Asthma exacerbations

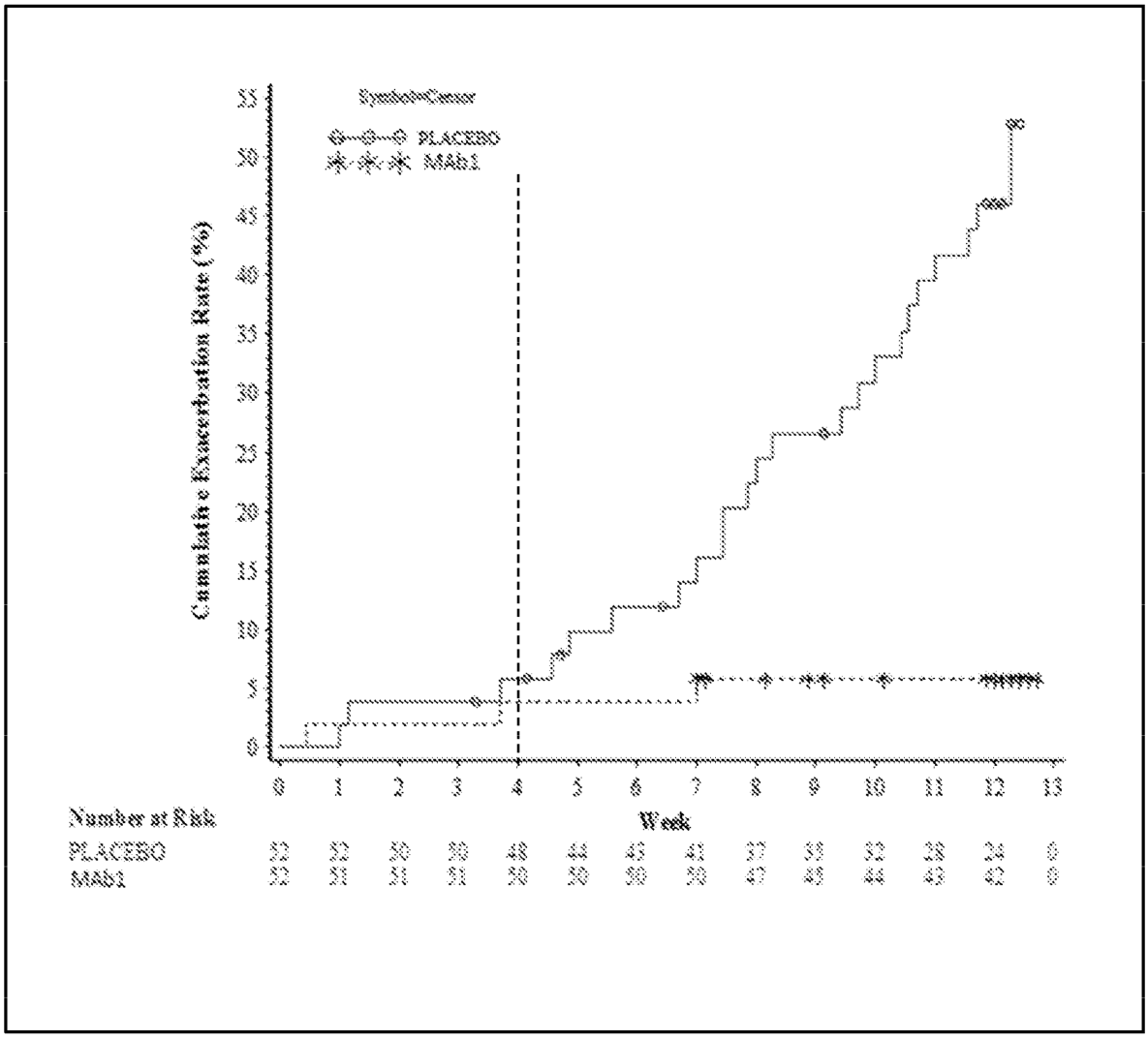


Figure 1

FEV1

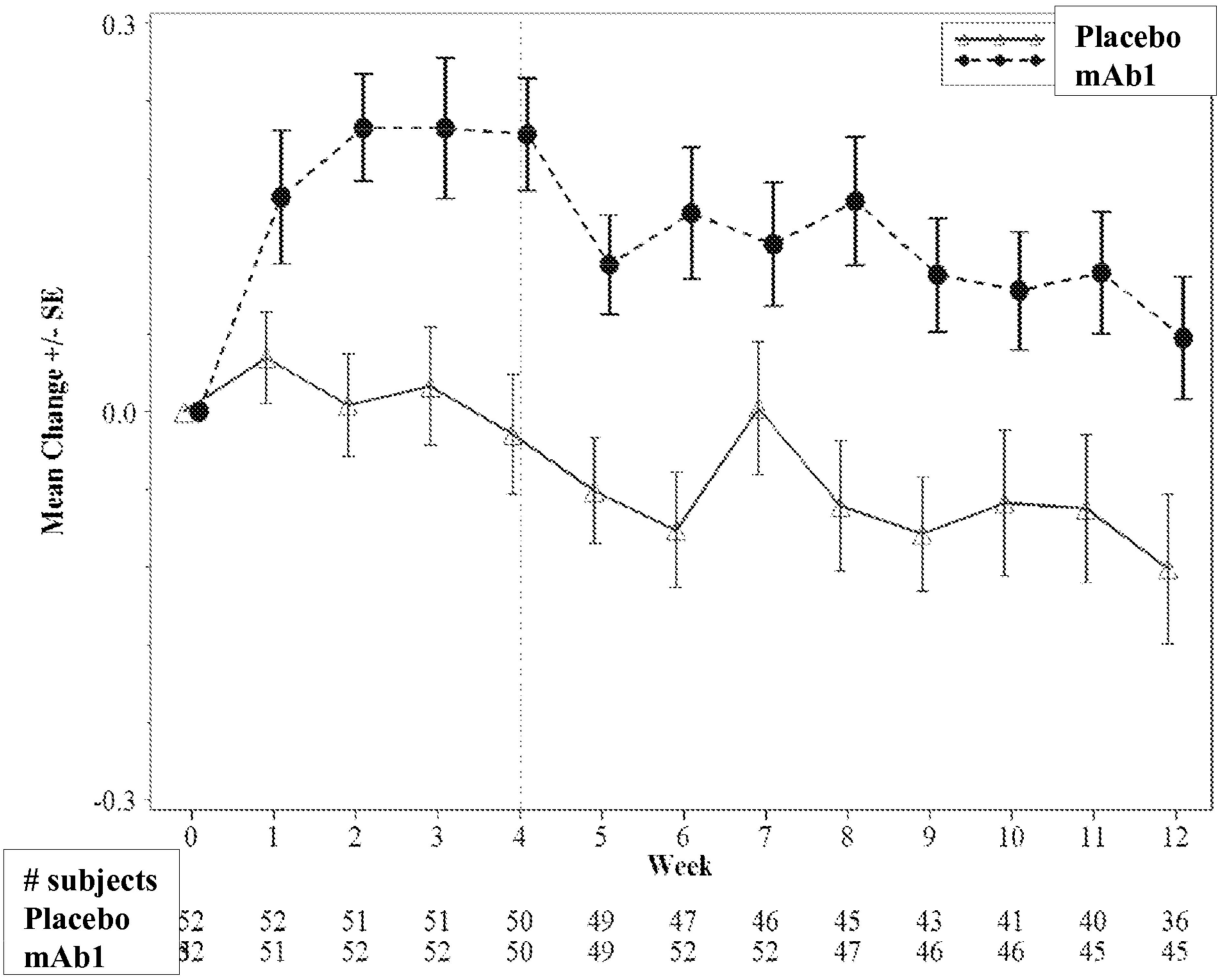


Figure 2

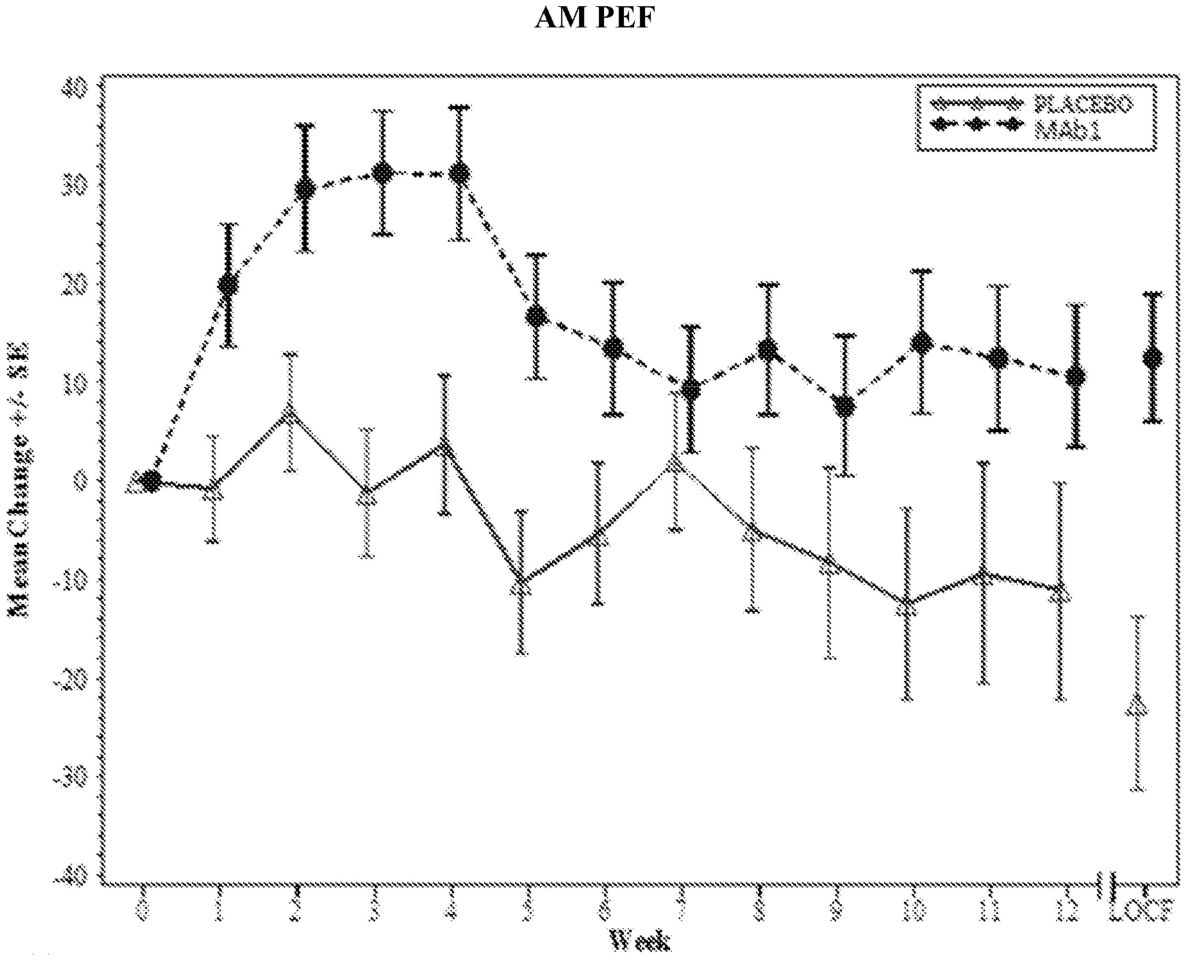

AM PEF
PLACEBO
MAb1
Mean Change +/- SE
40
30
20
10
0
-10
-20
-30
-40
0
1
2
3
4
5
6
7
8
9
10
11
12
LOCF
Week

