SOD1 mutation status

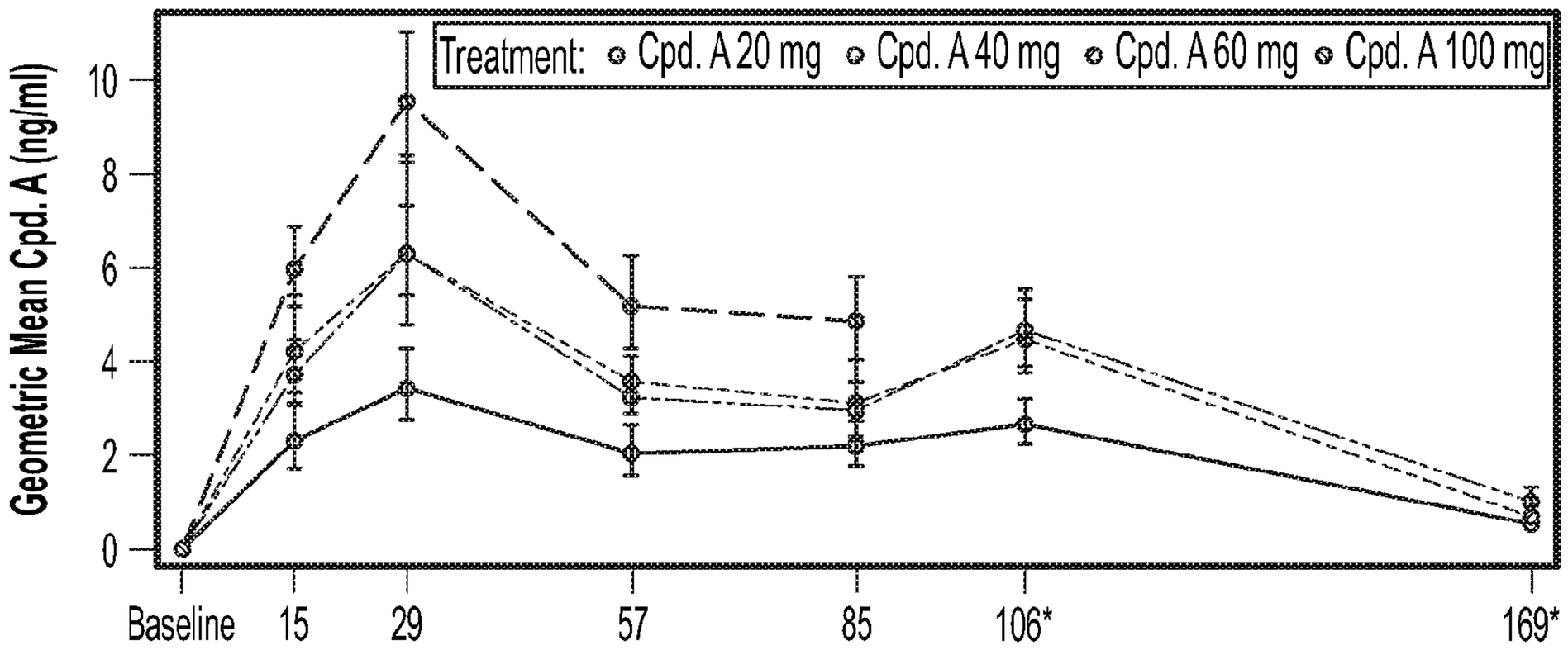

Treatment: Cpd. A 20 mg Cpd. A 40 mg Cpd. A 60 mg Cpd. A 100 mg
Geometric Mean Cpd. A (ng/ml)
0
2
4
6
8
10
Baseline
15
29
57
85
106*
169*

