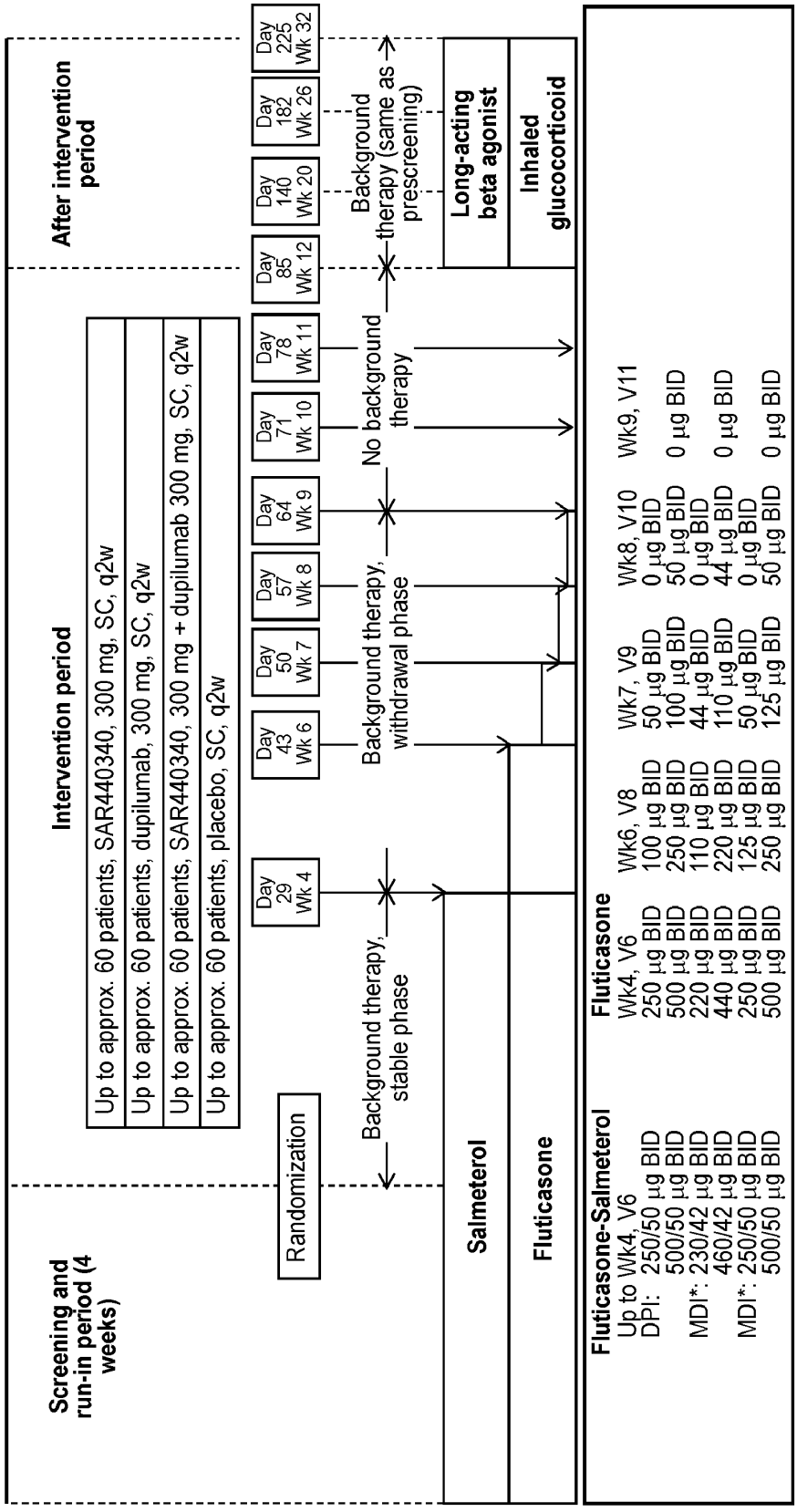

Screening and run-in period (4 weeks)
Randomization
Intervention period
Up to approx. 60 patients, SAR440340, 300 mg, SC, q2w
Up to approx. 60 patients, dupilumab, 300 mg, SC, q2w
Up to approx. 60 patients, SAR440340, 300 mg + dupilumab 300 mg, SC, q2w
Up to approx. 60 patients, placebo, SC, q2w
Day 29 Wk 4
Day 43 Wk 6
Day 50 Wk 7
Day 57 Wk 8
Day 64 Wk 9
Day 71 Wk 10
Day 78 Wk 11
Day 85 Wk 12
Day 140 Wk 20
Day 182 Wk 26
Day 225 Wk 32
Background therapy, stable phase
Background therapy, withdrawal phase
No background therapy
After intervention period
Background therapy (same as prescreening)
Long-acting beta agonist
Inhaled glucocorticoid
Salmeterol
Fluticasone
Fluticasone-Salmeterol
Up to Wk4, V6
DPI: 250/50 µg BID
500/50 µg BID
MDI*: 230/42 µg BID
460/42 µg BID
MDI*: 250/50 µg BID
500/50 µg BID
Fluticasone
Wk4, V6
250 µg BID
500 µg BID
220 µg BID
440 µg BID
250 µg BID
500 µg BID
Wk6, V8
100 µg BID
250 µg BID
110 µg BID
220 µg BID
125 µg BID
250 µg BID
Wk7, V9
50 µg BID
100 µg BID
44 µg BID
110 µg BID
50 µg BID
125 µg BID
Wk8, V10
0 µg BID
50 µg BID
0 µg BID
44 µg BID
0 µg BID
50 µg BID
Wk9, V11
0 µg BID
0 µg BID
0 µg BID

Fig. 1

Period	Screening (± 3 days)	Randomized IMP Treatment Period (± 3 days) Including the Following Background ICS/LABA Therapy Phases:													Post IMP Treatment Period (± 5 days)		
		ICS/LABA stabilization						ICS/LABA withdrawal[b,c]			No ICS/LABA[b]						
											No ICS/LABA[c]						
VISIT	V1	V2 Randomization/ Baseline	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14 EOT[d,e]	V15	V16[f]	V17 EOS
DAY[a]	D-28 to D0	D1	D8	D15	D22	D29	D36	D43	D50	D57	D64	D71	D78	D86	D141	D183	D225
WEEK	W-4 to W0	W0	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	W20	W26	W32
Hematology, biochemistry, urinalysis[n]	X	X				X				X				X	X		X
Hepatitis and HIV Serology tests[n]	X																
Quantiferon gold teating[o]	X																
Pregnancy (β-hCG blood) test[p]	X																
Pregnancy (urine) test[p]		X				X				X				X			X
Adverse event reporting, including SAEs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pharmacokinetics and Immunogenicity																	
Serum sample for SAR440340 concentration		X		X		X				X				X	X		X
Serum sample for dupilumab concentration		X		X		X				X				X	X		X
Anti-SAR440340 antibody and anti-dupilumab antibody		X												X			X
Biomarkers																	
Blood eosinophils and neutrophils	X	X		Xq		X		Xq		X				X	X		X
FeNOr	X	X		X		X				X				X	X		X
Total IL33 and sST2 (Serum)	X	X				X				X				X	X		X
Calcitonin	X	X				X				X				X	X		X
PARC	X	X				X				X				X			
Eotaxin-3	X	X				X								X			
Total IgE	X	X				X								X			
Periostin	X	X				X								X			
RNA sample (optional)	X	X				X								X			
Blood sample archival for exploratory research (optional)	X	X				X								X			
PGx analysis (optional)		X															

Fig. 2

Period	Screening (± 3 days)	Randomized IMP Treatment Period (± 3 days) Including the Following Background ICS/LABA Therapy Phases:													Post IMP Treatment Period (± 5 days)		
		ICS/LABA stabilization					ICS/LABA withdrawal[b,c]				No ICS/LABA[b] No ICS/LABA[c]						
VISIT	V1	V2 Random-ization/ Baseline	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14 EOT[d,e]	V15	V16[f]	V17 EOS
DAY[a]	D-28 to D0	D1	D8	D15	D22	D29	D36	D43	D50	D57	D64	D71	D78	D86	D141	D183	D225
WEEK	W-4 to W0	W0	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	W20	W26	W32
Hematology, biochemistry, urinalysis[n]	X	X				X				X				X	X		X
Hepatitis and HIV Serology tests[n]	X																
Quantiferon gold teating[o]	X																
Pregnancy (β-hCG blood) test[p]	X																
Pregnancy (urine) test[p]		X				X				X				X			X
Adverse event reporting, including SAEs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pharmacokinetics and Immunogenicity																	
Serum sample for SAR440340 concentration		X		X		X				X				X	X		X
Serum sample for dupilumab concentration		X		X		X				X				X	X		X
Anti-SAR440340 antibody and anti-dupilumab antibody		X												X			X
Biomarkers																	
Blood eosinophils and neutrophils	X	X		Xq		X		Xq		X				X	X		X
FeNOr	X	X		X		X				X				X	X		X
Total IL33 and sST2 (Serum)	X	X				X				X				X	X		X
Calcitonin	X	X				X				X				X	X		X
PARC	X	X				X				X				X			
Eotaxin-3	X	X				X				X				X			
Total IgE	X	X				X								X			
Periostin	X	X				X								X			
RNA sample (optional)	X	X				X								X			
Blood sample archival for exploratory research (optional)	X	X				X								X			
PGx analysis (optional)		X															

Fig. 2 (cont.)

SUBSTITUTE SHEET (RULE 26)

Period	Screening (± 3 days)	Randomized IMP Treatment Period (± 3 days) Including the Following Background ICS/LABA Therapy Phases:														Post IMP Treatment Period (± 5 days)		
		ICS/LABA stabilization						ICS/LABA withdrawal[b,c]			No ICS/LABA[b]							
											No ICS/LABA[c]							
VISIT	V1	V2 Randomization/ Baseline	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14 EOT[d,e]	V15	V16[f]	V17 EOS
DAY[a]	D-28 to D0	D1	D8	D15	D22	D29	D36	D43	D50	D57	D64	D71	D78	D86	D141	D183	D225
WEEK	W-4 to W0	W0	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	W20	W26	W32
Efficacy																	
LOAC event reporting			X	X	X	X	X	X	X	X	X		X	X			
Spirometry (FEV1) (pre-BD)[s]		X	X	X	X	X	X	X	X	X	X		X	X	X		X
Spirometry (FEV1) (post-BD)[s]		X				X		X		X				X	X		X
ACQ-5[t]	X	X		X		X		X		X				X	X		X
AQLQ(S)[t]		X		X		X		X		X				X	X		X
RQLQ (patients with history of allergic rhinitis only)[t]		X		X		X		X		X				X	X		X

Fig. 2 (cont.)

Endpoint	Category	Data	SG	PBO	SAR440340	SAR440340 + Dupi	Dupilumab
LOAC	LOAC-ITT	RR vs pbo	ITT		0.579 (0.348 to 0.966)	0.684 (0.434 to 1.077)	0.467 (0.272 to 0.802)
LOAC	LOAC-ITT	RRR% vs pbo	ITT		42.1	31.6	53.3
LOAC	LOAC-ITT	p-value vs pbo	ITT		0.0364	0.1011	0.0057
Pre-BD FEV1	FEV1-ITT	Mean Change (SD)	ITT	0.06 (0.35)	0.11 (0.34)	0.06 (0.37)	0.14 (0.43)
Pre-BD FEV1	FEV1-ITT	LS Mean (SE) vs pbo	ITT		0.14 (0.01 to 0.27)	0.10 (-0.03 to 0.23)	0.16 (0.03 to 0.29)
Pre-BD FEV1	FEV1-ITT	P-value vs. pbo	ITT		0.0344	0.1337	0.014
Post-BD FEV1	FEV1-ITT	Mean Change (SD)	ITT	-0.02 (0.27)	-0.00 (0.33)	0.06 (0.41)	0.09 (0.42)
Post-BD FEV1	FEV1-ITT	LS Mean (SE) vs pbo	ITT		0.05 (-0.07 to 0.17)	0.13 (0.01 to 0.25)	0.14 (0.02 to 0.26)
Post-BD FEV1	FEV1-ITT	P-value vs pbo	ITT		0.4085	0.0379	0.0178
PRO	ACQ	Mean Change (SD)	ITT	1.42 (0.95)	1.20 (0.83)	1.28 (0.93)	1.35 (0.93)
PRO	ACQ	LS Mean (SE) vs pbo	ITT		-0.42 (-0.73 to -0.12)	-0.32 (-0.63 to -0.01)	-0.46 (-0.76 to -0.15)
PRO	ACQ	P-value vs pbo	ITT		0.0066	0.0425	0.0034
PRO	AQLQ	Mean Change (SD)	ITT	0.58 (1.02)	0.90 (1.04)	0.68 (0.86)	0.70 (0.87)
PRO	AQLQ	LS Mean (SE) vs pbo	ITT		0.45 (0.14 to 0.77)	0.43 (0.11 to 0.75)	0.42 (0.11 to 0.74)
PRO	AQLQ	P-value vs. pbo	ITT		0.0048	0.0078	0.009

Fig. 3

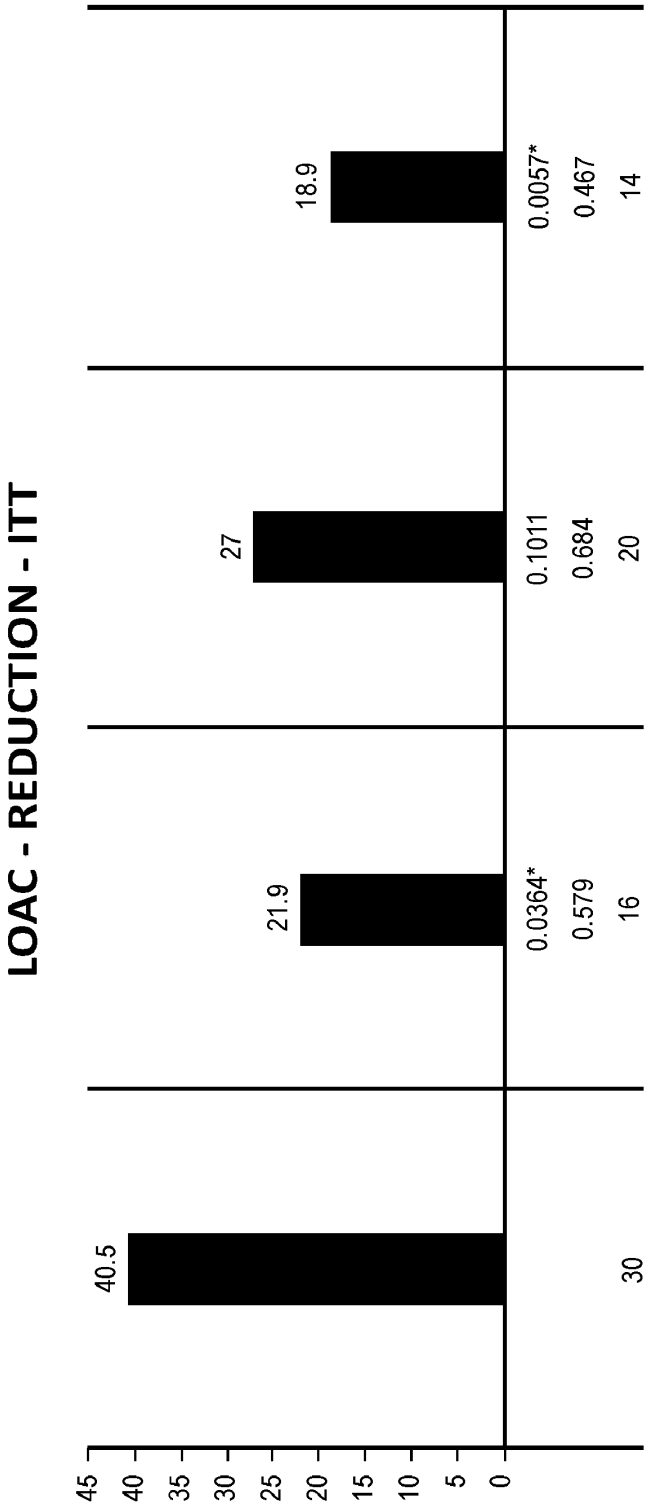

LOAC - REDUCTION - ITT
45
40
35
30
25
20
15
10
5
0
40.5
30
21.9
0.0364*
0.579
16
27
0.1011
0.684
20
18.9
0.0057*
0.467
14

Fig. 4

10 **Summary of LOAC events - mITT**

	Placebo (N=74)	SAR440340 300mg q2w (N=73)	SAR440340 q2w + Dupilumab q2w (N=74)	Dupilumab 300mg q2w (N=74)
Number of patients with LOAC				
Number	74	73	74	74
No	44(59.5)	57(78.1)	54(73.0)	60(81.1)
Yes	30(40.5)	16(21.9)	20(27.0)	14(18.9)
With rescue medication[a]	13(17.6)	6(8.2)	11(14.9)	5(6.8)
Without rescue medication[b]	17(23.0)	10(13.7)	9(12.2)	9(12.2)
Number of patients with >30% reduction from baseline in AM PEF on 2 consecutive days	22(29.7)	12(16.4)	14(18.9)	11(14.9)
Number of patients with >6 additional reliever puffs of salbutamol/albuterol or levosalbutamol/levalbuterol in a 24 hour period (compared with baseline) on 2 consecutive days	7(9.5)	3(4.1)	9(12.2)	3(4.1)
Number of patients with increase in ICS ≥4 times the last prescribed ICS dose (or ≥50% of the prescribed ICS dose at baseline if background therapy withdrawal completed)	1.(1.4)	0	0	0
Number of patients requiring use of systemic (oral and/or parenteral) steriod treatment	7(9.5)	3(4.1)	3(4.1)	3(4.1)
Number of patients requiring hospitalization or emergency room visit	0	1(1.4)	0	0

LOAC: Loss of asthma control, PEF: Peak expiratory flow, ICS: Inhaled corticosteroid

Fig. 5

SUBSTITUTE SHEET (RULE 26)

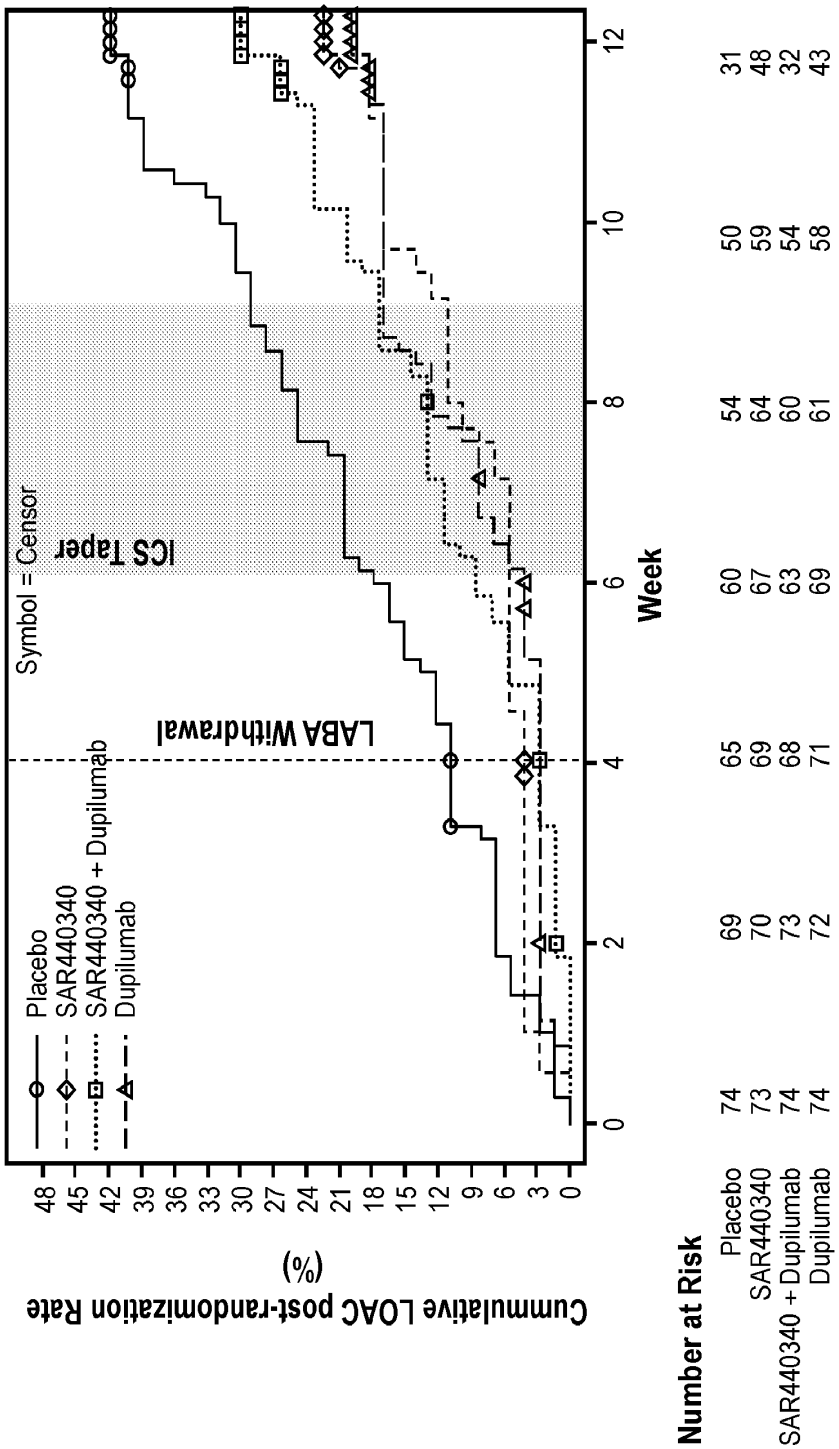

Cummulative LOAC post-randomization Rate
(%)
0
3
6
9
12
15
18
21
24
27
30
33
36
39
42
45
48
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Symbol = Censor
ICS Taper
LABA Withdrawal
0
2
4
6
8
10
12
Week
Number at Risk
Placebo 74 69 65 60 54 50 31
SAR440340 73 70 69 67 64 59 48
SAR440340 + Dupilumab 74 73 68 63 60 54 32
Dupilumab 74 72 71 69 61 58 43

Fig. 6

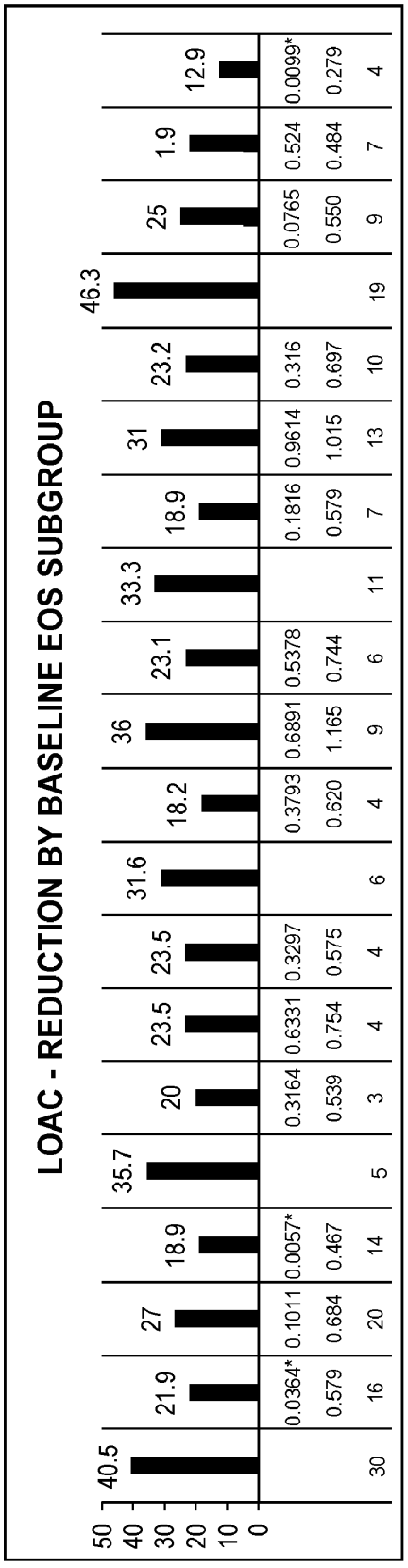

LOAC - REDUCTION BY BASELINE EOS SUBGROUP
50
40
30
20
10
0
40.5
21.9
27
18.9
35.7
20
23.5
23.5
31.6
18.2
36
23.1
33.3
18.9
31
23.2
46.3
25
1.9
12.9
0.0364*
0.579
16
0.1011
0.684
20
0.0057*
0.467
14
0.3164
0.539
3
0.6331
0.754
4
0.3297
0.575
4
0.3793
0.620
4
0.6891
1.165
9
0.5378
0.744
6
0.1816
0.579
7
0.9614
1.015
13
0.316
0.697
10
0.0765
0.550
9
0.524
0.484
7
0.0099*
0.279
4
30
5
6
11
19

Fig. 7A

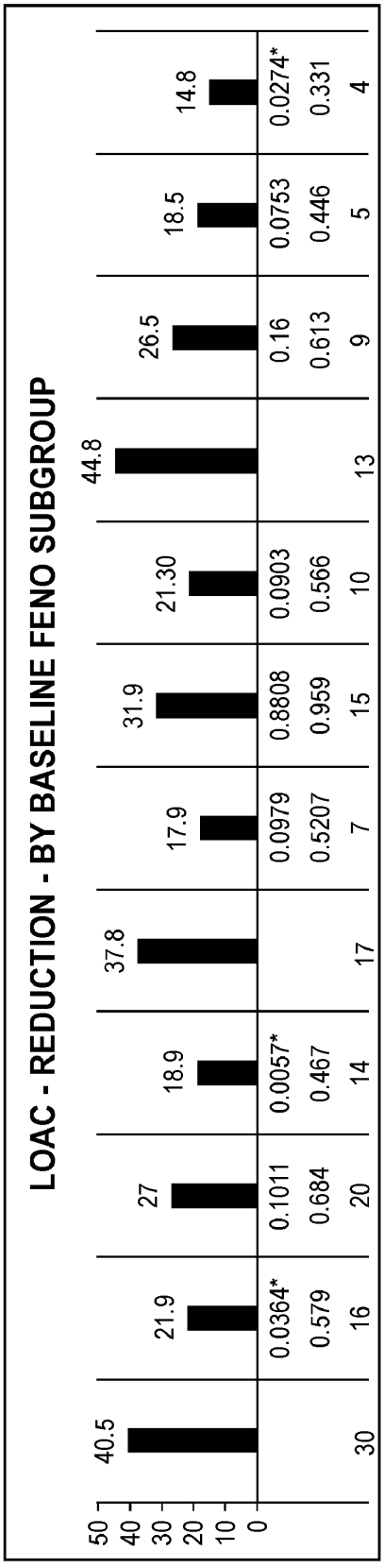

LOAC - REDUCTION - BY BASELINE FENO SUBGROUP
50
40
30
20
10
0
40.5
21.9
27
18.9
37.8
17.9
31.9
21.30
44.8
26.5
18.5
14.8
0.0364*
0.579
16
0.1011
0.684
20
0.0057*
0.467
14
0.0979
0.5207
7
0.8808
0.959
15
0.0903
0.566
10
0.16
0.613
9
0.0753
0.446
5
0.0274*
0.331
4
30
17
13

Fig. 7B

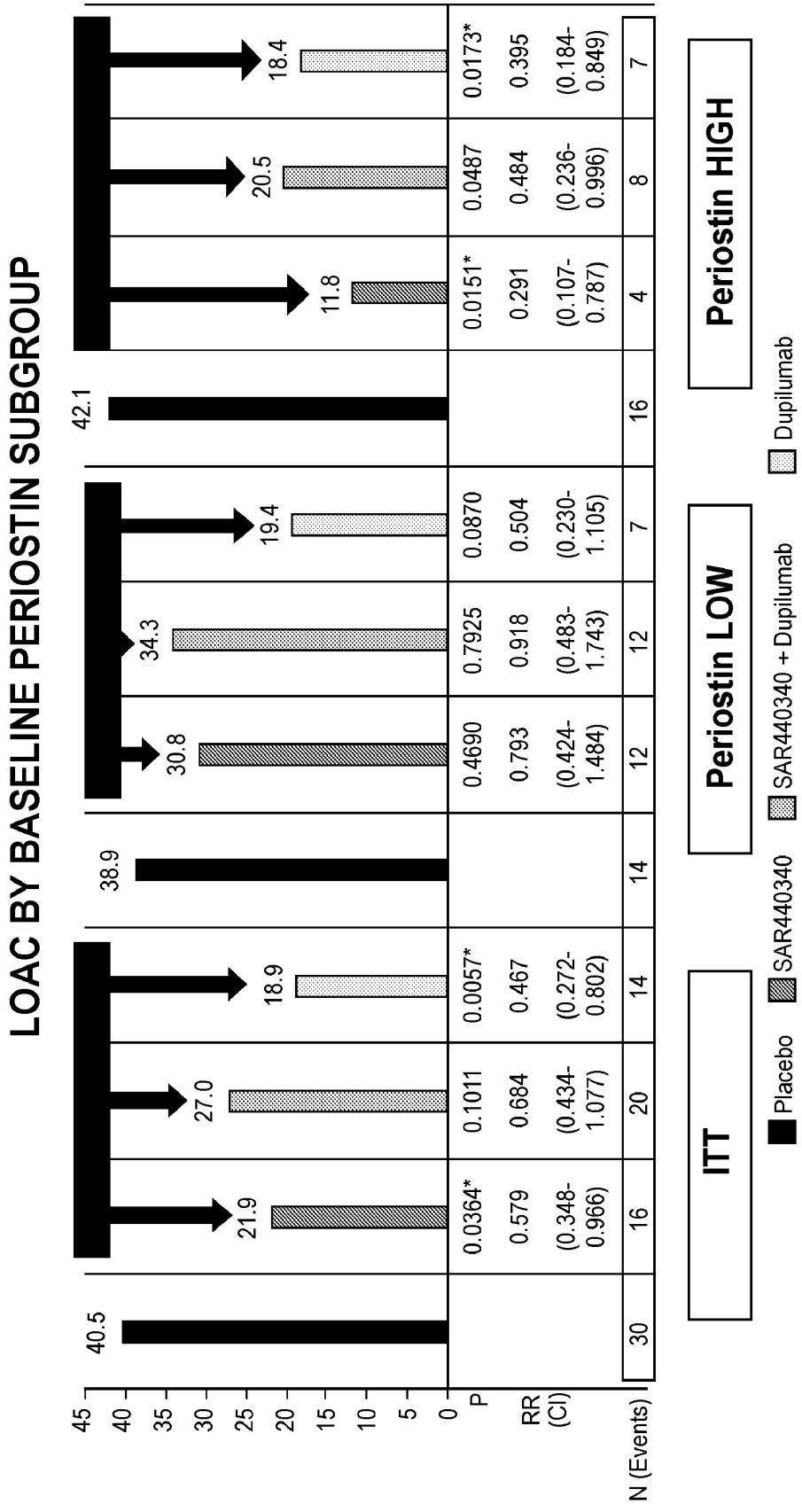

LOAC BY BASELINE PERIOSTIN SUBGROUP
45
40
35
30
25
20
15
10
5
0
40.5
21.9
27.0
18.9
38.9
30.8
34.3
19.4
42.1
11.8
20.5
18.4
P
RR (CI)
N (Events)
30
16
20
14
14
12
12
7
16
4
8
7
0.0364*
0.579
(0.348-0.966)
0.1011
0.684
(0.434-1.077)
0.0057*
0.467
(0.272-0.802)
0.4690
0.793
(0.424-1.484)
0.7925
0.918
(0.483-1.743)
0.0870
0.504
(0.230-1.105)
0.0151*
0.291
(0.107-0.787)
0.0487
0.484
(0.236-0.996)
0.0173*
0.395
(0.184-0.849)
ITT
Periostin LOW
Periostin HIGH
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 7C

Fig. 8A

Fig. 8B

Fig. 8C

Fig. 8D

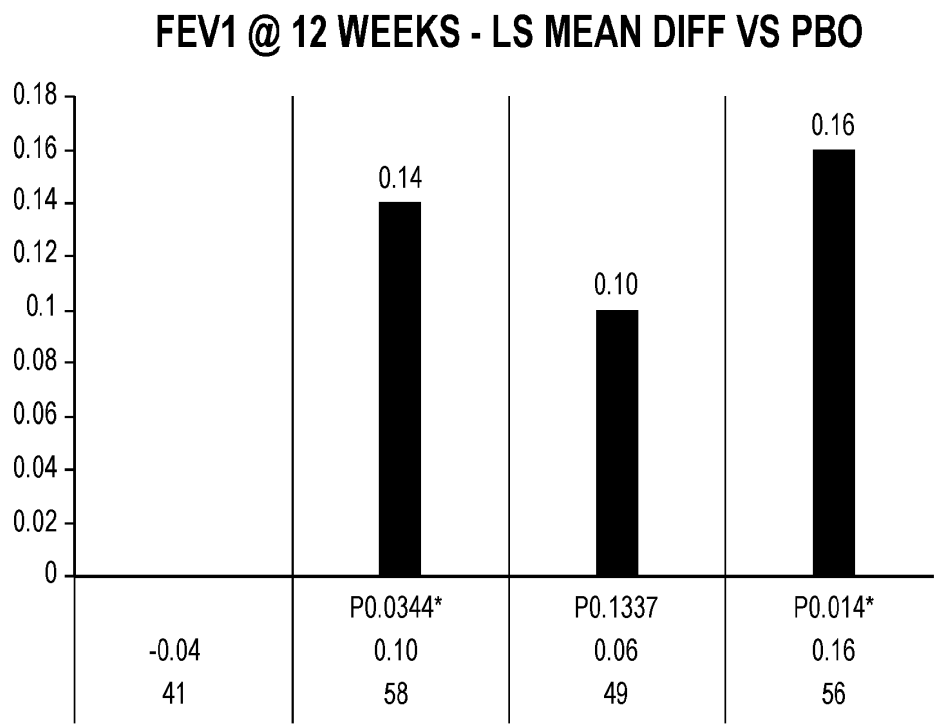

FEV1 @ 12 WEEKS - LS MEAN DIFF VS PBO
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0.14
0.10
0.16
P0.0344*
P0.1337
P0.014*
-0.04
0.10
0.06
0.16
41
58
49
56

Fig. 9A

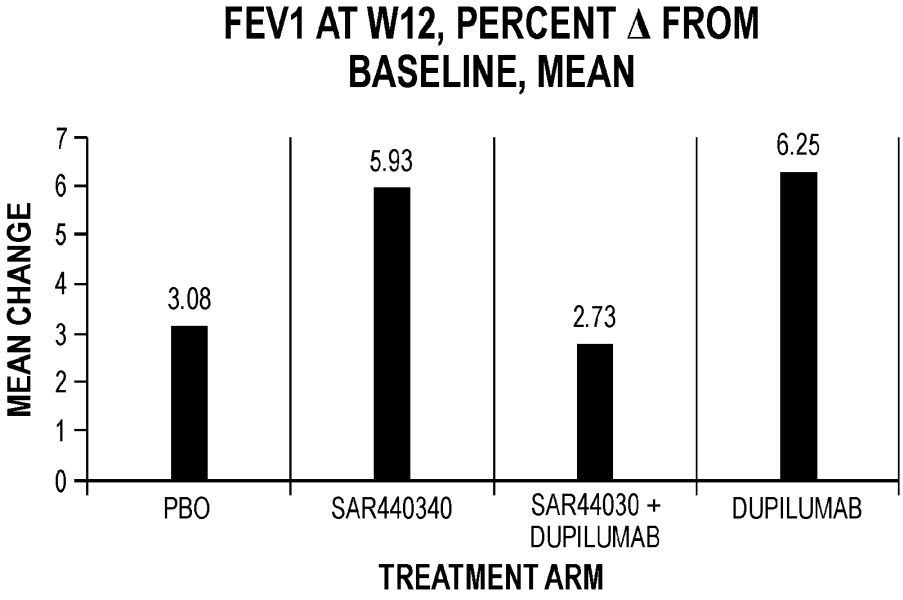

FEV1 AT W12, PERCENT Δ FROM BASELINE, MEAN
MEAN CHANGE
7
6
5
4
3
2
1
0
3.08
5.93
2.73
6.25
PBO
SAR440340
SAR44030 + DUPILUMAB
DUPILUMAB
TREATMENT ARM

Fig. 9B

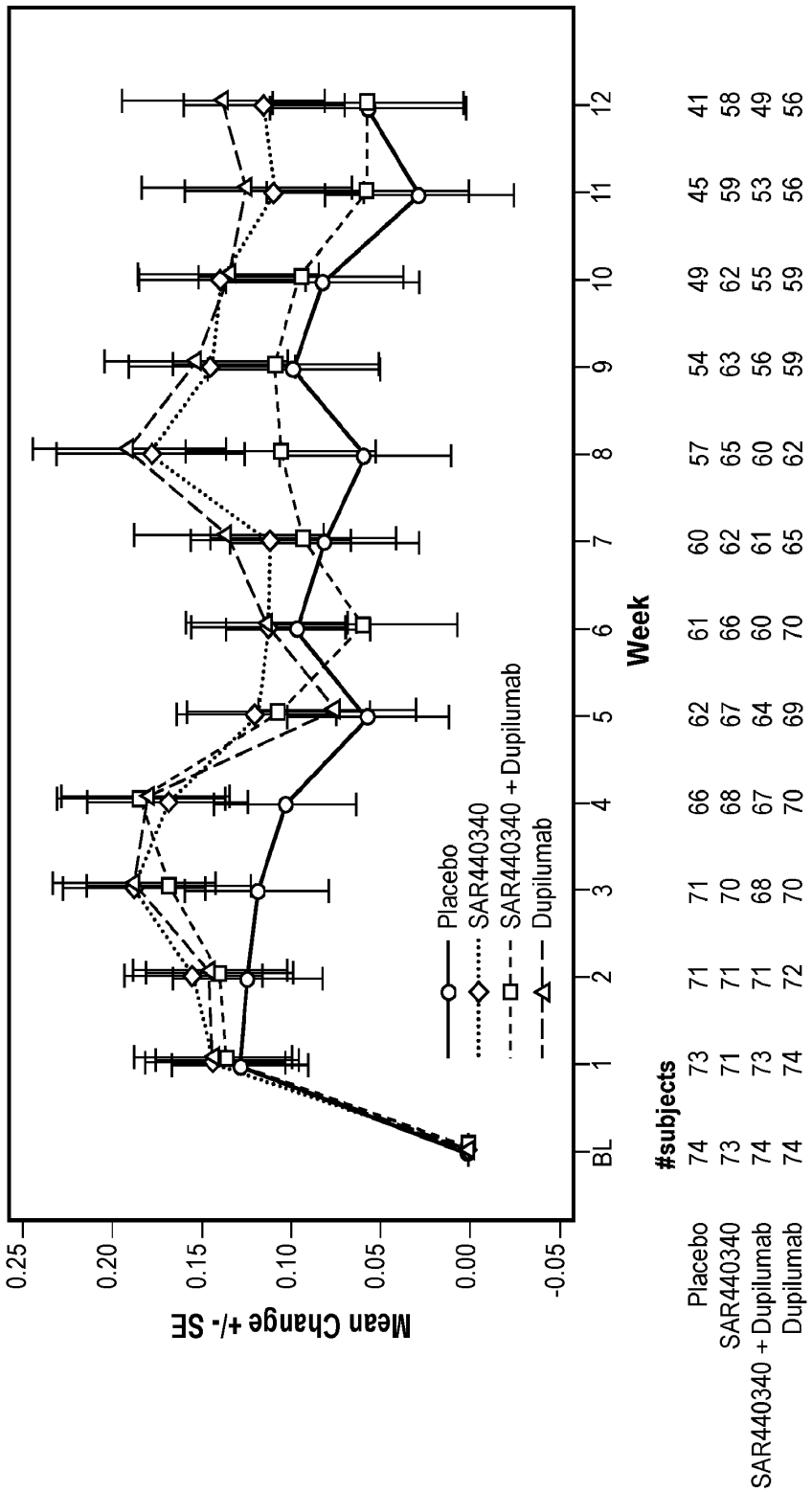

Mean Change +/- SE
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
BL
1
2
3
4
5
6
7
8
9
10
11
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
#subjects
Placebo 74 73 71 71 66 62 61 60 57 54 49 45 41
SAR440340 73 71 71 70 68 67 64 62 60 56 55 53 49
SAR440340 + Dupilumab 74 73 71 68 67 64 60 61 60 56 55 53 49
Dupilumab 74 74 72 70 70 69 70 65 62 59 59 56 56

Fig. 10

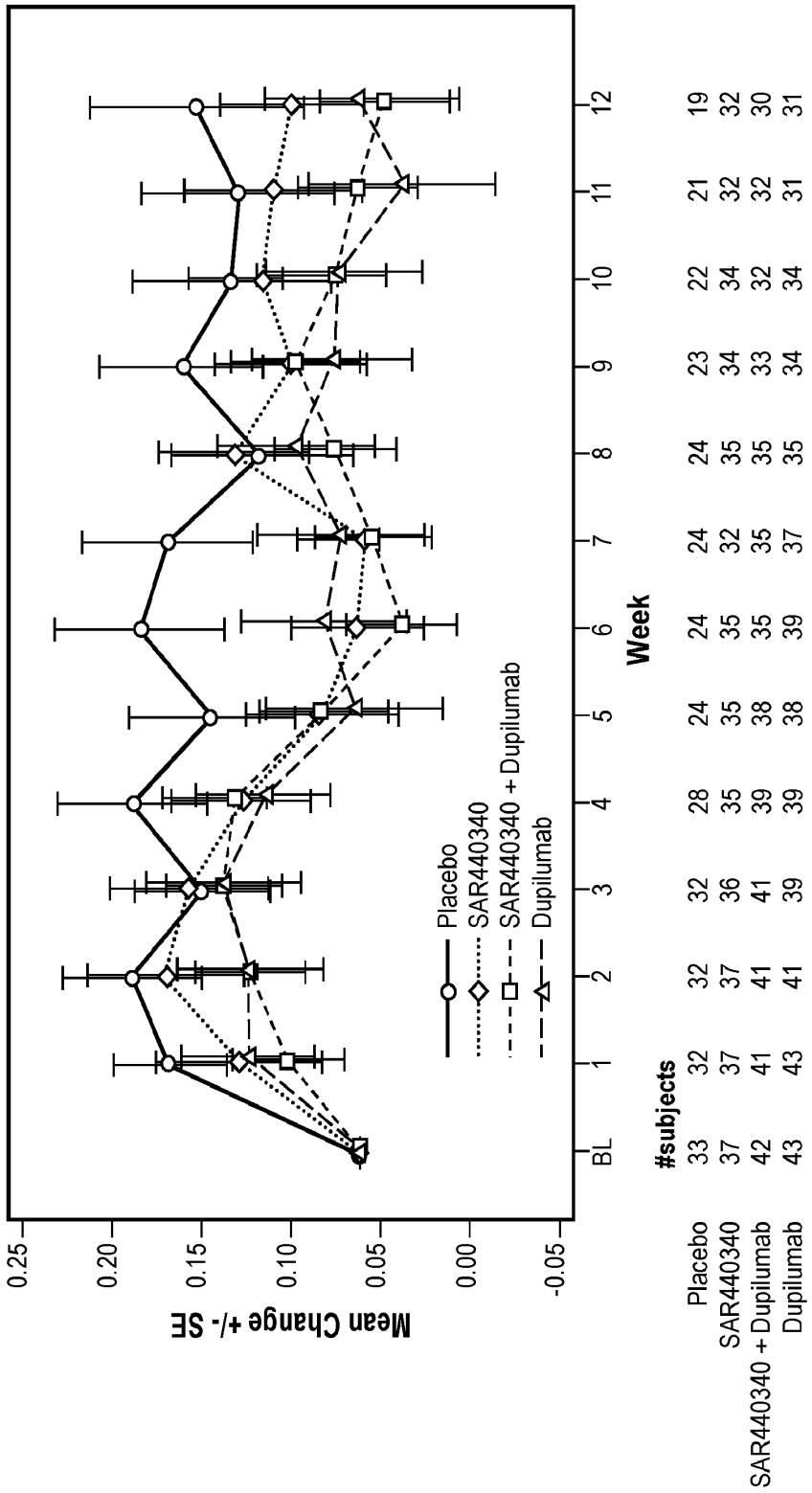

Mean Change +/- SE
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
BL
1
2
3
4
5
6
7
8
9
10
11
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
#subjects
Placebo 33 32 32 32 28 24 24 24 24 23 22 21 19
SAR440340 37 37 37 36 35 35 35 32 35 34 34 32 32
SAR440340 + Dupilumab 42 41 41 41 39 38 35 35 35 33 32 32 30
Dupilumab 43 43 41 39 39 38 39 37 35 34 34 31 31

Fig. 11

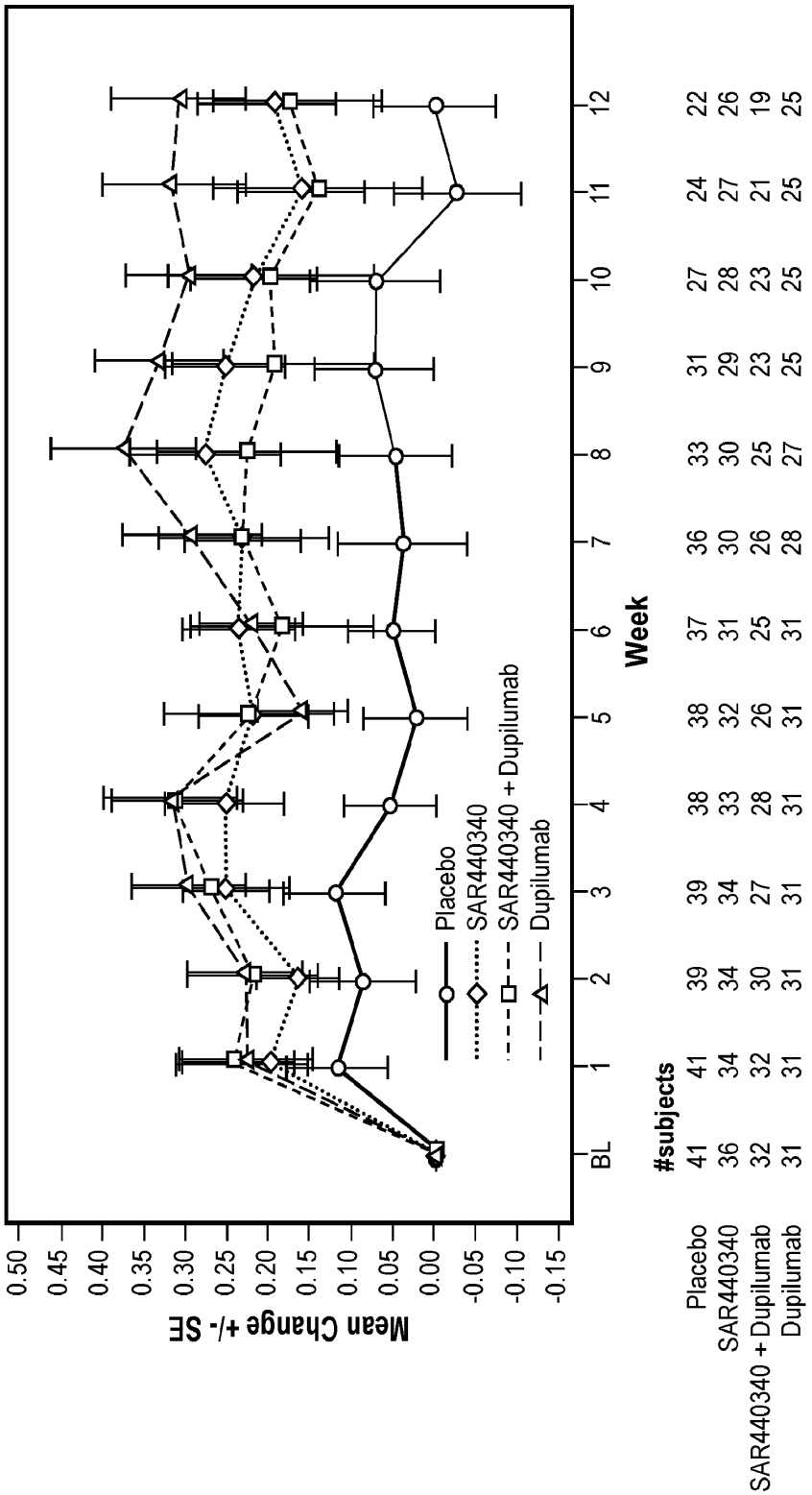

Mean Change +/- SE
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Week
BL 1 2 3 4 5 6 7 8 9 10 11 12
#subjects
Placebo 41 41 39 39 38 38 37 36 33 31 27 24 22
SAR440340 36 34 34 34 33 32 31 30 30 29 28 27 26
SAR440340 + Dupilumab 32 32 30 27 28 26 25 26 25 23 23 21 19
Dupilumab 31 31 31 31 31 31 31 28 27 25 25 25 25

Fig. 12

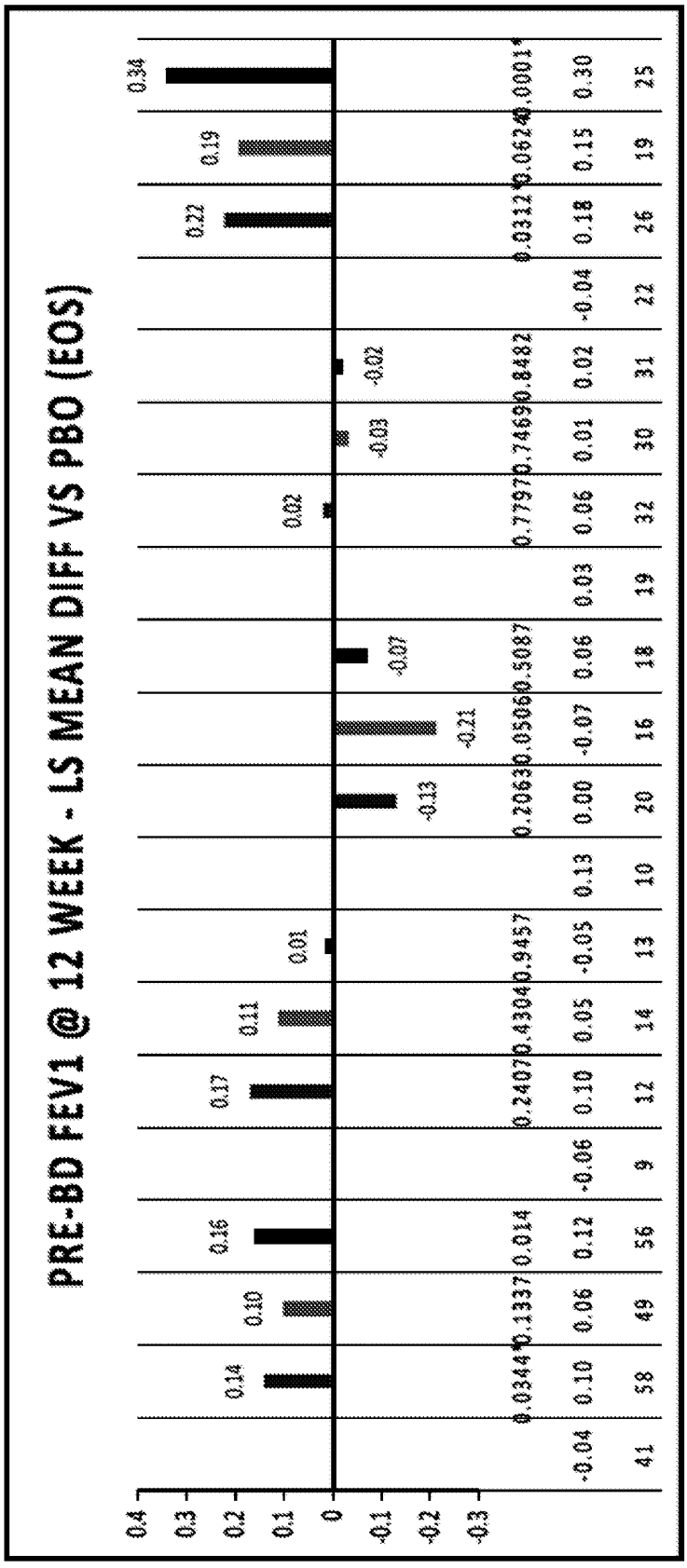

PRE-BD FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (EOS)
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
0.14
0.10
0.16
0.17
0.11
0.01
0.02
-0.03
-0.02
0.22
0.19
0.34
-0.07
-0.13
-0.21
0.0344
0.1337
0.014
0.2407
0.4304
0.9457
0.2063
0.0506
0.5087
0.7797
0.7469
0.8482
0.0312
0.0624
0.00011
-0.04
0.10
0.06
0.12
-0.06
0.10
0.05
-0.05
0.13
0.00
-0.07
0.06
0.03
0.06
0.01
0.02
-0.04
0.18
0.15
0.30
41
58
49
56
9
12
14
13
10
20
16
18
19
32
30
31
22
26
19
25

Fig. 13

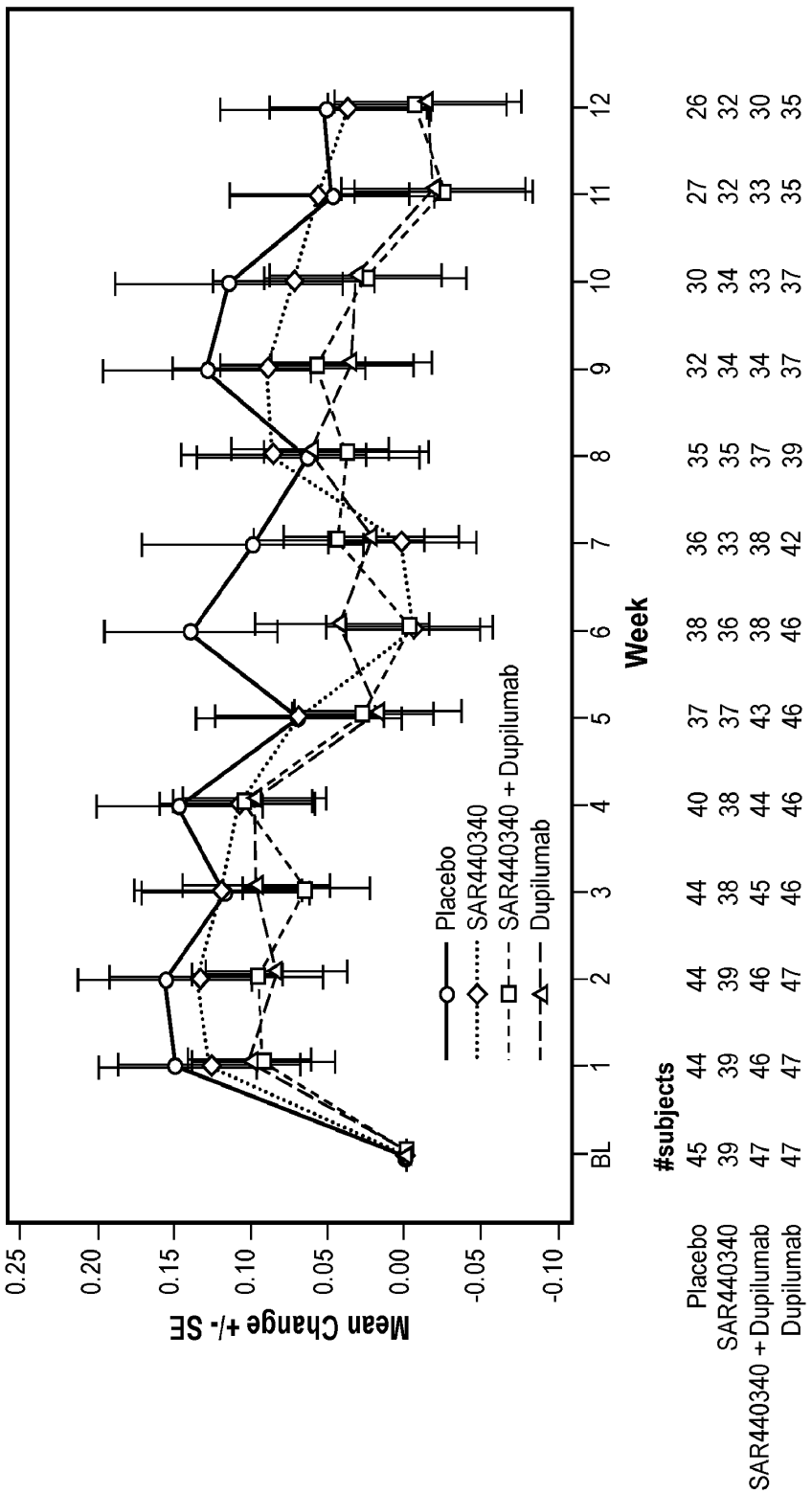

Mean Change +/- SE
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
BL
1
2
3
4
5
6
7
8
9
10
11
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
#subjects
Placebo 45 44 44 44 40 37 38 36 35 32 30 27 26
SAR440340 39 39 39 38 38 37 36 33 35 34 34 32 32
SAR440340 + Dupilumab 47 46 46 45 44 43 38 38 37 34 33 33 30
Dupilumab 47 47 47 46 46 46 46 42 39 37 37 35 35

Fig. 14

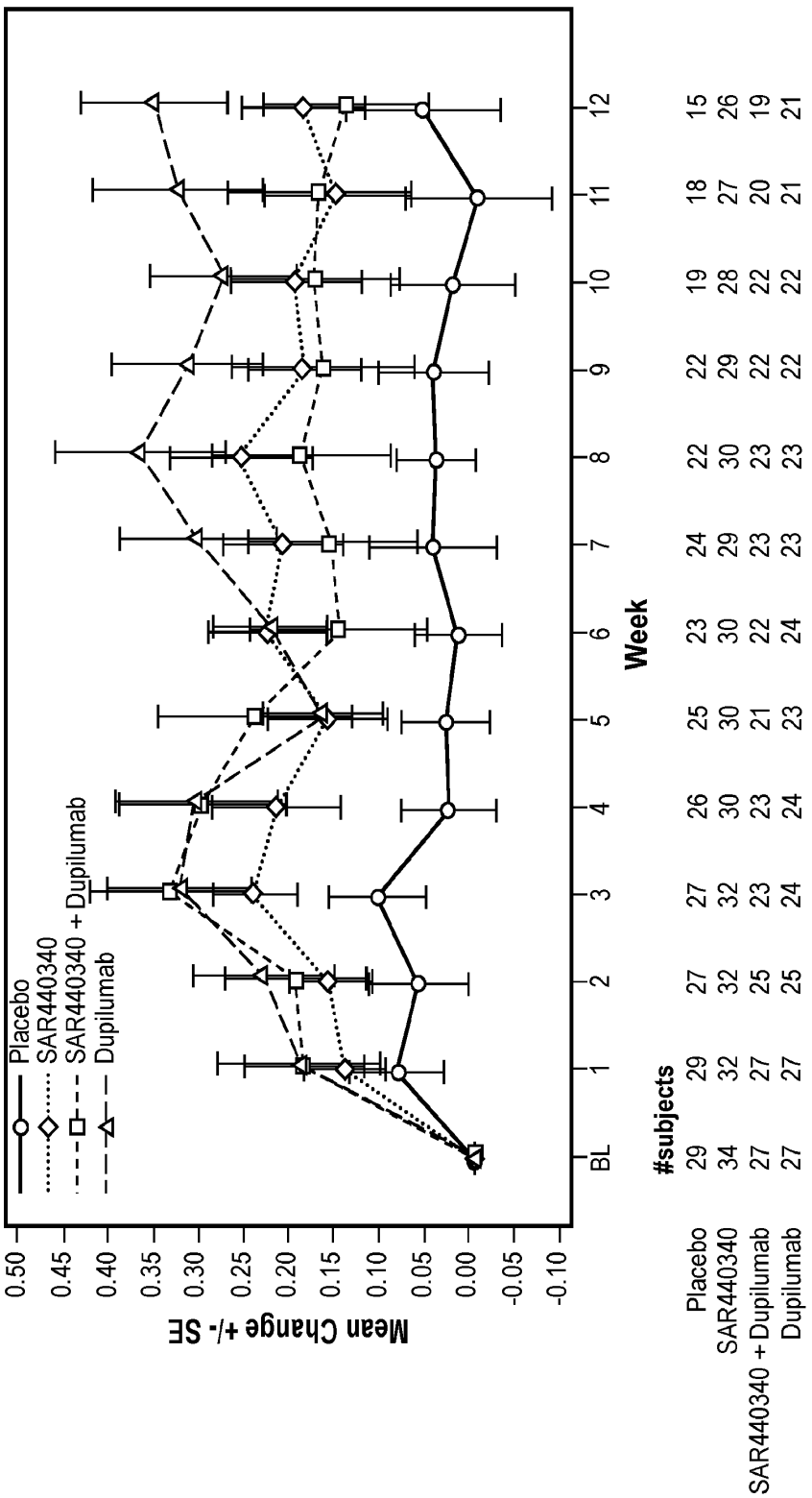

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
BL
1
2
3
4
5
6
7
8
9
10
11
12
Week
#subjects
Placebo 29 29 27 27 26 25 23 24 22 22 19 18 15
SAR440340 34 32 32 32 30 30 30 29 30 29 28 27 26
SAR440340 + Dupilumab 27 27 25 23 23 21 22 23 23 22 22 20 19
Dupilumab 27 27 25 24 24 23 24 23 23 22 22 21 21

Fig. 15

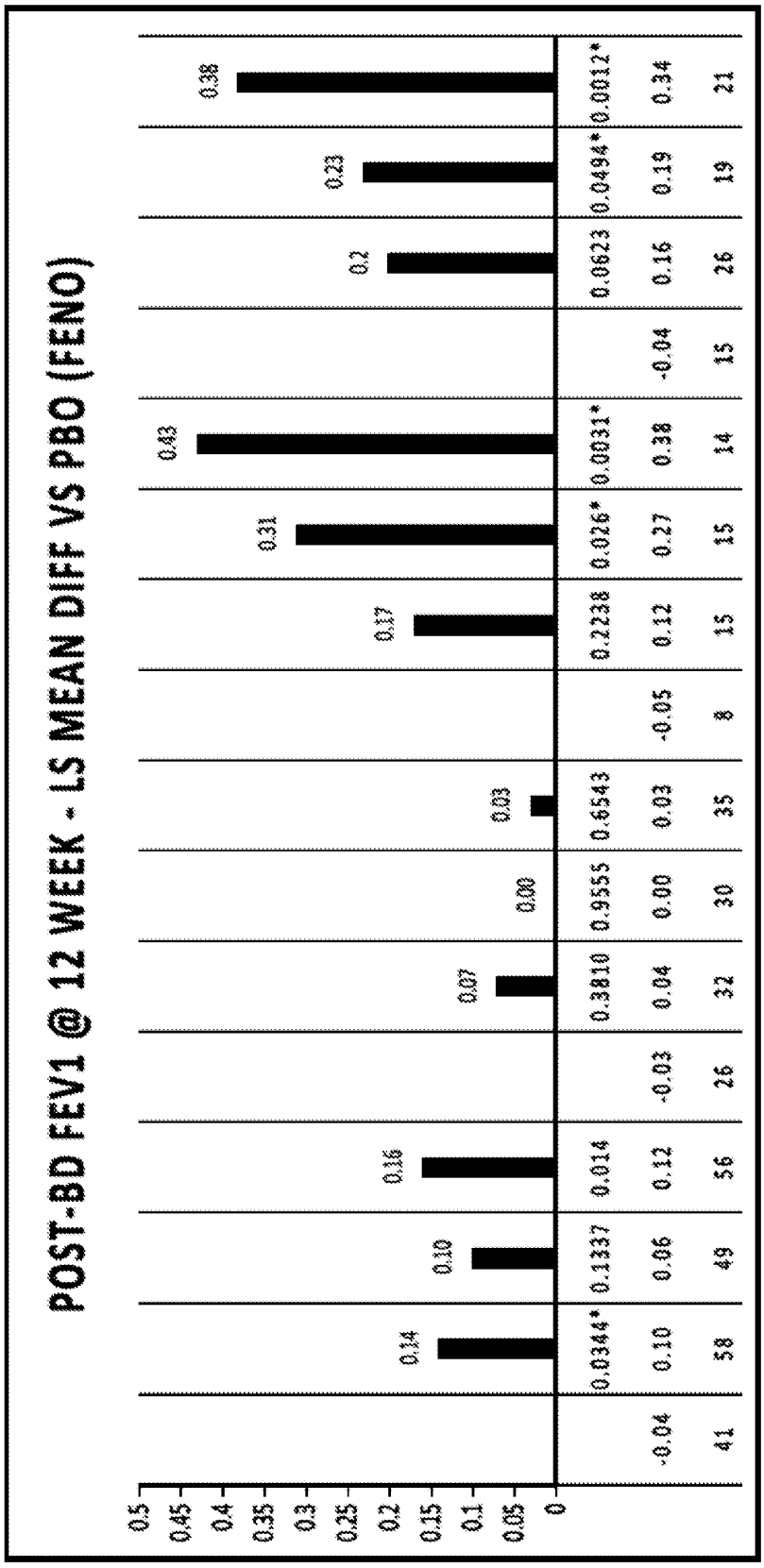

POST-BD FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (FENO)
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0.14
0.10
0.16
0.07
0.00
0.03
0.17
0.31
0.43
0.2
0.23
0.38
-0.04 0.0344* 0.1337 0.014 0.3810 0.9555 0.6543 0.2238 0.026* 0.0031* 0.0623 0.0494* 0.0012*
41 58 49 56 26 32 30 35 8 15 15 14 26 19 21
-0.04 0.10 0.06 0.12 -0.03 0.04 0.00 0.03 -0.05 0.12 0.27 0.38 0.16 0.19 0.34
-0.04 0.10 0.06 0.12 -0.03 0.04 0.00 0.03 -0.05 0.12 0.27 0.38 0.16 0.19 0.34

Fig. 16

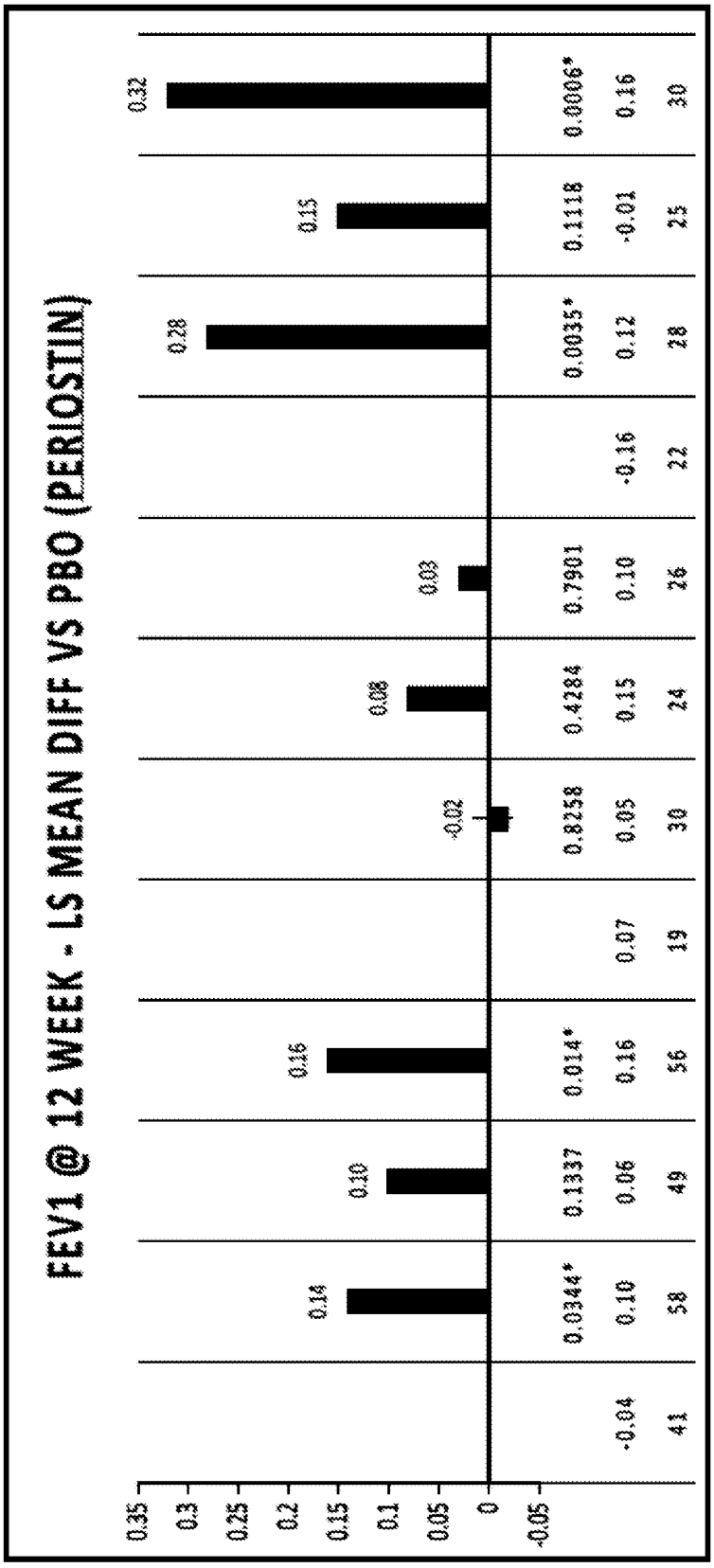

FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (PERIOSTIN)
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
-0.05
-0.04
0.14
0.10
0.16
-0.02
0.08
0.03
0.28
0.15
0.32
41
58
49
56
19
30
24
26
22
28
25
30
0.0344*
0.1337
0.014*
0.07
0.8258
0.4284
0.7901
0.0035*
0.1118
0.0006*
0.10
0.06
0.16
0.05
0.15
0.10
-0.16
0.12
-0.01
0.16

Fig. 17

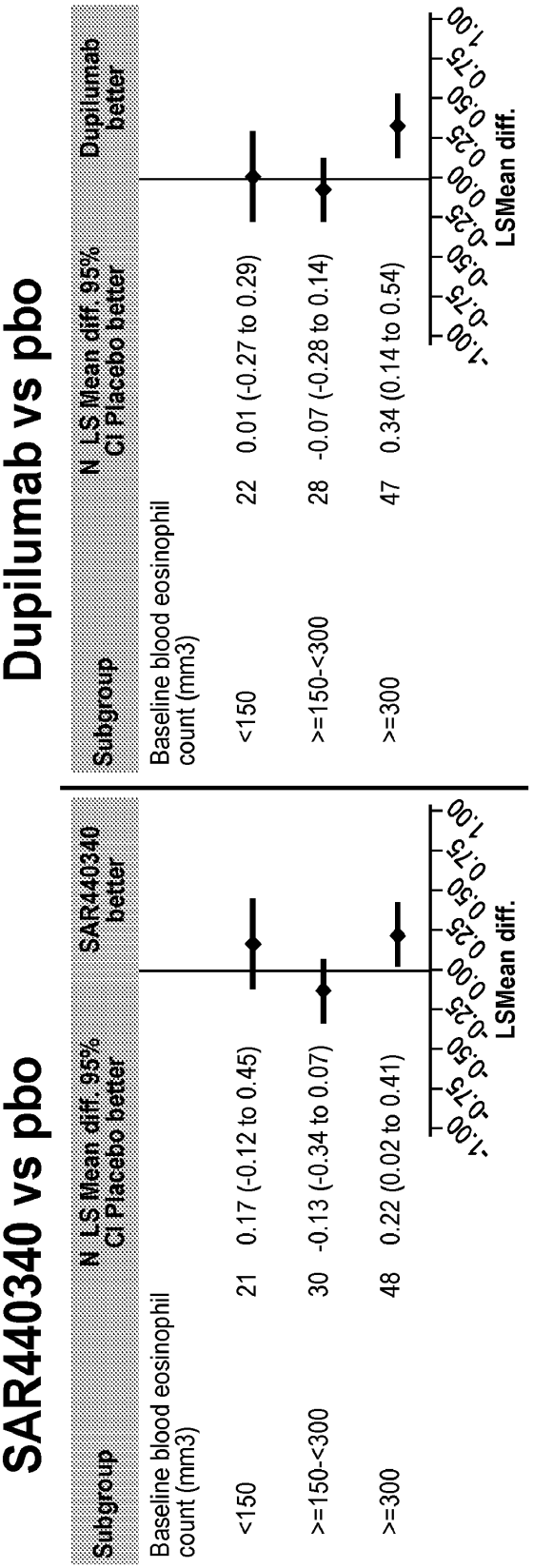

SAR440340 vs pbo
Subgroup
N LS Mean diff. 95% CI Placebo better
SAR440340 better
Baseline blood eosinophil count (mm3)
<150 21 0.17 (-0.12 to 0.45)
>=150-<300 30 -0.13 (-0.34 to 0.07)
>=300 48 0.22 (0.02 to 0.41)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LSMean diff.
Dupilumab vs pbo
Subgroup
N LS Mean diff. 95% CI Placebo better
Dupilumab better
Baseline blood eosinophil count (mm3)
<150 22 0.01 (-0.27 to 0.29)
>=150-<300 28 -0.07 (-0.28 to 0.14)
>=300 47 0.34 (0.14 to 0.54)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LSMean diff.

