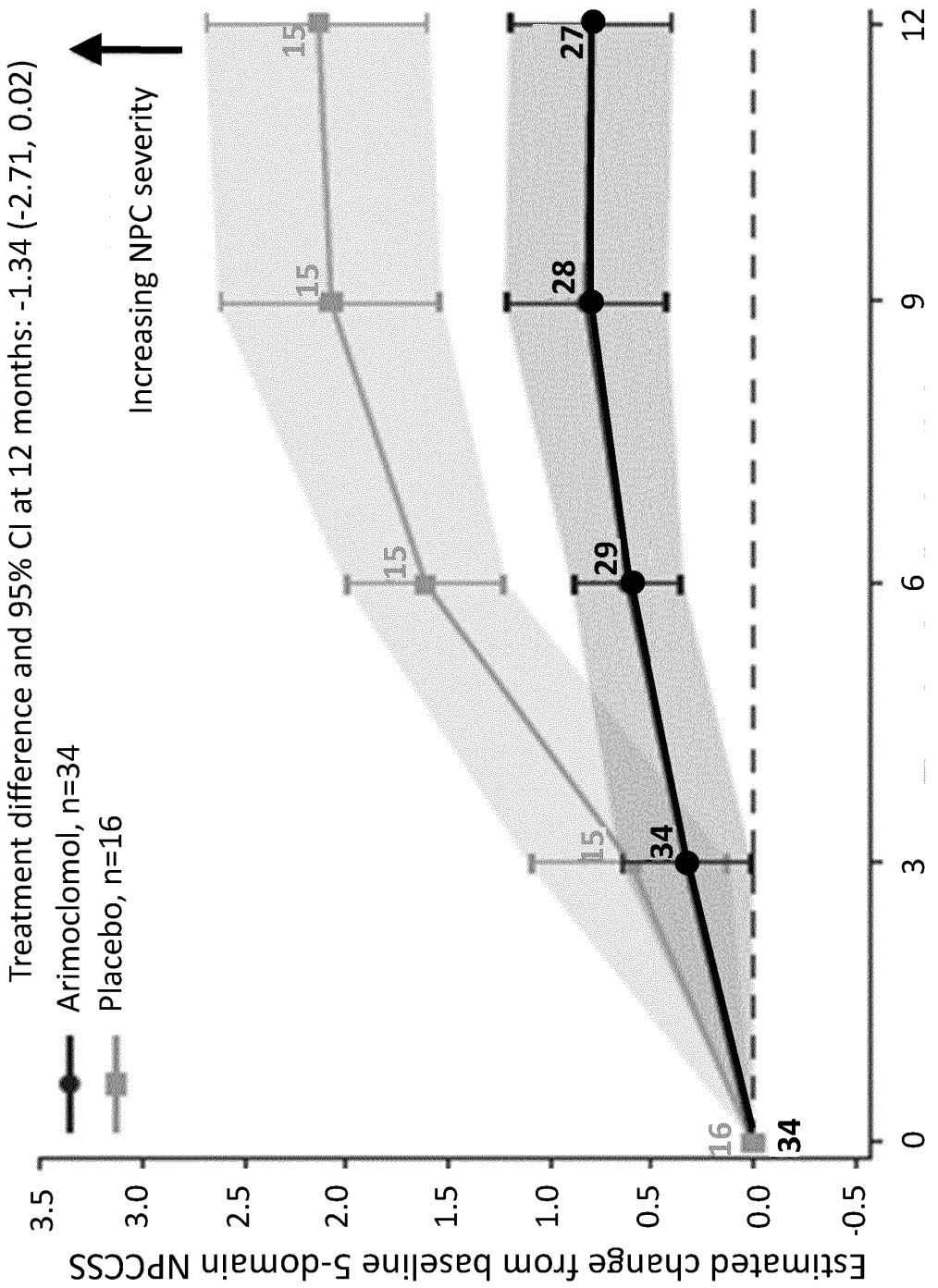

Treatment difference and 95% CI at 12 months: -1.34 (-2.71, 0.02)
Arimoclomol, n=34
Placebo, n=16
Increasing NPC severity
Estimated change from baseline 5-domain NPCCSS
Time since baseline (months)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0
3
6
9
12
16
15
15
15
15
34
29
28
27
34