FIGURE 2

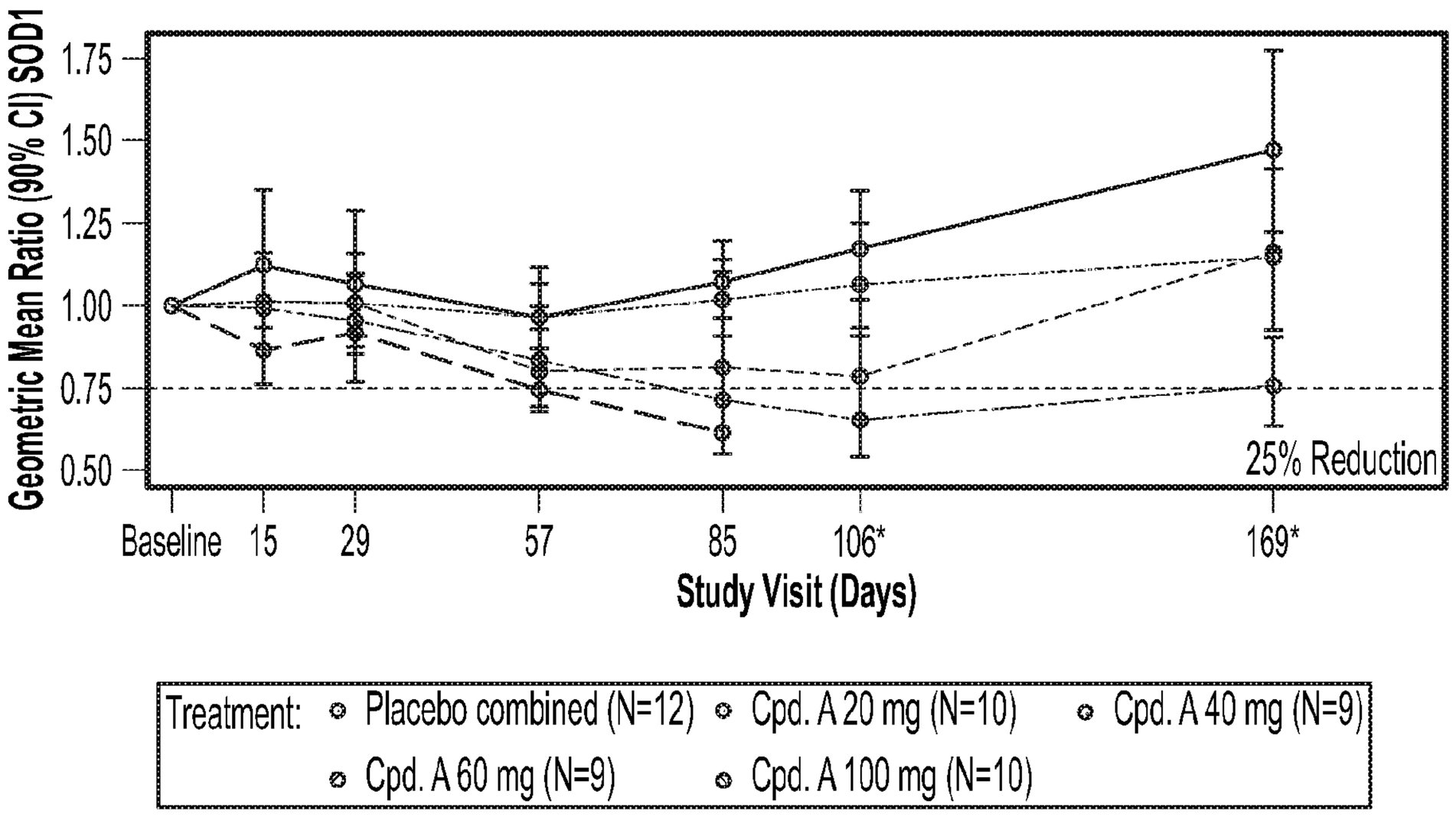

Geometric Mean Ratio (90% CI) SOD1
1.75
1.50
1.25
1.00
0.75
0.50
25% Reduction
Baseline
15
29
57
85
106*
169*
Study Visit (Days)
Treatment:
Placebo combined (N=12)
Cpd. A 20 mg (N=10)
Cpd. A 40 mg (N=9)
Cpd. A 60 mg (N=9)
Cpd. A 100 mg (N=10)