Fig. 18

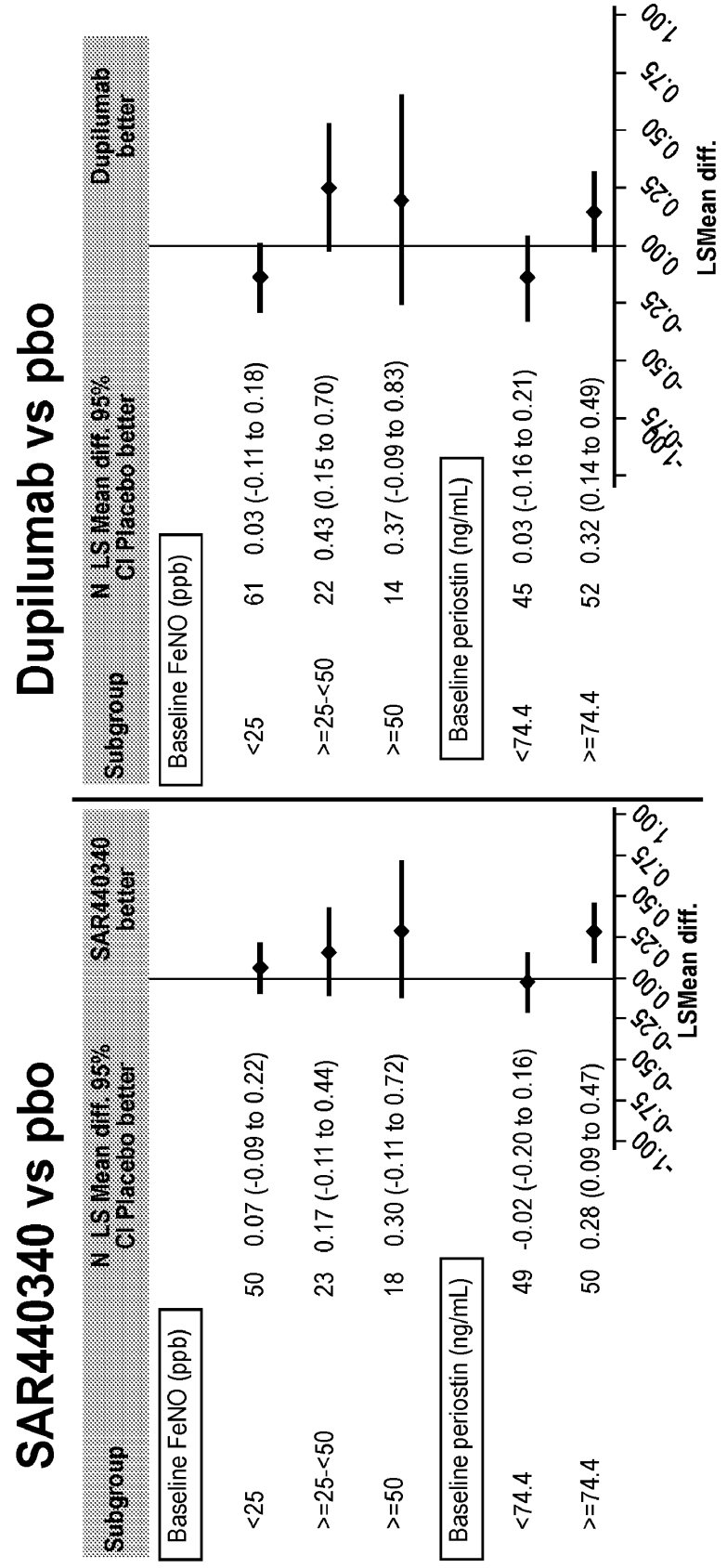

SAR440340 vs pbo
Subgroup
N
LS Mean diff. 95% CI Placebo better
SAR440340 better
Baseline FeNO (ppb)
<25 50 0.07 (-0.09 to 0.22)
>=25-<50 23 0.17 (-0.11 to 0.44)
>=50 18 0.30 (-0.11 to 0.72)
Baseline periostin (ng/mL)
<74.4 49 -0.02 (-0.20 to 0.16)
>=74.4 50 0.28 (0.09 to 0.47)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LSMean diff.
Dupilumab vs pbo
Subgroup
N
LS Mean diff. 95% CI Placebo better
Dupilumab better
Baseline FeNO (ppb)
<25 61 0.03 (-0.11 to 0.18)
>=25-<50 22 0.43 (0.15 to 0.70)
>=50 14 0.37 (-0.09 to 0.83)
Baseline periostin (ng/mL)
<74.4 45 0.03 (-0.16 to 0.21)
>=74.4 52 0.32 (0.14 to 0.49)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LSMean diff.

Fig. 19

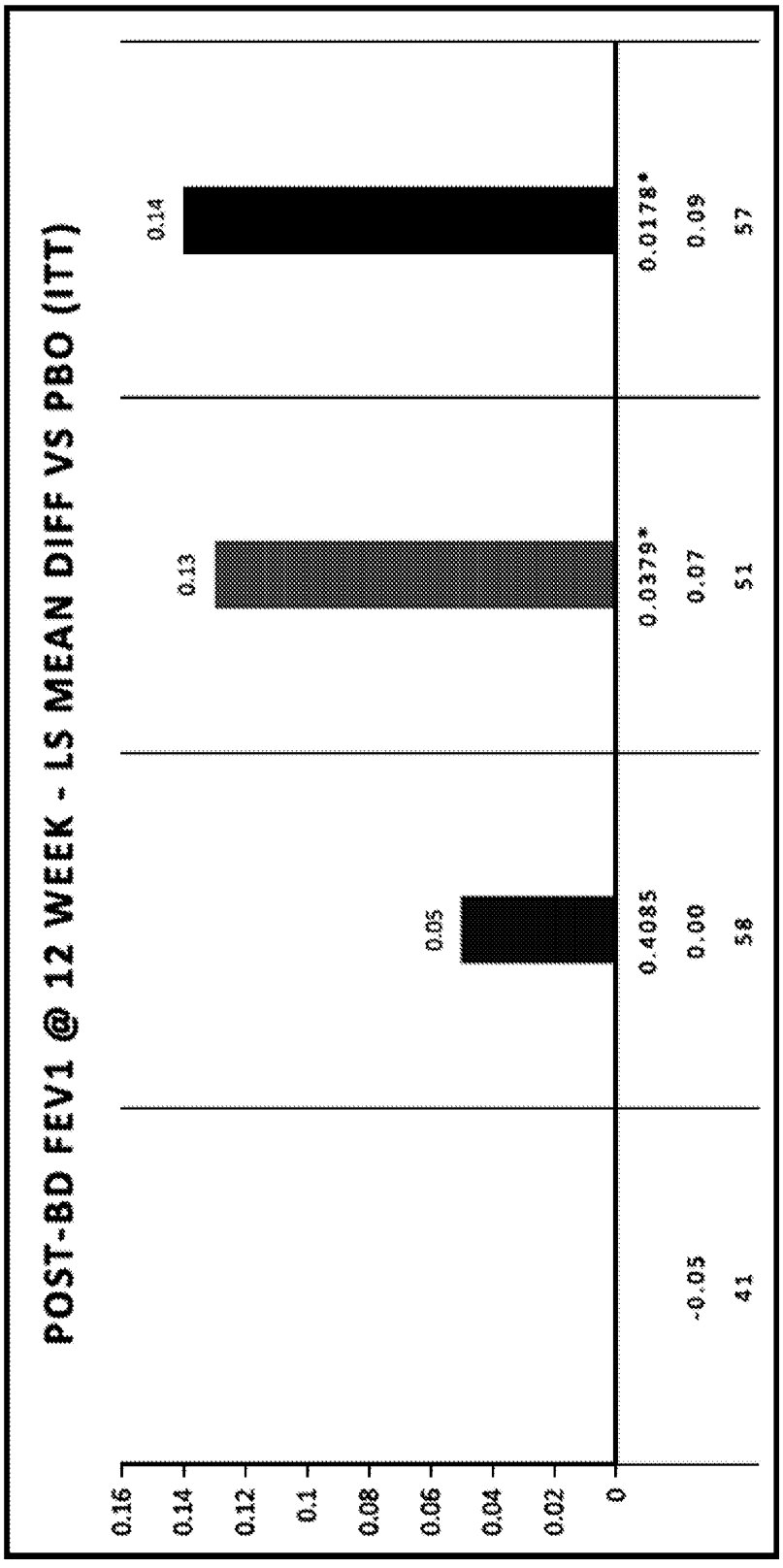

POST-BD FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (ITT)
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
-0.05
41
0.05
0.4085
0.00
58
0.13
0.0379*
0.07
51
0.14
0.0178*
0.09
57

Fig. 20

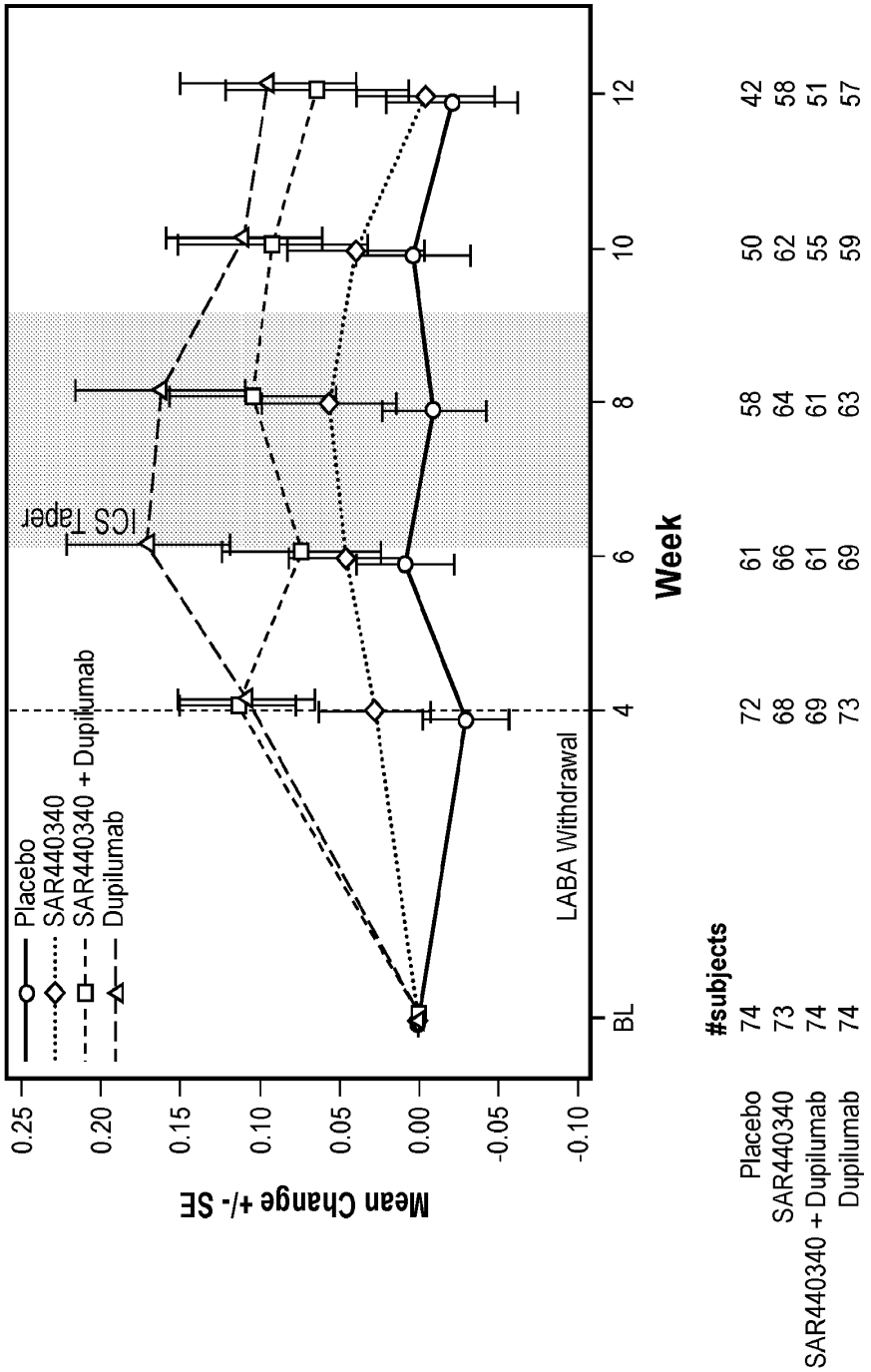

Mean Change +/- SE
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
ICS Taper
LABA Withdrawal
BL
4
6
8
10
12
Week
#subjects
Placebo 74 72 61 58 50 42
SAR440340 73 68 66 64 62 58
SAR440340 + Dupilumab 74 69 61 61 55 51
Dupilumab 74 73 69 63 59 57

Fig. 21

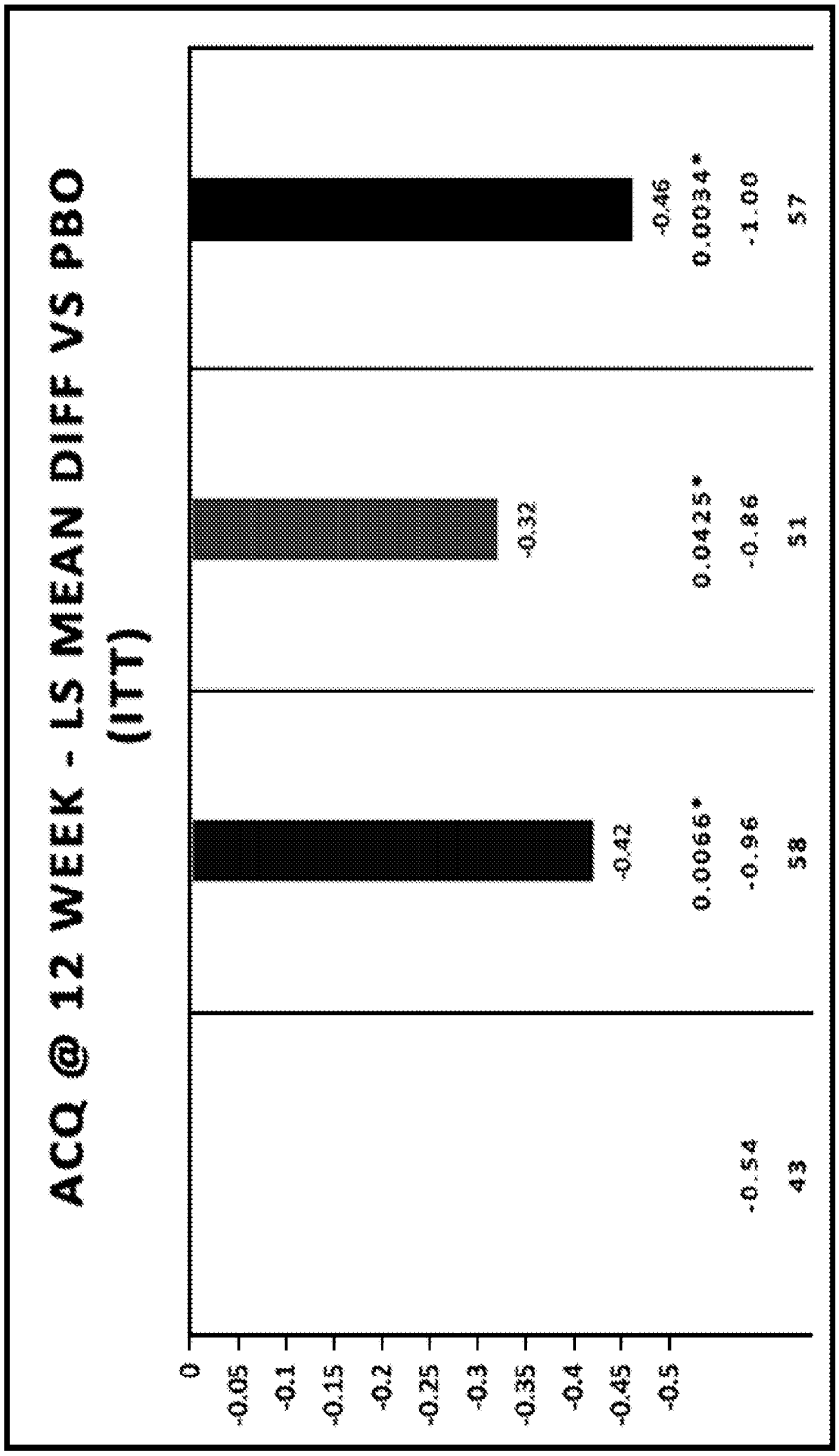

ACQ @ 12 WEEK - LS MEAN DIFF VS PBO
(ITT)
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
-0.35
-0.4
-0.45
-0.5
-0.54
43
-0.42
0.0066*
-0.96
38
-0.32
0.0425*
-0.86
51
-0.46
0.0034*
-1.00
57

Fig. 22

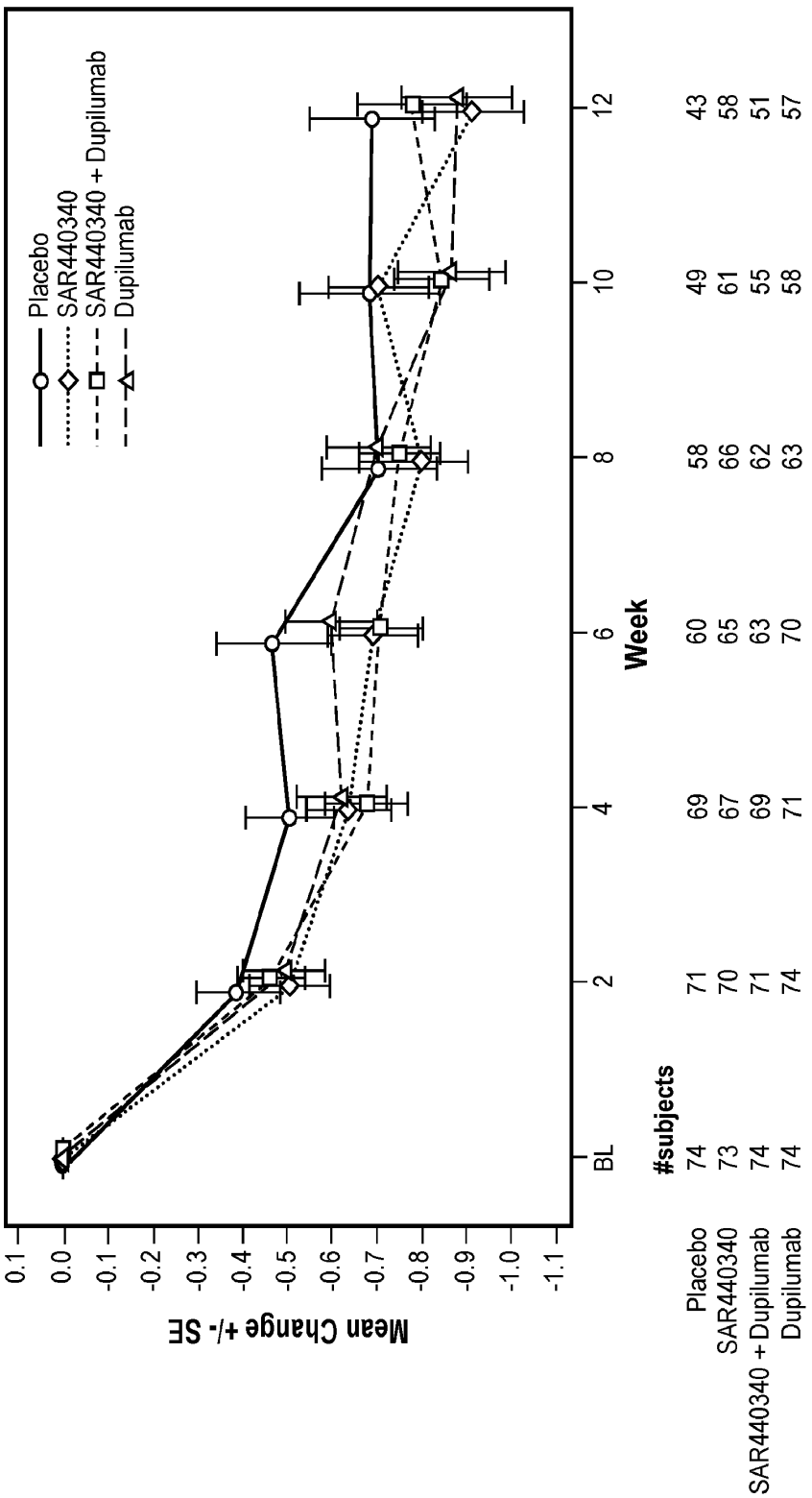

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
0.1
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
-0.8
-0.9
-1.0
-1.1
BL
2
4
6
8
10
12
Week
#subjects
Placebo 74 71 69 60 58 49 43
SAR440340 73 70 67 65 66 61 58
SAR440340 + Dupilumab 74 71 69 63 62 55 51
Dupilumab 74 74 71 70 63 58 57

Fig. 23

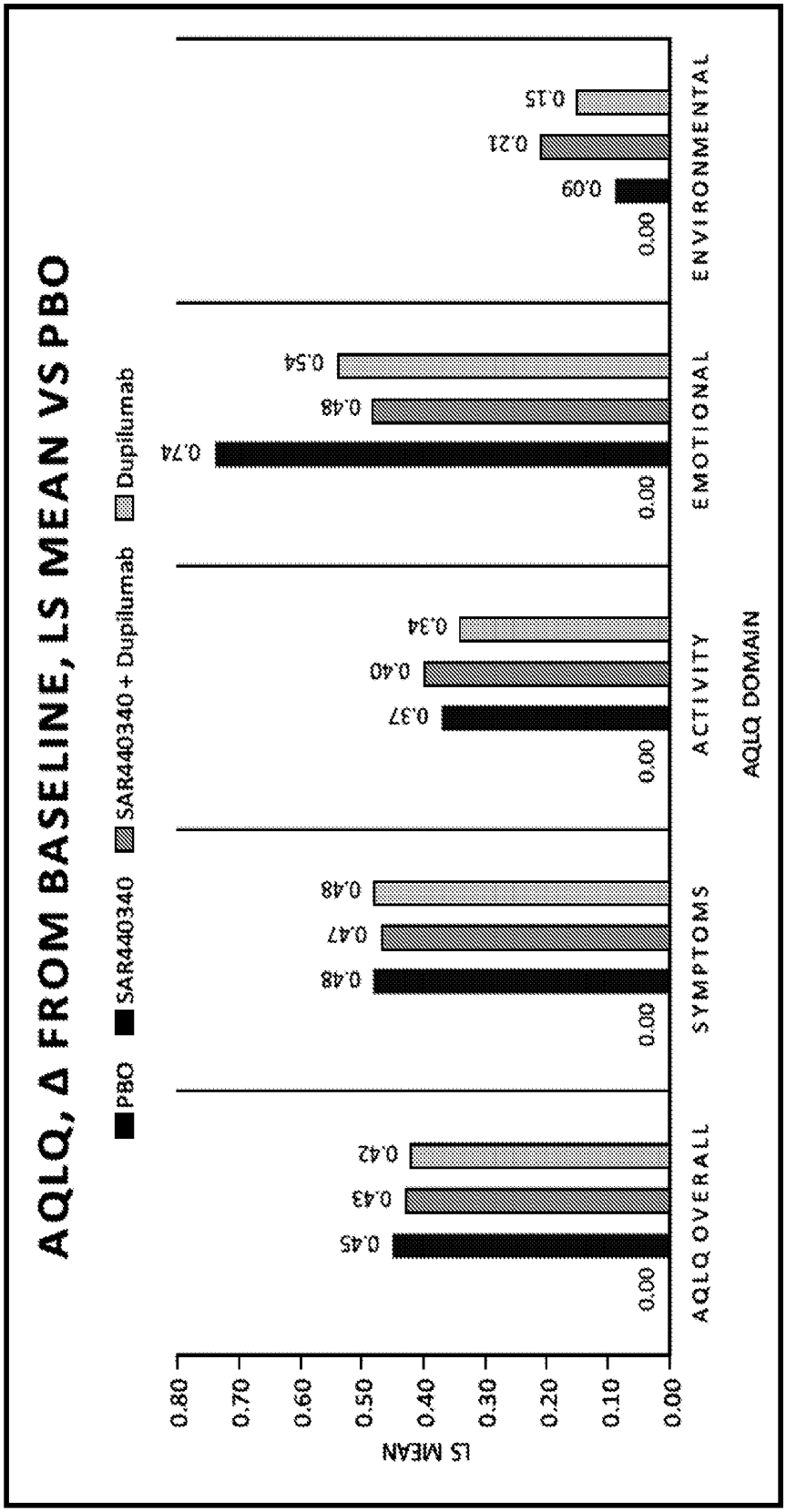

AQLQ, Δ FROM BASELINE, LS MEAN VS PBO
PBO
SAR440340
SAR440340 + Dupilumab
Dupilumab
LS MEAN
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
AQLQ OVERALL
0.45
0.43
0.42
0.00
SYMPTOMS
0.48
0.47
0.48
0.00
ACTIVITY
0.37
0.40
0.34
0.00
EMOTIONAL
0.74
0.48
0.54
0.00
ENVIRONMENTAL
0.09
0.21
0.15
0.00
AQLQ DOMAIN

Fig. 24

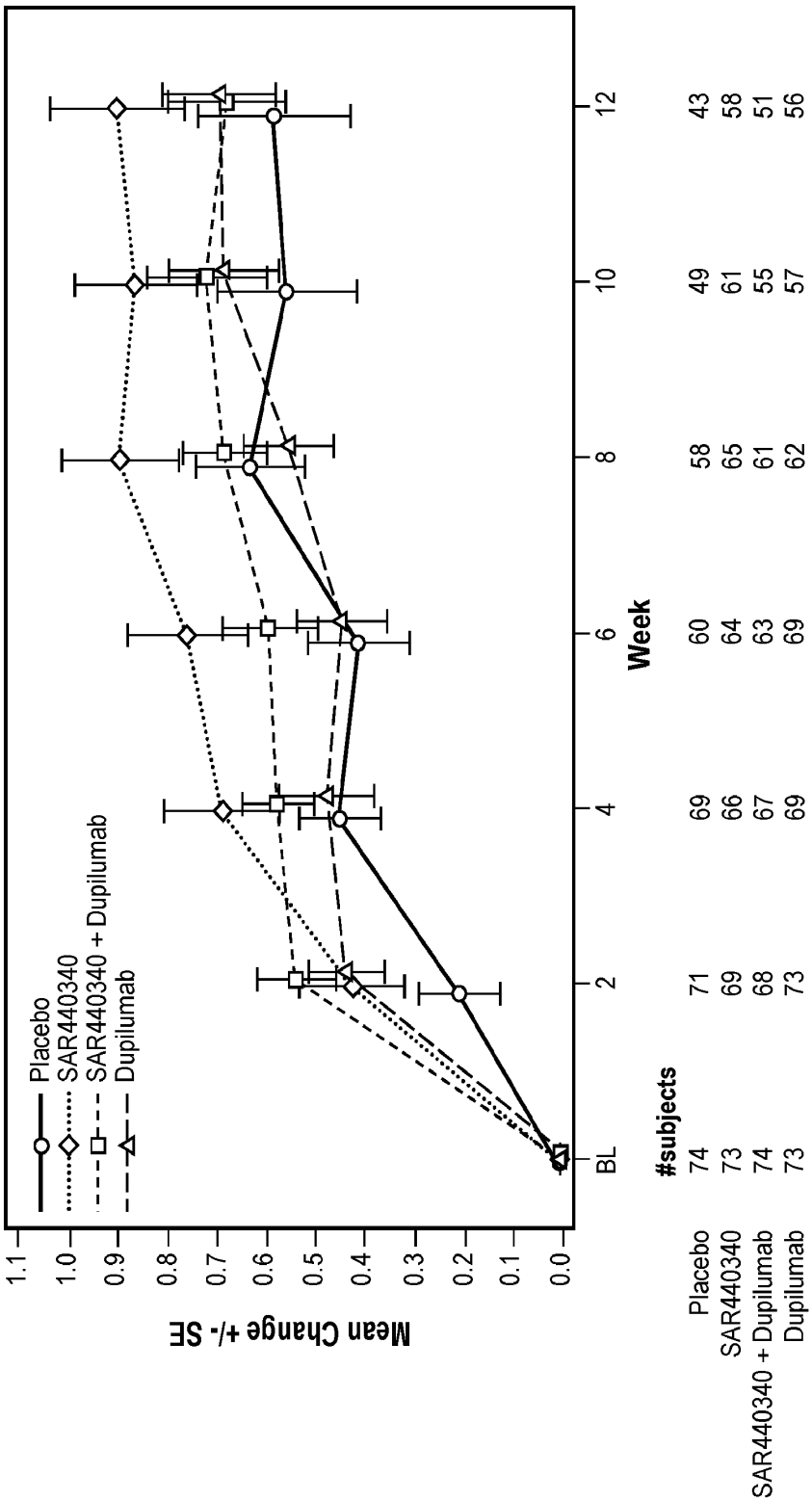

Mean Change +/- SE
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
BL
2
4
6
8
10
12
Week
#subjects
Placebo 74 71 69 60 58 49 43
SAR440340 73 69 66 64 65 61 58
SAR440340 + Dupilumab 74 68 67 63 61 55 51
Dupilumab 73 73 69 69 62 57 56

Fig. 25

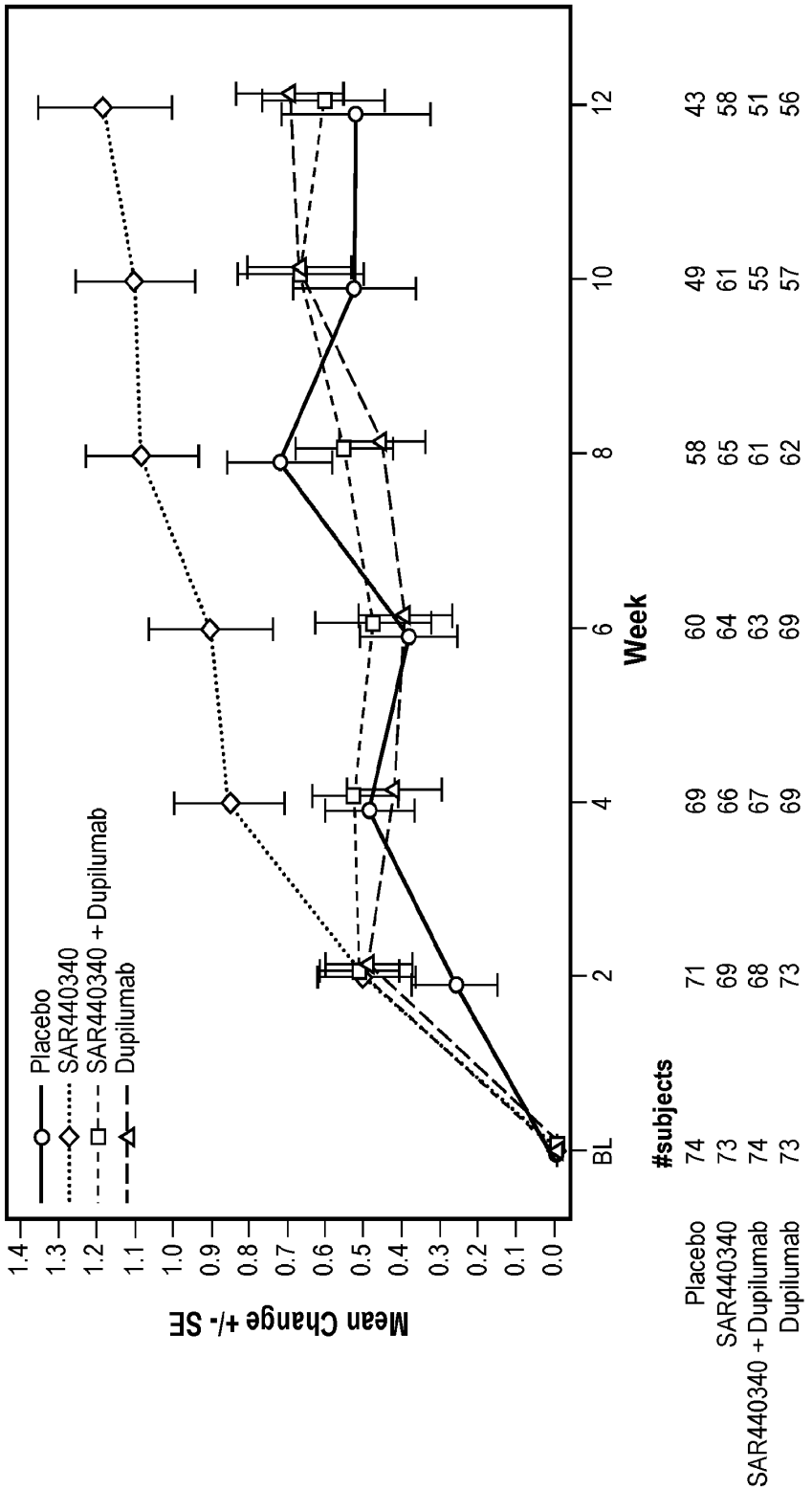

Mean Change +/- SE
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
BL
2
4
6
8
10
12
Week
#subjects
Placebo 74 71 69 60 58 49 43
SAR440340 73 69 66 64 65 61 58
SAR440340 + Dupilumab 74 68 67 63 61 55 51
Dupilumab 73 73 69 69 62 57 56

Fig. 26

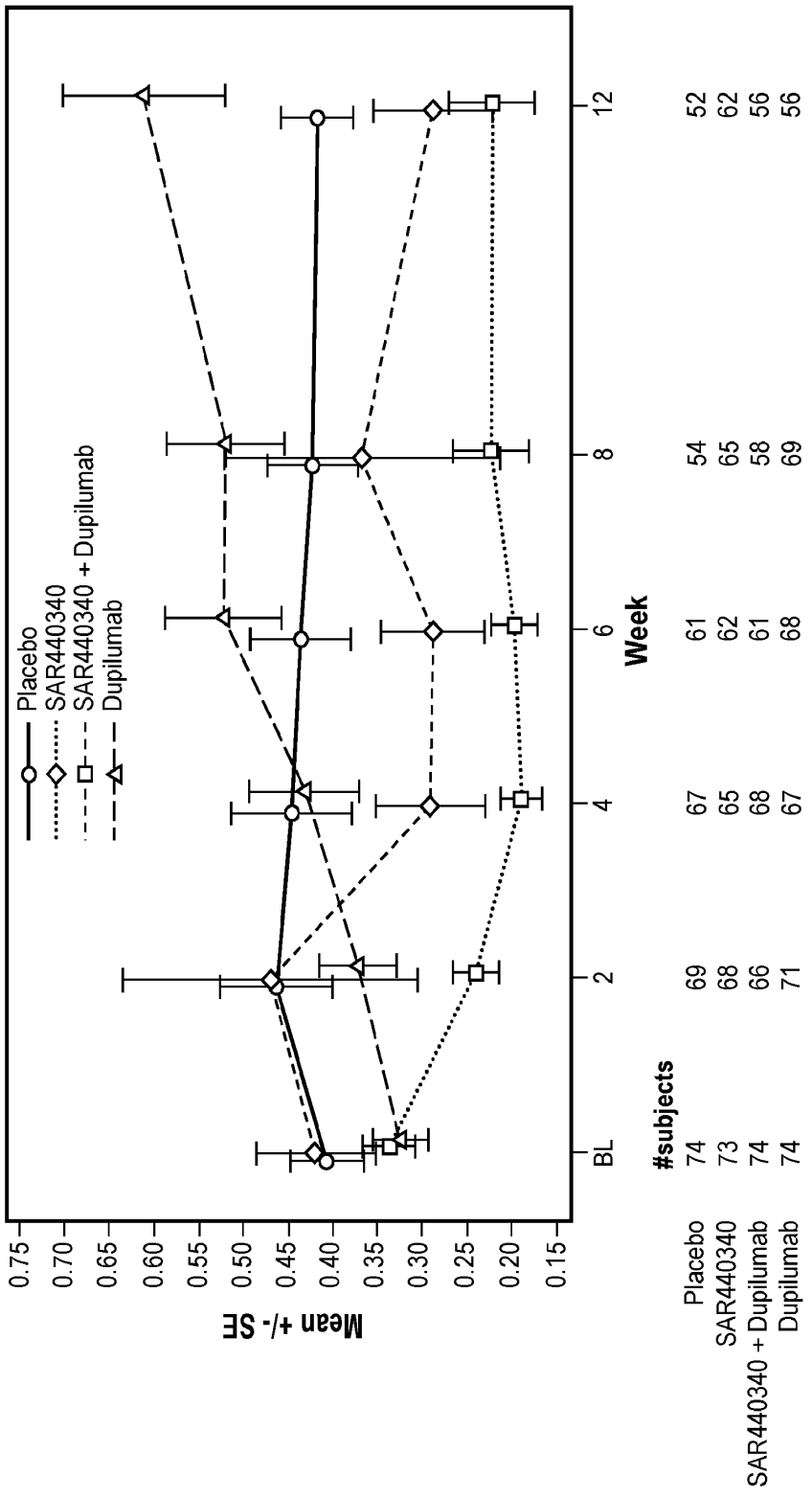

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
BL
2
4
6
8
12
Week
#subjects
Placebo 74 69 67 61 54 52
SAR440340 73 68 65 62 65 62
SAR440340 + Dupilumab 74 66 68 61 58 56
Dupilumab 74 71 67 68 69 56

Fig. 27

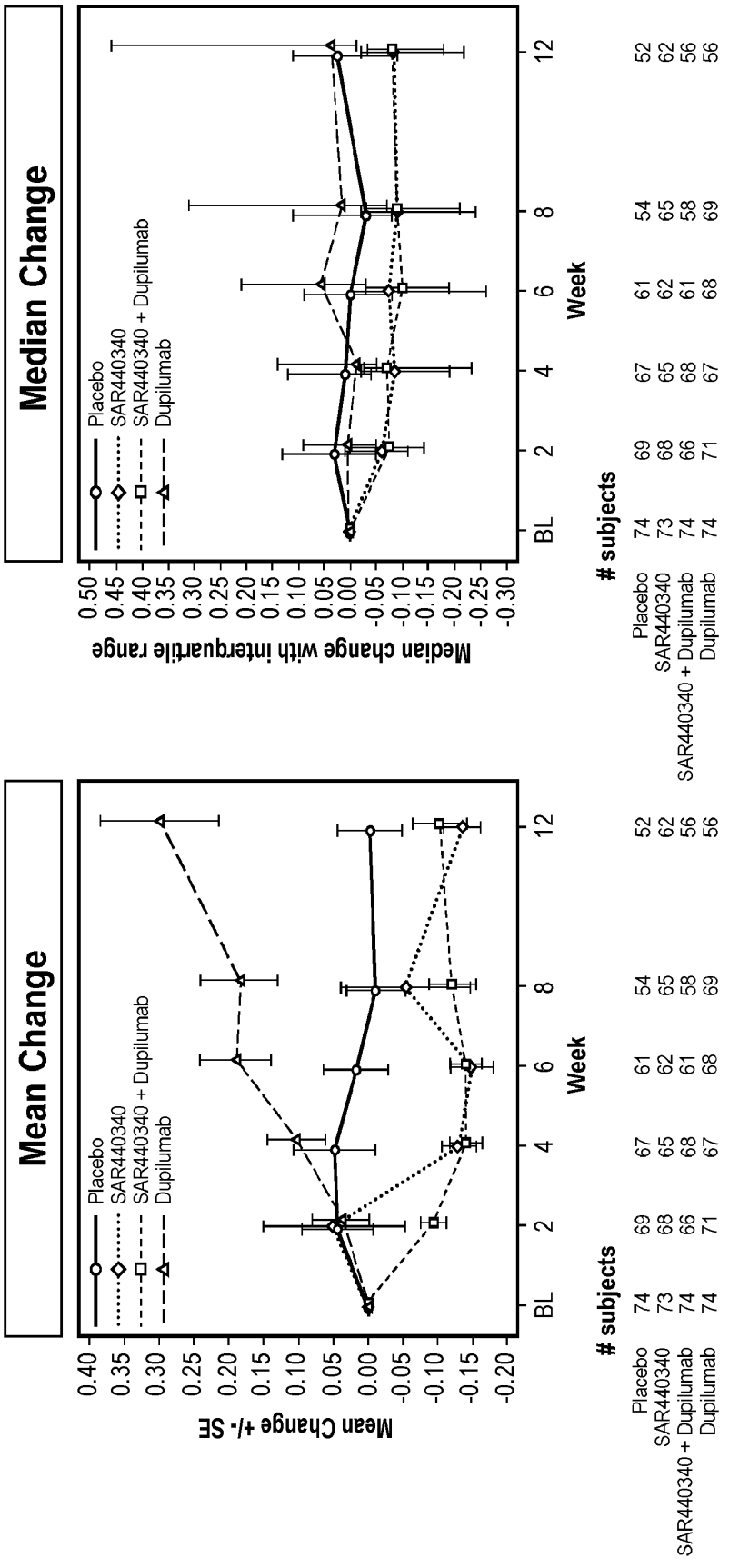

Median Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
0.50 0.45 0.40 0.35 0.30 0.25 0.20 0.15 0.10 0.05 0.00 -0.05 -0.10 -0.15 -0.20 -0.25 -0.30
BL 2 4 6 8 12
Week
subjects
Placebo 74 69 67 61 54 52
SAR440340 73 68 65 62 65 62
SAR440340 + Dupilumab 74 66 68 61 58 56
Dupilumab 74 71 67 68 69 56
Mean Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
0.40 0.35 0.30 0.25 0.20 0.15 0.10 0.05 0.00 -0.05 -0.10 -0.15 -0.20
BL 2 4 6 8 12
Week
subjects
Placebo 74 69 67 61 54 52
SAR440340 73 68 65 62 65 62
SAR440340 + Dupilumab 74 66 68 61 58 56
Dupilumab 74 71 67 68 69 56

Fig. 28

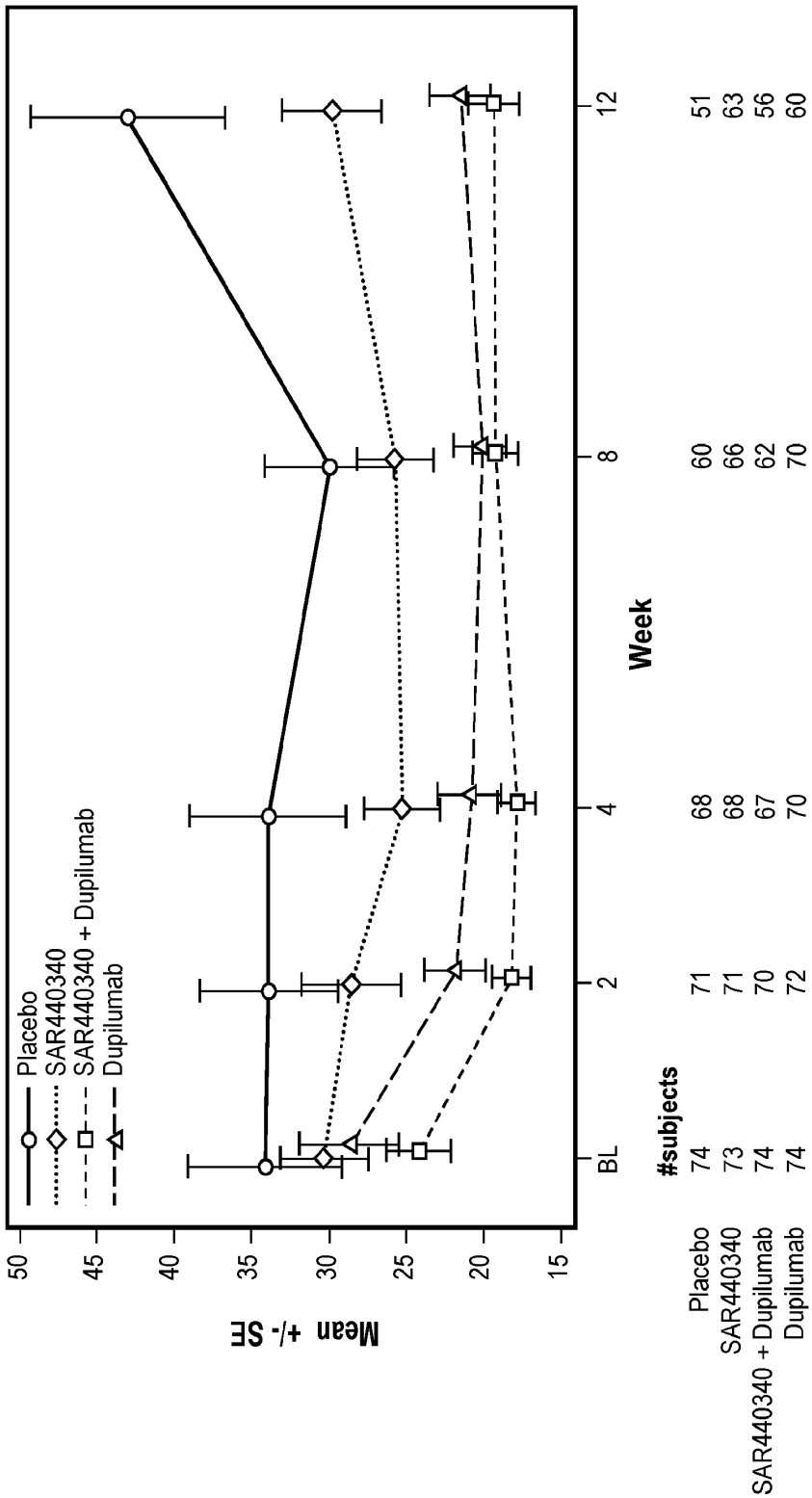

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
50
45
40
35
30
25
20
15
BL
2
4
8
12
Week
#subjects
Placebo 74 71 68 60 51
SAR440340 73 71 68 66 63
SAR440340 + Dupilumab 74 70 67 62 56
Dupilumab 74 72 70 70 60

Fig. 29

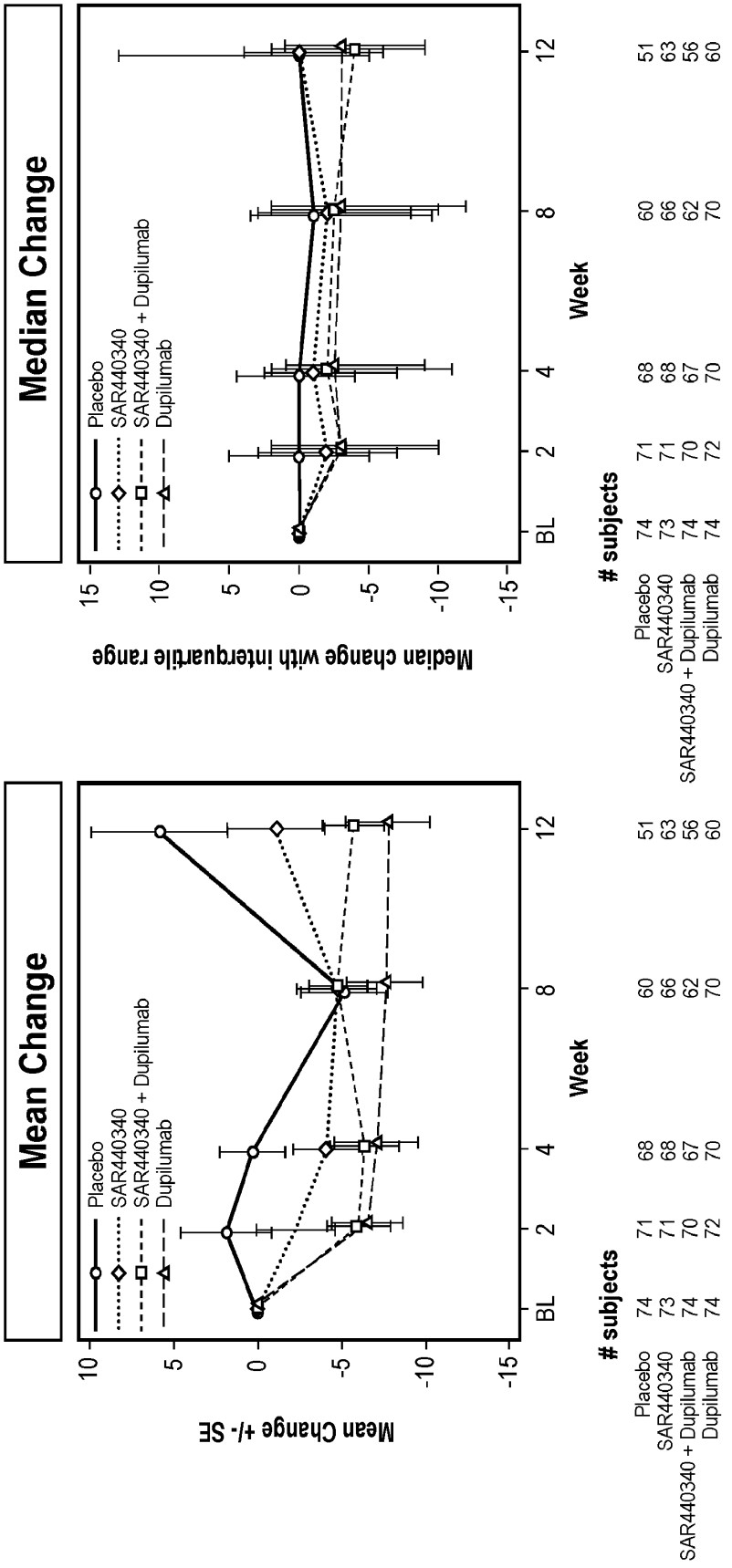

Median Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
Week
subjects
Placebo 74 71 68 60 51
SAR440340 73 71 68 66 63
SAR440340 + Dupilumab 74 70 67 62 56
Dupilumab 74 72 70 70 60
Mean Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
Week
subjects
Placebo 74 71 68 60 51
SAR440340 73 71 68 66 63
SAR440340 + Dupilumab 74 70 67 62 56
Dupilumab 74 72 70 70 60

Fig. 30

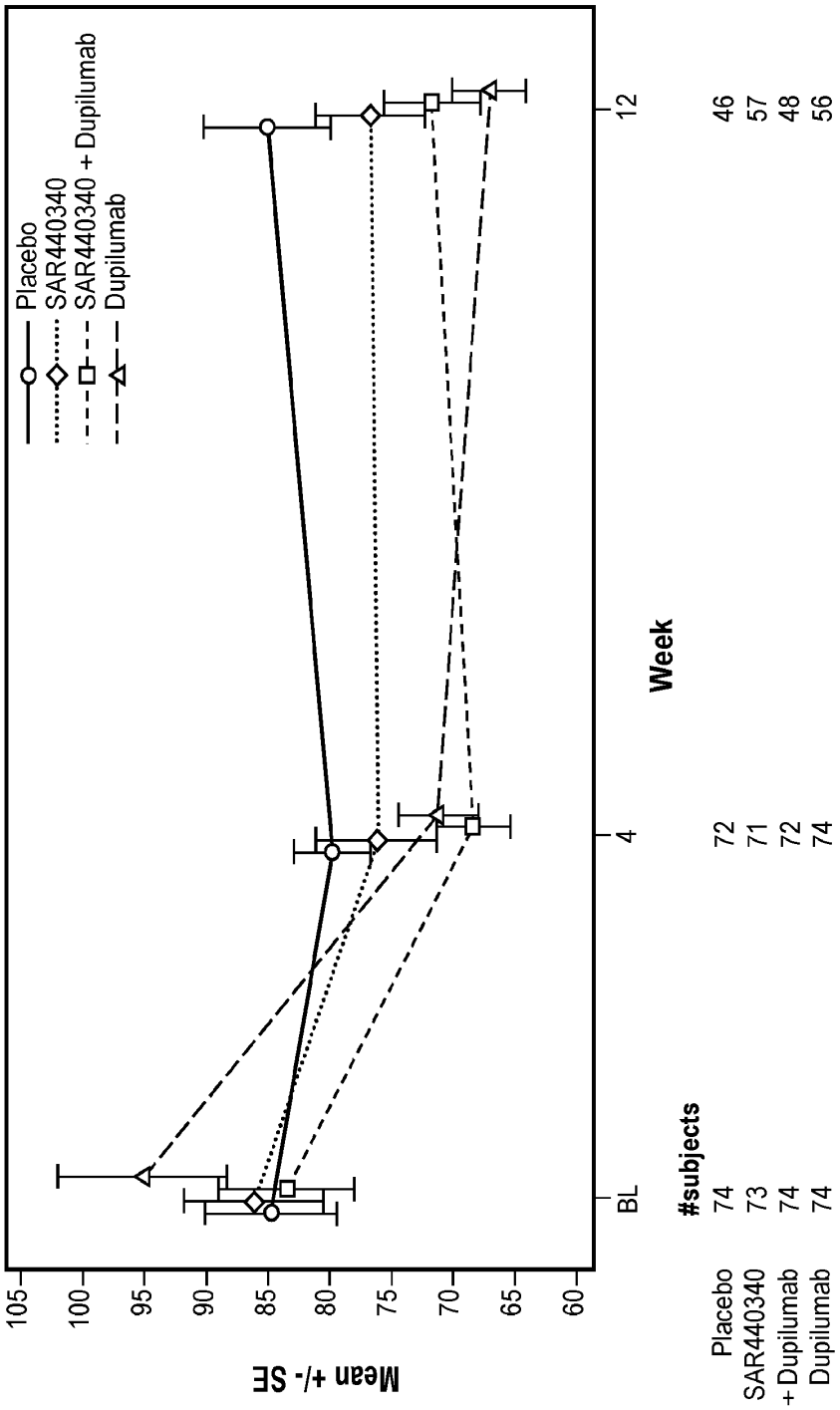

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
105
100
95
90
85
80
75
70
65
60
BL
4
12
Week
#subjects
Placebo 74 72 46
SAR440340 73 71 57
SAR440340 + Dupilumab 74 72 48
Dupilumab 74 74 56

Fig. 31

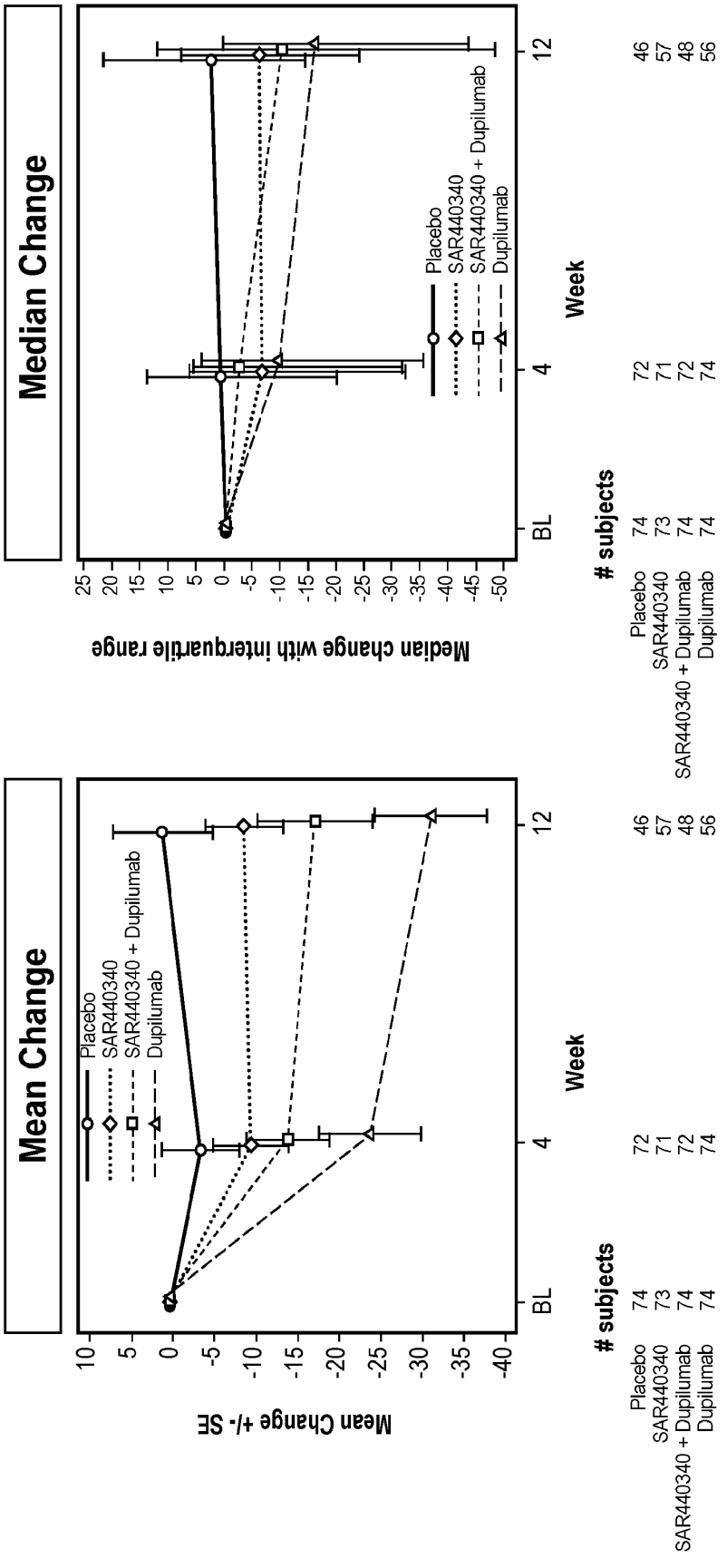

Median Change
Median change with interquartile range
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 74 72 46
SAR440340 73 71 57
SAR440340 + Dupilumab 74 72 48
Dupilumab 74 74 56
Mean Change
Mean Change +/- SE
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 74 72 46
SAR440340 73 71 57
SAR440340 + Dupilumab 74 72 48
Dupilumab 74 74 56

Fig. 32

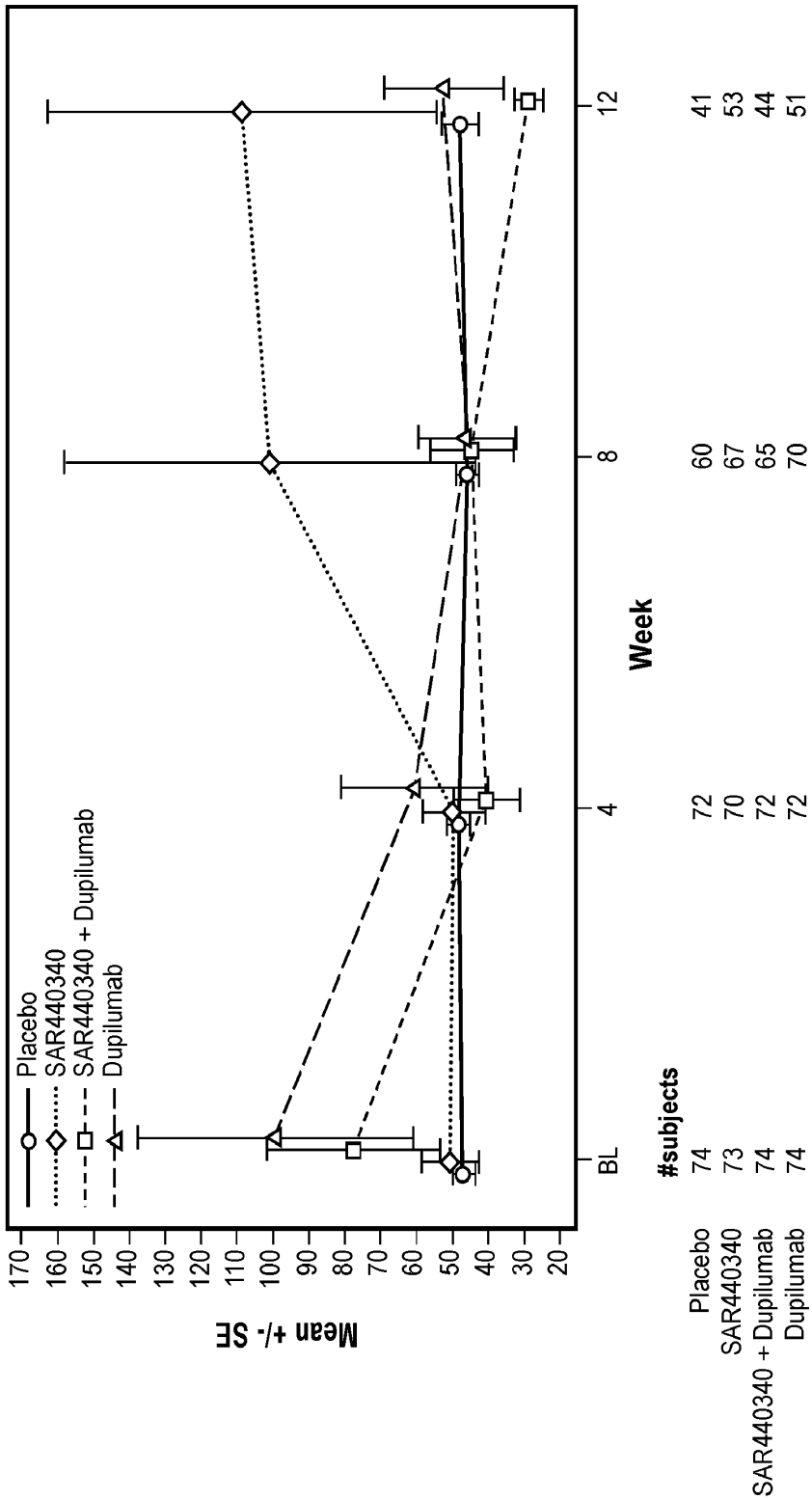

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
BL
4
8
12
Week
#subjects
Placebo 74 72 60 41
SAR440340 73 70 67 53
SAR440340 + Dupilumab 74 72 65 44
Dupilumab 74 72 70 51

Fig. 33

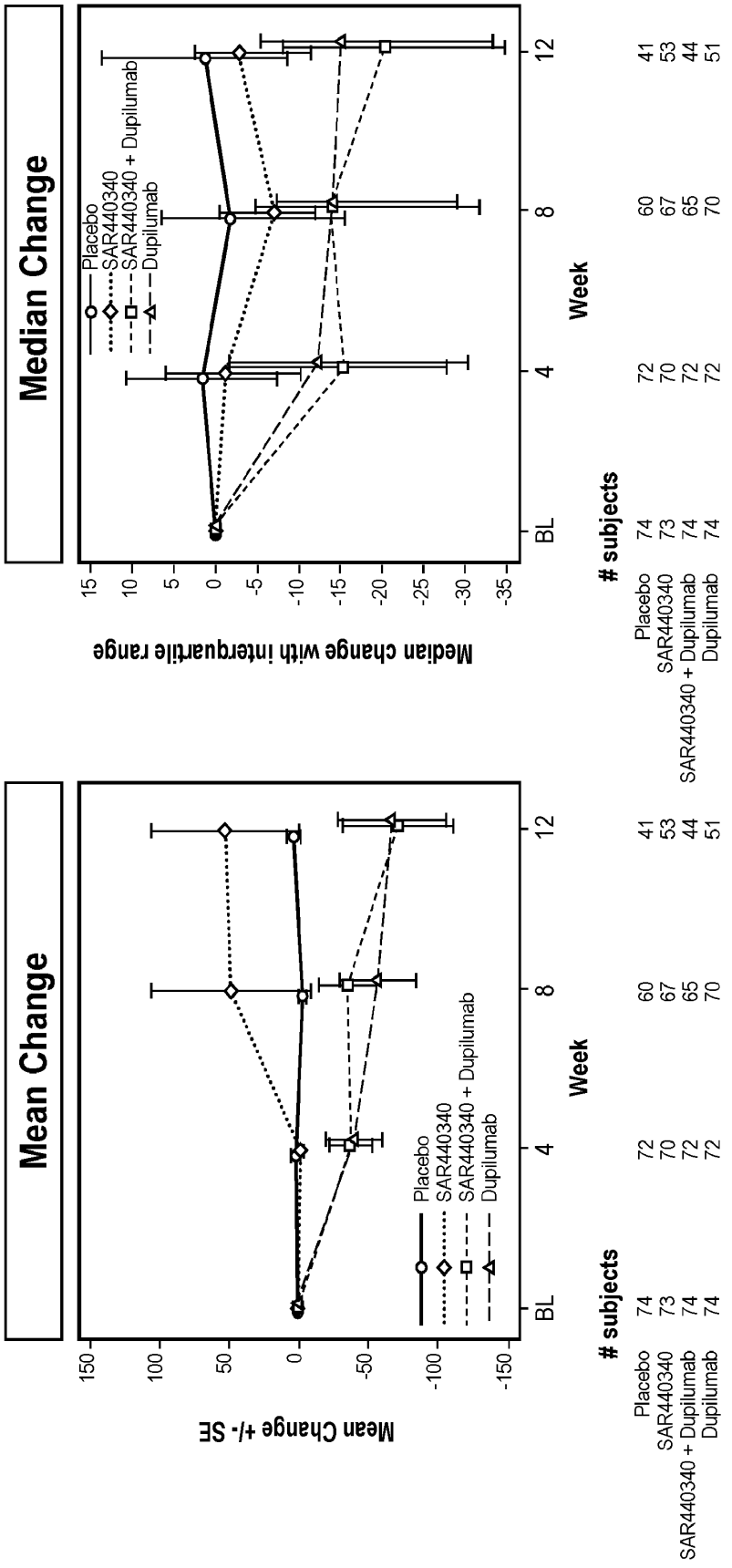

Median Change
Median change with interquartile range
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Week
BL
4
8
12
subjects
Placebo 74 72 60 41
SAR440340 73 70 67 53
SAR440340 + Dupilumab 74 72 65 44
Dupilumab 74 72 70 51
Mean Change
Mean Change +/- SE
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Week
subjects
Placebo 74 72 60 41
SAR440340 73 70 67 53
SAR440340 + Dupilumab 74 72 65 44
Dupilumab 74 72 70 51