Fig. 1A

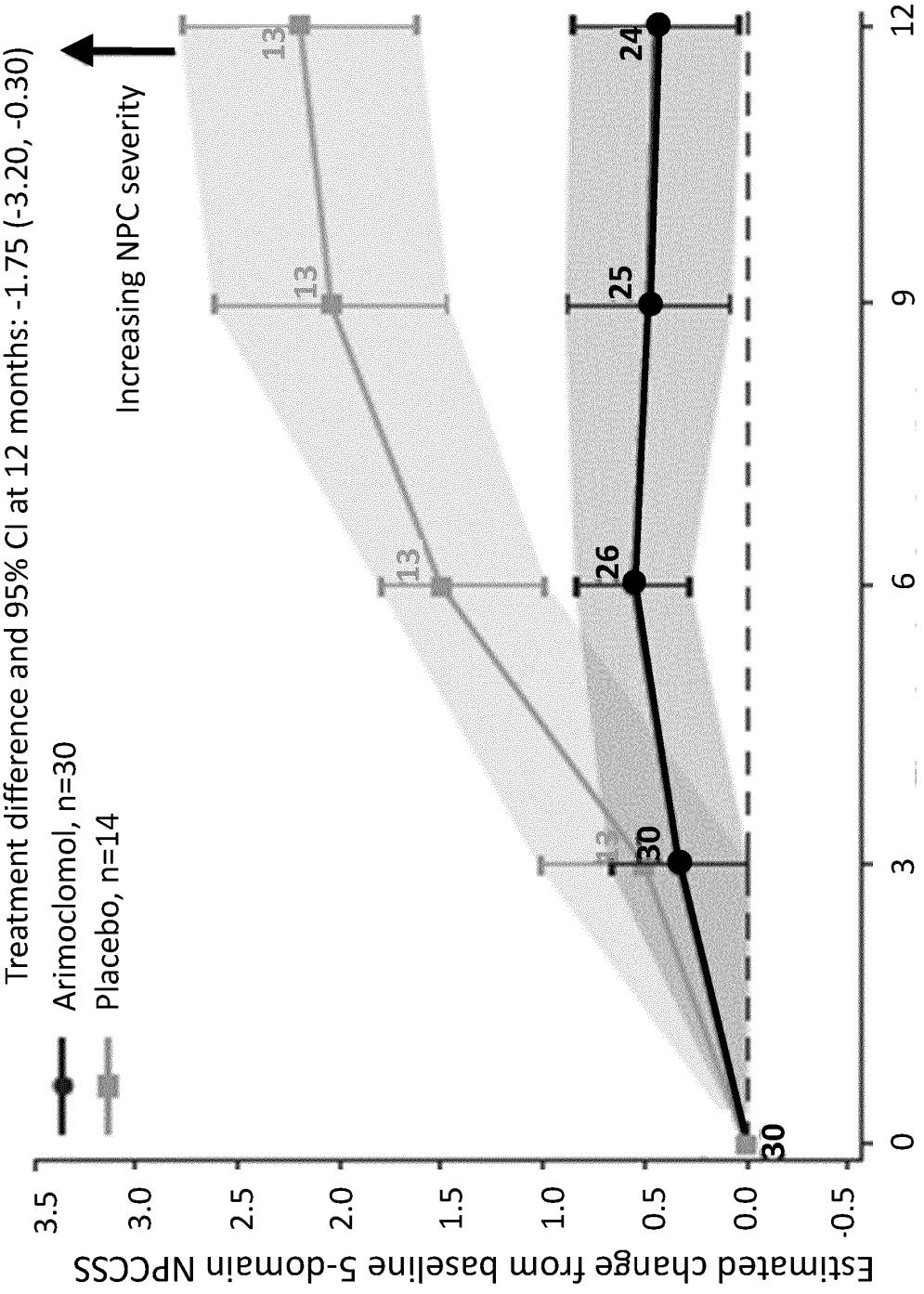

Treatment difference and 95% CI at 12 months: -1.75 (-3.20, -0.30)
Arimoclomol, n=30
Placebo, n=14
Increasing NPC severity
Estimated change from baseline 5-domain NPCCSS
Time since baseline (months)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0
3
6
9
12
13
13
13
13
30
26
25
24
30

Fig. 1B

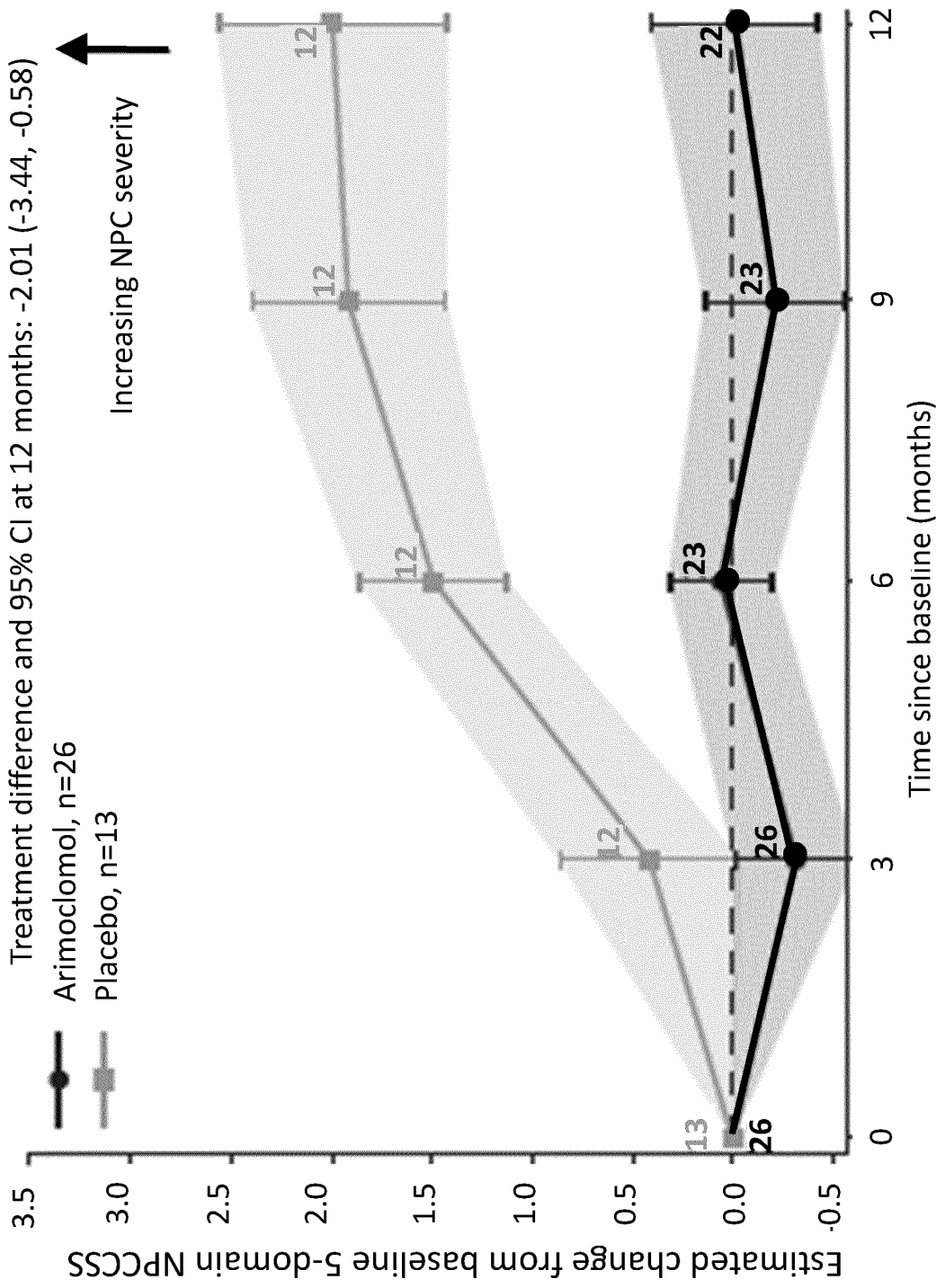

Treatment difference and 95% CI at 12 months: -2.01 (-3.44, -0.58)
Arimoclomol, n=26
Placebo, n=13
Increasing NPC severity
Estimated change from baseline 5-domain NPCCSS
Time since baseline (months)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0
3
6
9
12
13
12
12
12
12
26
26
23
23
22