FIGURE 3

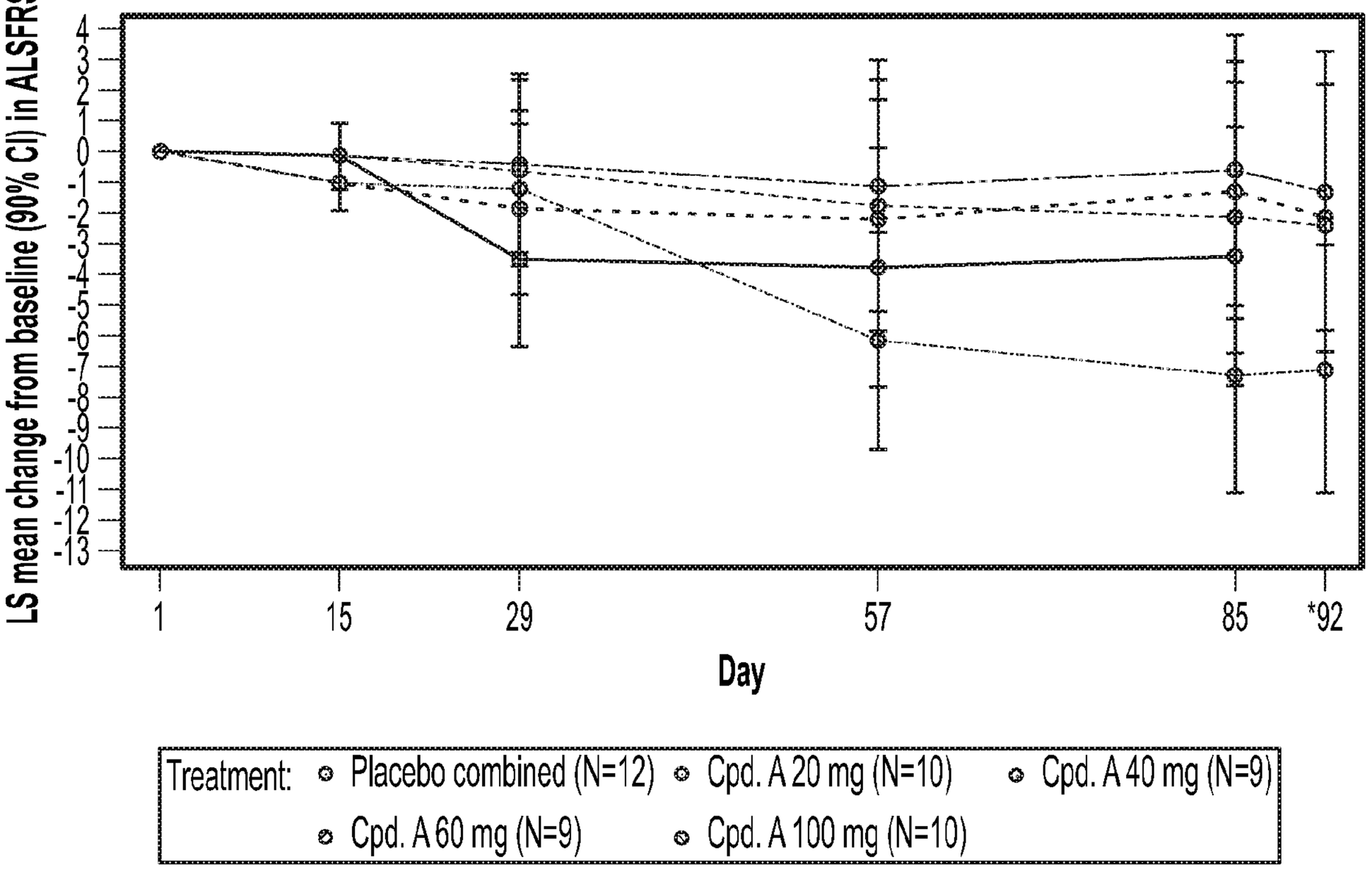

LS mean change from baseline (90% CI) in ALSFRS-R
4
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
-11
-12
-13
1
15
29
57
85
*92
Day
Treatment:
Placebo combined (N=12)
Cpd. A 20 mg (N=10)
Cpd. A 40 mg (N=9)
Cpd. A 60 mg (N=9)
Cpd. A 100 mg (N=10)