Figure 3

PM PEF

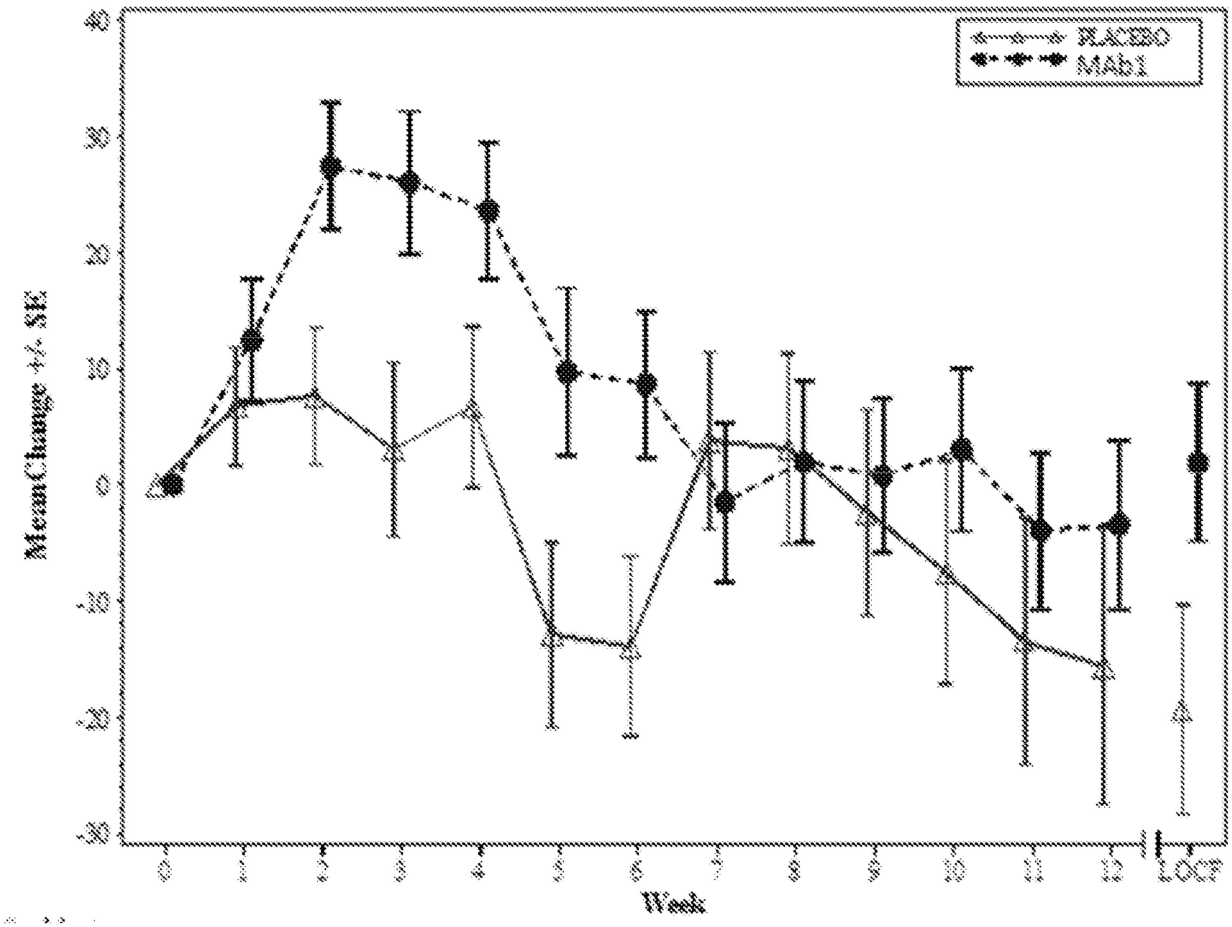


Figure 4

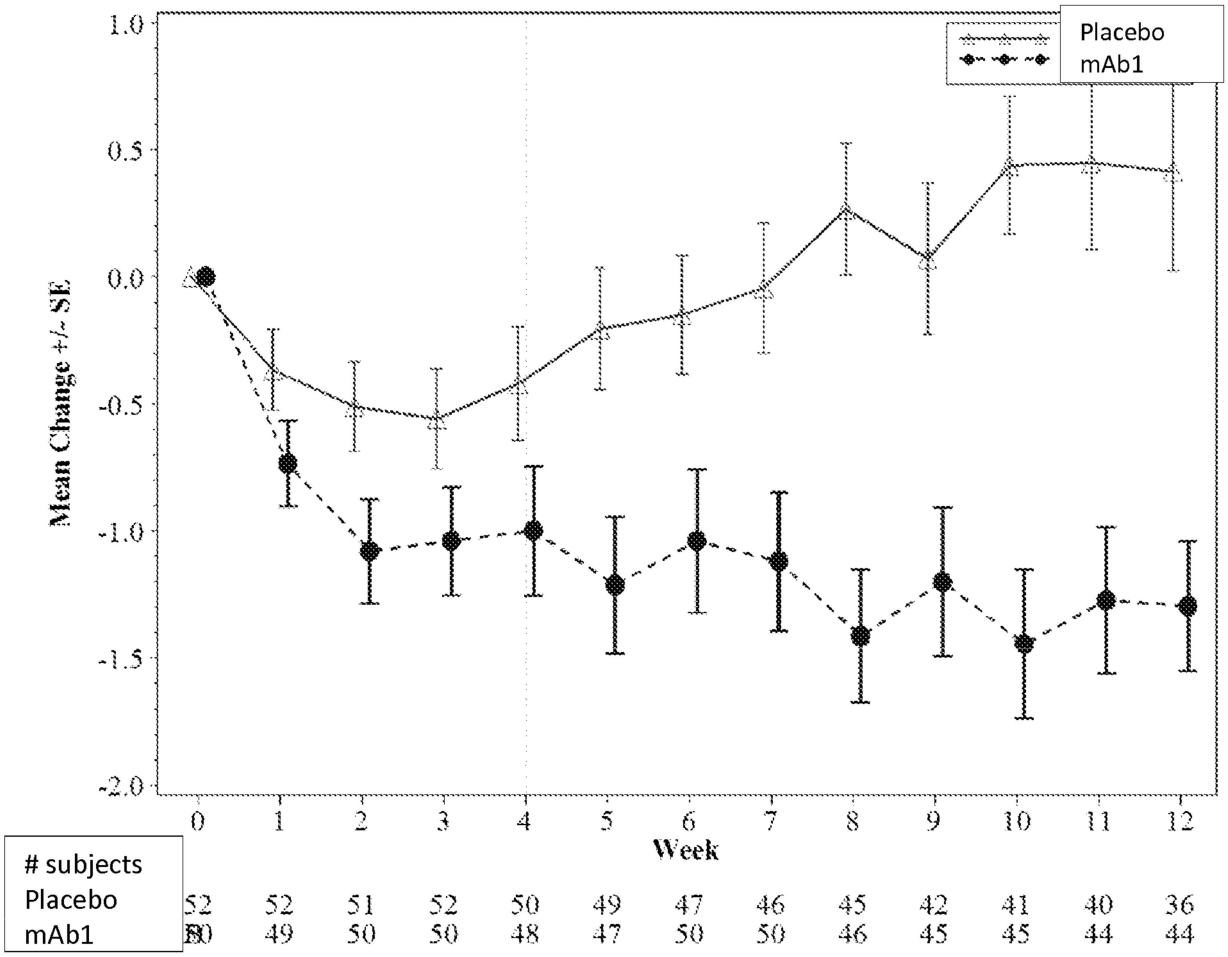

Albuterol use in inhalations/day
Placebo
mAb1
Mean Change +/- SE
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0
1
2
3
4
5
6
7
8
9
10
11
12
Week
subjects
Placebo 52 52 51 52 50 49 47 46 45 42 41 40 36
mAb1 50 49 50 50 48 47 50 50 46 45 45 44 44

Figure 5

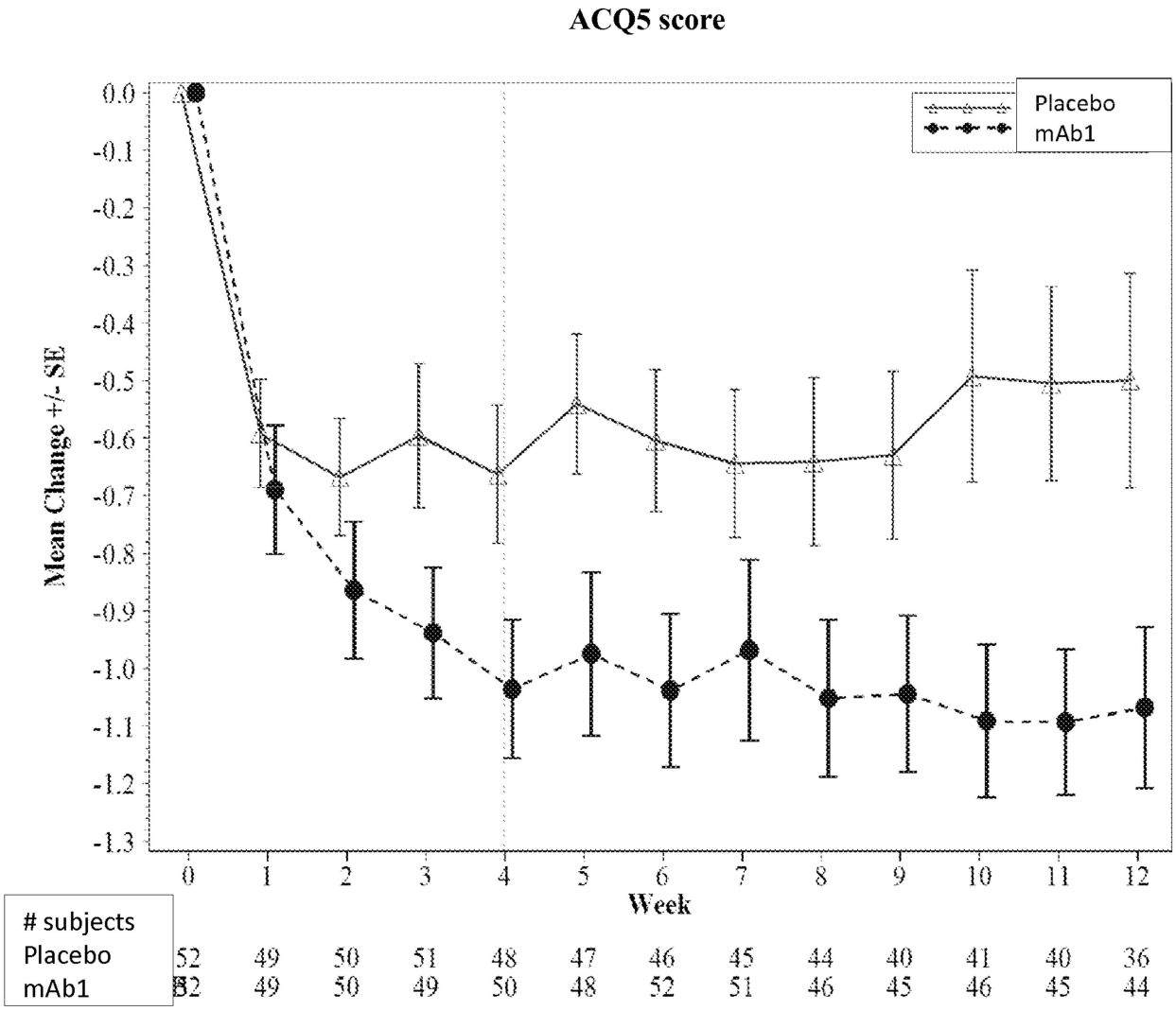

ACQ5 score
Placebo
mAb1
Mean Change +/- SE
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
-0.8
-0.9
-1.0
-1.1
-1.2
-1.3
0
1
2
3
4
5
6
7
8
9
10
11
12
Week
subjects
Placebo 52 49 50 51 48 47 46 45 44 40 41 40 36
mAb1 52 49 50 49 50 48 52 51 46 45 46 45 44