Fig. 1C

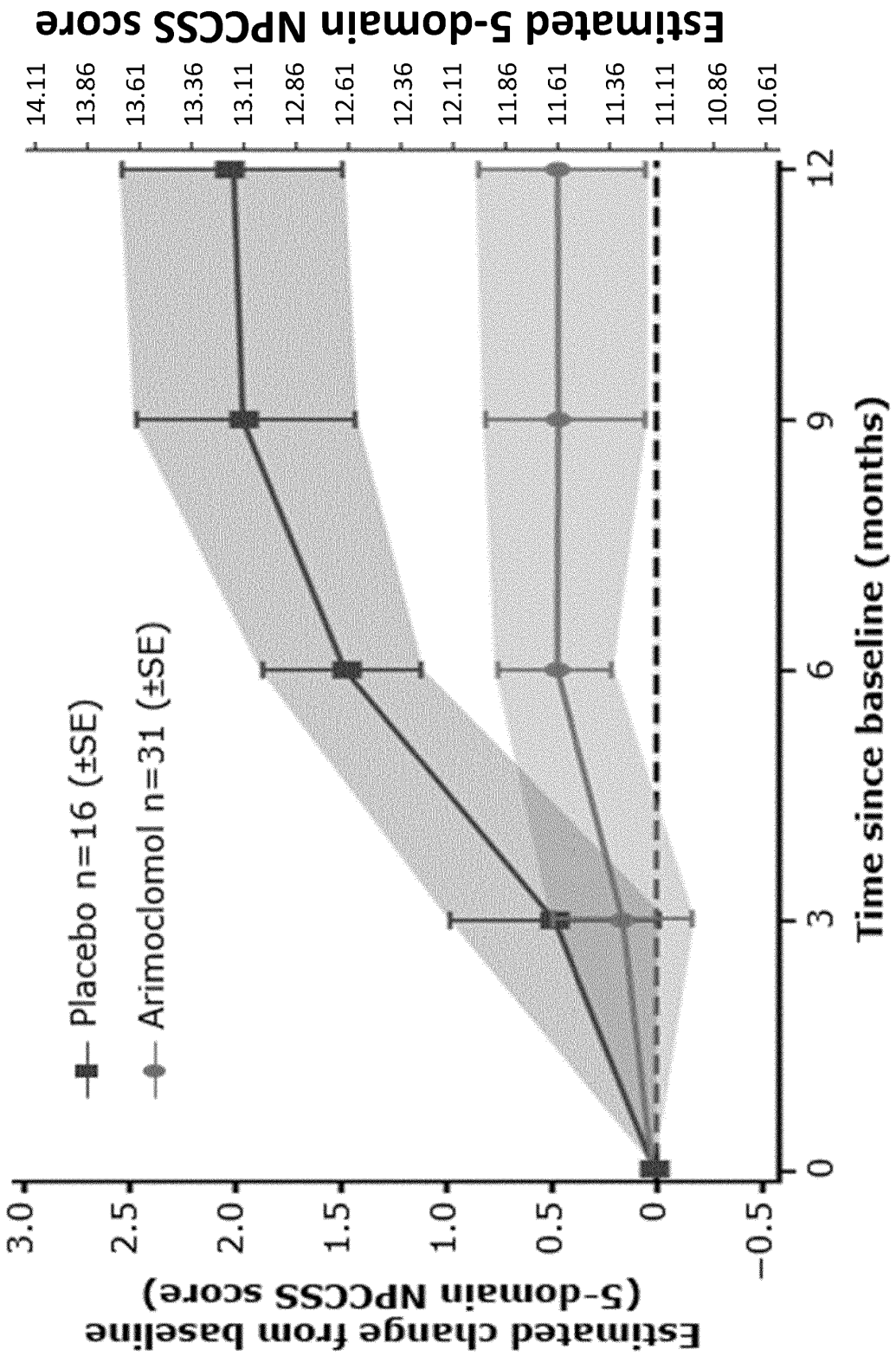

Estimated 5-domain NPCCSS score
14.11
13.86
13.61
13.36
13.11
12.86
12.61
12.36
12.11
11.86
11.61
11.36
11.11
10.86
10.61
Placebo n=16 (±SE)
Arimoclomol n=31 (±SE)
Estimated change from baseline (5-domain NPCCSS score)
3.0
2.5
2.0
1.5
1.0
0.5
0
−0.5
0
3
6
9
12
Time since baseline (months)