FIGURE 4A

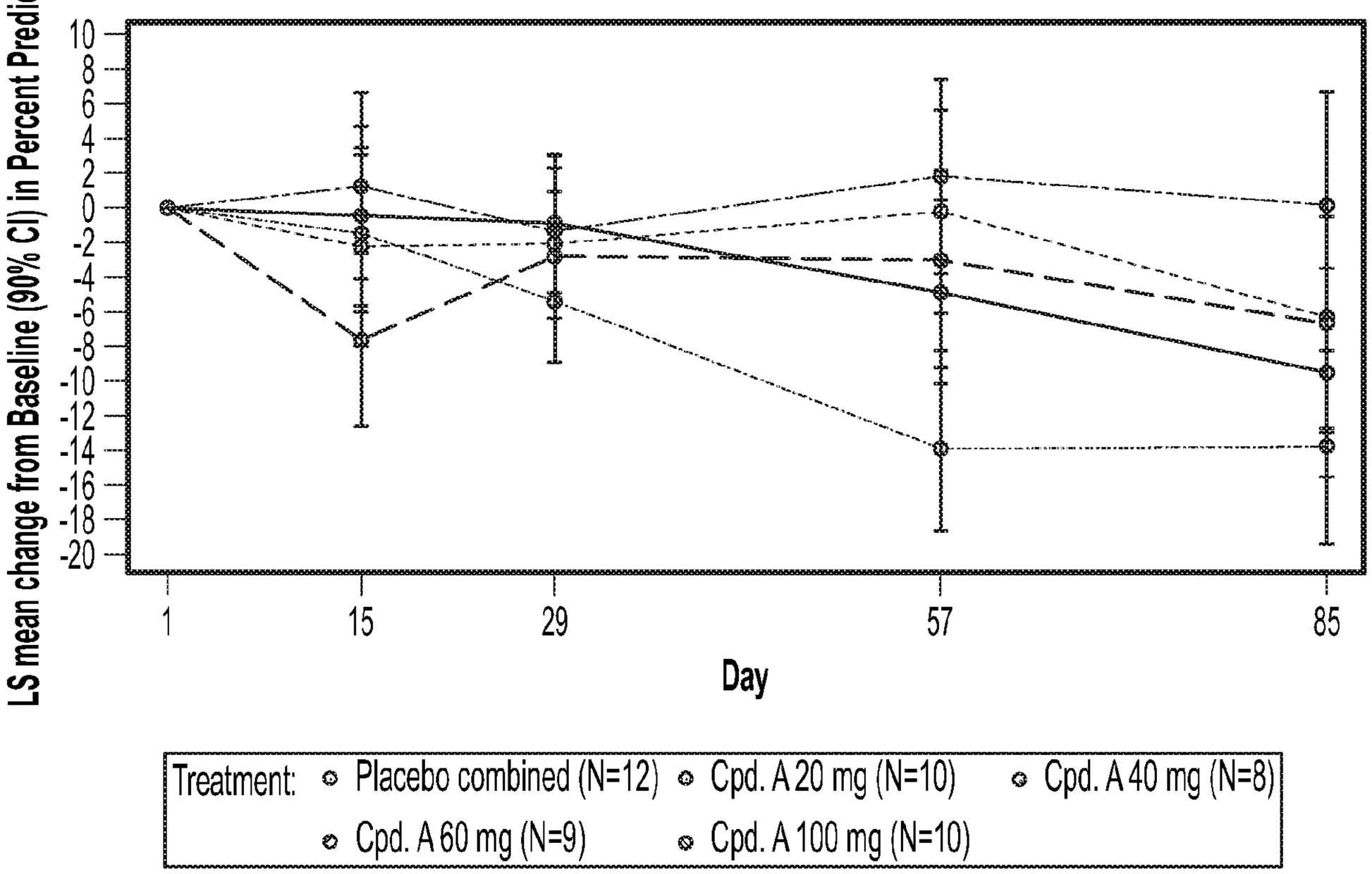

LS mean change from Baseline (90% CI) in Percent Predicted SVC
10
8
6
4
2
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
-20
1
15
29
57
85
Day
Treatment:
Placebo combined (N=12)
Cpd. A 20 mg (N=10)
Cpd. A 40 mg (N=8)
Cpd. A 60 mg (N=9)
Cpd. A 100 mg (N=10)