Figure 6

Nocturnal awakenings

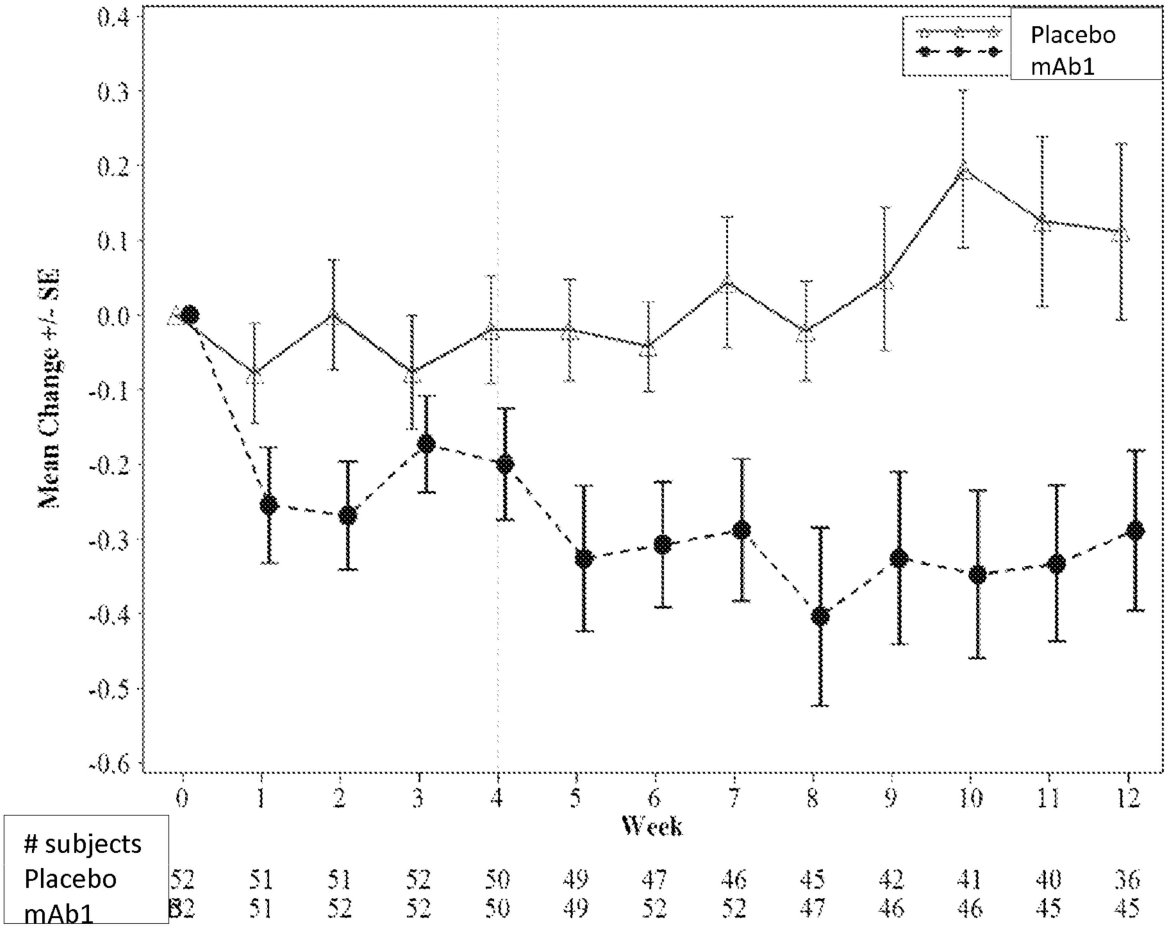


Figure 7

TARC

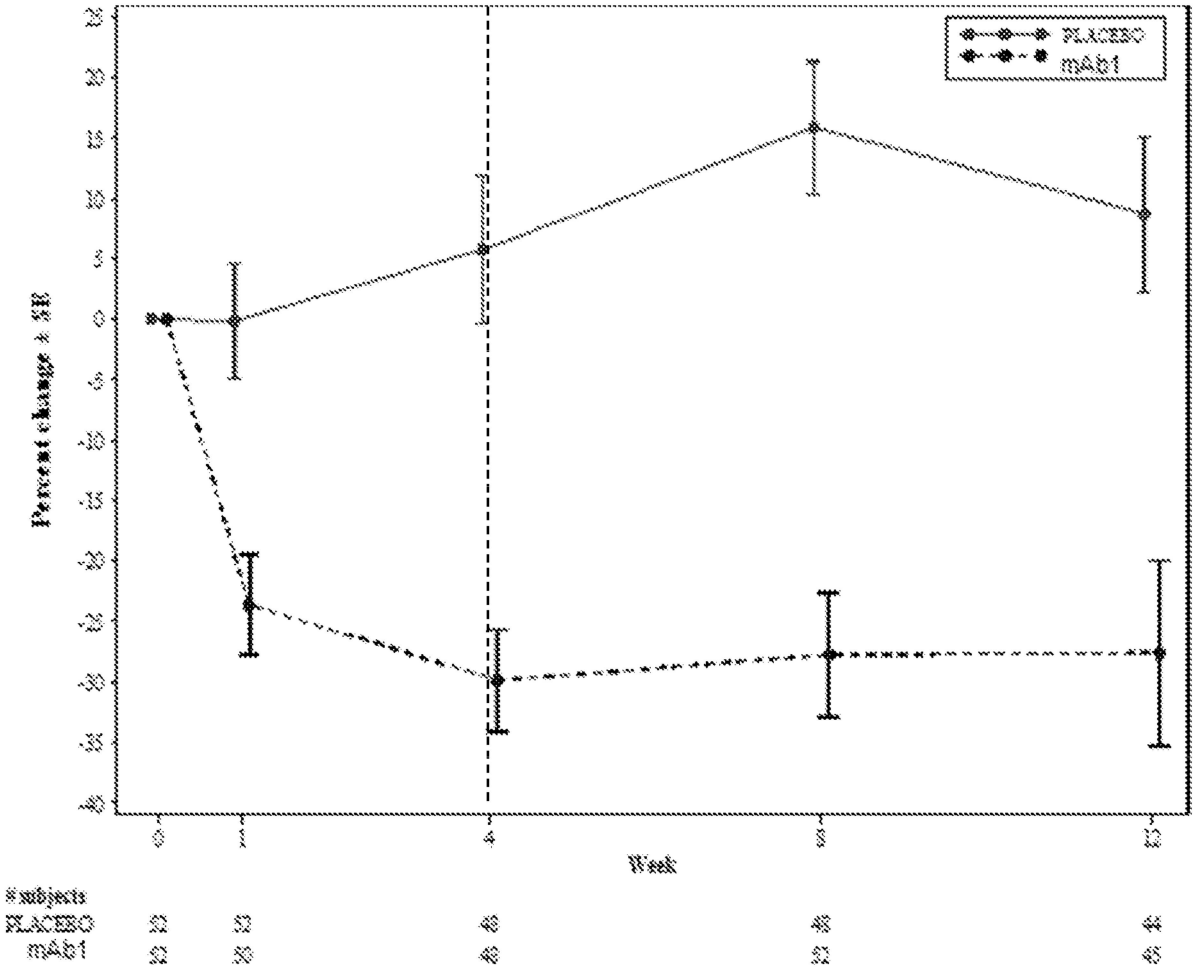


Figure 8

Eotaxin-3

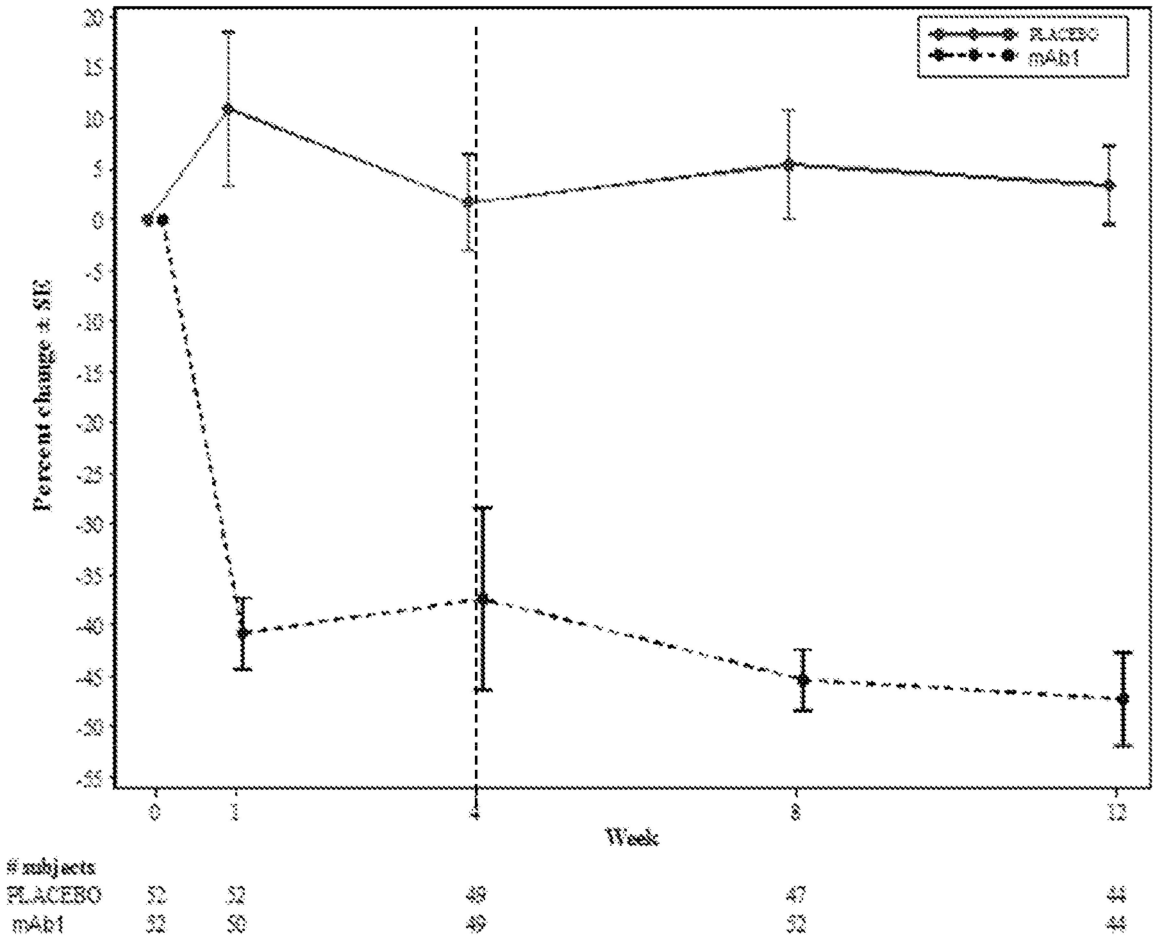


Figure 9

Total IgE

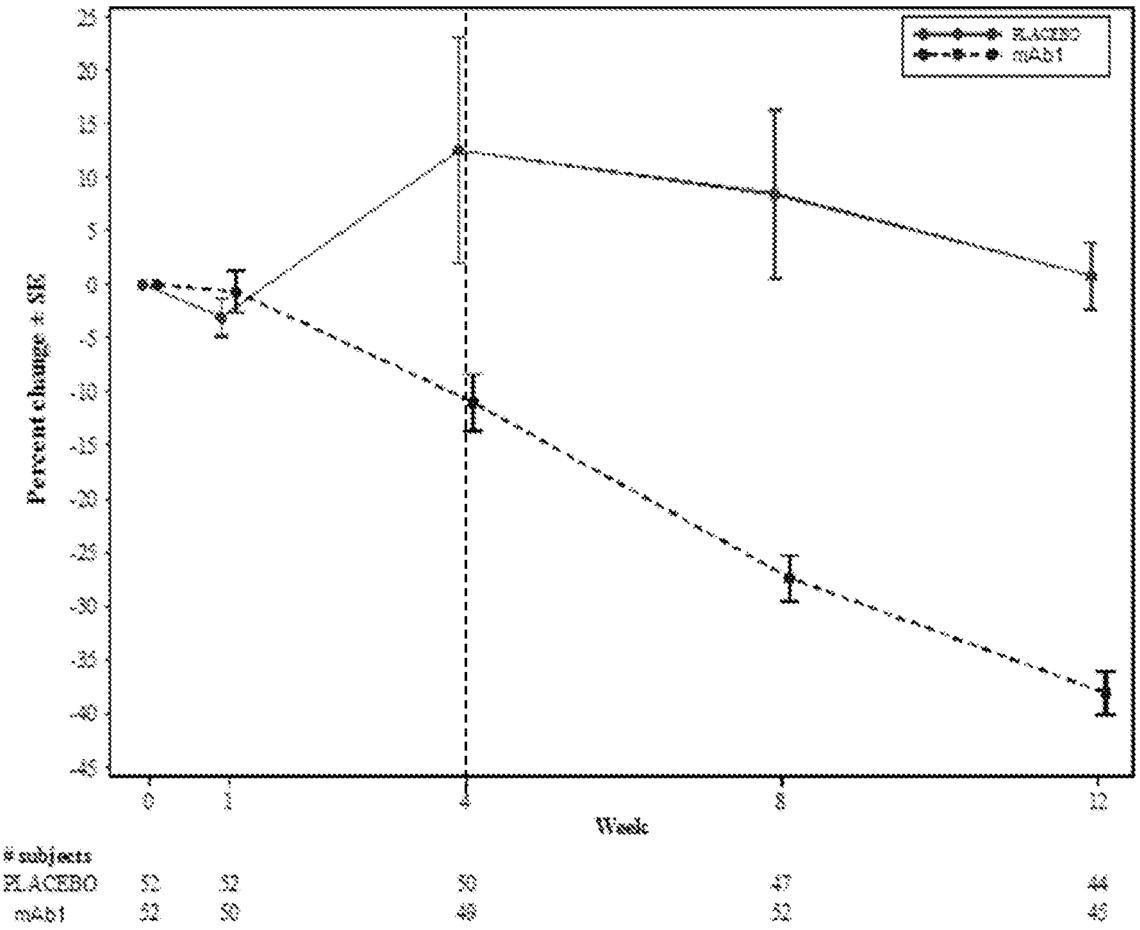


Figure 10

Periostin

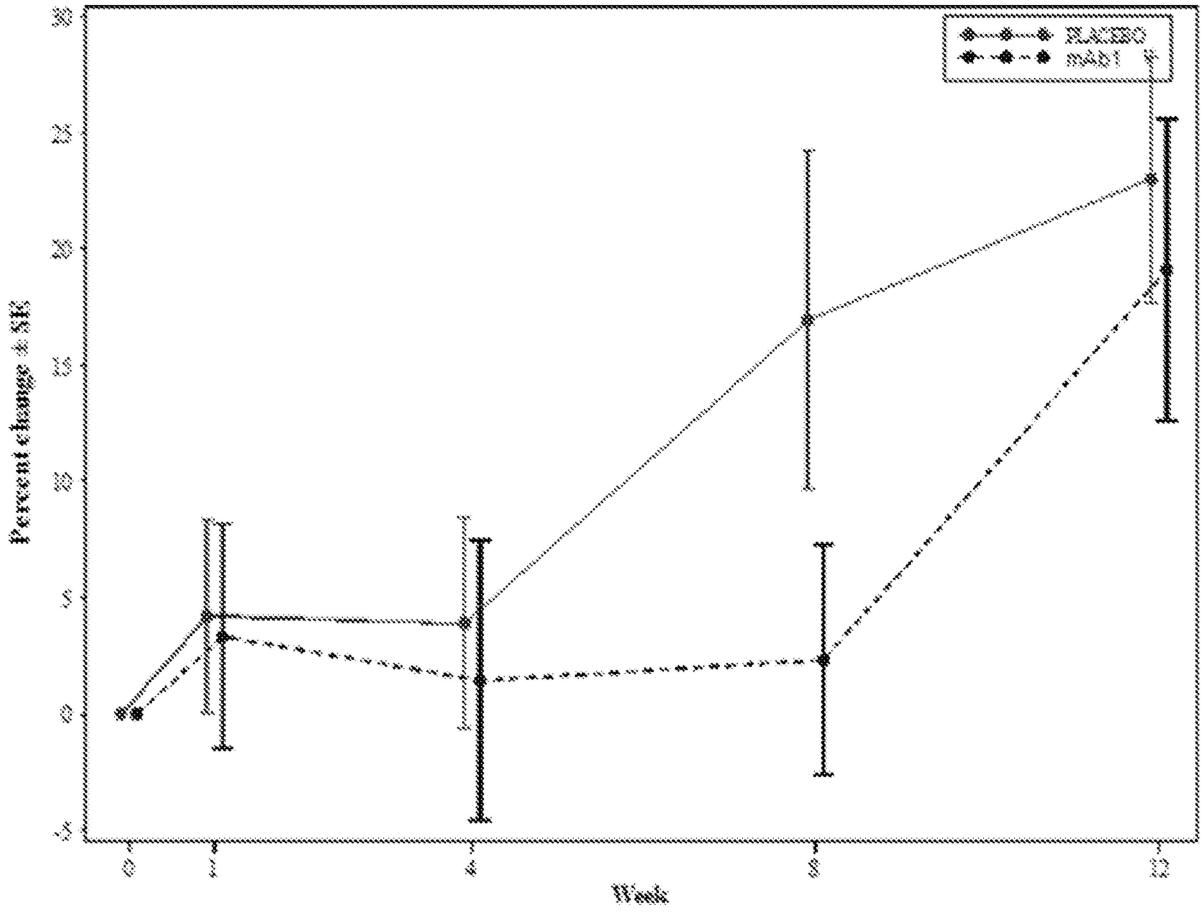


Figure 11

CEA

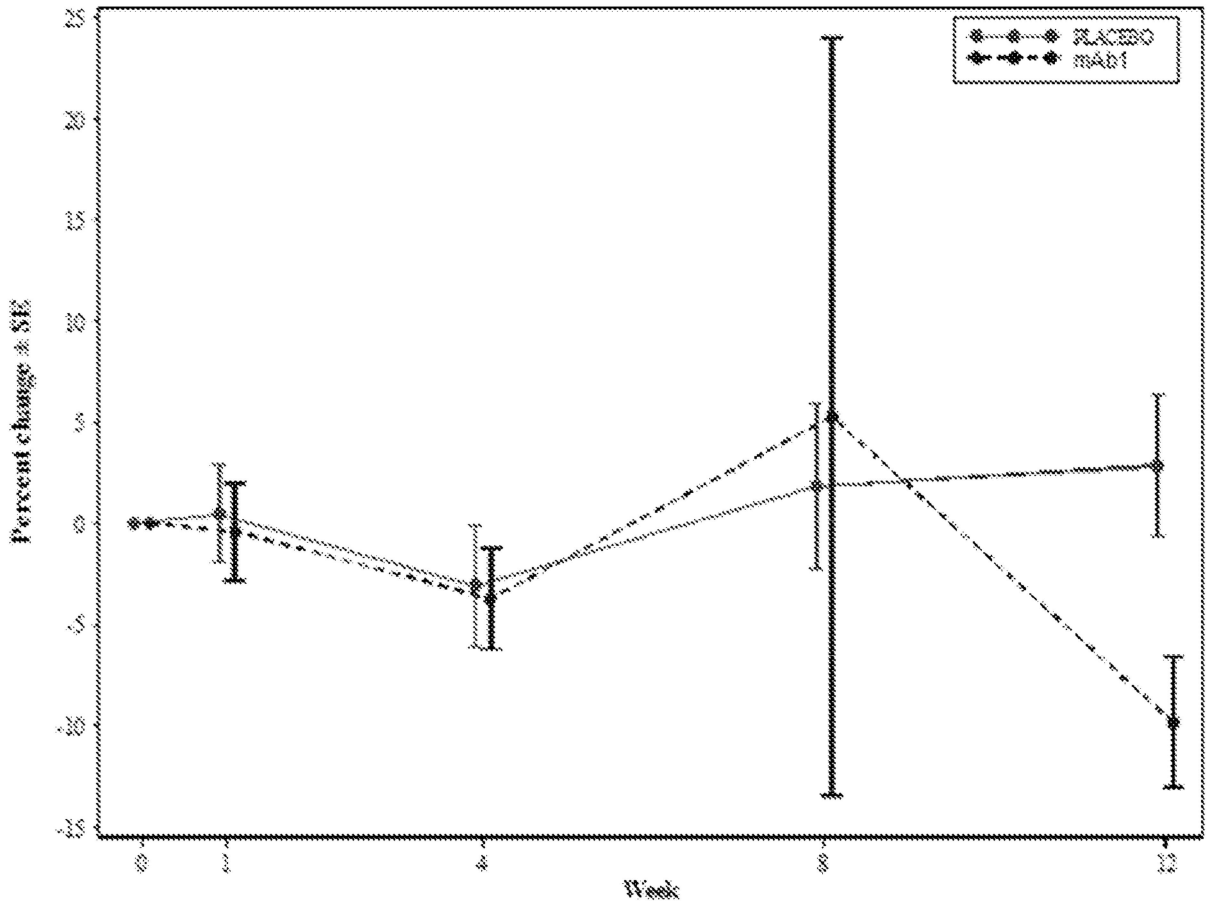


Figure 12

YKL-40

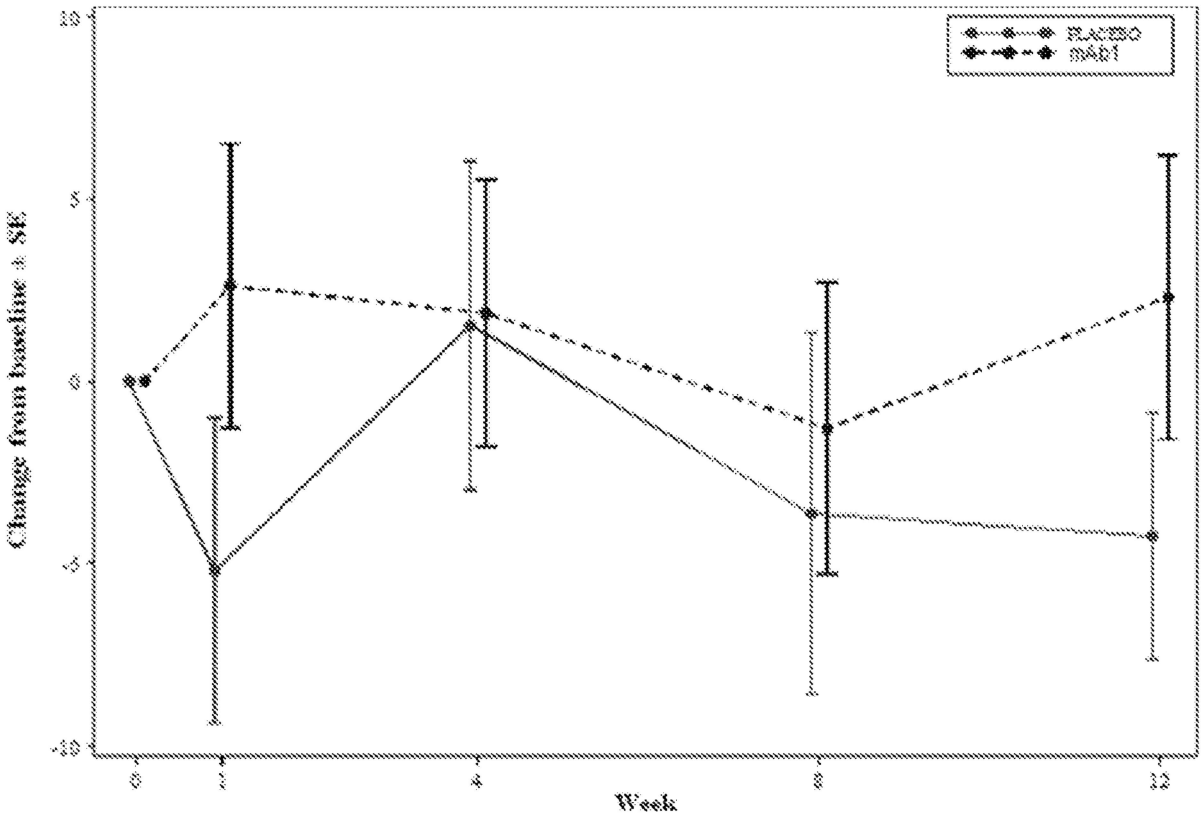


Figure 13

Blood Eosinophils

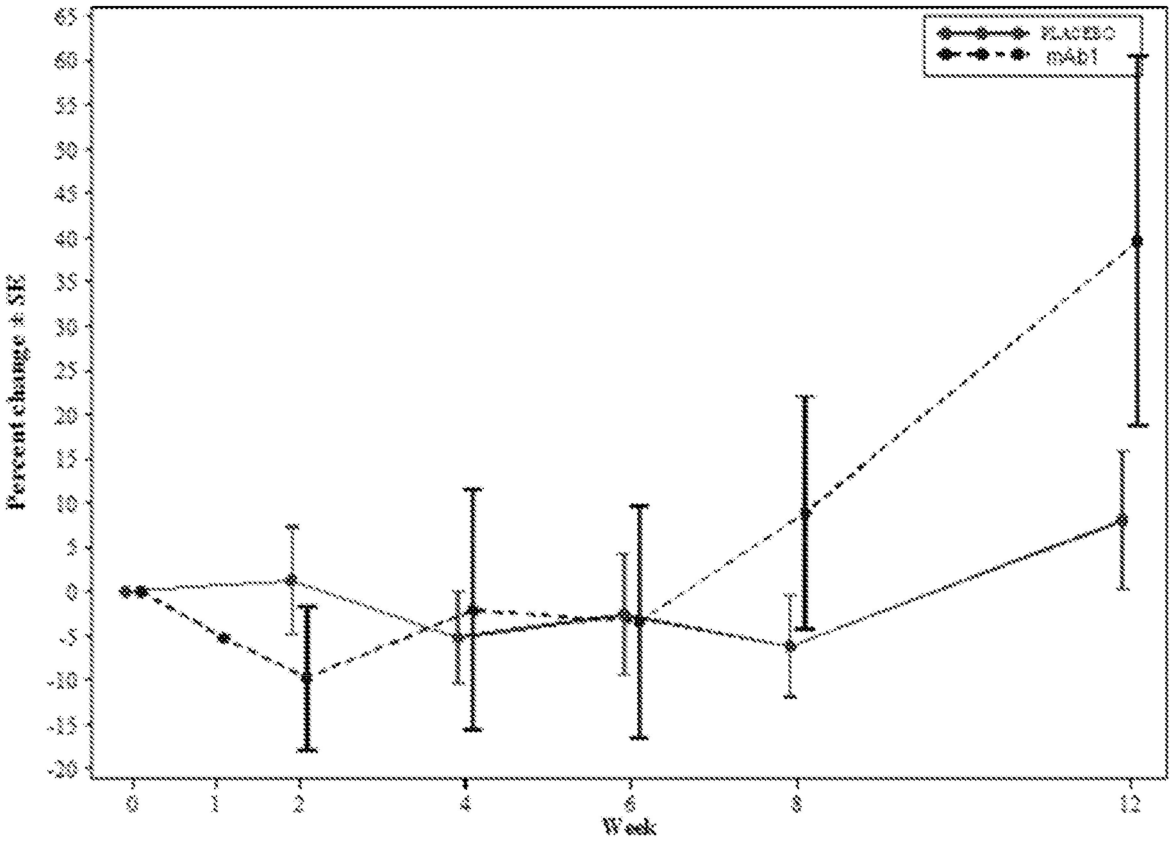


Figure 14

FeNO

