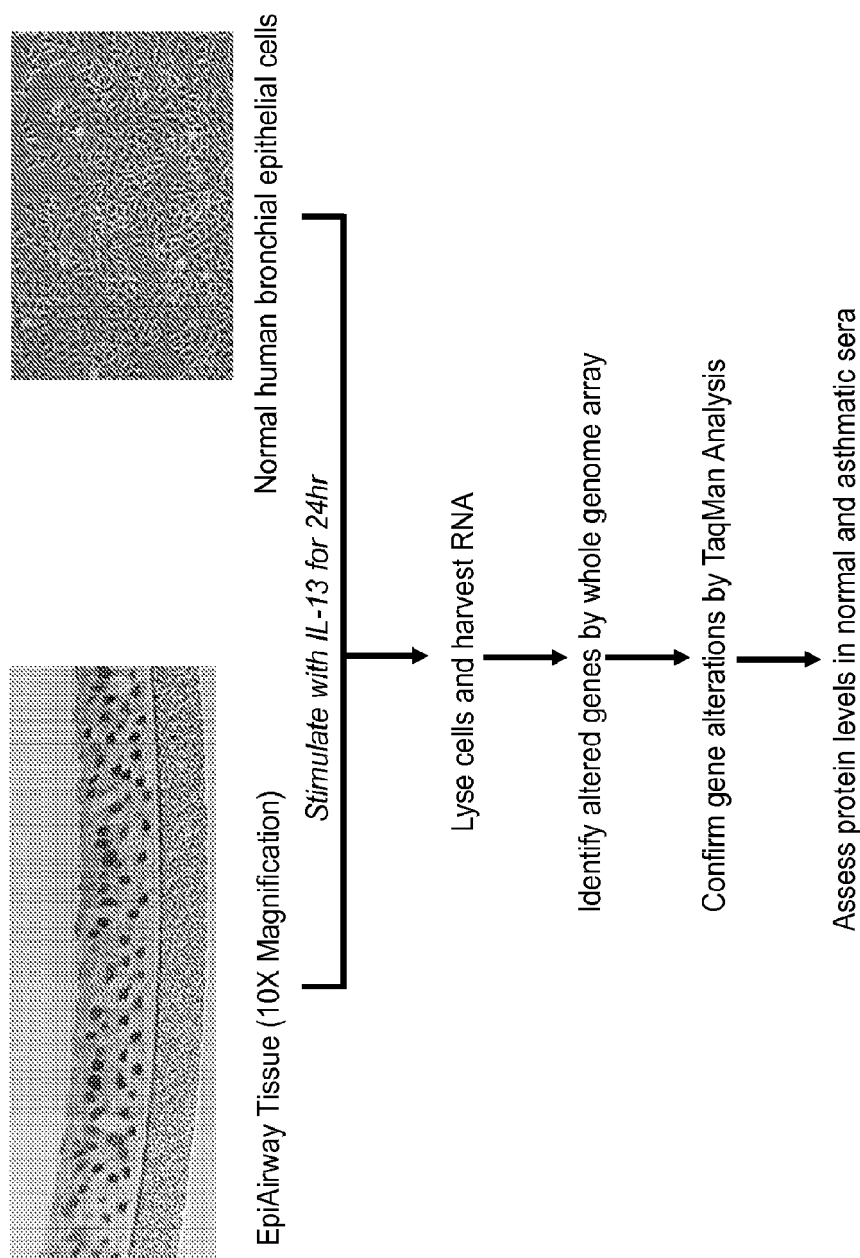


FIG. 1



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FIG. 2

Probe ID	log2.fc	p.value	q.val	UniGene.ID	Gene.Title	Gene.Symbol
223710_at	11.704	3.48E-06	0.007679	Hs.131342	chemokine (C-C motif) ligand 26	CCL26
1553177_at	7.373	0.003256	0.150603	Hs.350581	SH2 domain containing 1B	SH2D1B
203717_at	6.896	1.73E-06	0.007679	Hs.368912	dipeptidyl-peptidase 4	DPP4
1564746_at	6.882	0.000149	0.033081	Hs.546482	Na ⁺ /H ⁺ exchanger domain containing 2	NHEDC2
1553176_at	6.785	3.36E-05	0.015623	Hs.350581	SH2 domain containing 1B	SH2D1B
219564_at	6.680	1.94E-05	0.012103	Hs.463985	potassium inwardly-rectifying channel, subfamily J, member 1	KCNJ16
211478_s_at	6.663	2.17E-05	0.01218	Hs.368912	dipeptidyl-peptidase 4	DPP4
229491_at	6.483	6.92E-05	0.02249	Hs.546482	Na ⁺ /H ⁺ exchanger domain containing 2	NHEDC2
220622_at	6.008	0.000137	0.030929	Hs.411295	leucine rich repeat containing 31	LRRC31
210521_s_at	5.971	0.00076	0.071008	Hs.81073	fetuin B	FETUB
203716_s_at	5.874	6.92E-06	0.007679	Hs.368912	dipeptidyl-peptidase 4	DPP4
214539_at	5.769	3.91E-06	0.007679	Hs.158339	serpin peptidase inhibitor, clade B (ovalbumin), member 10	SERPINB10
227480_at	5.669	0.01015	0.246439	Hs.131819	sushi domain containing 2	SUSD2
218804_at	5.460	0.00054	0.063169	Hs.503074	anoctamin 1, calcium activated chloride channel	ANO1
223597_at	5.200	0.004137	0.166478	Hs.50813	Intelectin 1 (galactofuranose binding)	ITLN1
206932_at	5.171	0.000399	0.053415	Hs.47357	cholesterol 25-hydroxylase	CH25H
223377_x_at	5.091	0.007388	0.214469	Hs.655334	cytokine inducible SH2-containing protein	CISH
205969_at	5.057	0.00027	0.043821	Hs.506908	arylacetamide deacetylase (esterase)	AADAC
1557321_a_at	5.047	2.45E-06	0.007679	Hs.468059	calpain 14	CAPN14
210809_s_at	4.936	0.003132	0.147591	Hs.136348	periostin, osteoblast specific factor	POSTN
207328_at	4.911	0.000227	0.041212	Hs.73809	arachidonate 15-lipoxygenase	ALOX15
1555778_a_at	4.704	0.002295	0.127657	Hs.136348	periostin, osteoblast specific factor	POSTN

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FIG. 3

Probe ID	IL13 vs. NT (log2 fc)	IL13 vs. NT (p-value)	IL13 vs. NT (q-value)	UniGene ID	Gene Title	Gene Symbol
223710_at	10.5303	0.022019802	0.100091	Hs.131342	chemokine (C-C motif) ligand 26	CCL26
206224_at	10.23784	0.007869349	0.072181	Hs.123114	cystatin SN	CST1
210809_s_at	10.08787	0.01771057	0.093066	Hs.136348	periostin, osteoblast specific factor	POSTN
1555778_a_at	9.920576	0.011827893	0.081568	Hs.136348	periostin, osteoblast specific factor	POSTN
220622_at	7.874274	0.003115017	0.054393	Hs.411295	leucine rich repeat containing 31	LRRC31
1553176_at	7.818319	0.000388042	0.036284	Hs.350581	SH2 domain containing 1B	SH2D1B
203716_s_at	7.600052	0.002277719	0.05012	Hs.368912	dipeptidyl-peptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4
211478_s_at	7.545594	0.001764026	0.04697	Hs.368912	dipeptidyl-peptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4
206994_at	7.178186	0.005964215	0.066448	Hs.654549	cystatin S	CST4
206942_s_at	6.794592	0.0008042	0.040603	Hs.707990	pro-melanin-concentrating hormone	PMCH
1557321_a_at	6.691411	0.008835125	0.074483	Hs.468059	calpain 14	CAPN14
1553177_at	6.521778	0.004185219	0.059371	Hs.350581	SH2 domain containing 1B	SH2D1B
218804_at	6.458367	0.003943545	0.058651	Hs.503074	transmembrane protein 16A	TMEM16A
203717_at	6.245909	4.72091E-05	0.024165	Hs.368912	dipeptidyl-peptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4
210521_s_at	6.003439	0.046524549	0.133084	Hs.81073	fetuin B	FETUB
232217_at	5.825	0.003617583	0.057486	Hs.660142	family with sequence similarity 26, member E	FAM26E
206172_at	5.779177	0.007917215	0.072332	Hs.336046	interleukin 13 receptor, alpha 2	

FIG. 4

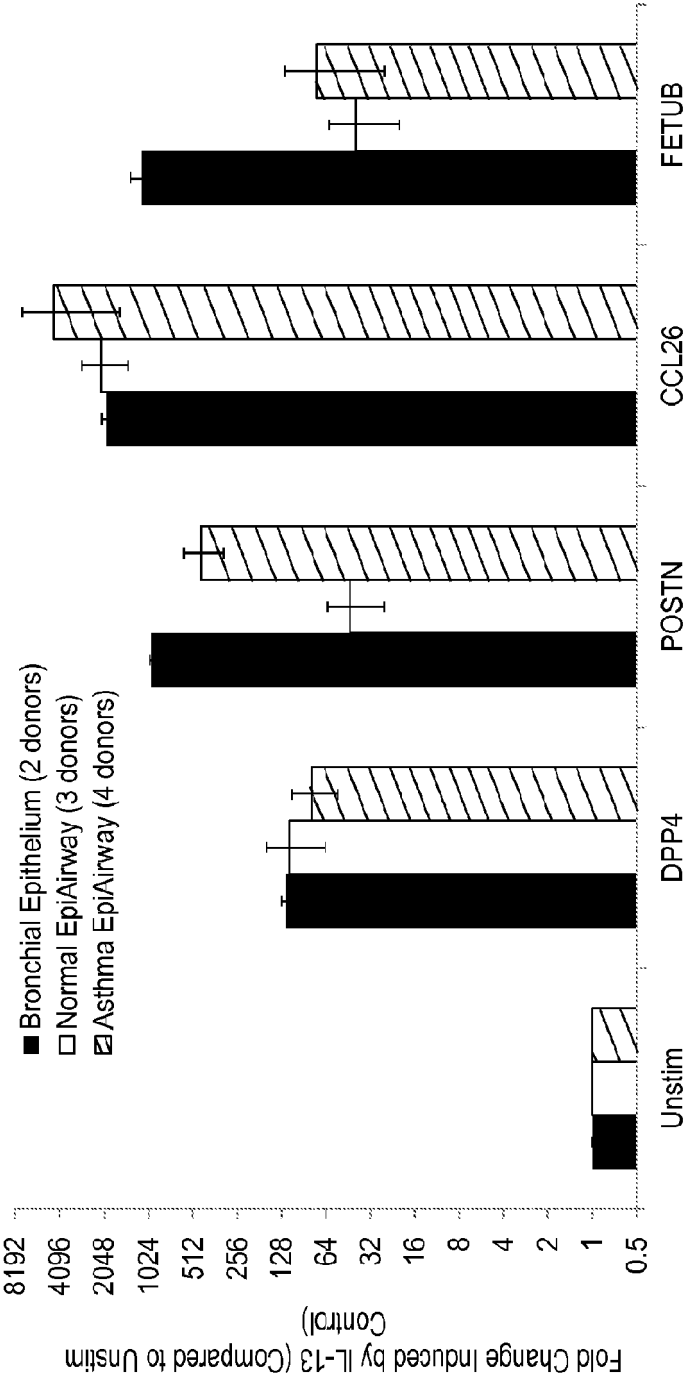


FIG. 5

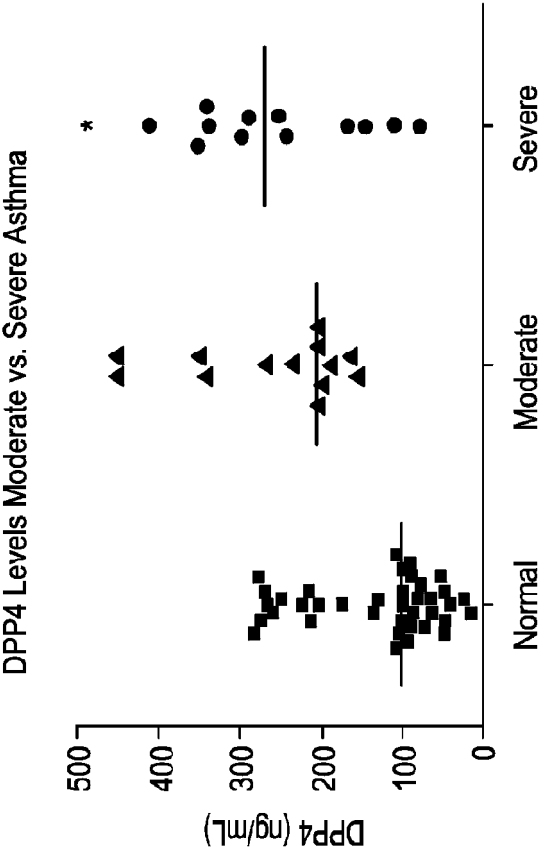


FIG. 6
Serum DDP4 Levels in Asthma Patients by
Medication Status

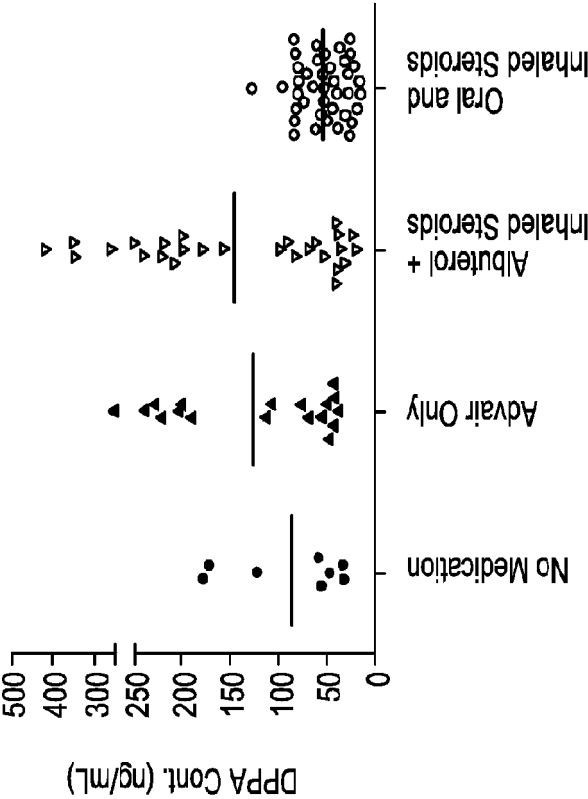


FIG. 7

Tralokinumab Phase 2b Study – CD-R1-Cat-354-1049

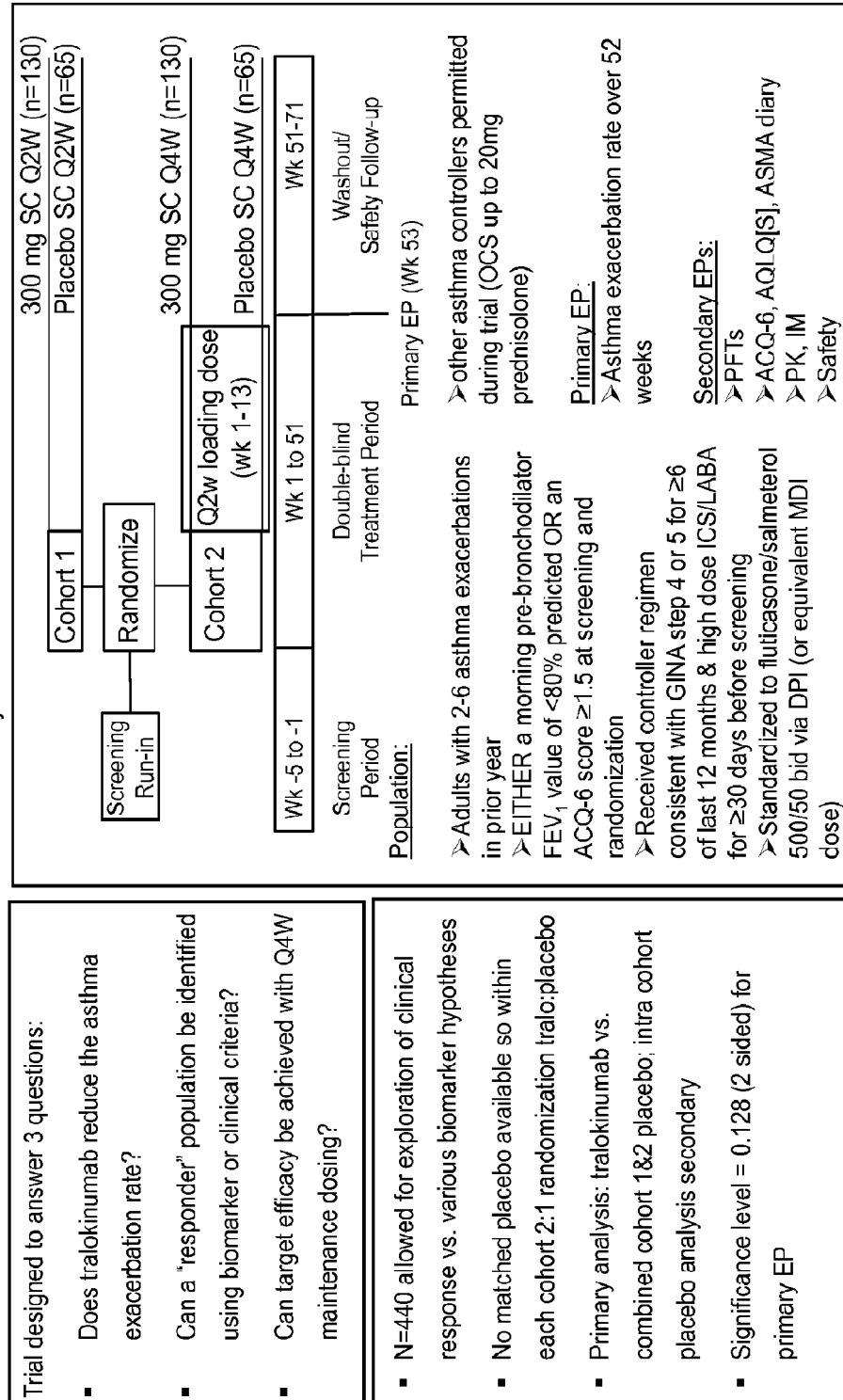


FIG. 8

Change from Baseline in Pre-bronchodilator FEV1 Over Time (ITT Population)