Fig. 1D

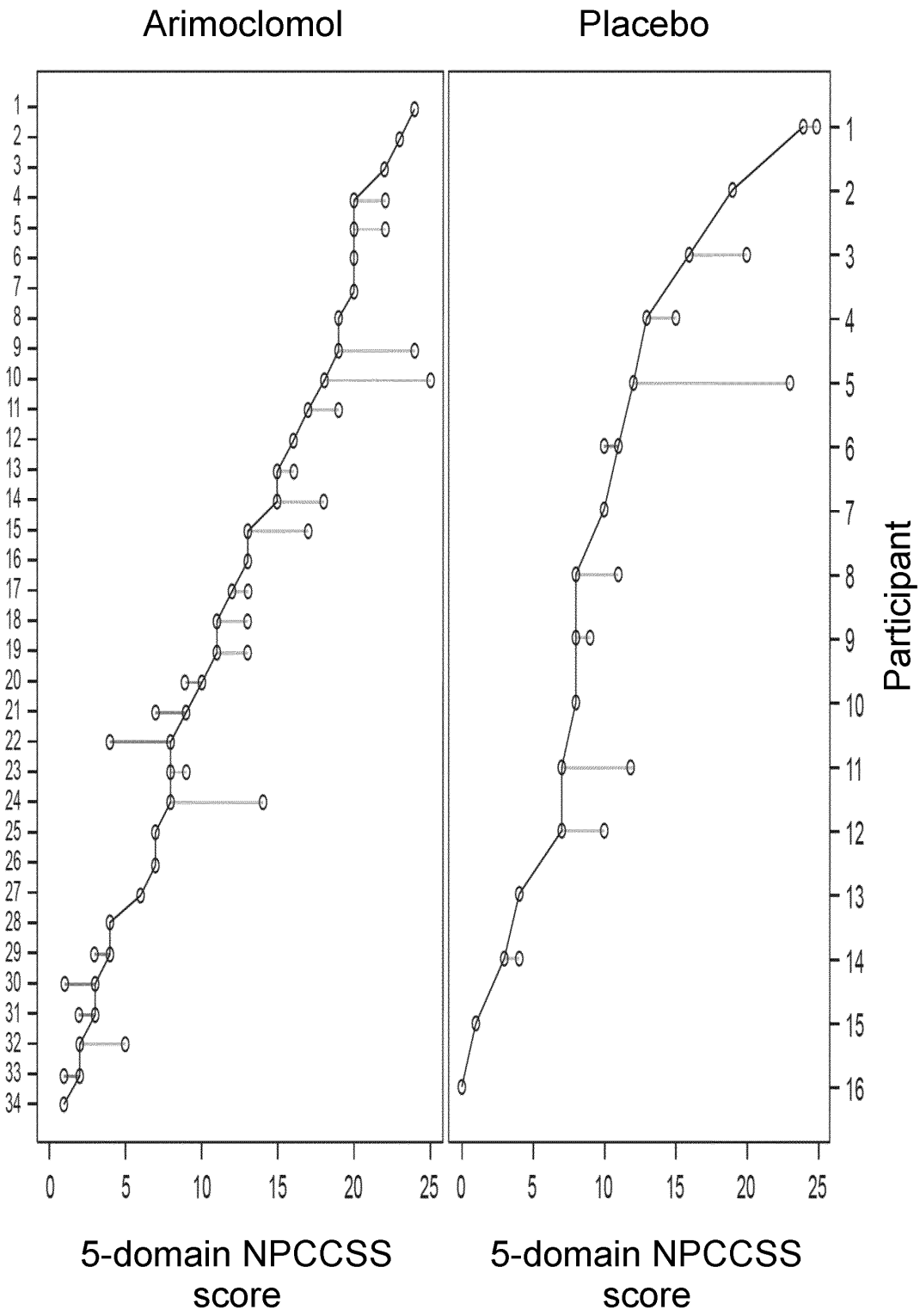

Arimoclomol
Placebo
Participant
5-domain NPCCSS score
5-domain NPCCSS score

Fig. 1E

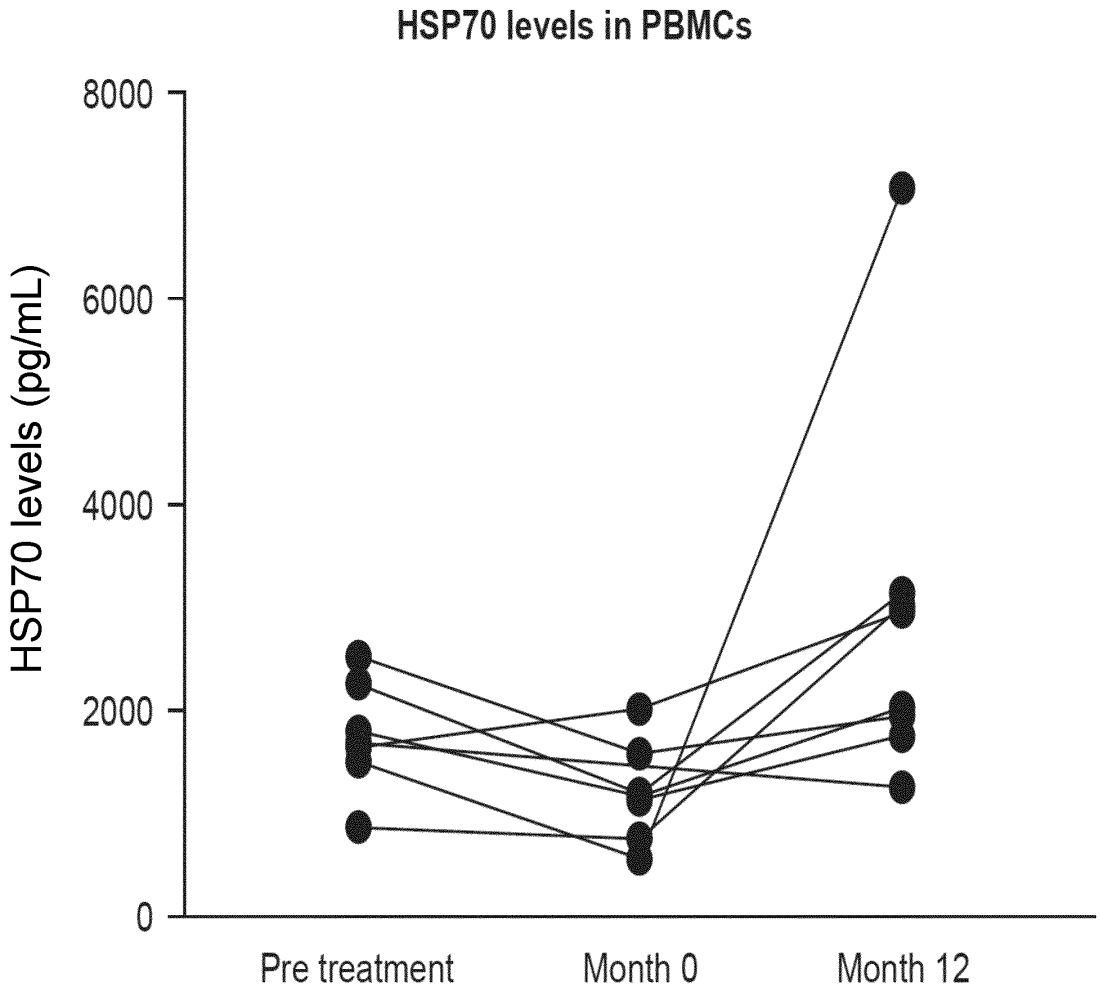

HSP70 levels in PBMCs
HSP70 levels (pg/mL)
8000
6000
4000
2000
0