Fig. 34

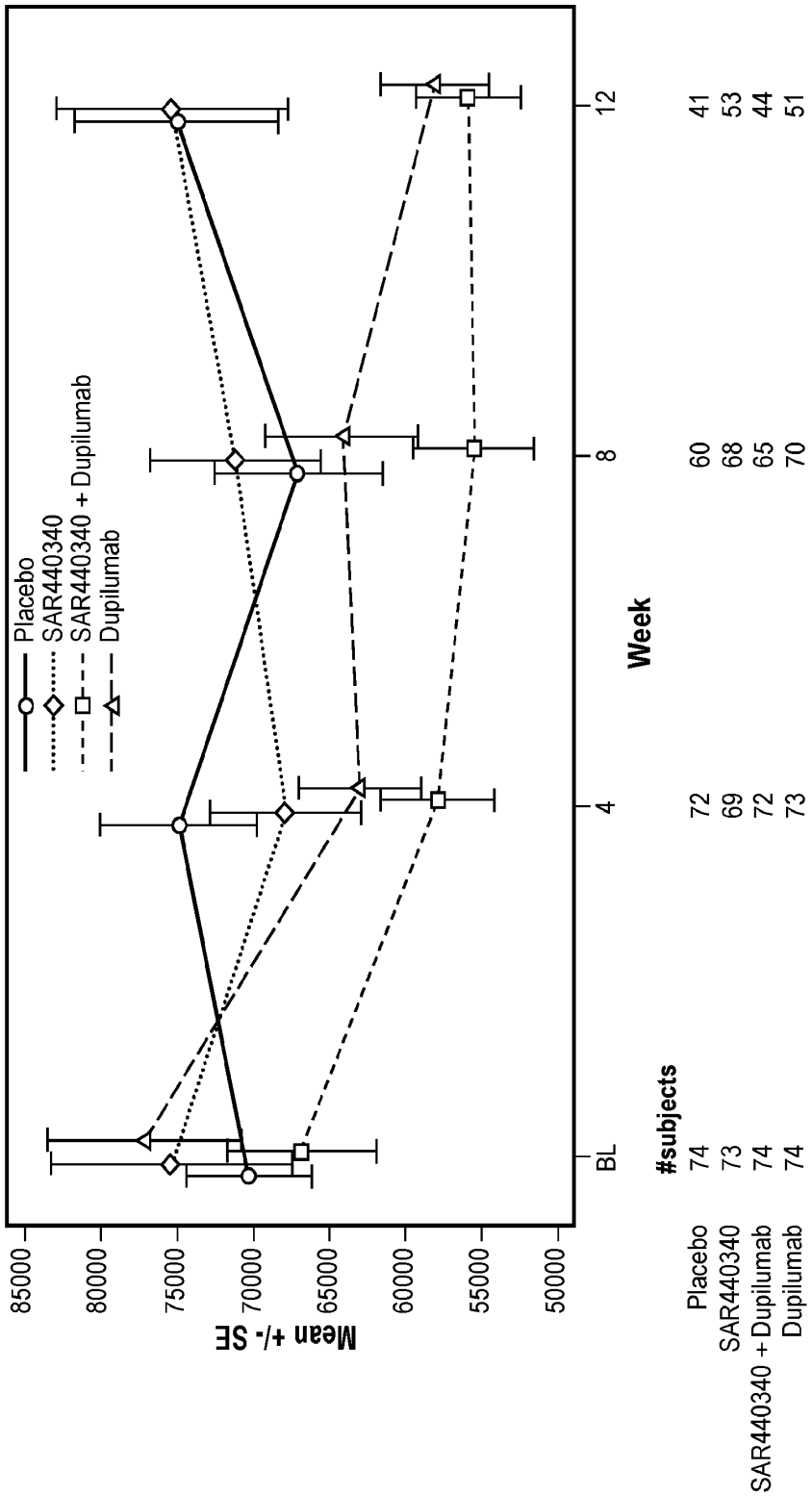
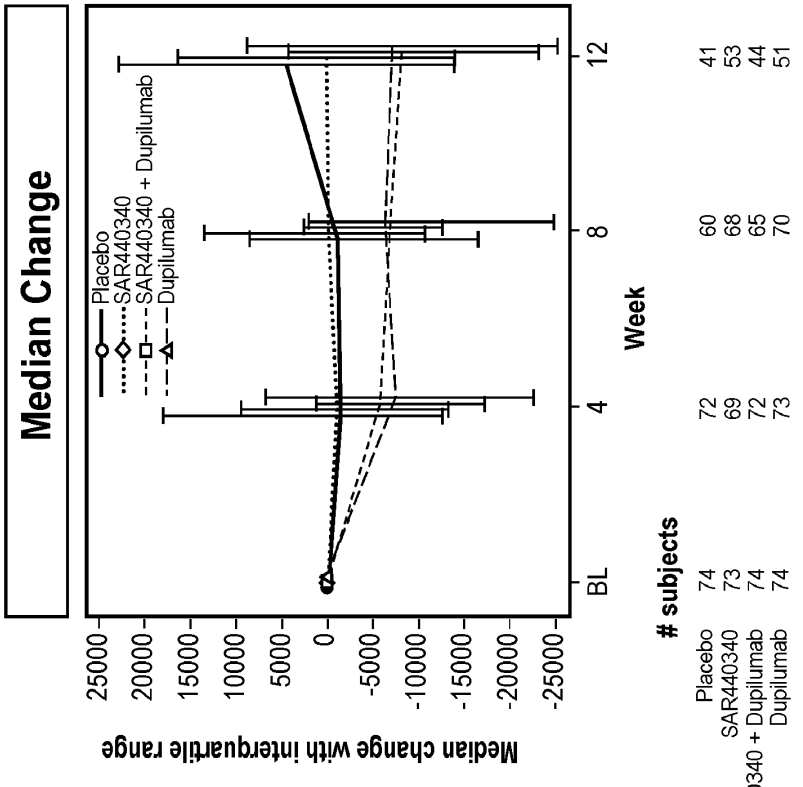

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
85000
80000
75000
70000
65000
60000
55000
50000
BL
4
8
12
Week
#subjects
Placebo 74 72 60 41
SAR440340 73 69 68 53
SAR440340 + Dupilumab 74 72 65 44
Dupilumab 74 73 70 51

Fig. 35


Median Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
25000
20000
15000
10000
5000
0
-5000
-10000
-15000
-20000
-25000
BL
4
8
12
Week
subjects
Placebo 74 72 60 41
SAR440340 73 69 68 53
SAR440340 + Dupilumab 74 72 65 44
Dupilumab 74 73 70 51

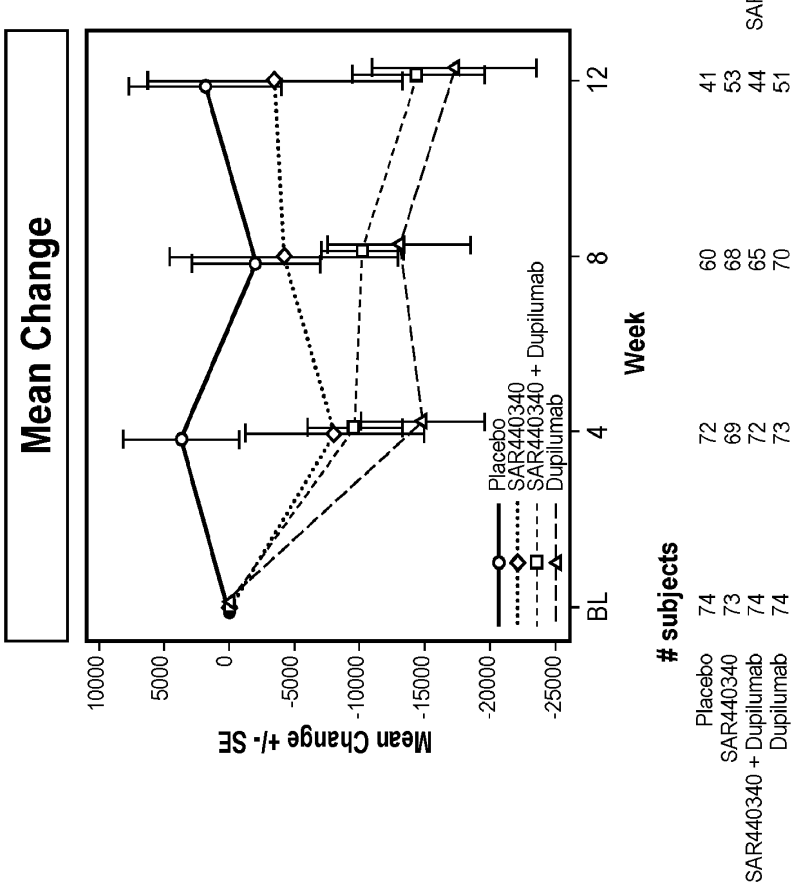

Mean Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
10000
5000
0
-5000
-10000
-15000
-20000
-25000
BL
4
8
12
Week
subjects
Placebo 74 72 60 41
SAR440340 73 69 68 53
SAR440340 + Dupilumab 74 72 65 44
Dupilumab 74 73 70 51

Fig. 36

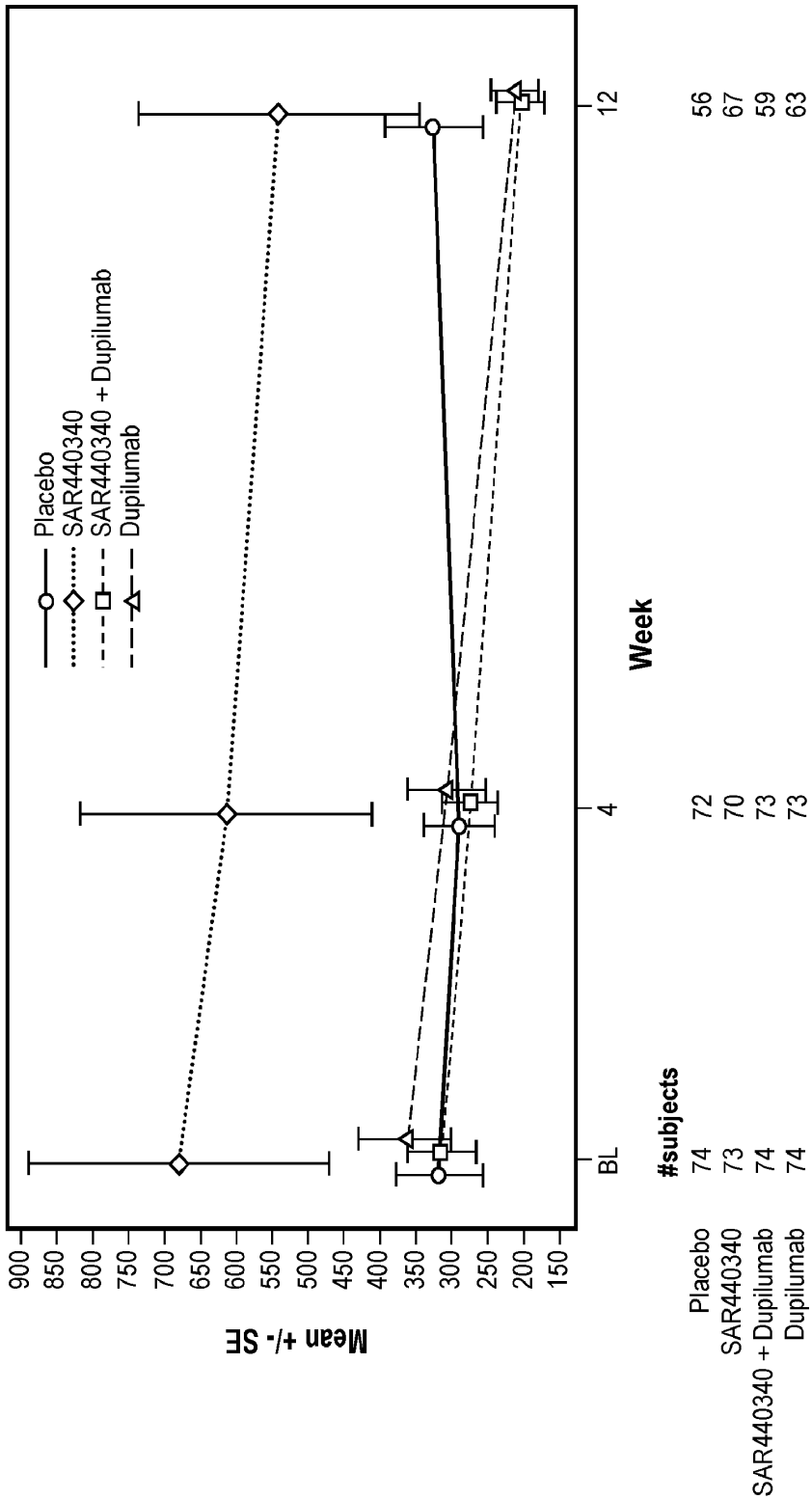
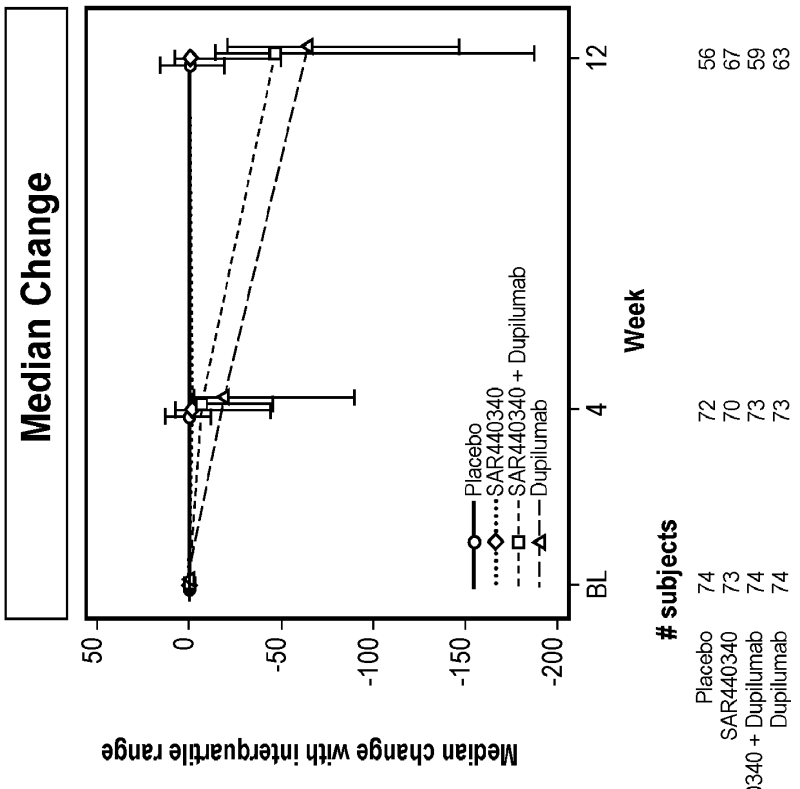

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
900
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
BL
4
12
Week
#subjects
Placebo 74 72 56
SAR440340 73 70 67
SAR440340 + Dupilumab 74 73 59
Dupilumab 74 73 63

Fig. 37


Median Change
Median change with interquartile range
50
0
-50
-100
-150
-200
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 74 72 56
SAR440340 73 70 67
SAR440340 + Dupilumab 74 73 59
Dupilumab 74 73 63

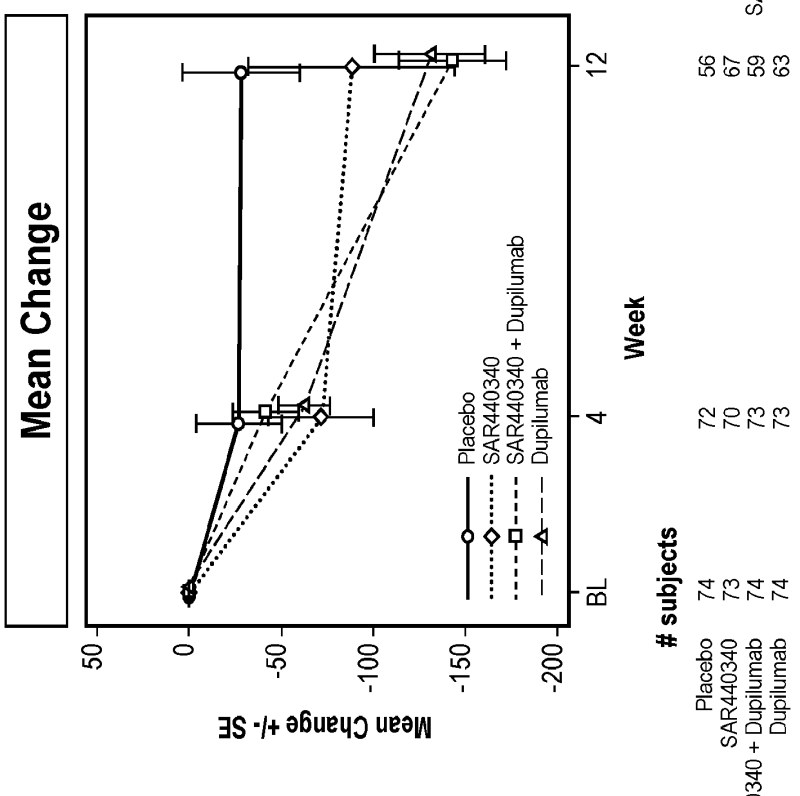

Mean Change
Mean Change +/- SE
50
0
-50
-100
-150
-200
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 74 72 56
SAR440340 73 70 67
SAR440340 + Dupilumab 74 73 59
Dupilumab 74 73 63

Fig. 38

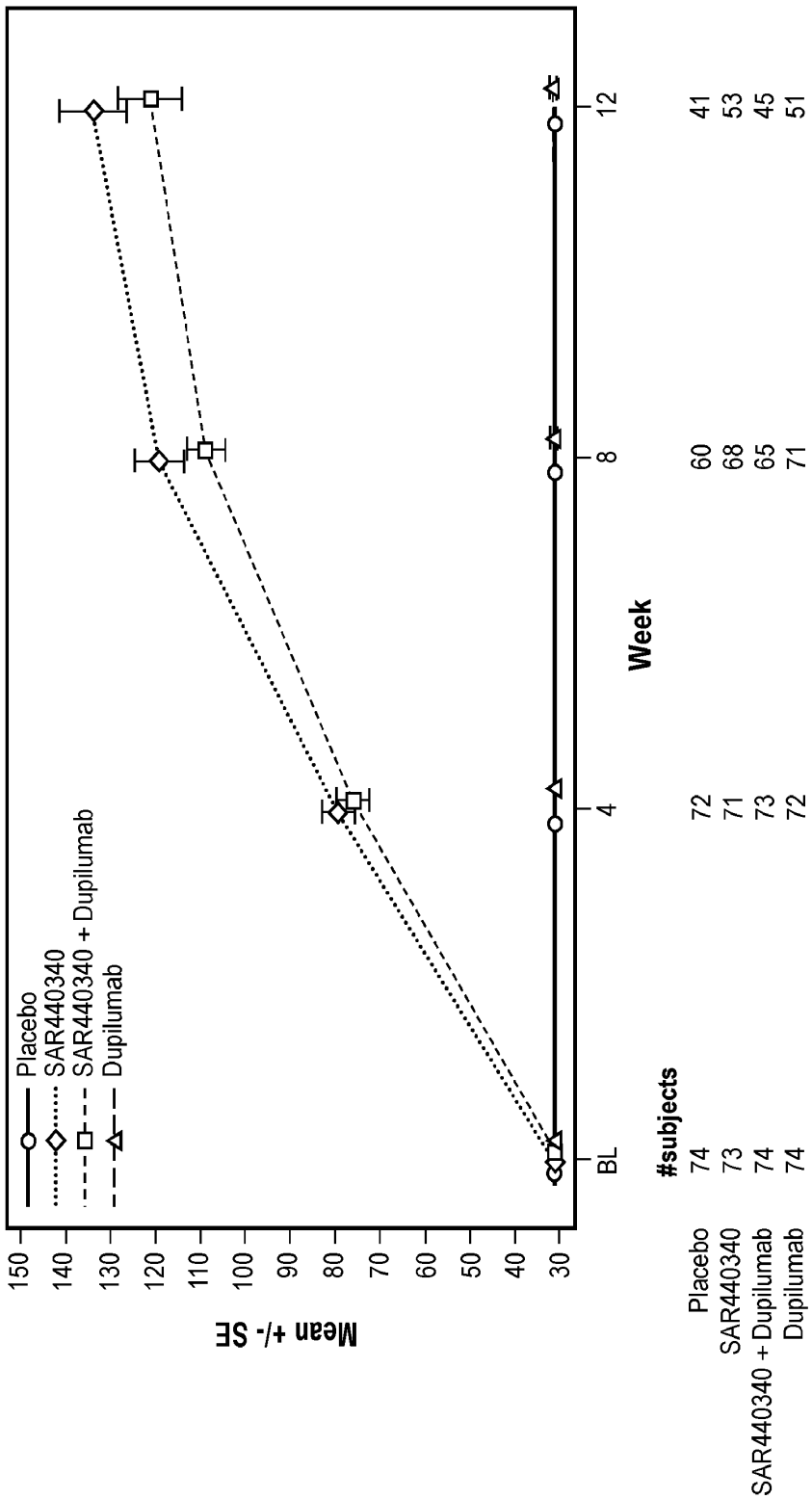

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
150
140
130
120
110
100
90
80
70
60
50
40
30
BL
4
8
12
Week
#subjects
Placebo 74 72 60 41
SAR440340 73 71 68 53
SAR440340 + Dupilumab 74 73 65 45
Dupilumab 74 72 71 51

Fig. 39

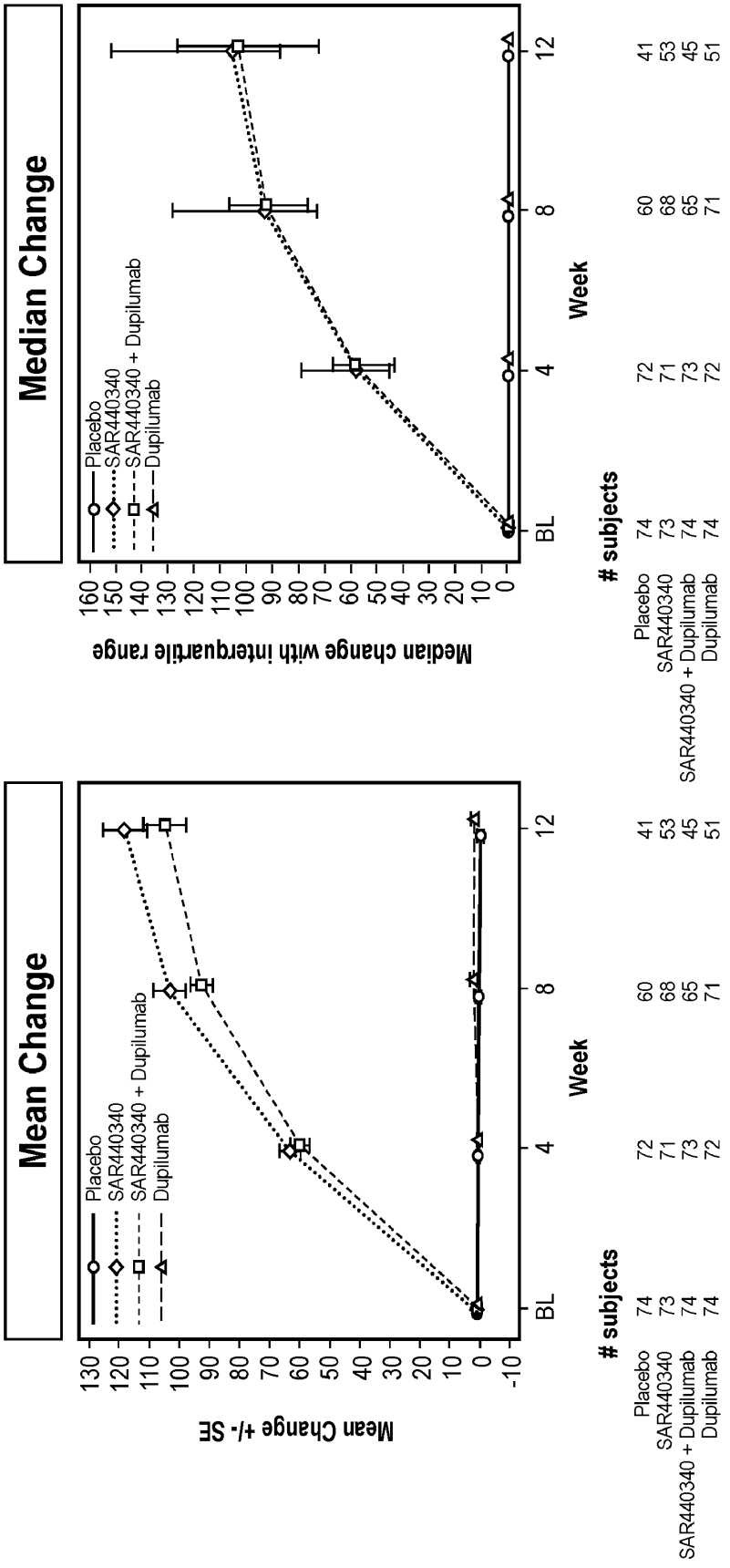

Mean Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
Week
BL
subjects
Placebo 74 72 60 41
SAR440340 73 71 68 53
SAR440340 + Dupilumab 74 73 65 45
Dupilumab 74 72 71 51
Median Change
Median change with interquartile range
Week
subjects
Placebo 74 72 60 41
SAR440340 73 71 68 53
SAR440340 + Dupilumab 74 73 65 45
Dupilumab 74 72 71 51

Fig. 40

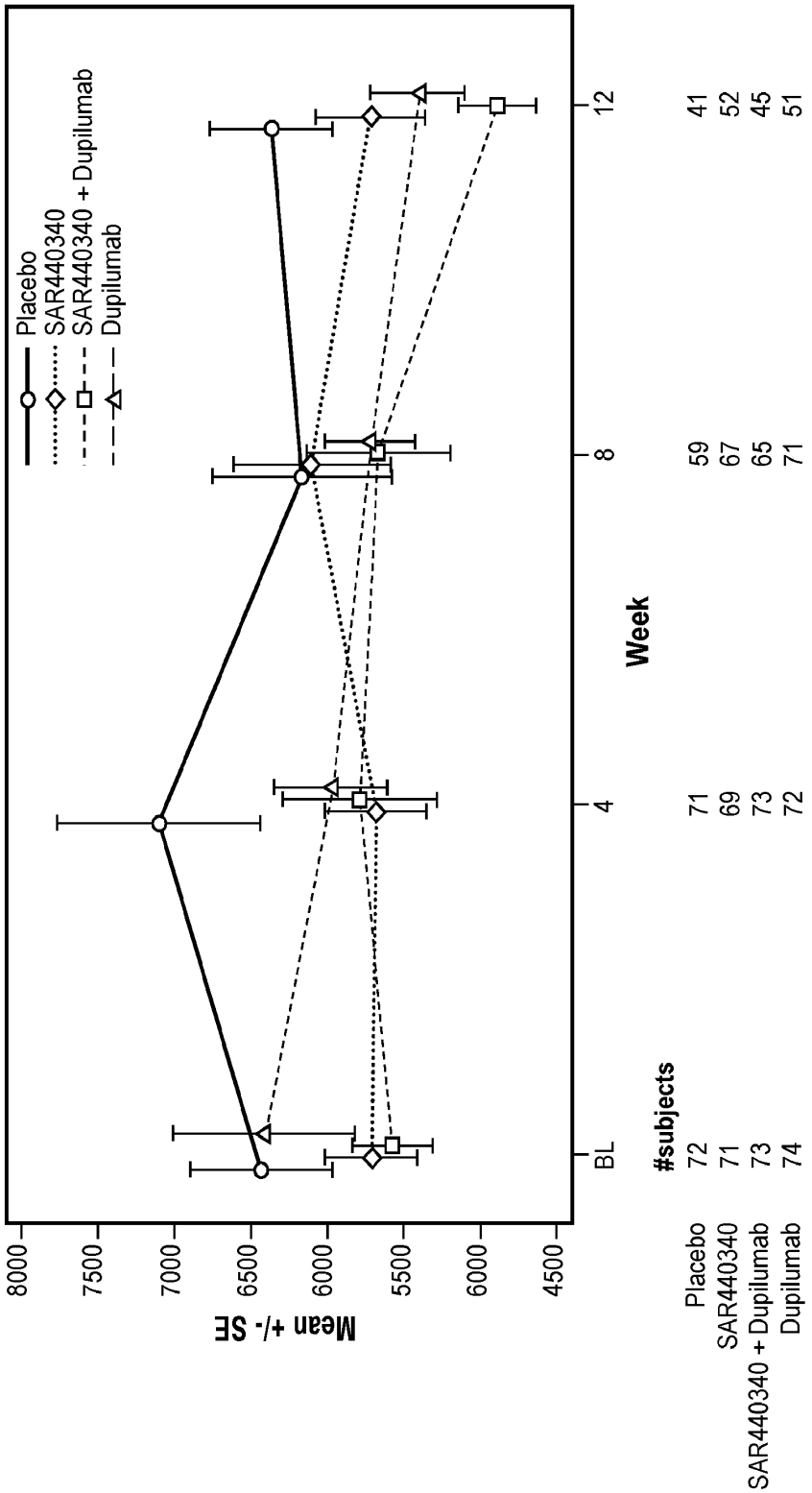

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
8000
7500
7000
6500
6000
5500
5000
4500
BL
4
8
12
Week
#subjects
Placebo 72 71 59 41
SAR440340 71 69 67 52
SAR440340 + Dupilumab 73 73 65 45
Dupilumab 74 72 71 51

Fig. 41

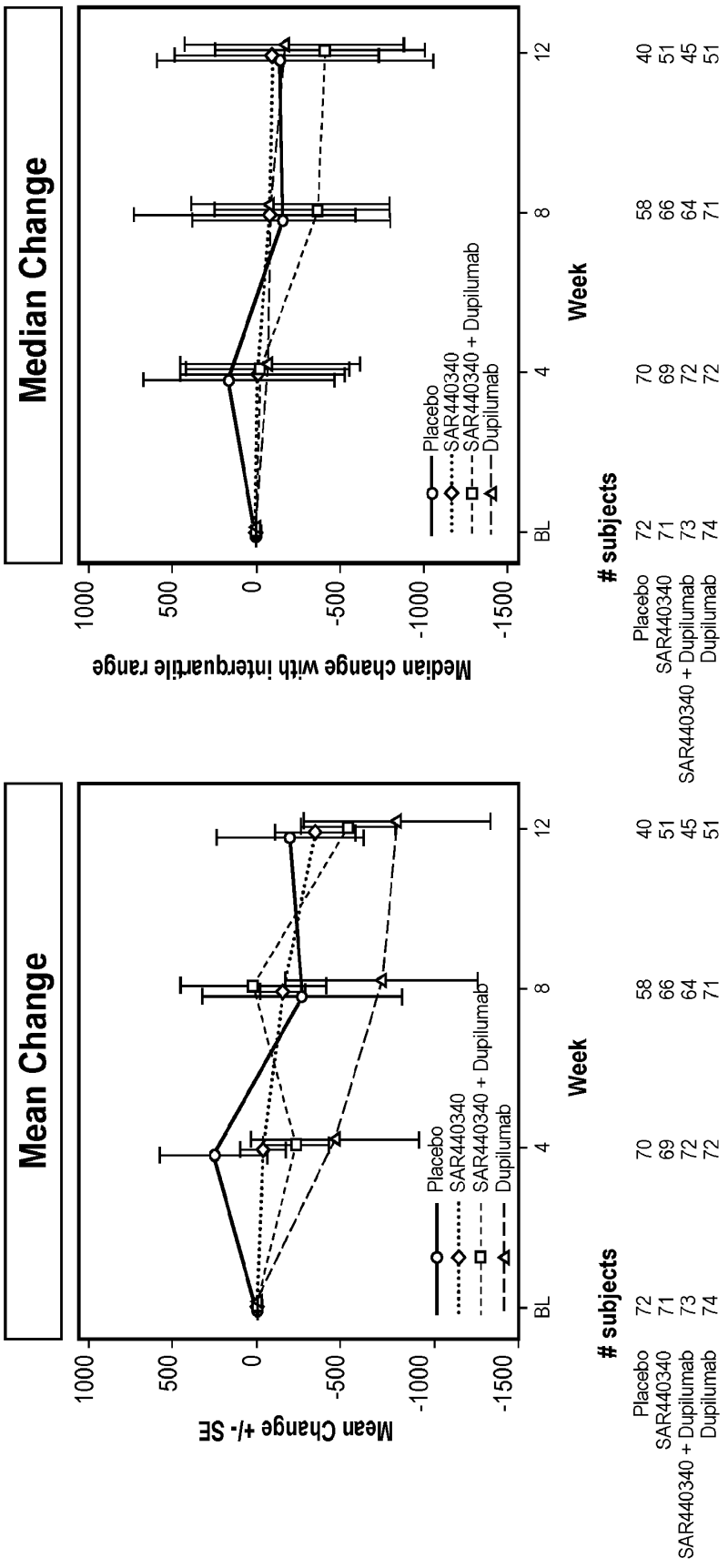

Median Change
Median change with interquartile range
1000
500
0
-500
-1000
-1500
BL
4
8
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 72 70 58 40
SAR440340 71 69 66 51
SAR440340 + Dupilumab 73 72 64 45
Dupilumab 74 72 71 51
Mean Change
Mean Change +/- SE
1000
500
0
-500
-1000
-1500
BL
4
8
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 72 70 58 40
SAR440340 71 69 66 51
SAR440340 + Dupilumab 73 72 64 45
Dupilumab 74 72 71 51

Fig. 42

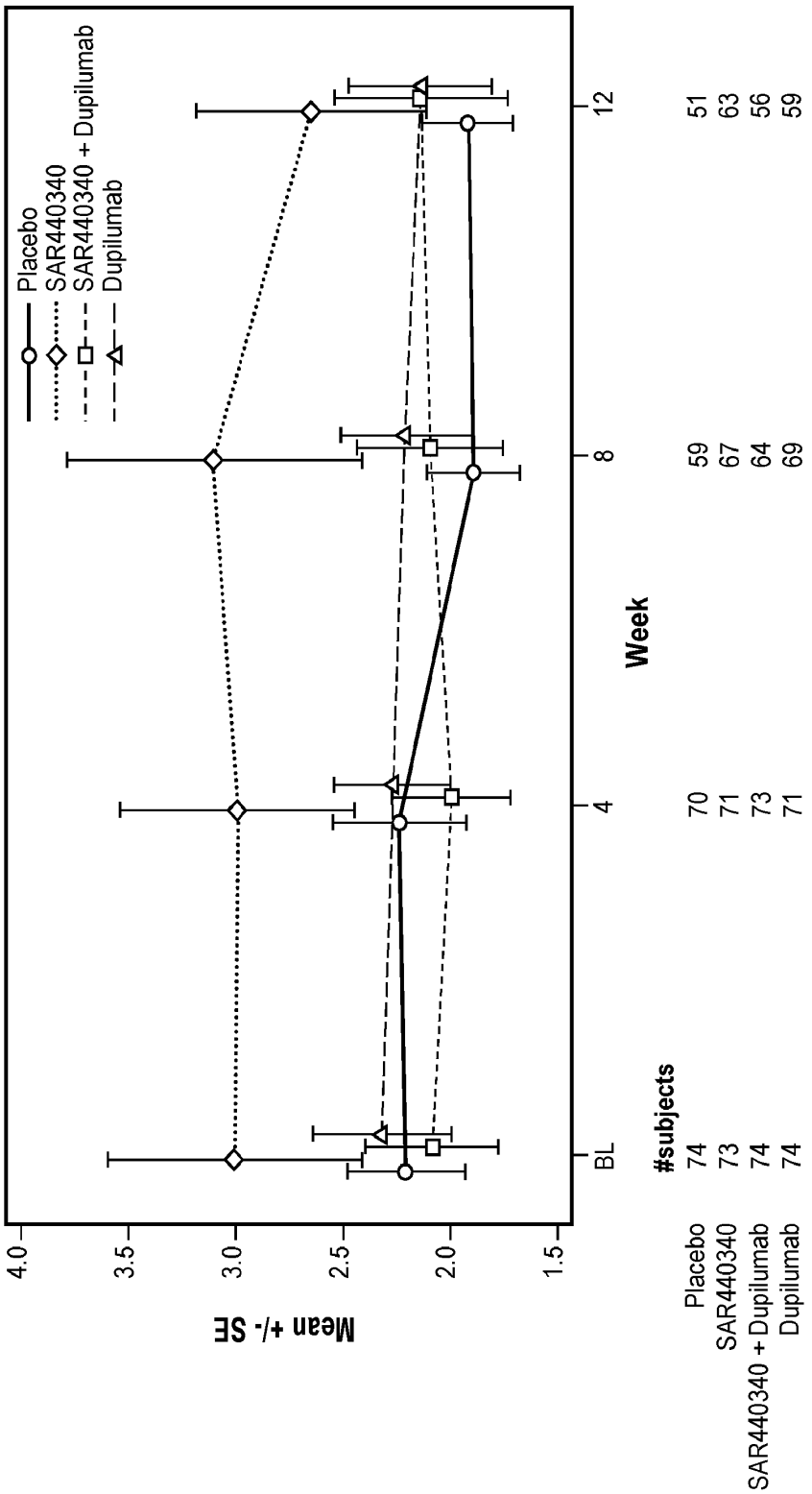

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
4.0
3.5
3.0
2.5
2.0
1.5
BL
4
8
12
Week
#subjects
Placebo 74 70 59 51
SAR440340 73 71 67 63
SAR440340 + Dupilumab 74 73 64 56
Dupilumab 74 71 69 59

Fig. 43

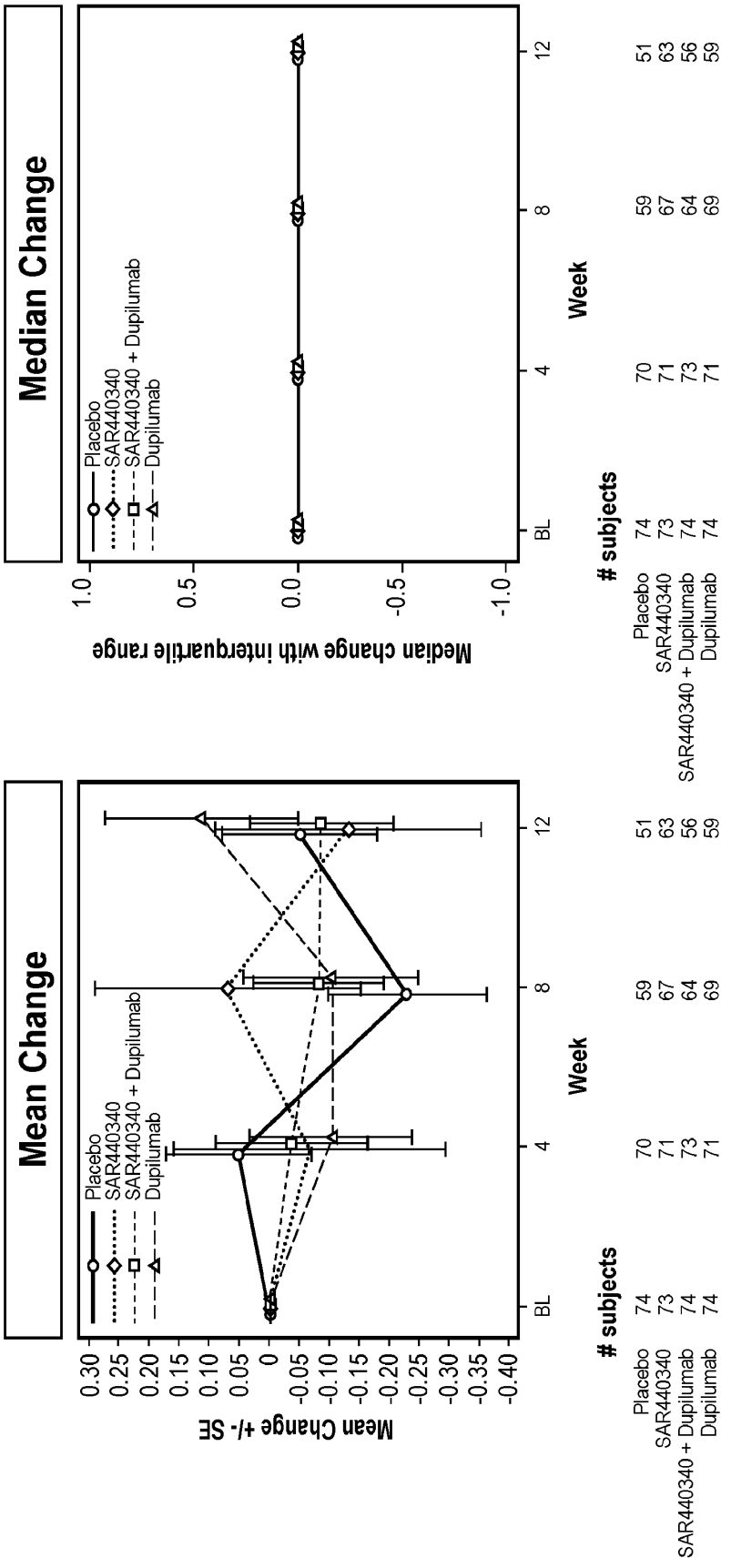

Median Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
1.0
0.5
0.0
-0.5
-1.0
BL
4
8
12
Week
subjects
Placebo 74 70 59 51
SAR440340 73 71 67 63
SAR440340 + Dupilumab 74 73 64 56
Dupilumab 74 71 69 59
Mean Change
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
-0.35
-0.40
BL
4
8
12
Week
subjects
Placebo 74 70 59 51
SAR440340 73 71 67 63
SAR440340 + Dupilumab 74 73 64 56
Dupilumab 74 71 69 59

Fig. 44

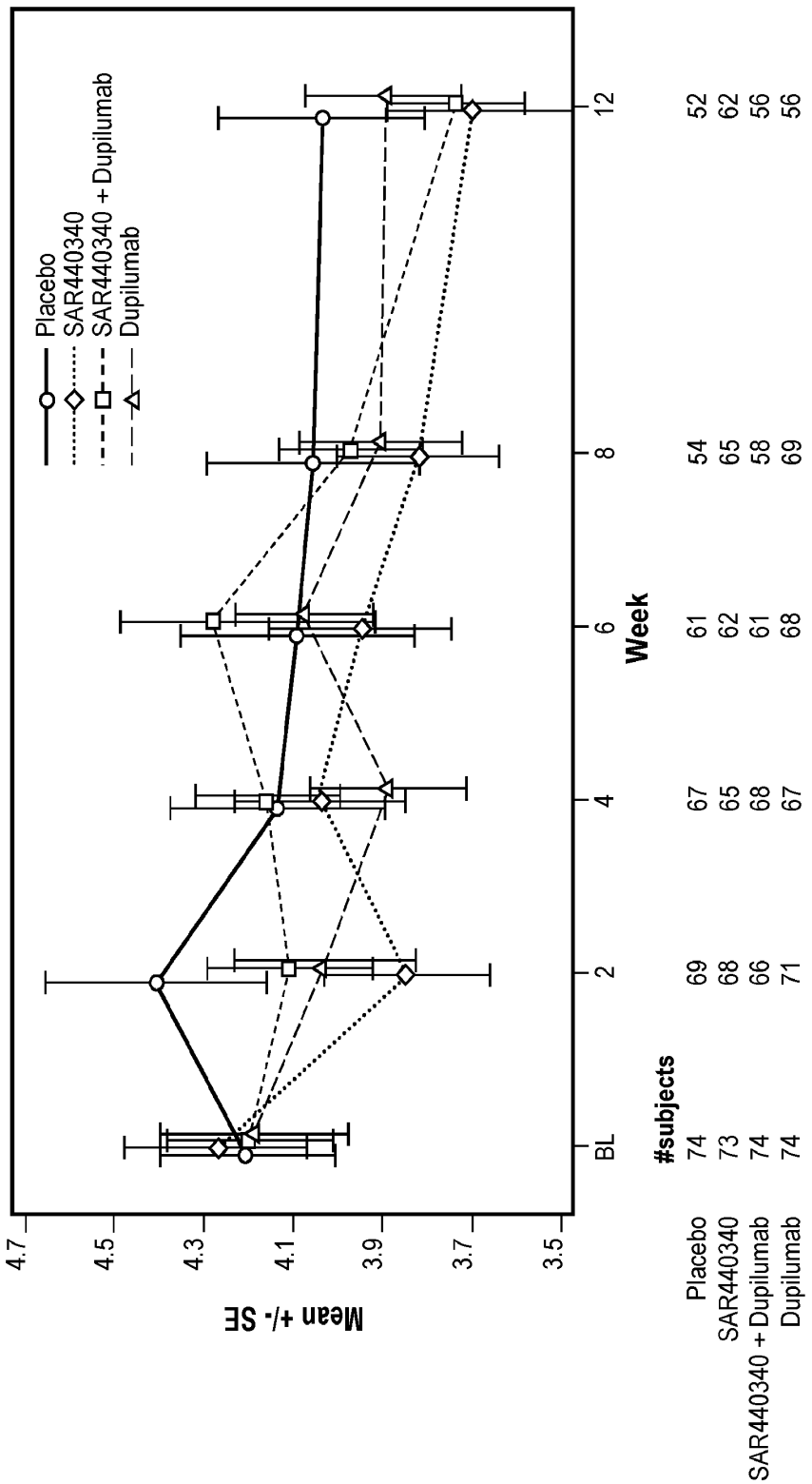

Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean +/- SE
4.7
4.5
4.3
4.1
3.9
3.7
3.5
BL
2
4
6
8
12
Week
#subjects
Placebo 74 69 67 61 54 52
SAR440340 73 68 65 62 65 62
SAR440340 + Dupilumab 74 66 68 61 58 56
Dupilumab 74 71 67 68 69 56

Fig. 45

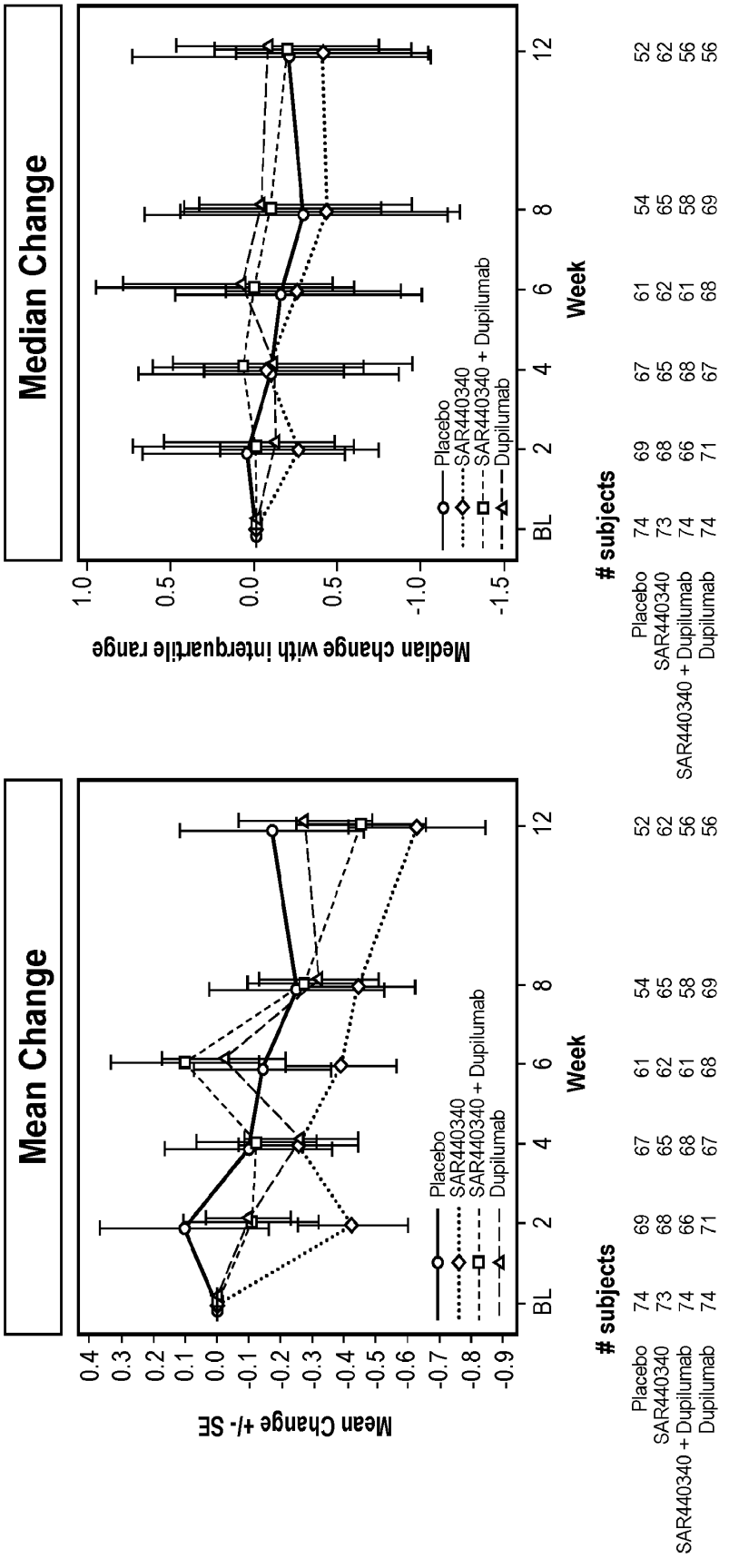

Median Change
Median change with interquartile range
1.0
0.5
0.0
-0.5
-1.0
-1.5
BL
2
4
6
8
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 74 69 67 61 54 52
SAR440340 73 68 65 62 65 62
SAR440340 + Dupilumab 74 66 68 61 58 56
Dupilumab 74 71 67 68 69 56
Mean Change
Mean Change +/- SE
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
-0.8
-0.9
BL
2
4
6
8
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 74 69 67 61 54 52
SAR440340 73 68 65 62 65 62
SAR440340 + Dupilumab 74 66 68 61 58 56
Dupilumab 74 71 67 68 69 56

Fig. 46

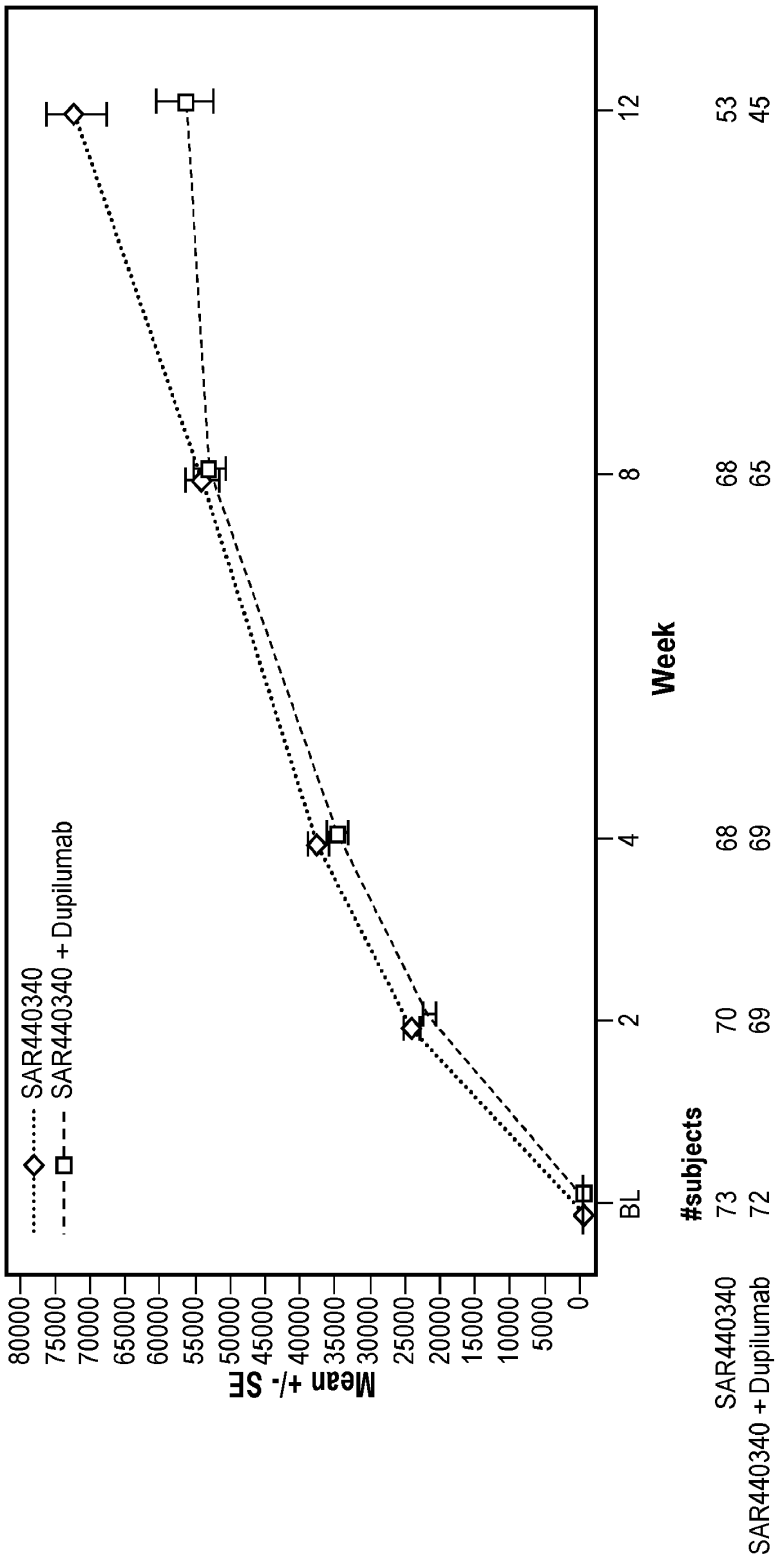

SAR440340
SAR440340 + Dupilumab
Mean +/- SE
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
BL
2
4
8
12
Week
#subjects
SAR440340 73 70 68 68 53
SAR440340 + Dupilumab 72 69 69 65 45

Fig. 47

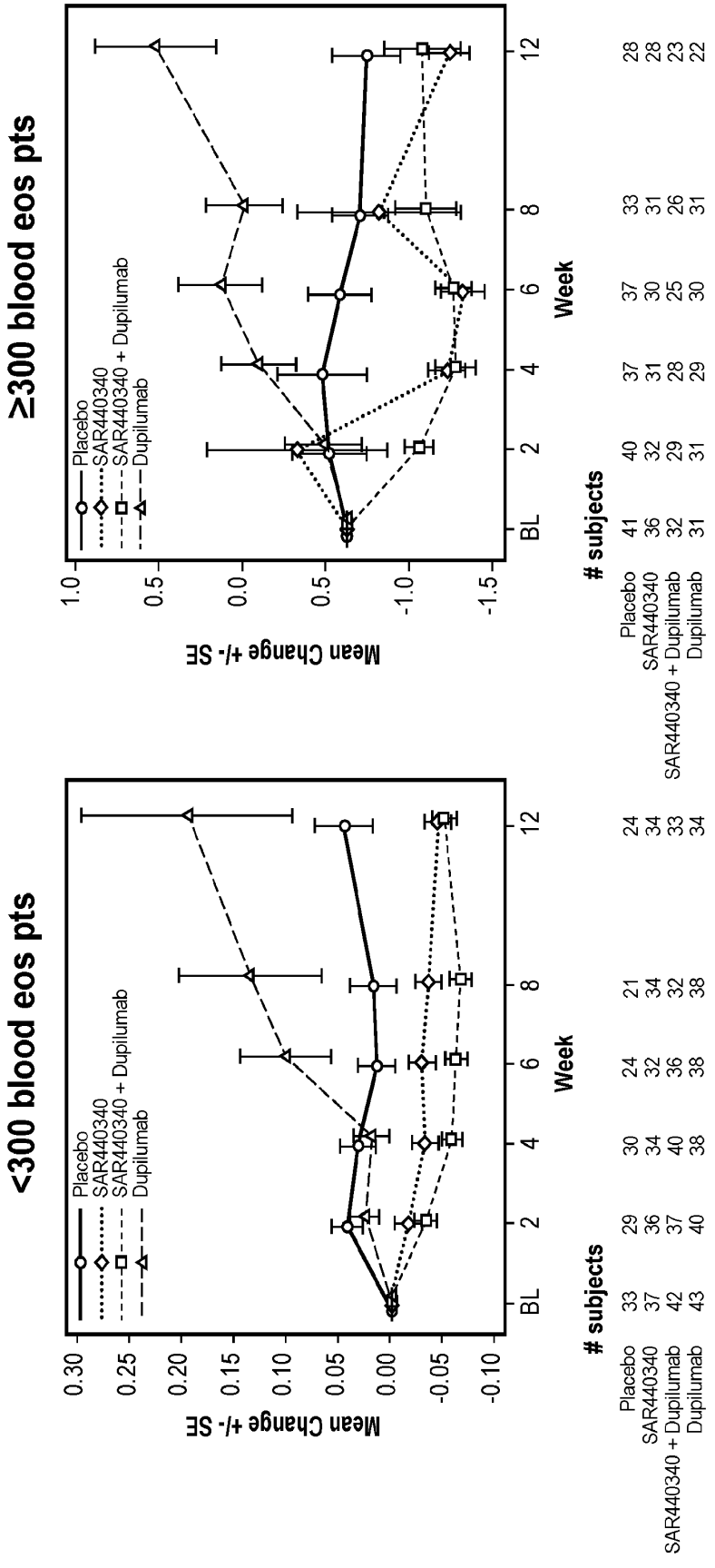

≥300 blood eos pts
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
1.0
0.5
0.0
-0.5
-1.0
-1.5
BL
2
4
6
8
12
Week
subjects
Placebo 41 40 37 37 33 28
SAR440340 36 32 31 30 31 28
SAR440340 + Dupilumab 32 29 28 25 26 23
Dupilumab 31 31 29 30 31 22
<300 blood eos pts
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
BL
2
4
6
8
12
Week
subjects
Placebo 33 29 30 24 21 24
SAR440340 37 36 34 32 34 34
SAR440340 + Dupilumab 42 37 40 36 32 33
Dupilumab 43 40 38 38 38 34

Fig. 48

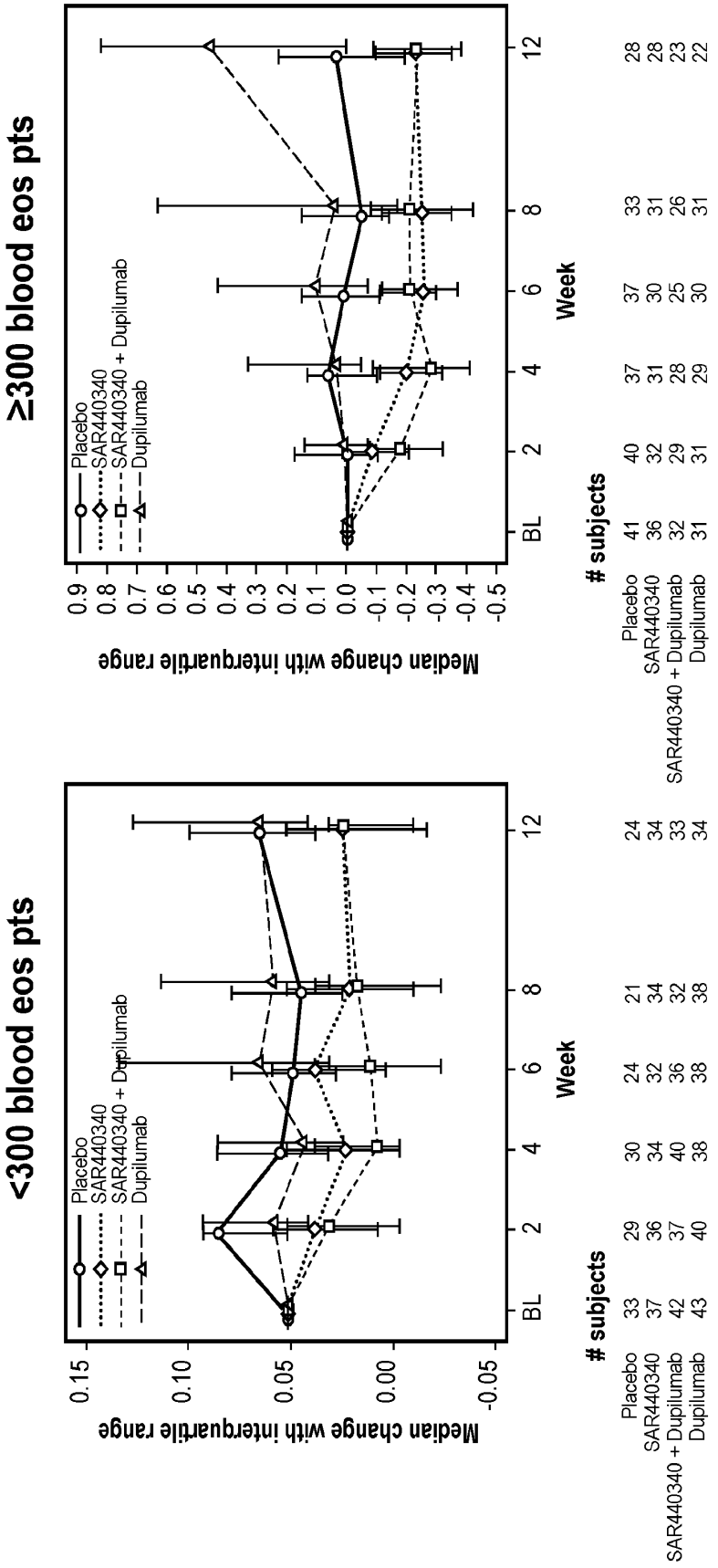

<300 blood eos pts
≥300 blood eos pts
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
Week
BL
subjects
Placebo 33 29 30 24 21 24
SAR440340 37 36 34 32 34 34
SAR440340 + Dupilumab 42 37 40 36 32 33
Dupilumab 43 40 38 38 38 34
Placebo 41 40 37 37 33 28
SAR440340 36 32 31 30 31 28
SAR440340 + Dupilumab 32 29 28 25 26 23
Dupilumab 31 31 29 30 31 22

Fig. 49

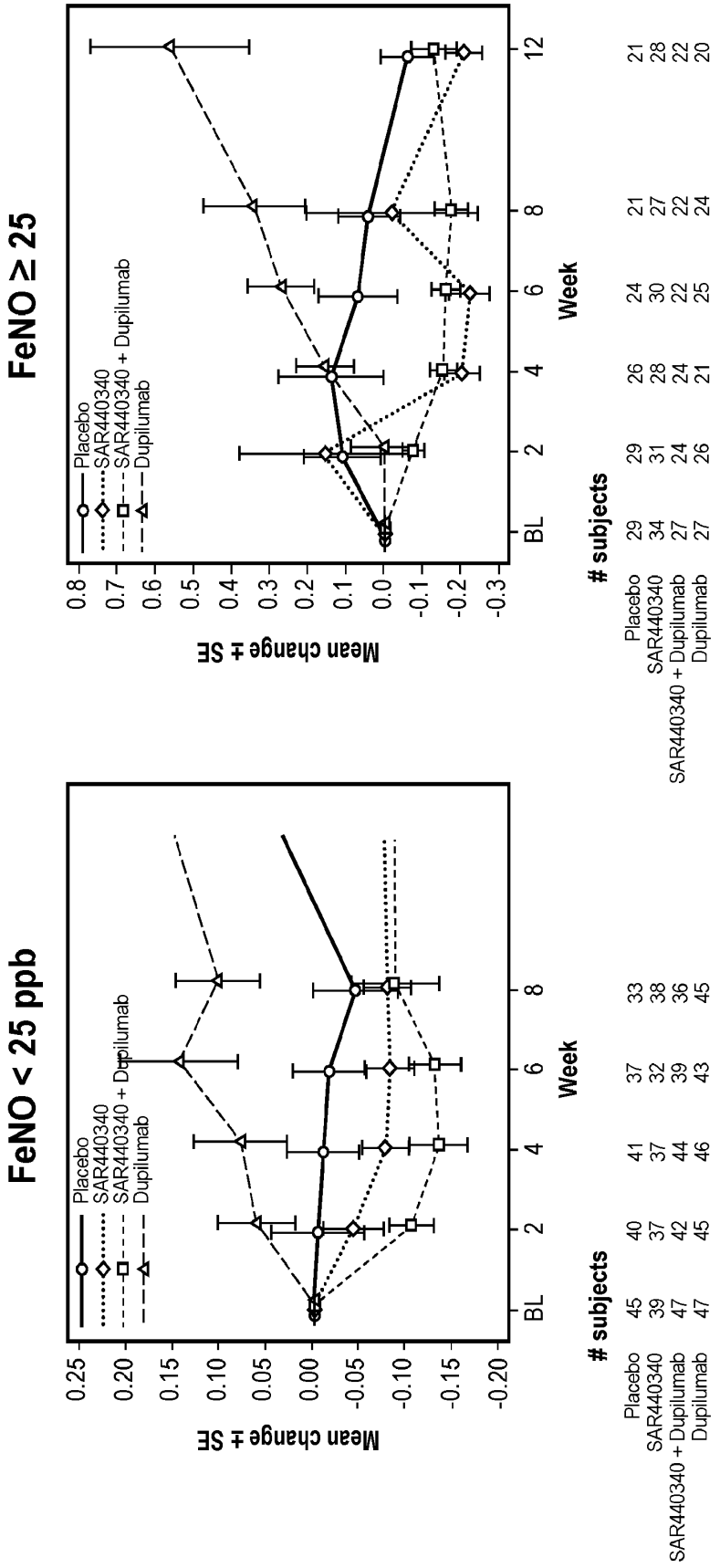

FeNO ≥ 25
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
Week
BL
subjects
Placebo 29 29 26 24 21
SAR440340 34 31 28 30 27
SAR440340 + Dupilumab 27 24 24 22 22
Dupilumab 27 26 21 25 24
FeNO < 25 ppb
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
Week
BL
subjects
Placebo 45 40 41 37 33
SAR440340 39 37 37 32 38
SAR440340 + Dupilumab 47 42 44 39 36
Dupilumab 47 45 46 43 45

Fig. 50

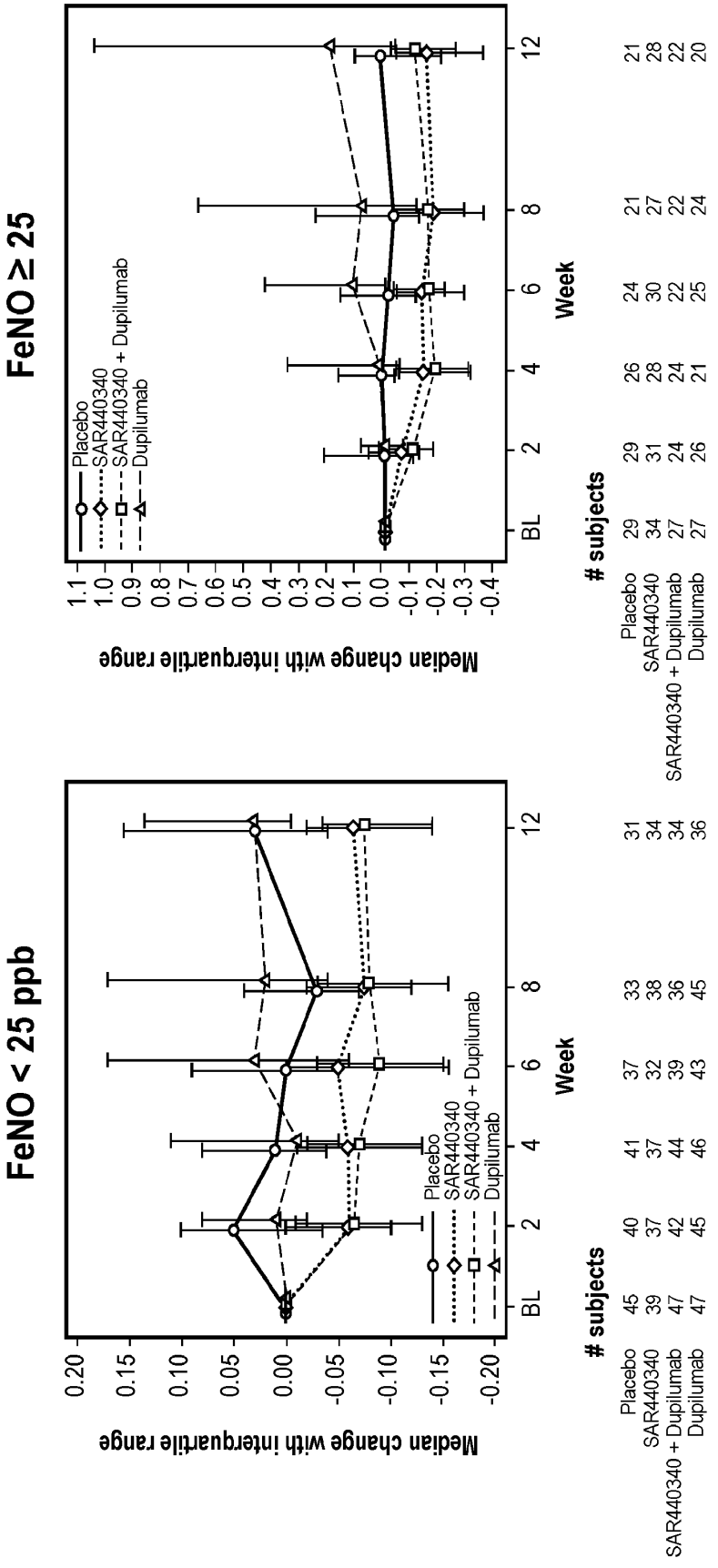

FeNO < 25 ppb
FeNO ≥ 25
Median change with interquartile range
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 45 40 41 37 33 31
SAR440340 39 37 37 32 38 34
SAR440340 + Dupilumab 47 42 44 39 36 34
Dupilumab 47 45 46 43 45 36
Placebo 29 29 26 24 21 21
SAR440340 34 31 28 30 27 28
SAR440340 + Dupilumab 27 24 24 22 22 22
Dupilumab 27 26 21 25 24 20