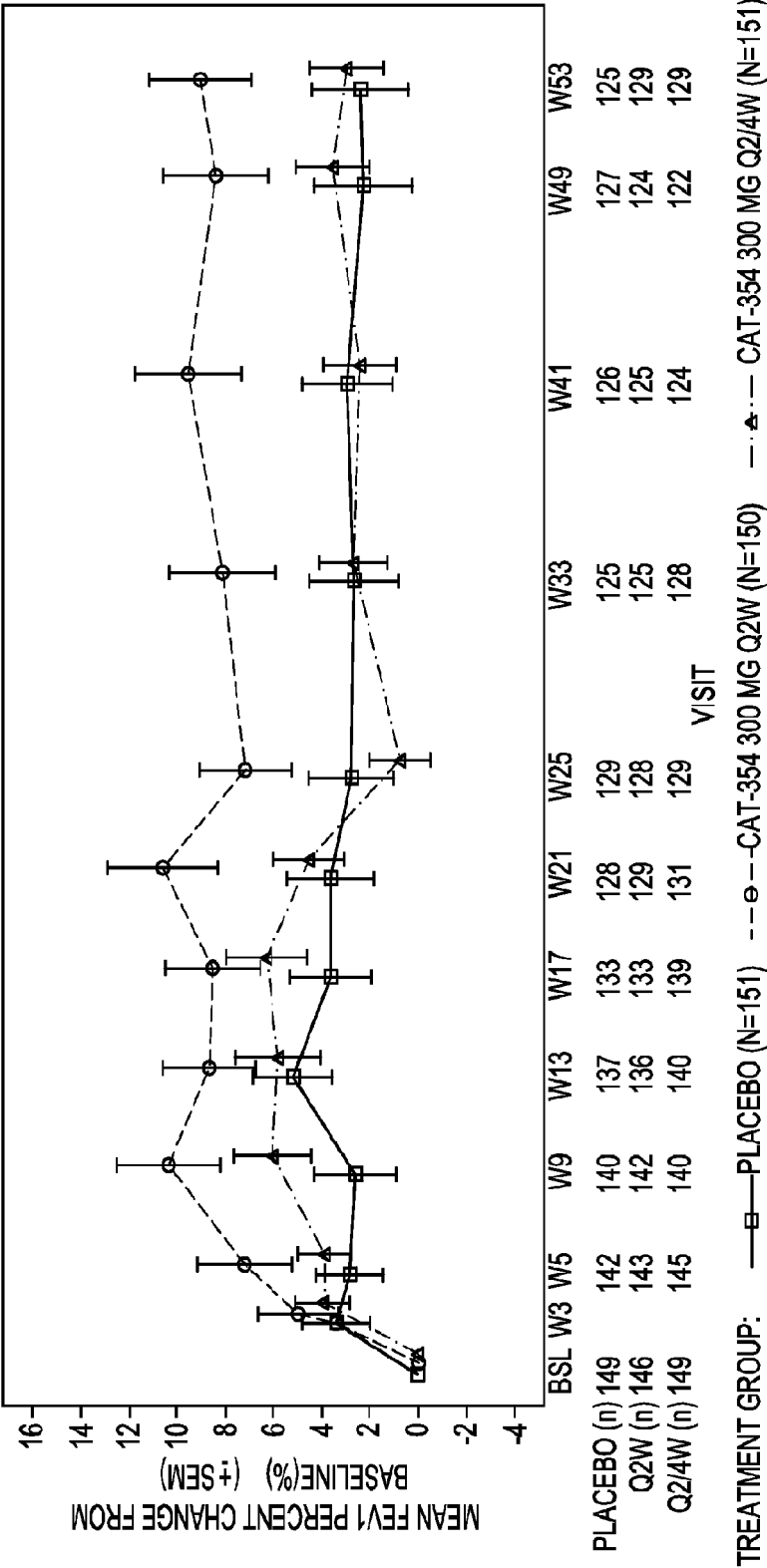
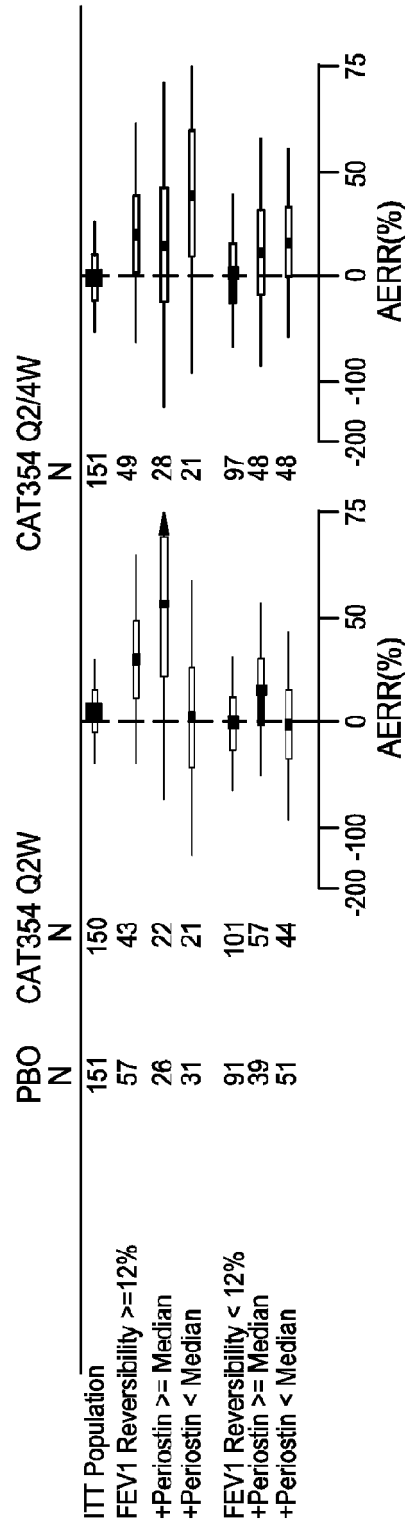


FIG. 9A

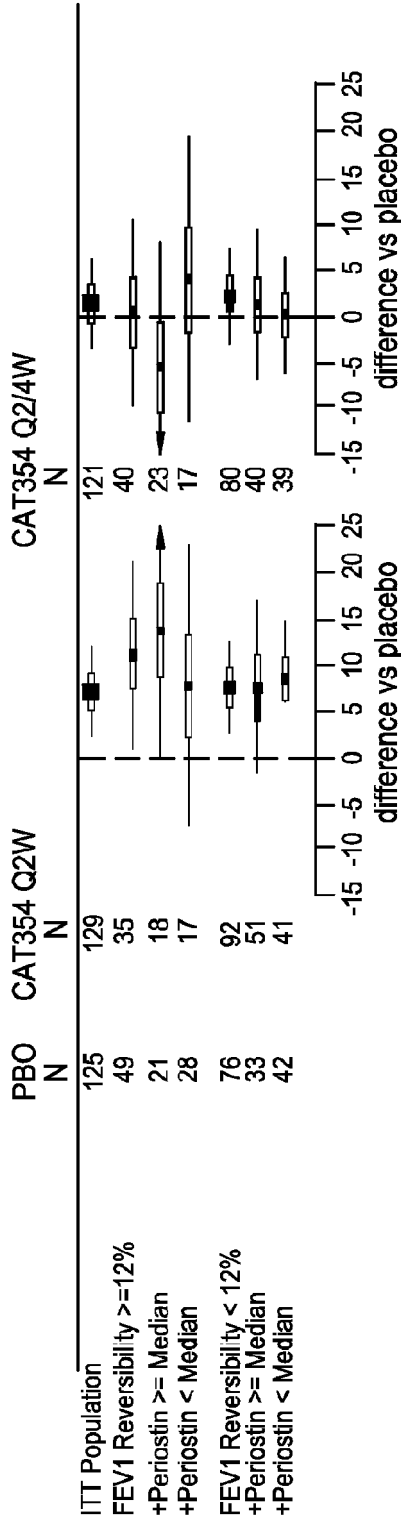
Annual AER and Change from Baseline in Pre-bronchodilator at Week 53 by FEV1 Reversibility and Serum Periostin Level



Estimates are from Poisson regression model, adjusted for covariates
Estimates are shown with 95% CI: within these 50% CI are highlighted.

FIG. 9B

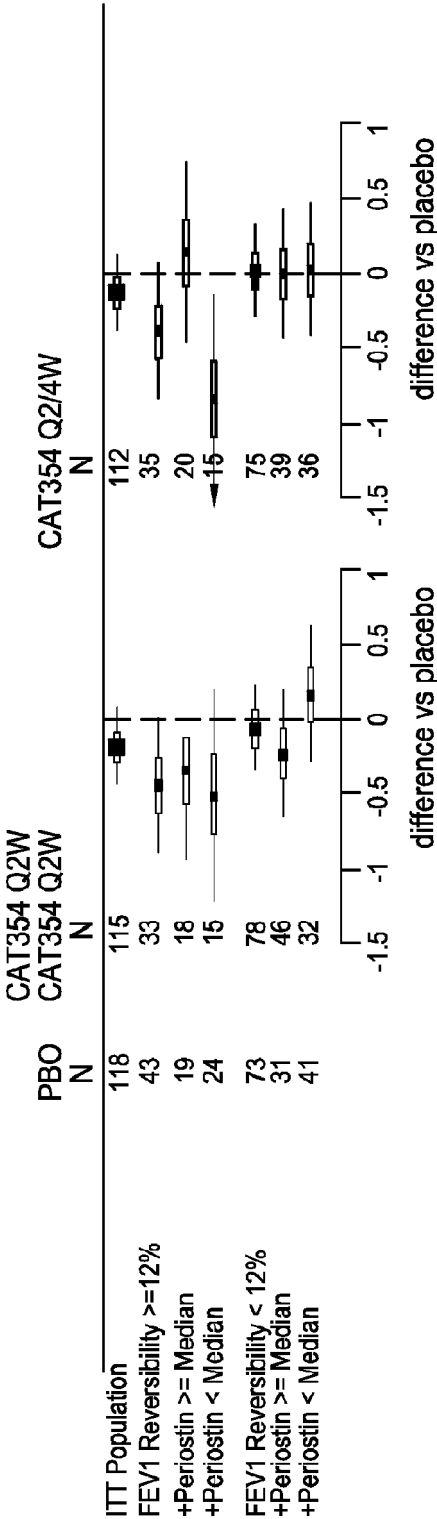
Annual AER and Change from Baseline in Pre-bronchodilator at Week 53 by FEV1 Reversibility and Serum Perioestin Level



Estimates are from a mixed model repeated measures (MMRM) analysis including all patients, N shows the number of patients with observations at week 53. Estimates are shown with 95% CI; within these 50% CI are highlighted.

FIG. 10A

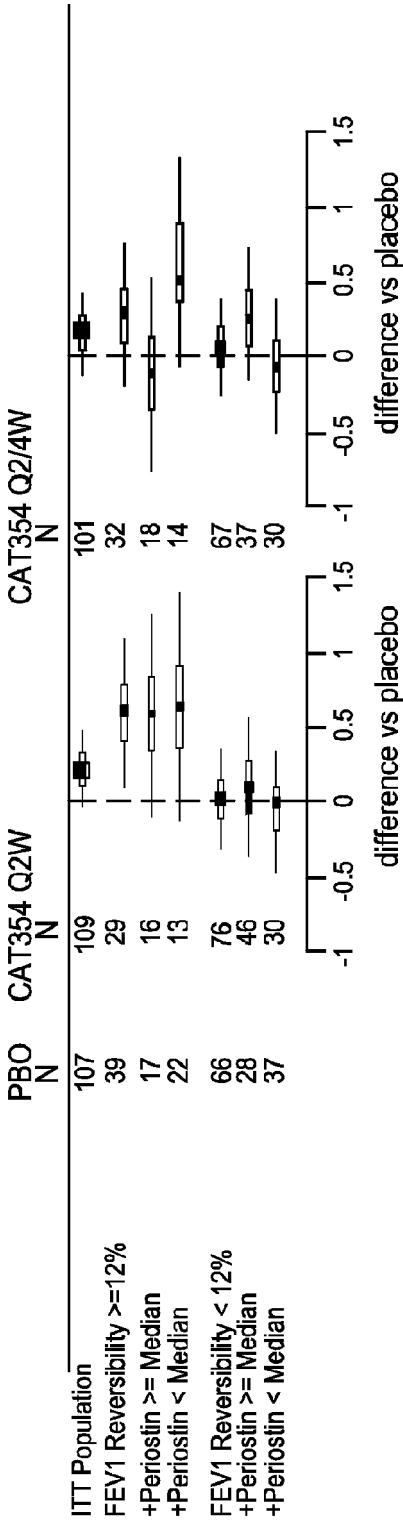
ACQ and AQLQ(S) at Week 53 By FEV1 Reversibility and Serum Periostin Level



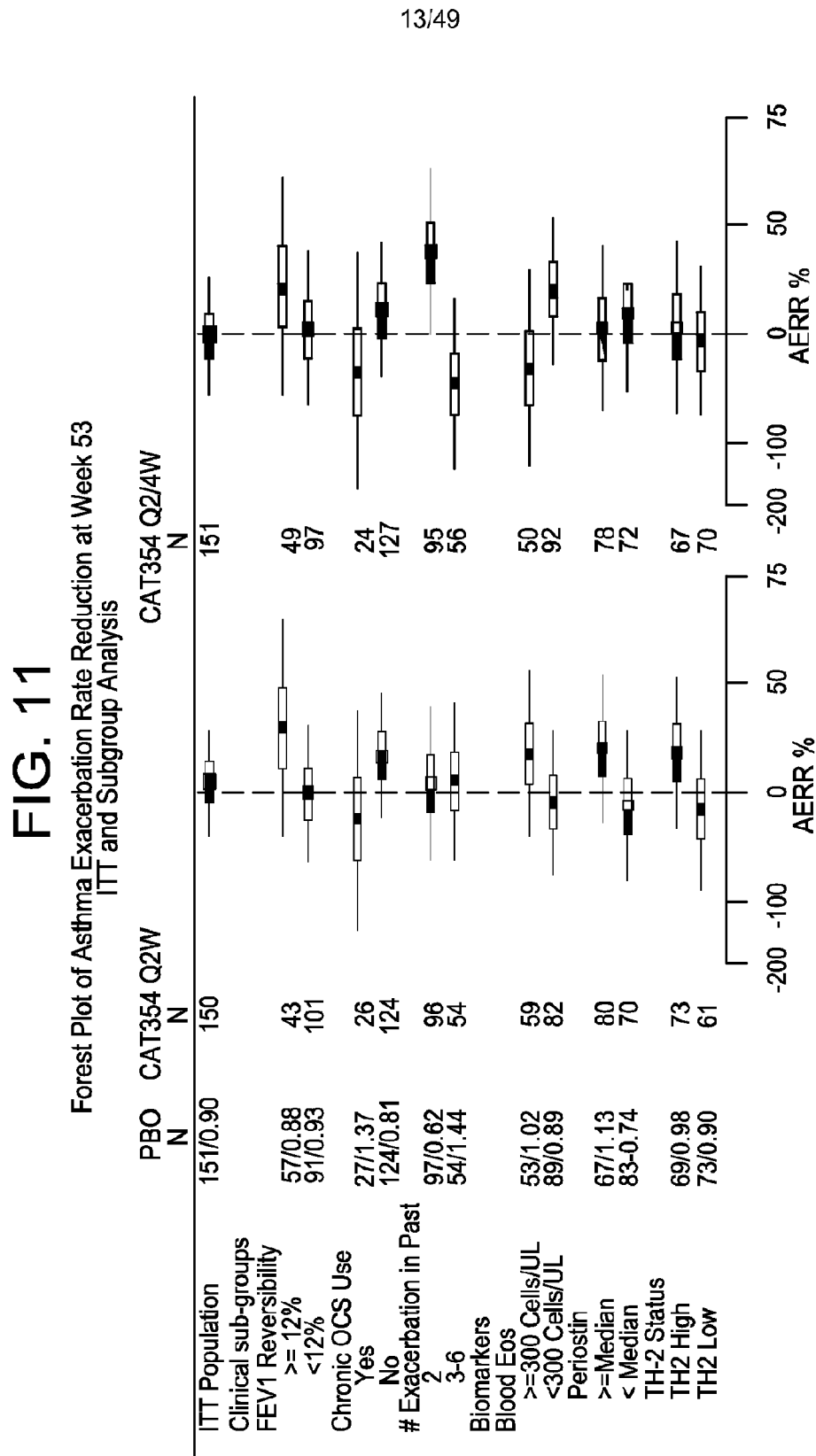
Estimates are from a mixed model repeated measures (MMRM) analysis including all patients, N shows the number of patients with observations at week 53. Estimates are shown with 95% CI: within these 50% CI are highlighted.