Pre treatment
Month 0
Month 12

Fig. 2A

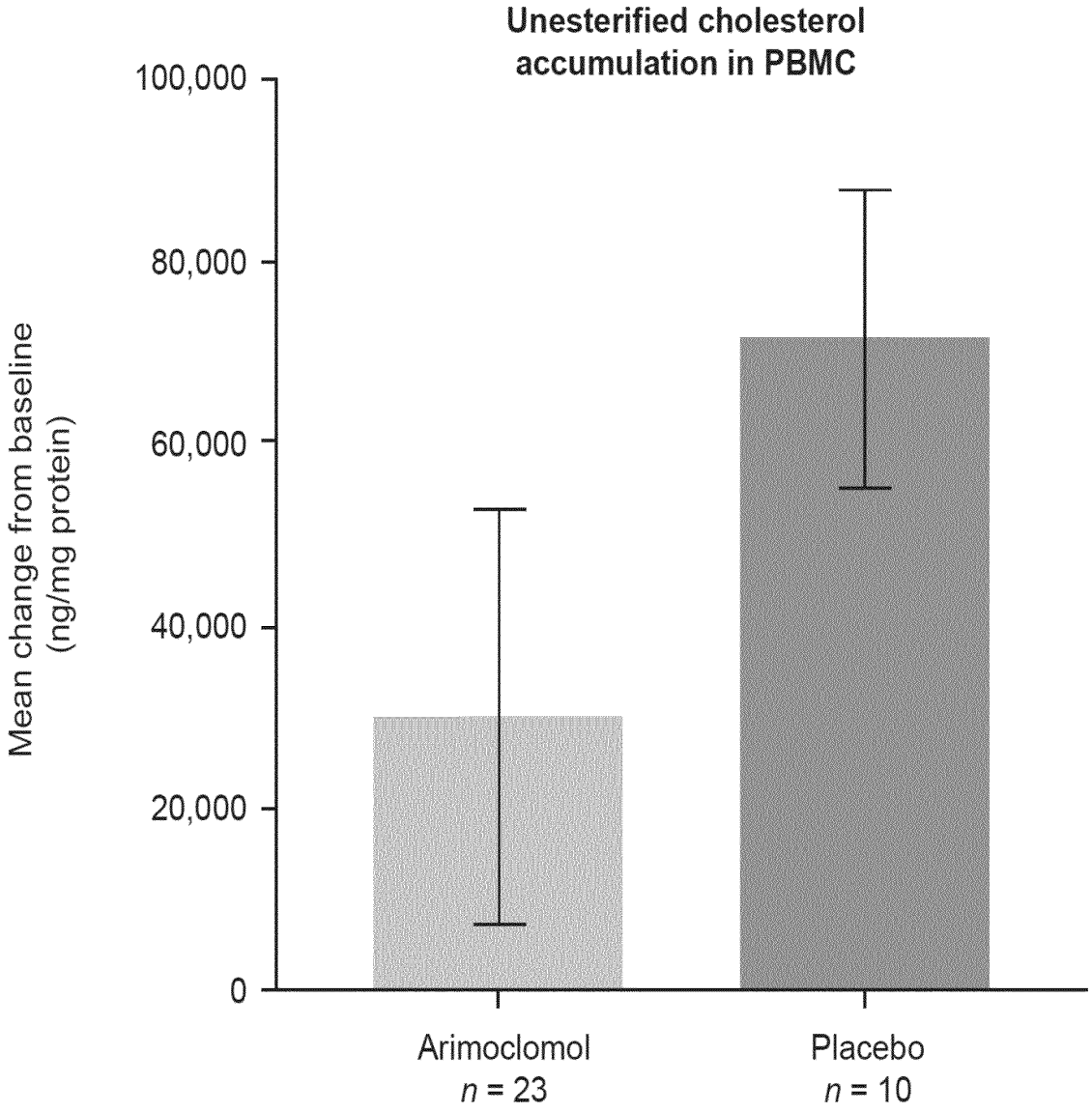

Unesterified cholesterol accumulation in PBMC
Mean change from baseline (ng/mg protein)
100,000
80,000
60,000
40,000
20,000
0
Arimoclomol
n = 23
Placebo
n = 10