Fig. 51

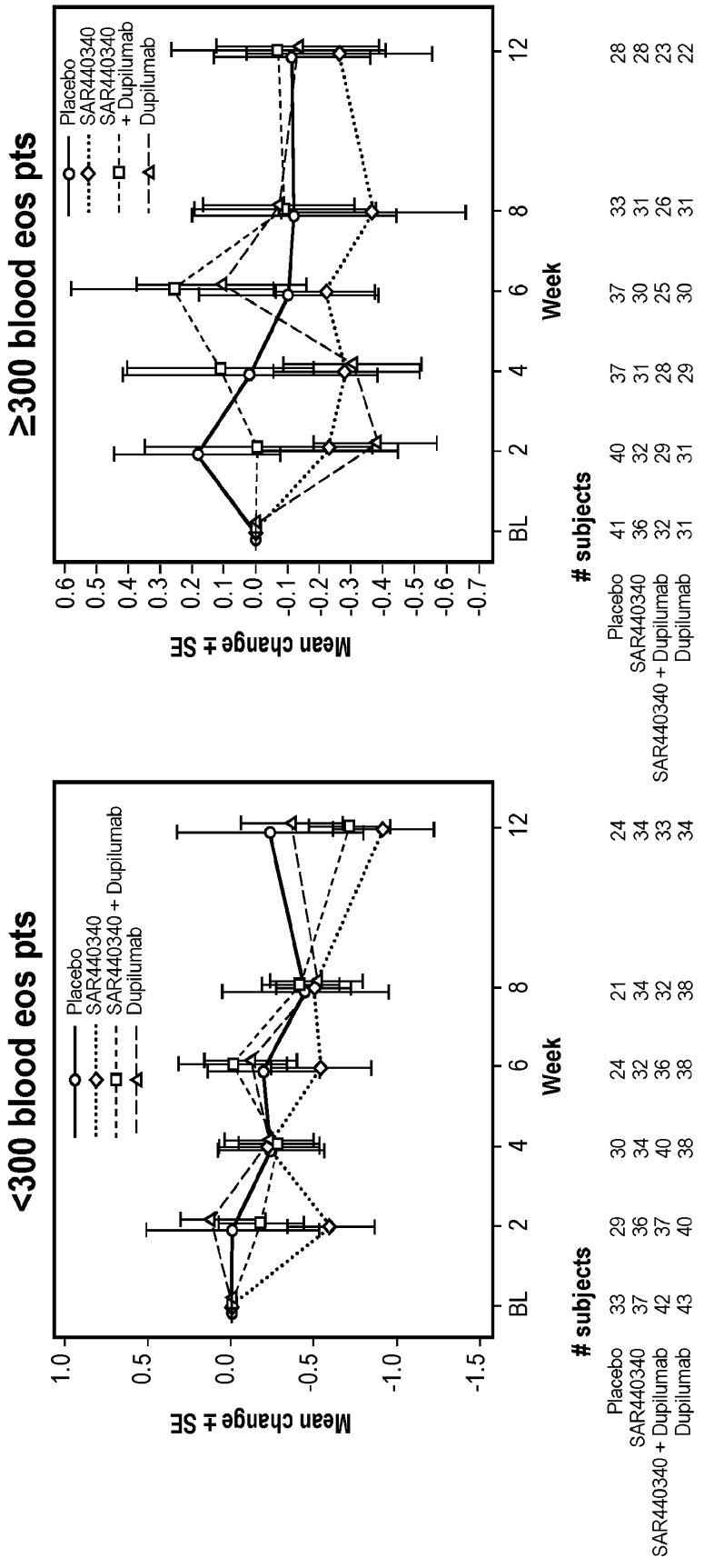

<300 blood eos pts
≥300 blood eos pts
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
Week
BL
subjects
Placebo 33 29 30 24 21 24
SAR440340 37 36 34 32 34 34
SAR440340 + Dupilumab 42 37 40 36 32 33
Dupilumab 43 40 38 38 38 34
Placebo 41 40 37 37 33 28
SAR440340 36 32 31 30 31 28
SAR440340 + Dupilumab 32 29 28 25 26 23
Dupilumab 31 31 29 30 31 22

Fig. 52

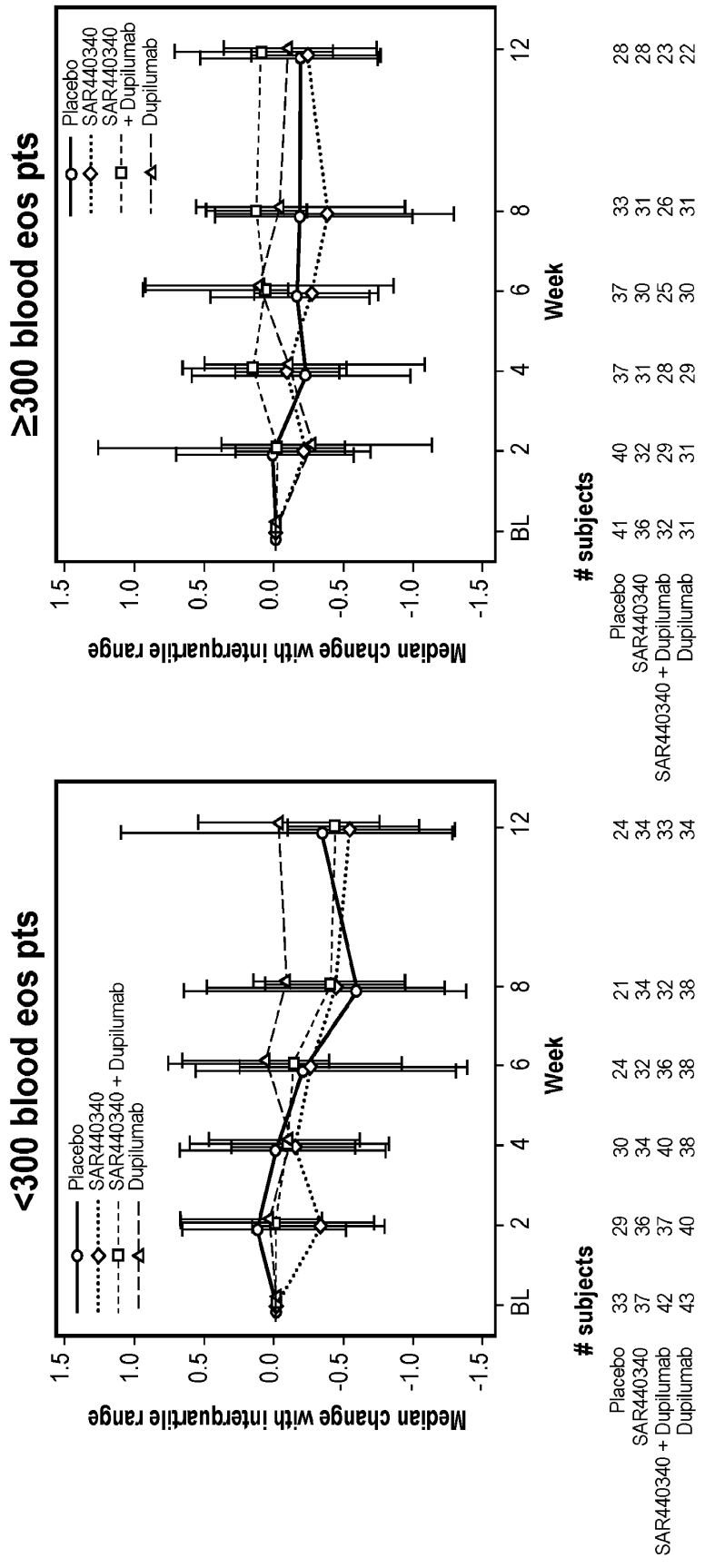

≥300 blood eos pts
<300 blood eos pts
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
Week
BL
subjects
Placebo 41 40 37 37 33 28
SAR440340 36 32 31 30 31 28
SAR440340 + Dupilumab 32 29 28 25 26 23
Dupilumab 31 31 29 30 31 22
Placebo 33 29 30 24 21 24
SAR440340 37 36 34 32 34 34
SAR440340 + Dupilumab 42 37 40 36 32 33
Dupilumab 43 40 38 38 38 34

Fig. 53

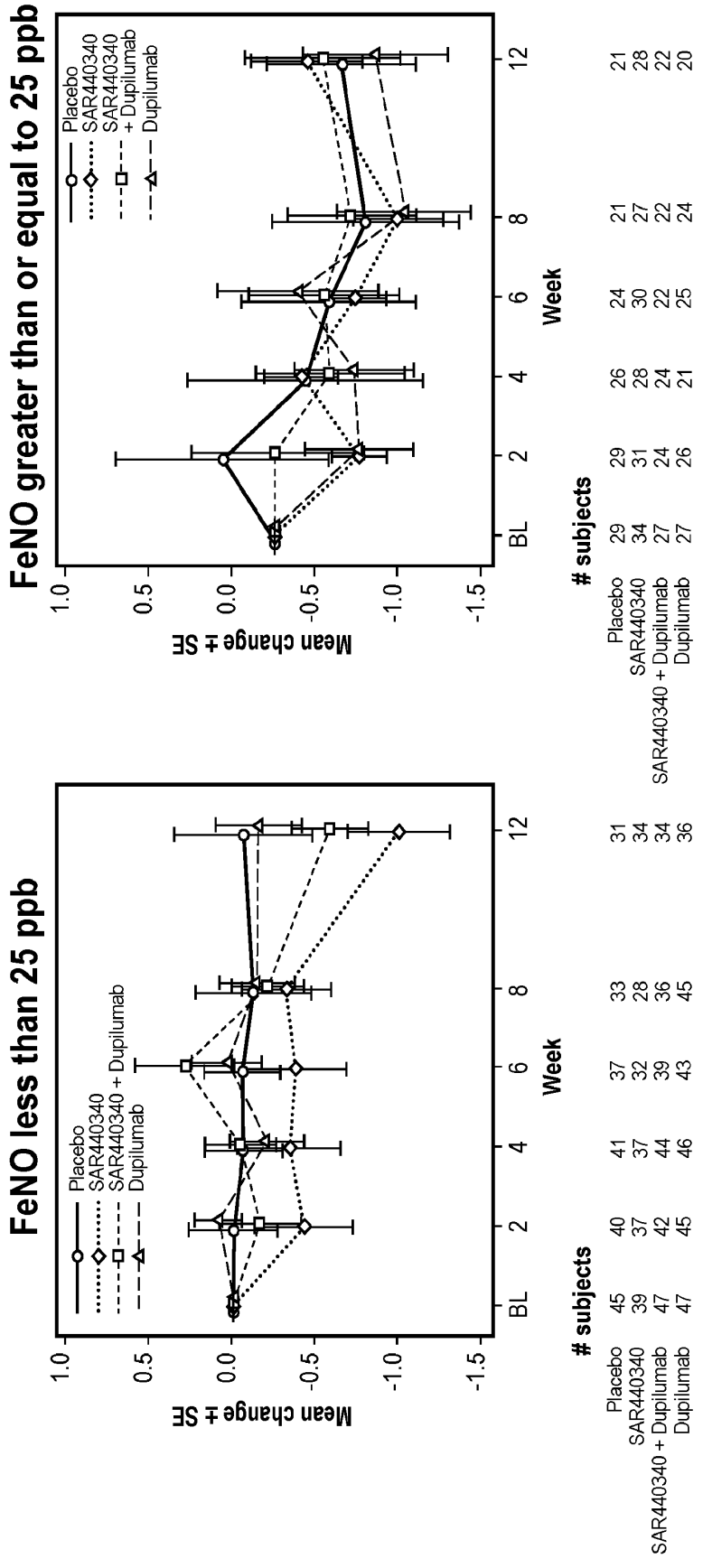

FeNO less than 25 ppb
FeNO greater than or equal to 25 ppb
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
1.0
0.5
0.0
-0.5
-1.0
-1.5
BL
2
4
6
8
12
Week
subjects
Placebo 45 40 41 37 33 31
SAR440340 39 37 37 32 28 34
SAR440340 + Dupilumab 47 42 44 39 36 34
Dupilumab 47 45 46 43 45 36
Placebo 29 29 26 24 21 21
SAR440340 34 31 28 30 27 28
SAR440340 + Dupilumab 27 24 24 22 22 22
Dupilumab 27 26 21 25 24 20

Fig. 54

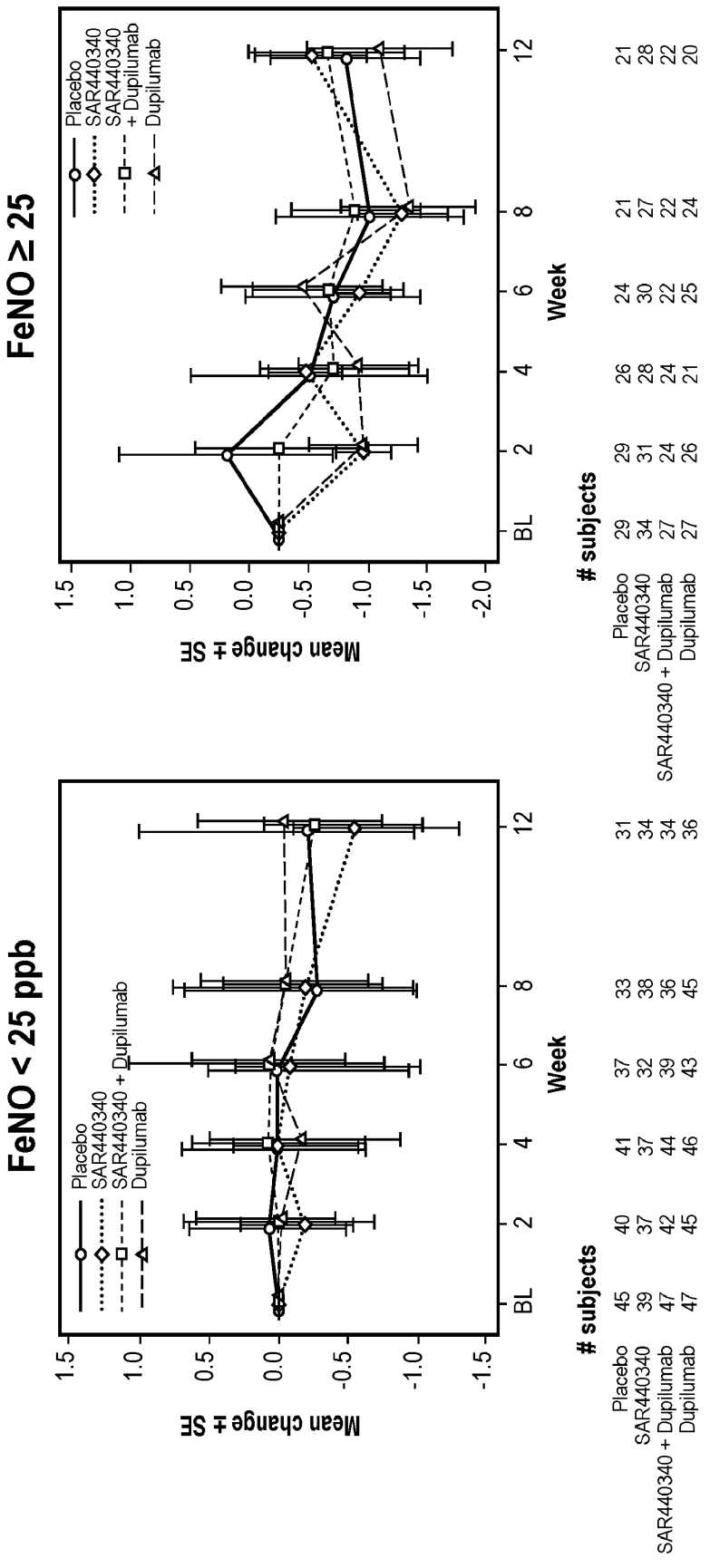

FeNO < 25 ppb
FeNO ≥ 25
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
Week
BL
subjects
Placebo 45 40 41 37 33 31
SAR440340 39 37 37 32 38 34
SAR440340 + Dupilumab 47 42 44 39 36 34
Dupilumab 47 45 46 43 45 36
Placebo 29 29 26 24 21 21
SAR440340 34 31 28 30 27 28
SAR440340 + Dupilumab 27 24 24 22 22 22
Dupilumab 27 26 21 25 24 20

Fig. 55

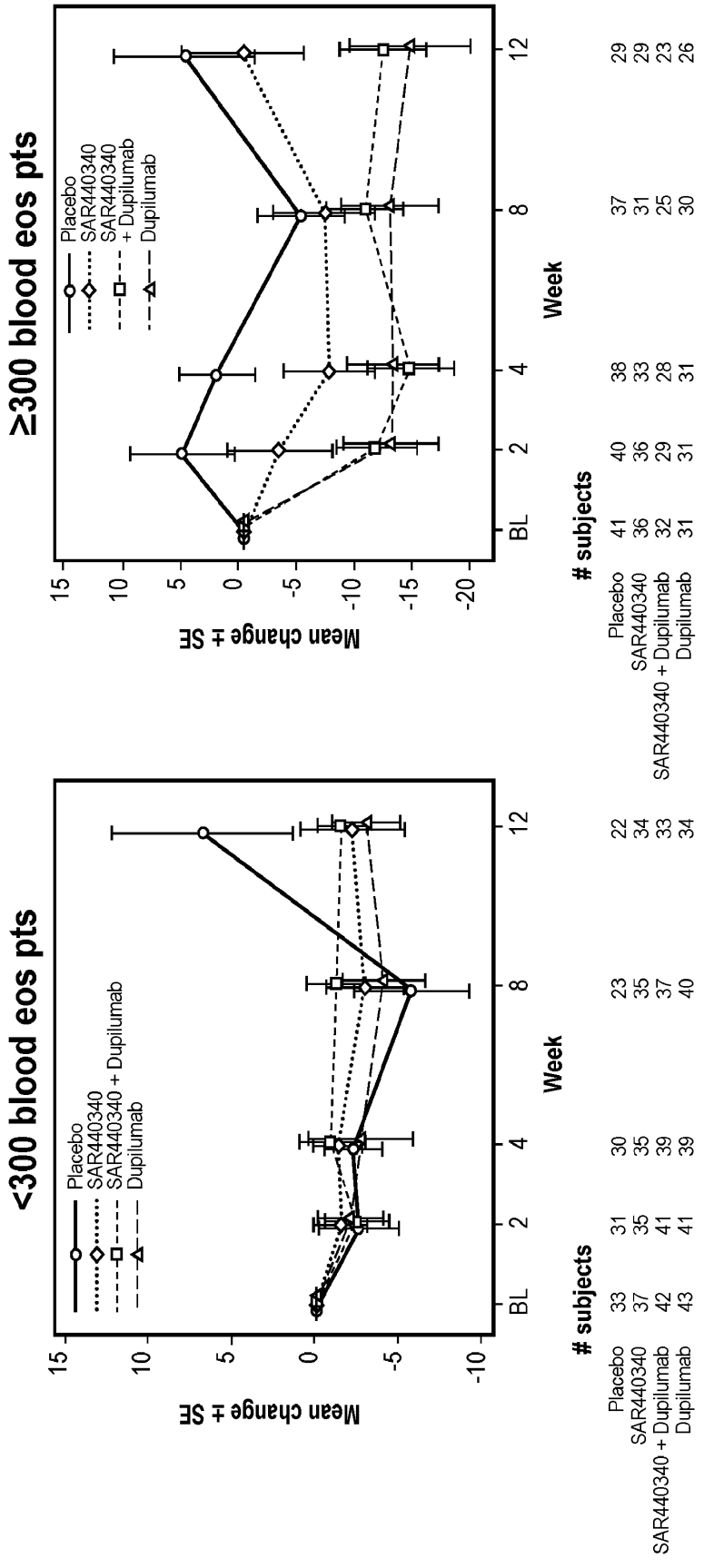

<300 blood eos pts
≥300 blood eos pts
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
Week
BL
subjects
Placebo 33 31 30 23 22
SAR440340 37 35 35 35 34
SAR440340 + Dupilumab 42 41 39 37 33
Dupilumab 43 41 39 40 34
Placebo 41 40 38 37 29
SAR440340 36 36 33 31 29
SAR440340 + Dupilumab 32 29 28 25 23
Dupilumab 31 31 31 30 26

Fig. 56

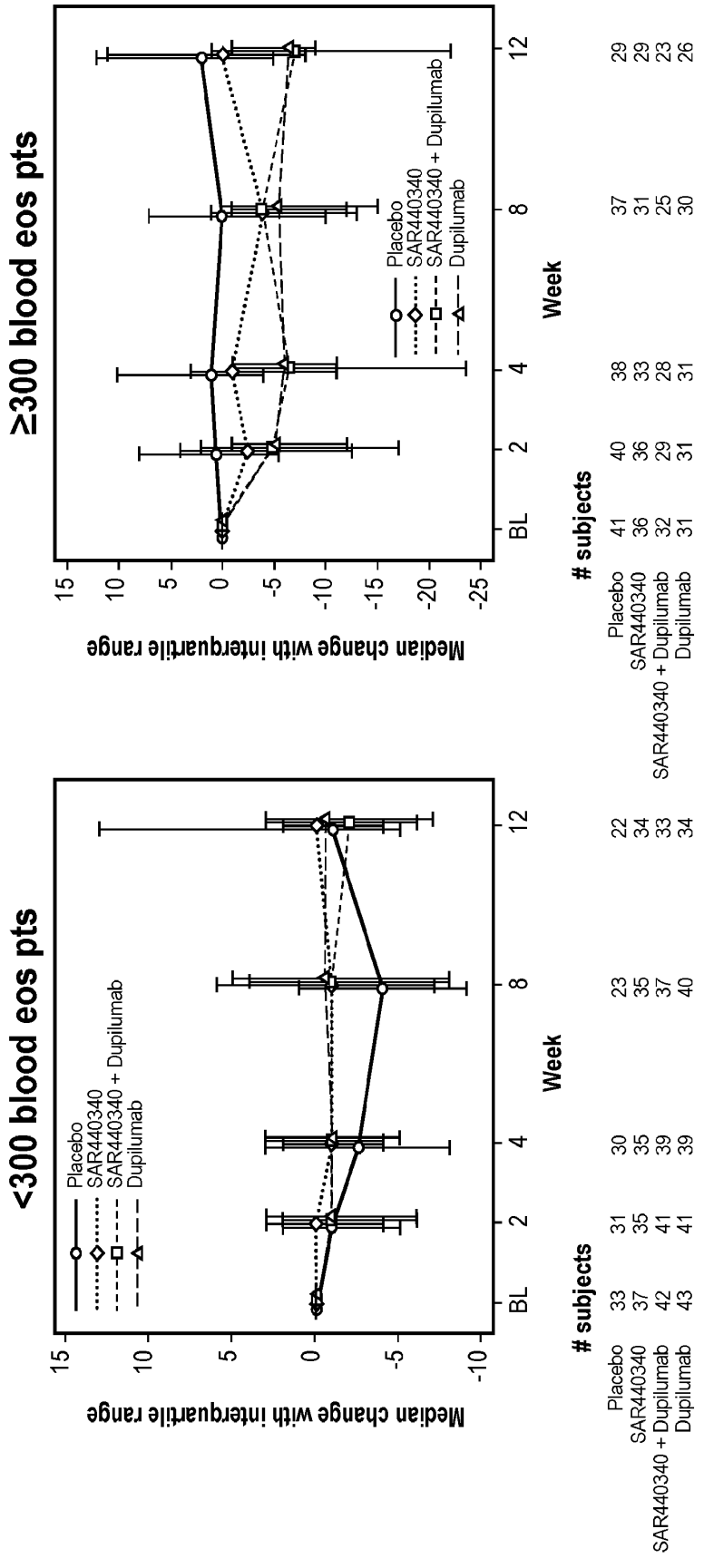

<300 blood eos pts
≥300 blood eos pts
Median change with interquartile range
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 33 31 30 23 22
SAR440340 37 35 35 35 34
SAR440340 + Dupilumab 42 41 39 37 33
Dupilumab 43 41 39 40 34
Placebo 41 40 38 37 29
SAR440340 36 36 33 31 29
SAR440340 + Dupilumab 32 29 28 25 23
Dupilumab 31 31 31 30 26

Fig. 57

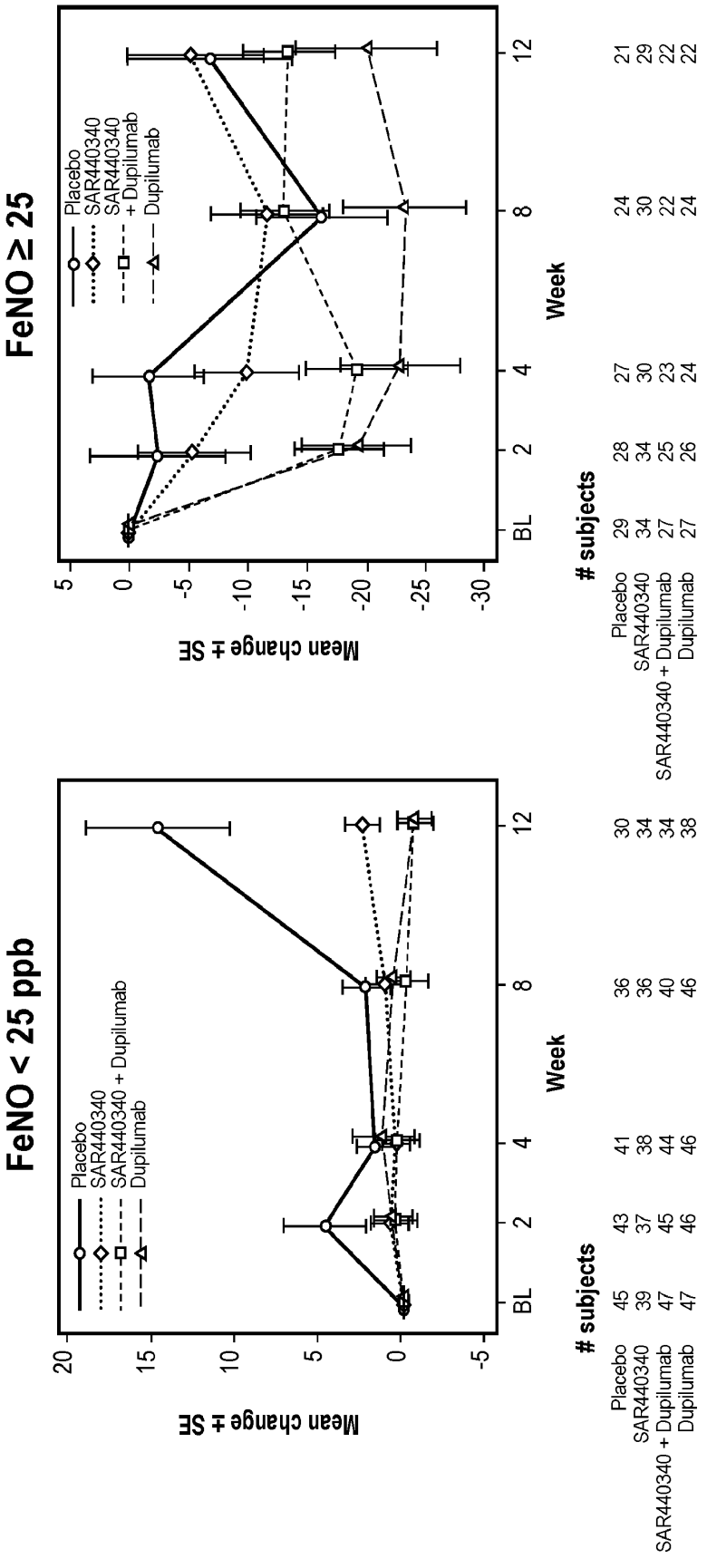

FeNO ≥ 25
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
5
0
-5
-10
-15
-20
-25
-30
BL
2
4
8
12
Week
subjects
Placebo 29 28 27 24 21
SAR440340 34 34 30 30 29
SAR440340 + Dupilumab 27 25 23 22 22
Dupilumab 27 26 24 24 22
FeNO < 25 ppb
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
20
15
10
5
0
-5
BL
2
4
8
12
Week
subjects
Placebo 45 43 41 36 30
SAR440340 39 37 38 36 34
SAR440340 + Dupilumab 47 45 44 40 34
Dupilumab 47 46 46 46 38

Fig. 58

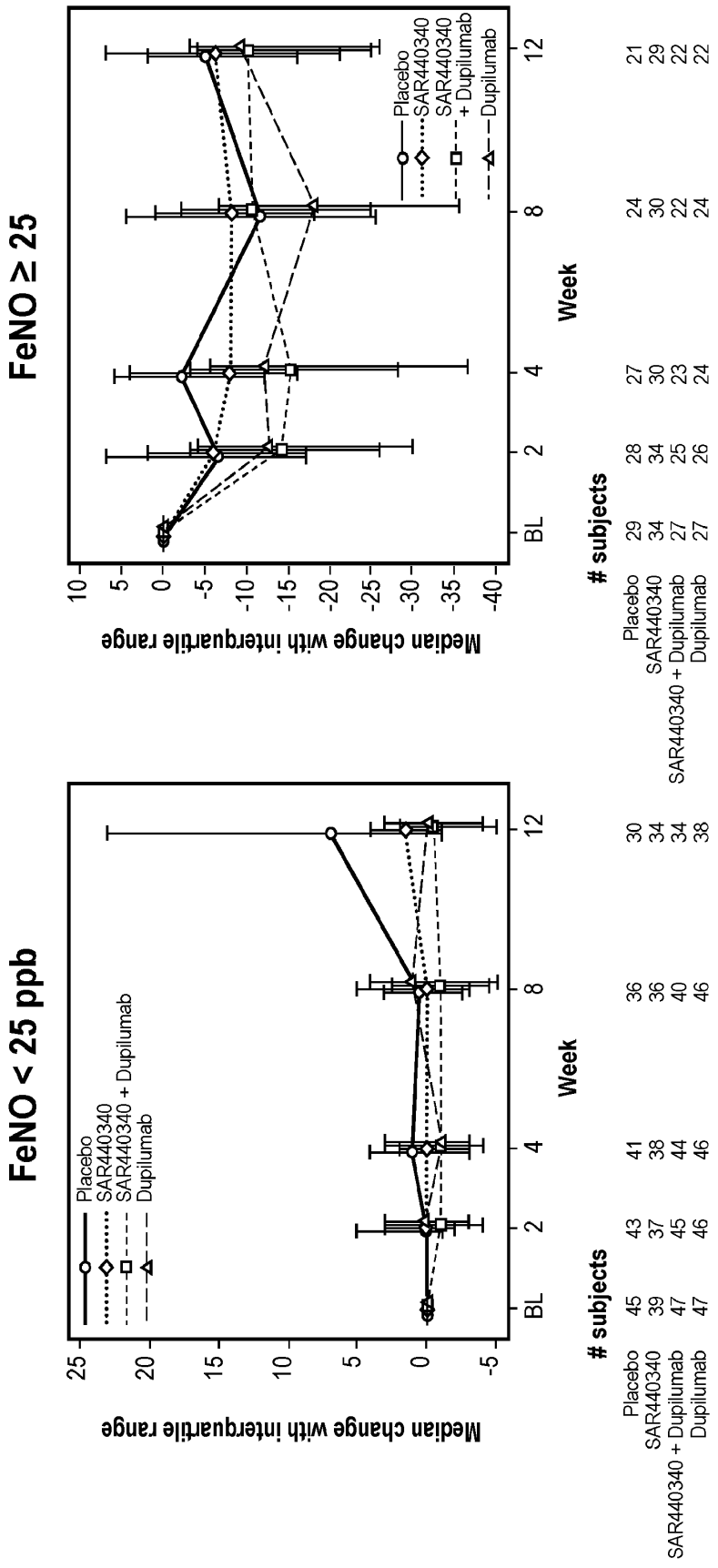

FeNO < 25 ppb
Median change with interquartile range
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 45 43 41 36 30
SAR440340 39 37 38 36 34
SAR440340 + Dupilumab 47 45 44 40 34
Dupilumab 47 46 46 46 38
FeNO ≥ 25
Median change with interquartile range
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 29 28 27 24 21
SAR440340 34 34 30 30 29
SAR440340 + Dupilumab 27 25 23 22 22
Dupilumab 27 26 24 24 22

Fig. 59

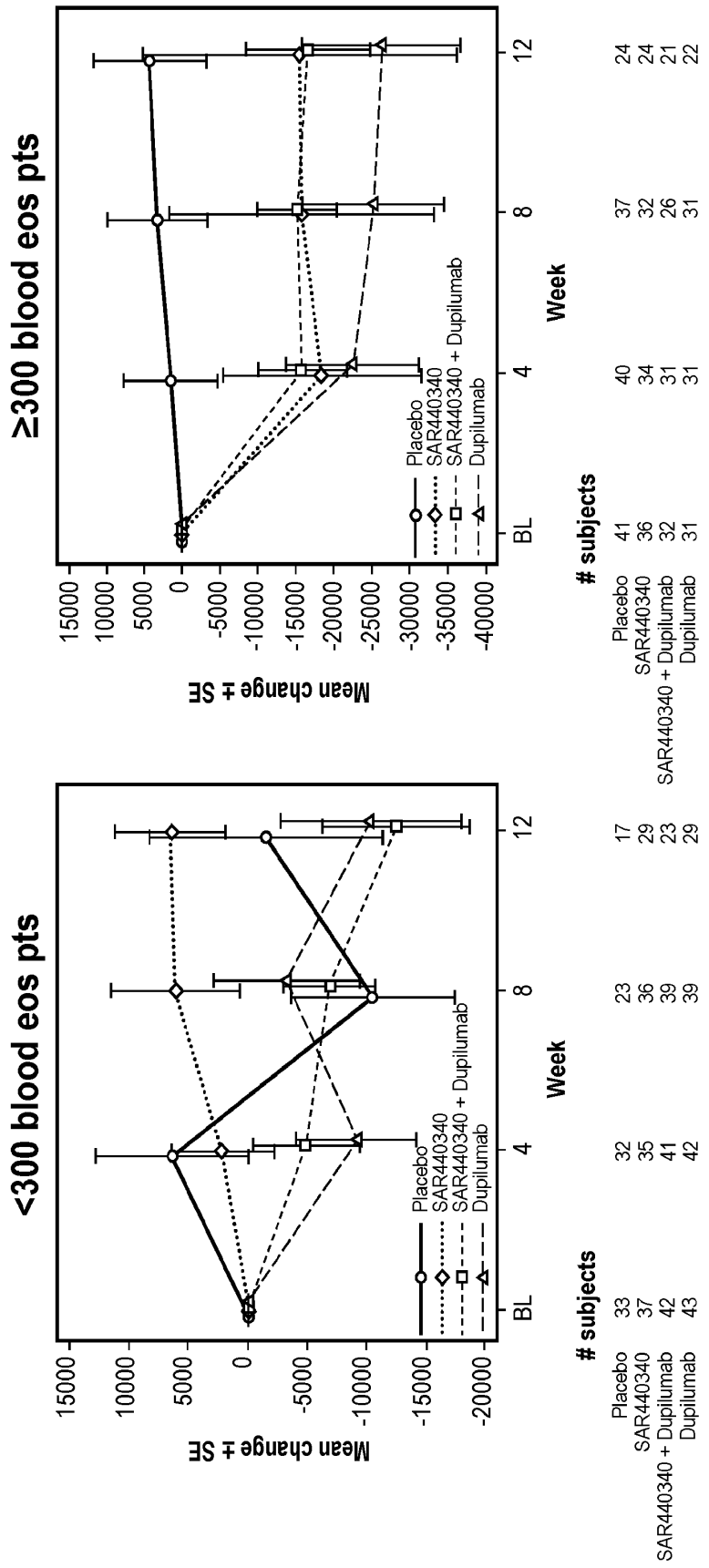

<300 blood eos pts
≥300 blood eos pts
Mean change ± SE
Week
BL
4
8
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 33 32 23 17
SAR440340 37 35 36 29
SAR440340 + Dupilumab 42 41 39 23
Dupilumab 43 42 39 29
Placebo 41 40 37 24
SAR440340 36 34 32 24
SAR440340 + Dupilumab 32 31 26 21
Dupilumab 31 31 31 22

Fig. 60

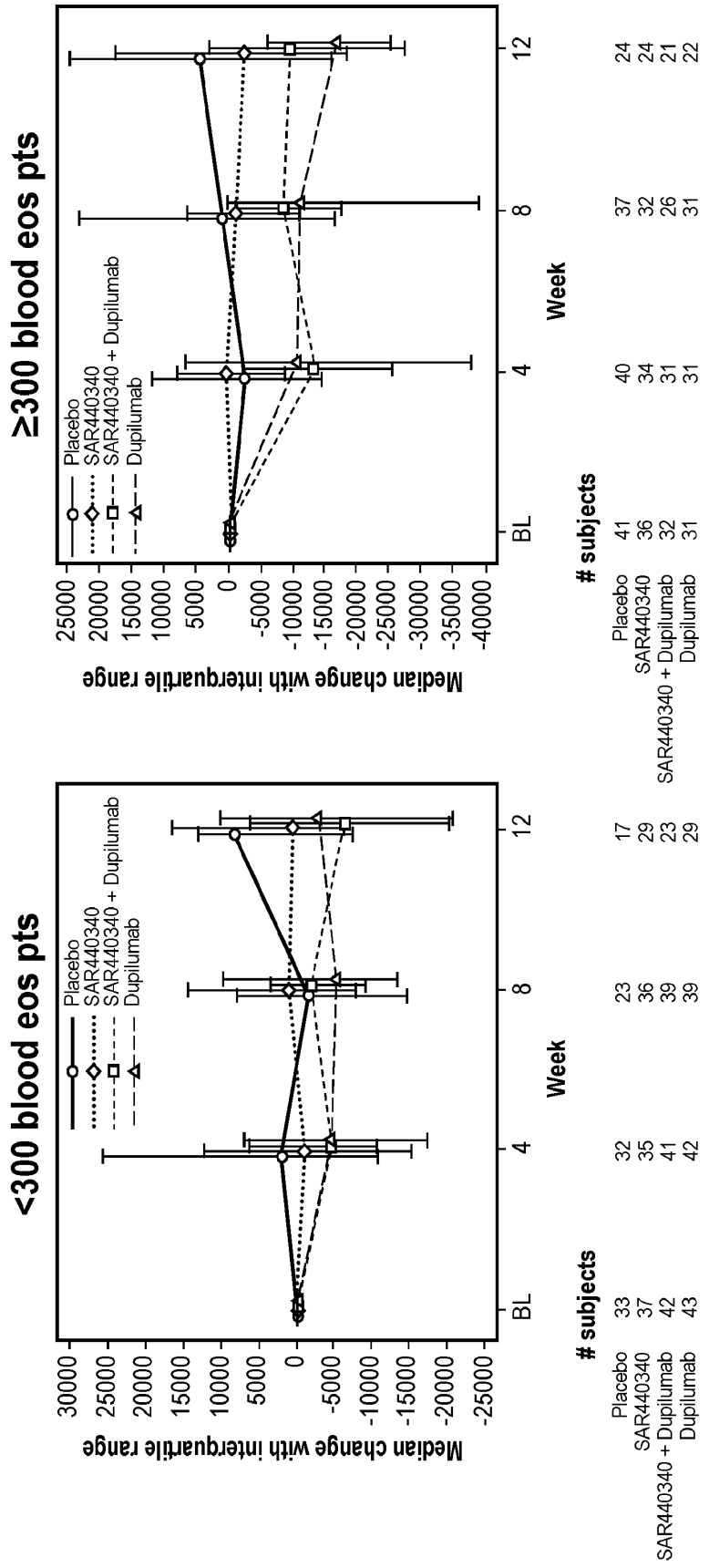

<300 blood eos pts
≥300 blood eos pts
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
Week
BL
4
8
12
subjects
Placebo 33 32 23 17
SAR440340 37 35 36 29
SAR440340 + Dupilumab 42 41 39 23
Dupilumab 43 42 39 29
Placebo 41 40 37 24
SAR440340 36 34 32 24
SAR440340 + Dupilumab 32 31 26 21
Dupilumab 31 31 31 22

Fig. 61

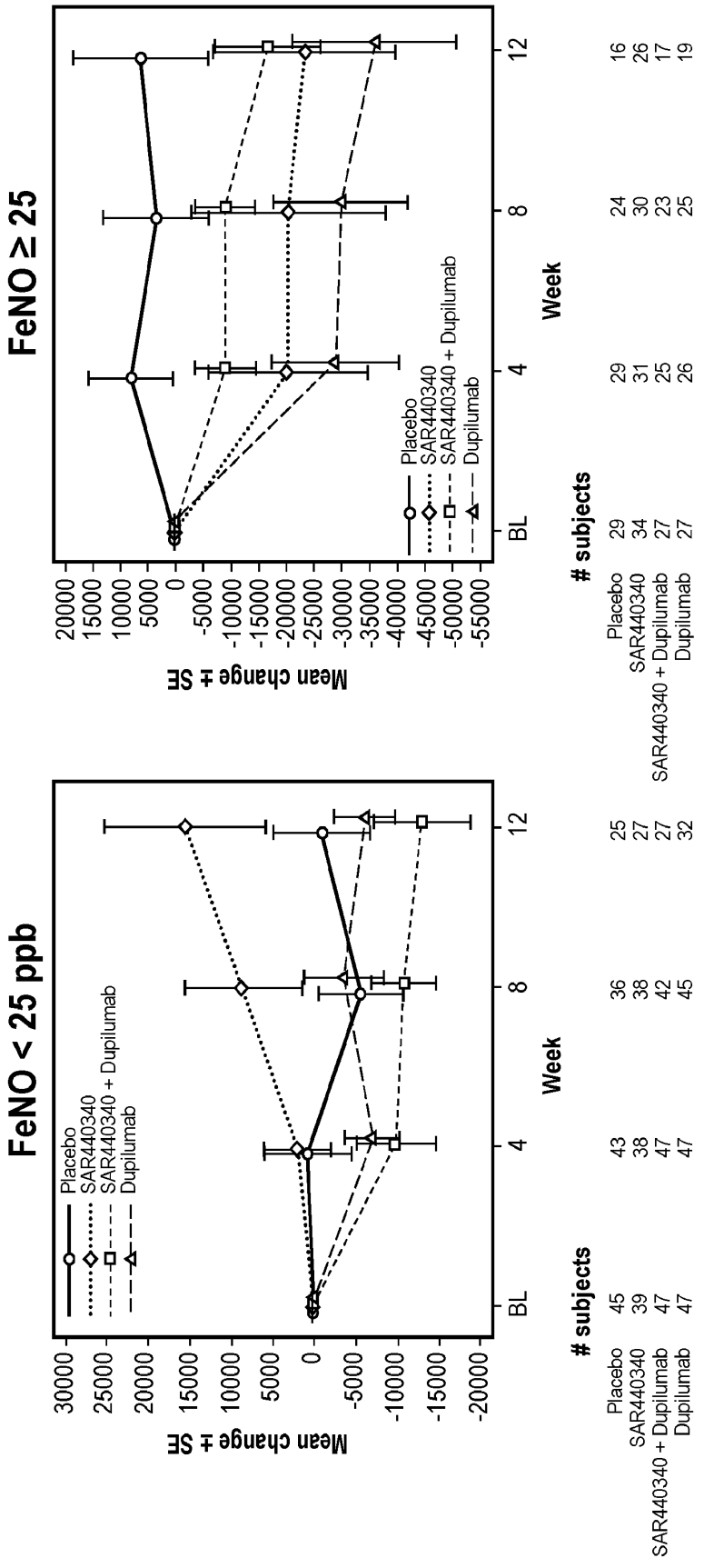

FeNO < 25 ppb
FeNO ≥ 25
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
Week
BL
subjects
Placebo 45 43 36 25
SAR440340 39 38 38 27
SAR440340 + Dupilumab 47 47 42 27
Dupilumab 47 47 45 32
Placebo 29 29 24 16
SAR440340 34 31 30 26
SAR440340 + Dupilumab 27 25 23 17
Dupilumab 27 26 25 19

Fig. 62

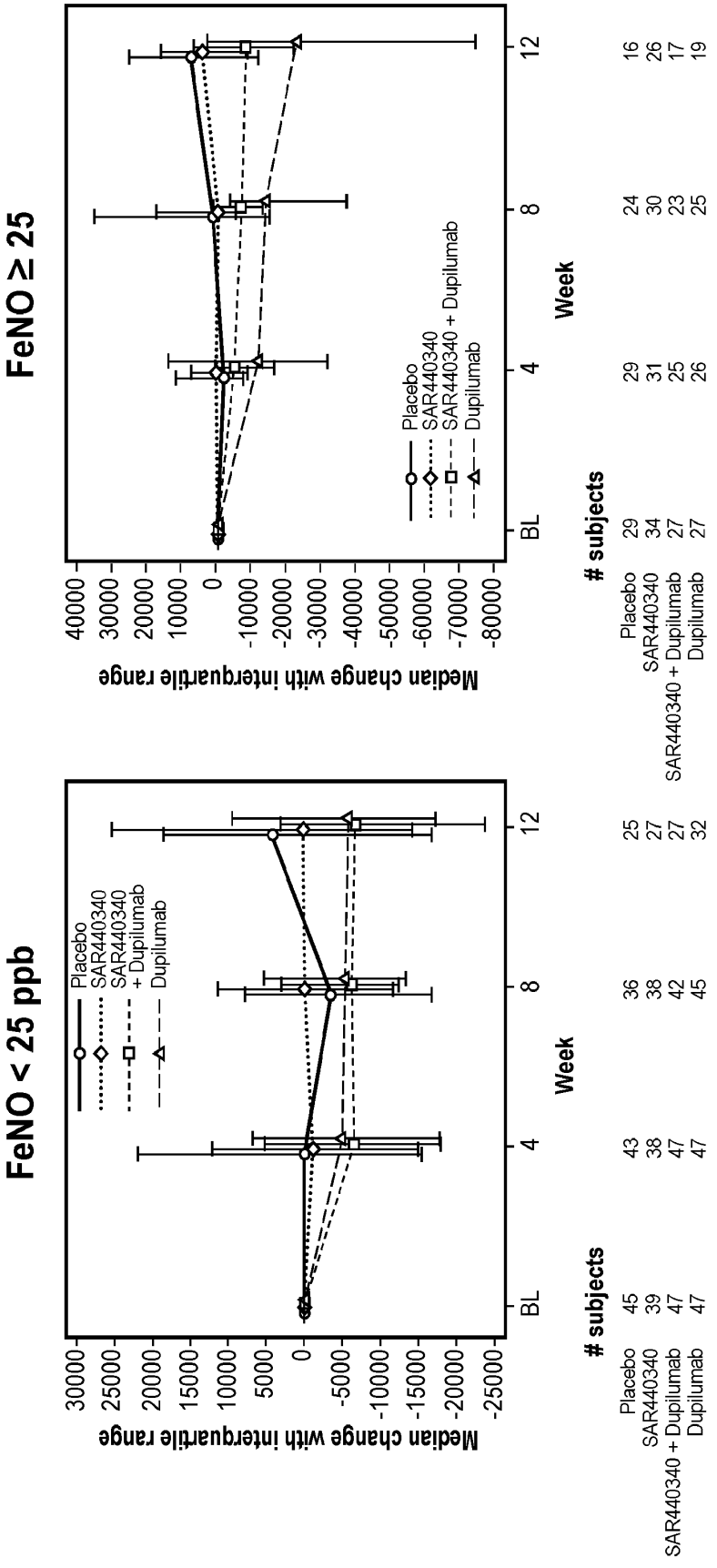

FeNO < 25 ppb
Median change with interquartile range
30000
25000
20000
15000
10000
5000
0
-5000
-10000
-15000
-20000
-25000
BL
4
8
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 45 43 36 25
SAR440340 39 38 38 27
SAR440340 + Dupilumab 47 47 42 27
Dupilumab 47 47 45 32
FeNO ≥ 25
Median change with interquartile range
40000
30000
20000
10000
0
-10000
-20000
-30000
-40000
-50000
-60000
-70000
-80000
BL
4
8
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 29 29 24 16
SAR440340 34 31 30 26
SAR440340 + Dupilumab 27 25 23 17
Dupilumab 27 26 25 19

Fig. 63

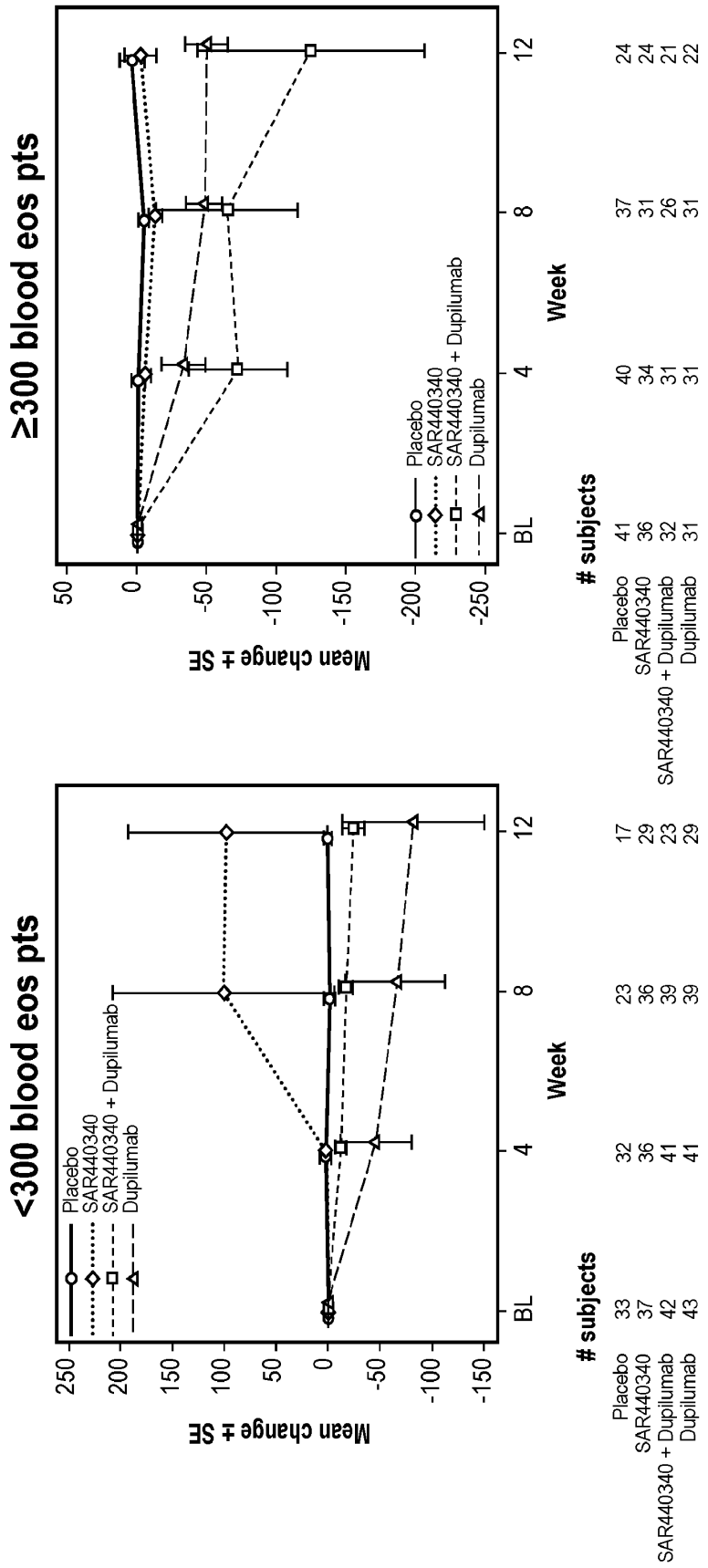

≥300 blood eos pts
Mean change ± SE
50
0
-50
-100
-150
-200
-250
BL
4
8
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 41 40 37 24
SAR440340 36 34 31 24
SAR440340 + Dupilumab 32 31 26 21
Dupilumab 31 31 31 22
<300 blood eos pts
Mean change ± SE
250
200
150
100
50
0
-50
-100
-150
BL
4
8
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 33 32 23 17
SAR440340 37 36 36 29
SAR440340 + Dupilumab 42 41 39 23
Dupilumab 43 41 39 29

Fig. 64

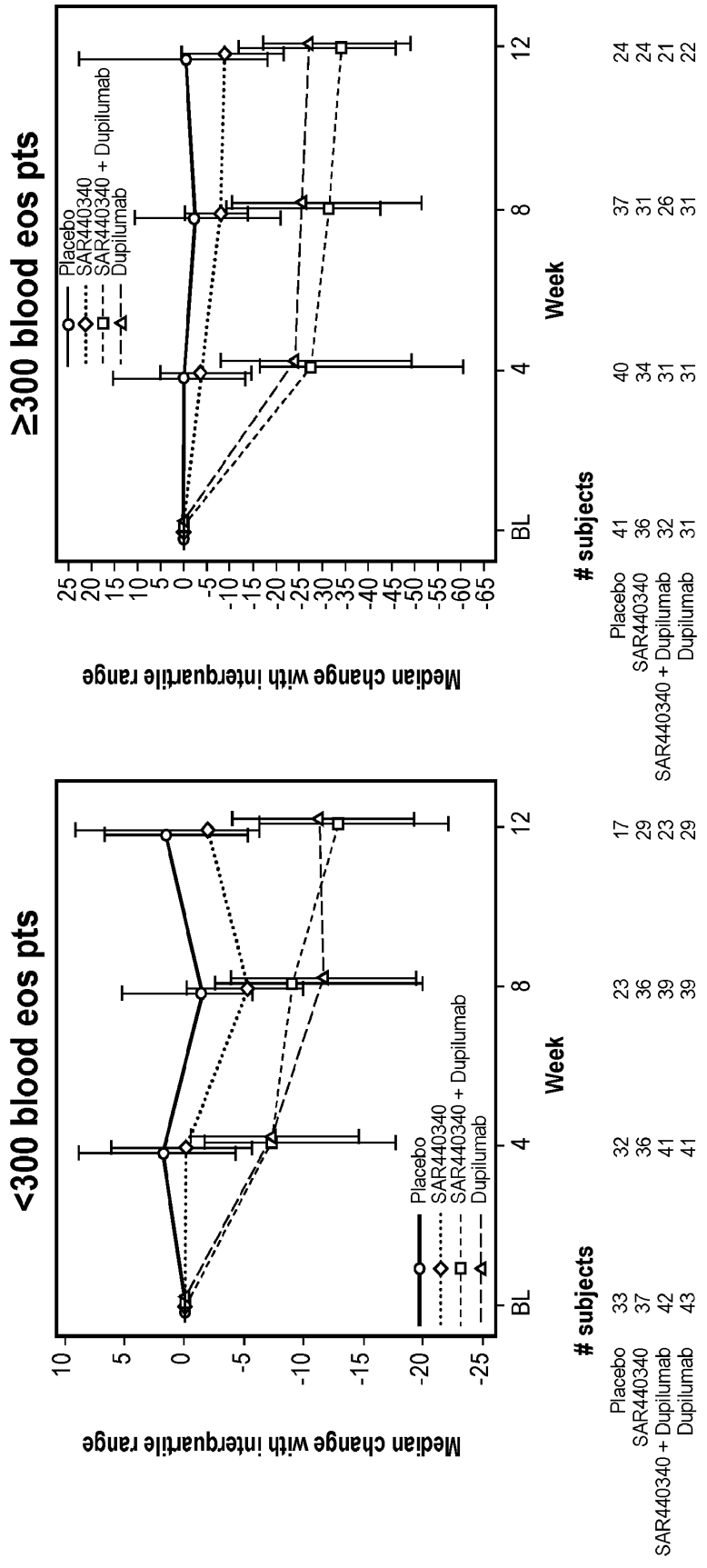

<300 blood eos pts
≥300 blood eos pts
Median change with interquartile range
Week
BL
4
8
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 33 32 23 17
SAR440340 37 36 36 29
SAR440340 + Dupilumab 42 41 39 23
Dupilumab 43 41 39 29
Placebo 41 40 37 24
SAR440340 36 34 31 24
SAR440340 + Dupilumab 32 31 26 21
Dupilumab 31 31 31 22

Fig. 65

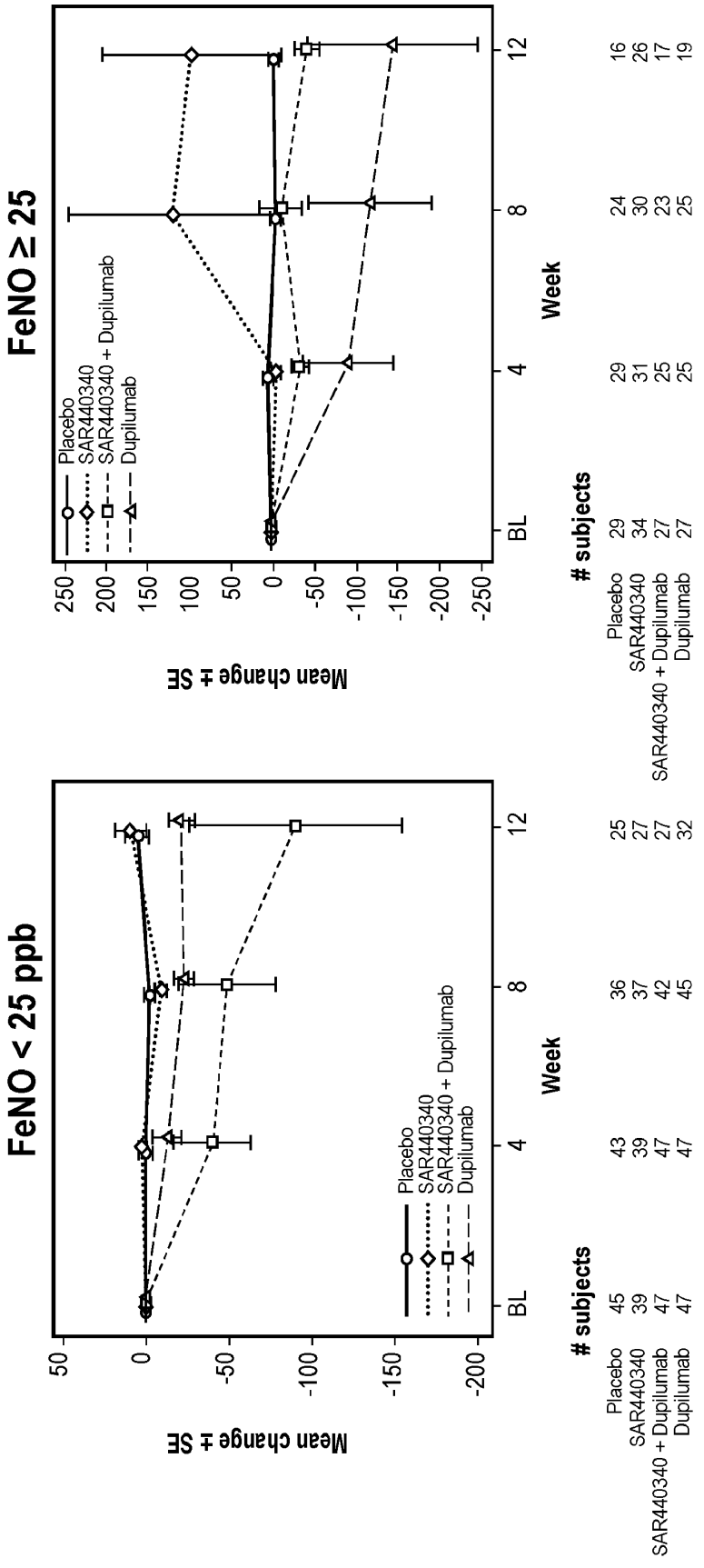

FeNO ≥ 25
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
250
200
150
100
50
0
-50
-100
-150
-200
-250
BL
4
8
12
Week
subjects
Placebo 29 29 24 16
SAR440340 34 31 30 26
SAR440340 + Dupilumab 27 25 23 17
Dupilumab 27 25 25 19
FeNO < 25 ppb
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
50
0
-50
-100
-150
-200
BL
4
8
12
Week
subjects
Placebo 45 43 36 25
SAR440340 39 39 37 27
SAR440340 + Dupilumab 47 47 42 27
Dupilumab 47 47 45 32

Fig. 66

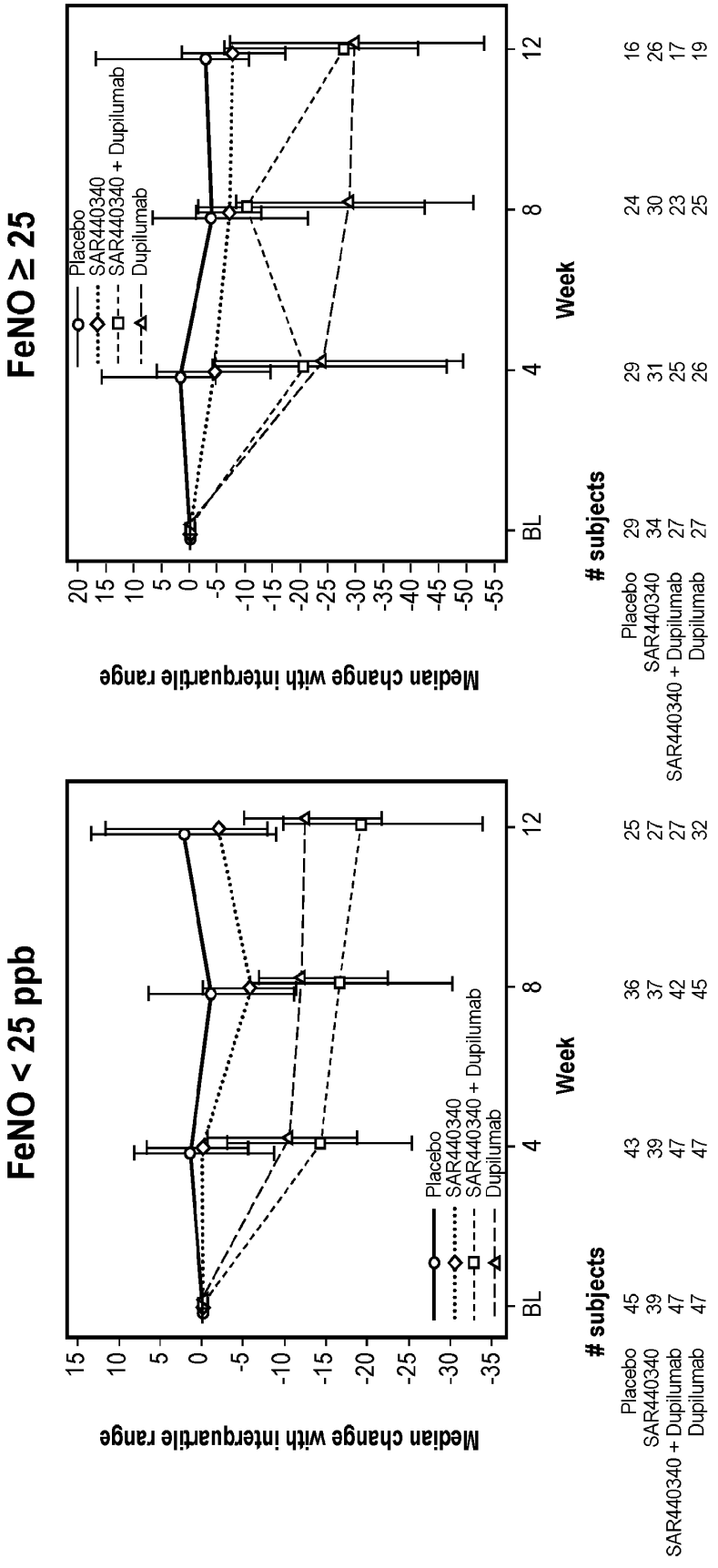

FeNO ≥ 25
Median change with interquartile range
Week
BL
4
8
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 29 24 16
SAR440340 34 30 26
SAR440340 + Dupilumab 27 23 17
Dupilumab 25 25 19
FeNO < 25 ppb
Median change with interquartile range
Week
BL
4
8
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 45 43 36 25
SAR440340 39 39 37 27
SAR440340 + Dupilumab 47 47 42 27
Dupilumab 47 47 45 32

Fig. 67

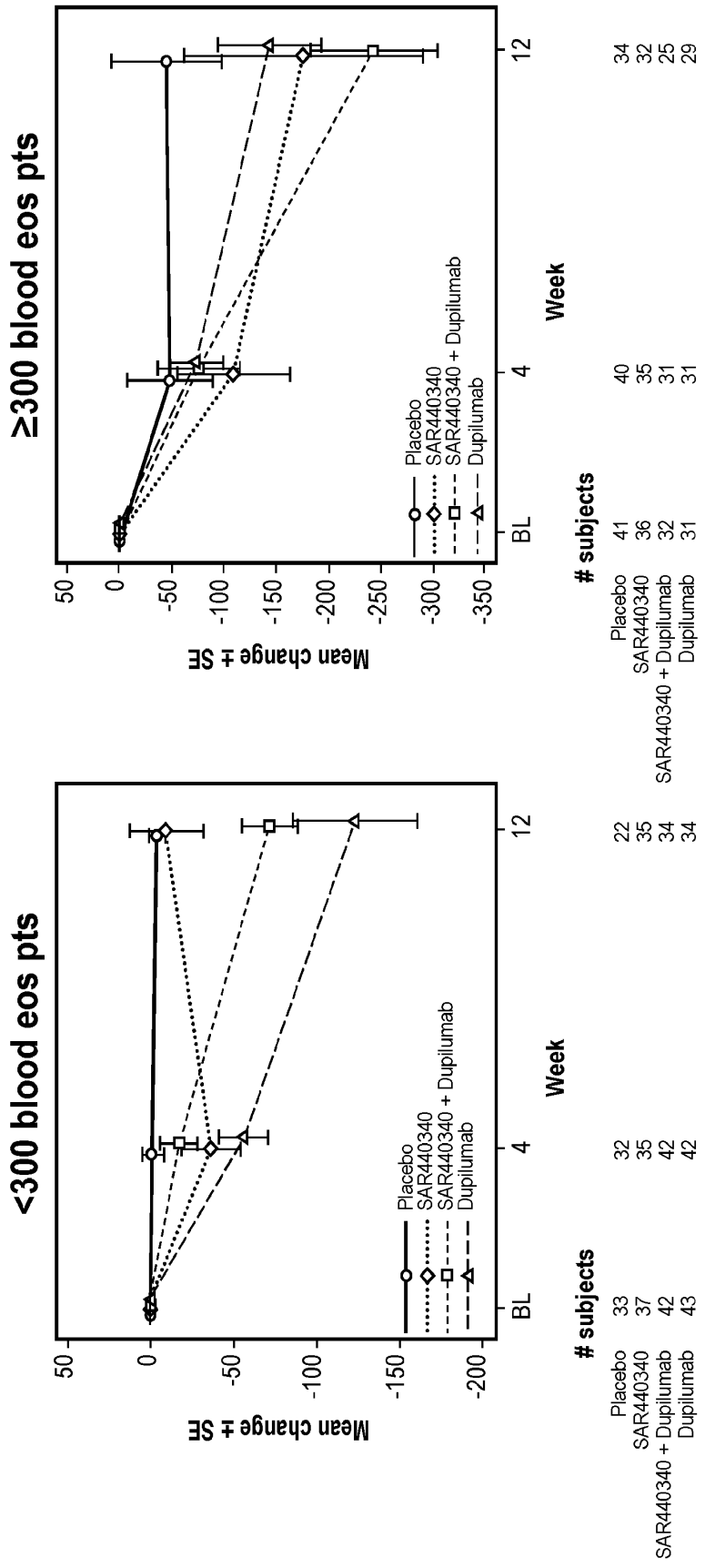

≥300 blood eos pts
Mean change ± SE
50
0
-50
-100
-150
-200
-250
-300
-350
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 41 40 34
SAR440340 36 35 32
SAR440340 + Dupilumab 32 31 25
Dupilumab 31 31 29
<300 blood eos pts
Mean change ± SE
50
0
-50
-100
-150
-200
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 33 32 22
SAR440340 37 35 35
SAR440340 + Dupilumab 42 42 34
Dupilumab 43 42 34

Fig. 68

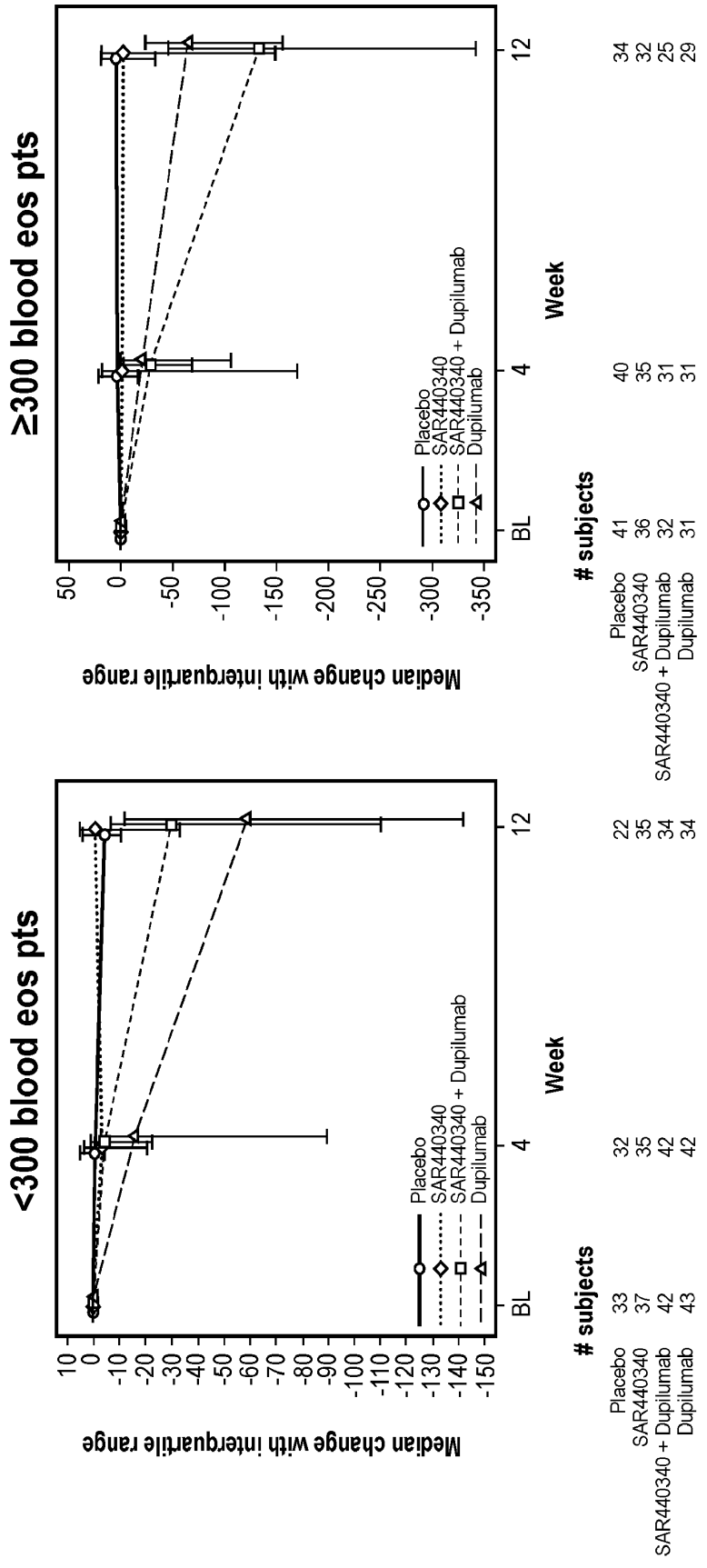

≥300 blood eos pts
Median change with interquartile range
50
0
-50
-100
-150
-200
-250
-300
-350
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 41 40 34
SAR440340 36 35 32
SAR440340 + Dupilumab 32 31 25
Dupilumab 31 31 29
<300 blood eos pts
Median change with interquartile range
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 33 32 22
SAR440340 37 35 35
SAR440340 + Dupilumab 42 42 34
Dupilumab 43 42 34