FIG. 10B

ACQ and AQLQ(S) at Week 53 By FEV1 Reversibility and Serum Perostin Level



Estimates are from a mixed model repeated measures (MMRM) analysis including all patients, N shows the number of patients with observations at week 53. Estimates are shown with 95% CI: within these 50% CI are highlighted.

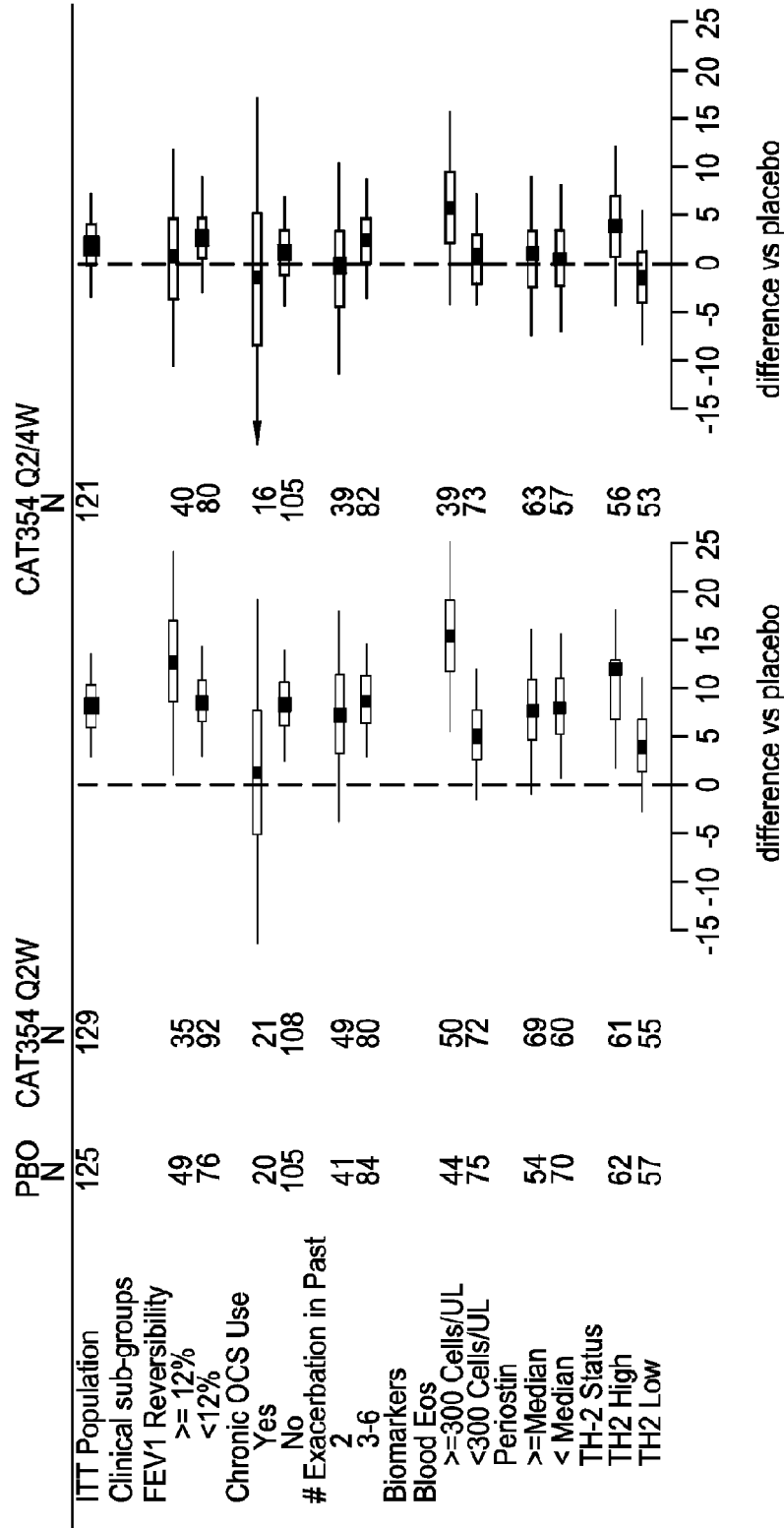


Estimates are shown with 95% CI; within these 50% CI are highlighted

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FIG. 12

Forest Plot of Percent Change from Baseline in pre-BD FEV1 at week 53
ITT and Subgroup Analysis



Estimates are shown with 95% CI: within these 50% CI are highlighted

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FIG. 13A

Asthma Exacerbation Rate Reduction and Mean Percent Change from Baseline in Pre-bronchodilator FEV₁ at Week 53 for Patients by Baseline Serum Periostin Level (Tralokinumab Q2W vs Placebo)

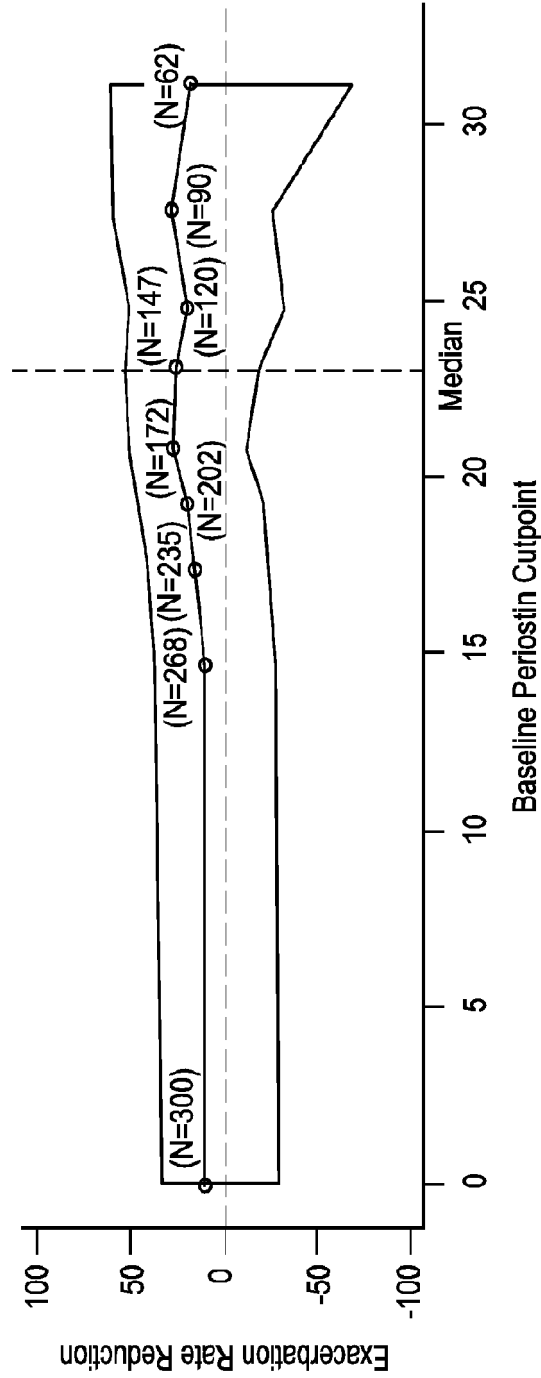


FIG. 13B

Asthma Exacerbation Rate Reduction and Mean Percent Change from Baseline in Pre-bronchodilator FEV₁ at Week 53 for Patients by Baseline Serum Periostin Level (Tralokinumab Q2W vs Placebo)

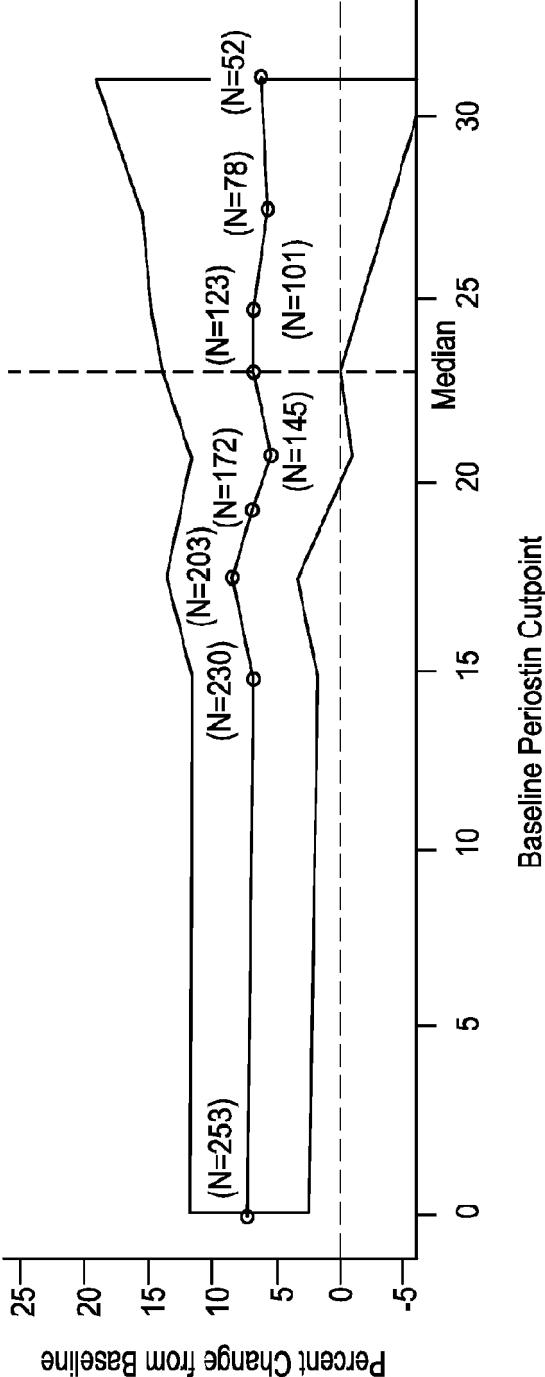


FIG. 14A
Percent Change from Baseline in Pre-Bronchodilator FEV1 Over Time by Treatment Group
Baseline Serum Perioestin >=Median ITT Population

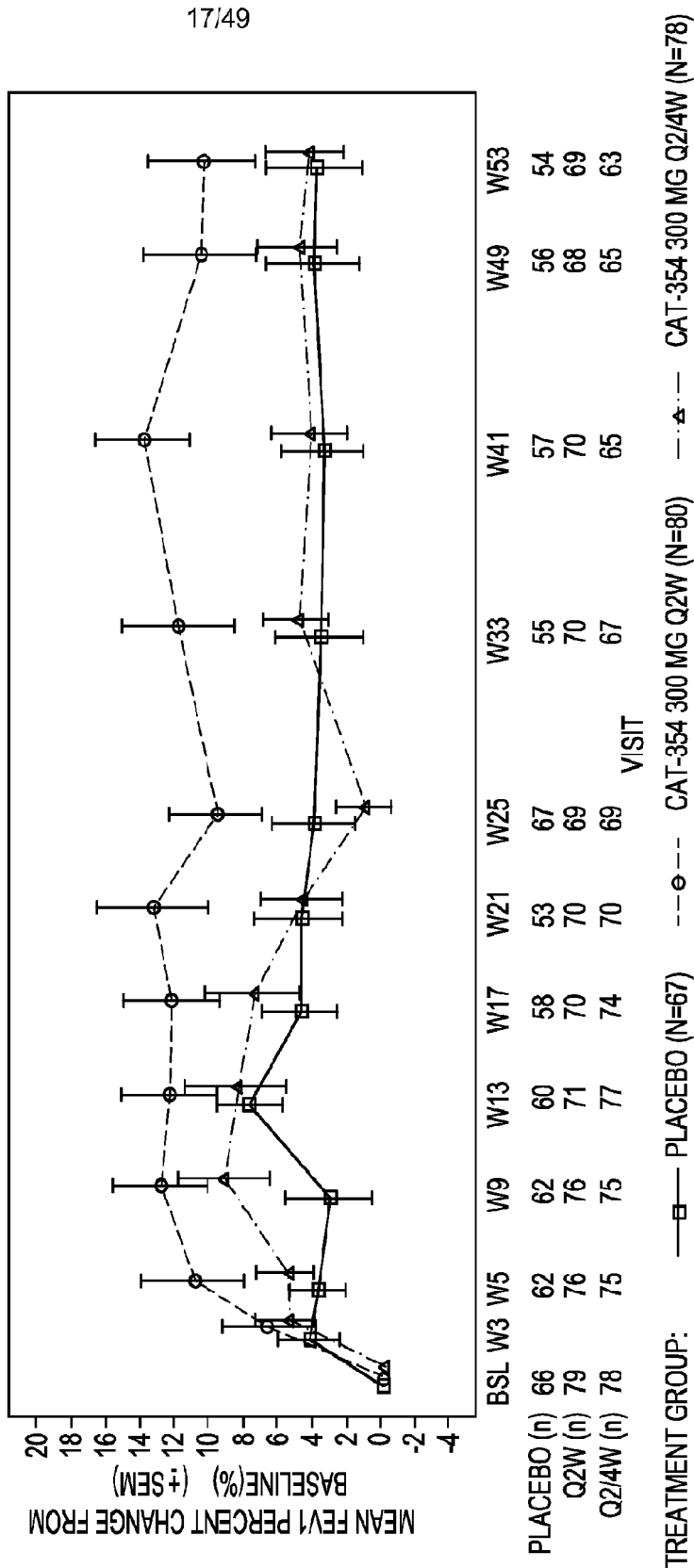


FIG. 14B
Percent Change from Baseline in Pre-Bronchodilator FEV1 Over Time by Treatment Group
Baseline Serum Periostin <Median ITT Population

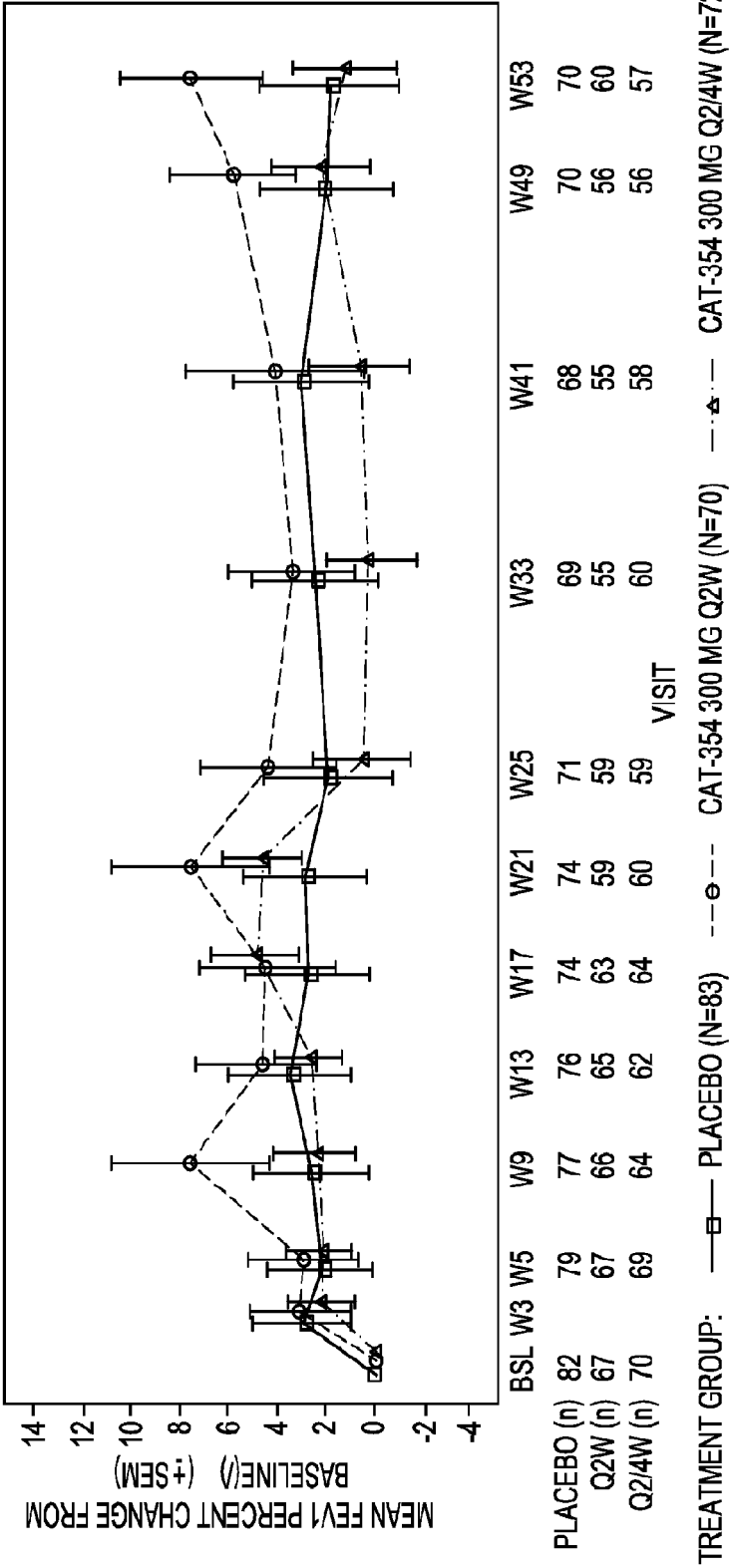


FIG. 15
DPP4 Outperforms Periostin in the Intention-To-Treat Population – Q2W vs Placebo