Fig. 2B

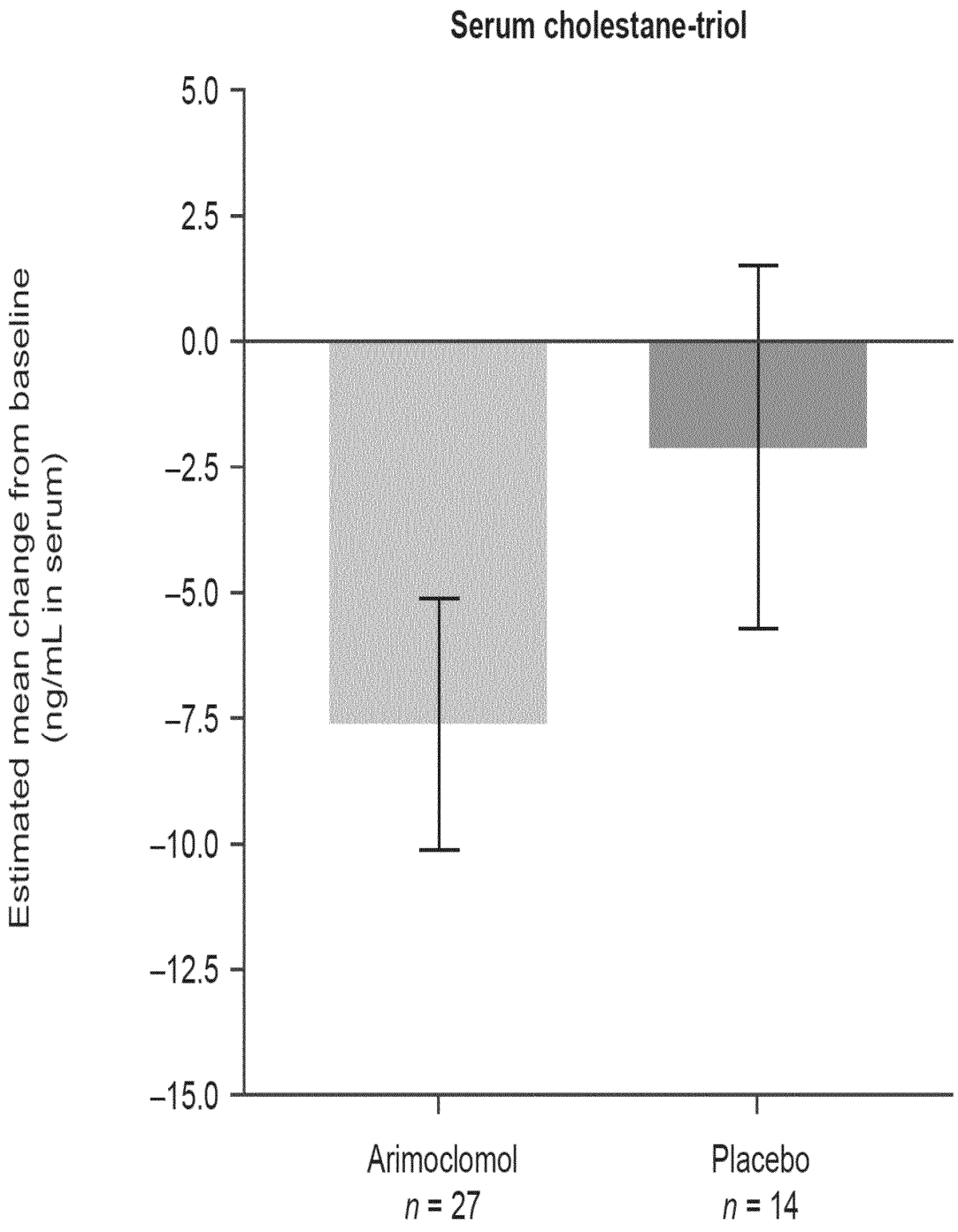

Serum cholestane-triol
Estimated mean change from baseline (ng/mL in serum)
5.0
2.5
0.0
−2.5
−5.0
−7.5
−10.0
−12.5
−15.0
Arimoclomol
n = 27
Placebo
n = 14