Fig. 69

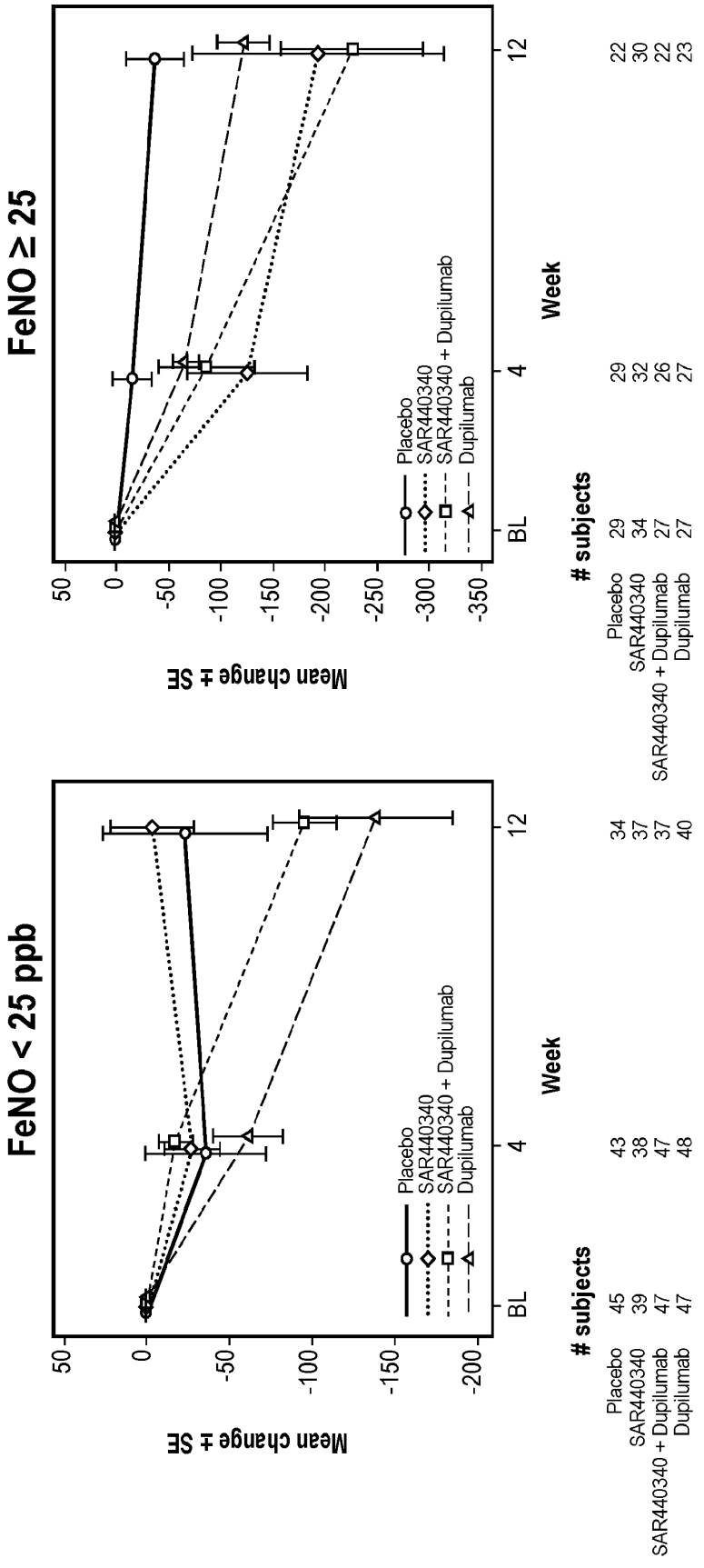

FeNO ≥ 25
Mean change ± SE
50
0
-50
-100
-150
-200
-250
-300
-350
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 29 29 22
SAR440340 34 32 30
SAR440340 + Dupilumab 27 26 22
Dupilumab 27 27 23
FeNO < 25 ppb
Mean change ± SE
50
0
-50
-100
-150
-200
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 45 43 34
SAR440340 39 38 37
SAR440340 + Dupilumab 47 47 37
Dupilumab 47 48 40

Fig. 70

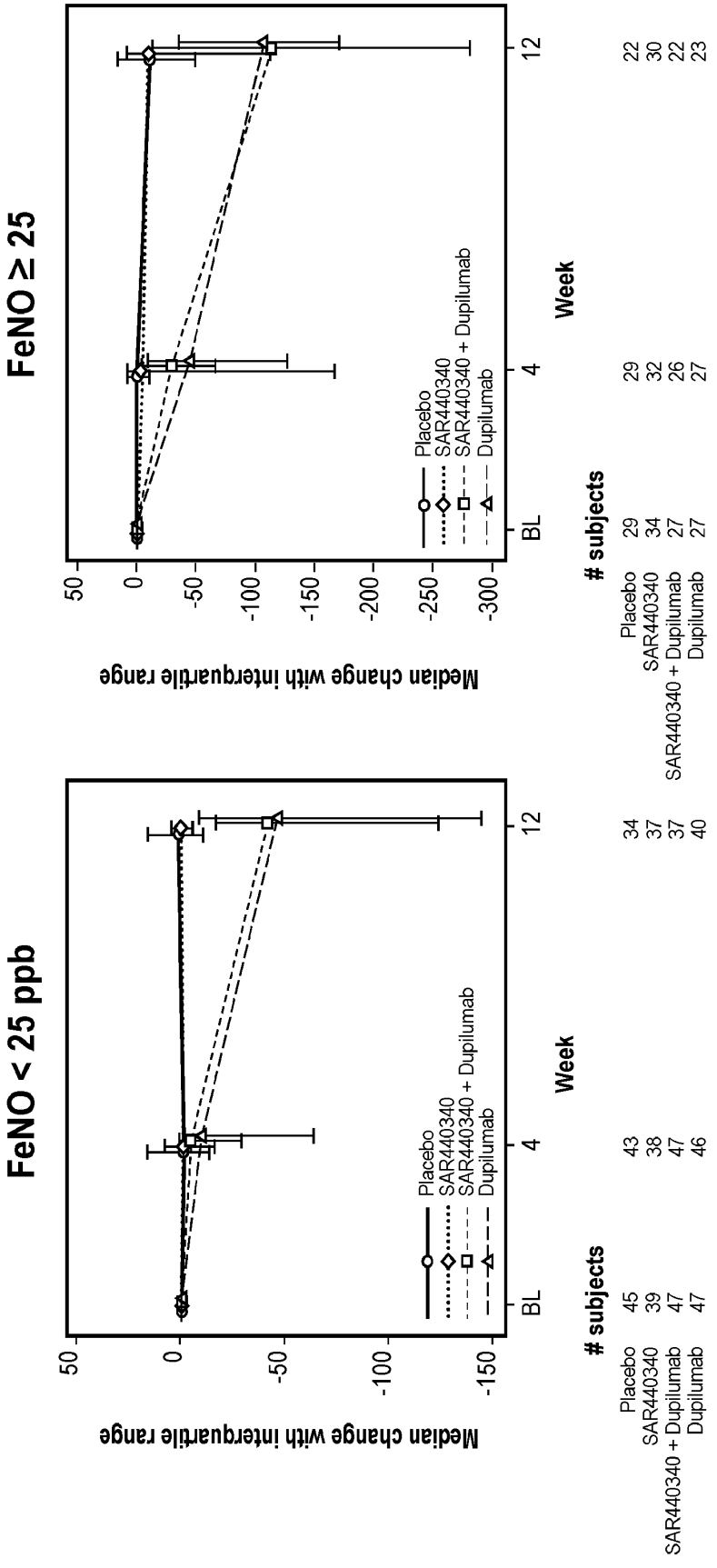

FeNO ≥ 25
Median change with interquartile range
50
0
-50
-100
-150
-200
-250
-300
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 29 29 22
SAR440340 34 32 30
SAR440340 + Dupilumab 27 26 22
Dupilumab 27 27 23
FeNO < 25 ppb
Median change with interquartile range
50
0
-50
-100
-150
BL
4
12
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 45 43 34
SAR440340 39 38 37
SAR440340 + Dupilumab 47 47 37
Dupilumab 47 46 40

Fig. 71

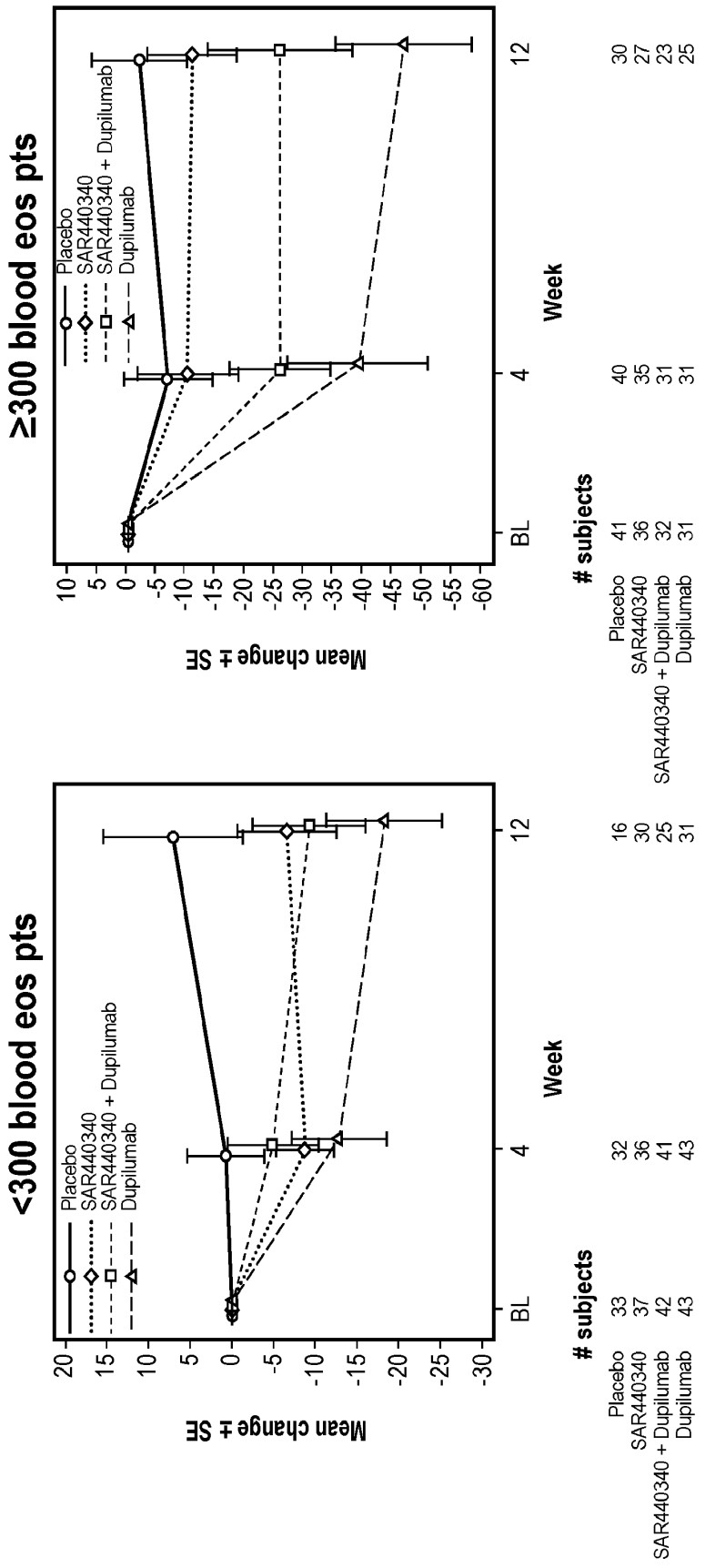

<300 blood eos pts
≥300 blood eos pts
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change ± SE
Week
BL
4
12
subjects
Placebo 33 32 16
SAR440340 37 36 30
SAR440340 + Dupilumab 42 41 25
Dupilumab 43 43 31
Placebo 41 40 30
SAR440340 36 35 27
SAR440340 + Dupilumab 32 31 23
Dupilumab 31 31 25

Fig. 72

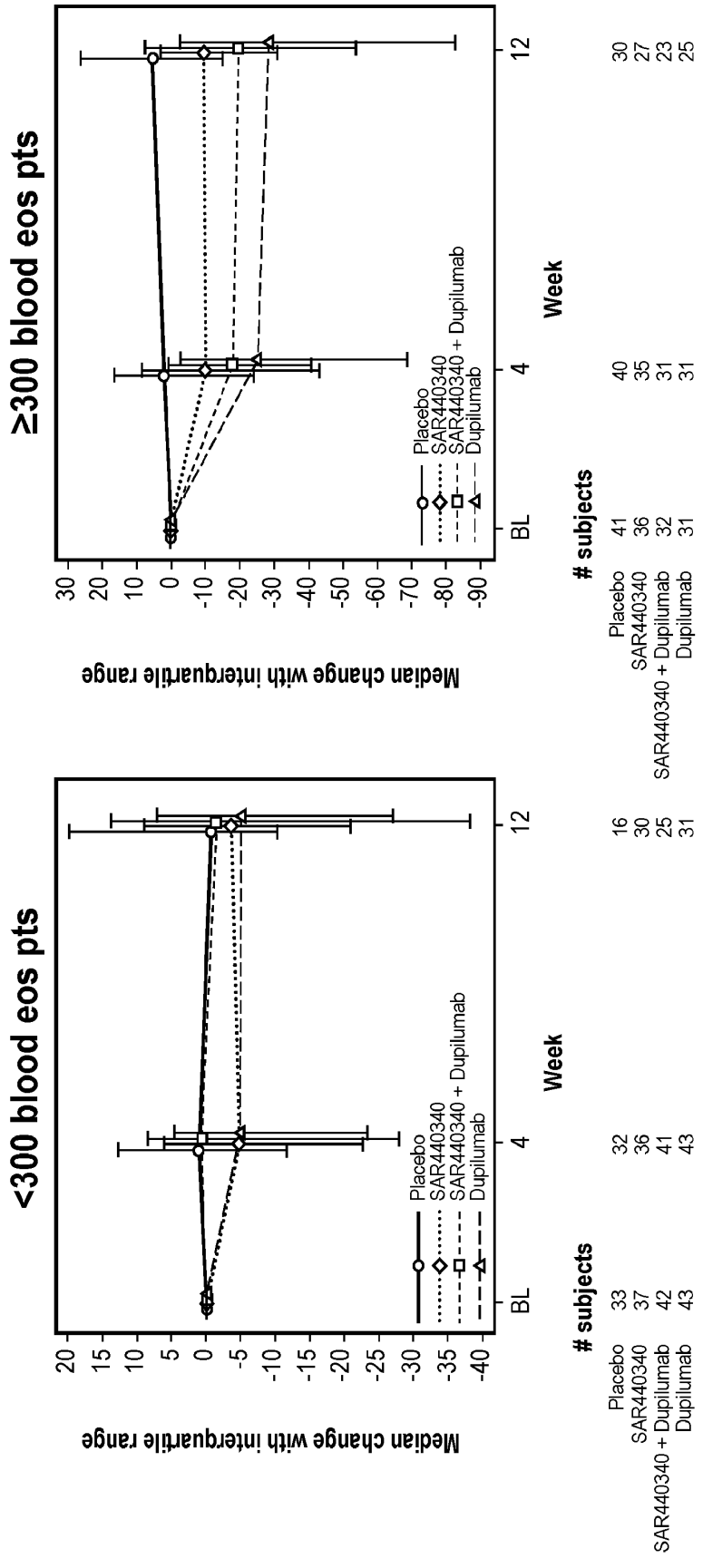

≥300 blood eos pts
Median change with interquartile range
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 41 40 30
SAR440340 36 35 27
SAR440340 + Dupilumab 32 31 23
Dupilumab 31 31 25
<300 blood eos pts
Median change with interquartile range
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 33 32 16
SAR440340 37 36 30
SAR440340 + Dupilumab 42 41 25
Dupilumab 43 43 31

Fig. 73

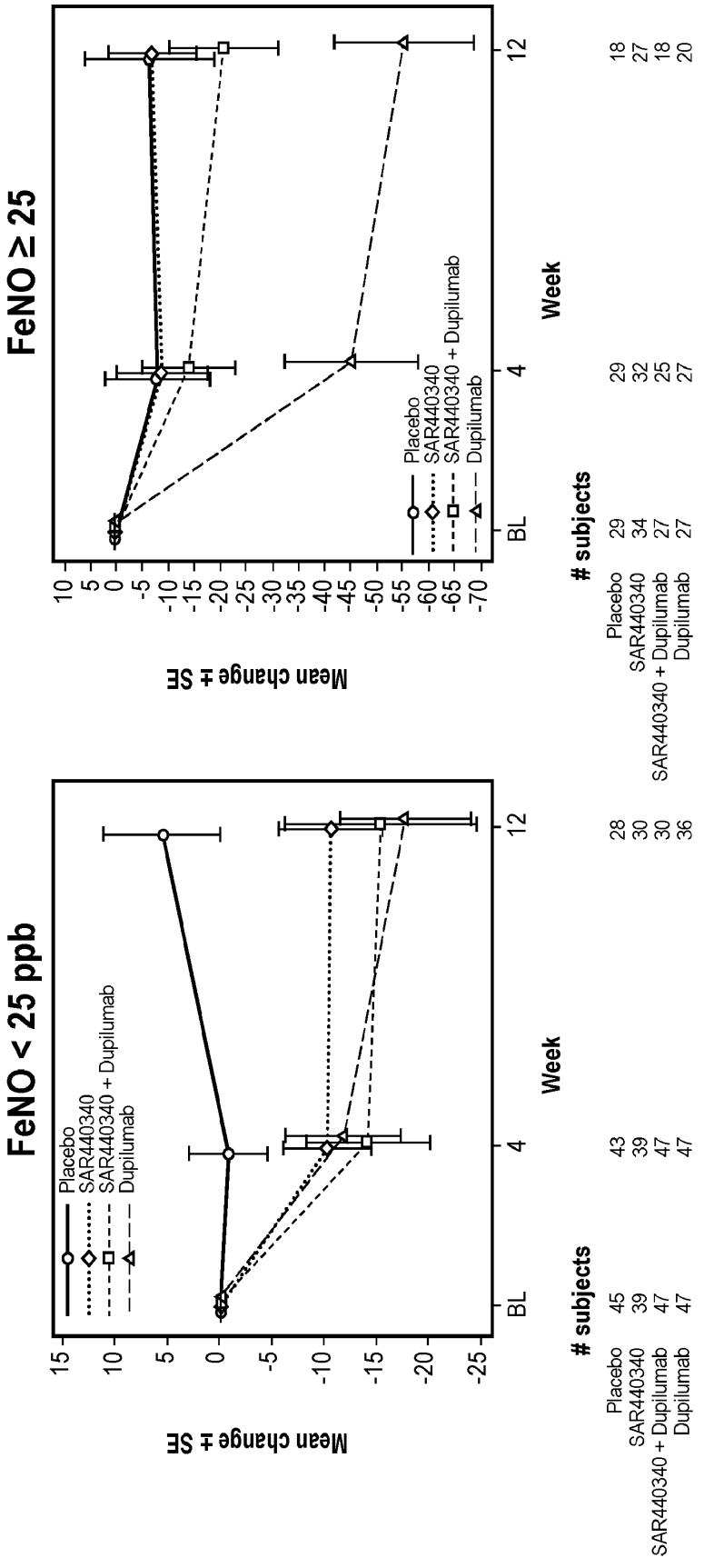

FeNO ≥ 25
Mean change ± SE
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 29 29 18
SAR440340 34 32 27
SAR440340 + Dupilumab 27 25 18
Dupilumab 27 27 20
FeNO < 25 ppb
Mean change ± SE
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 45 43 28
SAR440340 39 39 30
SAR440340 + Dupilumab 47 47 30
Dupilumab 47 47 36

Fig. 74

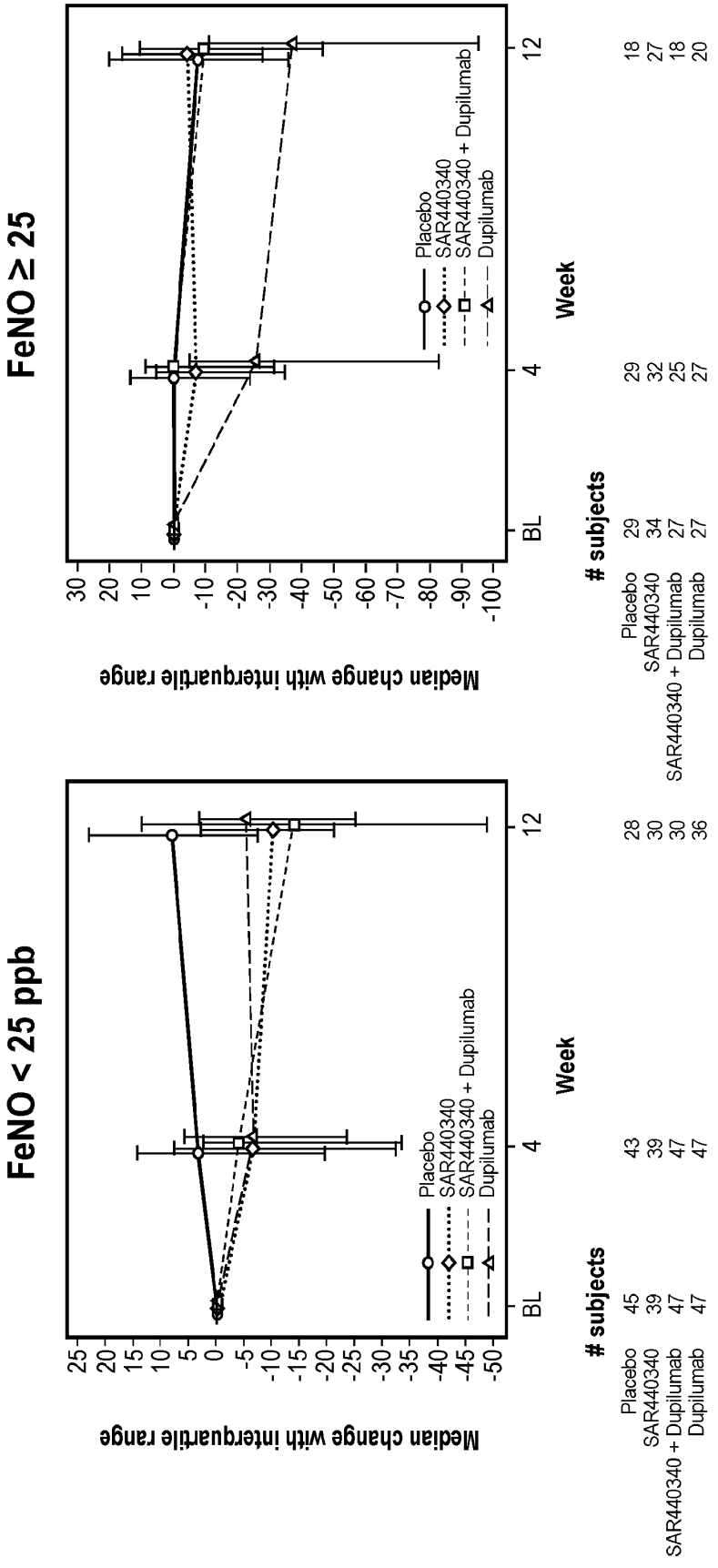

FeNO ≥ 25
Median change with interquartile range
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 29 29 18
SAR440340 34 32 27
SAR440340 + Dupilumab 27 25 18
Dupilumab 27 27 20
FeNO < 25 ppb
Median change with interquartile range
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 45 43 28
SAR440340 39 39 30
SAR440340 + Dupilumab 47 47 30
Dupilumab 47 47 36

Fig. 75

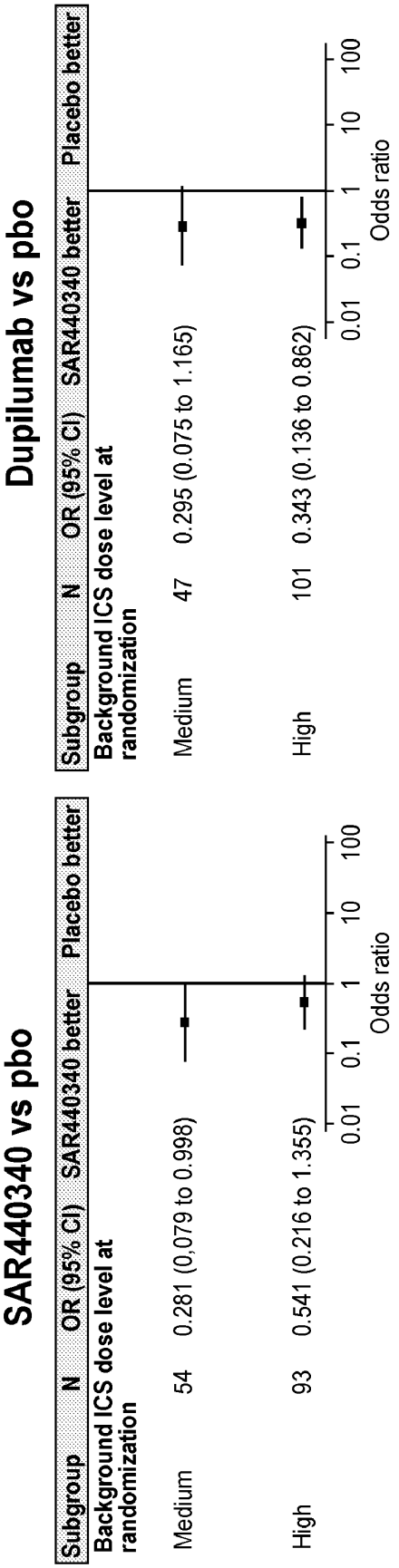

SAR440340 vs pbo
Subgroup N OR (95% CI) SAR440340 better Placebo better
Background ICS dose level at randomization
Medium 54 0.281 (0,079 to 0.998)
High 93 0.541 (0.216 to 1.355)
0.01 0.1 1 10 100
Odds ratio
Dupilumab vs pbo
Subgroup N OR (95% CI) SAR440340 better Placebo better
Background ICS dose level at randomization
Medium 47 0.295 (0.075 to 1.165)
High 101 0.343 (0.136 to 0.862)
0.01 0.1 1 10 100
Odds ratio

Fig. 76

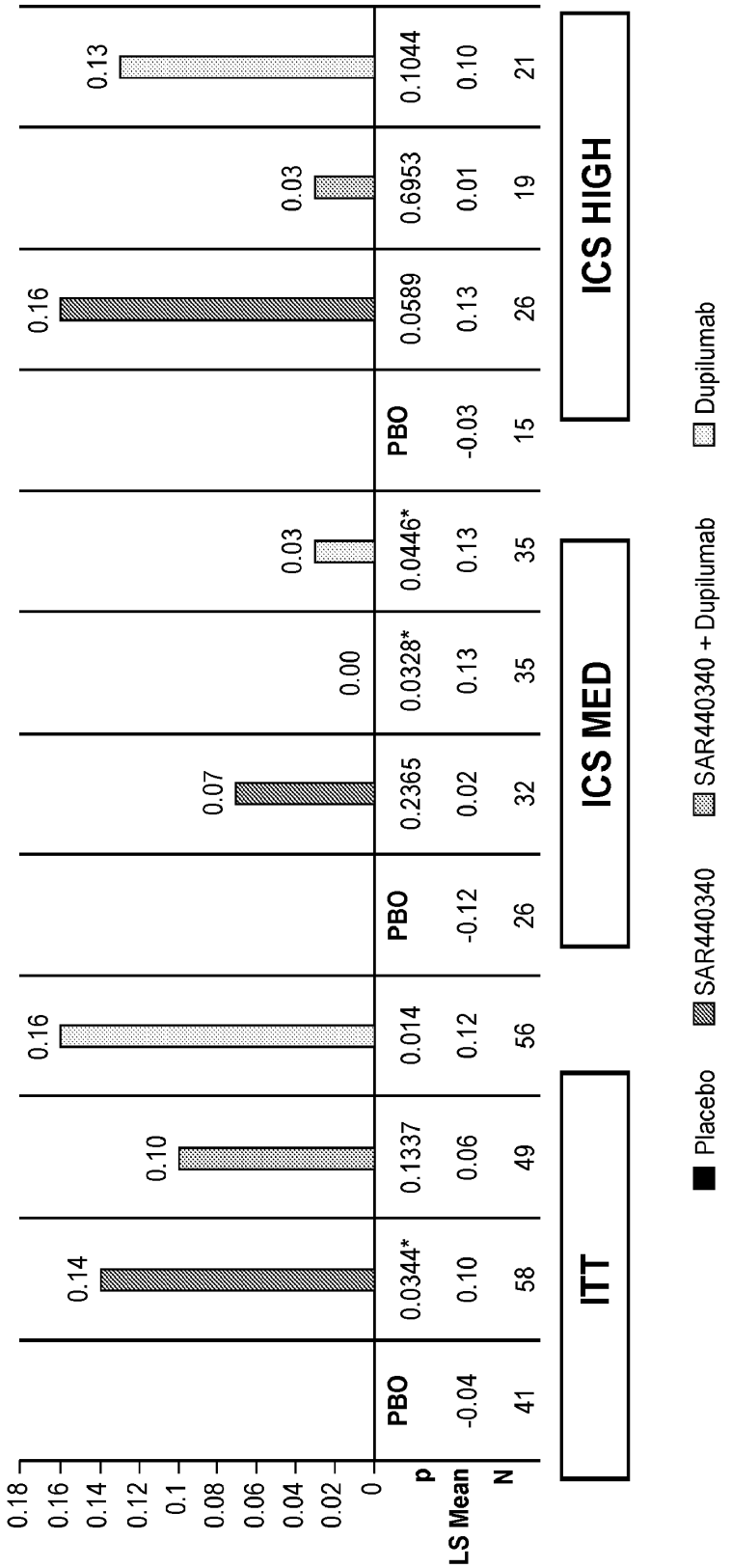

PRE-BD FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (ICS)
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0.14
0.10
0.16
0.07
0.00
0.03
0.16
0.03
0.13
PBO 0.0344* 0.1337 0.014 PBO 0.2365 0.0328* 0.0446* PBO 0.0589 0.6953 0.1044
LS Mean -0.04 0.10 0.06 0.12 -0.12 0.02 0.13 0.13 -0.03 0.13 0.01 0.10
N 41 58 49 56 26 32 35 35 15 26 19 21
ITT
ICS MED
ICS HIGH
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 77

				PBO, n=74	SAR440340, n=73	SAR440340 + Dupi, n=74	Dupilumab, n=74
Endpoint	**Category**	**Data**	**SG**	30 (40.5)	16 (21.9)	20 (27.0)	14 (18.9)
LOAC	LOAC-ITT	OR vs pbo	ITT		0.423 (0.203 to 0.880)	0.520 (0.256 to 1.057)	0.328 (0.153 to 0.700)
LOAC	LOAC-ITT	P-value vs pbo	ITT		0.0214	0.0709	0.004
LOAC	LOAC-ITT	RR vs pbo	ITT		0.579 (0.348 to 0.966)	0.684 (0.434 to 1.077)	0.467 (0.272 to 0.802)
LOAC	LOAC-ITT	RR% vs pbo	ITT		42.1	31.6	53.3
		P-value vs pbo	ITT		0.0364	0.1011	0.0057
				11 (42.3)	5 (17.9)	4 (16.0)	4 (19.0)
LOAC	LOAC-ICS	OR vs pbo	ICS MED		0.281 (0.079 to 0.998)	0.222 (0.055 to 0.891)	0.295 (0.075 to 1.165)
LOAC	LOAC-ICS	P-value vs pbo	ICS MED		0.0496	0.0339	0.0814
LOAC	LOAC-ICS	RR vs pbo	ICS MED				
LOAC	LOAC-ICS	RR% vs pbo	ICS MED				
	LOAC-ICS	P-value vs pbo	ICS MED				
				19 (39.6)	11 (24.4)	16 (32.7)	10 (18.9)
LOAC	LOAC-ICS	OR vs pbo	ICS HIGH		0.541 (0.216 to 1.355)	0.734 (0.312 to 1.729)	0.343 (0.136 to 0.862)
LOAC	LOAC-ICS	P-value vs pbo	ICS HIGH		0.1897	0.4796	0.0229
LOAC	LOAC-ICS	RR vs pbo	ICS HIGH				
LOAC	LOAC-ICS	RR% vs pbo	ICS HIGH				
	LOAC-ICS	P-value vs pbo	ICS HIGH				

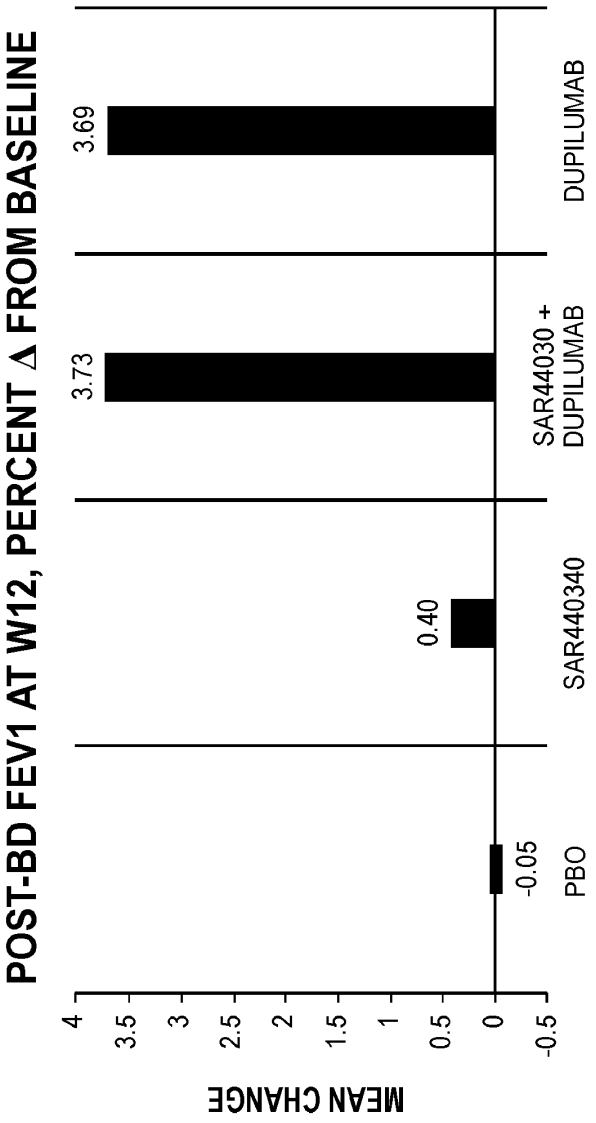
Fig. 78

				PBO, n=74	SAR440340, n=73	SAR440340 + Dupi, n=74	Dupilumab, n=74
Endpoint	**Category**	**Data**	**SG**	30 (40.5)	16 (21.9)	20 (27.0)	14 (18.9)
LOAC	LOAC-ITT	OR vs pbo	ITT		0.423 (0.203 to 0.880)	0.520 (0.256 TO 1.057)	0.328 (0.153 TO 0.700)
LOAC	LOAC-ITT	P-value vs pbo	ITT		0.0214	0.0709	0.004
LOAC	LOAC-ITT	RR vs pbo	ITT		0.579 (0.348 to 0.966)	0.684 (0.434 to 1.077)	0.467 (0.272 to 0.802)
LOAC	LOAC-ITT	RR% vs pbo	ITT		42.1	31.6	53.3
		P-value vs pbo	ITT		0.0364	0.1011	0.0057
				11 (42.3)	5 (17.9)	4 (16.0)	4 (19.0)
LOAC	LOAC-ICS	OR vs pbo	ICS MED		0.281 (0.079 to 0.998)	0.222 (0.055 to 0.891)	0.295 (0.075 to 1.165)
LOAC	LOAC-ICS	P-value vs pbo	ICS MED		0.0496	0.0339	0.0814
LOAC	LOAC-ICS	RR vs pbo	ICS MED				
LOAC	LOAC-ICS	RR% vs pbo	ICS MED				
	LOAC-ICS	P-value vs pbo	ICS MED				
				19 (39.6)	11 (24.4)	16 (32.7)	10 (18.9)
LOAC	LOAC-ICS	OR vs pbo	ICS HIGH		0.541 (0.216 to 1.355)	0.734 (0.312 to 1.729)	0.343 (0.136 to 0.862)
LOAC	LOAC-ICS	P-value vs pbo	ICS HIGH		0.1897	0.4796	0.0229
LOAC	LOAC-ICS	RR vs pbo	ICS HIGH				
LOAC	LOAC-ICS	RR% vs pbo	ICS HIGH				
	LOAC-ICS	P-value vs pbo	ICS HIGH				

Fig. 79

				PBO, n=74	SAR440340, n=73	SAR440340 + Dupi, n=74	Dupilumab, n=74
Endpoint	Category	Data	SG	30 (40.5)	16 (21.9)	20 (27.0)	14 (18.9)
LOAC	LOAC-ITT	OR vs pbo	ITT		0.423 (0.203 to 0.880)	0.520 (0.256 to 1.057)	0.328 (0.153 to 0.700)
LOAC	LOAC-ITT	P-value vs pbo	ITT		0.0214	0.0709	0.004
LOAC	LOAC-ITT	RR vs pbo	ITT		0.579 (0.348 to 0.966)	0.684 (0.434 to 1.077)	0.467 (0.272 to 0.802)
LOAC	LOAC-ITT	RRR% vs pbo	ITT		42.1	31.6	53.3
LOAC	LOAC-ITT	P-value vs pbo	ITT		0.0364	0.1011	0.0057
				14 (38.9)	12 (30.8)	12 (34.3)	7 (19.4)
LOAC	LOAC-Periostin	OR vs pbo	Periostin-LOW		0.714 (0.271 to 1.884)	0.890 (0.329 to 2.409)	0.390 (0.133 to 1.147)
LOAC	LOAC-Periostin	P-value vs pbo	Periostin-LOW		0.4964	0.819	0.0873
LOAC	LOAC-Periostin	RR vs pbo	Periostin-LOW				
LOAC	LOAC-Periostin	RR% vs pbo	Periostin-LOW				
LOAC	LOAC-Periostin	P-value vs pbo	Periostin-LOW				
				16 (42.1)	4 (11.8)	16 (32.7)	7 (18.4)
LOAC	LOAC-ICS	OR vs pbo	Periostin-HIGH		0.183 (0.051 to 0.657)	0.734 (0.312 to 1.729)	0.266 (0.085 to 0.829)
LOAC	LOAC-ICS	P-value vs pbo	Periostin-HIGH		0.0091	0.4796	0.0224
LOAC	LOAC-ICS	RR vs pbo	Periostin-HIGH				
LOAC	LOAC-ICS	RR% vs pbo	Periostin-HIGH				
LOAC	LOAC-ICS	P-value vs pbo	Periostin-HIGH				

Fig. 80



			PBO	SAR440340	SAR440340 + Dupi	Dupilumab
Endpoint	Category	Data	SG			
Post-BD FEV1	FEV1-ITT	Mean (SD	ITT	-0.05 (10.53)	0.40 (17.27)	3.73 (16.26)	3.69 (17.63)
				42	58	51	57

Fig. 81

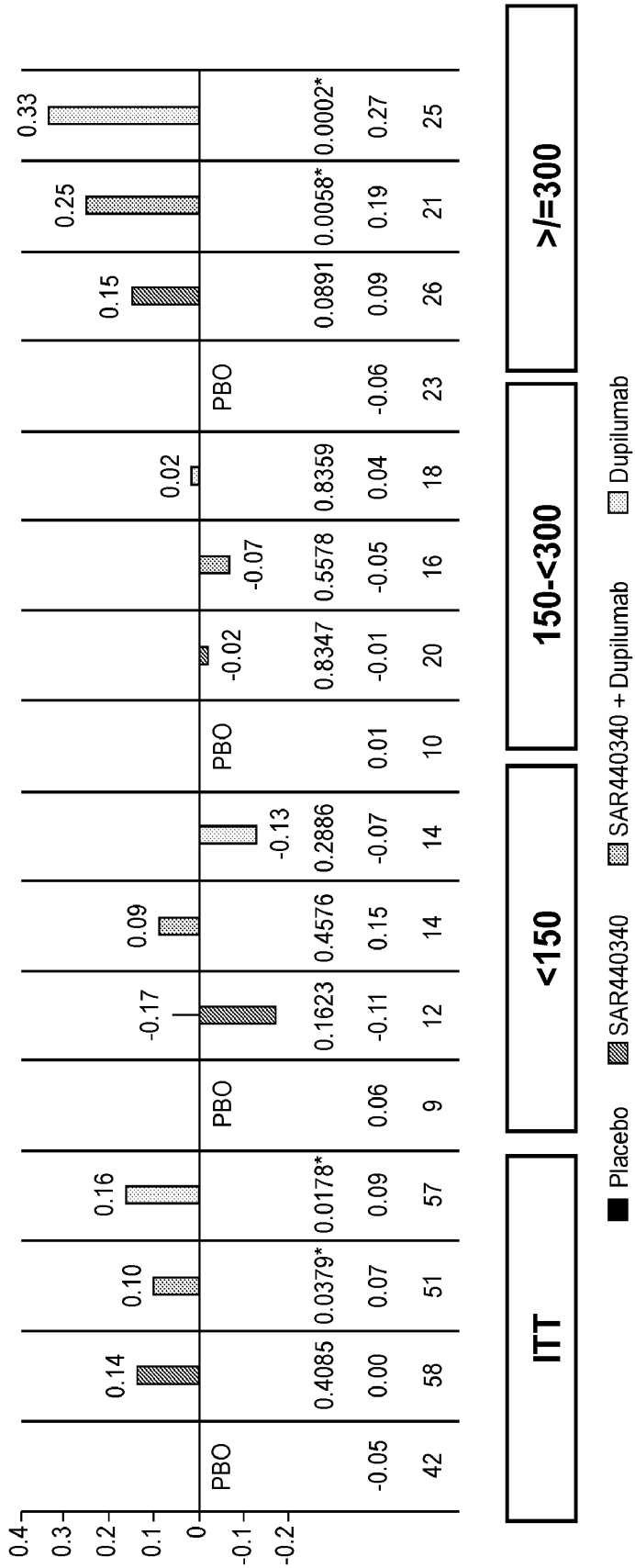

POST-BD FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (EOS)
0.4
0.3
0.2
0.1
0
-0.1
-0.2
PBO
0.14
0.10
0.16
PBO
-0.17
0.09
PBO
-0.13
PBO
-0.02
-0.07
PBO
0.02
PBO
0.15
0.25
0.33
-0.05
0.4085
0.0379*
0.0178*
0.06
0.1623
-0.11
0.4576
0.15
0.2886
-0.07
0.8347
-0.01
0.5578
-0.05
0.8359
0.04
-0.06
0.0891
0.09
0.0058*
0.19
0.0002*
0.27
42
0.00
58
0.07
51
0.09
57
9
12
14
14
10
20
16
18
23
26
21
25
ITT
<150
150-<300
>/=300
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 82

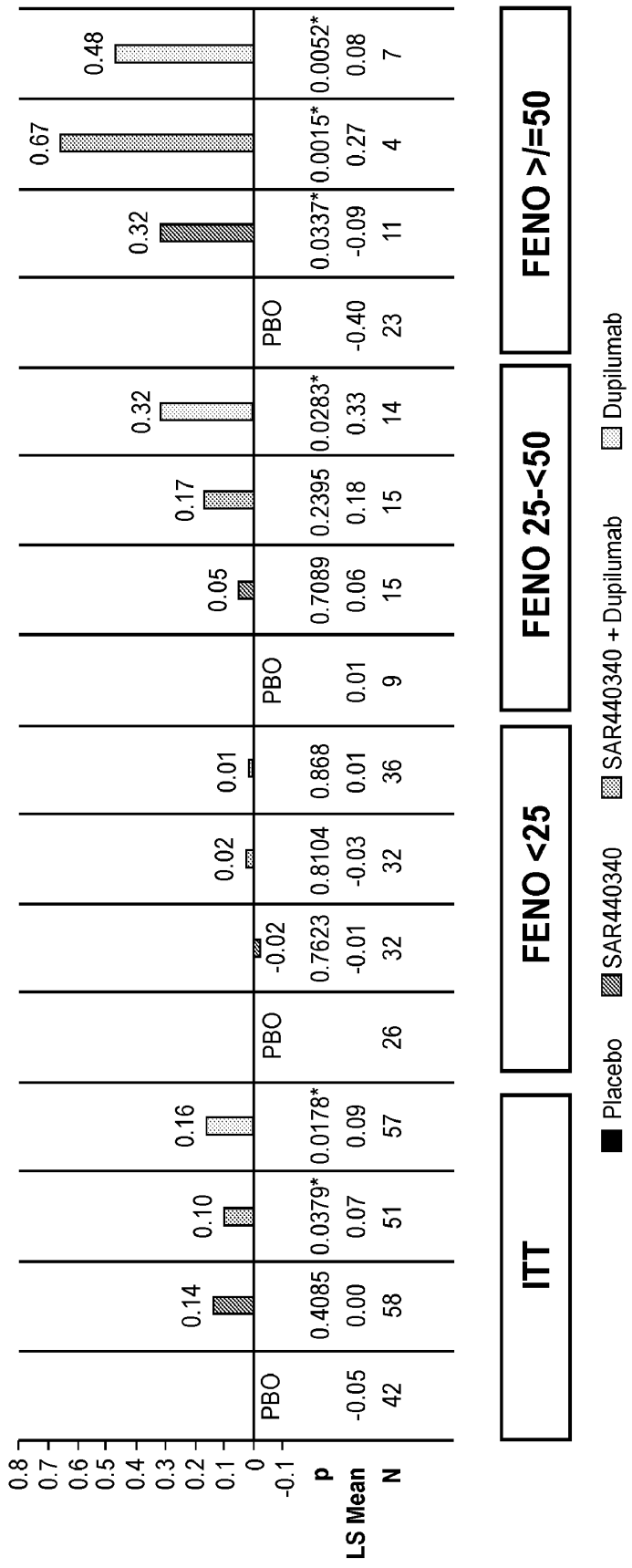

POST-BD FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (FENO)
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
p
LS Mean
N
PBO
-0.05
42
0.14
0.4085
0.00
58
0.10
0.0379*
0.07
51
0.16
0.0178*
0.09
57
PBO
26
-0.02
0.7623
-0.01
32
0.02
0.8104
-0.03
32
0.01
0.868
0.01
36
PBO
0.01
9
0.05
0.7089
0.06
15
0.17
0.2395
0.18
15
0.32
0.0283*
0.33
14
PBO
23
0.32
0.0337*
-0.09
11
0.67
0.0015*
0.27
4
0.48
0.0052*
0.08
7
ITT
FENO <25
FENO 25-<50
FENO >/=50
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 83

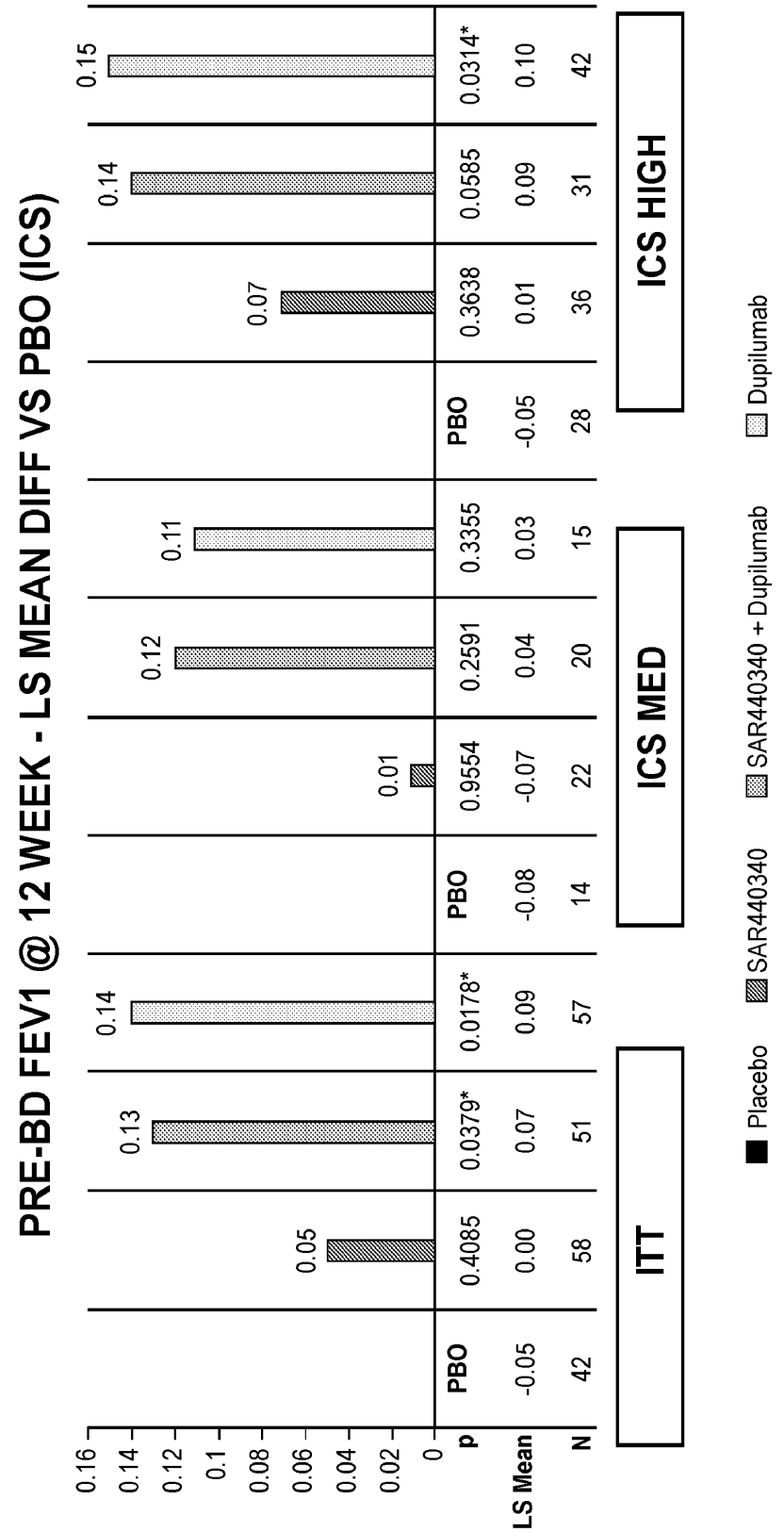

PRE-BD FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (ICS)
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0.05
0.13
0.14
0.01
0.12
0.11
0.07
0.14
0.15
p
PBO
0.4085
0.0379*
0.0178*
PBO
0.9554
0.2591
0.3355
PBO
0.3638
0.0585
0.0314*
LS Mean
-0.05
0.00
0.07
0.09
-0.08
-0.07
0.04
0.03
-0.05
0.01
0.09
0.10
N
42
58
51
57
14
22
20
15
28
36
31
42
ITT
ICS MED
ICS HIGH
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 84

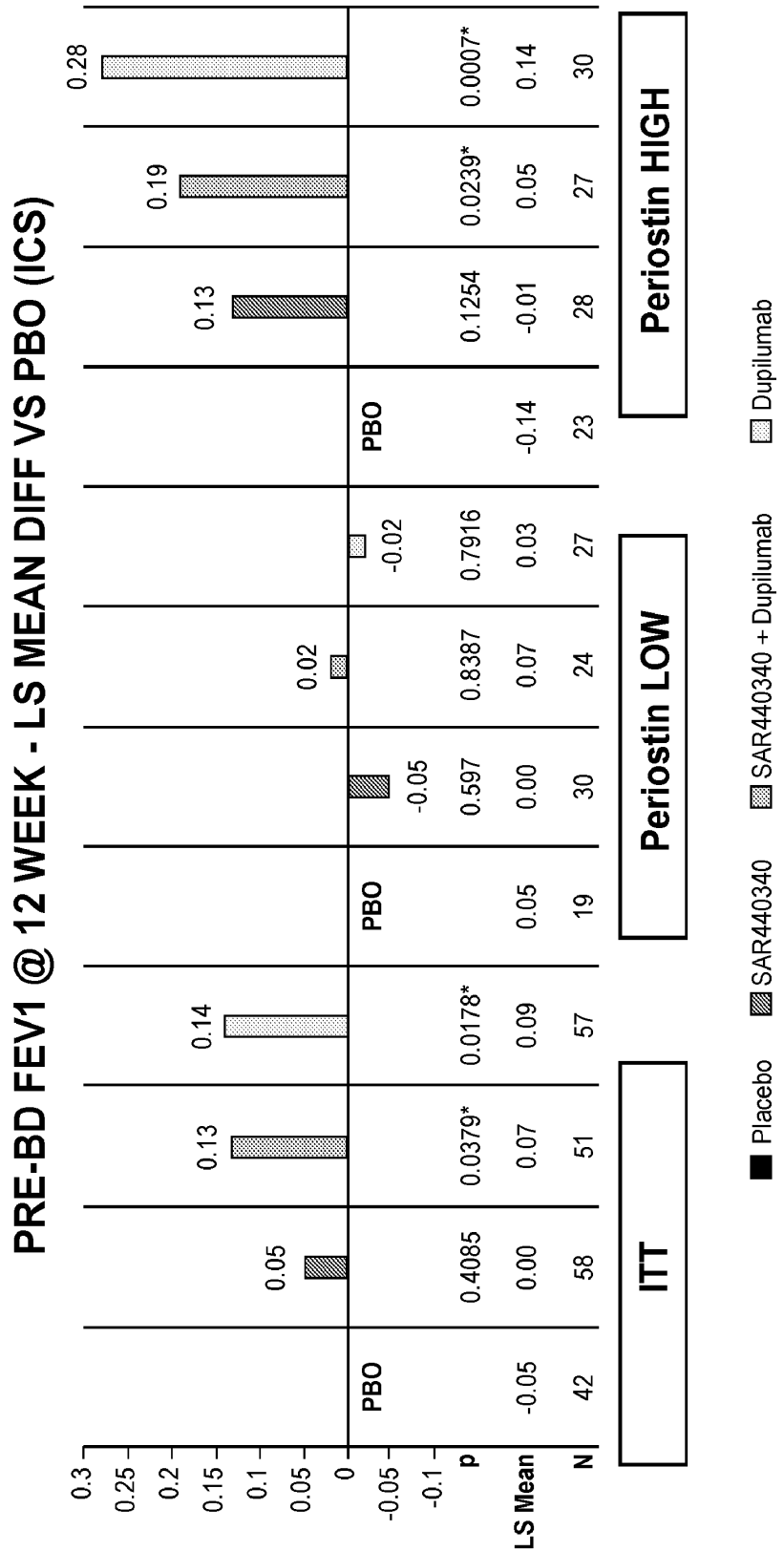

PRE-BD FEV1 @ 12 WEEK - LS MEAN DIFF VS PBO (ICS)
0.3
0.25
0.2
0.15
0.1
0.05
0
-0.05
-0.1
0.05
0.13
0.14
0.02
-0.02
0.13
0.19
0.28
p
PBO
0.4085
0.0379*
0.0178*
PBO
0.597
0.8387
0.7916
PBO
0.1254
0.0239*
0.0007*
LS Mean
-0.05
0.00
0.07
0.09
0.05
0.00
0.07
0.03
-0.14
-0.01
0.05
0.14
N
42
58
51
57
19
30
24
27
23
28
27
30
ITT
Periostin LOW
Periostin HIGH
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 85

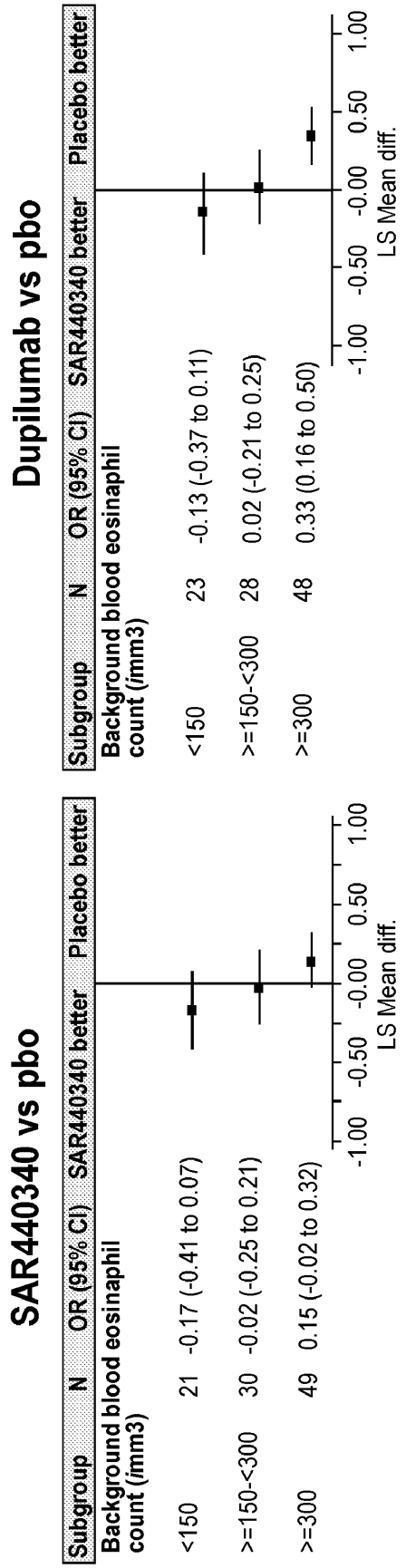

SAR440340 vs pbo
Subgroup N OR (95% CI) SAR440340 better Placebo better
Background blood eosinaphil count (/mm3)
<150 21 -0.17 (-0.41 to 0.07)
>=150-<300 30 -0.02 (-0.25 to 0.21)
>=300 49 0.15 (-0.02 to 0.32)
-1.00 -0.50 -0.00 0.50 1.00
LS Mean diff.
Dupilumab vs pbo
Subgroup N OR (95% CI) SAR440340 better Placebo better
Background blood eosinaphil count (/mm3)
<150 23 -0.13 (-0.37 to 0.11)
>=150-<300 28 0.02 (-0.21 to 0.25)
>=300 48 0.33 (0.16 to 0.50)
-1.00 -0.50 -0.00 0.50 1.00
LS Mean diff.

Fig. 86

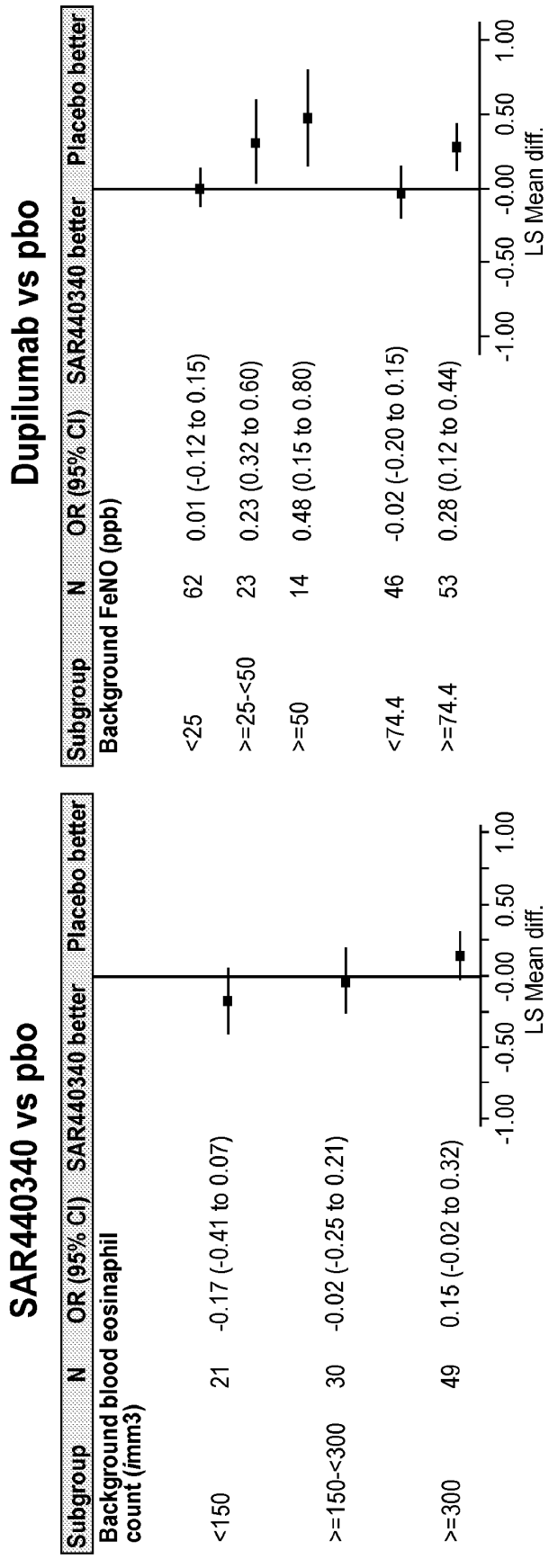

SAR440340 vs pbo
Subgroup N OR (95% CI) SAR440340 better Placebo better
Background blood eosinaphil count (/mm3)
<150 21 -0.17 (-0.41 to 0.07)
>=150-<300 30 -0.02 (-0.25 to 0.21)
>=300 49 0.15 (-0.02 to 0.32)
-1.00 -0.50 -0.00 0.50 1.00
LS Mean diff.
Dupilumab vs pbo
Subgroup N OR (95% CI) SAR440340 better Placebo better
Background FeNO (ppb)
<25 62 0.01 (-0.12 to 0.15)
>=25-<50 23 0.23 (0.32 to 0.60)
>=50 14 0.48 (0.15 to 0.80)
<74.4 46 -0.02 (-0.20 to 0.15)
>=74.4 53 0.28 (0.12 to 0.44)
-1.00 -0.50 -0.00 0.50 1.00
LS Mean diff.

Fig. 87

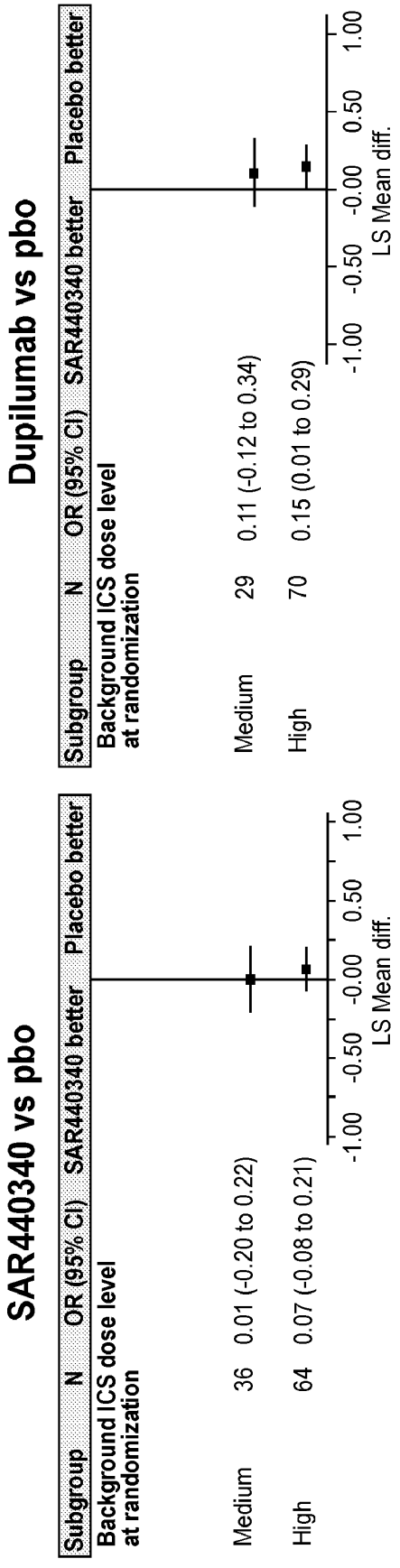

SAR440340 vs pbo
Subgroup N OR (95% CI) SAR440340 better Placebo better
Background ICS dose level at randomization
Medium 36 0.01 (-0.20 to 0.22)
High 64 0.07 (-0.08 to 0.21)
-1.00 -0.50 -0.00 0.50 1.00
LS Mean diff.
Dupilumab vs pbo
Subgroup N OR (95% CI) SAR440340 better Placebo better
Background ICS dose level at randomization
Medium 29 0.11 (-0.12 to 0.34)
High 70 0.15 (0.01 to 0.29)
-1.00 -0.50 -0.00 0.50 1.00
LS Mean diff.