Endpoint	All-comers (N* = 150)	Periostin >= Median (N* = 80)	DPP4 >=Median (N* = 77)
Primary			
Acute Exacerbation Rate Reduction ^a (95% CI)	7% (-30%, 33%) P = 0.669	25% (-19%, 53%) P = 0.219	34% (-6%, 59%) P=0.083
Secondary (Difference from placebo)			
Percent change from baseline in FEV1 (95% CI)	7.1 (2.35, 11.84) P = 0.003	6.75 (-0.31, 13.82) P = 0.061	10.8 (3.27, 18.23) P=0.005
ACQ-6, change from baseline (95% CI)	-0.18 (-0.43, 0.06) P = 0.137	-0.23 (-0.56, 0.09) P = 0.163	-0.50 (-0.86, -0.14) P=0.007
AQLQ, change from baseline (95% CI)	0.21 (-0.05, 0.46) P = 0.114	0.22 (-0.15, 0.59) P = 0.245	0.69 (0.30, 1.08) P<0.001

* N for tralokinumab 300 mg Q2W

Abbreviations: CI, confidence interval; FEV₁, forced expiratory volume at 1 second; ITT, intent-to-treat. ACQ-6, asthma control questionnaire, AQLQ, asthma quality of life questionnaire

^aAsthma exacerbation rate reductions were calculated using Poisson regression model adjusted for over dispersion with treatment group, age, gender, number of asthma exacerbations in the past year, atopic asthma status, presence or absence of chronic OCS use and geographical region as covariates and the log of number of days in the study as offset

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FIG. 16

Q2W vs Placebo for Above and Below

Endpoint	Periostin >= Median (N* = 80)	Periostin < Median (N* = 80)	DPP4 >=Median (N* = 77)	DPP4 < Median (N* = 68)
Primary				
Acute Exacerbation Rate Reduction (95% CI)	25% (-19%, 53%) P = 0.219	-8% (-73%, 32%) P = 0.742	34% (-6%, 59%) P=0.083	-25% (-102%, 23%) P = 0.359
Secondary (Difference from placebo)				
Percent change from baseline in FEV1 (95% CI)	6.75 (-0.31, 13.82) P = 0.061	7.06 (0.51, 13.60) P = 0.035	10.8 (3.27, 18.23) P=0.005	3.79 (-2.33, 9.92) P = 0.330
ACQ-6, change from baseline (95% CI)	-0.23 (-0.56, 0.09) P = 0.163	-0.02 (-0.38, 0.34) P = 0.919	-0.50 (-0.86, -0.14) P=0.007	0.05 (-0.29, 0.38) P = 0.424
AQLQ, change from baseline (95% CI)	0.22 (-0.15, 0.59) P = 0.245	0.21 (-0.16, 0.58) P = 0.272	0.69 (0.30, 1.08) P<0.001	-0.20 (-0.54, 0.15) P =0.143

* N for tralokinumab 300 mg Q2W

FIG. 17A
Percent Change from Baseline in Pre-Bronchodilator FEV1 Over Time by Treatment Group
Baseline DPP4 => Median ITT Population

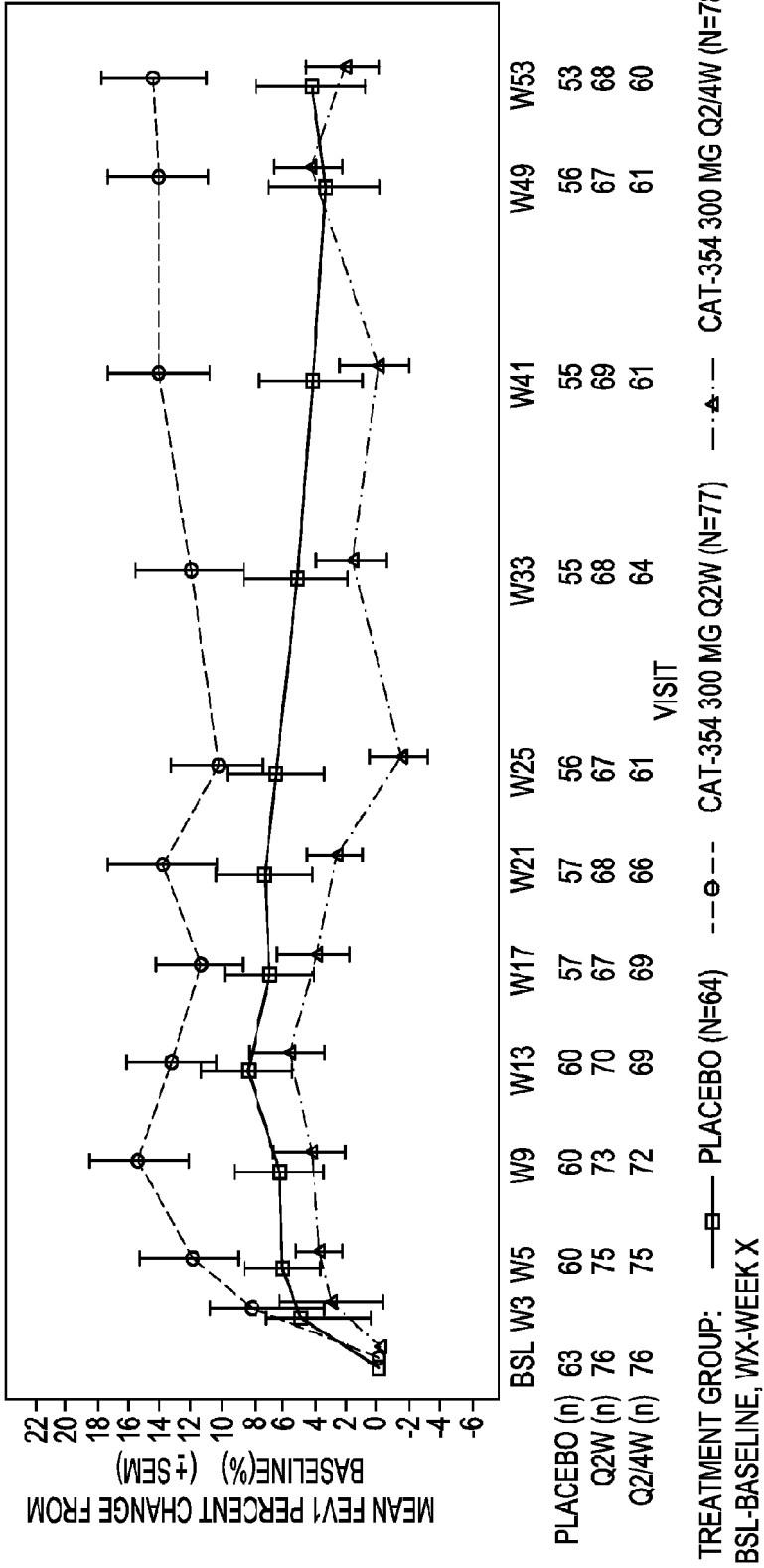


FIG. 17B

Percent Change from Baseline in Pre-Bronchodilator FEV1 Over Time by Treatment Group
Baseline DPP4 < Median ITT Population

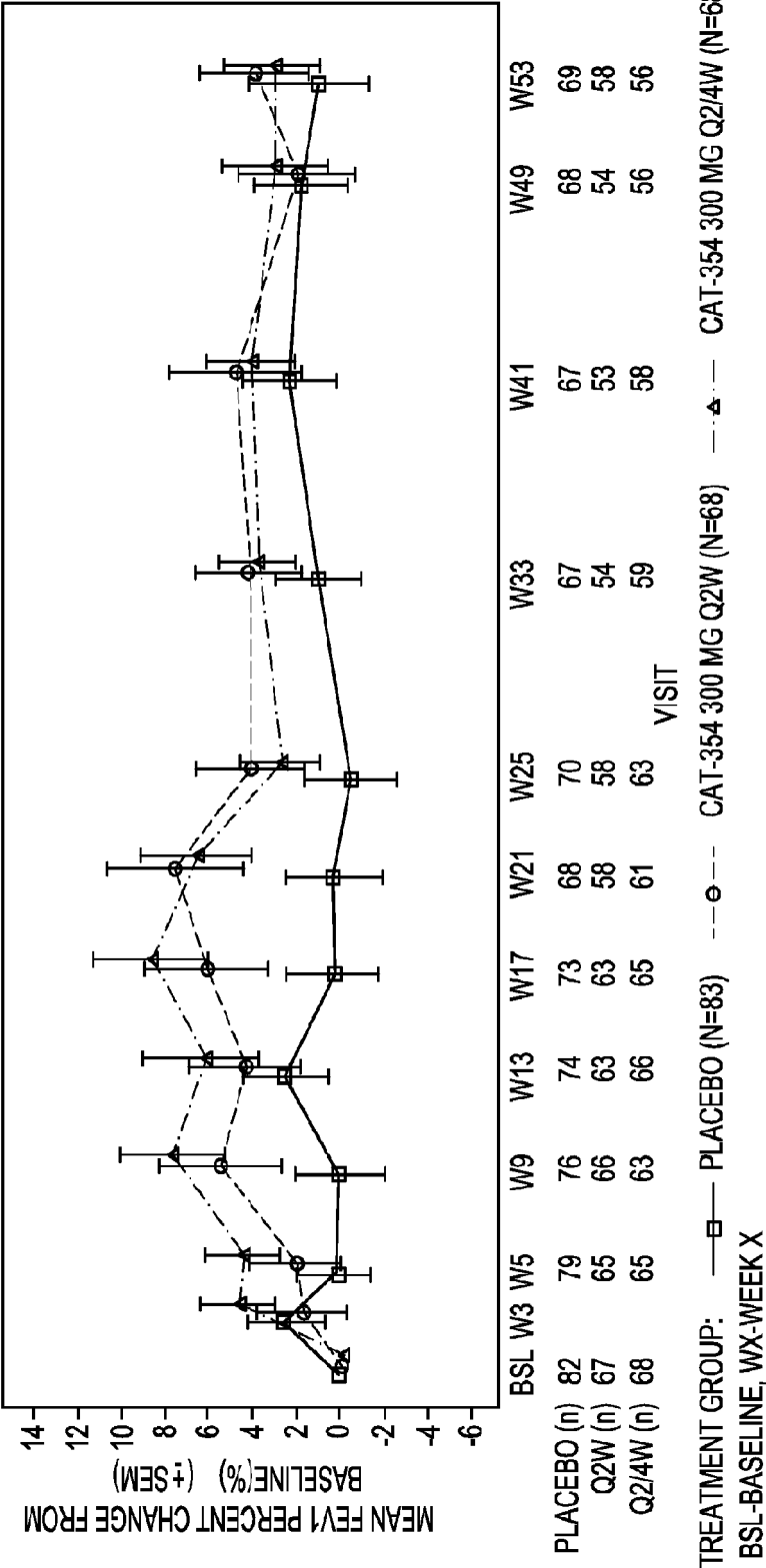


FIG. 17C

Change from Baseline in Mean ACQ-6 Score Over Time by Treatment Group
Baseline DPP4 >= Median ITT Population

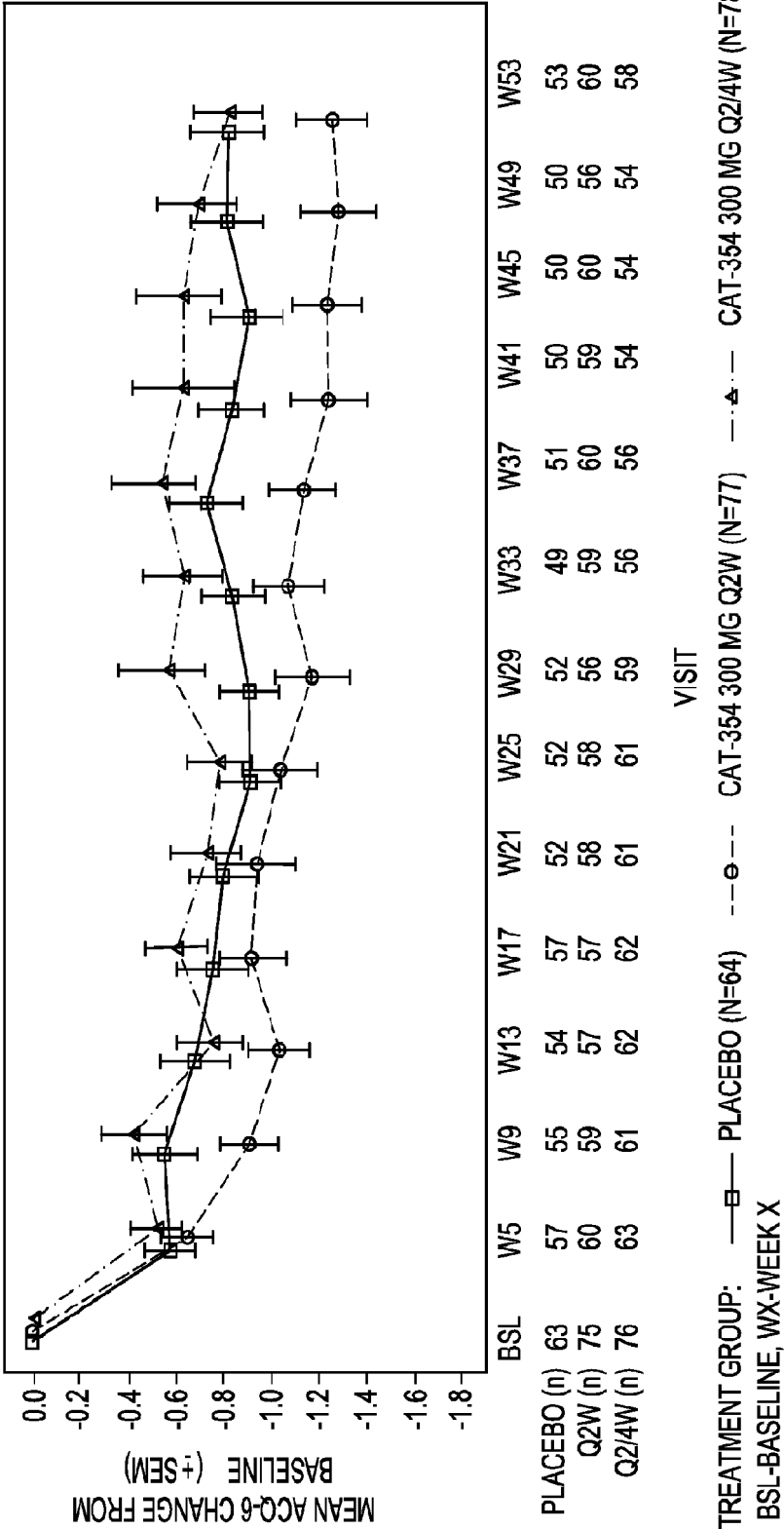


FIG. 17D
Change from Baseline in Mean ACQ-6 Score Over Time by Treatment Group
Baseline DPP4 < Median ITT Population