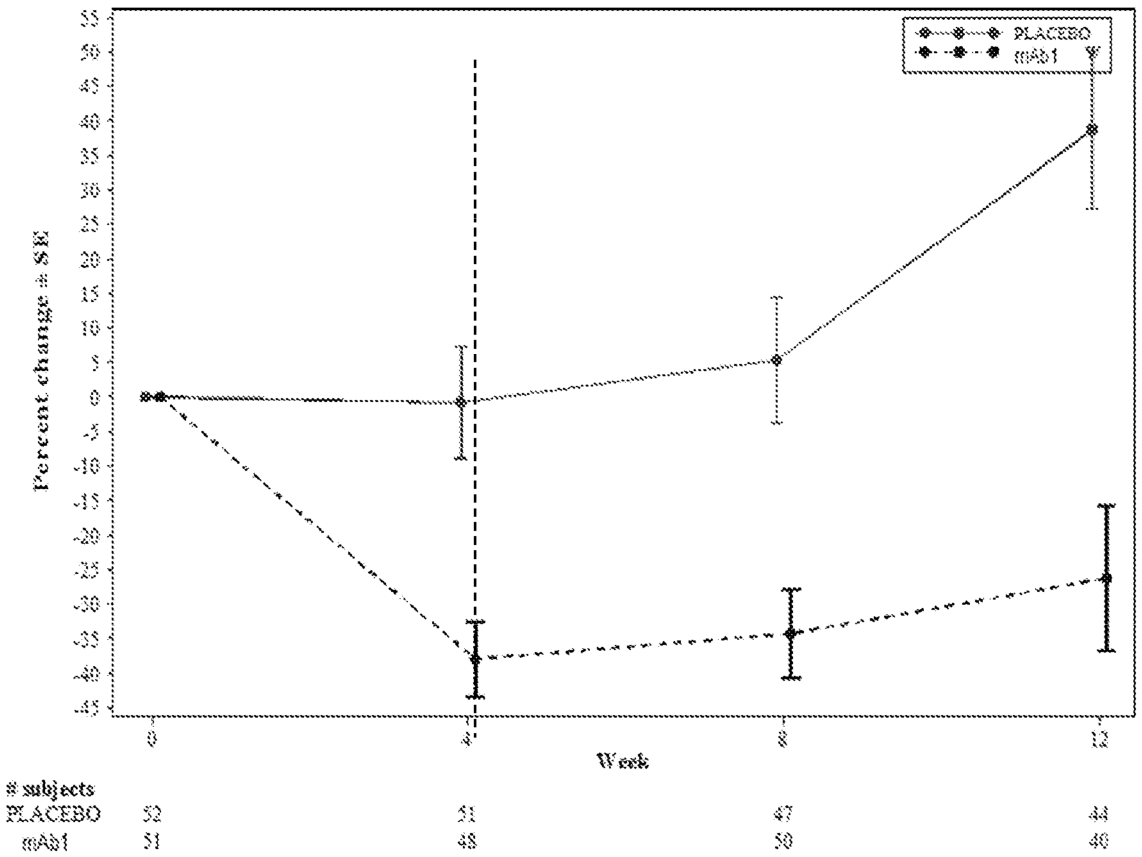


Figure 15

FEV1 vs. FeNO

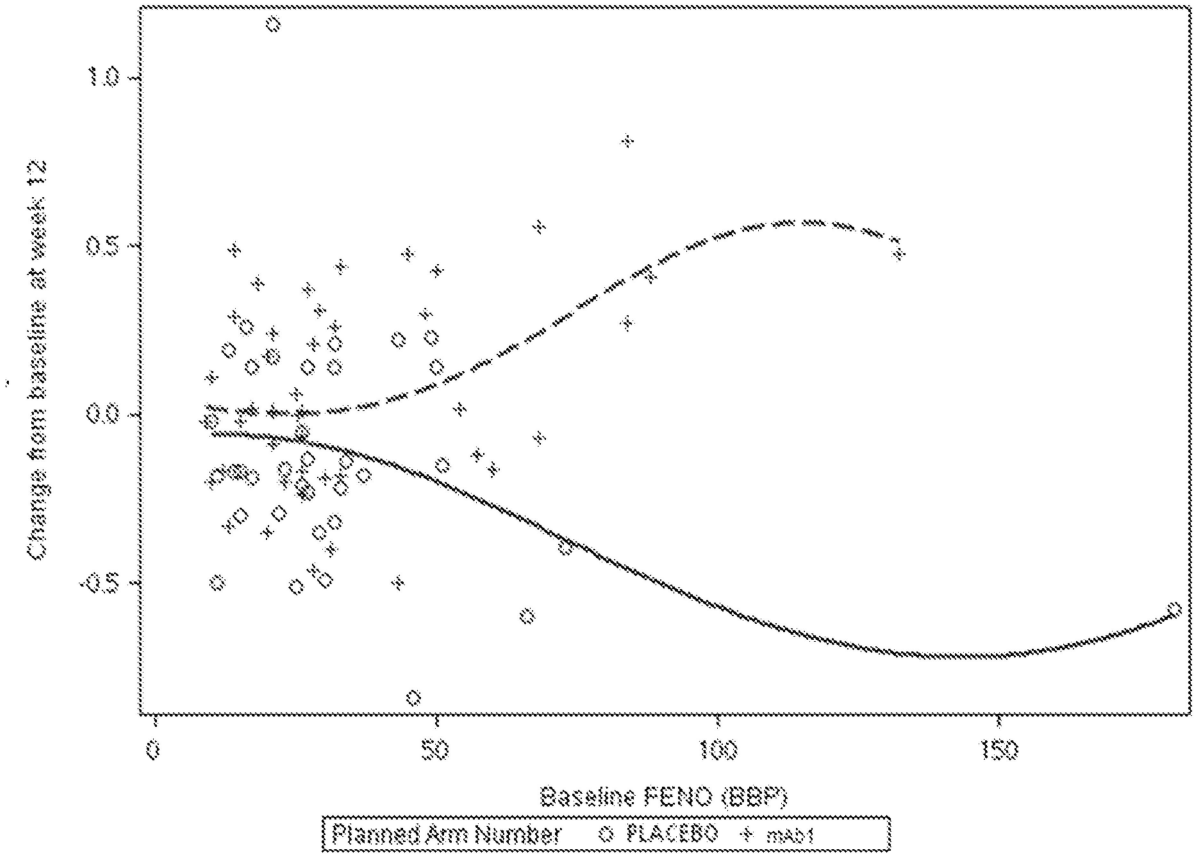


Figure 16

AM PEF vs. FeNO

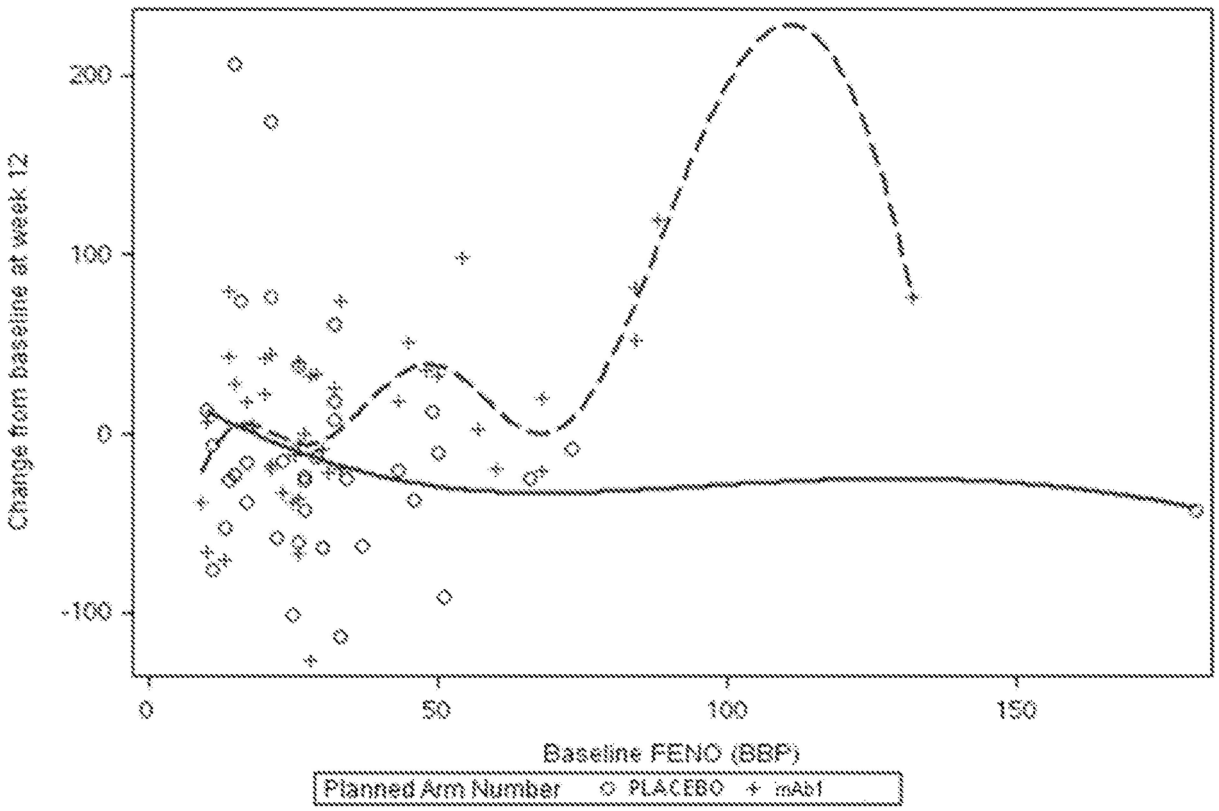


Figure 17

PM PEF vs. FeNO

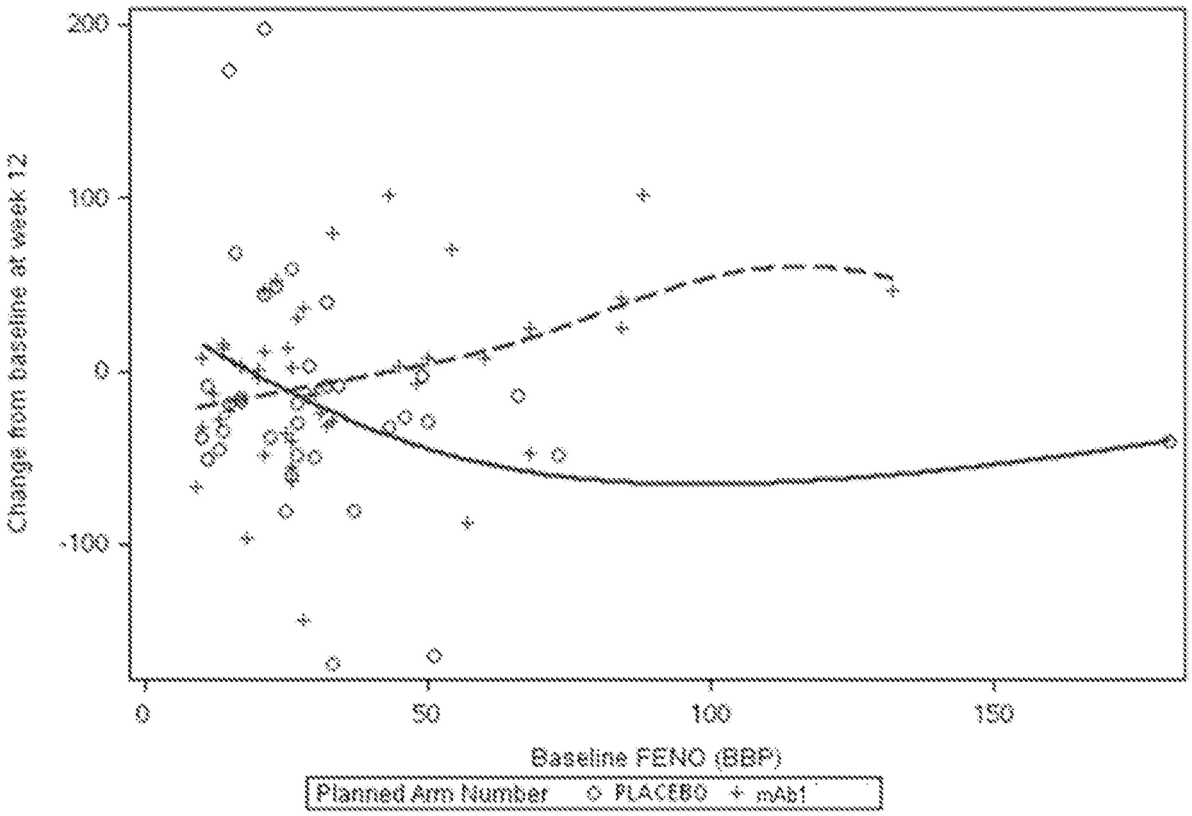


Figure 18

FEV1 vs. Blood Eosinophils

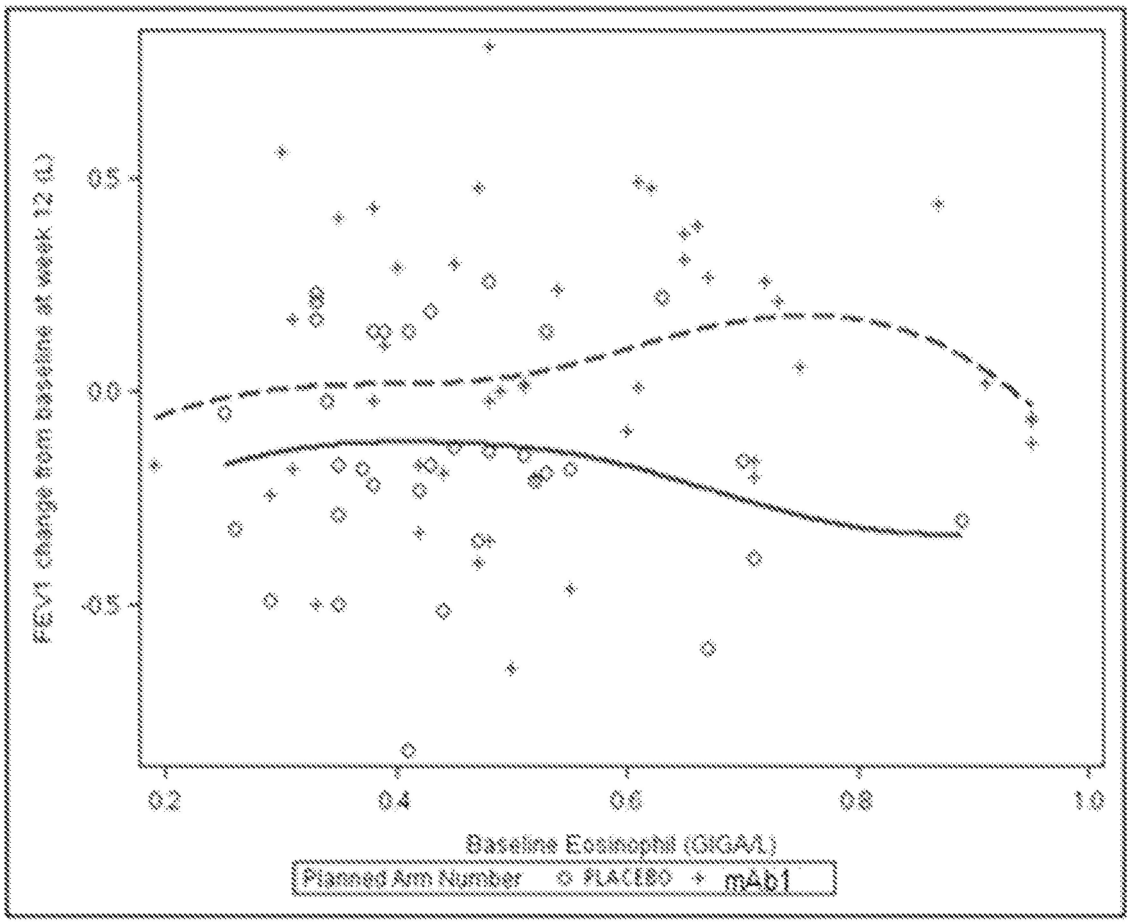


Figure 19

ACQ vs. Blood Eosinophils

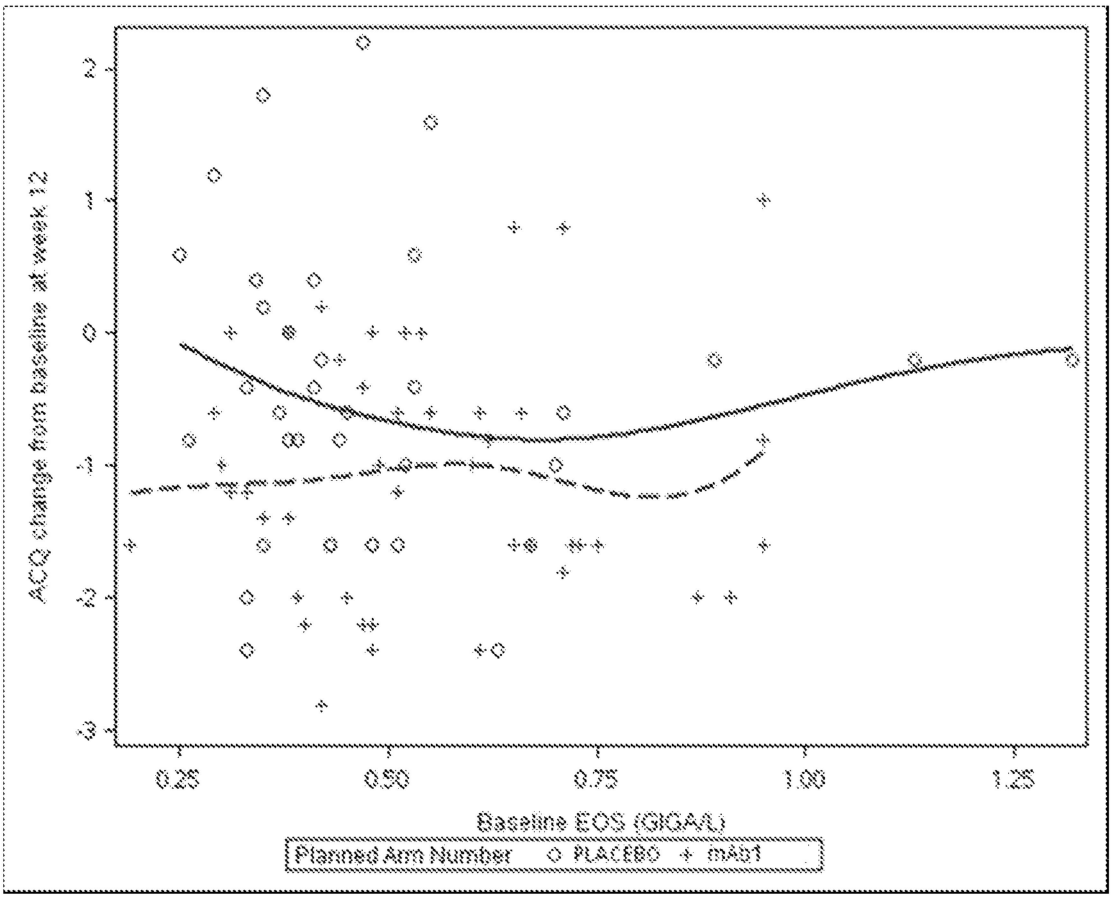


Figure 20

Albuterol use vs. Blood Eosinophils

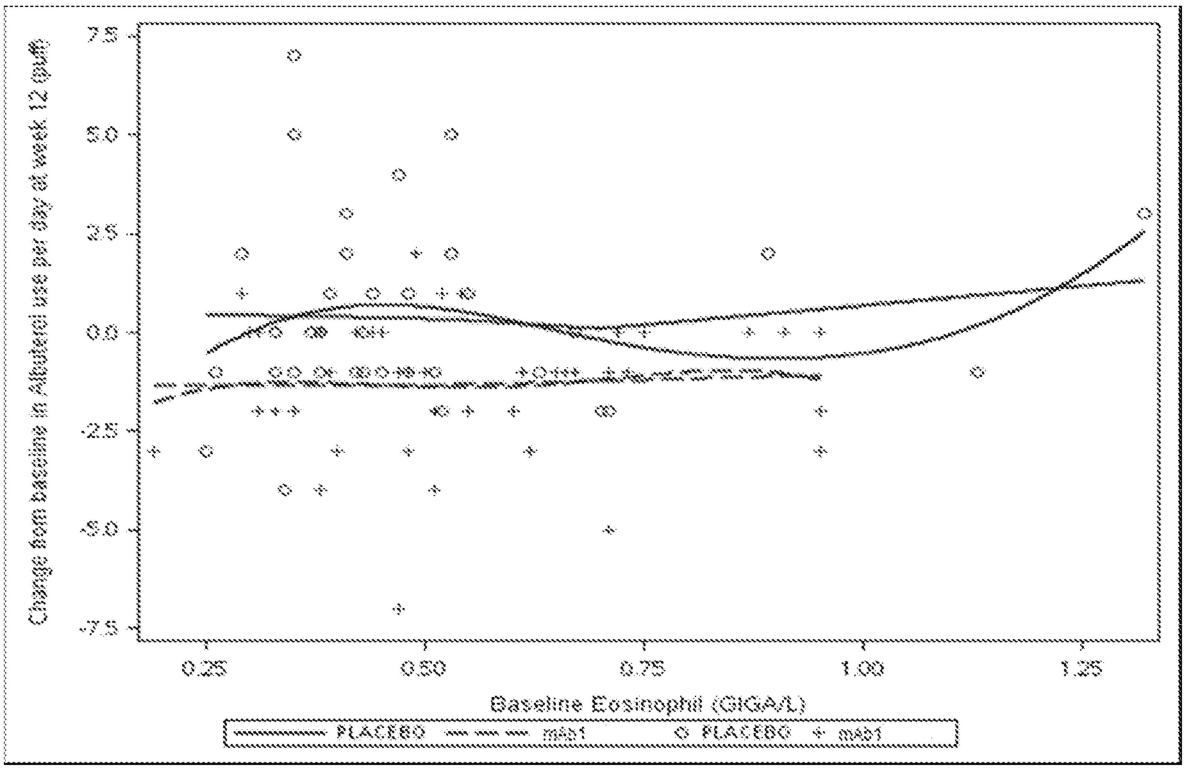


Figure 21

ACQ vs. periostin