Fig. 88

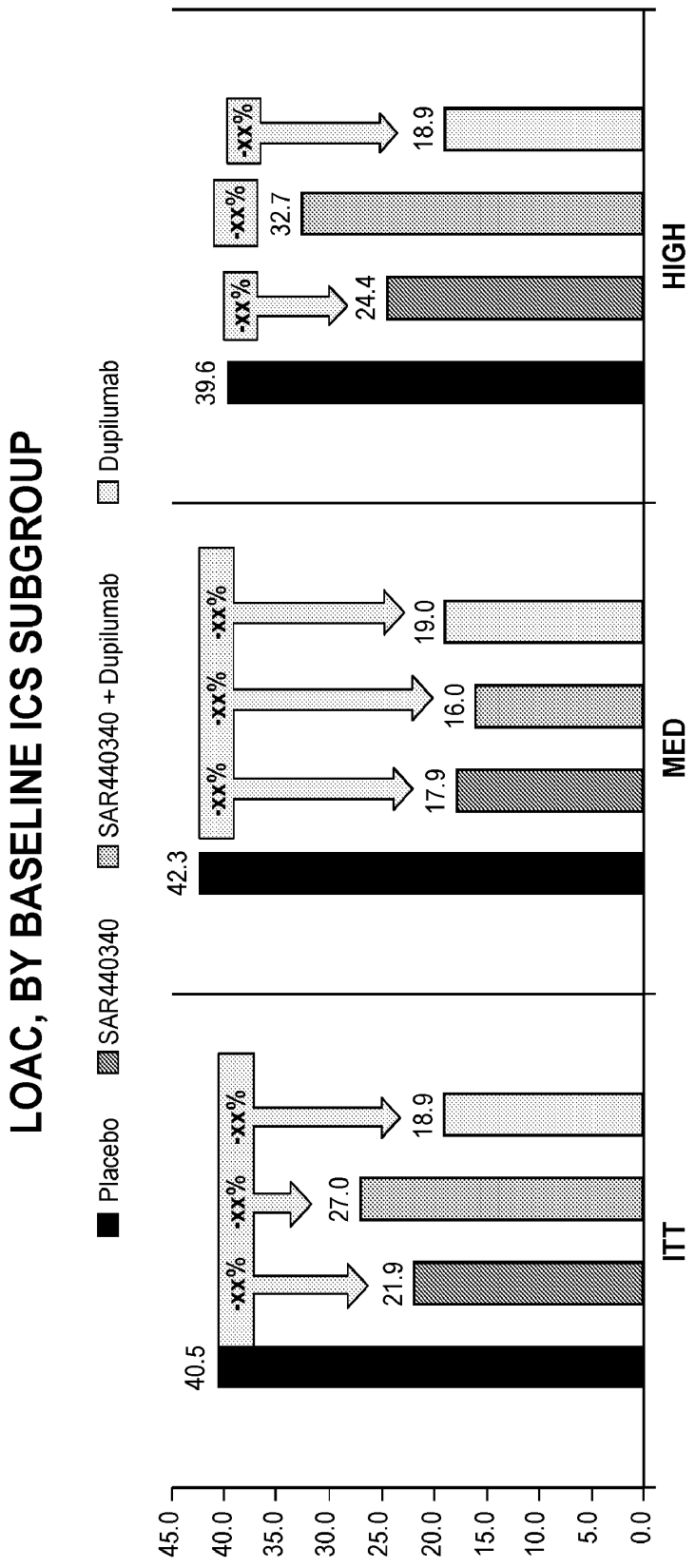

LOAC, BY BASELINE ICS SUBGROUP
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
40.5
-xx%
-xx%
-xx%
21.9
27.0
18.9
ITT
42.3
-xx%
-xx%
-xx%
17.9
16.0
19.0
MED
39.6
-xx%
-xx%
-xx%
24.4
32.7
18.9
HIGH

Fig. 89

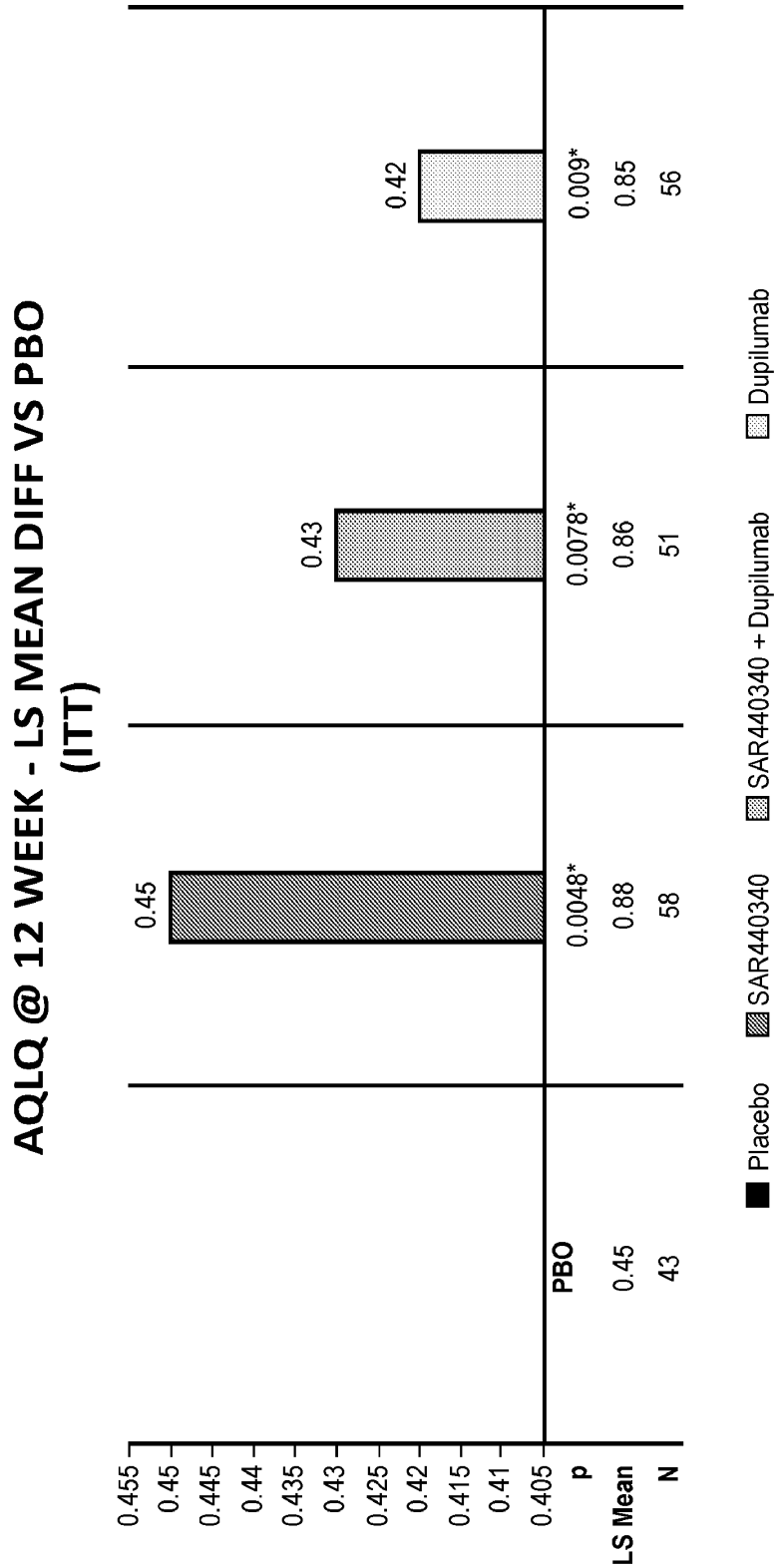

AQLQ @ 12 WEEK - LS MEAN DIFF VS PBO
(ITT)
0.455
0.45
0.445
0.44
0.435
0.43
0.425
0.42
0.415
0.41
0.405
LS Mean
N
PBO
0.45
43
p
0.45
0.0048*
0.88
58
0.43
0.0078*
0.86
51
0.42
0.009*
0.85
56
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 90

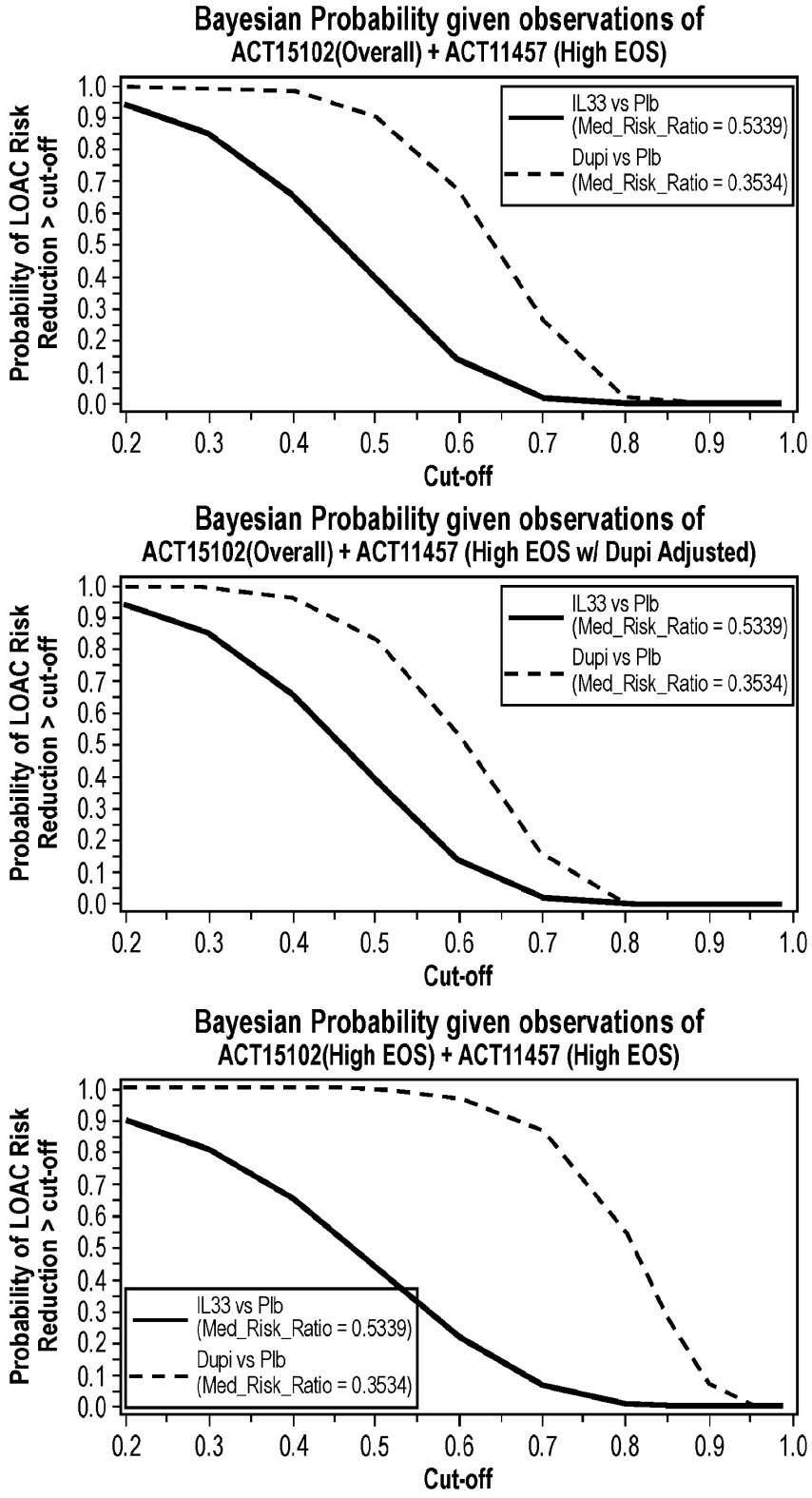

Bayesian Probability given observations of
ACT15102(Overall) + ACT11457 (High EOS)
Probability of LOAC Risk Reduction > cut-off
IL33 vs Plb (Med_Risk_Ratio = 0.5339)
Dupi vs Plb (Med_Risk_Ratio = 0.3534)
Cut-off
Bayesian Probability given observations of
ACT15102(Overall) + ACT11457 (High EOS w/ Dupi Adjusted)
Probability of LOAC Risk Reduction > cut-off
IL33 vs Plb (Med_Risk_Ratio = 0.5339)
Dupi vs Plb (Med_Risk_Ratio = 0.3534)
Cut-off
Bayesian Probability given observations of
ACT15102(High EOS) + ACT11457 (High EOS)
Probability of LOAC Risk Reduction > cut-off
IL33 vs Plb (Med_Risk_Ratio = 0.5339)
Dupi vs Plb (Med_Risk_Ratio = 0.3534)
Cut-off

Fig. 91

Inclusion	
Age/Sex	Adults, ≥18-70 years, females and males
Asthma history	Physician-diagnosed asthma for at least 12 months based on GINA
Existing asthma treatment	Medium- to-high dose ICS (≥250 mcg of fluticasone propionate twice daily or equivalent, max 1000 mcg/day) in combination with LABA
Pre-BD FEV1	FEV1 >40% of predicted normal at Visit 1; FEV1 ≥50% but ≤85% of predicted normal at Visit 2
ACQ-5	≥1.5 and < 3
FEV1	≥12% and 200 mL inc in FEV1 post BD OR documented history in last 12 mos OR methacholine PC20 < 8 mg/ml
No. of prior severe exacerbations	≥1 within 2 years
Baseline eos	No more than 25% of patients < 150 cells/microL At least 45% of patients ≥ 300 cells/microL
Exclusion	
	▪BMI <16 ▪Chronic lung disease (e.g. COPD, IPF]) which may impair lung function ▪ACQ-5) score <1.25 or >3.0 at V2/randomization. During the screening period an ACQ-5 of up to ≤4 is acceptable. ▪Use of systemic corticosteroids within 28 days of, or during, screening period ▪Current smoker (or smoker who stopped within 6 months or previous history of > 10 packs/year) ▪Anti-immunoglobulin E (IgE) therapy or allergen immunotherapy ▪Bronchial thermoplasty within 2 years prior to Visit 1 or plan to begin therapy during the screening period or the randomized treatment period

Fig. 92

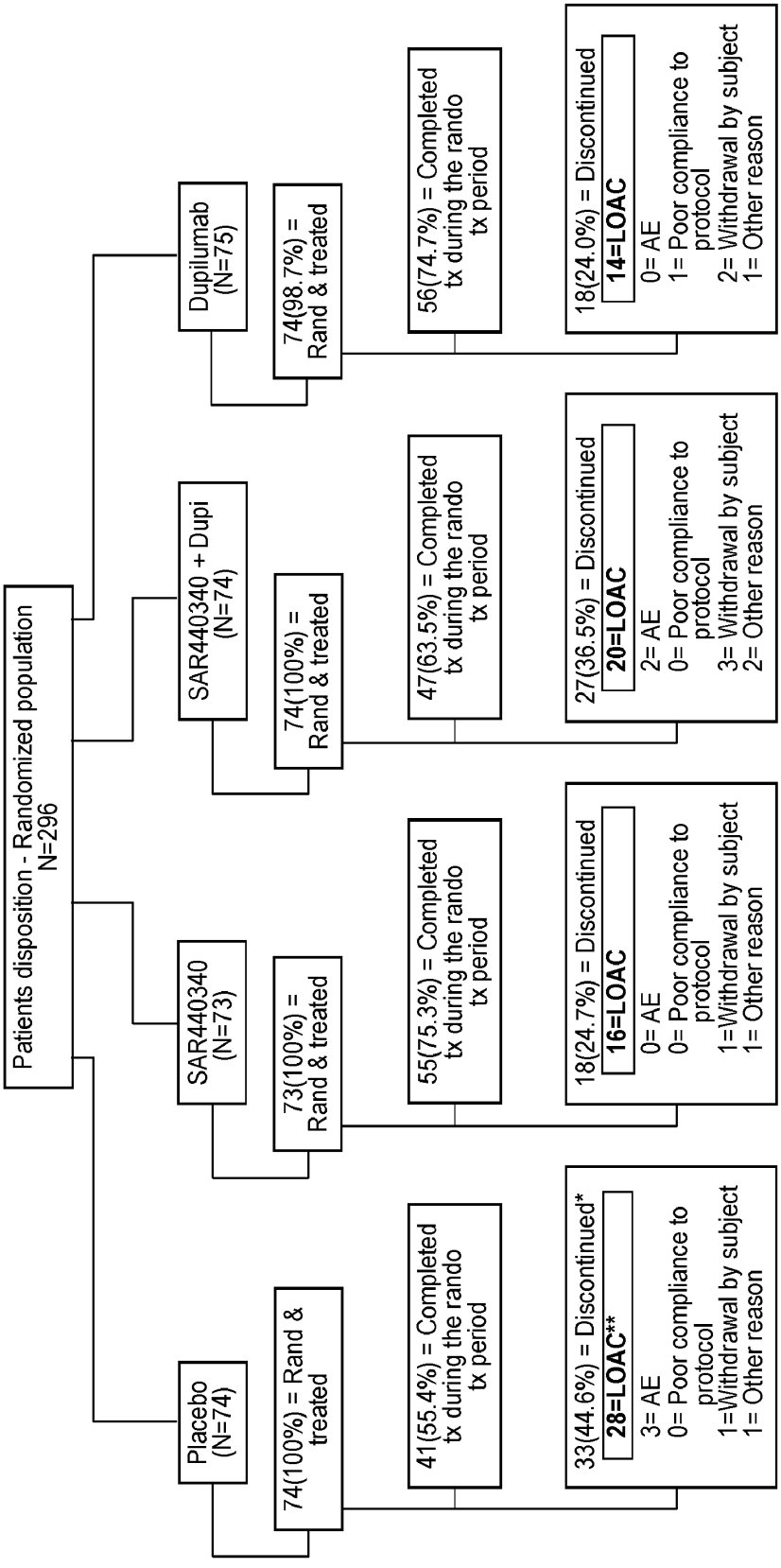

Patients disposition - Randomized population N=296
Placebo (N=74)
74(100%) = Rand & treated
41(55.4%) = Completed tx during the rando tx period
33(44.6%) = Discontinued*
28=LOAC**
3= AE
0= Poor compliance to protocol
1=Withdrawal by subject
1= Other reason
SAR440340 (N=73)
73(100%) = Rand & treated
55(75.3%) = Completed tx during the rando tx period
18(24.7%) = Discontinued
16=LOAC
0= AE
0= Poor compliance to protocol
1=Withdrawal by subject
1= Other reason
SAR440340 + Dupi (N=74)
74(100%) = Rand & treated
47(63.5%) = Completed tx during the rando tx period
27(36.5%) = Discontinued
20=LOAC
2= AE
0= Poor compliance to protocol
3= Withdrawal by subject
2= Other reason
Dupilumab (N=75)
74(98.7%) = Rand & treated
56(74.7%) = Completed tx during the rando tx period
18(24.0%) = Discontinued
14=LOAC
0= AE
1= Poor compliance to protocol
2= Withdrawal by subject
1= Other reason

Fig. 93

		N=74	N=73	N=74	N=75	N=296
Category	Data	PBO	SAR440340	SAR440340 + Dupilumab	Dupilumab	All
Age (y)	Mean (SD)	47.0 (11.4)	49.0 (13.9)	49.1 (12.0)	51.3 (12.7)	49.1 (12.6)
Sex (%)	Female	47 (63.5)	50 (68.5)	51 (68.9)	41 (54.7)	189 (63.9)
BMI (kg/m2) [n(%)]	Mean (SD)	29.92 (6.89)	28.66 (5.57)	30.27 (6.20)	28.93 (5.99)	29.45 (6.19)
BMI (kg/m2) [n(%)]	?30	32 (43.2)	24 (32.9)	28 (37.8)	29 (38.7)	113 (38.2)
Region	E Europe	43 (58.1)	41 (56.2)	42 (56.8)	44 (58.7)	170 (57.4)
Region	Lat Am	16 (21.6)	18 (24.7)	18 (24.3)	16 (21.3)	68 (23.0)
Region	No Am	15 (20.3)	14 (19.2)	14 (18.9)	15 (20.0)	58 (19.6)
Race	White	71 (95.9)	68 (93.2)	69 (93.2)	73 (97.3)	281 (94.9)
Race	Black	1 (1.4)	3 (4.1)	2 (2.7)	0	6 (2.0)
Race	Asian	0	2 (2.7)	1 (1.4)	1 (1.3)	4 (1.4)
Race	Native American	2 (2.7)	0	1 (1.4)	1 (1.3)	4 (1.4)
Race	Multiple	0	0	1 (1.4)	0	1 (0.3)
Ethnicity	Hispanic	17 (23.0)	17 (23.3)	17 (23.0)	14 (18.7)	65 (22.0)
Ethnicity	Not Hispanic	57 (77.0)	56 (76.7)	57 (77.0)	61 (81.3)	231 (78.0)

Fig. 94

		N=74	N=73	N=74	N=75	N=296
Category	Data	PBO	SAR440340	SAR440340 + Dupilumab	Dupilumab	All
Age at asthma onset (y)	Mean (SD)	28.8 (17.6)	31.6 (19.9)	31.5 (18.1)	32.6 (17.8)	31.1 (18.3)
Age at asthma onset (y) - >/=40	[n (%)]	22 (29.7)	28 (38.4)	30 (40.5)	27 (36.0)	107 (36.1)
Smoking	Never	62 (83.8)	62 (84.9)	**53 (71.6)**	61 (81.3)	238 (80.4)
ICS Dose	High	48 (64.9)	**45 (61.6)**	49 (66.2)	53 (70.7)	195 (65.9)
ICS Dose	Medium	26 (35.1)	28 (38.4)	25 (33.8)	22 (29.3)	101 (34.1)
BL pre-FEV1 (L)	Mean (SD)	2.12 (0.61)	**1.93 (0.47)**	2.00 (0.57)	2.04 (0.63)	2.02 (0.57)
BL pre-FEV1 % pred (%)	Mean (SD)	65.90 (9.54)	63.71 (9.35)	65.04 (9.00)	64.10 (10.26)	64.69 (9.54)
BL FEV1 reversibility (%)	Mean (SD)	15.58 (15.84)	16.22 (13.27)	14.52 (17.98)	13.32 (11.76)	14.90 (14.87)
BL ACQ-5	Mean (SD)	2.19 (0.38)	2.12 (0.40)	2.07 (0.38)	2.25 (0.41)	2.16 (0.40)
BL-AQLQ	Mean (SD)	4.68 (0.95)	4.58 (0.94)	4.77 (0.79)	4.67 (0.90)	4.68 (0.90)
BL Total IgE (IU/mL)	Mean (SD)	317.56 (523.05)	682.04 (1798.02)	314.36 (412.73)	367.48 (548.84)	419.30 (998.79)
BL Total IgE (IU/mL)	Median	161.5	140	144.5	170	160.5

Fig. 95

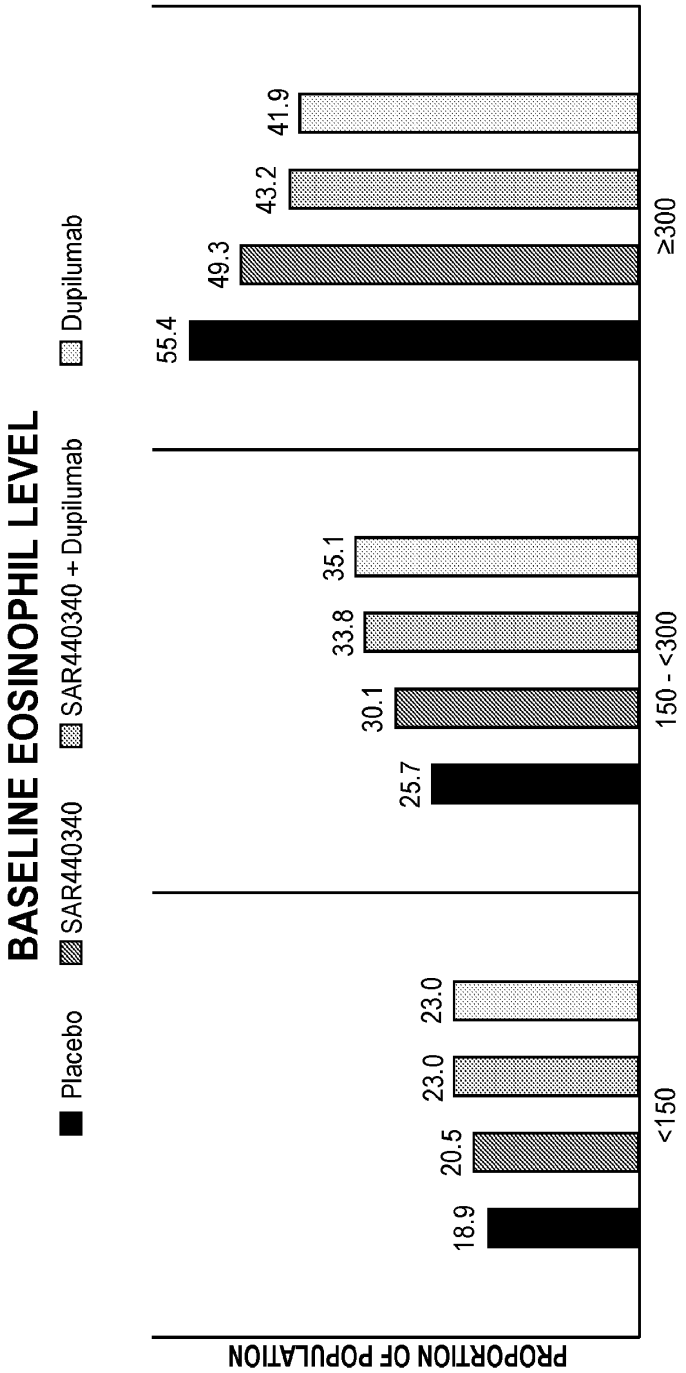

BASELINE EOSINOPHIL LEVEL
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
PROPORTION OF POPULATION
18.9
20.5
23.0
23.0
<150
25.7
30.1
33.8
35.1
150 - <300
55.4
49.3
43.2
41.9
≥300
EOSINOPHILSTRATA

Fig. 96A

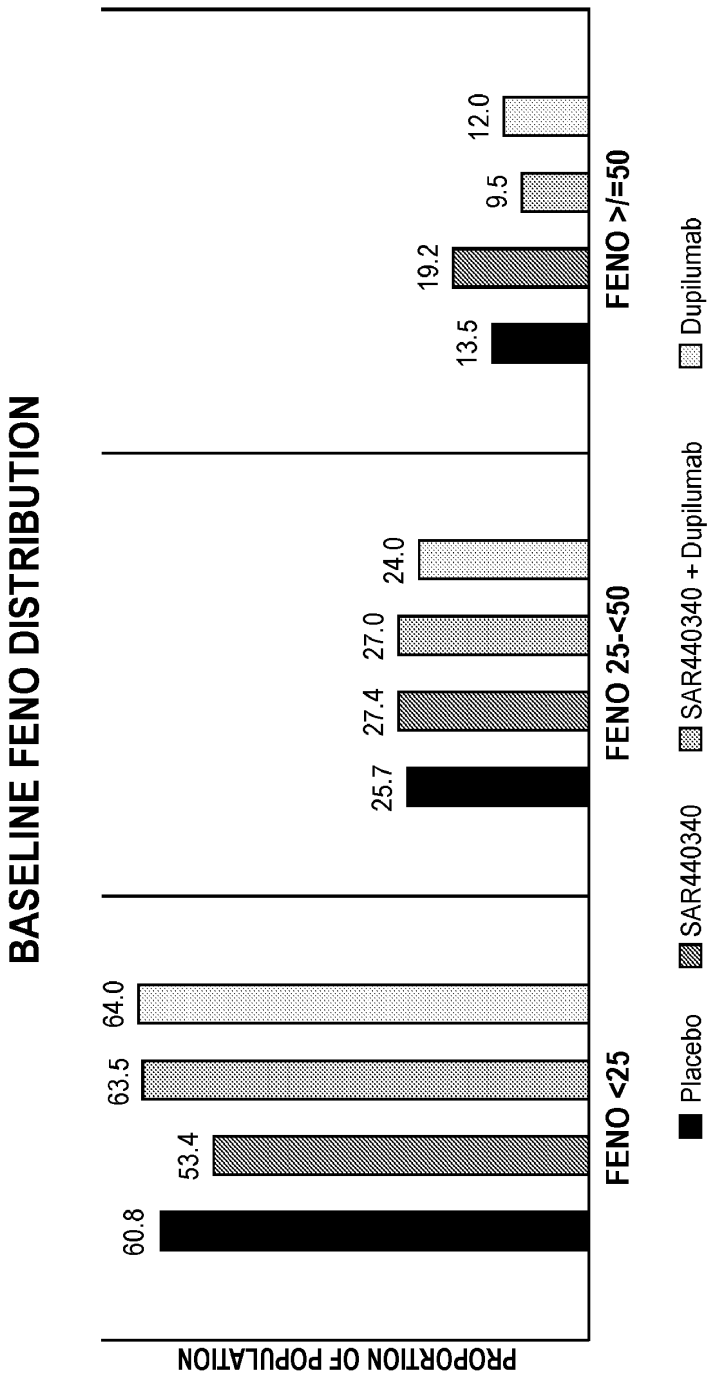

BASELINE FENO DISTRIBUTION
PROPORTION OF POPULATION
FENO <25
FENO 25-<50
FENO >/=50
60.8
53.4
63.5
64.0
25.7
27.4
27.0
24.0
13.5
19.2
9.5
12.0
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 96B

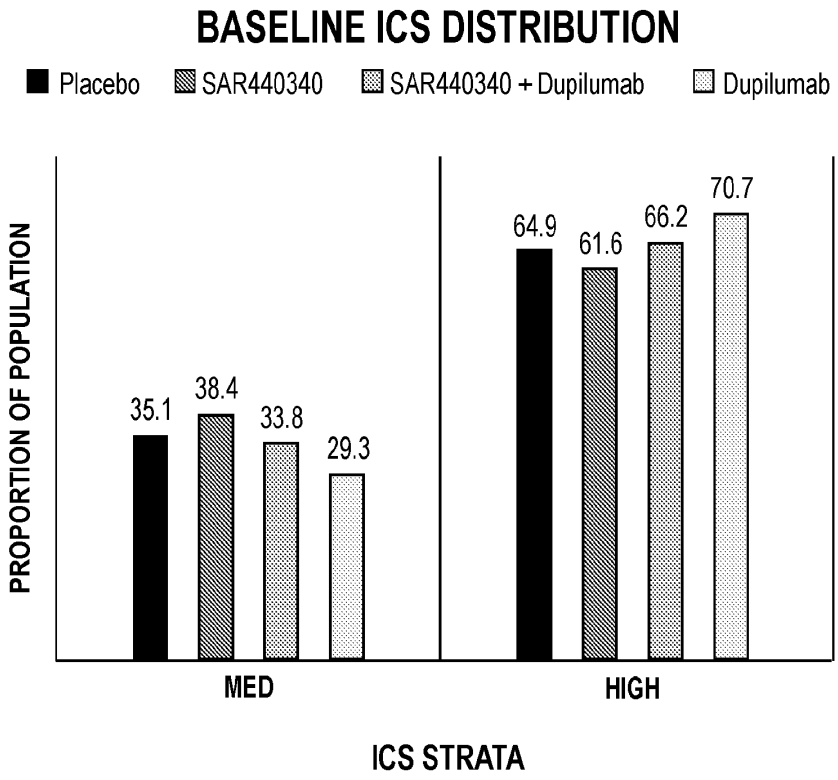

BASELINE ICS DISTRIBUTION
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
PROPORTION OF POPULATION
35.1
38.4
33.8
29.3
64.9
61.6
66.2
70.7
MED
HIGH
ICS STRATA

Fig. 96C

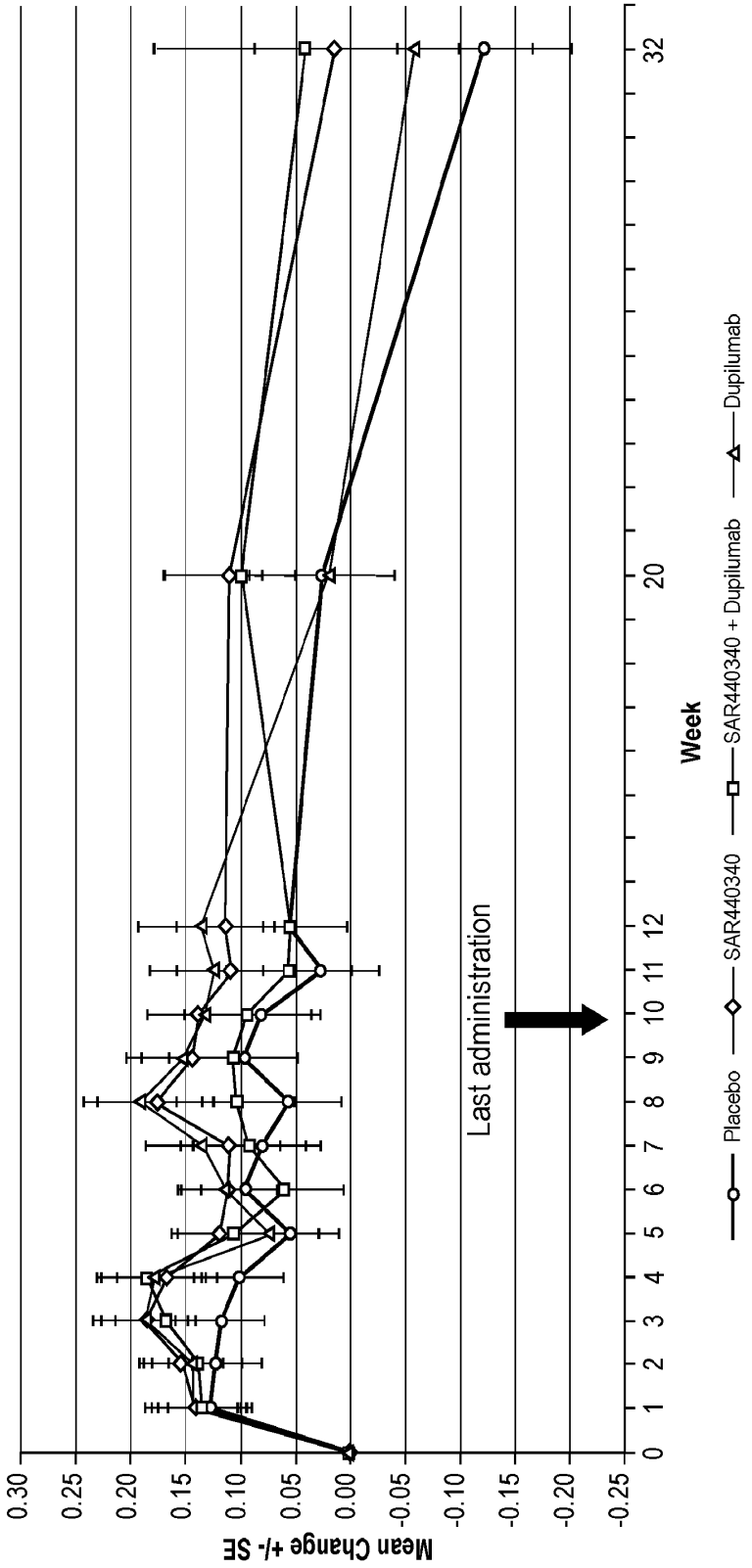

Mean Change +/- SE
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
-0.20
-0.25
0 1 2 3 4 5 6 7 8 9 10 11 12 20 32
Week
Last administration
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 97

	N=74	N-73	N=74	N=74	N=74	N=73	N=74	N=74
ITT - Week 4	32 (43.2)	37 (50.7)	39 (52.7)	35 (47.3)	31 (41.9)	38 (52.1)	44 (59.5)	30 (40.5)
ITT - Week 12	28 (37.8)	41 (56.2)	34 (45.9)	41 (55.4)	21 (28.4)	36 (49.3)	28 (37.8)	33 (44.6)
	N=14	N=15	N=17	N=17	N=14	N=15	N=17	N=17
<150 - Week 4	5 (35.7)	5 (33.3)	7 (41.2)	7 (41.2)	4 (28.6)	7 (46.7)	10 (58.8)	8 (47.1)
<150 - Week 12	5 (35.7)	9 (60.0)	10 (58.8)	7 (41.2)	6 (42.9)	9 (60.0)	7 (41.2)	8 (47.1)
	N=19	N=22	N=25	N=26	N=19	N=22	N=25	N=26
150-<300 - Week 4	7 (36.8)	11 (50.0)	14 (56.0)	8 (30.8)	10 (52.6)	11 (50.0)	15 (60.0)	7 (26.9)
150-<300 - Week 12	8 (42.1)	12 (54.5)	11 (44.0)	14 (53.8)	6 (31.6)	10 (45.5)	10 (40.0)	10 (38.5)
	N=33	N=37	N=42	N=43	N=33	N=37	N=42	N=43
<300 - Week 4	12 (36.4)	16 (43.2)	21 (50.0)	15 (34.9)	14 (42.4)	18 (48.6)	25 (59.5)	15 (34.9)
<300 - Week 12	13 (39.4)	21 (56.8)	21 (51.0)	21 (48.8)	12 (36.4)	19 (51.4)	17 (40.5)	18 (41.9)
	N=41	N=36	N=32	N=31	N=41	N=36	N=32	N=31
>/=300 - Week 4	20 (48.8)	21 (58.3)	18 (56.3)	20 (64.5)	17 (41.5)	20 (55.6)	19 (59.4)	15 (48.4)
>/=300 - Week 12	15 (36.6)	20 (56.6)	13 (40.6)	20 (64.5)	9 (22.0)	17 (47.2)	11 (34.4)	15 (48.4)

Fig. 98

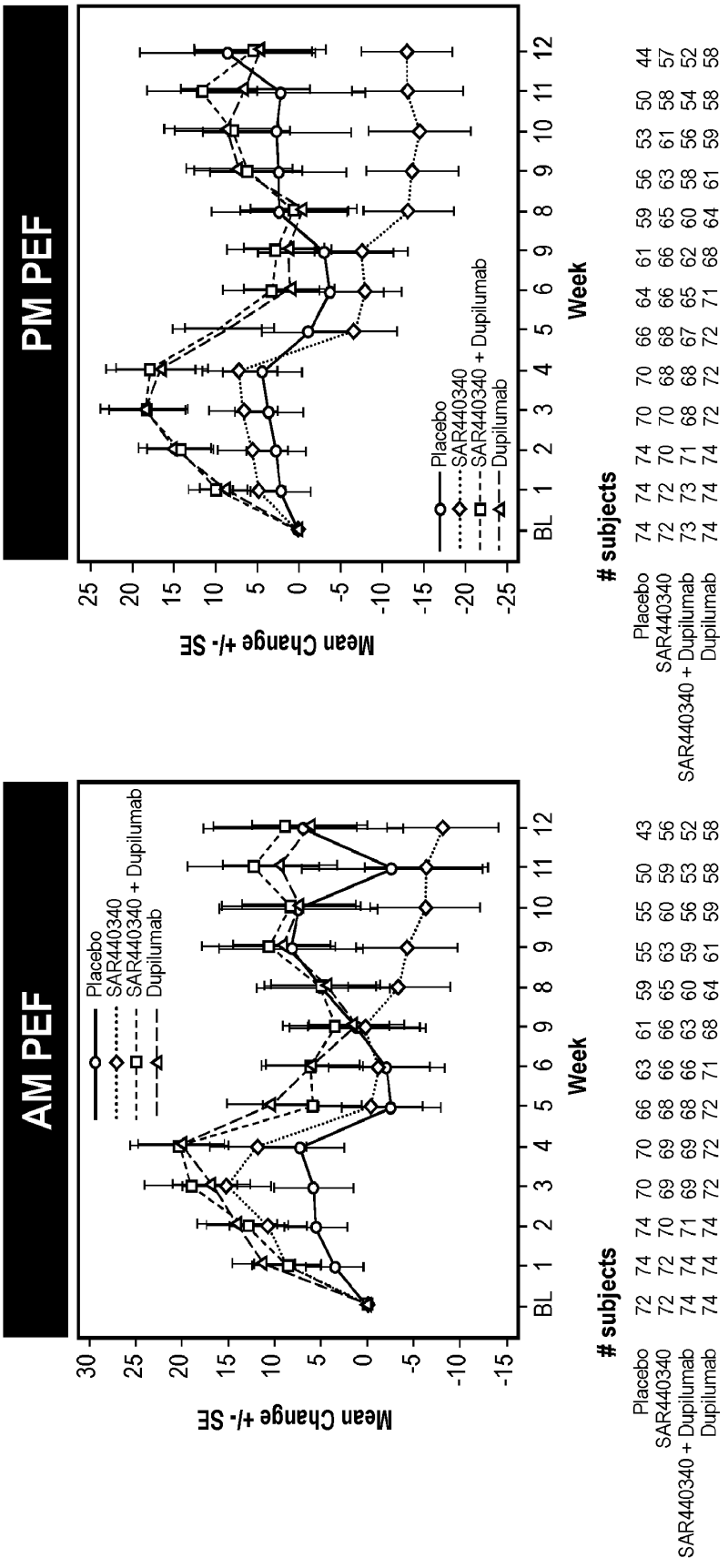

AM PEF
PM PEF
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
Week
BL 1 2 3 4 5 6 7 8 9 10 11 12
subjects
Placebo 72 74 74 70 70 66 63 61 59 55 55 50 43
SAR440340 72 72 70 69 69 68 66 66 65 63 60 59 56
SAR440340 + Dupilumab 74 74 71 69 69 68 66 63 60 59 56 53 52
Dupilumab 74 74 74 72 72 72 71 68 64 61 59 58 58
Placebo 74 74 74 70 70 70 68 68 66 66 64 61 59 56 53 50 44
SAR440340 72 72 70 70 70 68 68 67 65 62 60 58 56 54 52
SAR440340 + Dupilumab 73 73 71 68 68 67 65 62 60 58 56 54 52
Dupilumab 74 74 74 72 72 72 71 68 64 61 59 58 58

Fig. 99

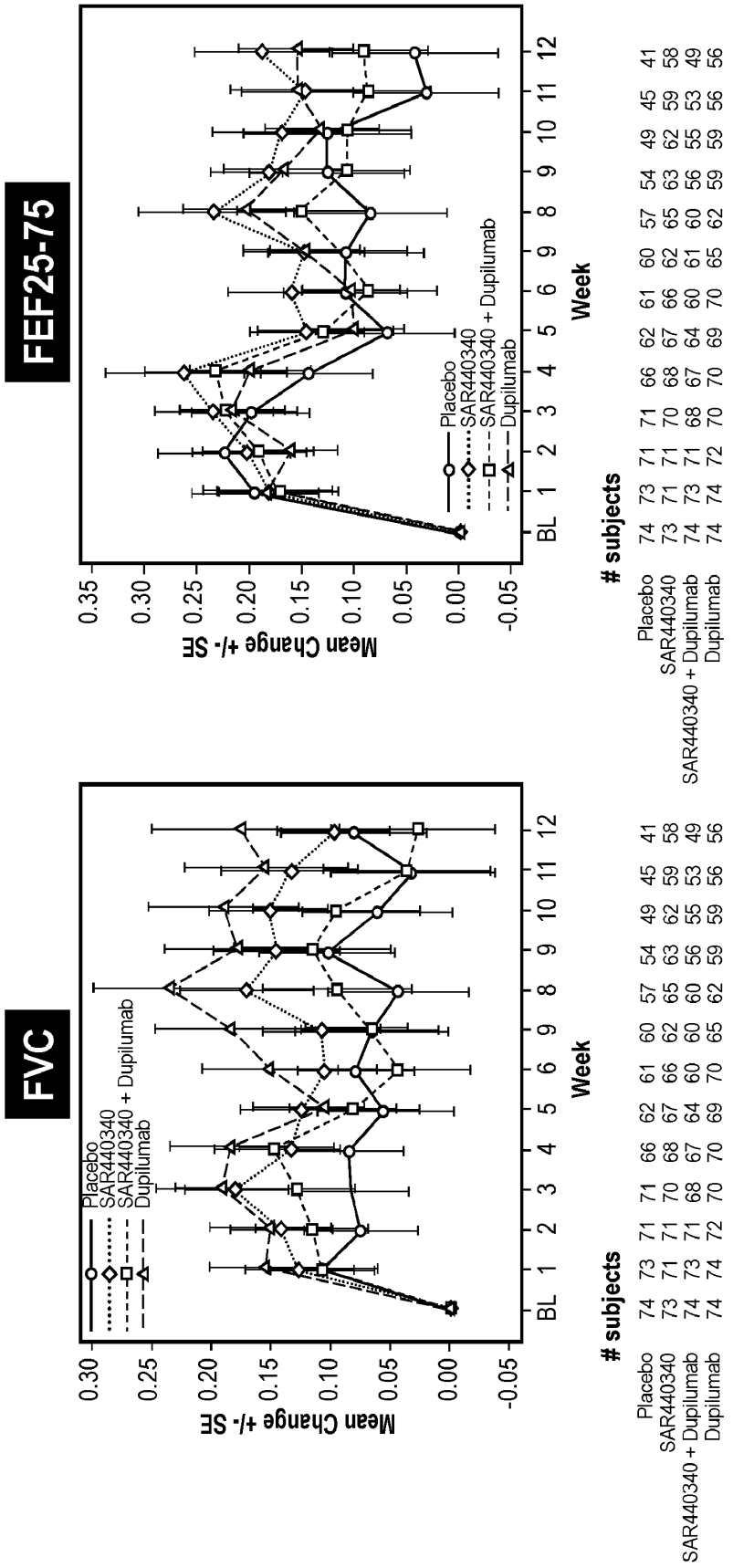
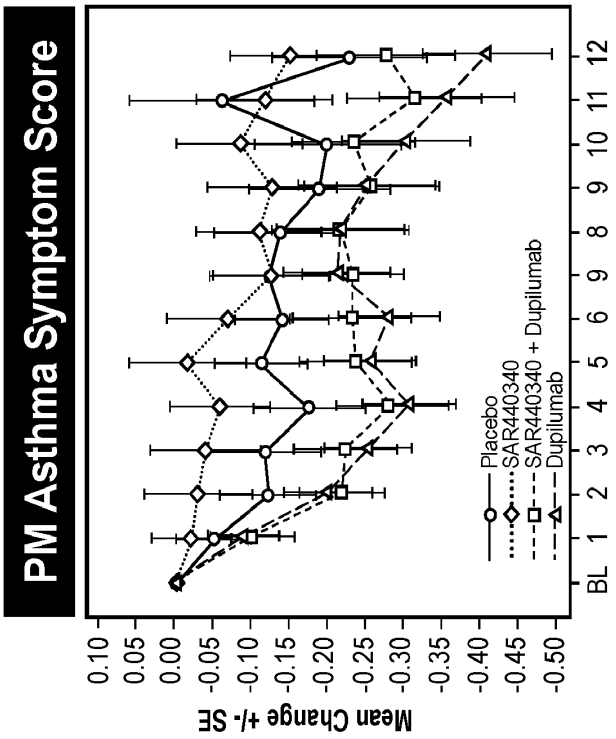
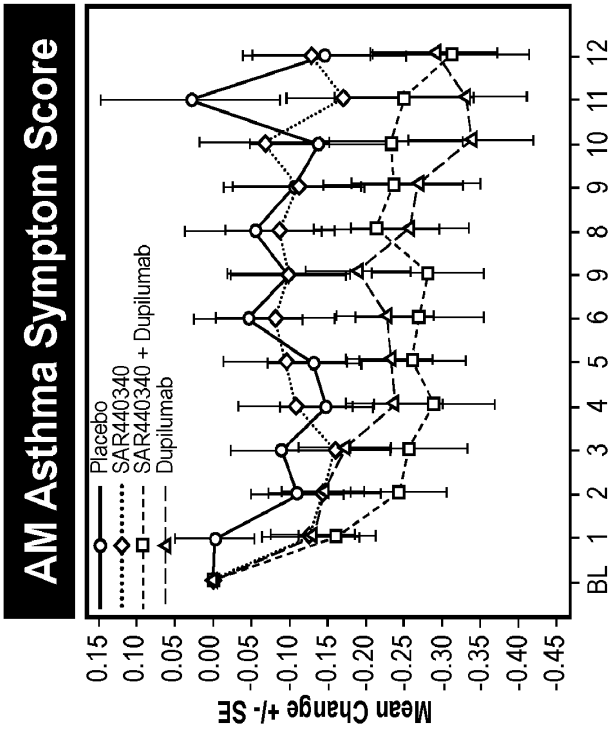

FVC
FEF25-75
Mean Change +/- SE
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 74 73 71 71 66 62 61 60 57 54 49 45 41
SAR440340 73 71 71 70 68 67 66 62 65 63 62 59 58
SAR440340 + Dupilumab 74 73 71 68 67 64 60 60 60 56 55 53 49
Dupilumab 74 74 72 70 70 69 70 65 62 59 59 56 56

Fig. 100





# subjects	BL	1	2	3	4	5	6	7	8	9	10	11	12
Placebo	74	74	74	70	70	66	64	61	59	56	53	50	44
SAR440340	73	73	71	70	70	69	67	67	67	65	63	61	58
SAR440340 + Dupilumab	74	74	71	69	69	68	66	63	60	59	56	54	52
Dupilumab	74	74	74	72	72	72	71	68	64	61	59	58	58

# subjects	BL	1	2	3	4	5	6	7	8	9	10	11	12
Placebo	74	74	74	70	70	66	64	61	59	56	53	50	44
SAR440340	73	73	71	71	69	69	67	67	67	65	63	60	59
SAR440340 + Dupilumab	74	74	72	69	69	68	66	61	61	59	56	54	52
Dupilumab	74	74	74	72	72	72	71	64	64	61	59	58	58

Fig. 101

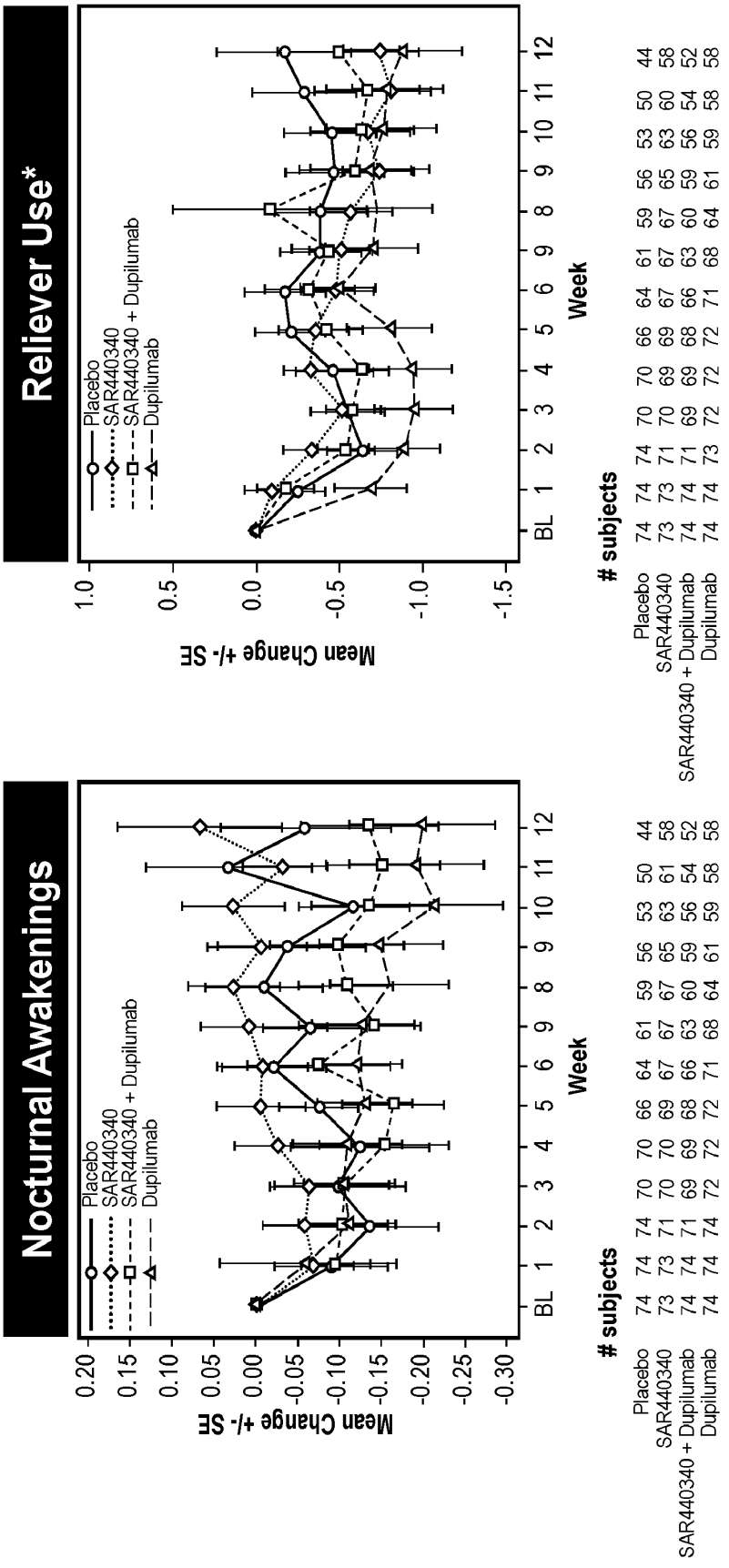
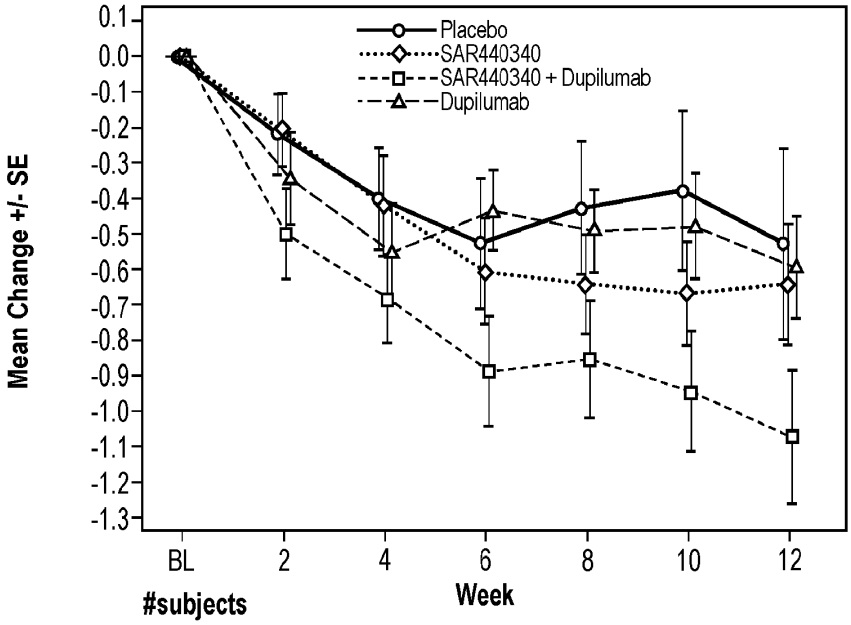
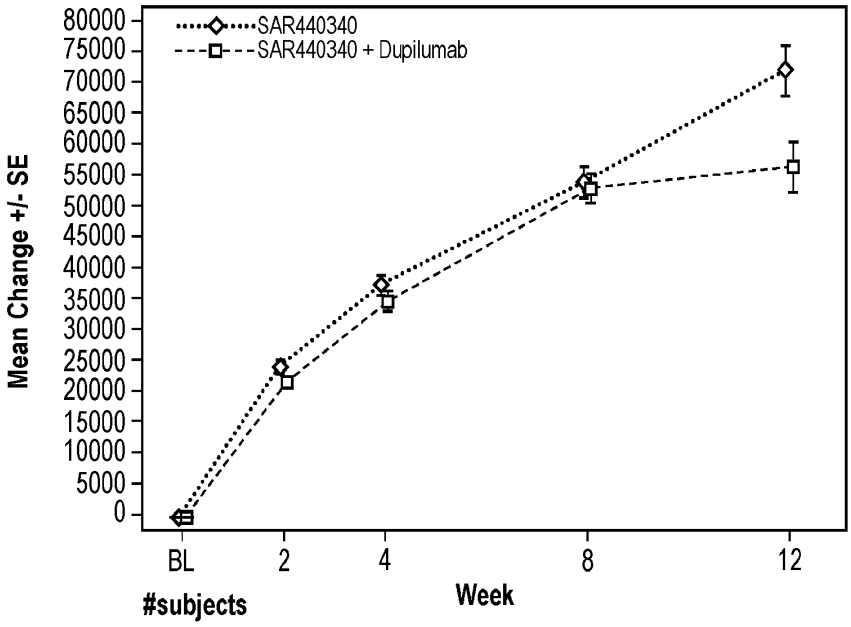

Nocturnal Awakenings
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
BL 1 2 3 4 5 6 7 8 9 10 11 12
Week
subjects
Placebo 74 74 74 70 70 66 64 61 59 56 53 50 44
SAR440340 73 73 71 70 70 69 67 67 65 63 61 58
SAR440340 + Dupilumab 74 74 71 69 69 68 66 63 60 59 56 54 52
Dupilumab 74 74 74 72 72 71 68 64 61 59 58 58
Reliever Use*
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean Change +/- SE
1.0
0.5
0.0
-0.5
-1.0
-1.5
BL 1 2 3 4 5 6 7 8 9 10 11 12
Week
subjects
Placebo 74 74 74 70 70 66 64 61 59 56 53 50 44
SAR440340 73 73 71 70 70 69 68 67 67 65 63 60 58
SAR440340 + Dupilumab 74 74 71 69 69 68 66 66 63 60 59 56 54 52
Dupilumab 74 74 73 72 72 72 71 68 64 61 59 58 58

Fig. 102



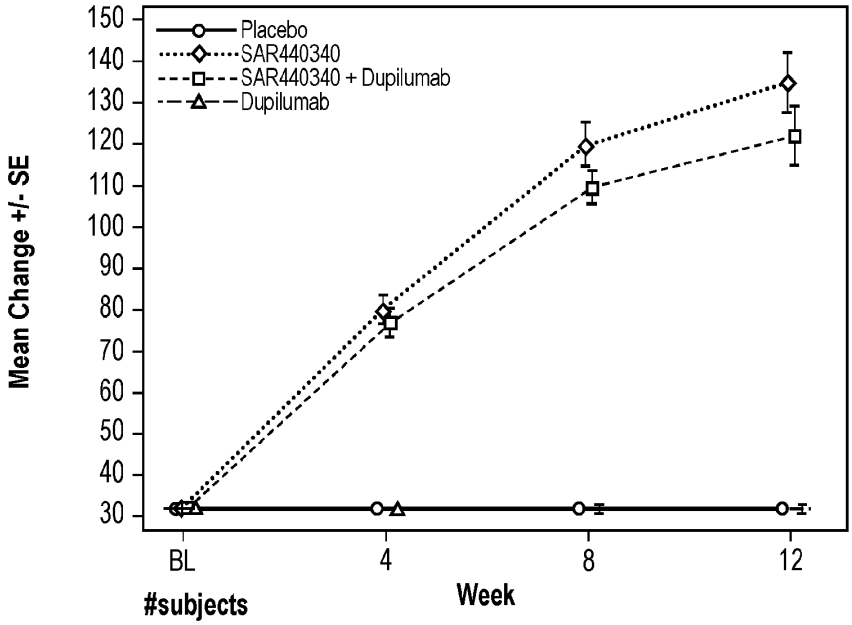
#subjects							
Placebo	52	48	48	41	41	33	27
SAR440340	41	39	36	34	36	33	31
SAR440340 + Dupilumab	43	39	39	36	35	32	28
Dupilumab	49	49	48	47	42	39	39

Fig. 103



#subjects					
SAR440340	73	70	68	68	53
SAR440340 + Dupilumab	72	69	69	65	45

Fig. 104



#subjects				
Placebo	74	72	60	41
SAR440340	73	71	68	53
SAR440340 + Dupilumab	74	73	65	45
Dupilumab	74	72	71	51

Fig. 105

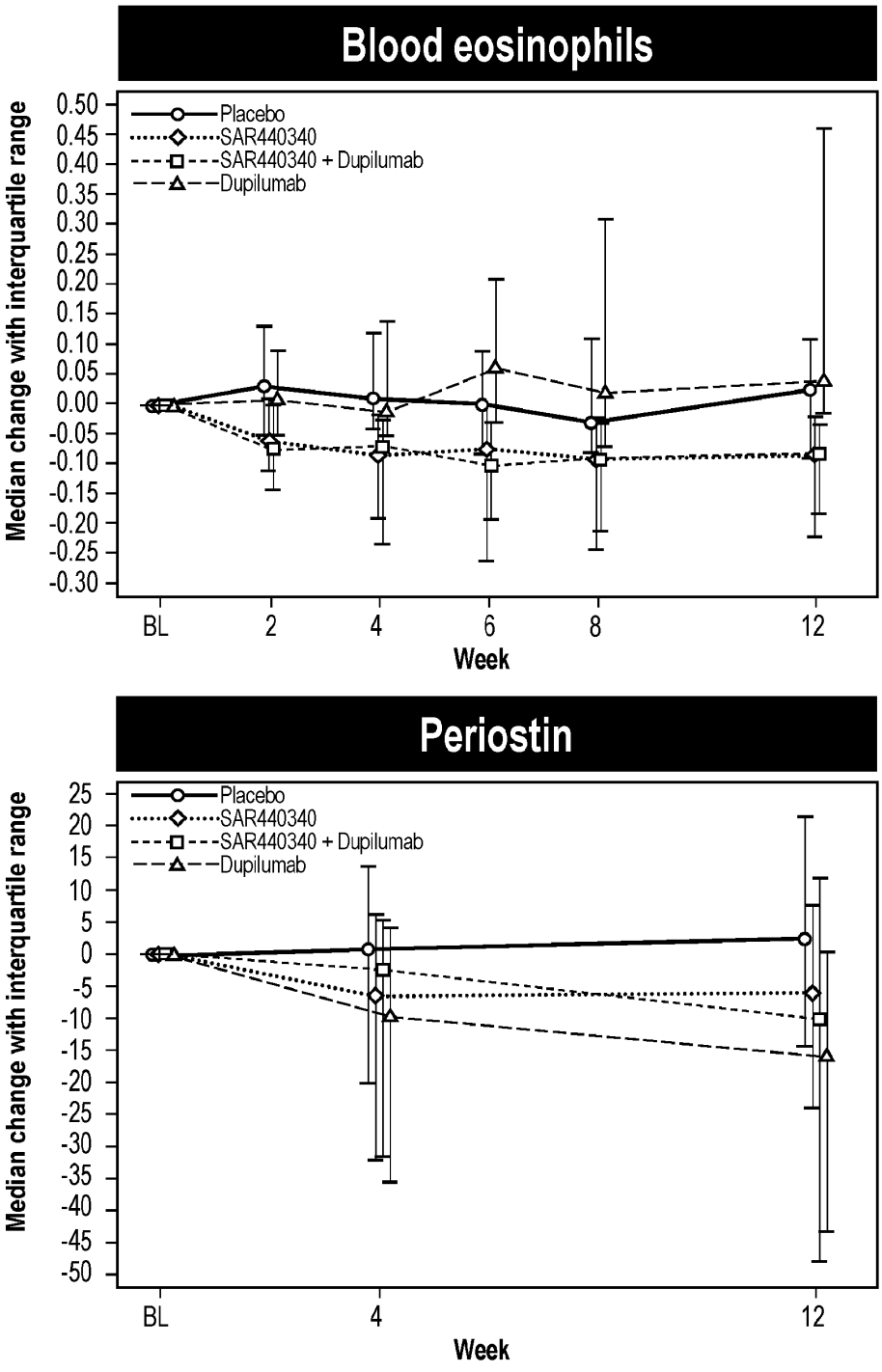
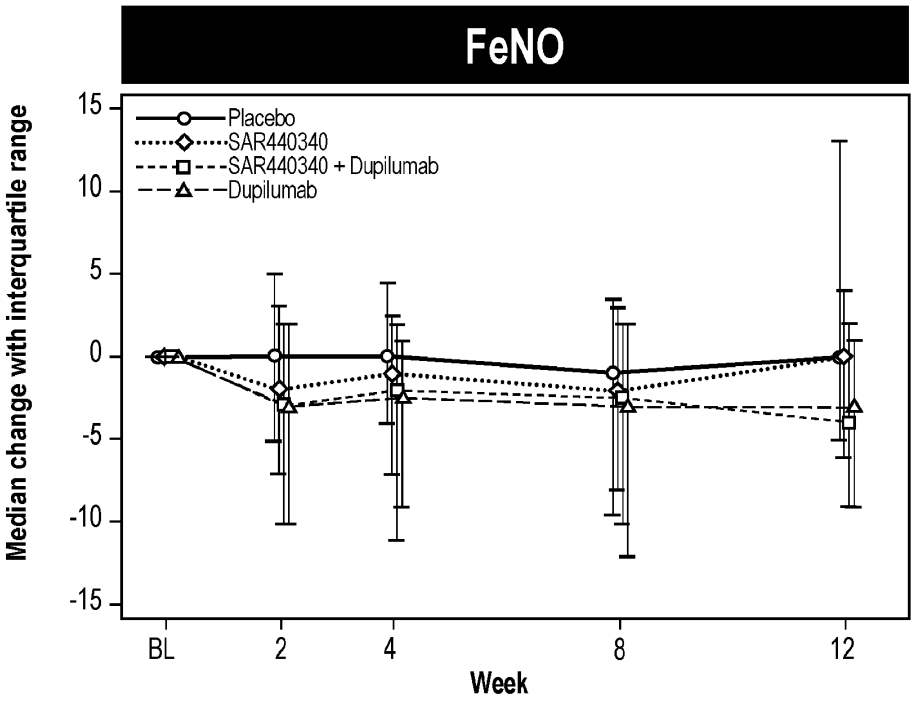

Blood eosinophils
Median change with interquartile range
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
BL
2
4
6
8
12
Week
Periostin
Median change with interquartile range
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
BL
4
12
Week

Fig. 106


FeNO
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
15
10
5
0
-5
-10
-15
BL
2
4
8
12
Week

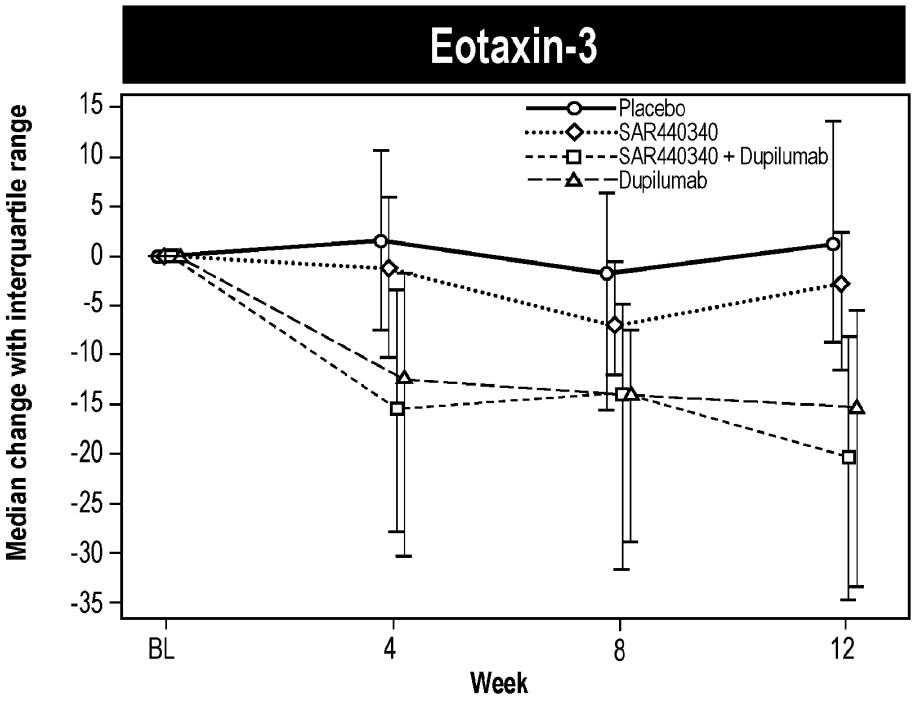

Eotaxin-3
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Median change with interquartile range
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
BL
4
8
12
Week

Fig. 106 (Cont)

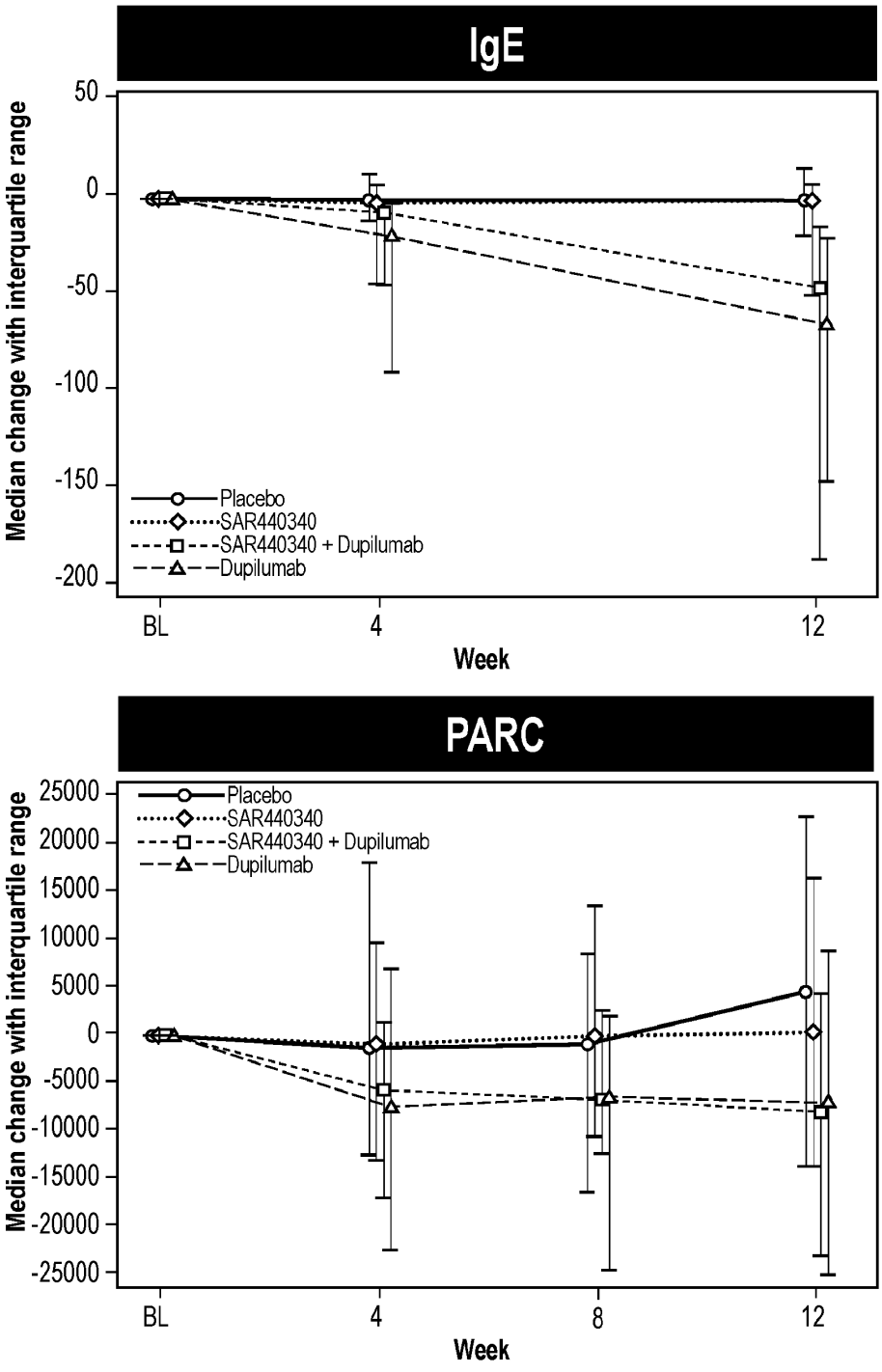

IgE
Median change with interquartile range
50
0
-50
-100
-150
-200
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
BL
4
12
Week
PARC
Median change with interquartile range
25000
20000
15000
10000
5000
0
-5000
-10000
-15000
-20000
-25000
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
BL
4
8
12
Week

Fig. 106 (Cont)

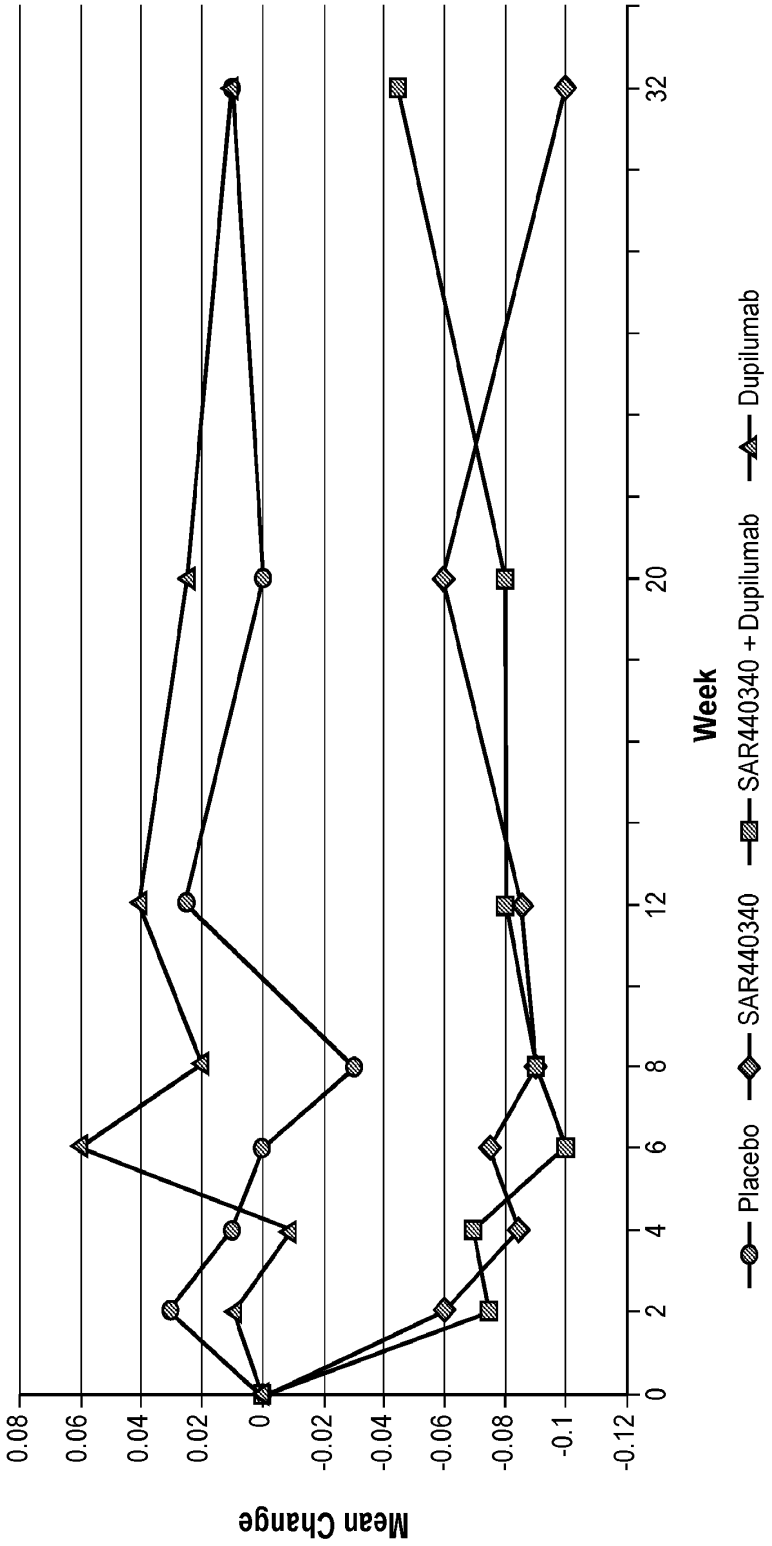

Mean Change
0.08
0.06
0.04
0.02
0
-0.02
-0.04
-0.06
-0.08
-0.1
-0.12
0
2
4
6
8
12
20
32
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 107