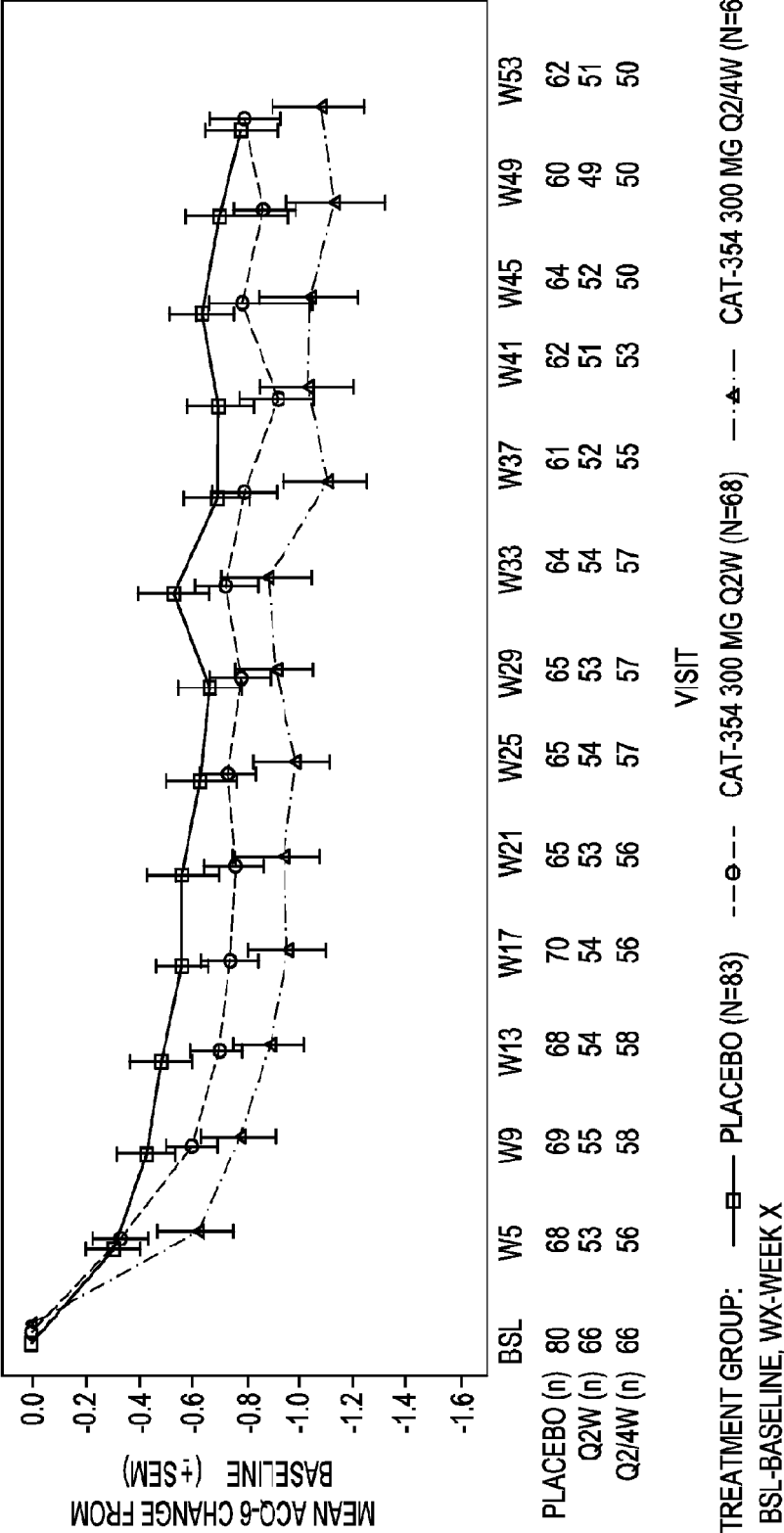


FIG. 17E

Change from Baseline in AQLQ(S) Total Score Over Time by Treatment Group
Baseline DPP4 >= Median ITT Population

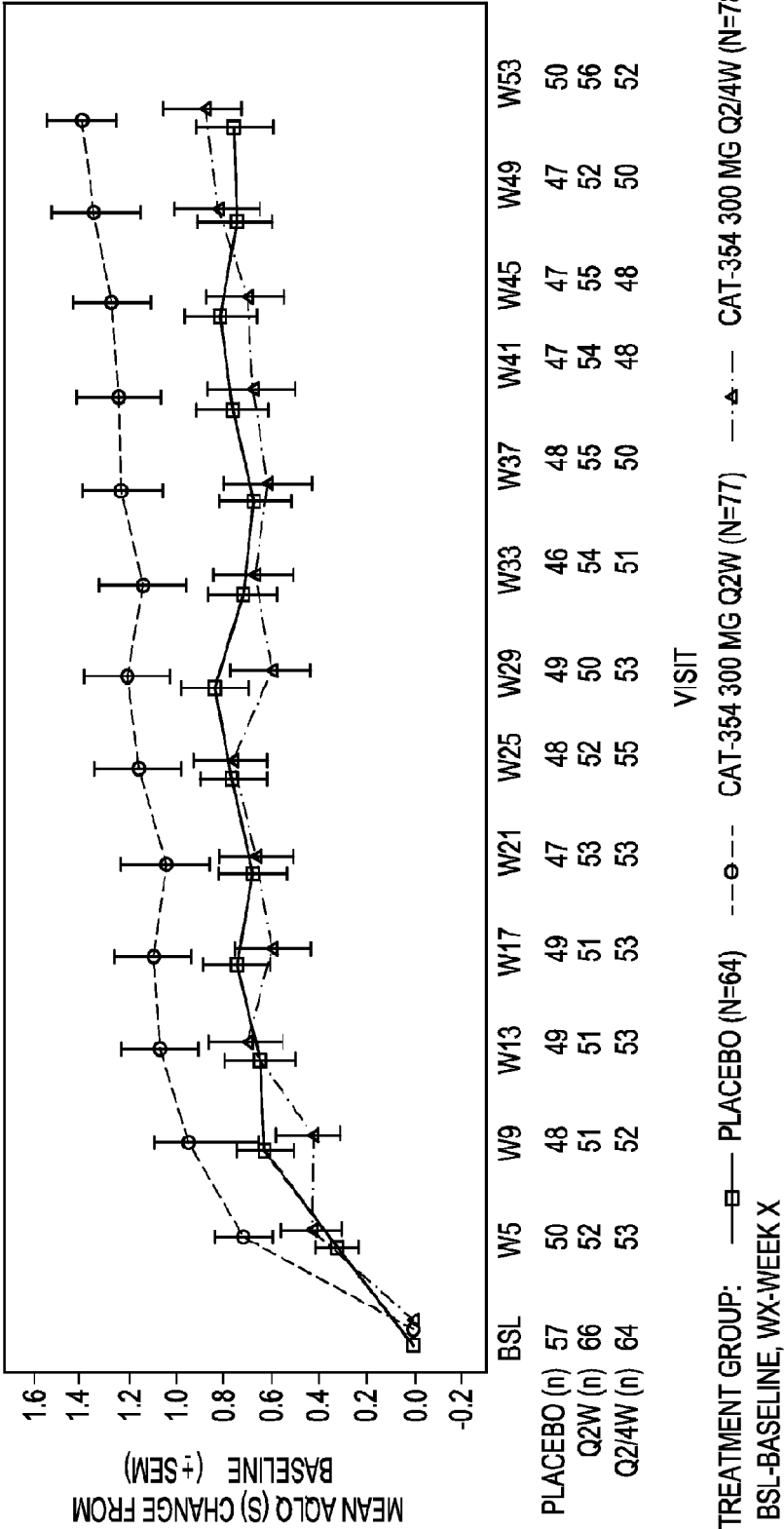


FIG. 17F

Change from Baseline in AQLQ(S) Total Score Over Time by Treatment Group
Baseline DPP4 < Median ITT Population

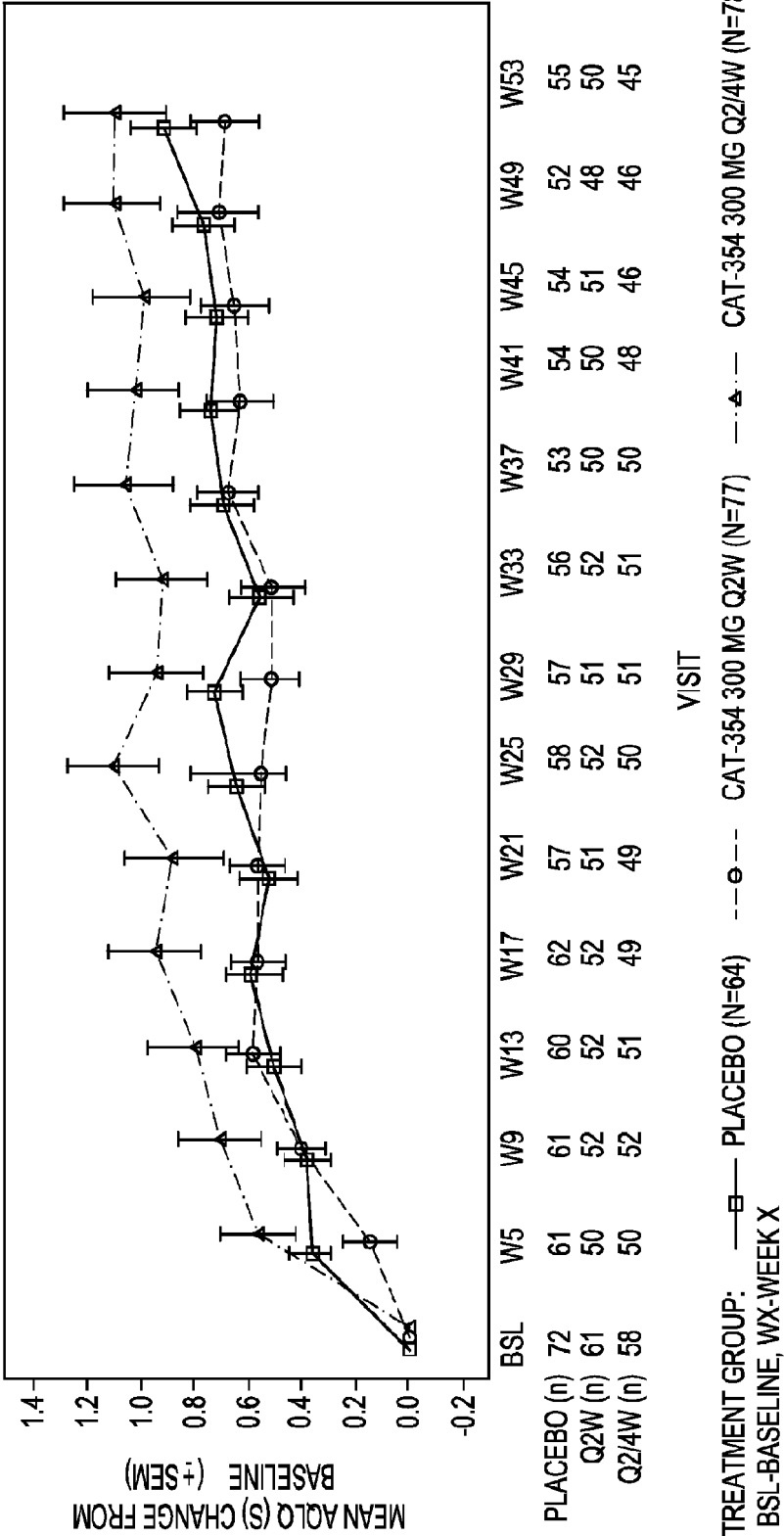


FIG. 17G

Percent Change from Baseline in Pre-Bronchodilator FEV1 Over Time By Treatment Group
Baseline FEV1 Reversibility >= 12% + Baseline DPP4 >= Median ITT Population

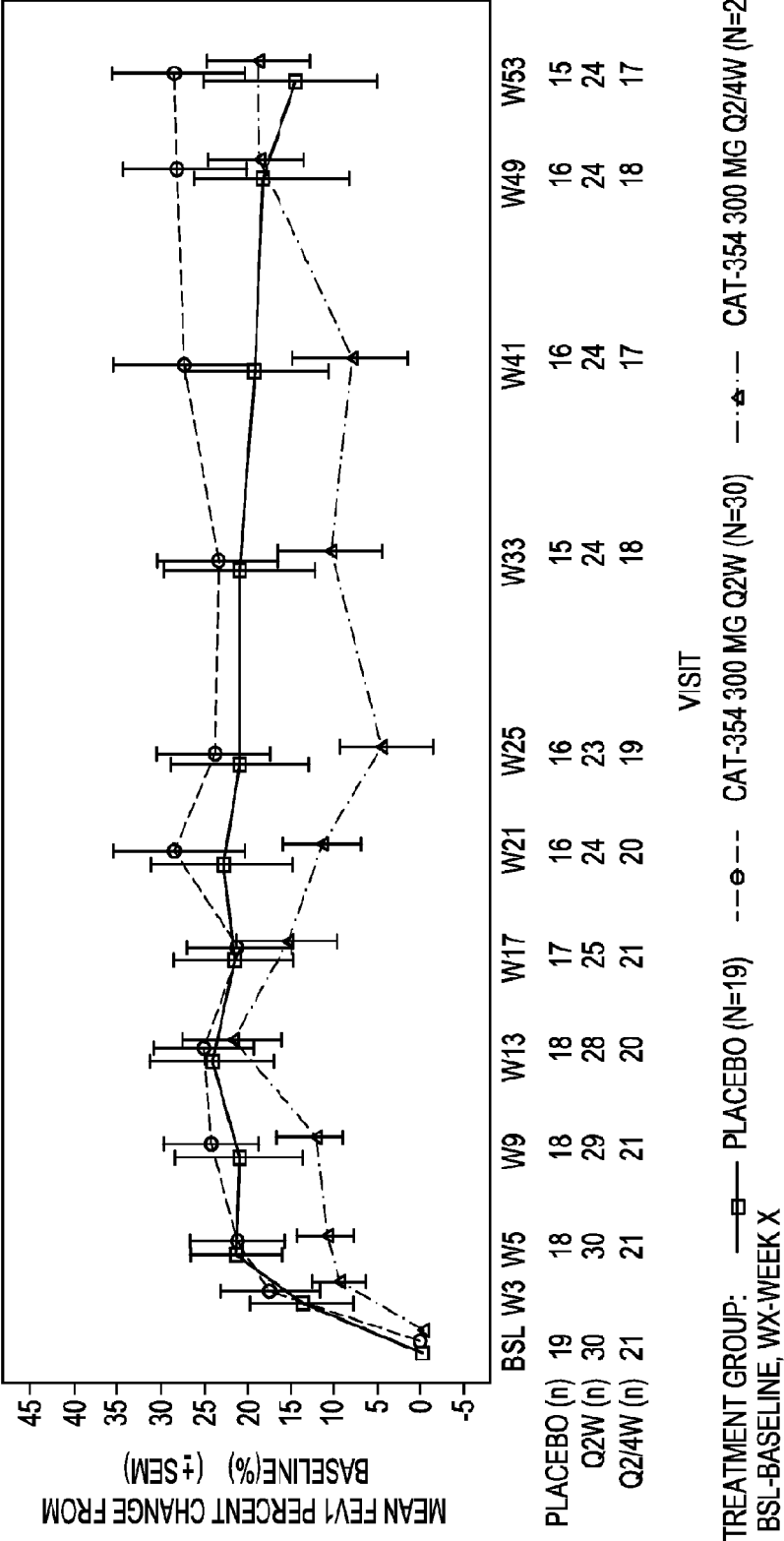


FIG. 17H

Change from Baselin in Mean ACQ-6 Score Over Time By Treatment Group
Baseline FEV1 Reversibility >= 12% + Baseline DPP4 >= Median ITT Population