Fig. 2C

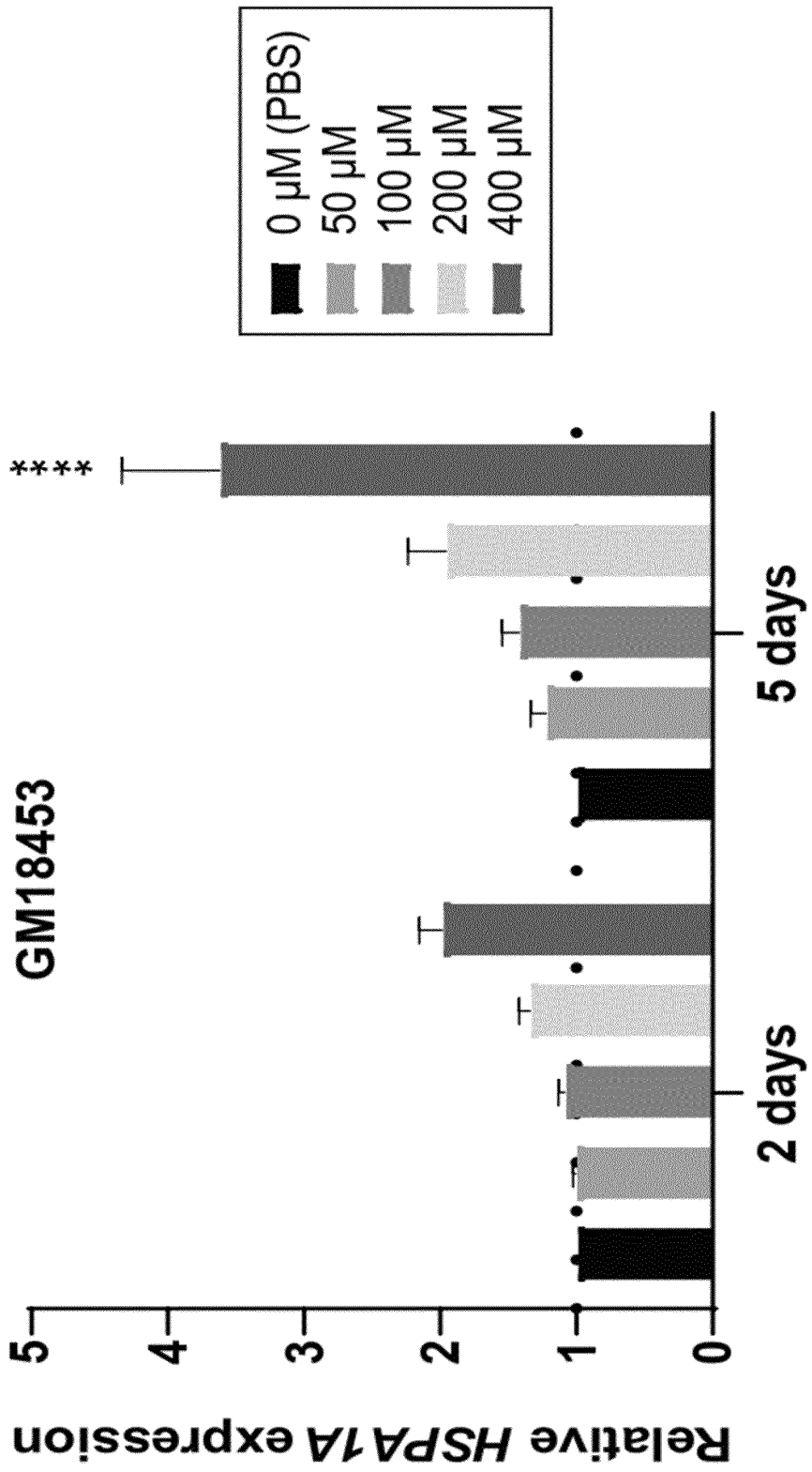

0 µM (PBS)
50 µM
100 µM
200 µM
400 µM
Relative HSPA1A expression
5
4
3
2
1
0
GM18453
****
2 days
5 days

Fig. 3

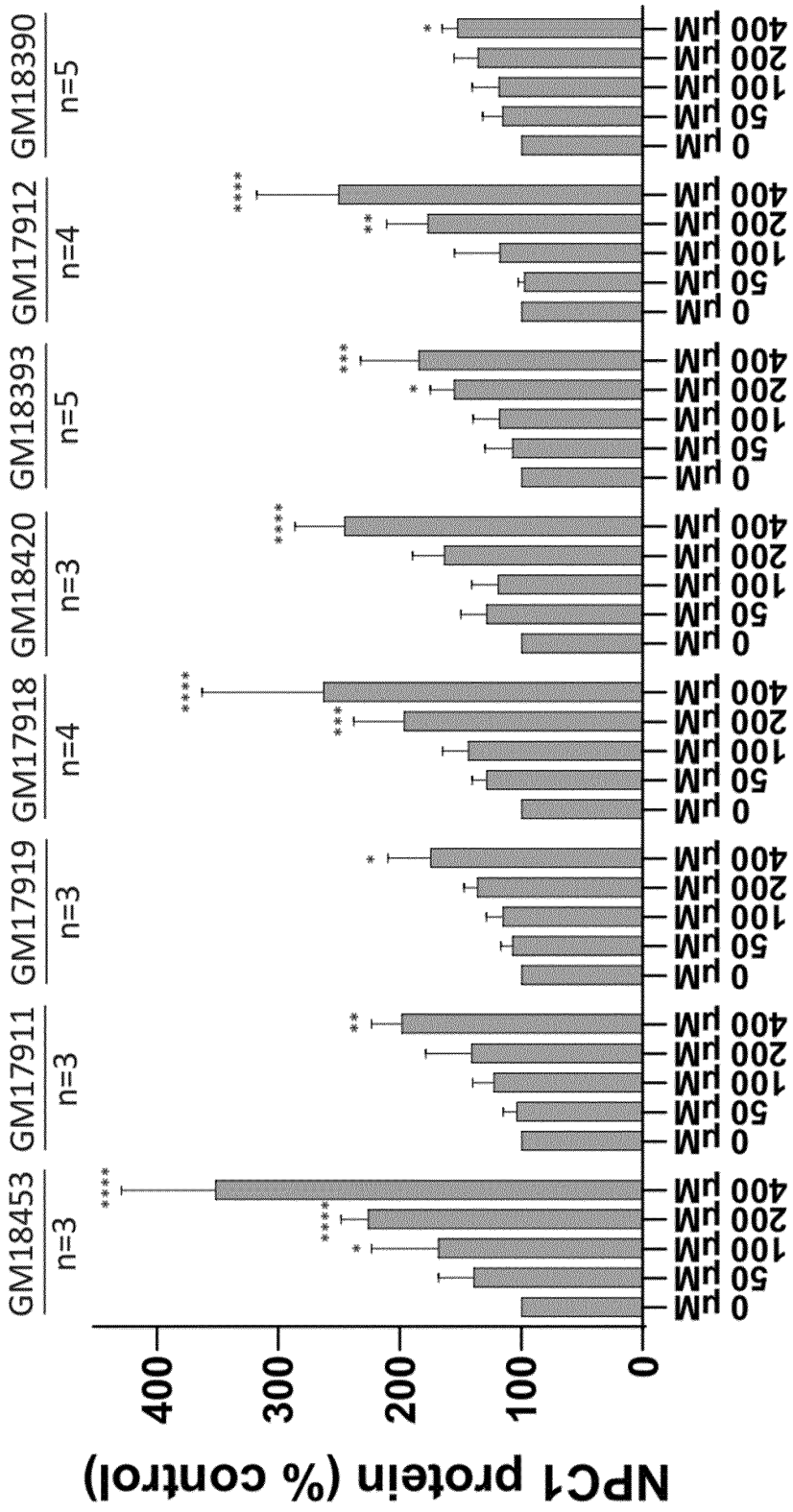

NPC1 protein (% control)
0
100
200
300
400
GM18453 n=3
GM17911 n=3
GM17919 n=3
GM17918 n=4
GM18420 n=3
GM18393 n=5
GM17912 n=4
GM18390 n=5
0 µM
50 µM
100 µM
200 µM
400 µM