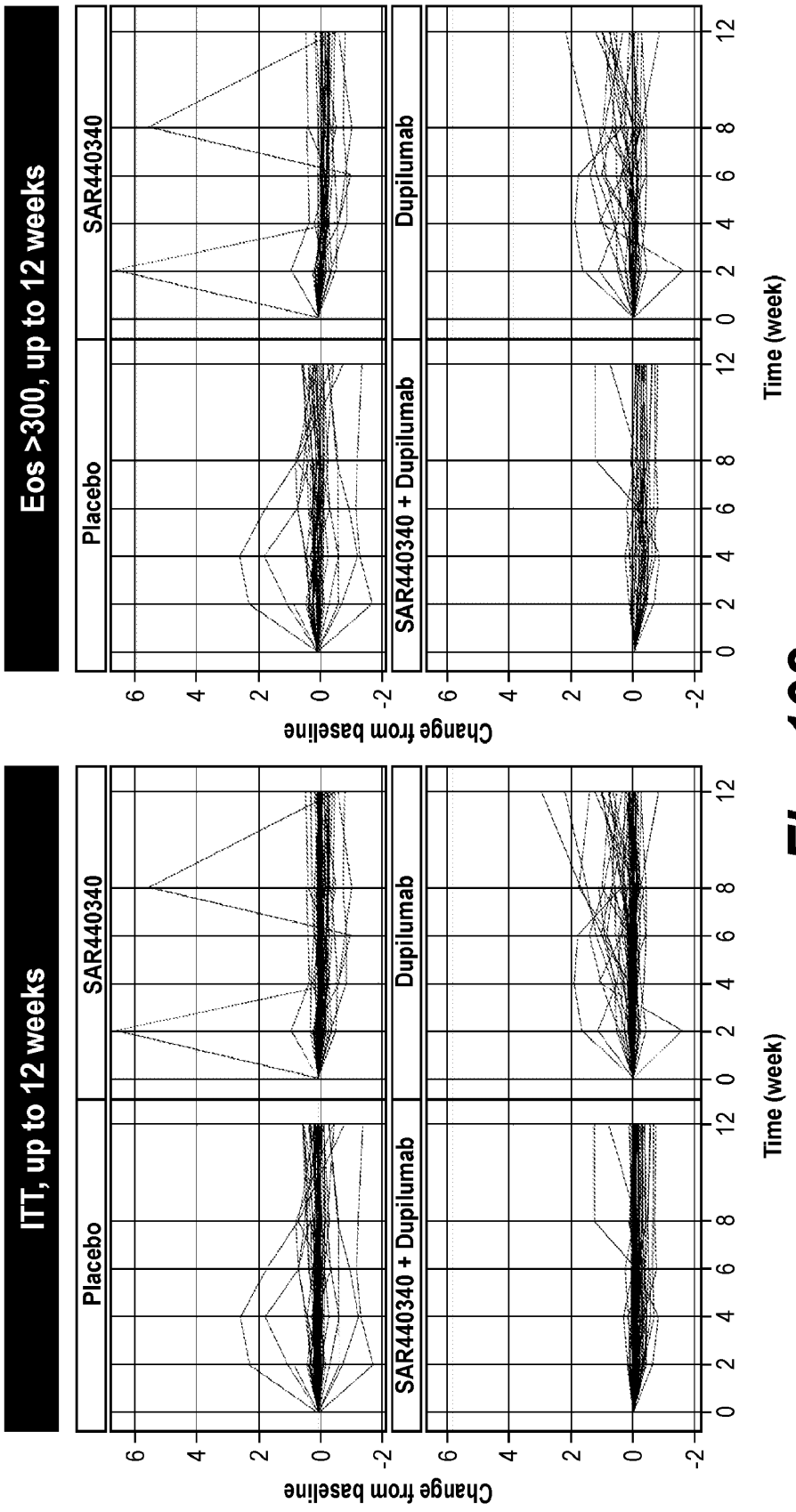
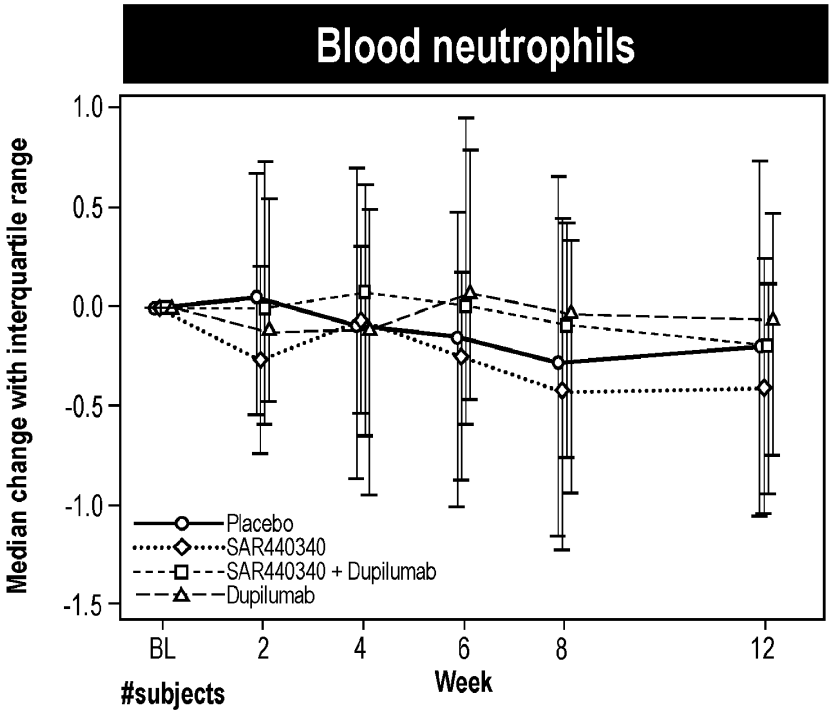
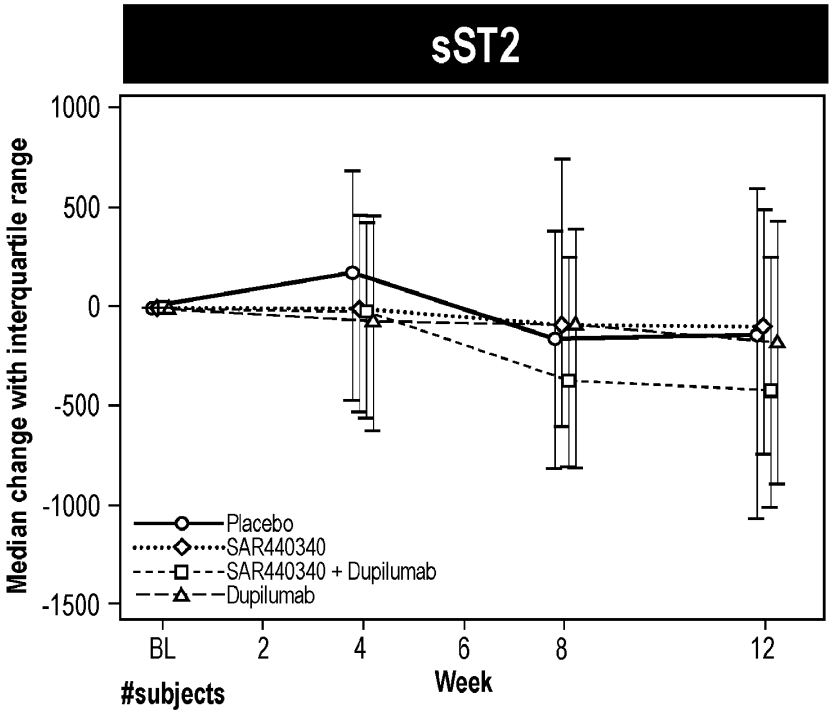

ITT, up to 12 weeks
Eos >300, up to 12 weeks
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Change from baseline
Time (week)

Fig. 108



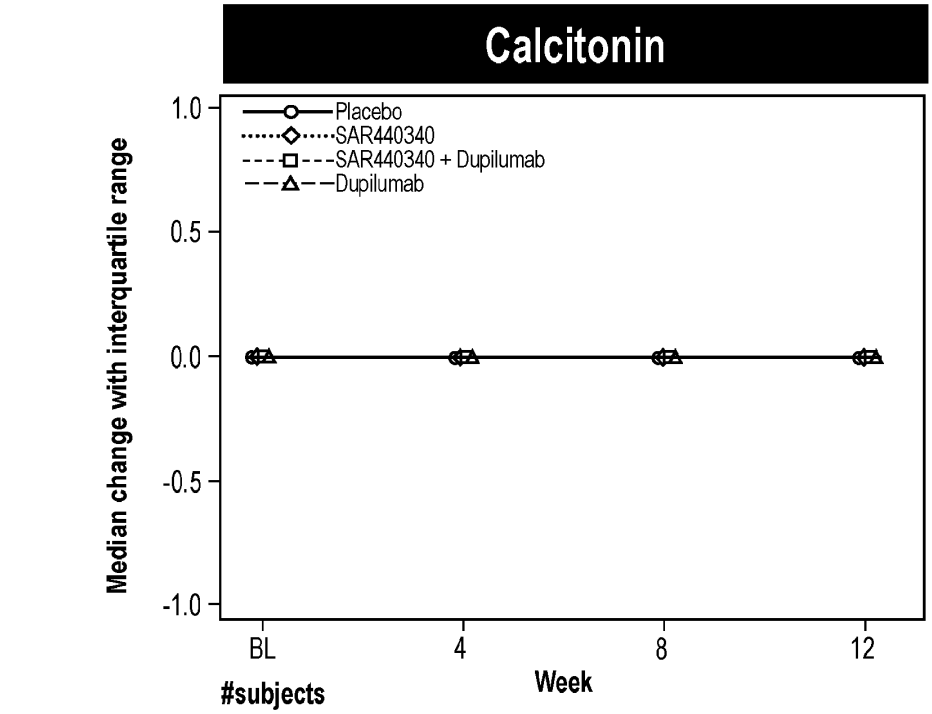
#subjects						
Placebo	74	69	67	61	54	52
SAR440340	73	68	65	62	65	62
SAR440340 + Dupilumab	74	66	68	61	58	56
Dupilumab	74	71	67	68	69	56

Fig. 109



#subjects				
Placebo	72	70	58	40
SAR440340	71	69	66	51
SAR440340 + Dupilumab	73	72	64	45
Dupilumab	74	72	71	51

Fig. 109 (Cont)



#subjects				
Placebo	74	70	59	51
SAR440340	73	71	67	63
SAR440340 + Dupilumab	74	73	64	56
Dupilumab	74	71	69	59

Fig. 109 (Cont)

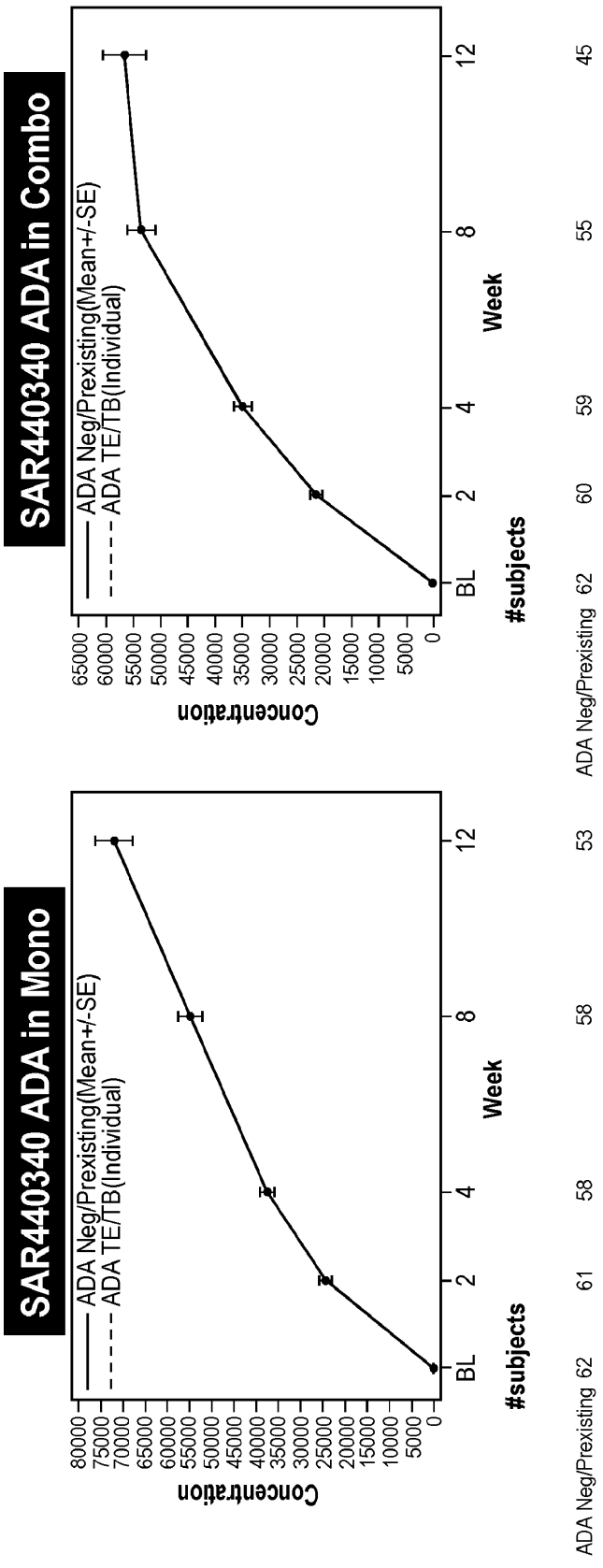

SAR440340 ADA in Mono
ADA Neg/Prexisting(Mean+/-SE)
ADA TE/TB(Individual)
Concentration
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
BL
2
4
8
12
Week
#subjects
ADA Neg/Prexisting 62 61 58 58 53
SAR440340 ADA in Combo
ADA Neg/Prexisting(Mean+/-SE)
ADA TE/TB(Individual)
Concentration
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
BL
2
4
8
12
Week
#subjects
ADA Neg/Prexisting 62 60 59 55 45

Fig. 110

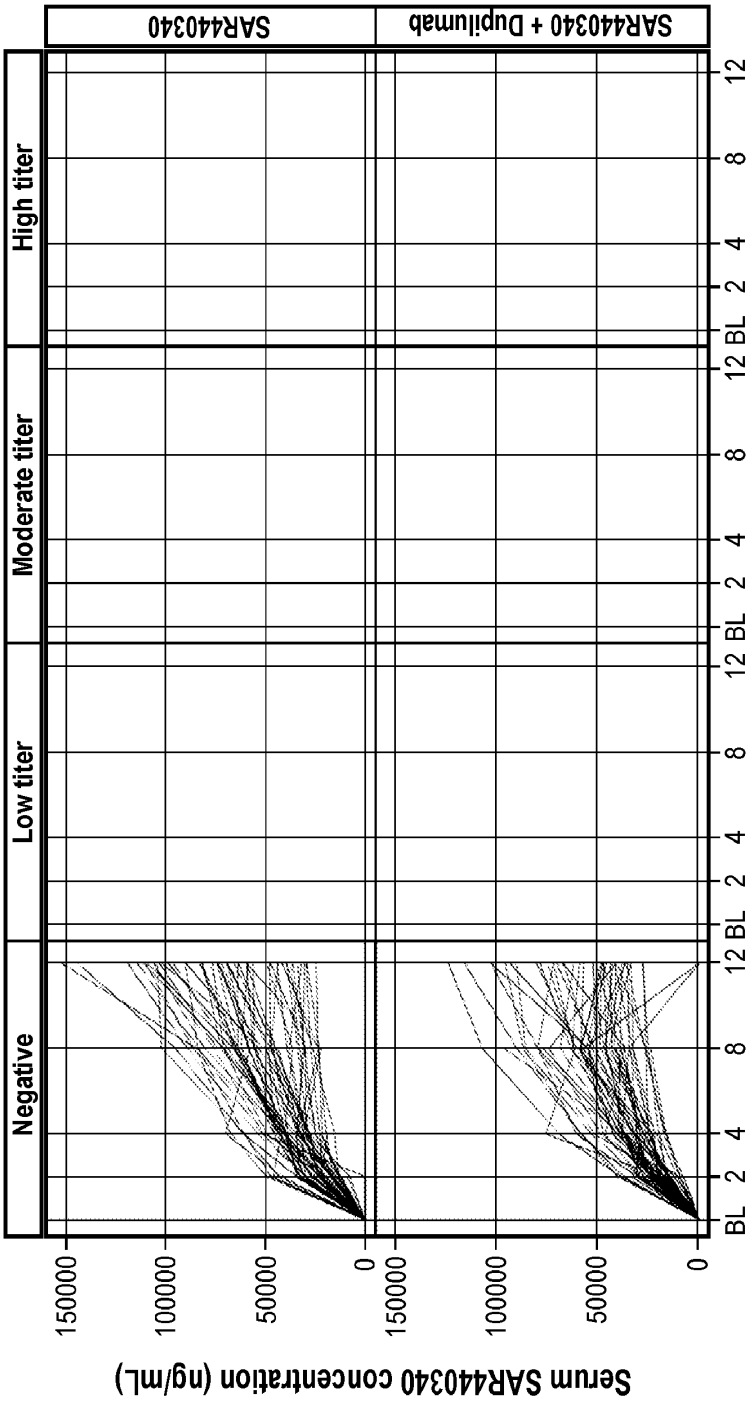

SAR440340
SAR440340 + Dupilumab
Negative
Low titer
Moderate titer
High titer
BL 2 4 8 12 BL 2 4 8 12 BL 2 4 8 12
Time (week)
0 50000 100000 150000
Serum SAR440340 concentration (ng/mL)

Fig. 111

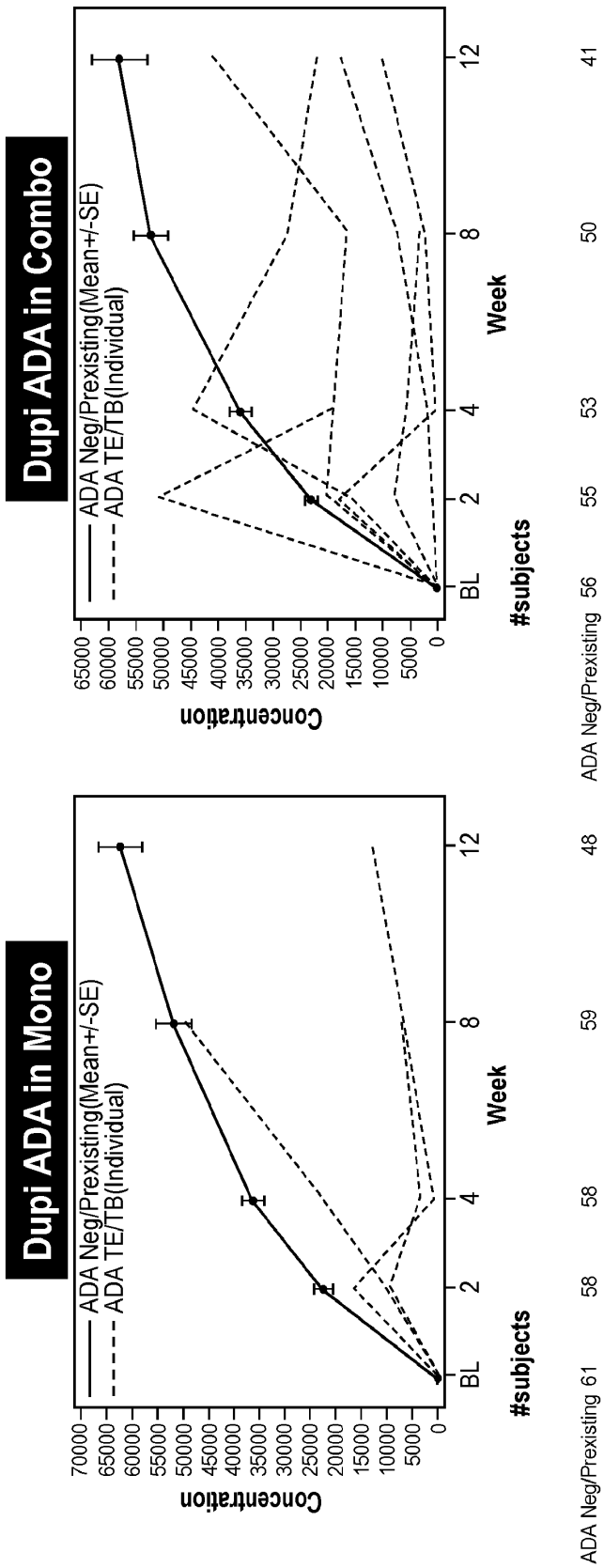

Dupi ADA in Mono
ADA Neg/Prexisting(Mean+/-SE)
ADA TE/TB(Individual)
Concentration
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
BL
2
4
8
12
Week
#subjects
ADA Neg/Prexisting 61 58 58 59 48
Dupi ADA in Combo
ADA Neg/Prexisting(Mean+/-SE)
ADA TE/TB(Individual)
Concentration
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
BL
2
4
8
12
Week
#subjects
ADA Neg/Prexisting 56 55 53 50 41

Fig. 112

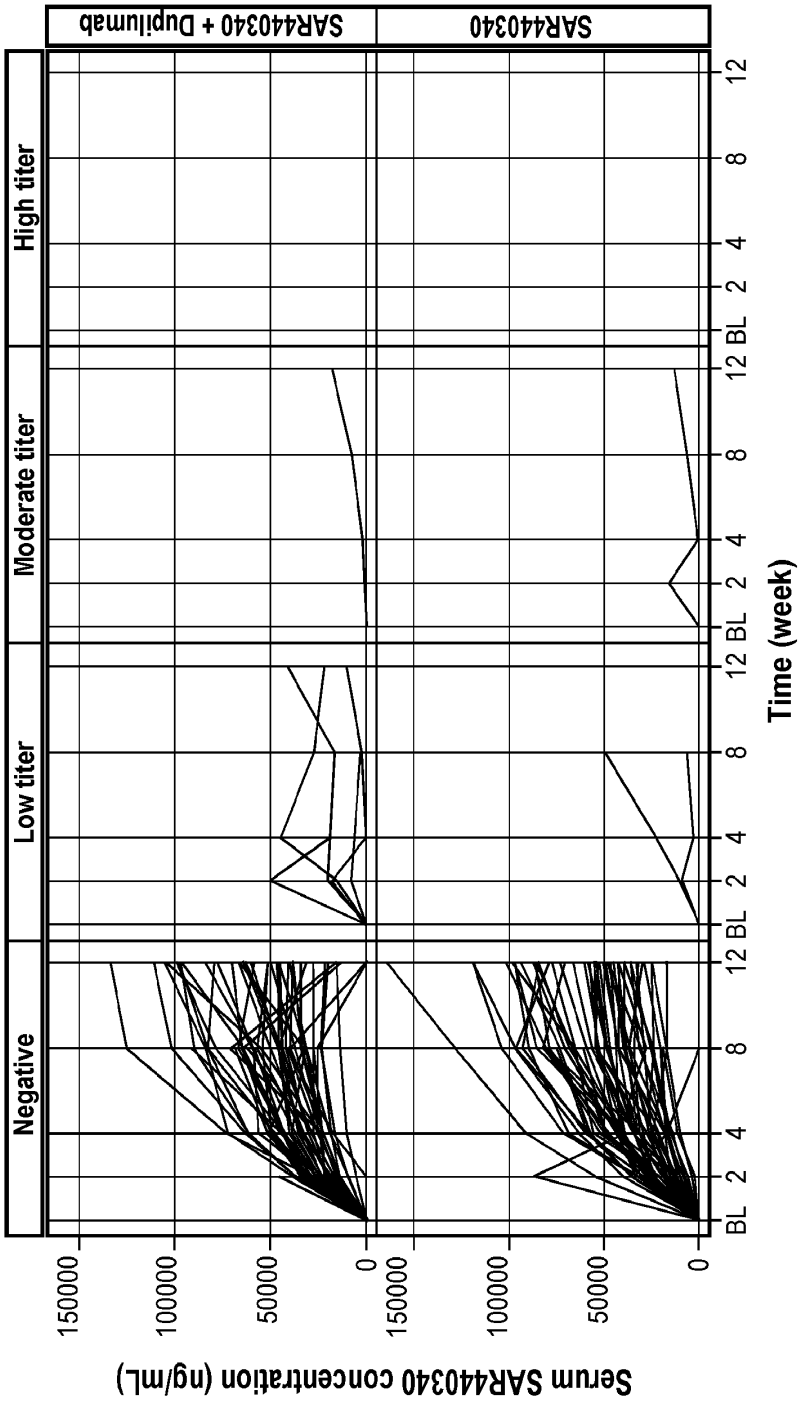

SAR440340 + Dupilumab
SAR440340
Negative
Low titer
Moderate titer
High titer
BL 2 4 8 12 BL 2 4 8 12 BL 2 4 8 12
Time (week)
0 50000 100000 150000
Serum SAR440340 concentration (ng/mL)

Fig. 113

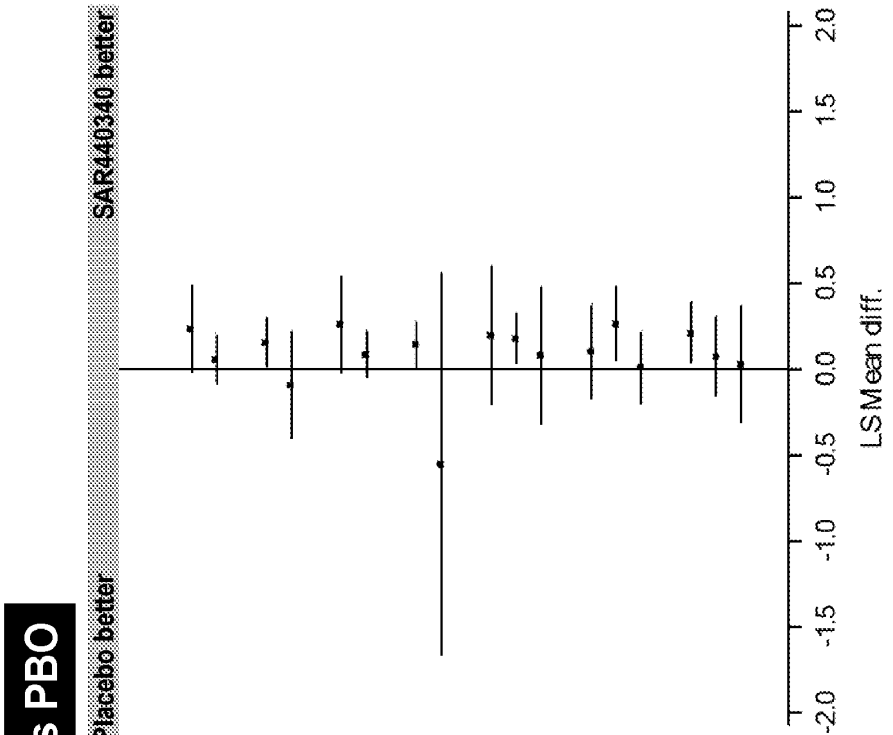

SAR440340 vs PBO
Subgroup
N
LS Mean diff. 95% CI
Placebo better
SAR440340 better
Age group 1 (years)
<45 36 0.24 (-0.02 to 0.49)
>=45 63 0.06 (-0.08 to 0.20)
Age group 2 (years)
<65 86 0.16 (0.01 to 0.30)
>=65 13 -0.09 (-0.41 to 0.23)
Sex
Male 33 0.26 (-0.01 to 0.54)
Female 66 0.09 (-0.05 to 0.22)
Race
White 95 0.15 (0.01 to 0.28)
All other races 4 -0.55 (-1.66 to 0.56)
Baseline weight group (kg)
<60 7 0.20 (-0.21 to 0.60)
>=60 - <100 80 0.18 (0.03 to 0.33)
>=100 12 0.08 (-0.32 to 0.49)
Baseline BMI group (kg/m2)
<25 31 0.10 (-0.17 to 0.38)
>=25 - <30 34 0.27 (0.04 to 0.49)
>=30 34 0.01 (-0.20 to 0.22)
Region
East Europe 52 0.21 (0.03 to 0.39)
Latin America 28 0.08 (-0.16 to 0.31)
North America 19 0.03 (-0.31 to 0.37)
-2.0
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
LS Mean diff.

Fig. 114

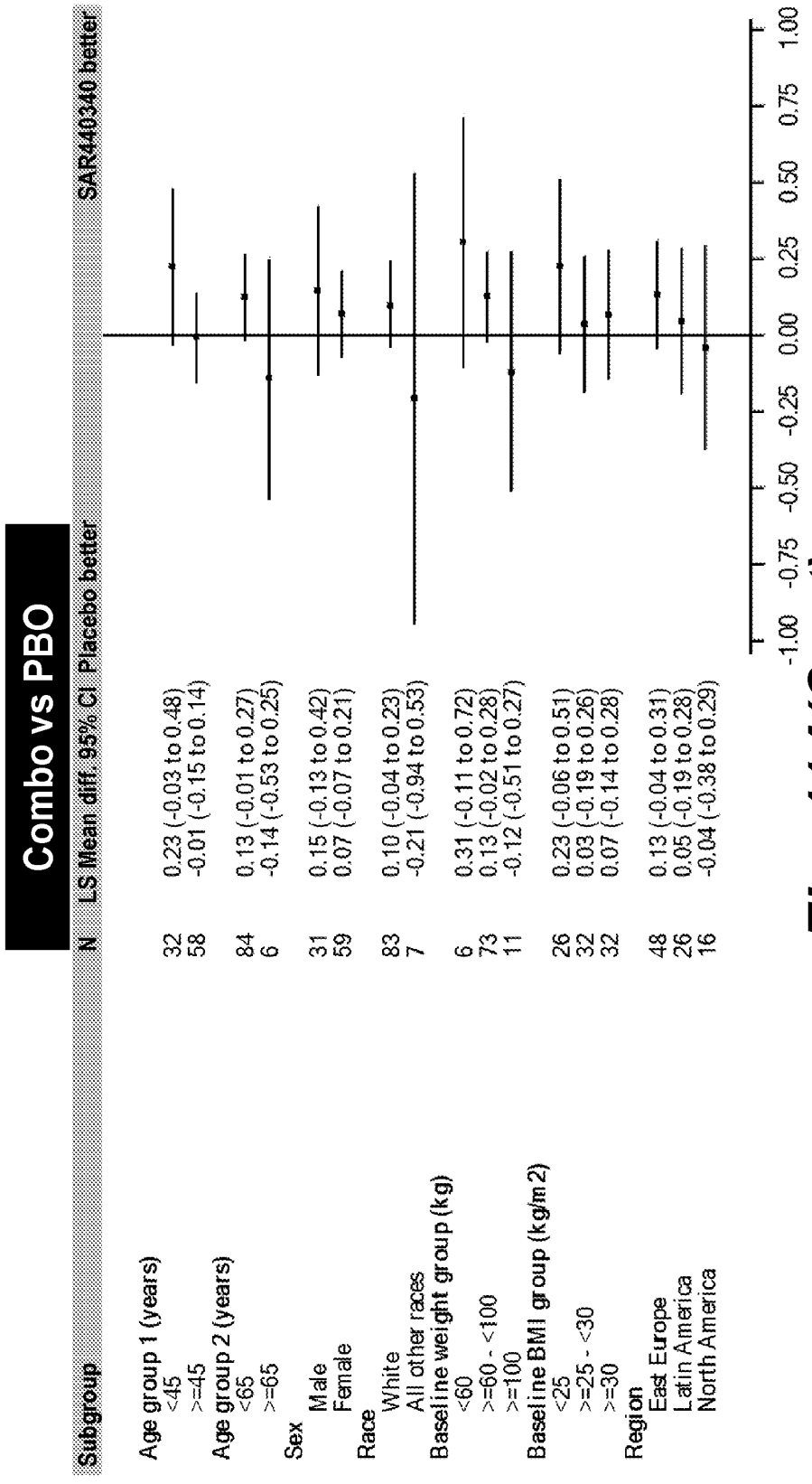

Combo vs PBO
Subgroup
N
LS Mean diff. 95% CI
Placebo better
SAR440340 better
Age group 1 (years)
<45 32 0.23 (-0.03 to 0.48)
>=45 58 -0.01 (-0.15 to 0.14)
Age group 2 (years)
<65 84 0.13 (-0.01 to 0.27)
>=65 6 -0.14 (-0.53 to 0.25)
Sex
Male 31 0.15 (-0.13 to 0.42)
Female 59 0.07 (-0.07 to 0.21)
Race
White 83 0.10 (-0.04 to 0.23)
All other races 7 -0.21 (-0.94 to 0.53)
Baseline weight group (kg)
<60 6 0.31 (-0.11 to 0.72)
>=60 - <100 73 0.13 (-0.02 to 0.28)
>=100 11 -0.12 (-0.51 to 0.27)
Baseline BMI group (kg/m2)
<25 26 0.23 (-0.06 to 0.51)
>=25 - <30 32 0.03 (-0.19 to 0.26)
>=30 32 0.07 (-0.14 to 0.28)
Region
East Europe 48 0.13 (-0.04 to 0.31)
Latin America 26 0.05 (-0.19 to 0.28)
North America 16 -0.04 (-0.38 to 0.29)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LS Mean diff.

Fig. 114(Cont)

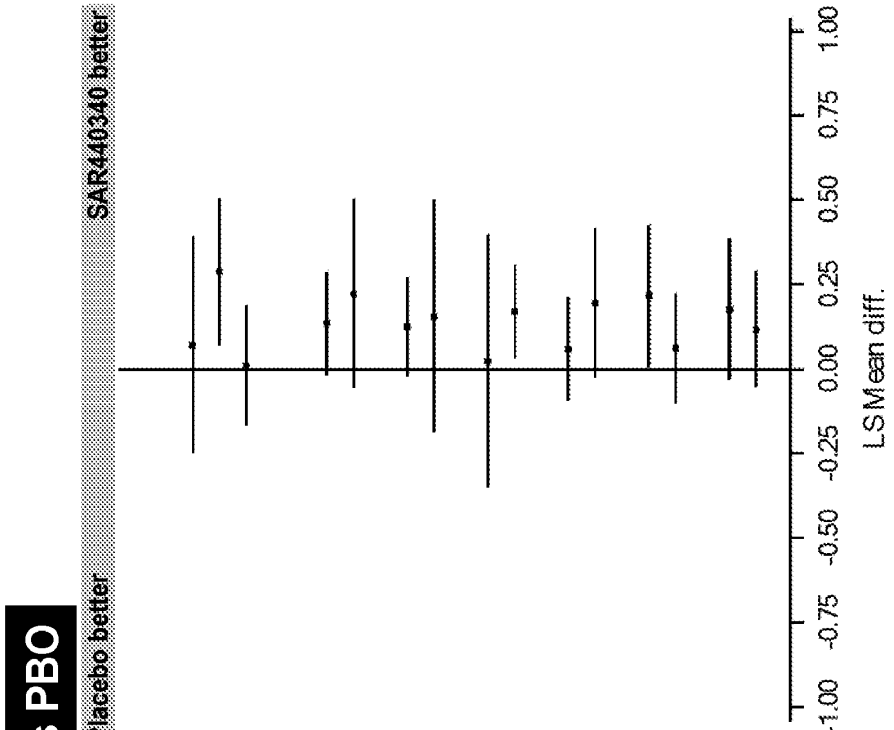

SAR440340 vs PBO
Subgroup
N
LS Mean diff. 95% CI
Placebo better
SAR440340 better
Age at onset of asthma (years)
<18 27 0.07 (-0.25 to 0.39)
>=18-<40 36 0.29 (0.07 to 0.50)
>=40 36 0.01 (-0.17 to 0.19)
Number of asthma exacerbations within 1 year before screening visit
<=1 77 0.14 (-0.01 to 0.29)
>1 22 0.22 (-0.06 to 0.50)
Ongoing atopic medical condition
Yes 80 0.13 (-0.02 to 0.27)
No 19 0.16 (-0.19 to 0.50)
Smoking history
Former 15 0.02 (-0.35 to 0.40)
Never 84 0.17 (0.03 to 0.31)
Baseline FEV1 (L)
<1.90 51 0.06 (-0.10 to 0.21)
>=1.90 48 0.20 (-0.02 to 0.41)
Baseline percent predicted FEV1 (%)
<64 46 0.22 (0.01 to 0.43)
>=64 53 0.06 (-0.10 to 0.22)
Baseline ACQ-5 score
<=2 45 0.18 (-0.03 to 0.39)
>2 54 0.12 (-0.05 to 0.29)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LS Mean diff.

Fig. 115

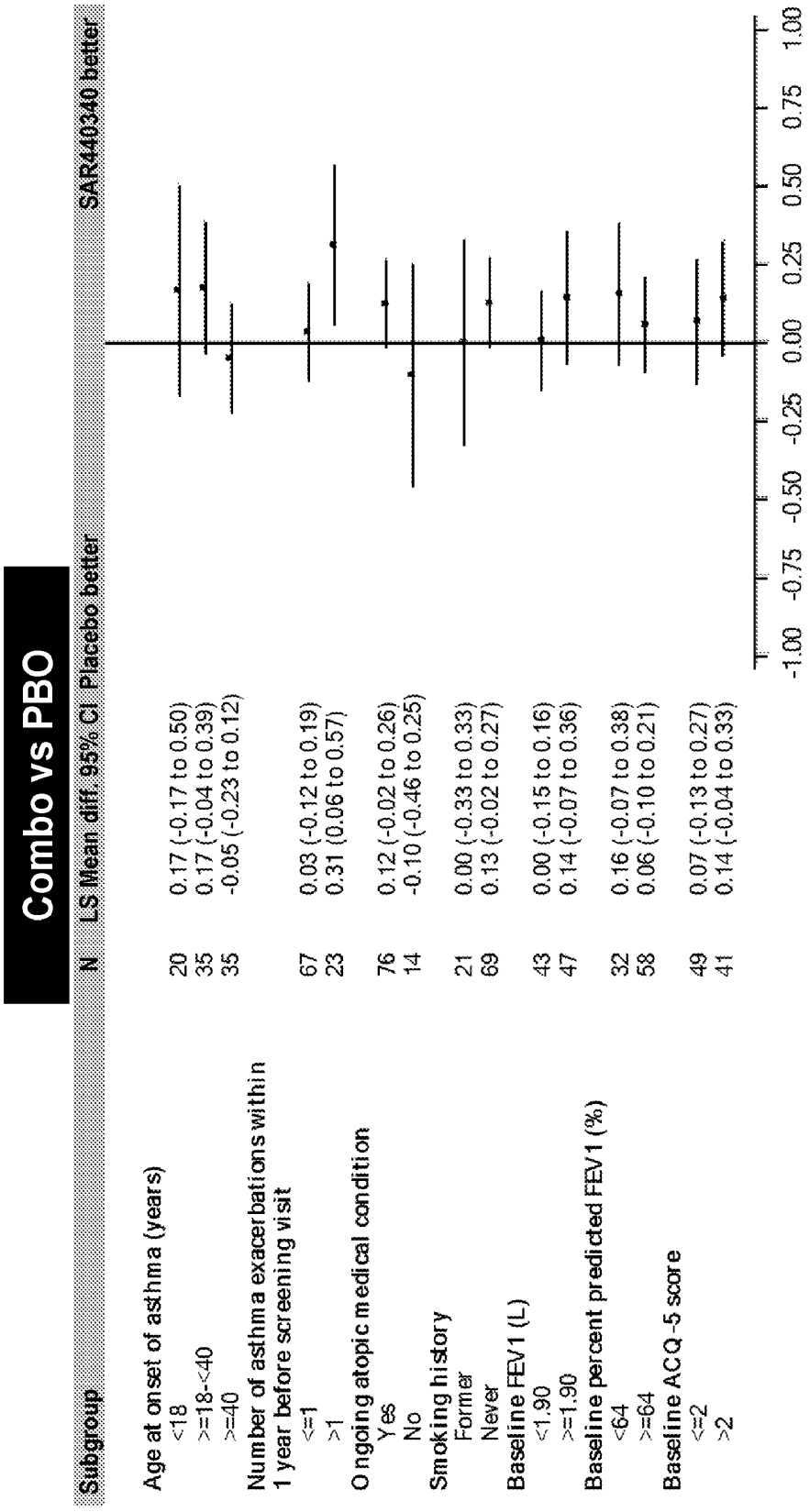

Combo vs PBO
Subgroup
N
LS Mean diff. 95% CI
Placebo better
SAR440340 better
Age at onset of asthma (years)
<18 20 0.17 (-0.17 to 0.50)
>=18-<40 35 0.17 (-0.04 to 0.39)
>=40 35 -0.05 (-0.23 to 0.12)
Number of asthma exacerbations within 1 year before screening visit
<=1 67 0.03 (-0.12 to 0.19)
>1 23 0.31 (0.06 to 0.57)
Ongoing atopic medical condition
Yes 76 0.12 (-0.02 to 0.26)
No 14 -0.10 (-0.46 to 0.25)
Smoking history
Former 21 0.00 (-0.33 to 0.33)
Never 69 0.13 (-0.02 to 0.27)
Baseline FEV1 (L)
<1.90 43 0.00 (-0.15 to 0.16)
>=1.90 47 0.14 (-0.07 to 0.36)
Baseline percent predicted FEV1 (%)
<64 32 0.16 (-0.07 to 0.38)
>=64 58 0.06 (-0.10 to 0.21)
Baseline ACQ-5 score
<=2 49 0.07 (-0.13 to 0.27)
>2 41 0.14 (-0.04 to 0.33)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LS Mean diff.

Fig. 115(Cont)

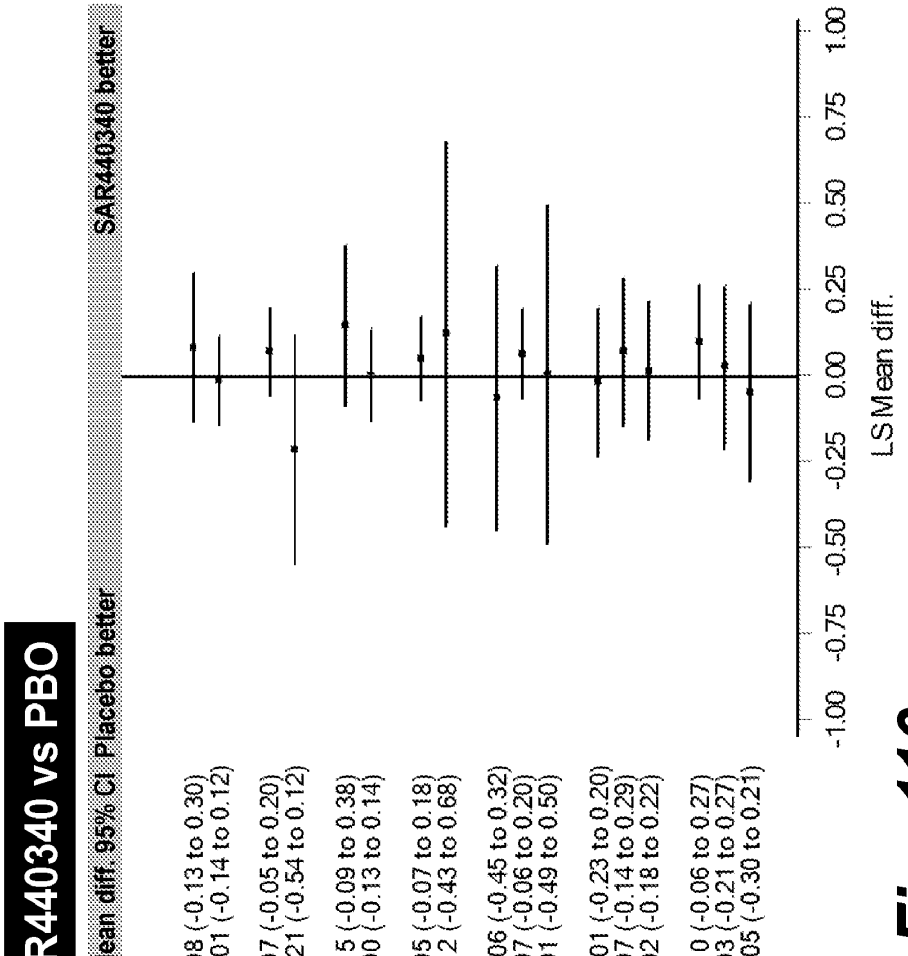

SAR440340 vs PBO
Subgroup
N
LS Mean diff. 95% CI
Placebo better
SAR440340 better
Age group 1 (years)
<45 36 0.08 (-0.13 to 0.30)
>=45 64 -0.01 (-0.14 to 0.12)
Age group 2 (years)
<65 87 0.07 (-0.05 to 0.20)
>=65 13 -0.21 (-0.54 to 0.12)
Sex
Male 33 0.15 (-0.09 to 0.38)
Female 67 0.00 (-0.13 to 0.14)
Race
White 96 0.05 (-0.07 to 0.18)
All other races 4 0.12 (-0.43 to 0.68)
Baseline weight group (kg)
<60 7 -0.06 (-0.45 to 0.32)
>=60 - <100 81 0.07 (-0.06 to 0.20)
>=100 12 0.01 (-0.49 to 0.50)
Baseline BMI group (kg/m2)
<25 32 -0.01 (-0.23 to 0.20)
>=25 - <30 34 0.07 (-0.14 to 0.29)
>=30 34 0.02 (-0.18 to 0.22)
Region
East Europe 53 0.10 (-0.06 to 0.27)
Latin America 28 0.03 (-0.21 to 0.27)
North America 19 -0.05 (-0.30 to 0.21)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LS Mean diff.

Fig. 116

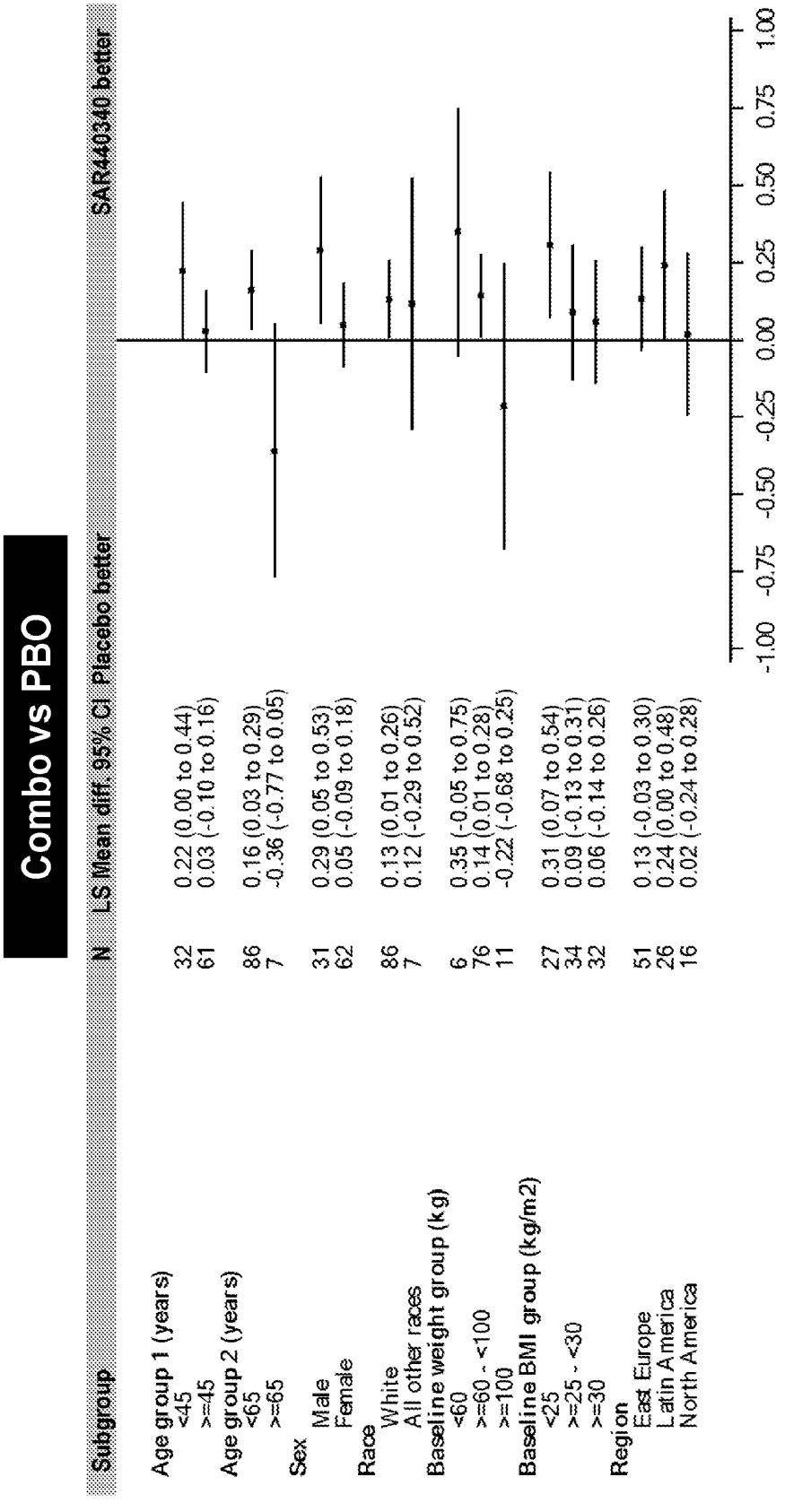

Combo vs PBO
Subgroup
N
LS Mean diff. 95% CI
Placebo better
SAR440340 better
Age group 1 (years)
<45
32
0.22 (0.00 to 0.44)
>=45
61
0.03 (-0.10 to 0.16)
Age group 2 (years)
<65
86
0.16 (0.03 to 0.29)
>=65
7
-0.36 (-0.77 to 0.05)
Sex
Male
31
0.29 (0.05 to 0.53)
Female
62
0.05 (-0.09 to 0.18)
Race
White
86
0.13 (0.01 to 0.26)
All other races
7
0.12 (-0.29 to 0.52)
Baseline weight group (kg)
<60
6
0.35 (-0.05 to 0.75)
>=60 - <100
76
0.14 (0.01 to 0.28)
>=100
11
-0.22 (-0.68 to 0.25)
Baseline BMI group (kg/m2)
<25
27
0.31 (0.07 to 0.54)
>=25 - <30
34
0.09 (-0.13 to 0.31)
>=30
32
0.06 (-0.14 to 0.26)
Region
East Europe
51
0.13 (-0.03 to 0.30)
Latin America
26
0.24 (0.00 to 0.48)
North America
16
0.02 (-0.24 to 0.28)
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
1.00
LS Mean diff.

Fig. 116(Cont)

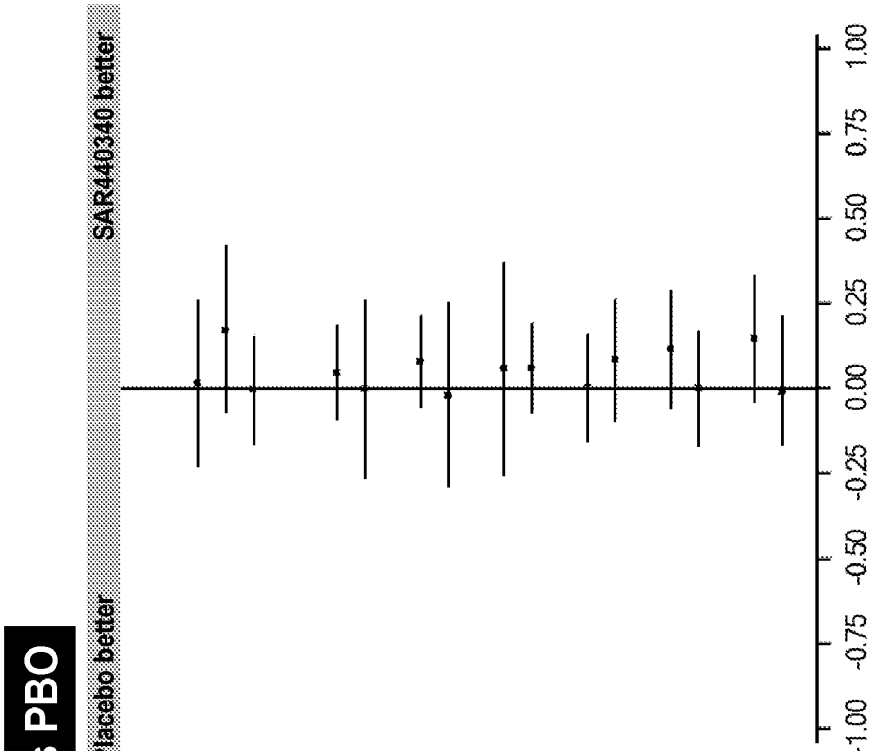

SAR440340 vs PBO
Subgroup
N
LS Mean diff. 95% CI
Placebo better
SAR440340 better
Age at onset of asthma (years)
<18
>=18-<40
>=40
Number of asthma exacerbations within 1 year before screening visit
<=1
>1
Ongoing atopic medical condition
Yes
No
Smoking history
Former
Never
Baseline FEV1 (L)
<1.90
>=1.90
Baseline percent predicted FEV1 (%)
<64
>=64
Baseline ACQ-5 score
<=2
>2
27
37
36
78
22
81
19
15
85
52
48
47
53
45
55
0.01 (-0.23 to 0.26)
0.17 (-0.07 to 0.41)
-0.00 (-0.16 to 0.16)
0.05 (-0.09 to 0.18)
-0.00 (-0.26 to 0.26)
0.08 (-0.05 to 0.21)
-0.02 (-0.29 to 0.25)
0.06 (-0.25 to 0.37)
0.06 (-0.07 to 0.19)
0.00 (-0.15 to 0.16)
0.08 (-0.09 to 0.26)
0.12 (-0.06 to 0.29)
0.00 (-0.17 to 0.17)
0.15 (-0.04 to 0.33)
-0.01 (-0.16 to 0.14)
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
1.00
LS Mean diff.

Fig. 117

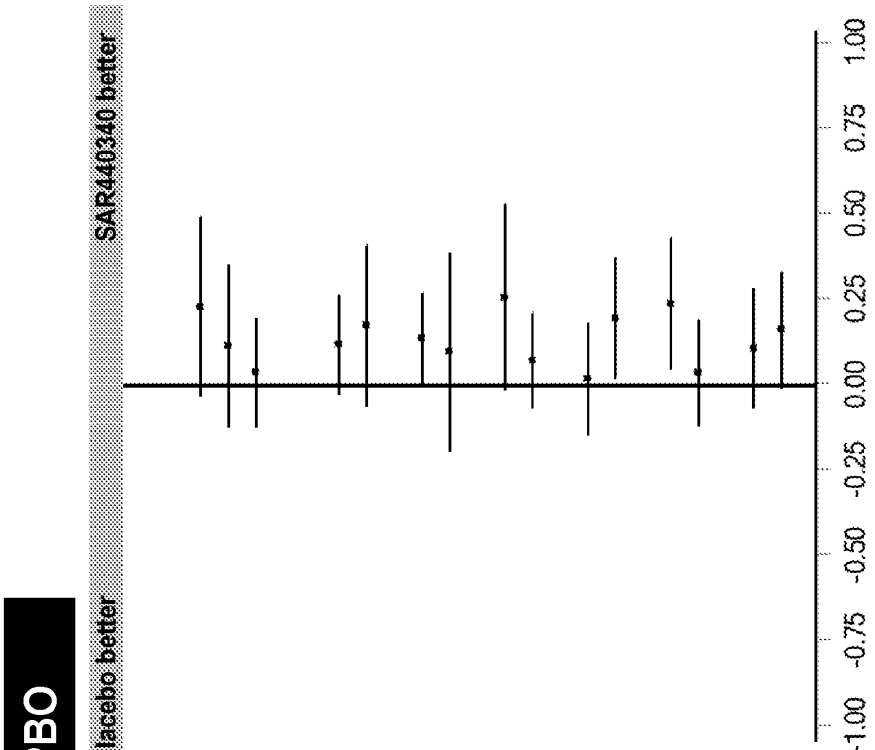

Combo vs PBO
Subgroup
N
LS Mean diff. 95% CI
Placebo better
SAR440340 better
Age at onset of asthma (years)
<18 20 0.23 (-0.03 to 0.49)
>=18-<40 37 0.12 (-0.12 to 0.35)
>=40 36 0.04 (-0.12 to 0.20)
Number of asthma exacerbations within 1 year before screening visit
<=1 70 0.12 (-0.02 to 0.26)
>1 23 0.18 (-0.06 to 0.41)
Ongoing atopic medical condition
Yes 79 0.14 (0.00 to 0.27)
No 14 0.10 (-0.19 to 0.39)
Smoking history
Former 21 0.26 (-0.01 to 0.53)
Never 72 0.07 (-0.06 to 0.21)
Baseline FEV1 (L)
<1.90 46 0.02 (-0.14 to 0.18)
>=1.90 47 0.20 (0.02 to 0.37)
Baseline percent predicted FEV1 (%)
<64 35 0.24 (0.05 to 0.43)
>=64 58 0.04 (-0.12 to 0.19)
Baseline ACQ-5 score
<=2 50 0.11 (-0.07 to 0.28)
>2 43 0.16 (-0.01 to 0.33)
-1.00 -0.75 -0.50 -0.25 0.00 0.25 0.50 0.75 1.00
LS Mean diff.

Fig. 117(Cont)

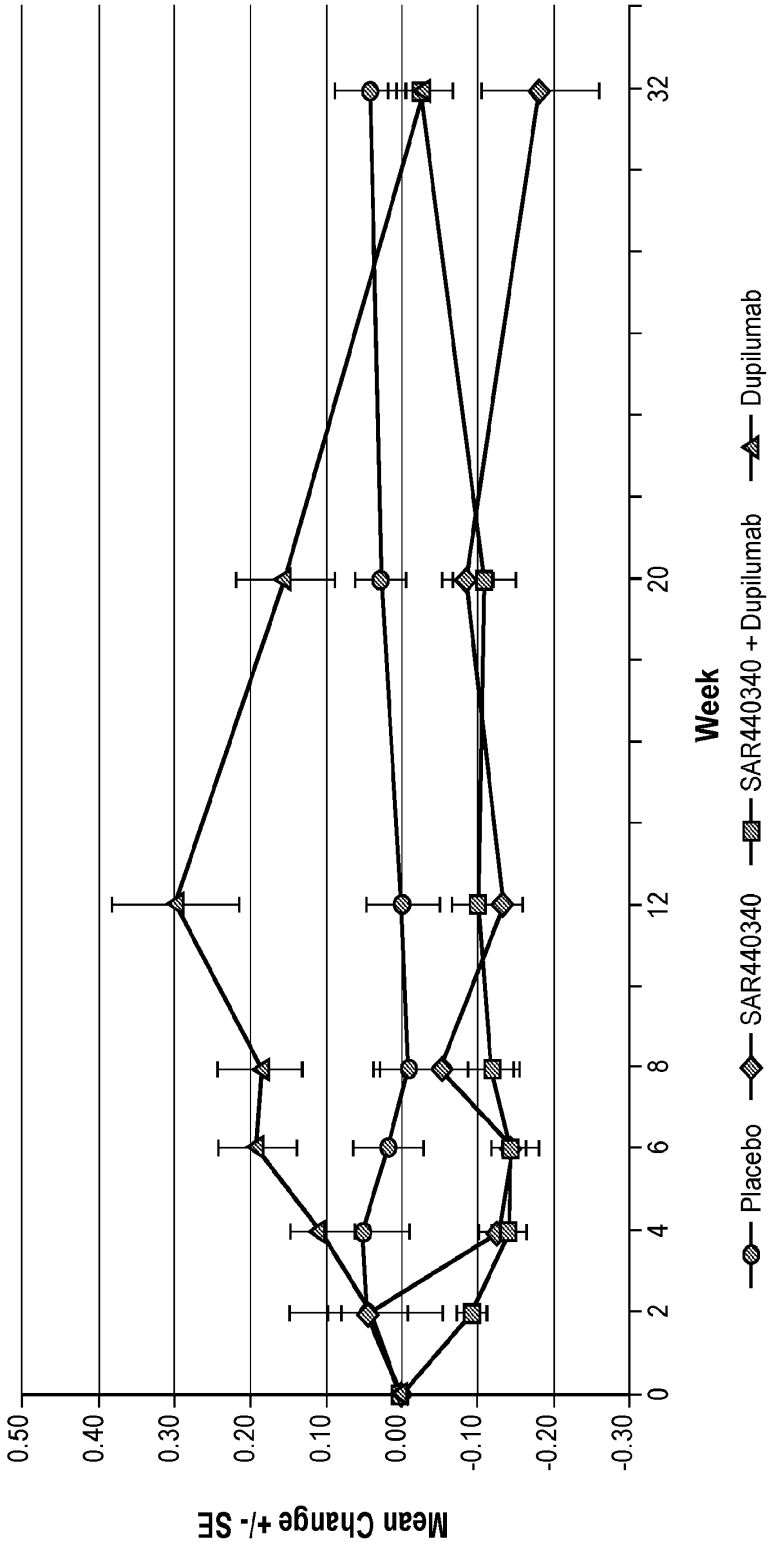

Mean Change +/- SE
0.50
0.40
0.30
0.20
0.10
0.00
-0.10
-0.20
-0.30
0
2
4
6
8
12
20
32
Week
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab

Fig. 118

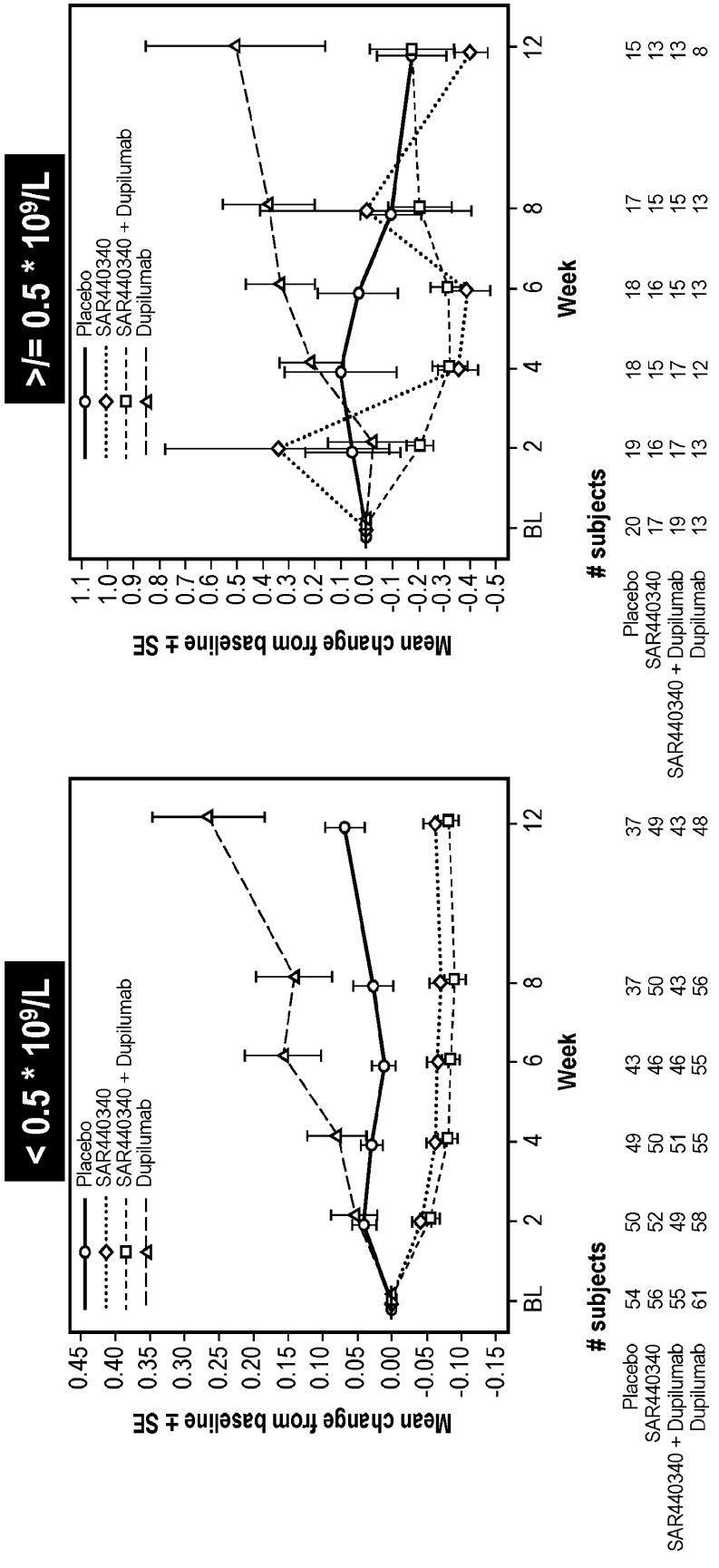

< 0.5 * 10⁹/L
>/= 0.5 * 10⁹/L
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change from baseline ± SE
Week
BL
subjects
Placebo 54 50 49 43 37 37
SAR440340 56 52 50 46 50 49
SAR440340 + Dupilumab 55 49 51 46 43 43
Dupilumab 61 58 55 55 56 48
Placebo 20 19 18 18 17 15
SAR440340 17 16 15 16 15 13
SAR440340 + Dupilumab 19 17 17 15 15 13
Dupilumab 13 13 12 13 13 8

Fig. 119

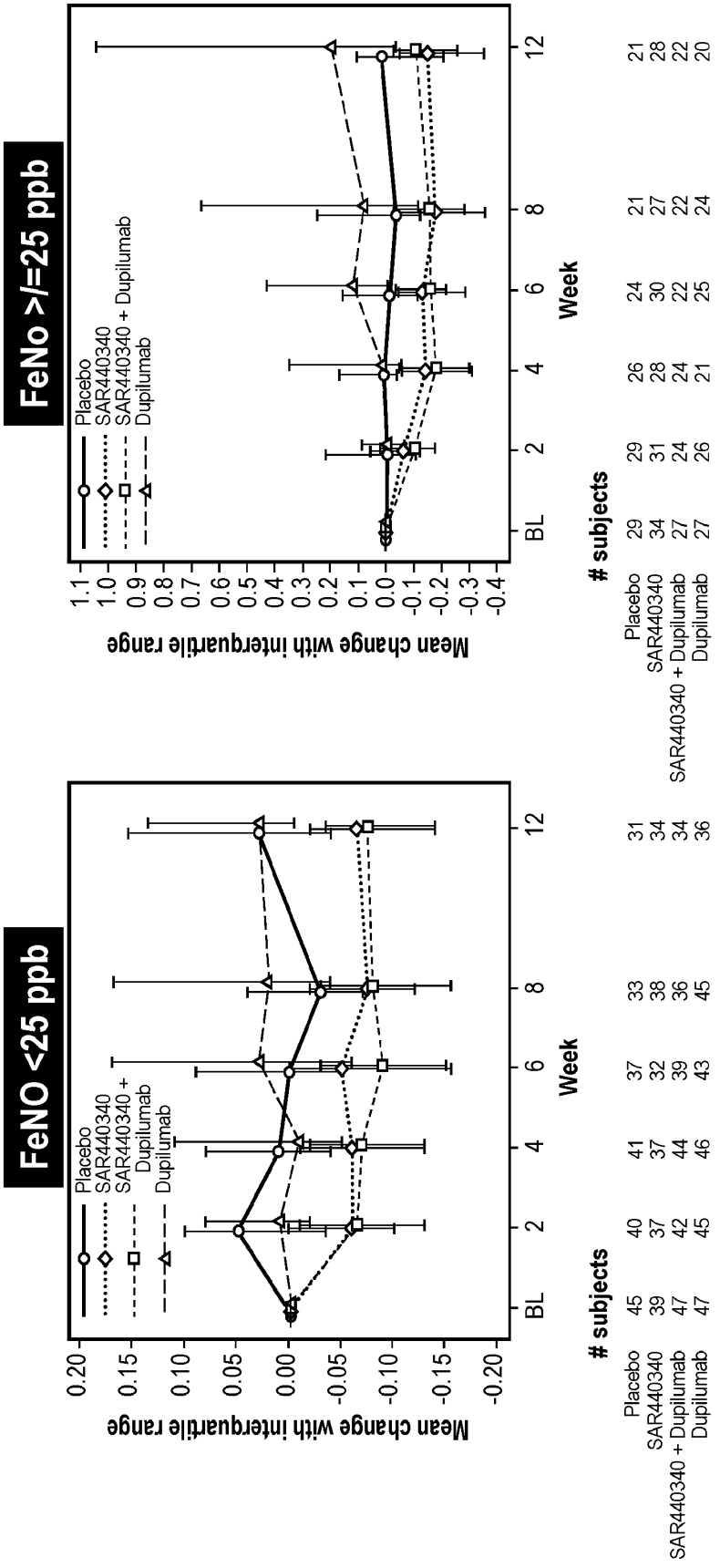

FeNO <25 ppb
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change with interquartile range
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
-0.20
BL
2
4
6
8
12
Week
subjects
Placebo 45 40 41 37 33 31
SAR440340 39 37 37 32 38 34
SAR440340 + Dupilumab 47 42 44 39 36 34
Dupilumab 47 45 46 43 45 36
FeNo >/=25 ppb
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change with interquartile range
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
-0.3
-0.4
BL
2
4
6
8
12
Week
subjects
Placebo 29 29 26 24 21 21
SAR440340 34 31 28 30 27 28
SAR440340 + Dupilumab 27 24 24 22 22 22
Dupilumab 27 26 21 25 24 20