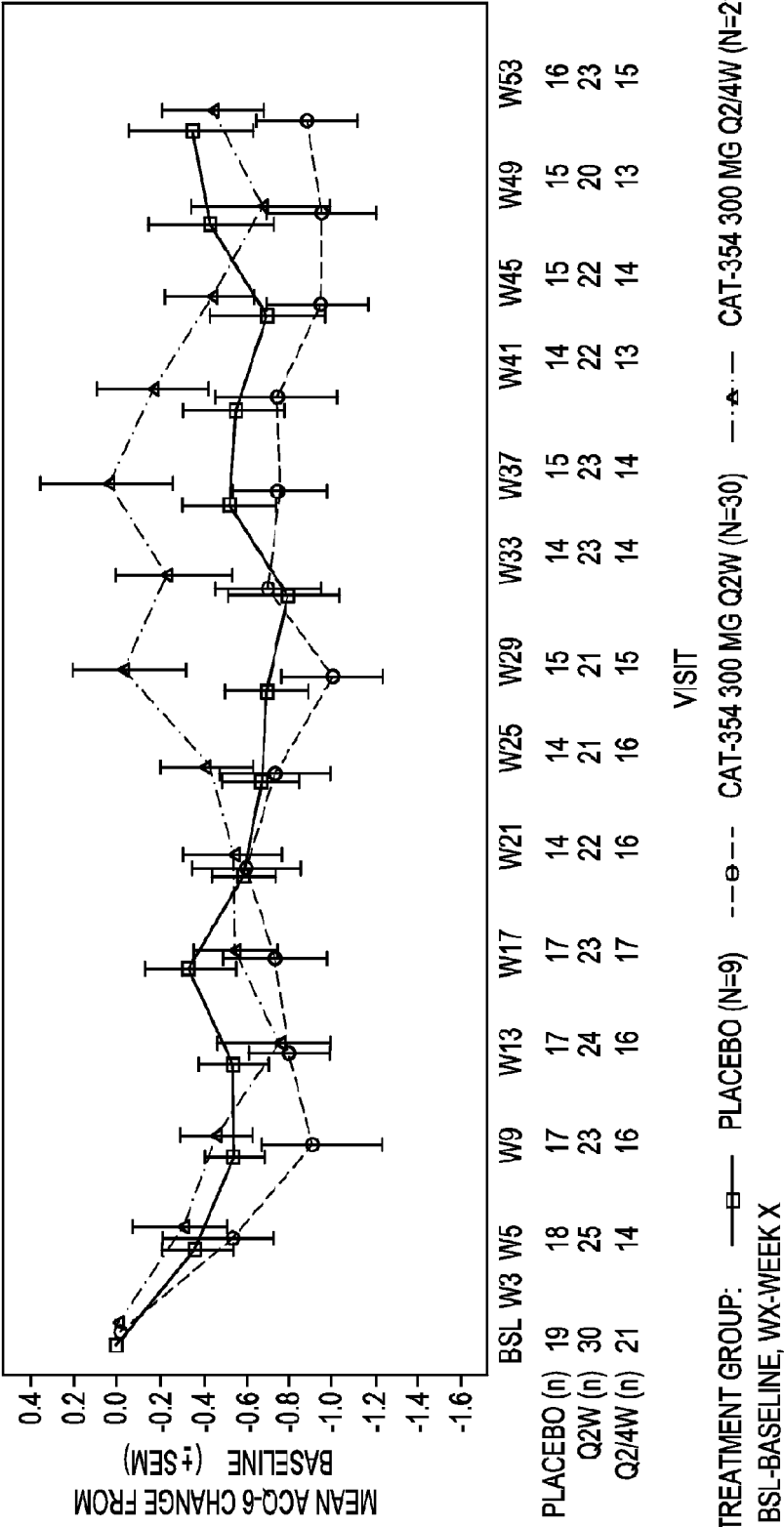
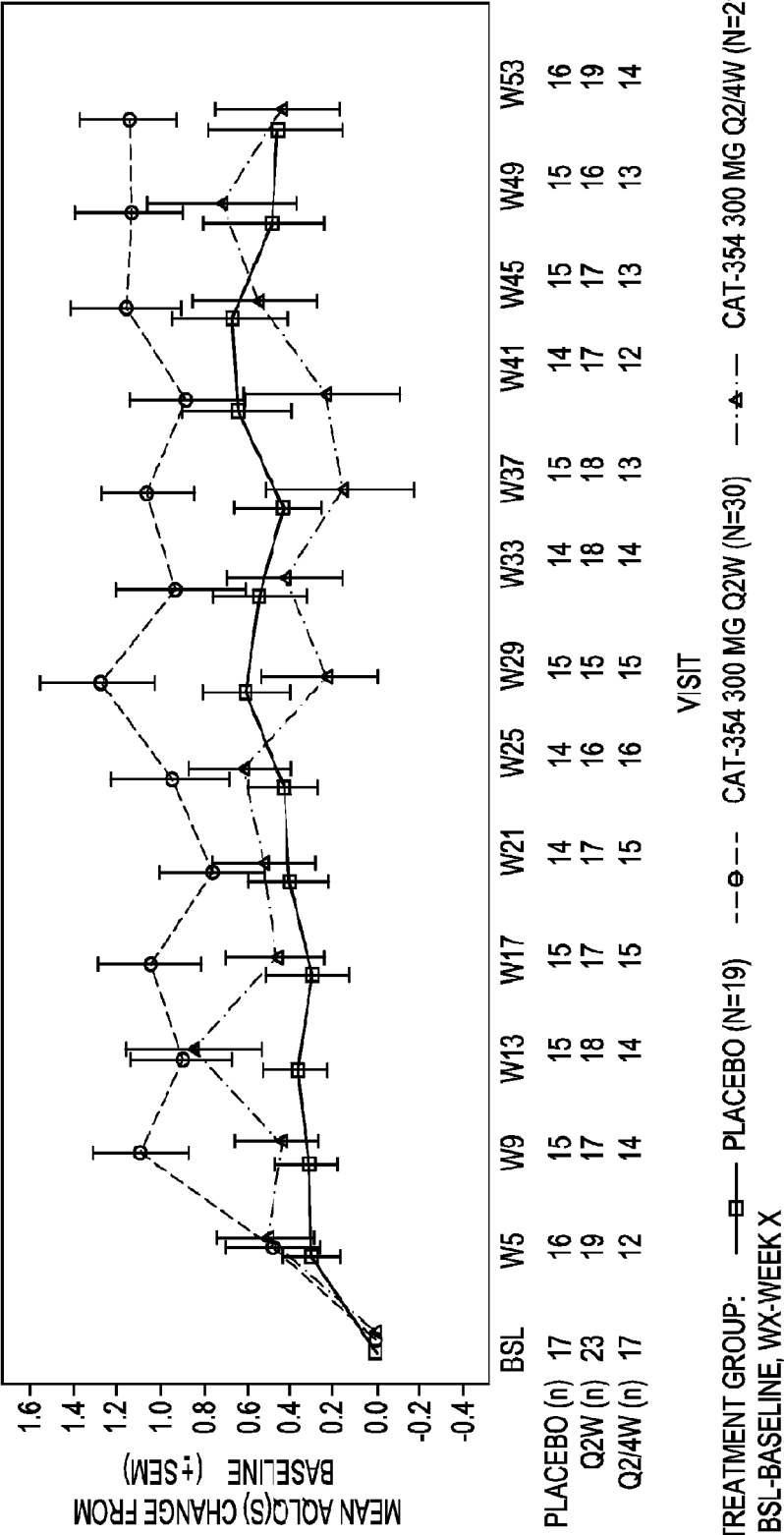


FIG. 17I

Change from Baseline in AQLQ (S) Total Score Over Time By Treatment Group
Baseline FEV1 Reversibility $\geq$ 12% + Baseline DPP4 $\geq$ Median ITT Population



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FIG. 18

Asthma Exacerbation Rate Reduction (95% CI)
for Subjects with Baseline DPP4 $\geq$ Cutpoint
CAT-354 Q2W vs Placebo

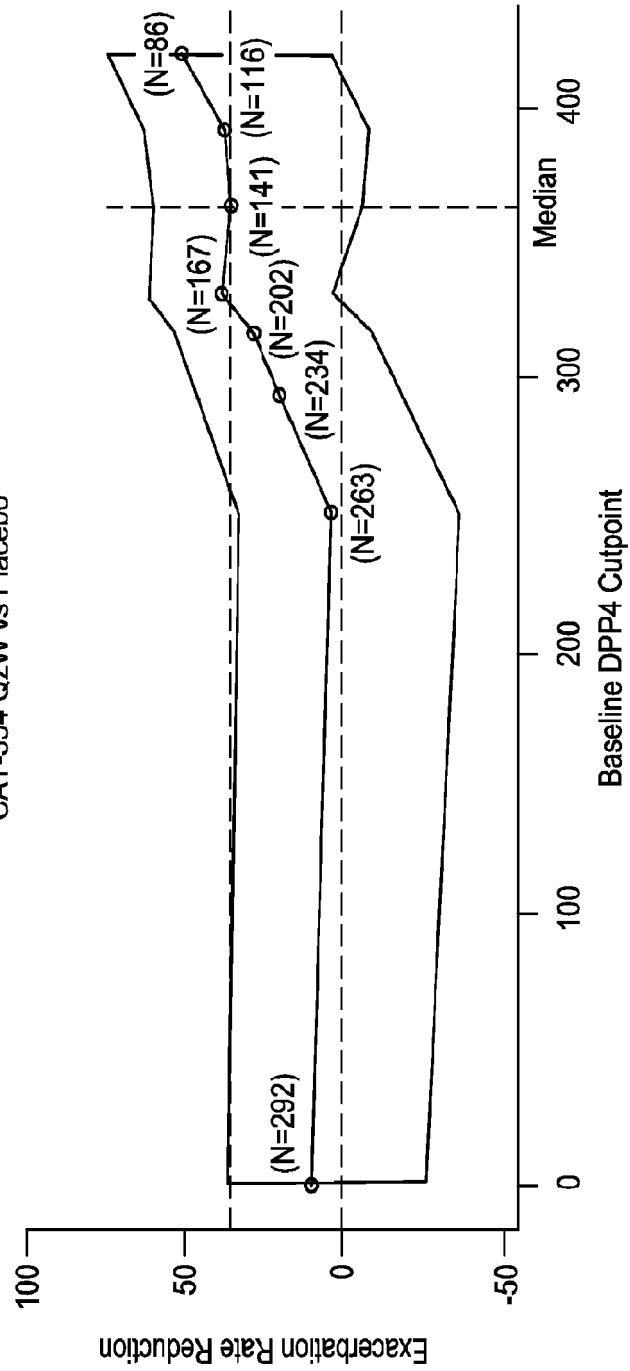
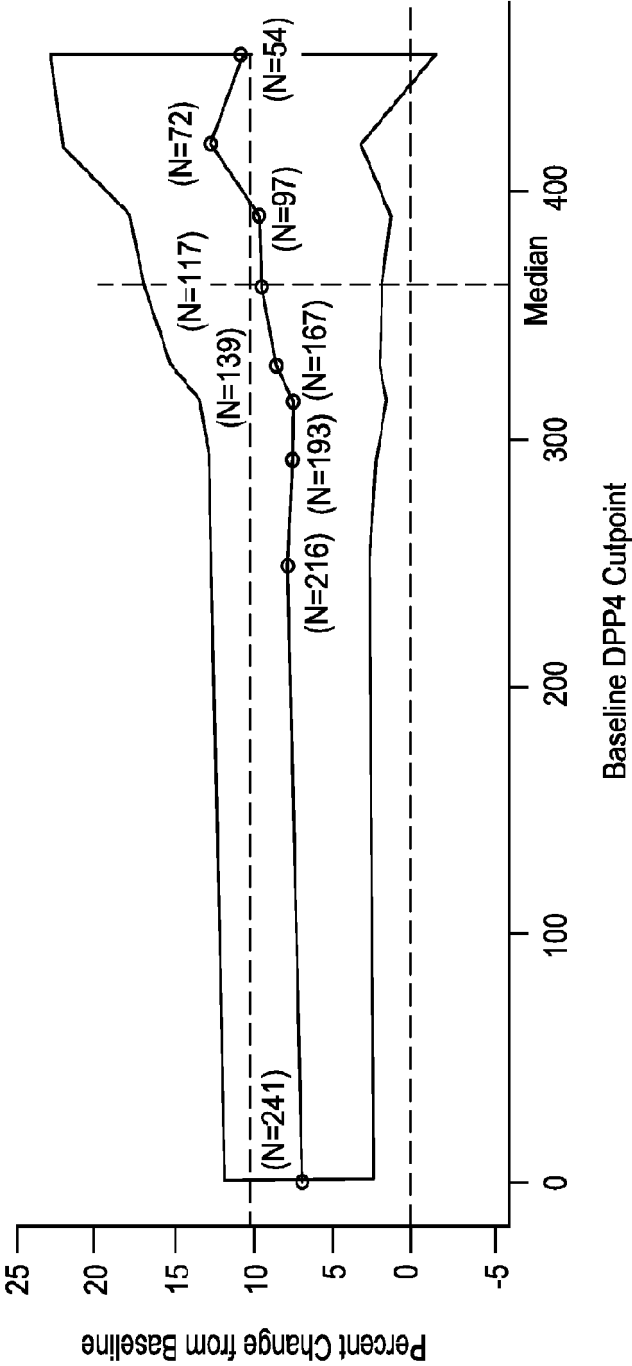


FIG. 19

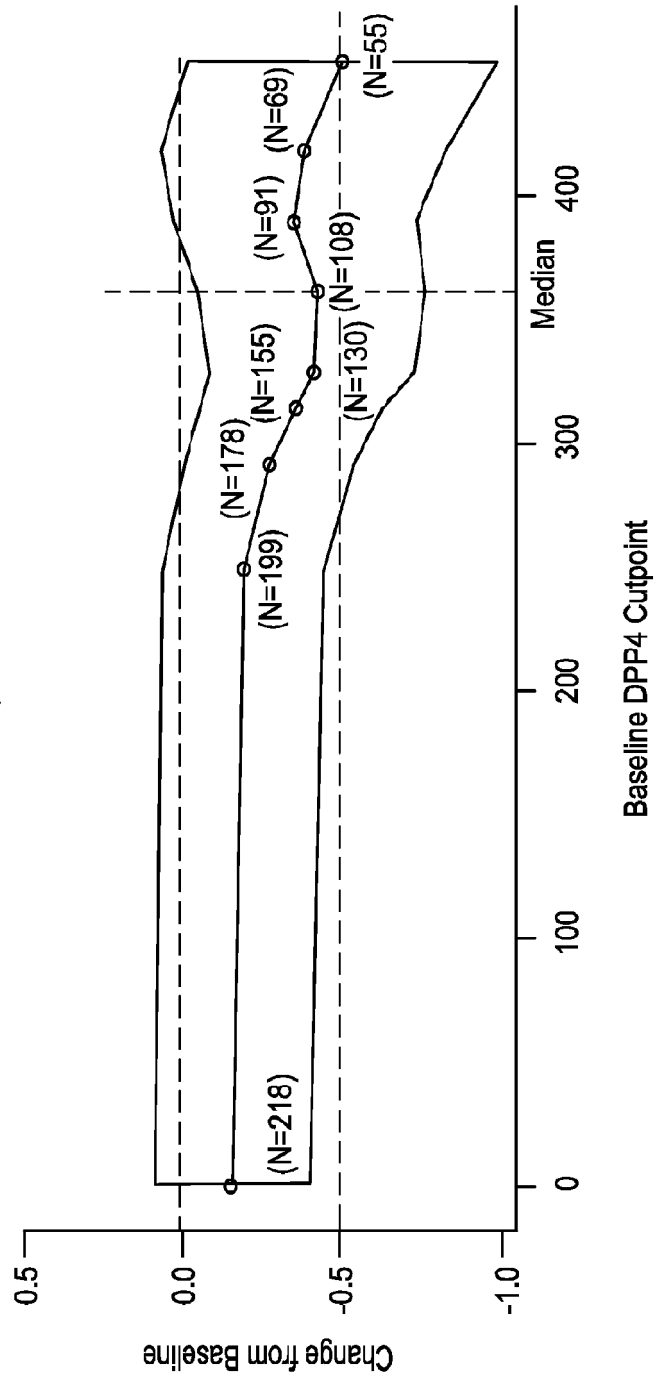
Mean Percent Change from Baseline in Pre-BD FEV1 at Week 53
(95% CI) for subjects with Baseline DPP4 >= Cutpoint
CAT-354 Q2W vs Placebo



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FIG. 20

Mean Change from Baseline in Mean ACQ-6 Score at Week 53
(95% CI) for Subjects with Baseline DPP4 $\geq$ Cutpoint
CAT-354 Q2W vs Placebo



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FIG. 21

Partial Overlap between Periostin-High and DPP4-High

		DPP4		Total
		Low	High	
Frequency Percent		1	2	
Periostin	Low 1	126 28.06	99 22.05	225 50.11
	High 2	99 22.05	125 27.84	224 49.89
Total		225 50.11	224 49.89	449 100.00

Frequency Missing = 3

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FIG. 22

Partial Overlap between Th2-High and DPP4-High

		DPP4		
		Low	High	
		1	2	Total
Th2	Frequency Percent			
	Low 1	112 27.18	91 22.09	203 49.27
	High 2	95 23.06	114 27.67	209 50.73
Total		207 50.24	205 49.76	412 100.00

Frequency Missing = 40

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FIG. 23

Partial Overlap between DPP- 4 High and Eos-High

		DPP4			
		Low	High		
Frequency Percent		1	2	Total	
Eos	< 300	1	134 31.68	127 30.02	261 61.70
	>= 300	2	78 18.44	84 19.86	162 38.30
	Total		212 50.12	211 49.88	423 100.00

Frequency Missing = 29

FIG. 24
DPP4 Levels Reduced in OCS-treated Subjects

CHRONIC OCS USE	N Obs	Mean	Median	Minimum	Maximum	Std Dev
NEGATIVE	373	380.9463807	371.0000000	134.0000000	905.0000000	105.6377830
POSITIVE	77	335.79222078	321.0000000	169.0000000	540.0000000	92.9282884

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FIG. 25
DPP4 and FEV₁ reversibility and No Chronic OCS Use

BL FEV ₁ reversibility	BL DPP4	N for AER (placebo/ CAT-354)	Exacerbation rate (placebo/ CAT-354)	AER Adjusted for Covariates	Δ % change from BL FEV ₁ vs. Pbo	Δ mean change from BL ACQ-6 vs. pbo	Δ mean change from BL AQLQ vs. pbo
--	--	(124/124)	0.80/0.67	21% (-19, 47)	6.59% (1.7, 11.4)	-0.11 (-0.37, 0.16)	0.18 (-0.11, 0.46)
≥ 12% at BL	--	(48/33)	0.87/0.56	46% (-18, 75)	10.72% (-0.0, 21.4)	-0.50 (-1.02, 0.03)	0.66 (0.07, 1.25)
	≥ median	(15/24)	1.25/0.63	57% (-30, 86)	20.3% (-1.2, 39.5)	-0.89 (-1.63, -0.14)	1.26 (0.48, 2.04)
< 12% at BL	< median	(32/8)	0.72/0.41	-7% (-88, 88)	-0.9% (-15.4, 13.5)	-0.43 (-1.41, 0.56)	0.24 (-0.87, 1.35)
	--	(73/85)	0.76/0.69	21% (-38, 55)	6.97% (2.0, 11.9)	0.06 (-0.27, 0.39)	-0.05 (-0.40, 0.31)
< 12% at BL	≥ median	(36/42)	0.80/0.49	41% (-115, 70)	7.01% (0.1, 13.9)	-0.36 (-0.85, 0.13)	0.37 (-0.18, 0.92)
	< median	(34/41)	0.75/0.93	-14% (-256, 50)	8.49 (1.4, 15.6)	0.39 (-0.07, 0.82)	-0.44 (-0.88, 0.01)
--	≥ median	(52/68)	0.94/0.54	35% (-7, 61)	11.06% (3.6, 18.6)	-0.48 (-0.87, -0.09)	0.68 (0.26, 1.09)
--	< median	(68/51)	0.72/0.81	-18% (-120, 37)	4.79% (-3.67, 8.4)	0.21 (-0.16, 0.58)	-0.29 (-0.68, 0.11)