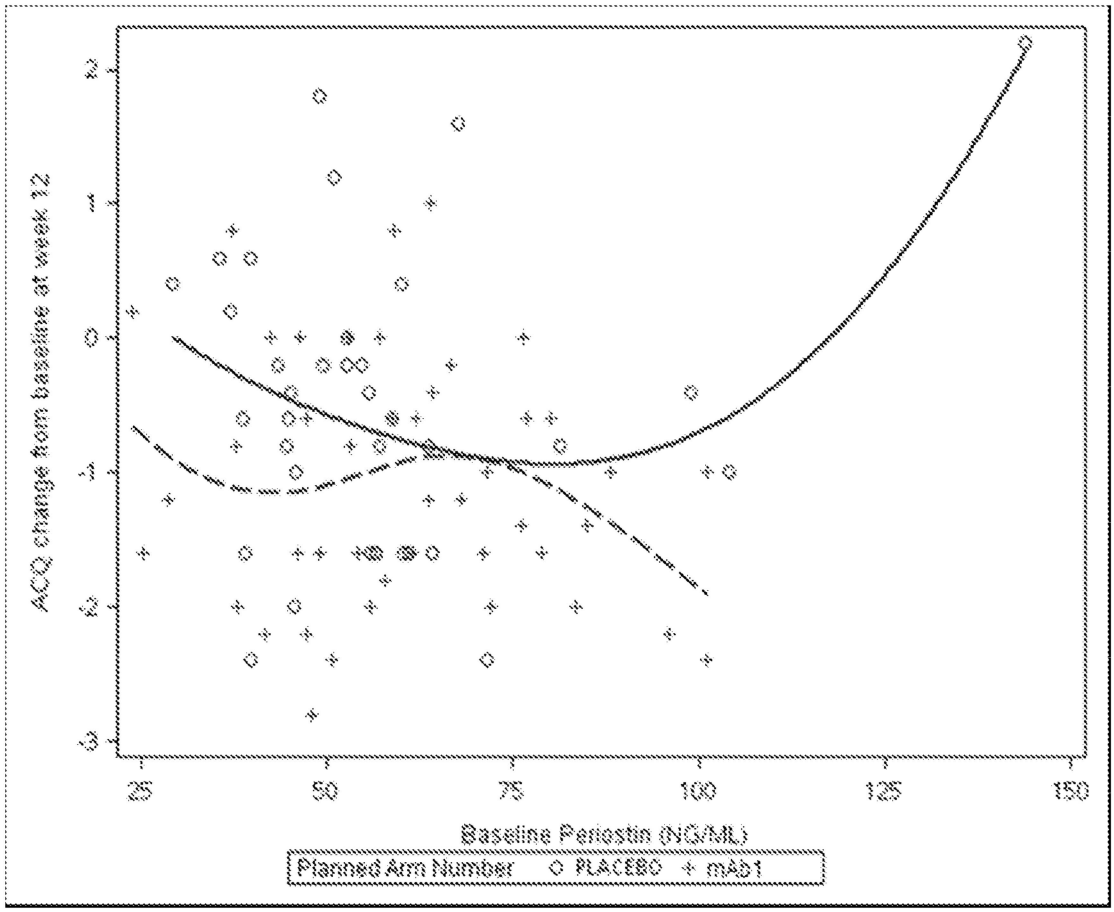


Figure 22

ACQ vs. YKL-40

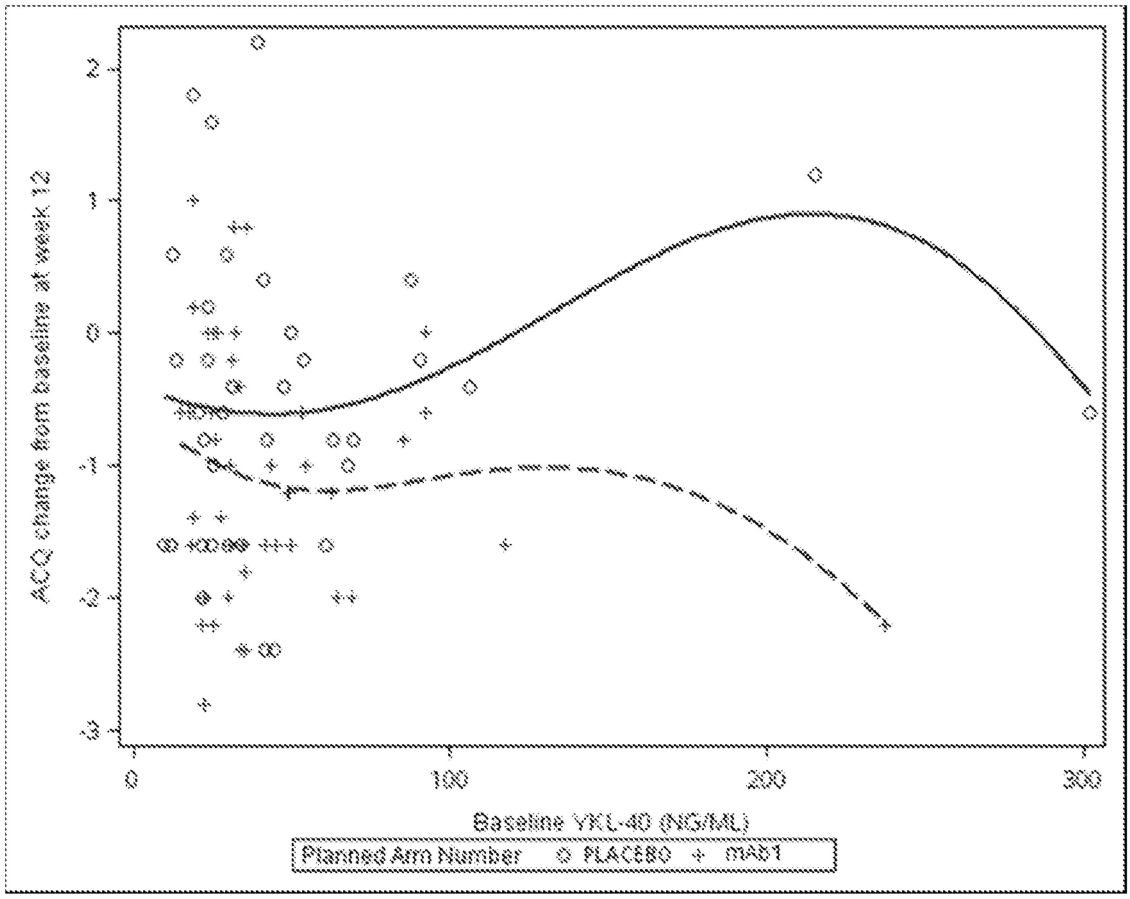


Figure 23

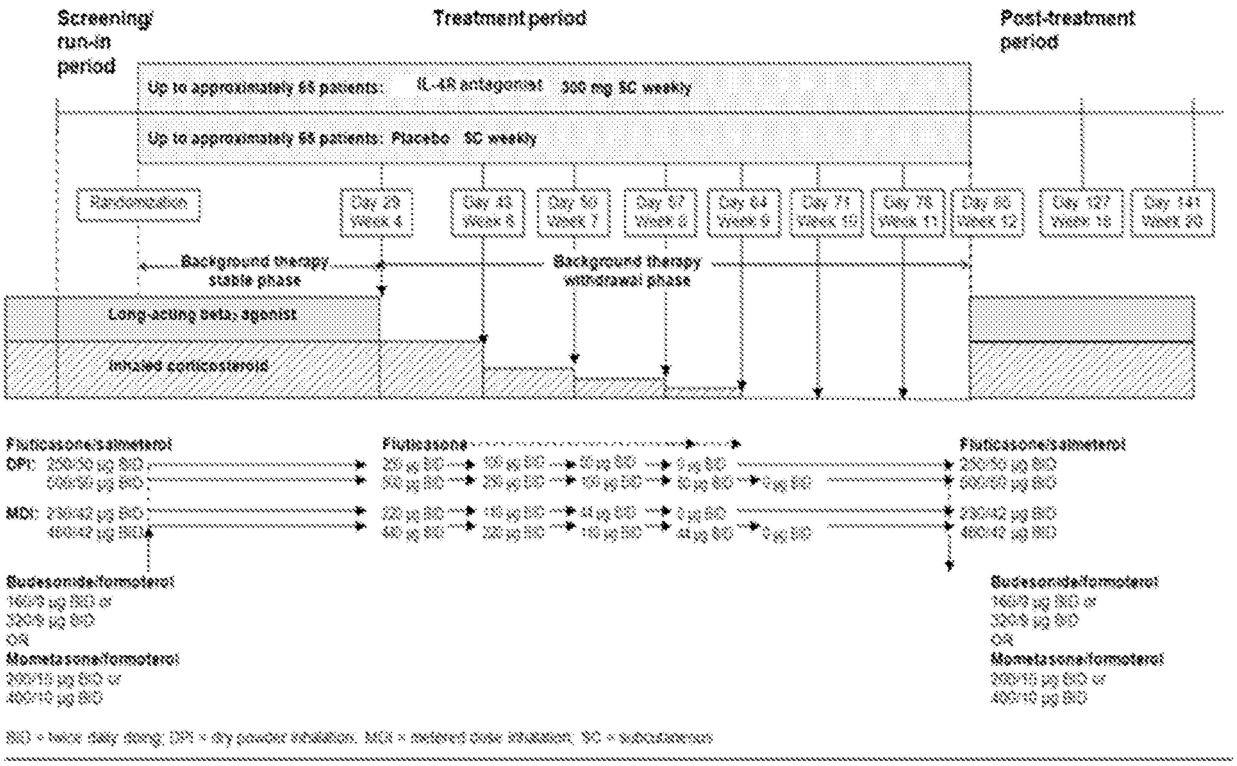

Screening/ run-in period
Treatment period
Post-treatment period
Up to approximately 65 patients: IL-4R antagonist 300 mg SC weekly
Up to approximately 65 patients: Placebo SC weekly
Randomization
Day 29 Week 4
Day 43 Week 6
Day 50 Week 7
Day 57 Week 8
Day 64 Week 9
Day 71 Week 10
Day 78 Week 11
Day 85 Week 12
Day 127 Week 18
Day 141 Week 20
Background therapy stable phase
Background therapy withdrawal phase