FIGURE 4B

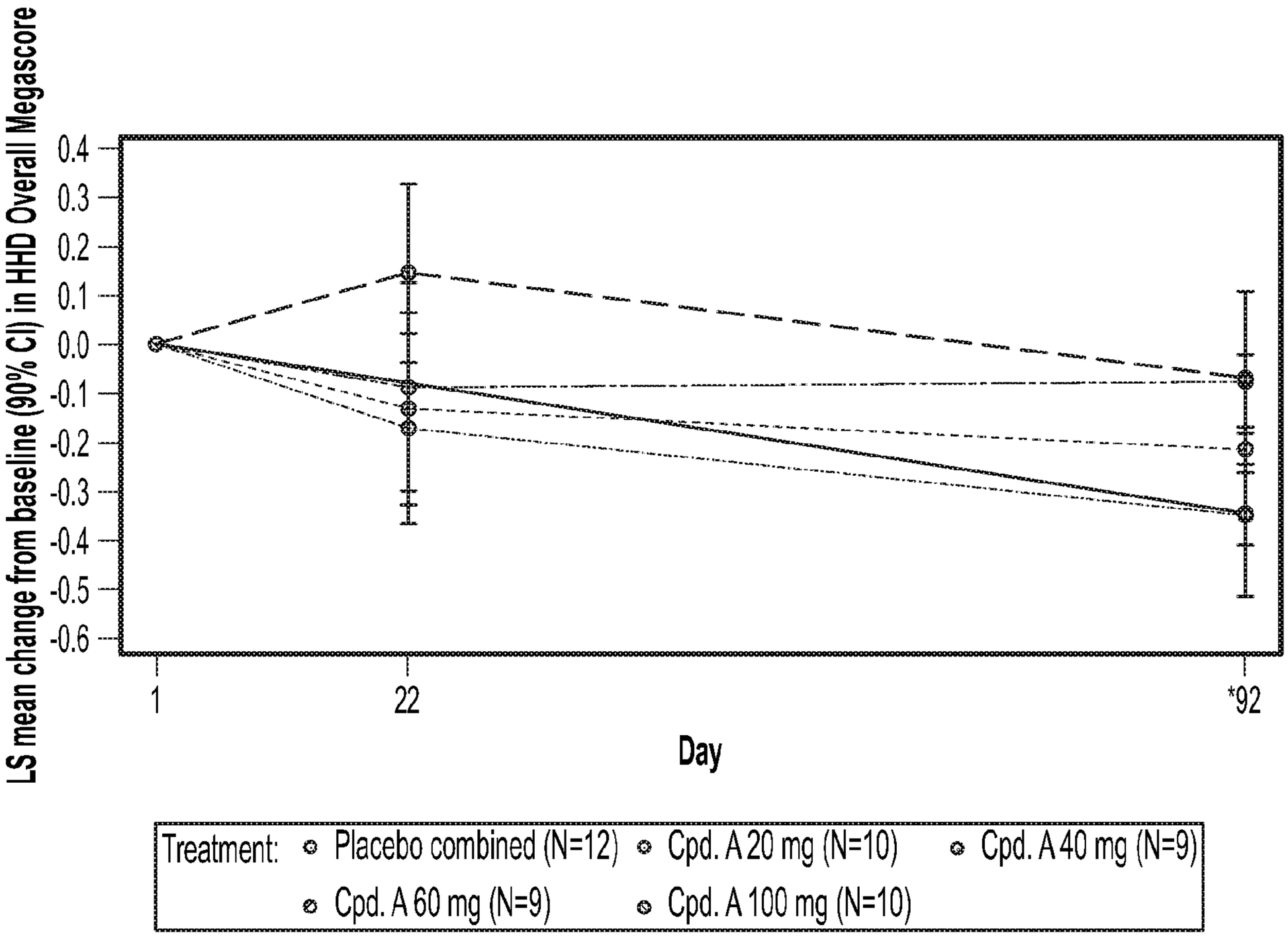

LS mean change from baseline (90% CI) in HHD Overall Megascore
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
1
22
*92
Day
Treatment:
Placebo combined (N=12)
Cpd. A 20 mg (N=10)
Cpd. A 40 mg (N=9)
Cpd. A 60 mg (N=9)
Cpd. A 100 mg (N=10)