95% CI in parentheses

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FIG. 26
 Periostin and FEV₁ reversibility and No Chronic OCS Use

BL FEV ₁ reversibility	BL Periostin	N for AERR (placebo/ CAT-354)	Exacerbation rate (placebo/ CAT-354)	AERR Adjusted for Covariates	AERR Unadjusted	Δ % change from BL FEV ₁ vs. pbo	Δ mean change from BL ACQ-6 vs. pbo	Δ mean change from BL AQLQ vs. pbo
--	--	(124/124)	0.80/0.67	21% (-19, 47)	16%	6.59% (1.7, 11.4)	-0.11 (-0.37, 0.16)	0.18 (-0.11, 0.46)
≥ 12% at BL	--	(48/33)	0.87/0.56	46% (-18, 75)	37%	10.72% (-0.0, 21.4)	-0.50 (-1.02, 0.03)	0.66 (0.07, 1.25)
	≥ median	(22/18)	1.22/0.59	67% (2, 89)	52%	14.7% (-0.2, 29.5)	-0.68 (-1.31, -0.06)	0.64 (-0.11, 1.39)
	< median	(26/15)	0.58/0.52	-32% (-273, 53)	10%	8.00% (-7.0, 23.0)	-0.23 (-1.10, 0.64)	0.71 (-0.23, 1.65)
	--	(73/85)	0.76/0.69	21% (-38, 55)	9%	6.97% (2.0, 11.9)	0.06 (-0.27, 0.39)	-0.05 (-0.40, 0.31)
< 12% at BL	≥ median	(34/50)	0.96/0.72	49% (-8, 76)	25%	4.10% (-3.2, 11.4)	-0.14 (-0.59, 0.31)	-0.04 (-0.53, 0.46)
	< median	(38/35)	0.59/0.64	-1% (-142, 59)	-8%	8.61 (1.8, 15.4)	0.42 (-0.07, 0.91)	-0.13 (-0.64, 0.39)
--	≥ median	(58/69)	1.04/0.69	41% (-2, 66)	34%	6.39% (-0.6, 13.4)	-0.26 (-0.61, 0.09)	0.19 (-0.21, 0.58)
--	< median	(65/55)	0.59/0.64	-7% (-97, 42)	-8%	6.46% (-0.4, 13.3)	0.24 (-0.17, 0.65)	0.12 (-0.31, 0.56)

95% CI in parentheses

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FIG. 27A

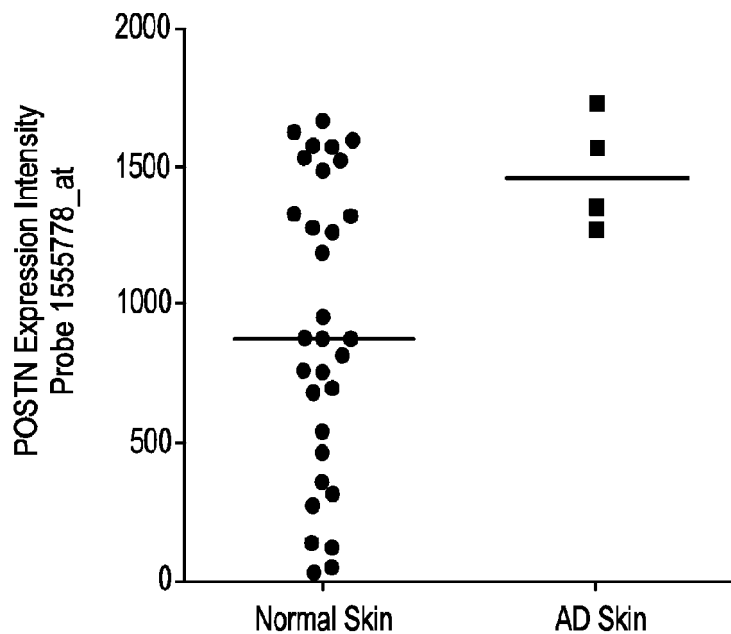
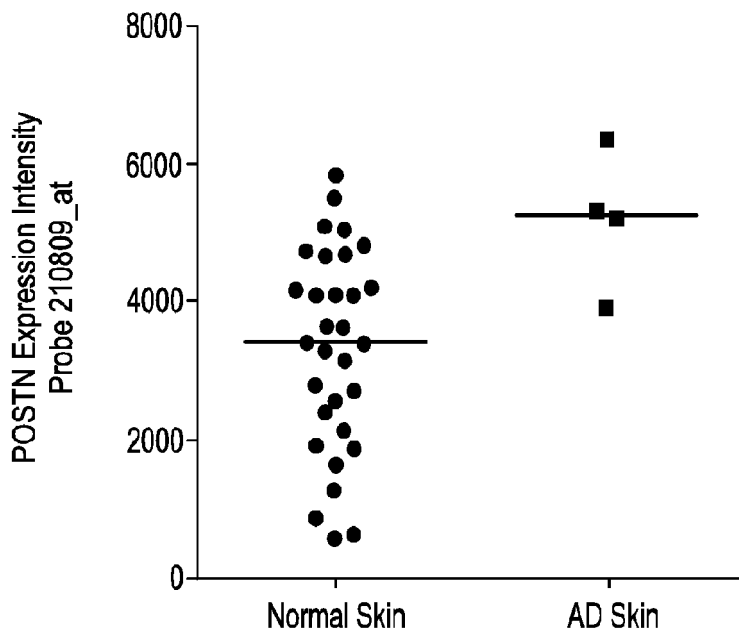


FIG. 27B



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FIG. 28A

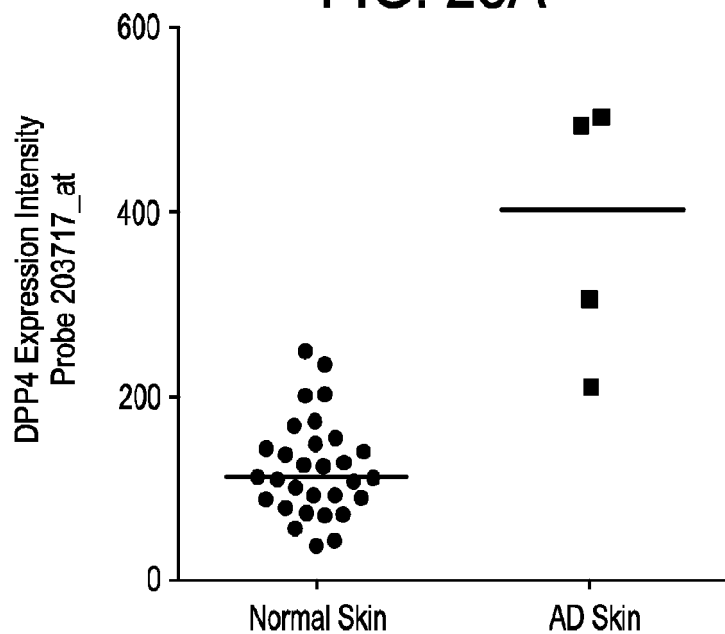
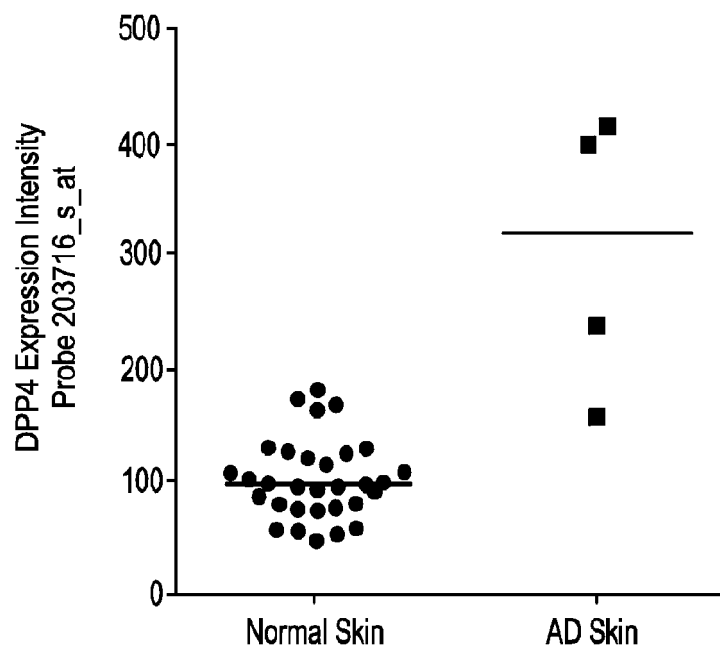
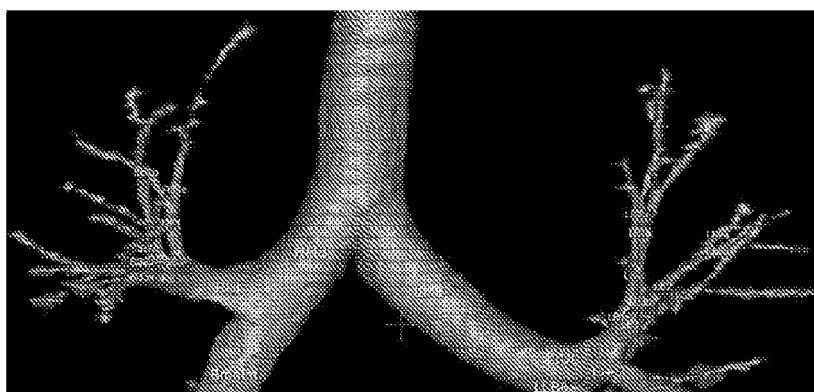


FIG. 28B



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FIG. 29A



E13024010332 Visit 4

FIG. 29B



E13024010332 Visit 30

FIG. 30A

Relative Change in Lumen Area (LA)

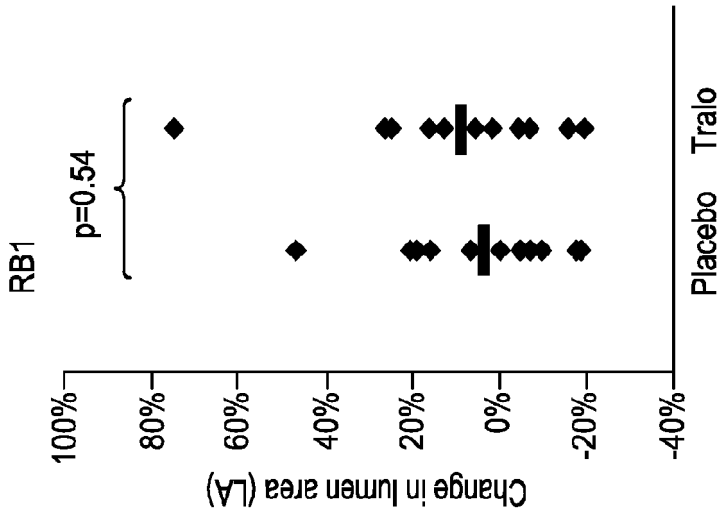


FIG. 30B

Relative Change in Lumen Area (LA)

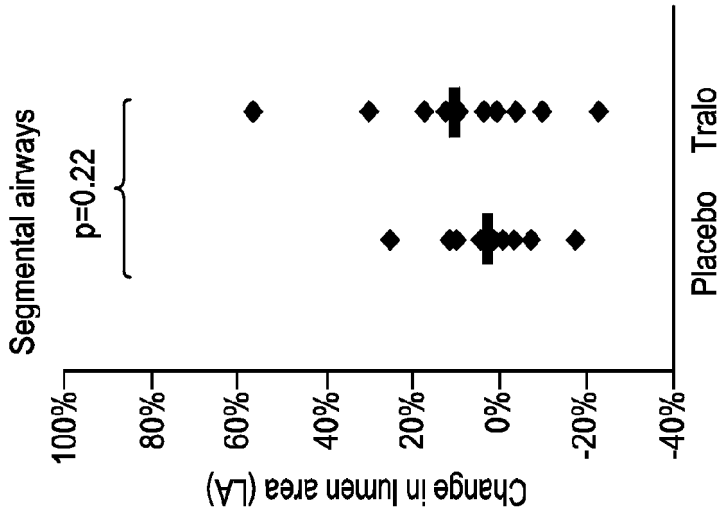


FIG. 30C

Relative Change in Lumen Area (LA)

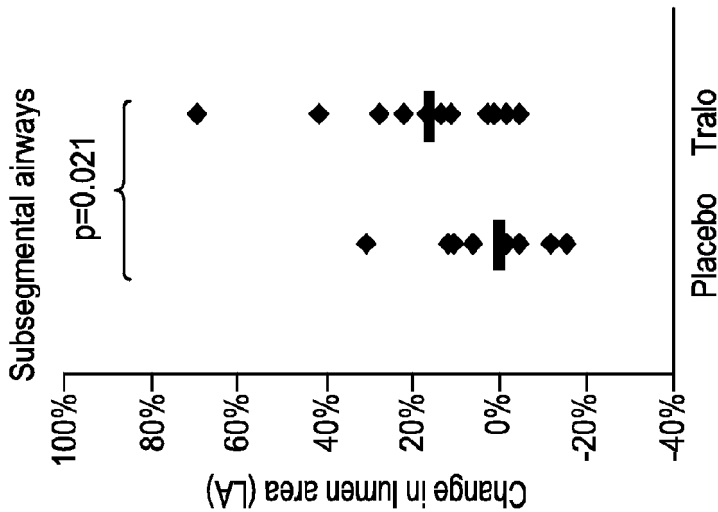


FIG. 31A

Relative Change in Wall Area Percentage (WA%)

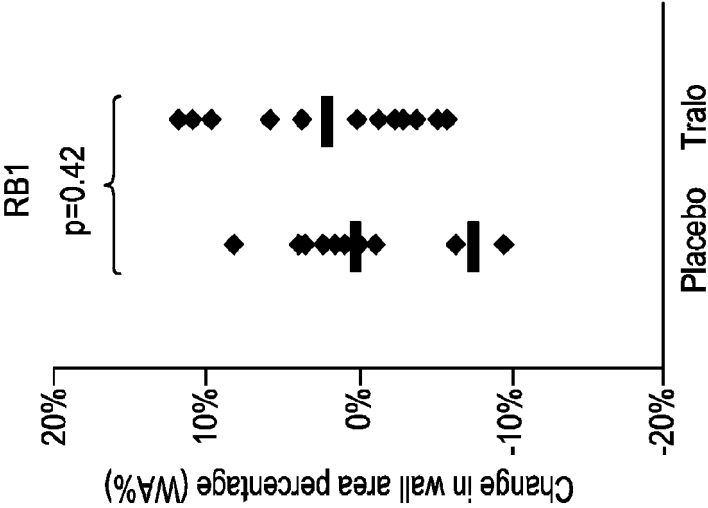


FIG. 31B

Relative Change in Wall Area Percentage (WA%)

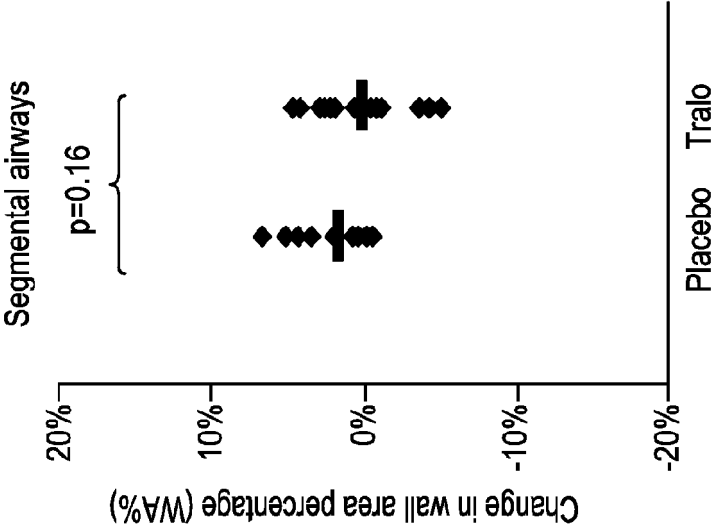
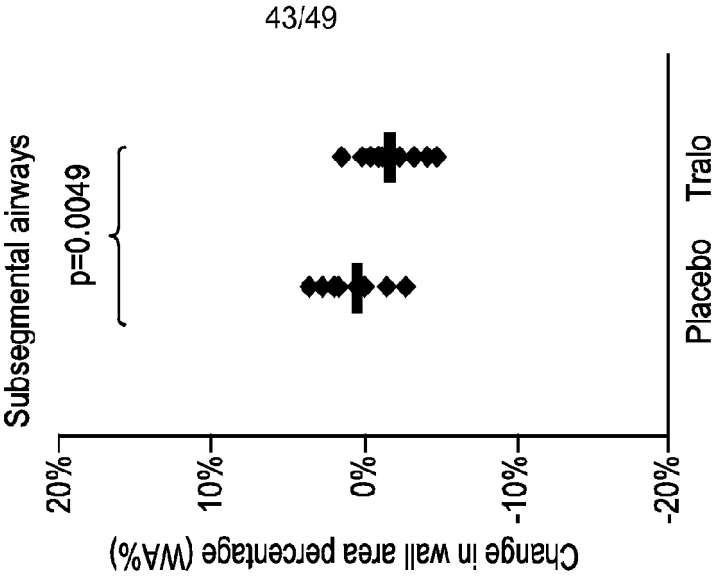