Long-acting beta2 agonist
Inhaled corticosteroid
Fluticasone/salmeterol
DPI: 250/50 µg BID
500/50 µg BID
MDI: 230/42 µg BID
460/42 µg BID
Fluticasone
250 µg BID
500 µg BID
100 µg BID
200 µg BID
50 µg BID
100 µg BID
25 µg BID
50 µg BID
Budesonide/formoterol
160/9 µg BID or
320/9 µg BID
OR
Mometasone/formoterol
200/10 µg BID or
400/10 µg BID
BID = twice daily dosing; DPI = dry powder inhalation; MDI = metered dose inhalation; SC = subcutaneous

Figure 24

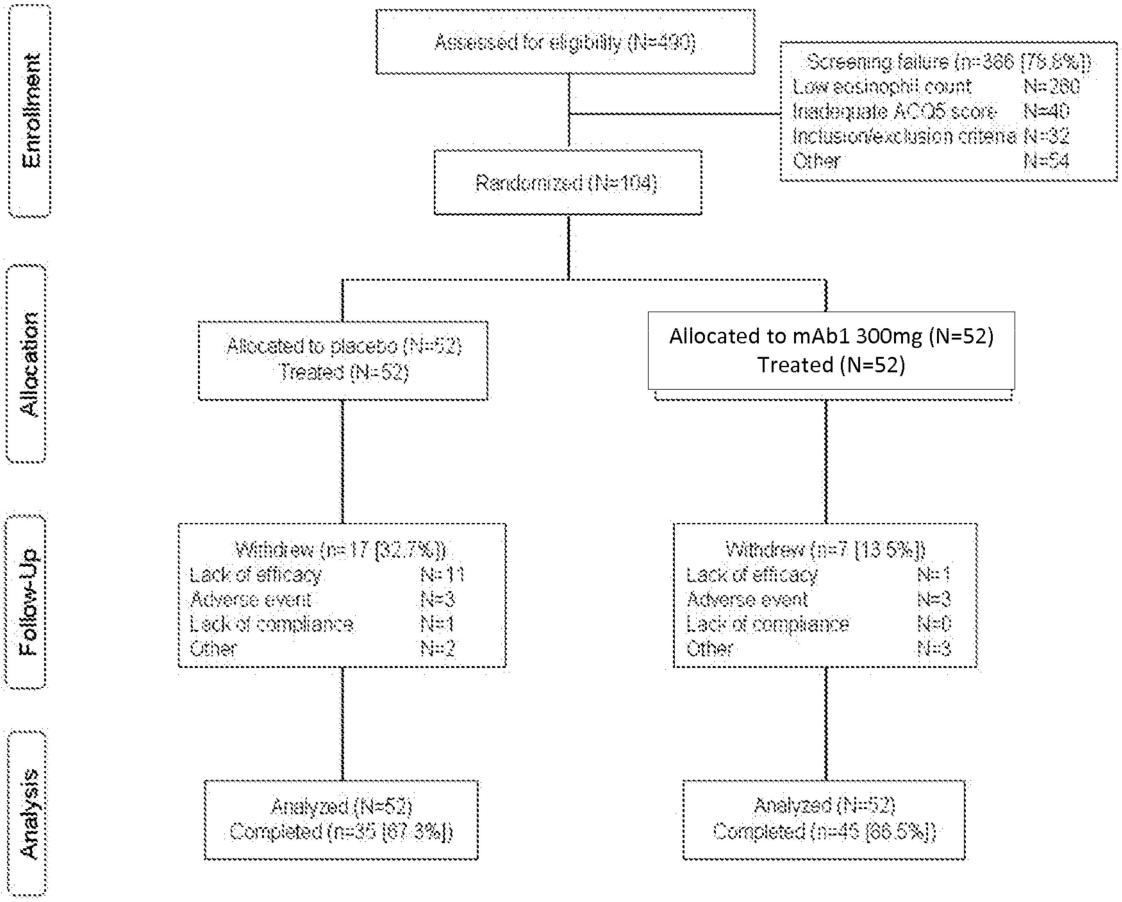

Enrollment
Allocation
Follow-Up
Analysis
Assessed for eligibility (N=490)
Screening failure (n=386 [78.8%])
Low eosinophil count N=280
Inadequate ACQ5 score N=40
Inclusion/exclusion criteria N=32
Other N=54
Randomized (N=104)
Allocated to placebo (N=52)
Treated (N=52)
Allocated to mAb1 300mg (N=52)
Treated (N=52)
Withdrew (n=17 [32.7%])
Lack of efficacy N=11
Adverse event N=3
Lack of compliance N=1
Other N=2
Withdrew (n=7 [13.5%])
Lack of efficacy N=1
Adverse event N=3
Lack of compliance N=0
Other N=3
Analyzed (N=52)
Completed (n=35 [67.3%])
Analyzed (N=52)
Completed (n=45 [86.5%])