FIGURE 4C

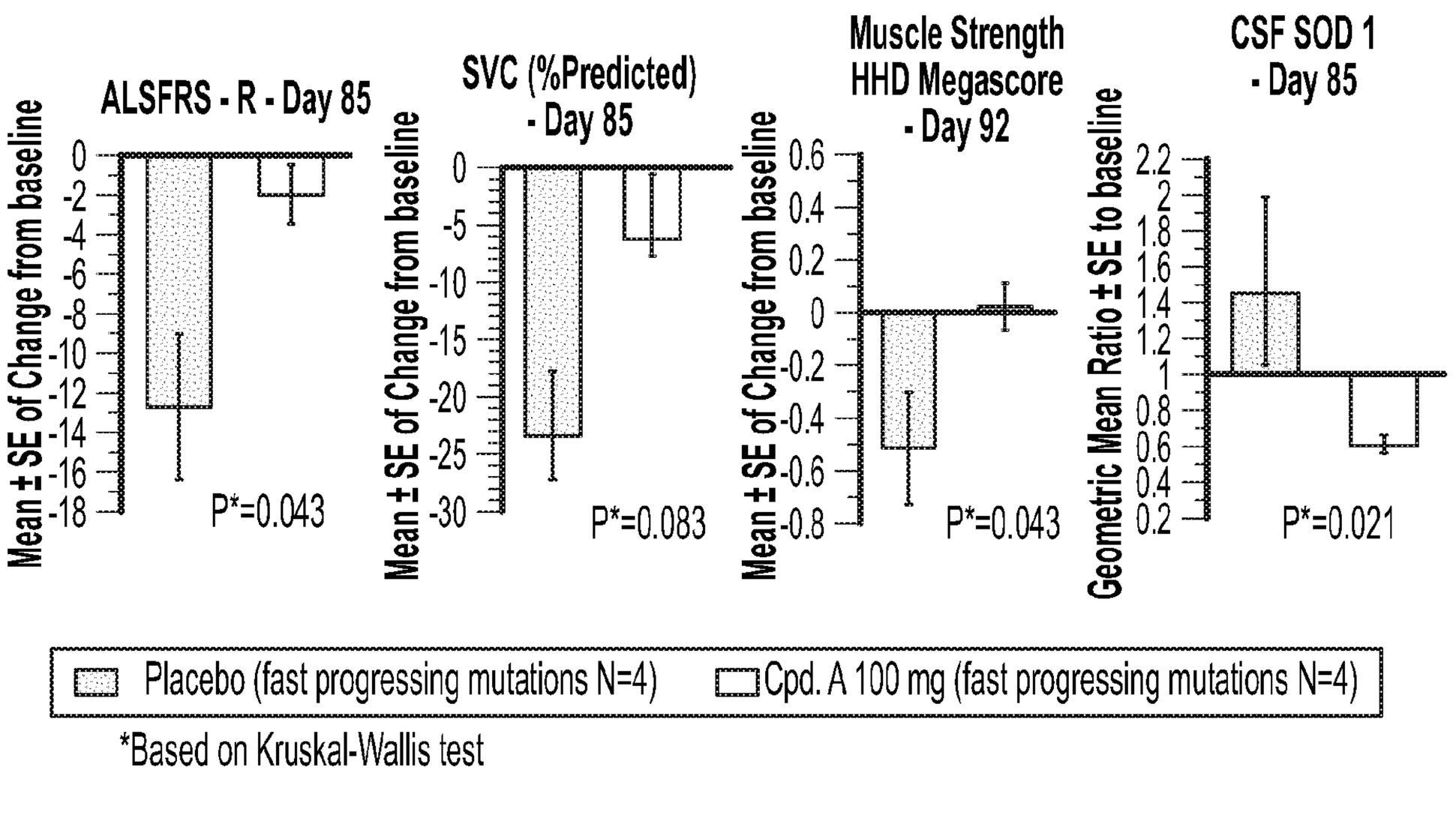

ALSFRS - R - Day 85
Mean ± SE of Change from baseline
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
P*=0.043
SVC (%Predicted) - Day 85
Mean ± SE of Change from baseline
0
-5
-10
-15
-20
-25
-30
P*=0.083
Muscle Strength HHD Megascore - Day 92
Mean ± SE of Change from baseline
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
P*=0.043
CSF SOD 1 - Day 85
Geometric Mean Ratio ± SE to baseline
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
P*=0.021
Placebo (fast progressing mutations N=4)
Cpd. A 100 mg (fast progressing mutations N=4)
*Based on Kruskal-Wallis test