Fig. 120

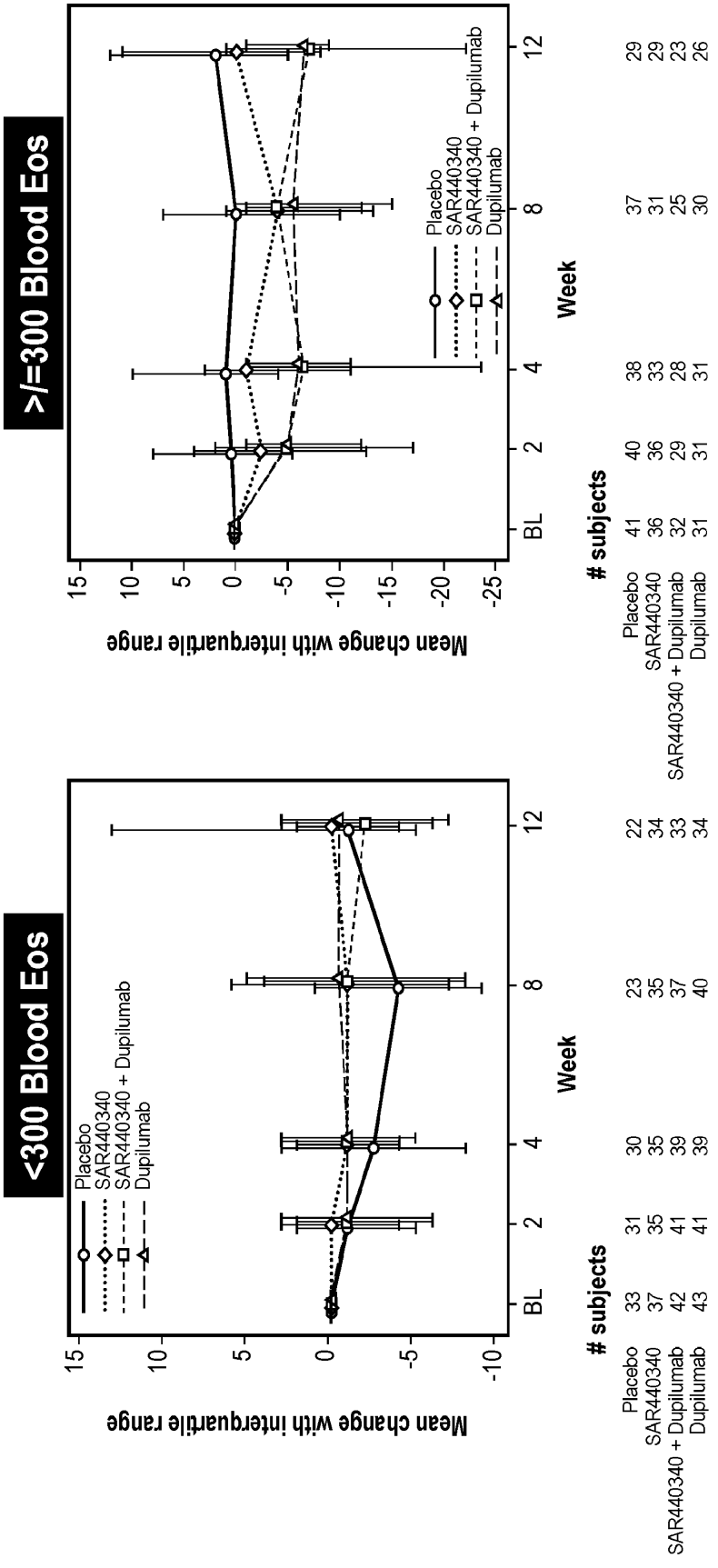

<300 Blood Eos
>/=300 Blood Eos
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
Mean change with interquartile range
Week
BL
2
4
8
12
subjects
Placebo 33 31 30 23 22
SAR440340 37 35 35 35 34
SAR440340 + Dupilumab 42 41 39 37 33
Dupilumab 43 41 39 40 34
Placebo 41 40 38 37 29
SAR440340 36 36 33 31 29
SAR440340 + Dupilumab 32 29 28 25 23
Dupilumab 31 31 31 30 26

Fig. 121

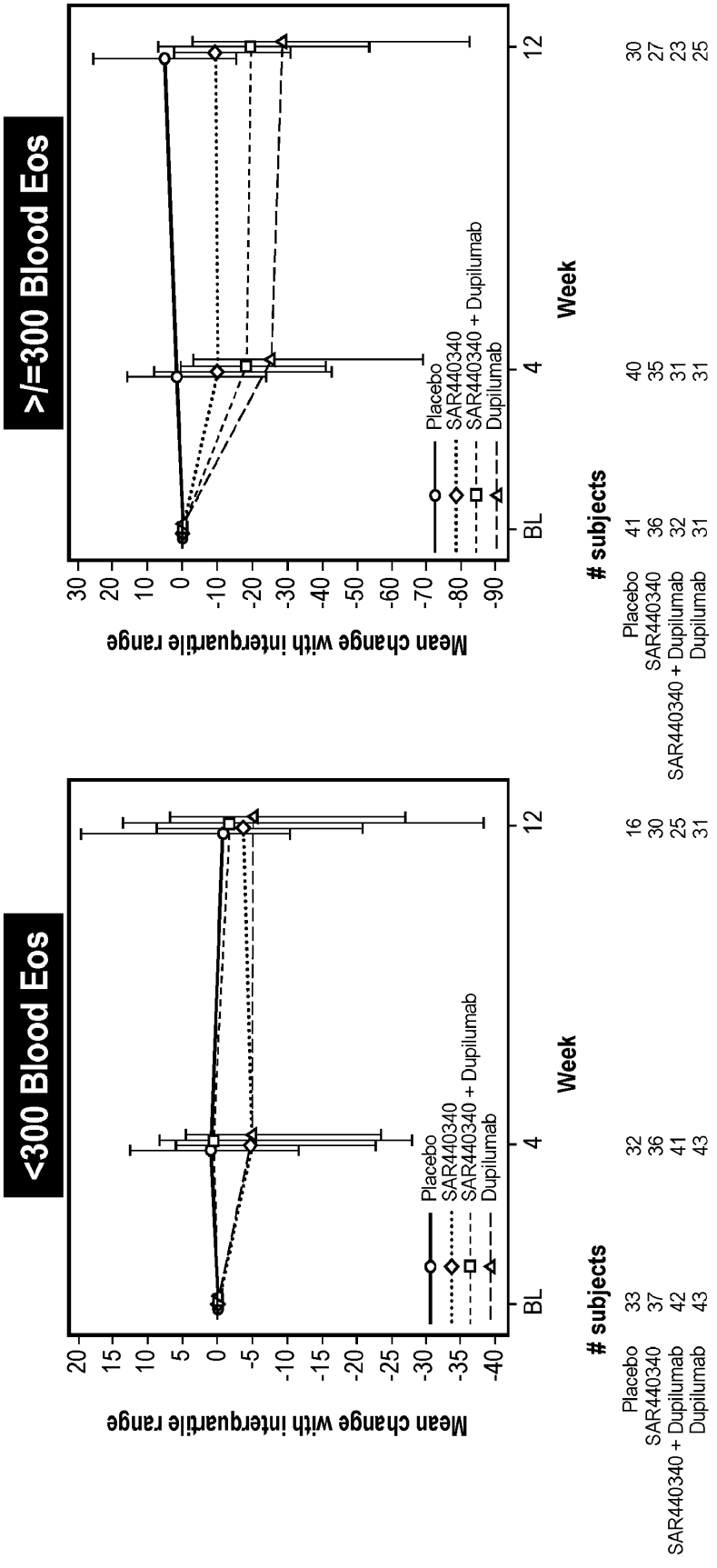

<300 Blood Eos
>/=300 Blood Eos
Mean change with interquartile range
Week
BL
4
12
Placebo
SAR440340
SAR440340 + Dupilumab
Dupilumab
subjects
Placebo 33 16
SAR440340 37 30
SAR440340 + Dupilumab 42 25
Dupilumab 43 31
Placebo 41 40
SAR440340 36 35
SAR440340 + Dupilumab 32 31
Dupilumab 31 31

Fig. 122

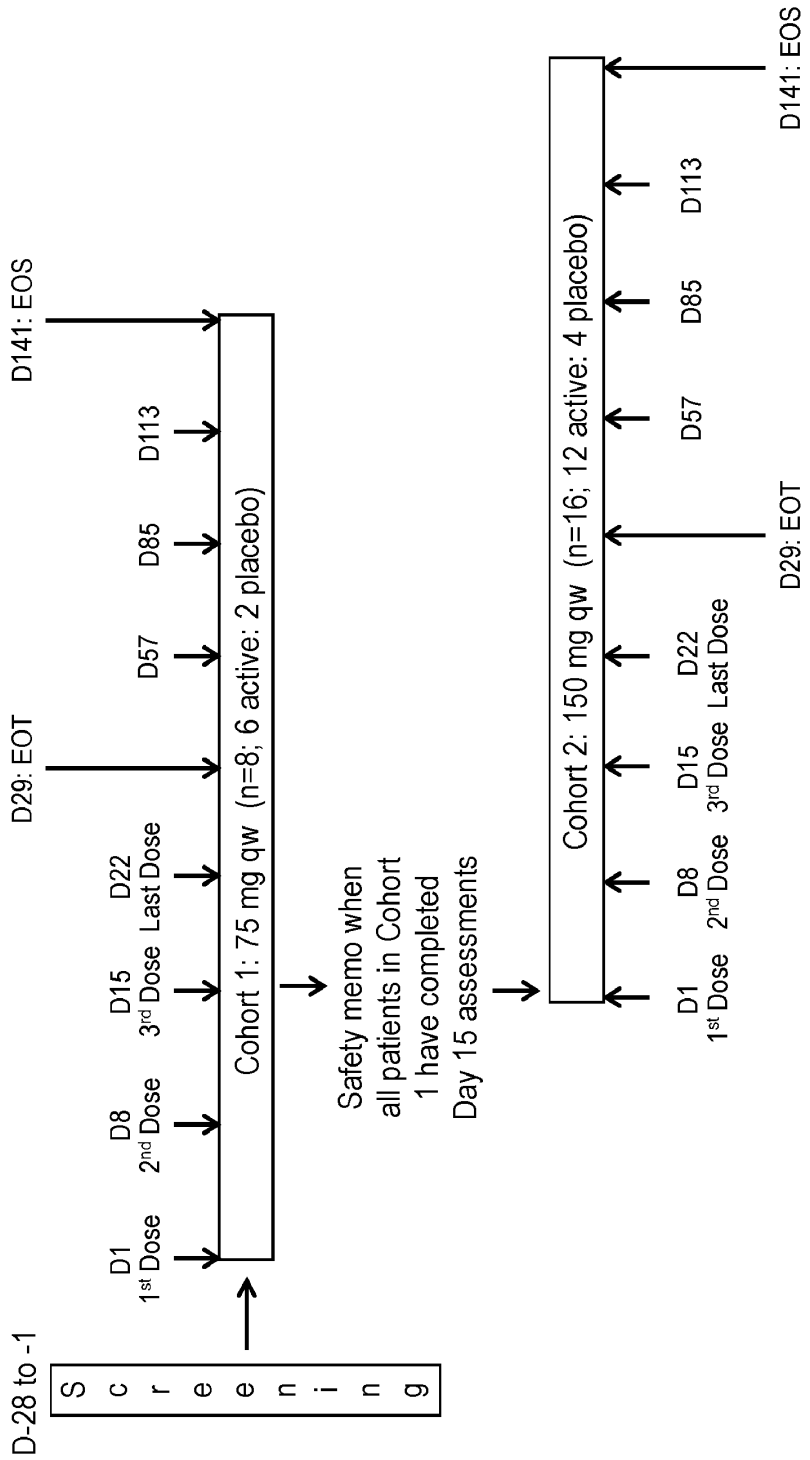

D-28 to -1
Screening
D1 1st Dose
D8 2nd Dose
D15 3rd Dose
D22 Last Dose
D57
D85
D113
D29: EOT
D141: EOS
Cohort 1: 75 mg qw (n=8; 6 active: 2 placebo)
Safety memo when all patients in Cohort 1 have completed Day 15 assessments
Cohort 2: 150 mg qw (n=16; 12 active: 4 placebo)

Fig. 123

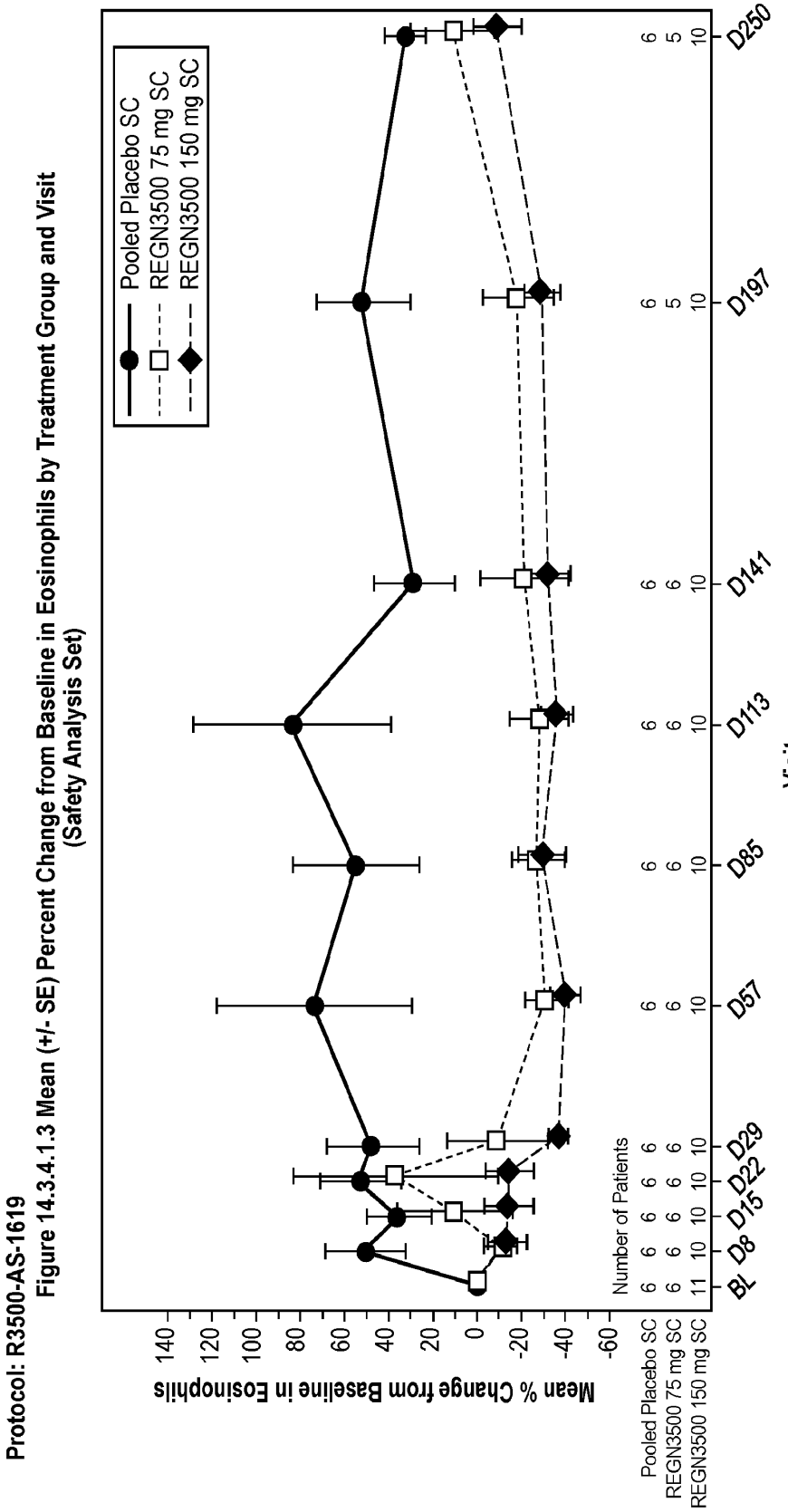

Protocol: R3500-AS-1619
Figure 14.3.4.1.3 Mean (+/- SE) Percent Change from Baseline in Eosinophils by Treatment Group and Visit
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
REGN3500 150 mg SC
Mean % Change from Baseline in Eosinophils
140
120
100
80
60
40
20
0
-20
-40
-60
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Visit
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 6 6 6 6 6
REGN3500 75 mg SC 6 6 6 6 6 6 6 6 6 5 5
REGN3500 150 mg SC 11 10 10 10 10 10 10 10 10 10 10

Fig. 124

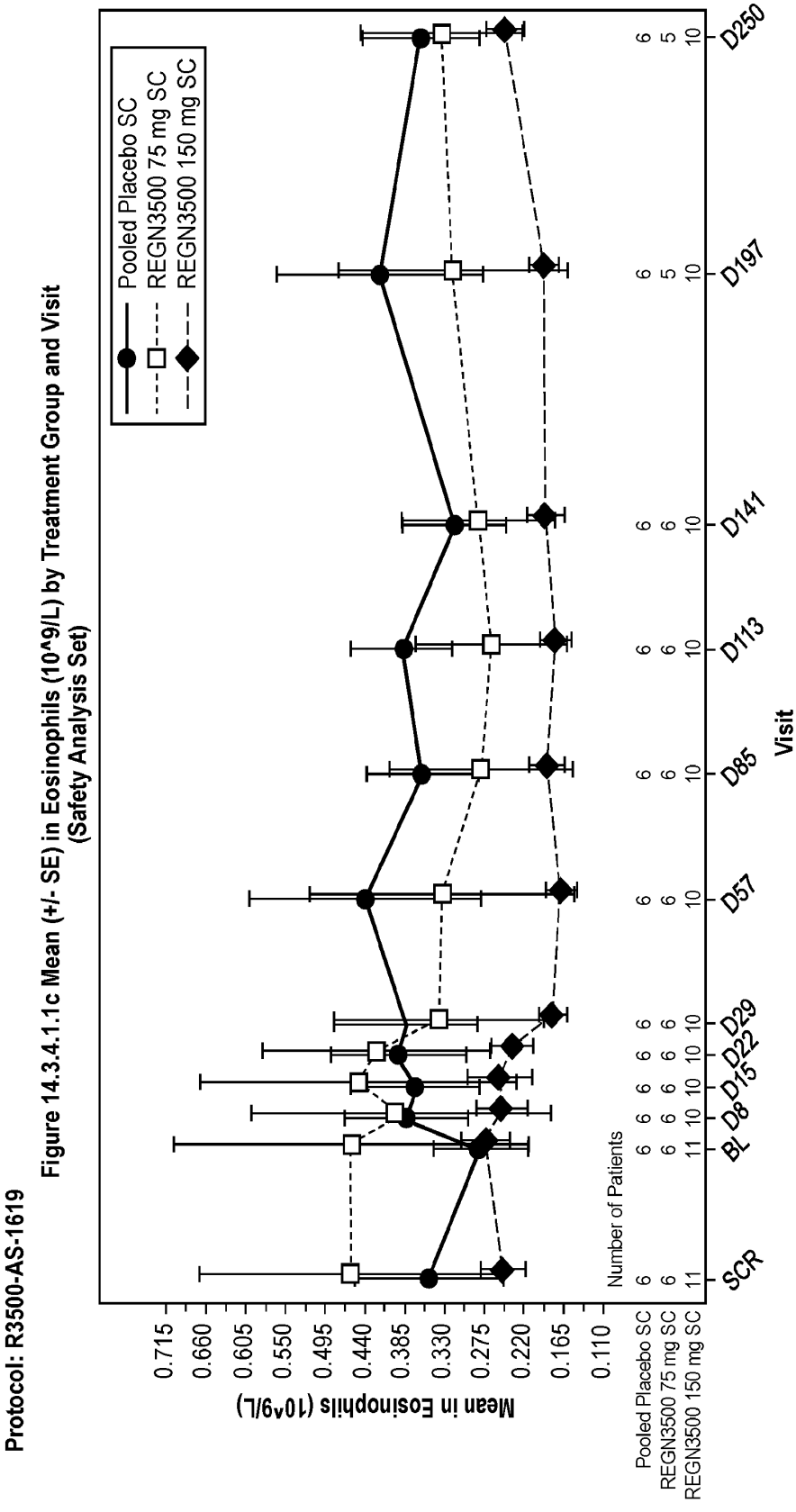

Protocol: R3500-AS-1619
Figure 14.3.4.1.1c Mean (+/- SE) in Eosinophils (10^9/L) by Treatment Group and Visit
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
REGN3500 150 mg SC
Mean in Eosinophils (10^9/L)
0.715
0.660
0.605
0.550
0.495
0.440
0.385
0.330
0.275
0.220
0.165
0.110
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 6 6 6 6 6 6
REGN3500 75 mg SC 6 6 6 6 6 6 6 6 6 6 6 5
REGN3500 150 mg SC 11 11 10 10 10 10 10 10 10 10 10 10
SCR
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Visit

Fig. 125

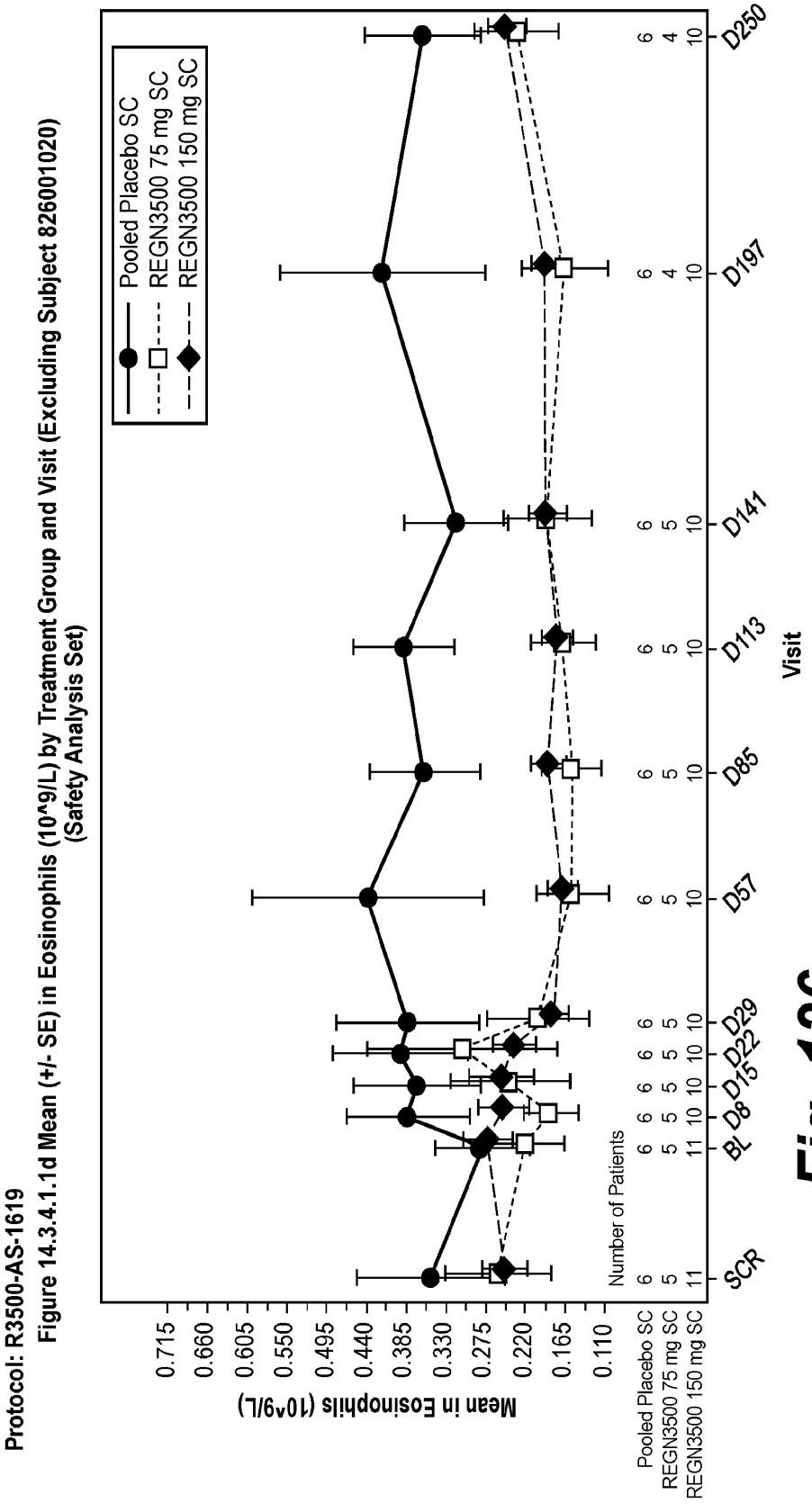

Protocol: R3500-AS-1619
Figure 14.3.4.1.1d Mean (+/- SE) in Eosinophils (10^9/L) by Treatment Group and Visit (Excluding Subject 82600102)
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
REGN3500 150 mg SC
Mean in Eosinophils (10^9/L)
0.715
0.660
0.605
0.550
0.495
0.440
0.385
0.330
0.275
0.220
0.165
0.110
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 6 6 6 6 6 6
REGN3500 75 mg SC 5 5 5 5 5 5 5 5 5 4 4
REGN3500 150 mg SC 11 10 10 10 10 10 10 10 10 10 10
SCR
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Visit

Fig. 126

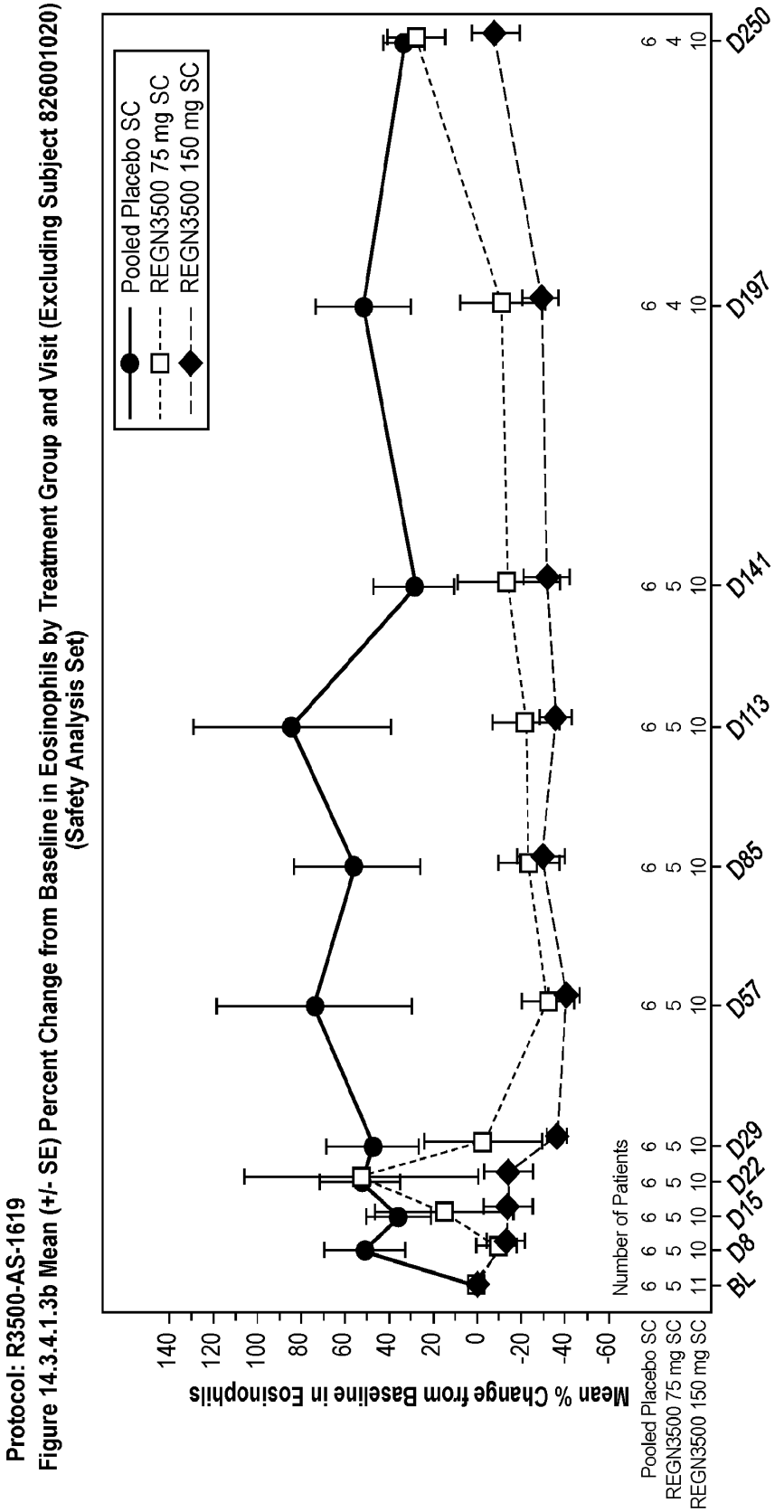

Protocol: R3500-AS-1619
Figure 14.3.4.1.3b Mean (+/- SE) Percent Change from Baseline in Eosinophils by Treatment Group and Visit (Excluding Subject 826001020)
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
REGN3500 150 mg SC
Mean % Change from Baseline in Eosinophils
140
120
100
80
60
40
20
0
-20
-40
-60
Visit
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 5 10 6 5 10 6 5 10 6 4 10
REGN3500 75 mg SC 5 5 5 5 5 5 5 10 6 5 10 6 5 10 6 4 10
REGN3500 150 mg SC 11 10 10 10 10 10 5 10 6 5 10 6 5 10 6 4 10

Fig. 127

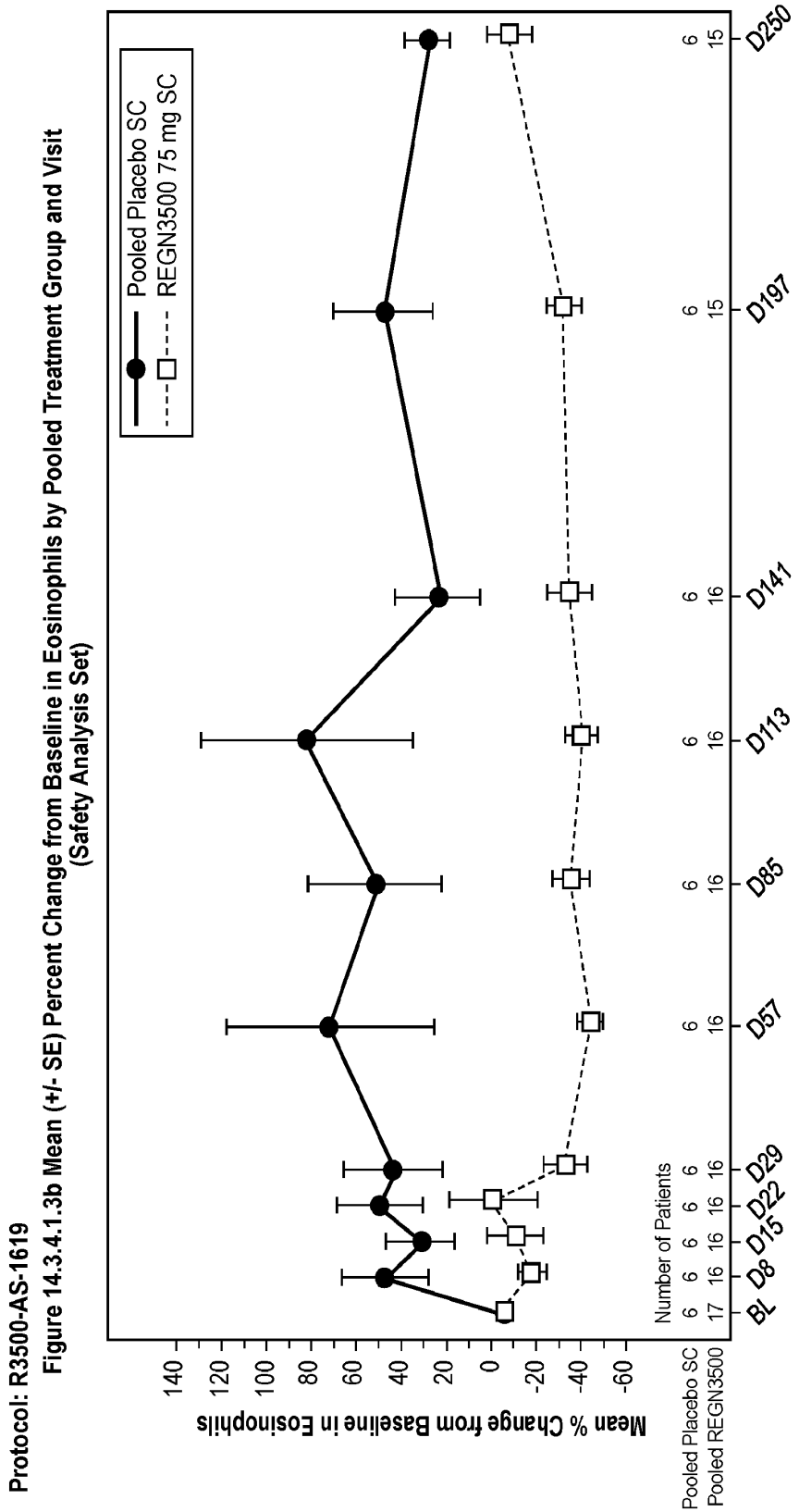

Protocol: R3500-AS-1619
Figure 14.3.4.1.3b Mean (+/- SE) Percent Change from Baseline in Eosinophils by Pooled Treatment Group and Visit
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
Mean % Change from Baseline in Eosinophils
140
120
100
80
60
40
20
0
-20
-40
-60
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 6 6 6
Pooled REGN3500 17 16 16 16 16 16 16 16 15
BL D8 D15 D22 D29 D57 D85 D113 D141 D197 D250
Visit

Fig. 128

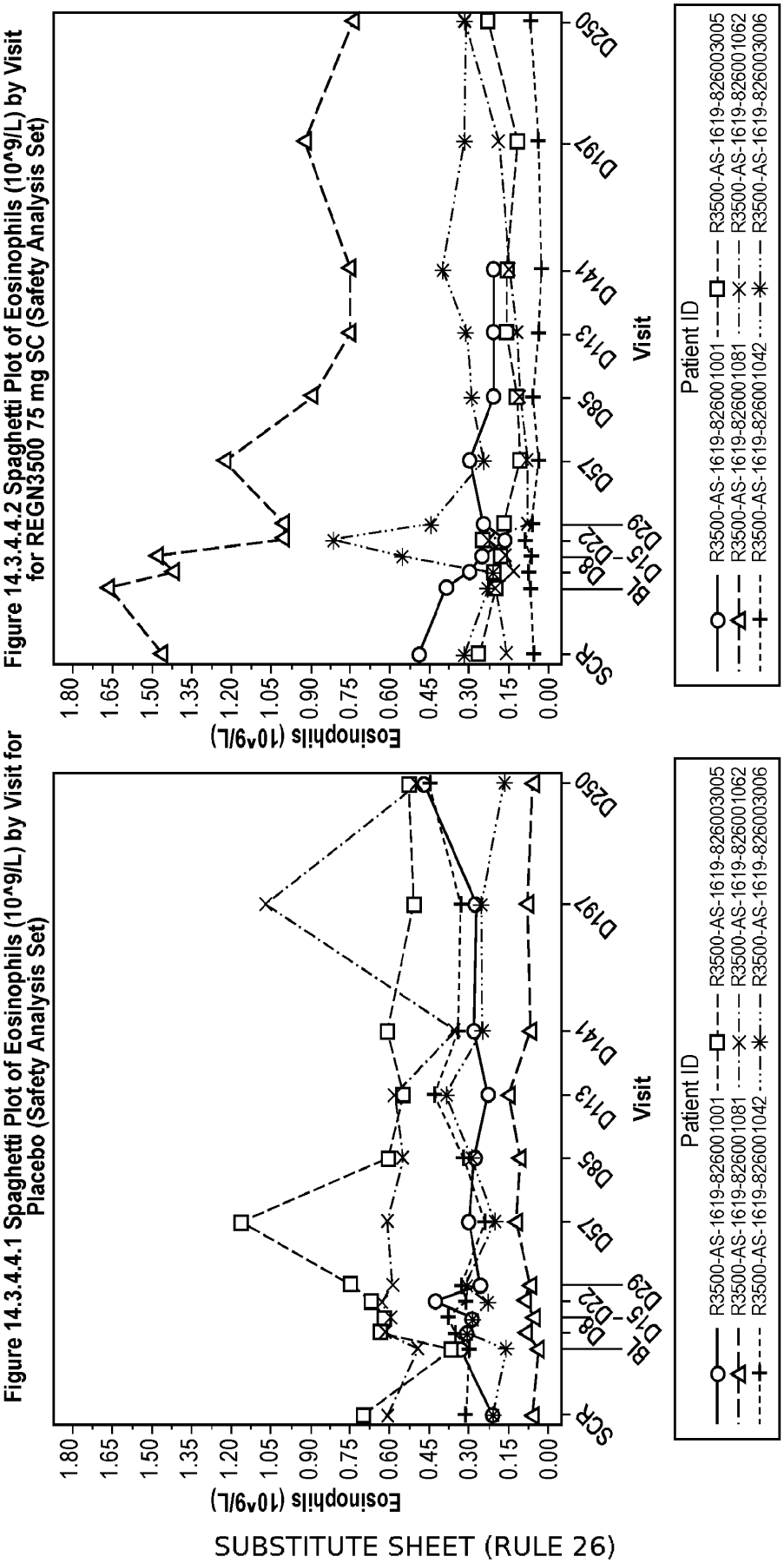

Figure 14.3.4.4.1 Spaghetti Plot of Eosinophils (10^9/L) by Visit for Placebo (Safety Analysis Set)
Figure 14.3.4.4.2 Spaghetti Plot of Eosinophils (10^9/L) by Visit for REGN3500 75 mg SC (Safety Analysis Set)
Eosinophils (10^9/L)
1.80
1.65
1.50
1.35
1.20
1.05
0.90
0.75
0.60
0.45
0.30
0.15
0.00
SCR
BL
D8
D22
D15
D29
D57
D85
D113
D141
D197
D250
Visit
Patient ID
R3500-AS-1619-826001001
R3500-AS-1619-826003005
R3500-AS-1619-826001081
R3500-AS-1619-826001062
R3500-AS-1619-826001042
R3500-AS-1619-826003006

Fig. 129

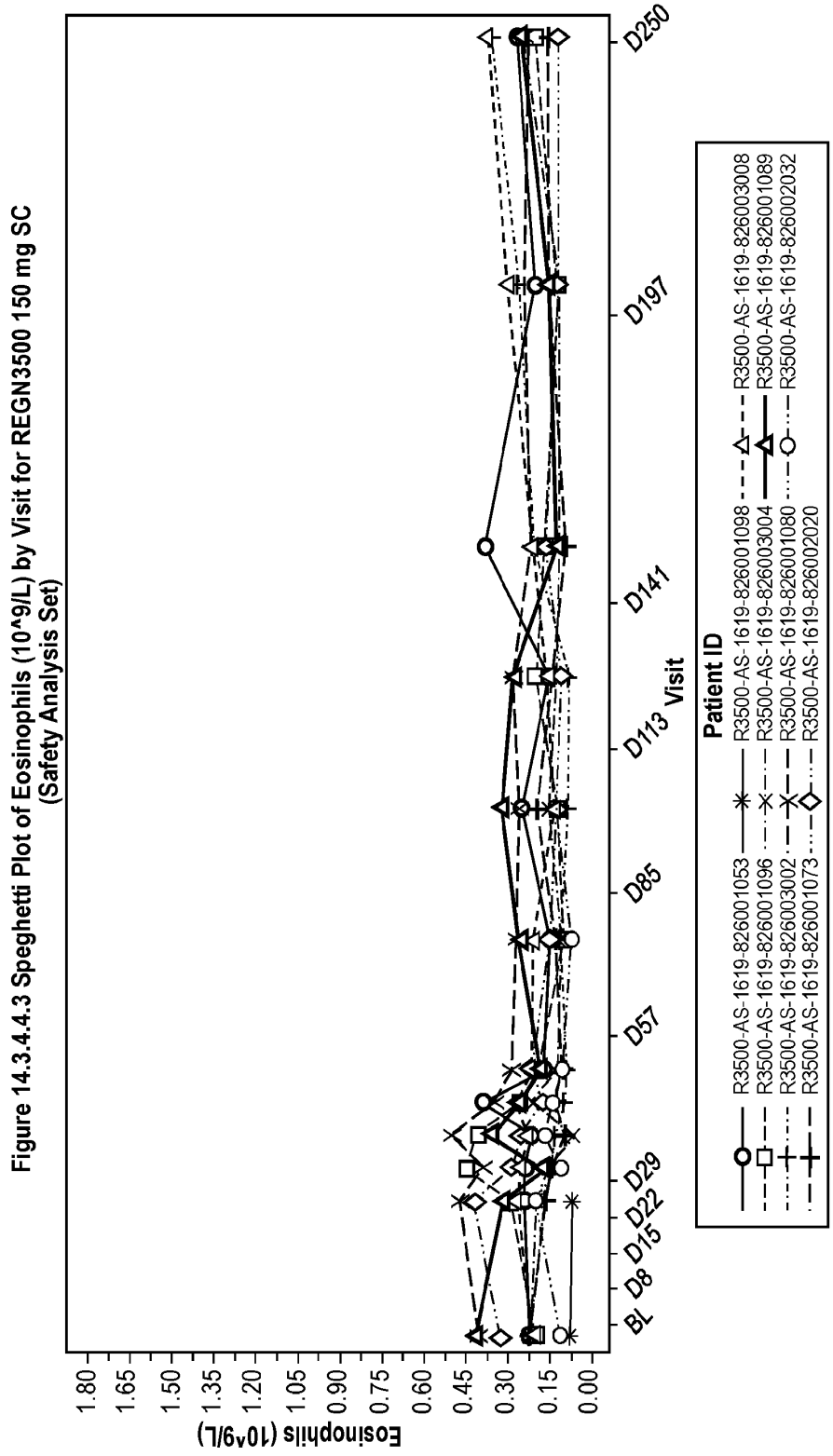

Figure 14.3.4.4.3 Speghetti Plot of Eosinophils (10^9/L) by Visit for REGN3500 150 mg SC
(Safety Analysis Set)
Eosinophils (10^9/L)
1.80
1.65
1.50
1.35
1.20
1.05
0.90
0.75
0.60
0.45
0.30
0.15
0.00
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Visit
Patient ID
R3500-AS-1619-826001053
R3500-AS-1619-826001096
R3500-AS-1619-826003002
R3500-AS-1619-826001073
R3500-AS-1619-826001098
R3500-AS-1619-826003004
R3500-AS-1619-826001080
R3500-AS-1619-826002020
R3500-AS-1619-826003008
R3500-AS-1619-826001089
R3500-AS-1619-826002032

Fig. 129 (Cont)

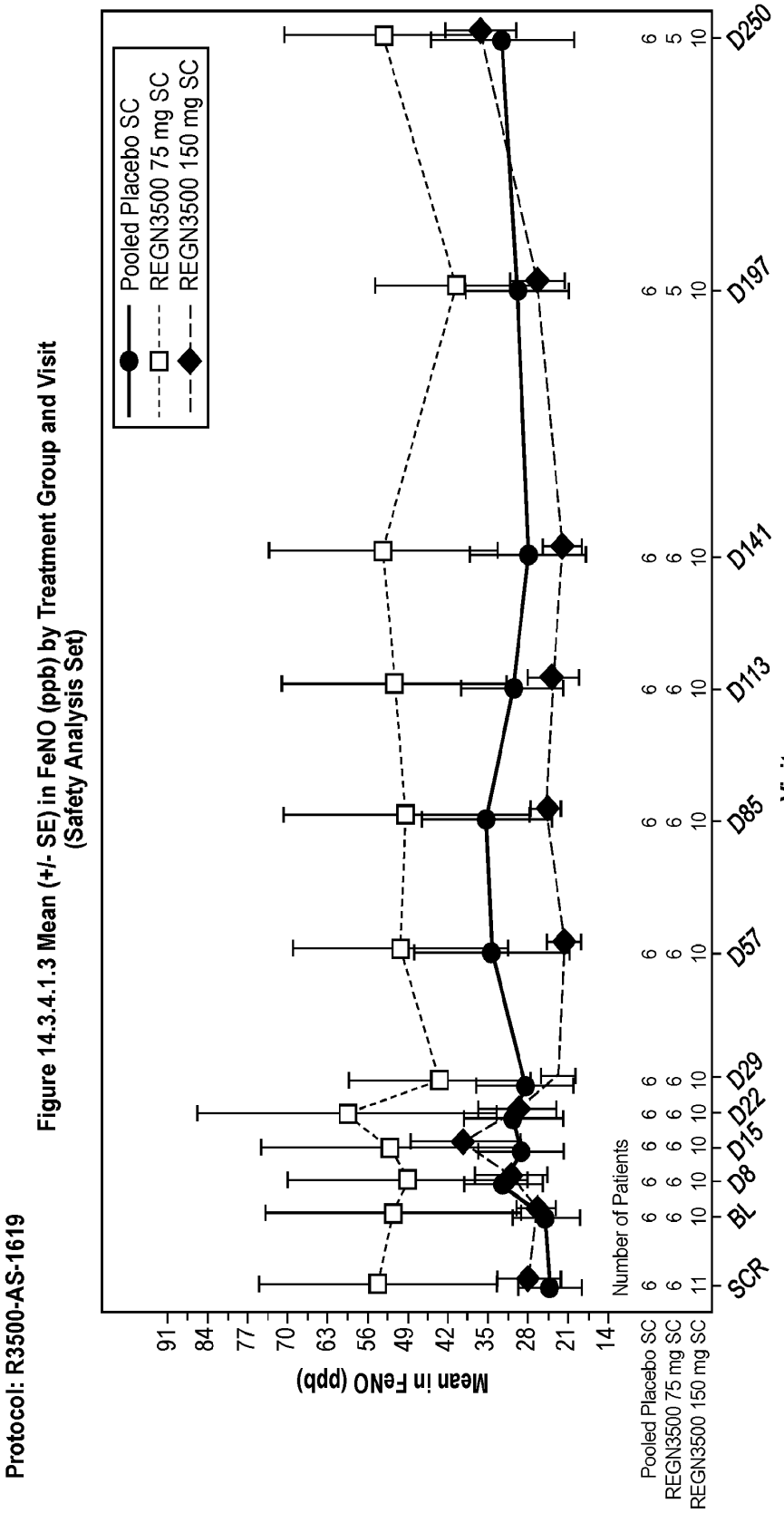

Protocol: R3500-AS-1619
Figure 14.3.4.1.3 Mean (+/- SE) in FeNO (ppb) by Treatment Group and Visit
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
REGN3500 150 mg SC
Mean in FeNO (ppb)
91
84
77
70
63
56
49
42
35
28
21
14
Visit
SCR
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 6 6 6 6 6 6
REGN3500 75 mg SC 6 6 6 6 6 6 6 6 6 5 5 5
REGN3500 150 mg SC 11 10 10 10 10 10 10 10 10 10 6 10

Fig. 130

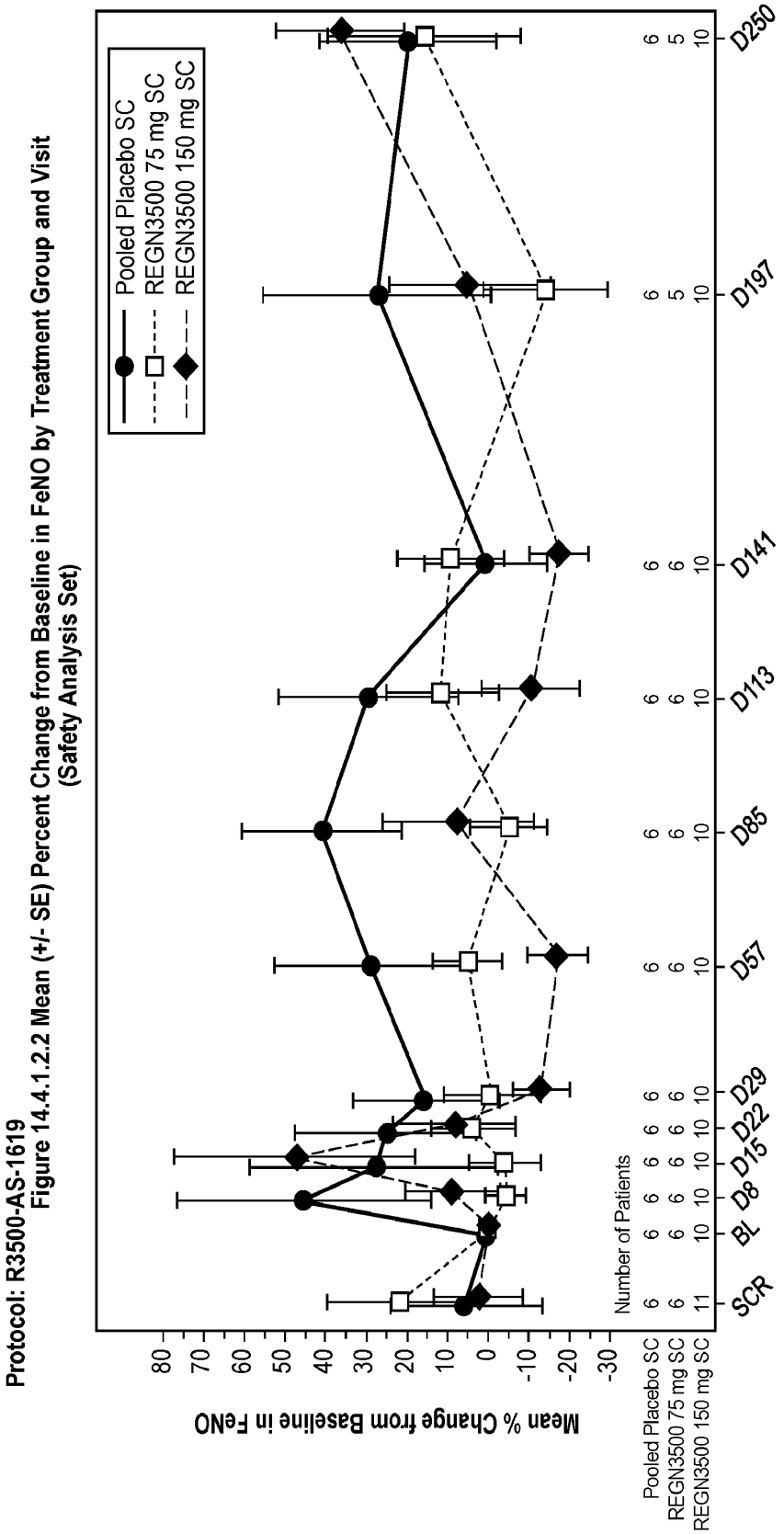

Protocol: R3500-AS-1619
Figure 14.4.1.2.2 Mean (+/- SE) Percent Change from Baseline in FeNO by Treatment Group and Visit
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
REGN3500 150 mg SC
Mean % Change from Baseline in FeNO
80
70
60
50
40
30
20
10
0
-10
-20
-30
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 6 6 6 6 6 6 6 6
REGN3500 75 mg SC 6 6 6 6 6 6 6 6 6 6 6 5 5 5
REGN3500 150 mg SC 11 10 10 10 10 10 10 10 10 10 10 10 10 10
SCR
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Visit

Fig. 131

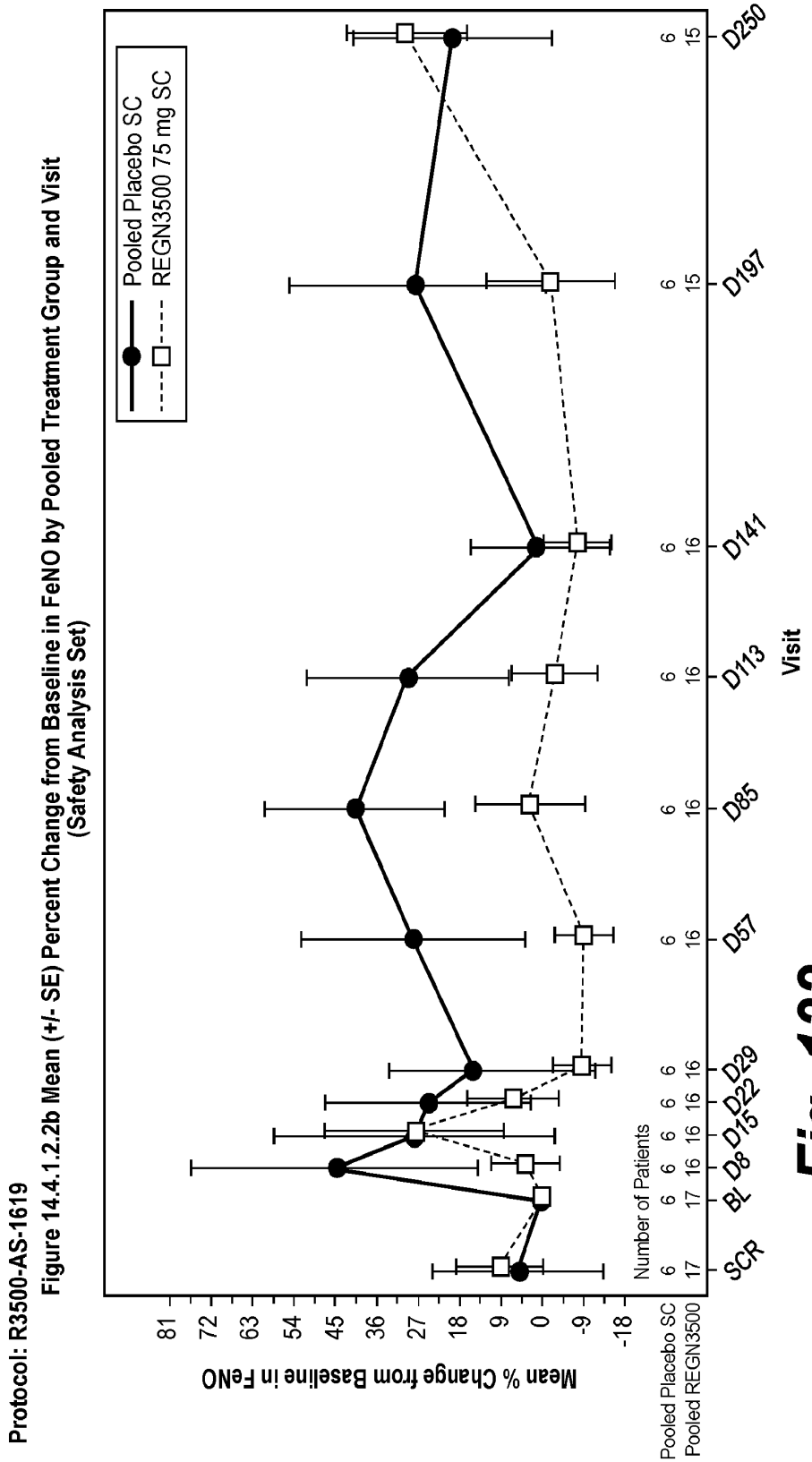

Protocol: R3500-AS-1619
Figure 14.4.1.2.2b Mean (+/- SE) Percent Change from Baseline in FeNO by Pooled Treatment Group and Visit
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
Mean % Change from Baseline in FeNO
81
72
63
54
45
36
27
18
9
0
-9
-18
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 6 6 6 6
Pooled REGN3500 17 17 16 16 16 16 16 16 16 15
SCR
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Visit

Fig. 132

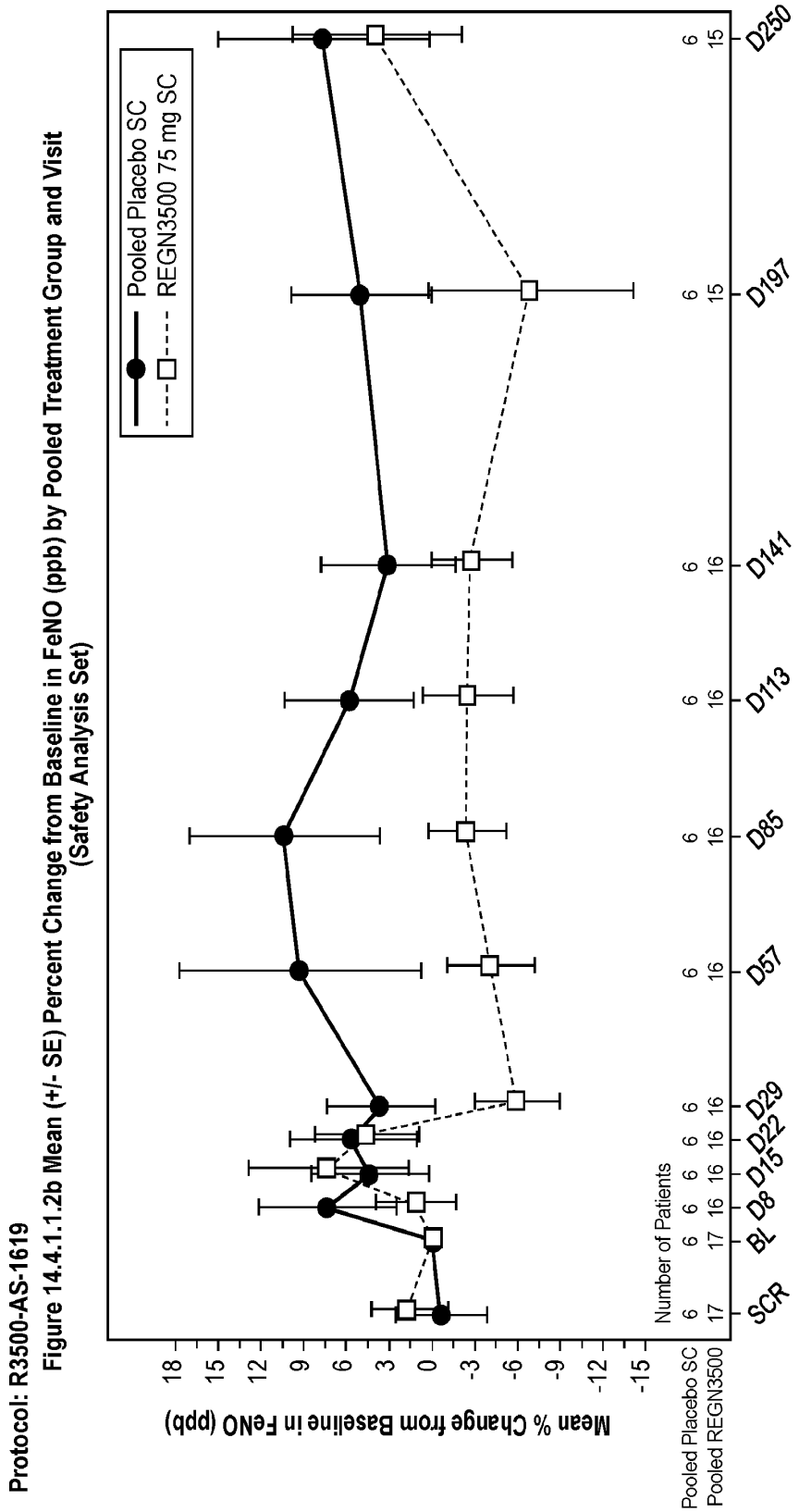

Protocol: R3500-AS-1619
Figure 14.4.1.1.2b Mean (+/- SE) Percent Change from Baseline in FeNO (ppb) by Pooled Treatment Group and Visit
(Safety Analysis Set)
Pooled Placebo SC
REGN3500 75 mg SC
Mean % Change from Baseline in FeNO (ppb)
18
15
12
9
6
3
0
-3
-6
-9
-12
-15
Number of Patients
Pooled Placebo SC 6 6 6 6 6 6 6 6 6 6 6
Pooled REGN3500 17 17 16 16 16 16 16 16 16 15 15
SCR
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Visit

Fig. 133

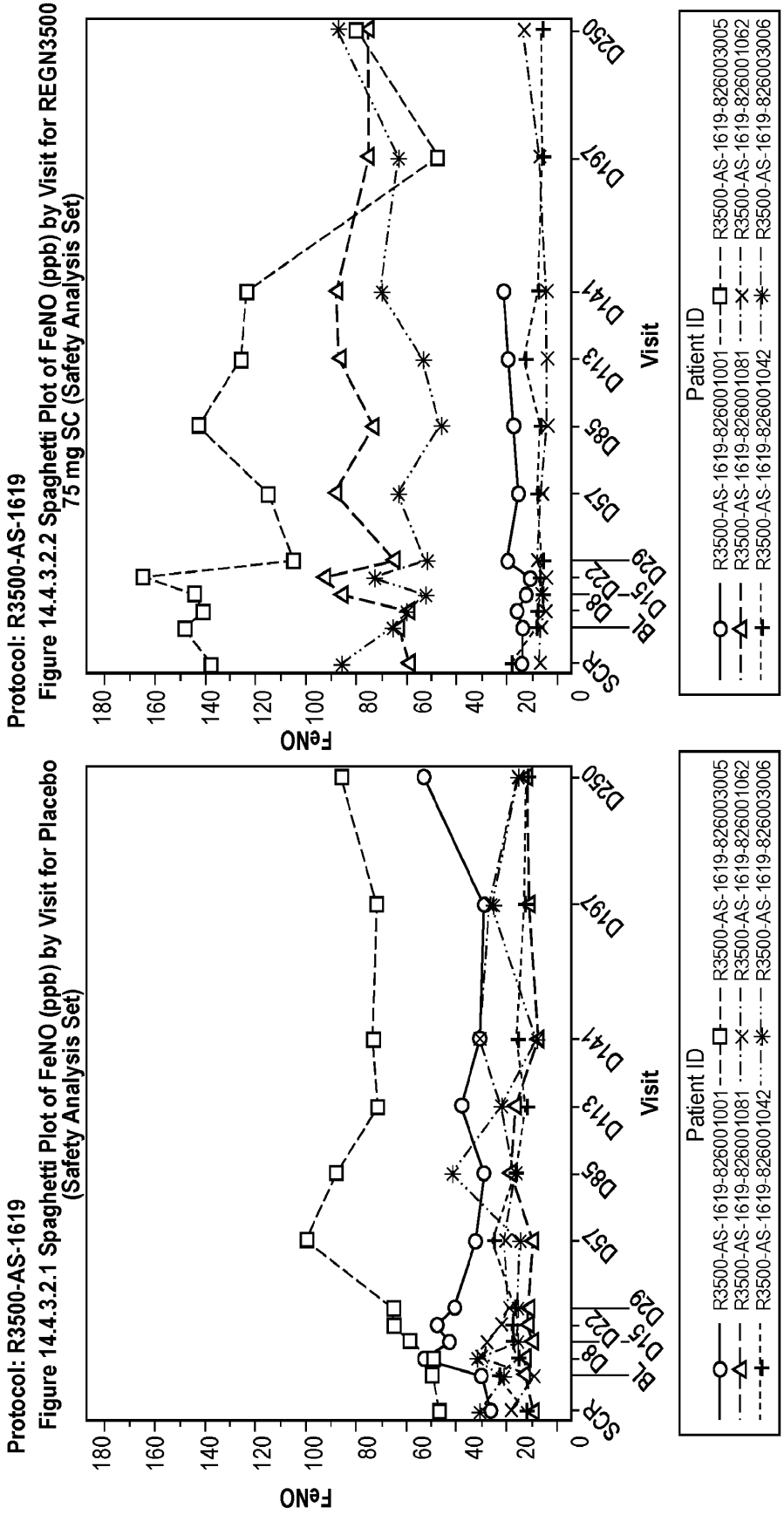

Protocol: R3500-AS-1619
Figure 14.4.3.2.1 Spaghetti Plot of FeNO (ppb) by Visit for Placebo (Safety Analysis Set)
Protocol: R3500-AS-1619
Figure 14.4.3.2.2 Spaghetti Plot of FeNO (ppb) by Visit for REGN3500 75 mg SC (Safety Analysis Set)
FeNO
Visit
SCR
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Patient ID
R3500-AS-1619-826001001
R3500-AS-1619-826001081
R3500-AS-1619-826001042
R3500-AS-1619-826003005
R3500-AS-1619-826001062
R3500-AS-1619-826003006

Fig. 134

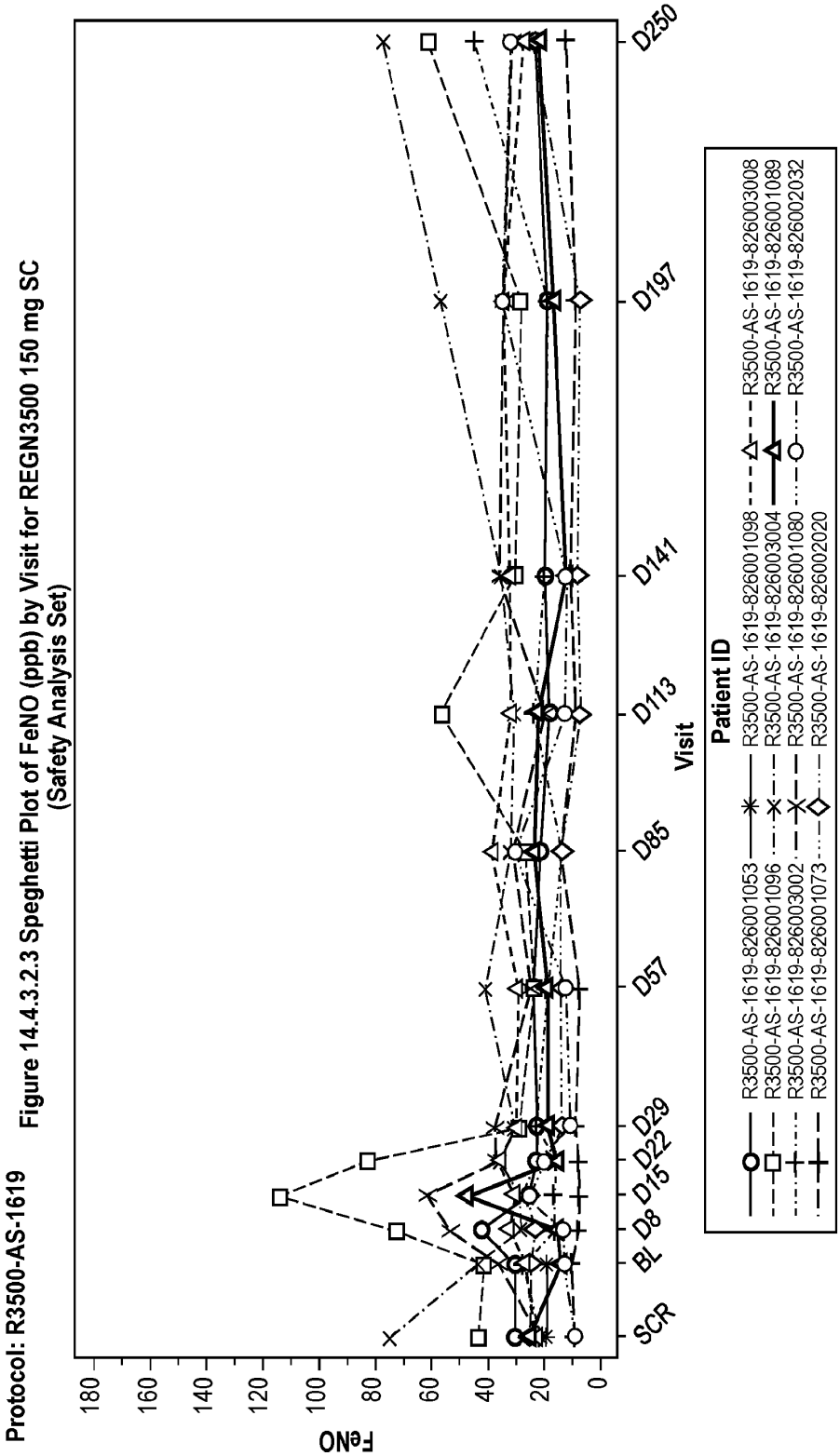

Protocol: R3500-AS-1619
Figure 14.4.3.2.3 Spaghetti Plot of FeNO (ppb) by Visit for REGN3500 150 mg SC
(Safety Analysis Set)
FeNO
180
160
140
120
100
80
60
40
20
0
SCR
BL
D8
D15
D22
D29
D57
D85
D113
D141
D197
D250
Visit
Patient ID
R3500-AS-1619-826001053
R3500-AS-1619-826001096
R3500-AS-1619-826003002
R3500-AS-1619-826001073
R3500-AS-1619-826001098
R3500-AS-1619-826003004
R3500-AS-1619-826001080
R3500-AS-1619-826002020
R3500-AS-1619-826003008
R3500-AS-1619-826001089
R3500-AS-1619-826002032

Fig. 134 (Cont)