Figure 25

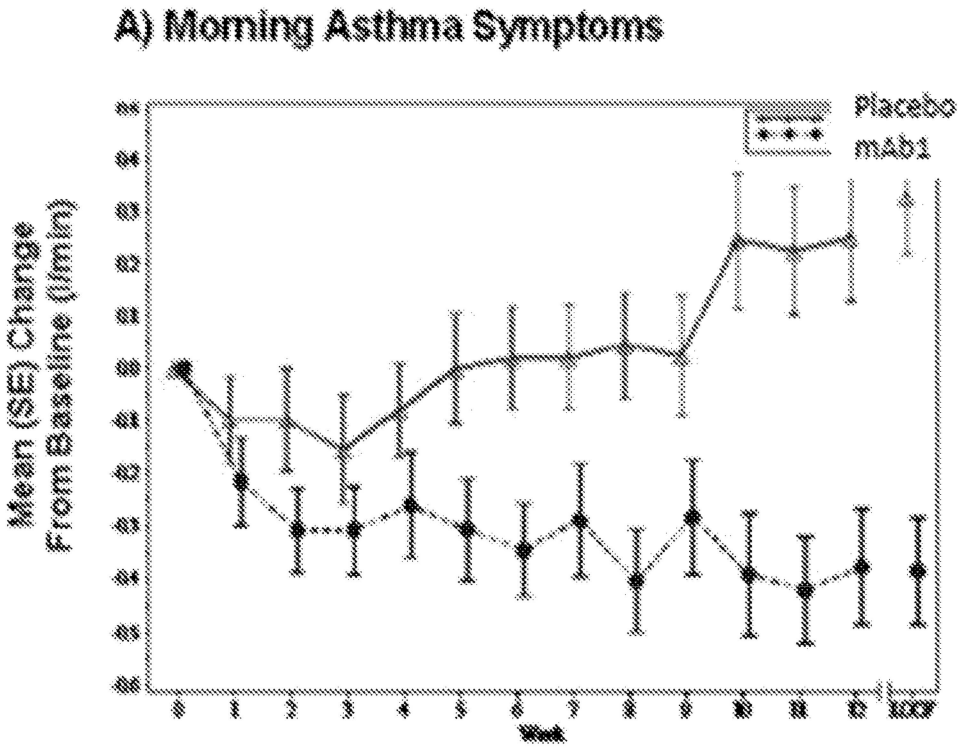


Figure 26A

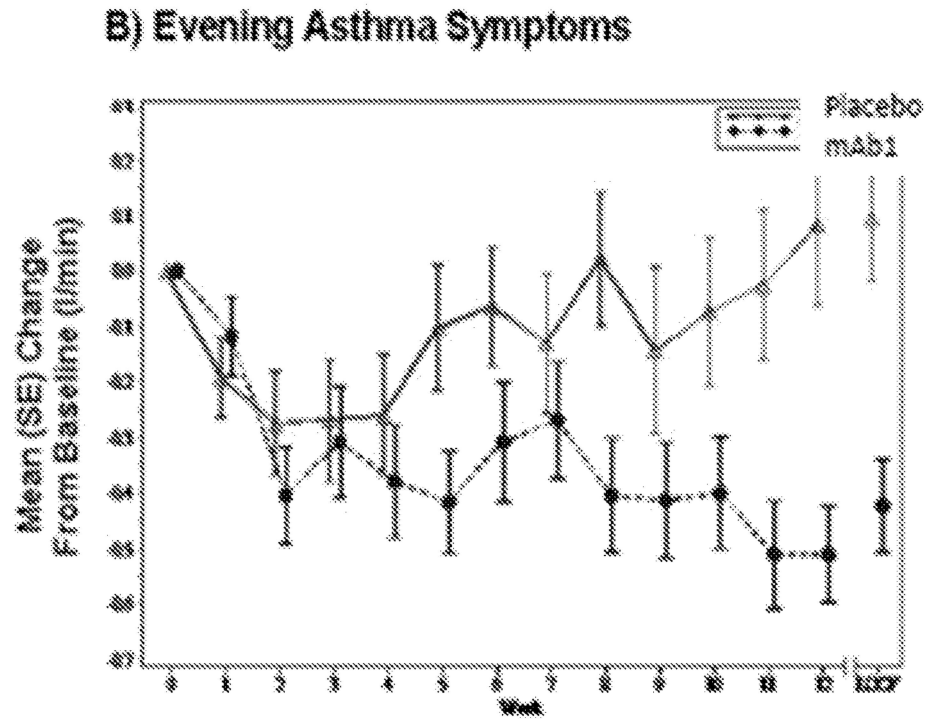


Figure 26B

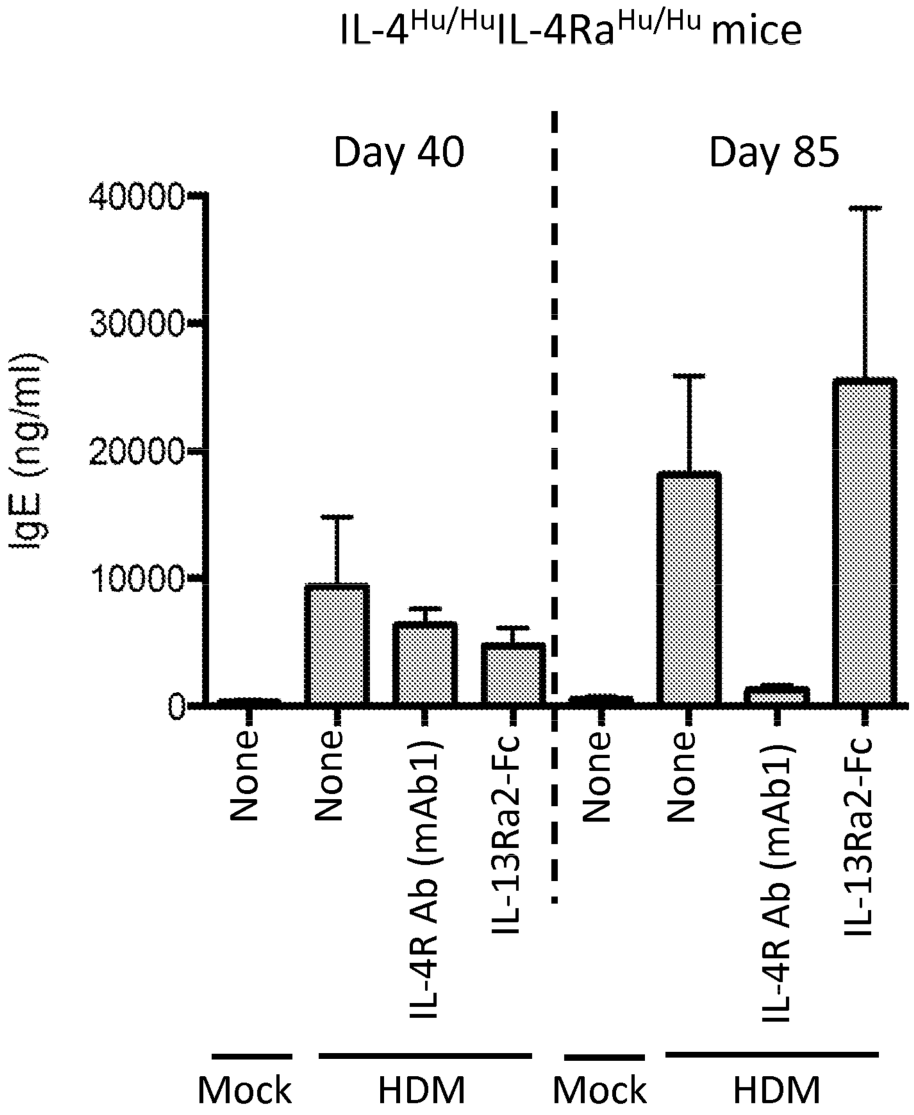

IL-4Hu/HuIL-4RaHu/Hu mice
Day 40
Day 85
IgE (ng/ml)
40000
30000
20000
10000
0
None
None
IL-4R Ab (mAb1)
IL-13Ra2-Fc
None
None
IL-4R Ab (mAb1)
IL-13Ra2-Fc
Mock
HDM
Mock
HDM

Figure 27

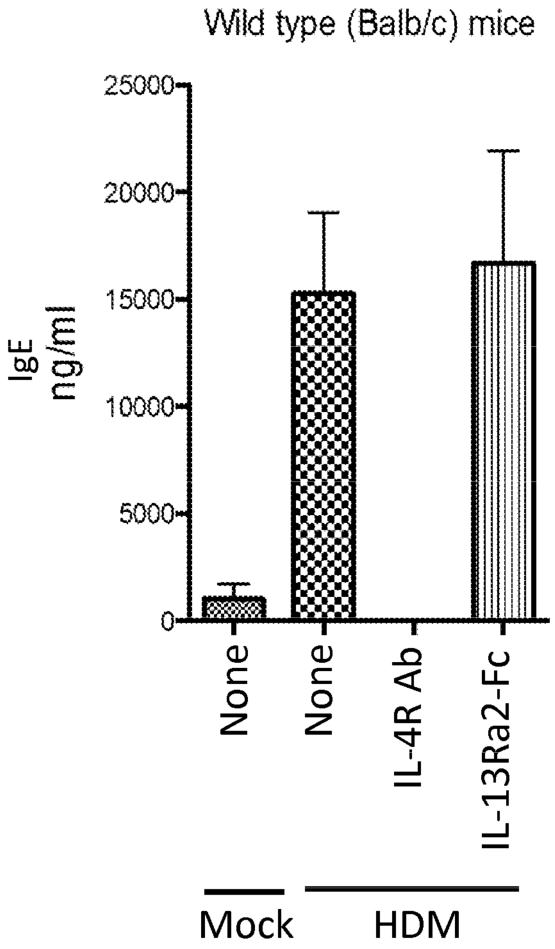

Wild type (Balb/c) mice
IgE ng/ml
25000
20000
15000
10000
5000
0
None
None
IL-4R Ab
IL-13Ra2-Fc
Mock
HDM

Figure 28

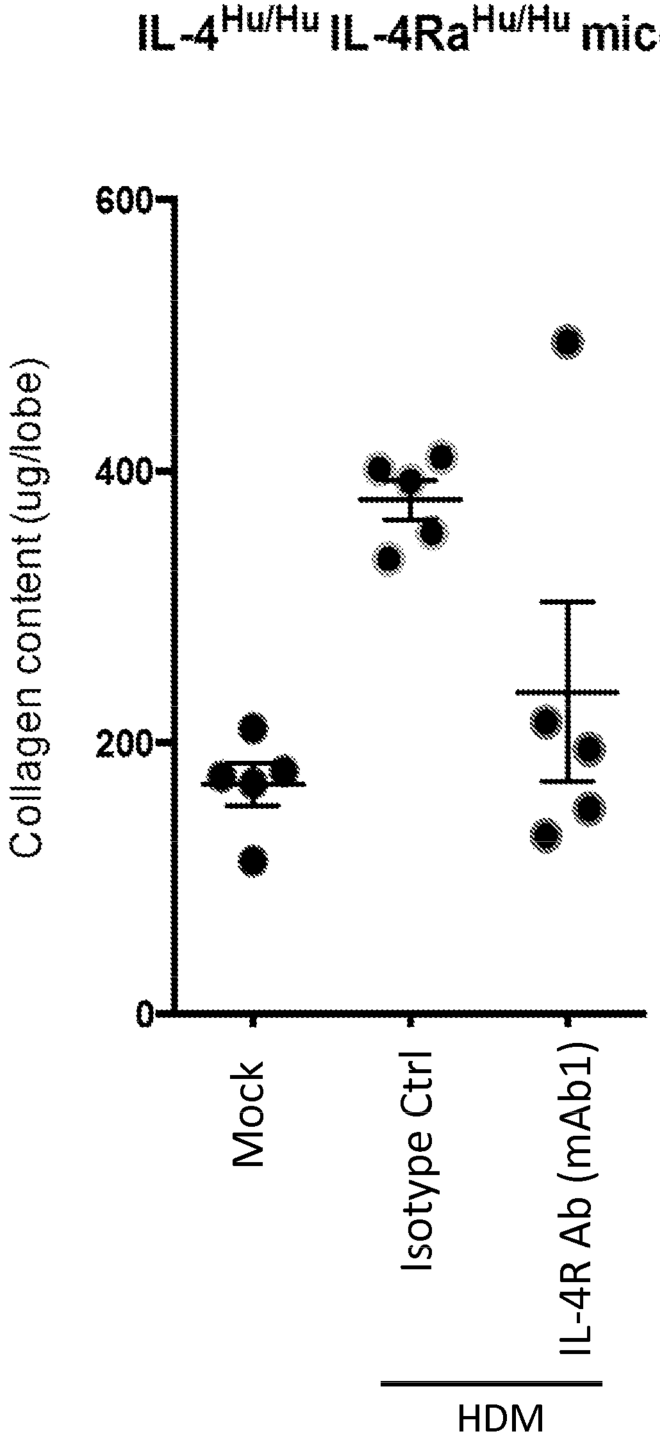

IL-4Hu/Hu IL-4RaHu/Hu mice
Collagen content (ug/lobe)
600
400
200
0
Mock
Isotype Ctrl
IL-4R Ab (mAb1)
HDM

Figure 29

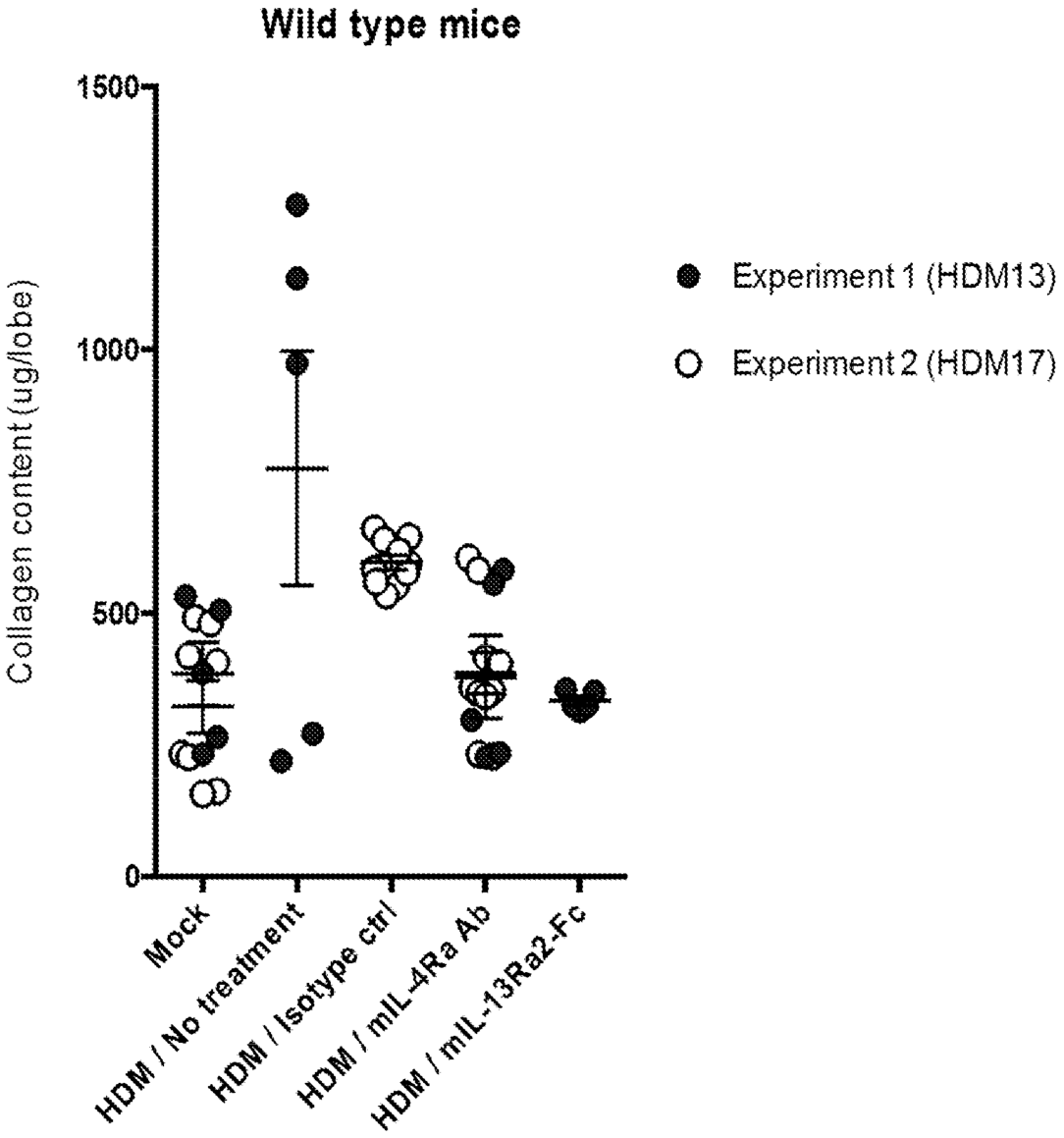

Wild type mice
Collagen content (ug/lobe)
1500
1000
500
0
Mock
HDM / No treatment
HDM / Isotype ctrl
HDM / mIL-4Ra Ab
HDM / mIL-13Ra2-Fc
Experiment 1 (HDM13)
Experiment 2 (HDM17)

Figure 30

IL-4$^{Hu/Hu}$ IL-4Ra$^{Hu/Hu}$ mice

Figure 31A.

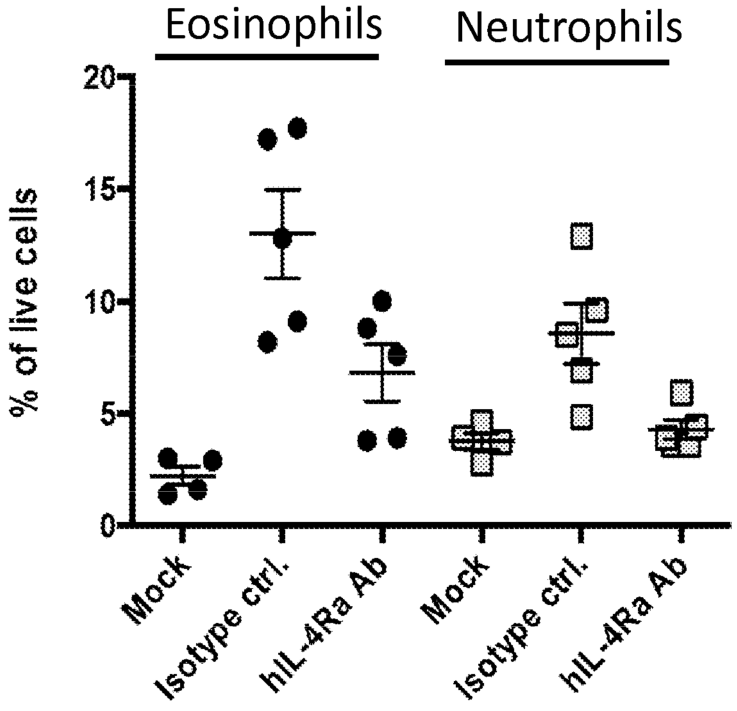


Figure 31B.