FIGURE 5

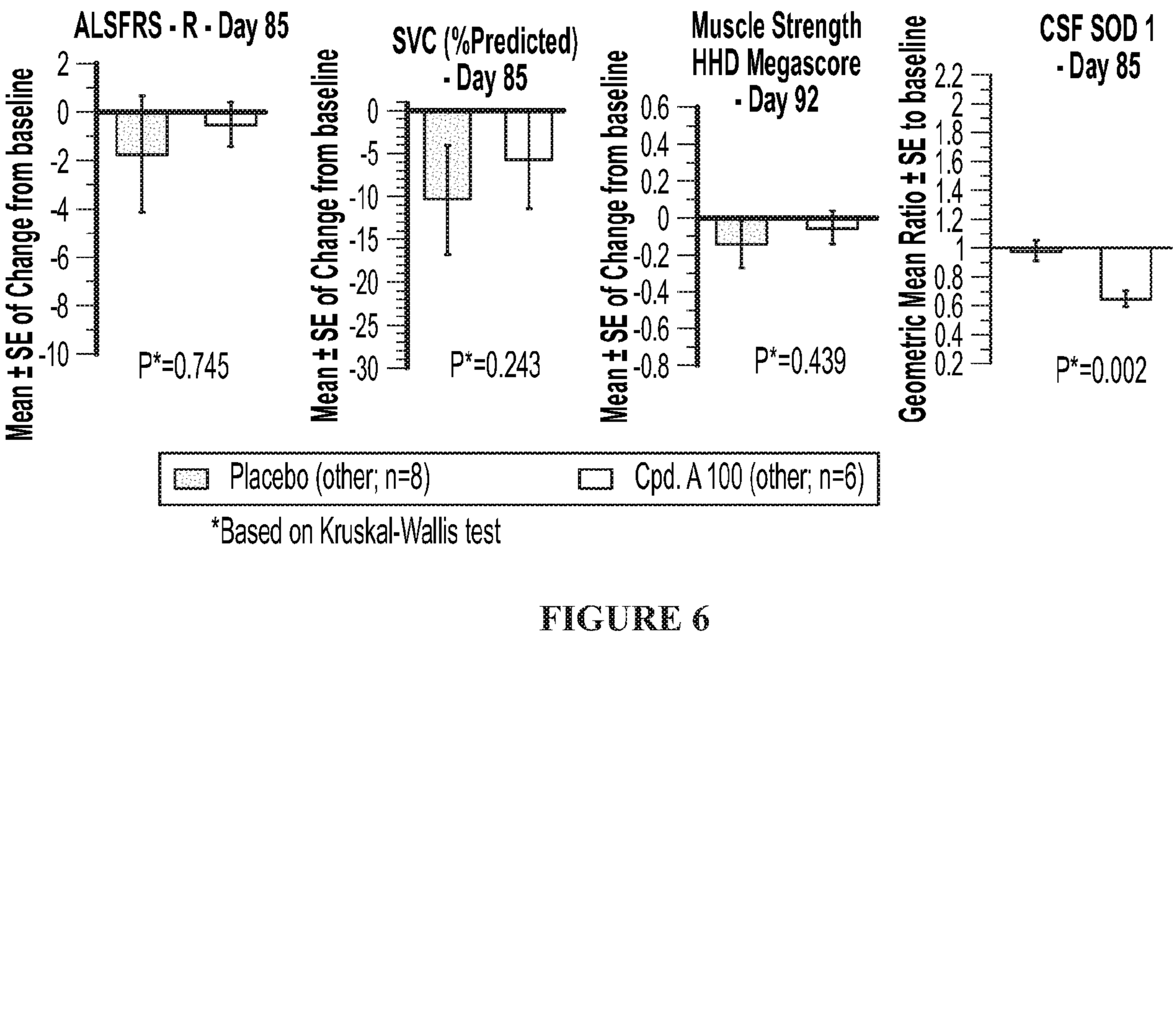

ALSFRS - R - Day 85
Mean ± SE of Change from baseline
2
0
-2
-4
-6
-8
-10
P*=0.745
SVC (%Predicted) - Day 85
Mean ± SE of Change from baseline
0
-5
-10
-15
-20
-25
-30
P*=0.243
Muscle Strength HHD Megascore - Day 92
Mean ± SE of Change from baseline
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
P*=0.439
CSF SOD 1 - Day 85
Geometric Mean Ratio ± SE to baseline
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
P*=0.002
Placebo (other; n=8)
Cpd. A 100 (other; n=6)
*Based on Kruskal-Wallis test