Fig. 4

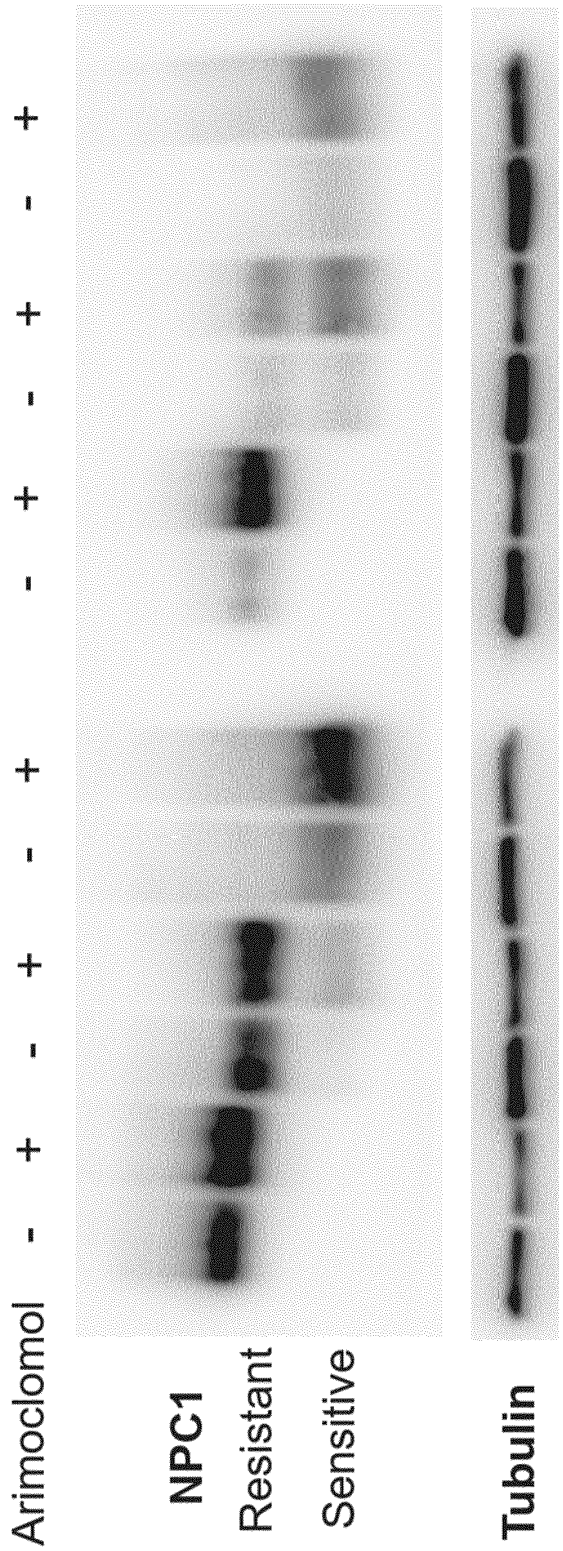

GM18420
GM18453
No digest
EndoH
PNGase
Arimoclomol
- + - + - +
- + - + - +
NPC1
Resistant
Sensitive
Tubulin

Fig. 5A

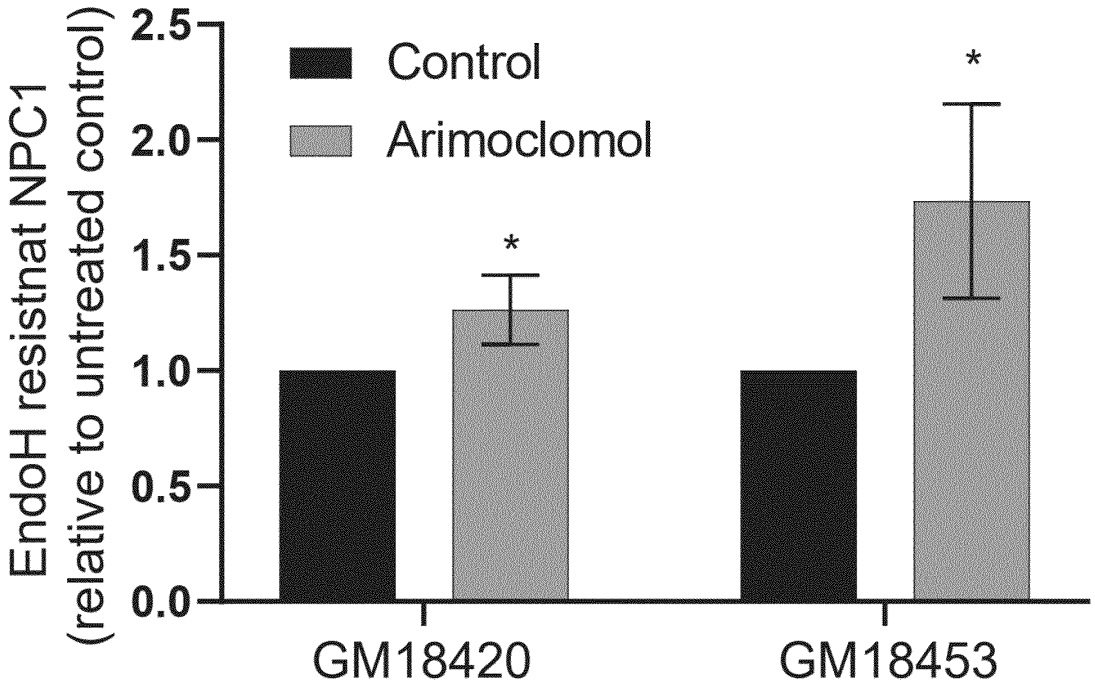

EndoH resistnat NPC1
(relative to untreated control)
2.5
2.0
1.5
1.0
0.5
0.0
Control
Arimoclomol
*
*
GM18420
GM18453

Fig. 5B