FIGURE 6

FIGURE 7

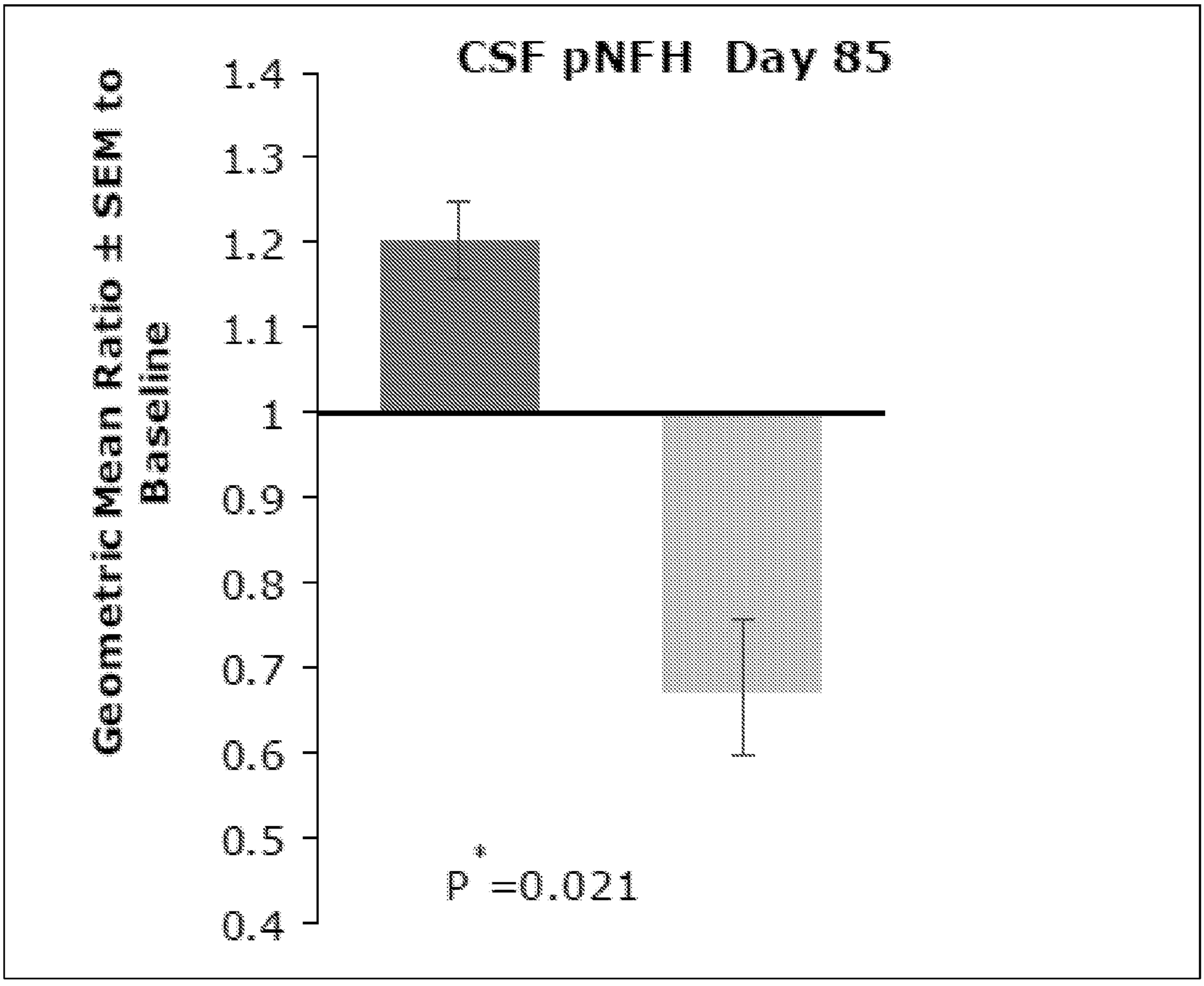
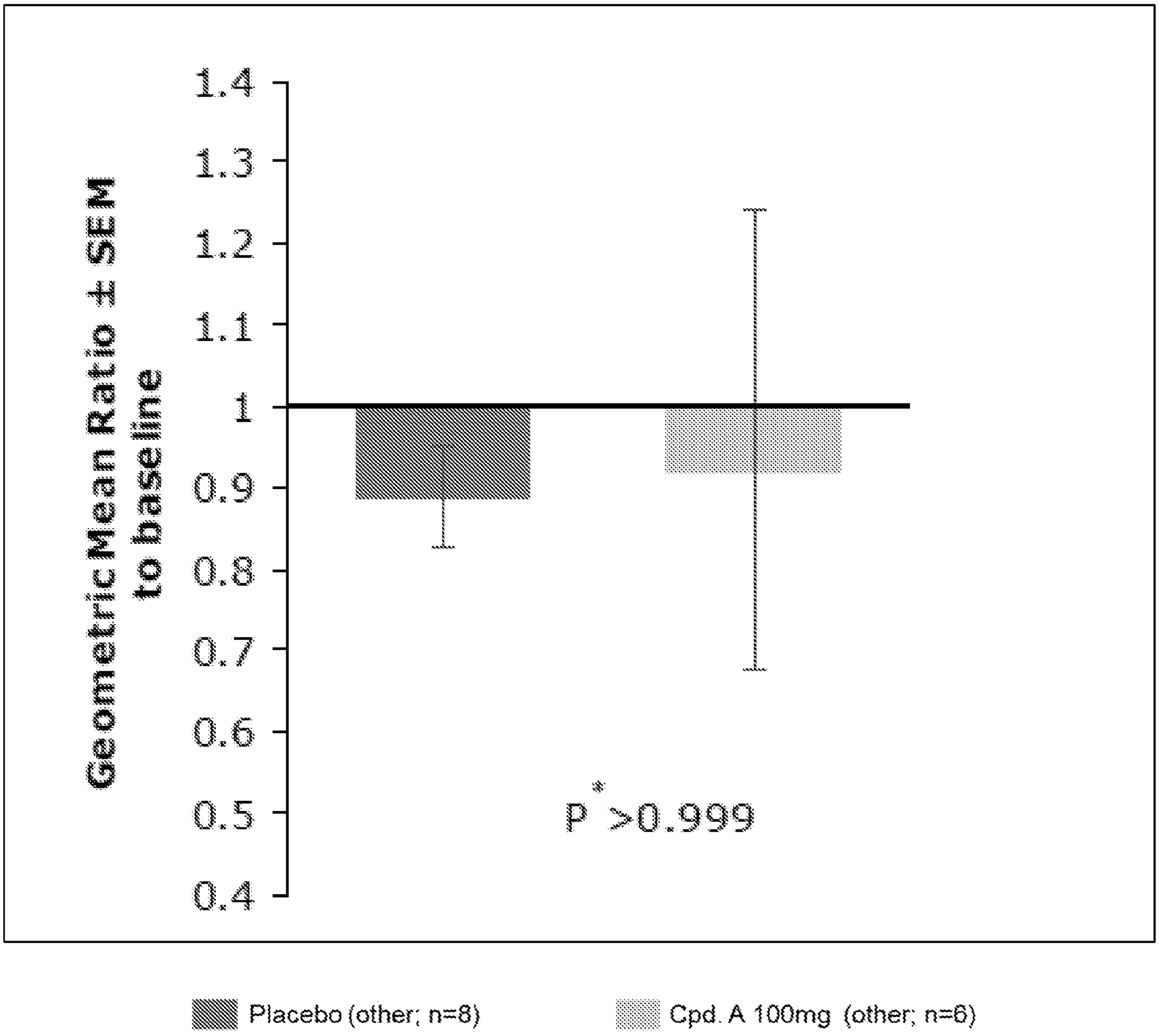

CSF pNFH Day 85
Geometric Mean Ratio ± SEM
Baseline
1.4
1.3
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
P* =0.021
Placebo (fast progressing mutations N=4)
Cpd. A 100 mg (fast progressing mutations N=4)

FIGURE 8


CSF pNFH Day 85
Geometric Mean Ratio ± SEM
to baseline
0.4
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
1.3
1.4
p* >0.999
Placebo (other; n=8)
Cpd. A 100mg (other; n=6)
*Based on Kruskal-Wallis test