FIG. 31C

Relative Change in Wall Area Percentage (WA%)



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FIG. 32A
Relative Change in
Airway Resistance

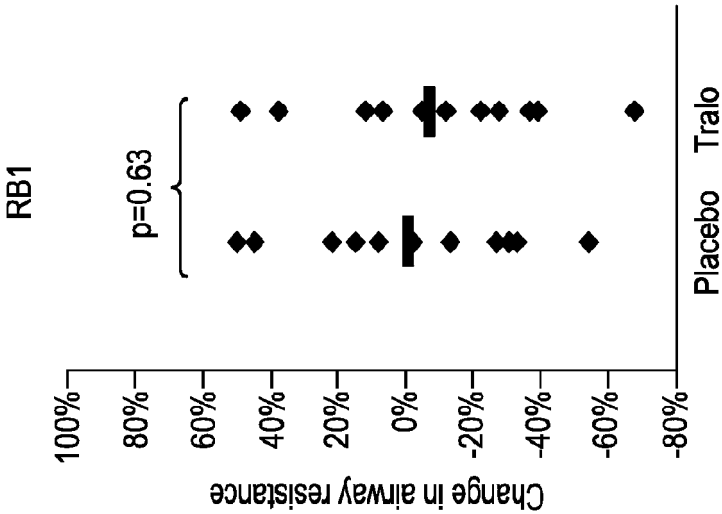


FIG. 32B
Relative Change in
Airway Resistance

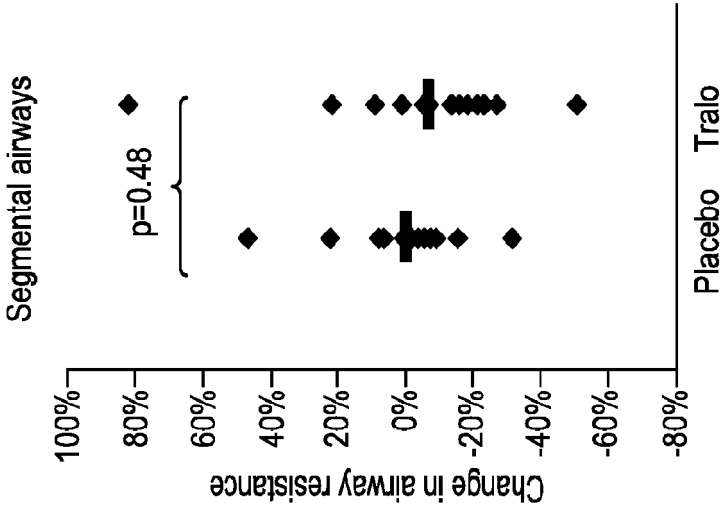


FIG. 32C
Relative Change in
Airway Resistance

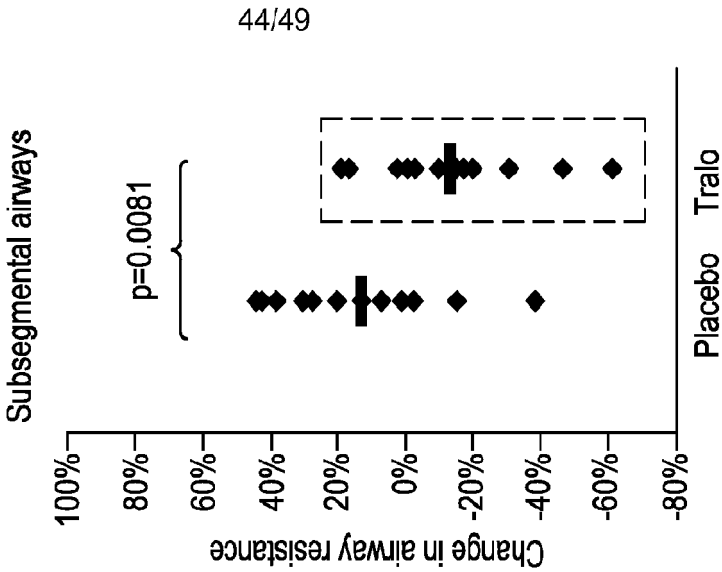


FIG. 33A

Relative Change in Airway Resistance (Calculated)
and FEV1: Effect of Tralokinumab in different sub-groups
*WA% at subsegmental level

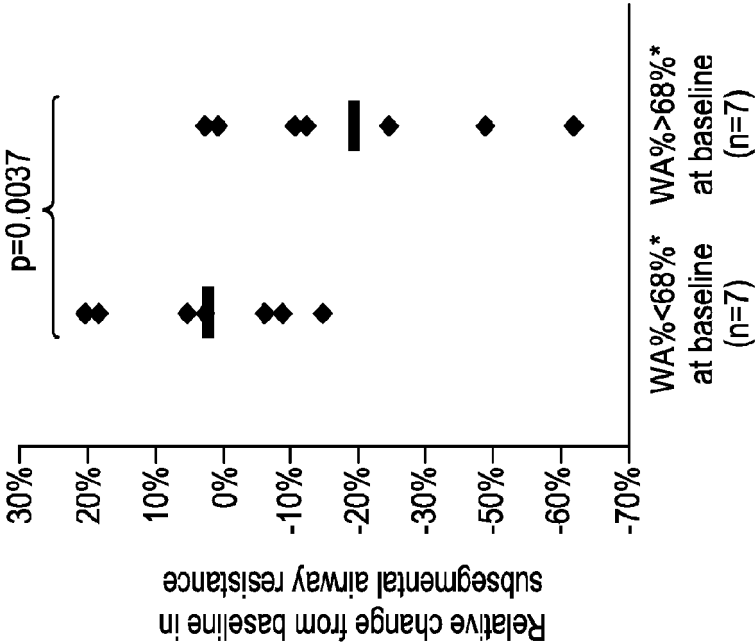
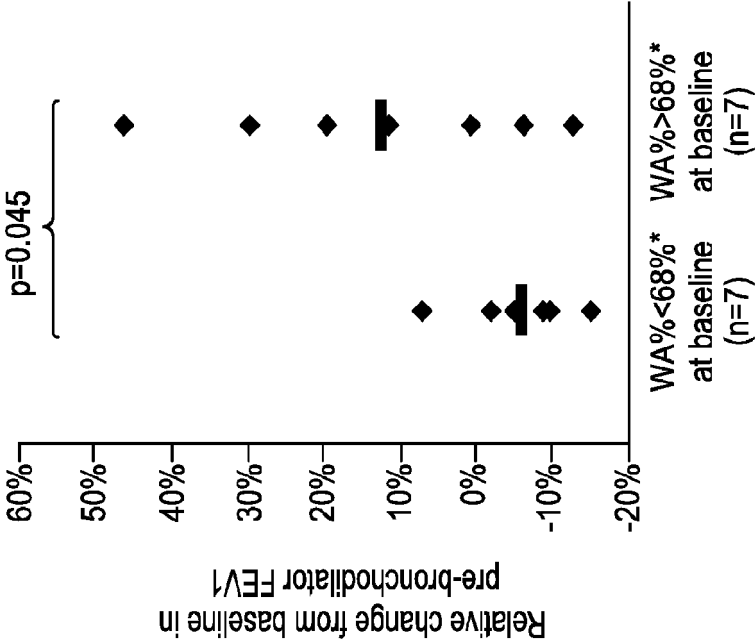
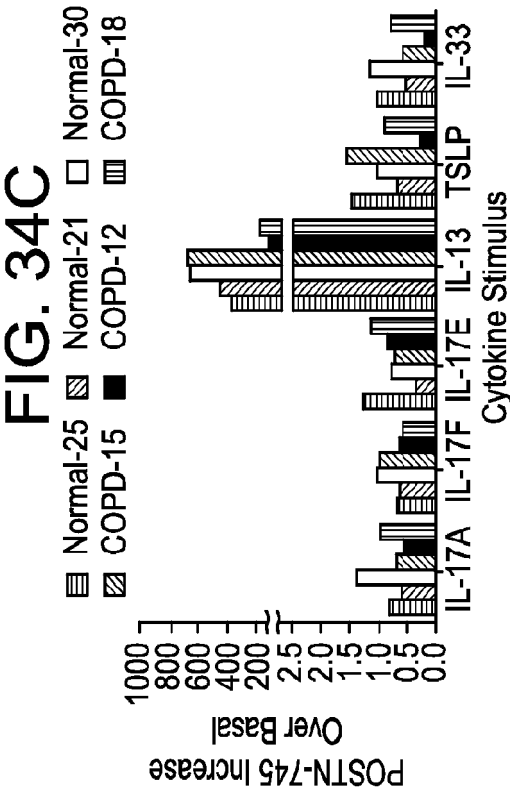
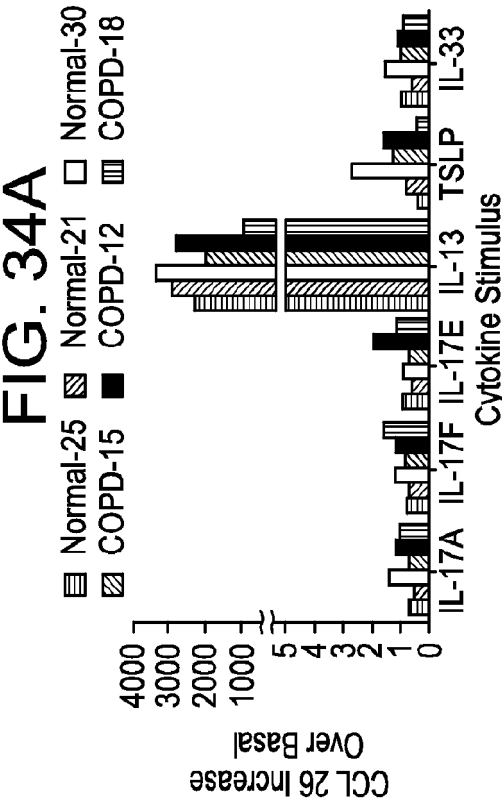
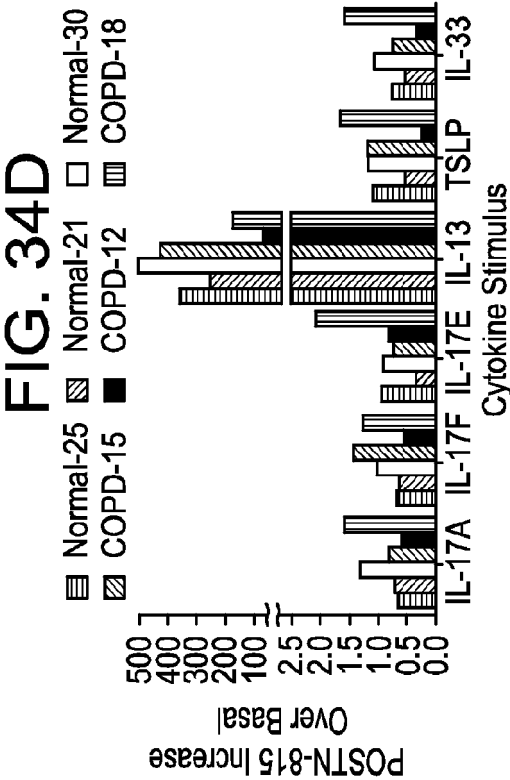
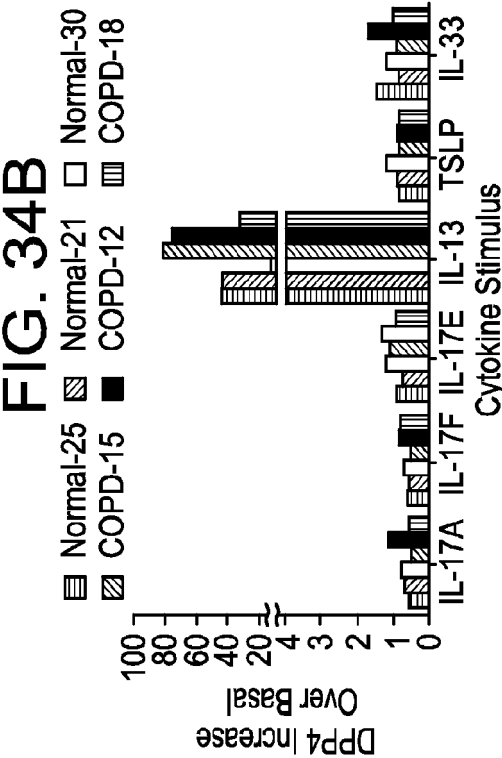


FIG. 33B

Relative Change in Airway Resistance (Calculated)
and FEV1: Effect of Tralokinumab in different sub-groups
*WA% at subsegmental level





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FIG. 35A

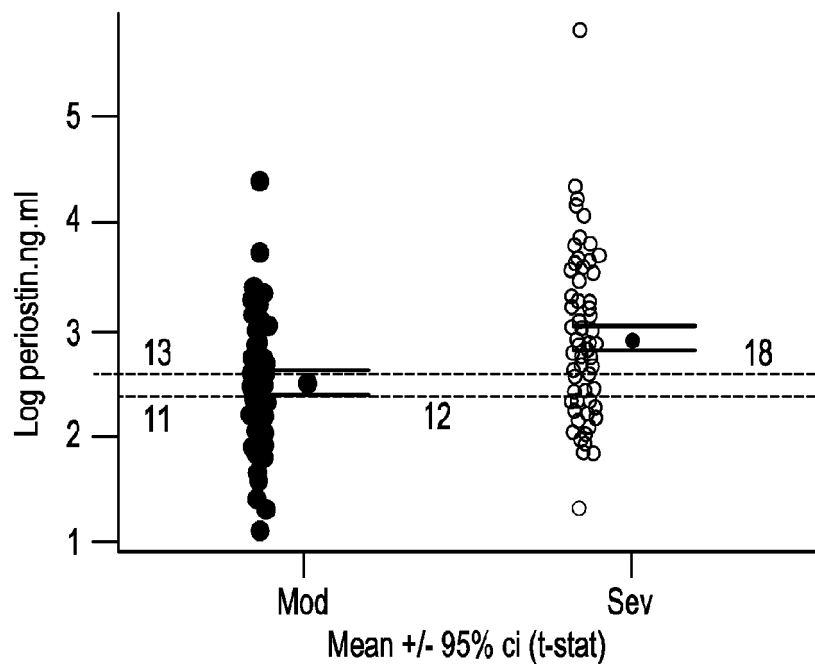


FIG. 35B

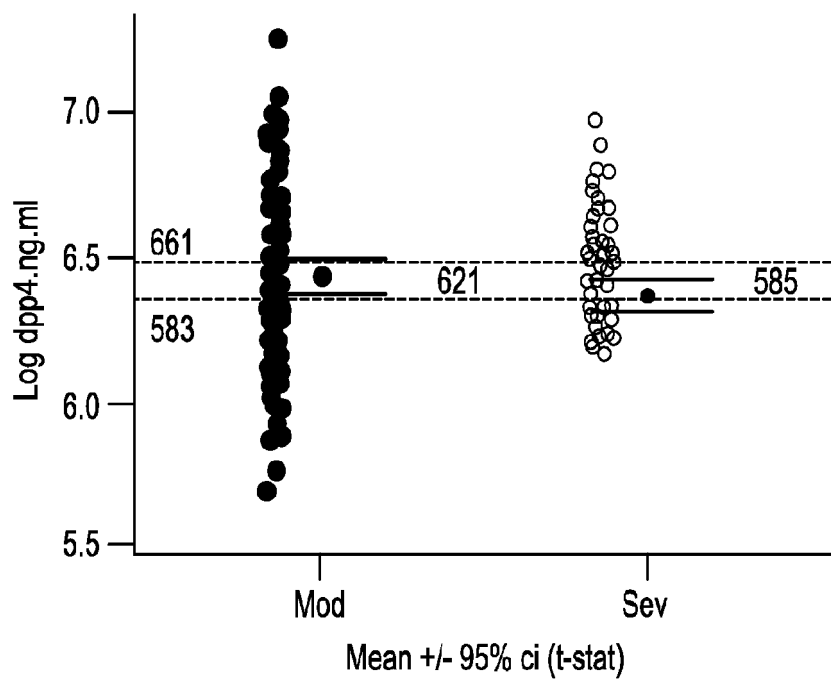


FIG. 36

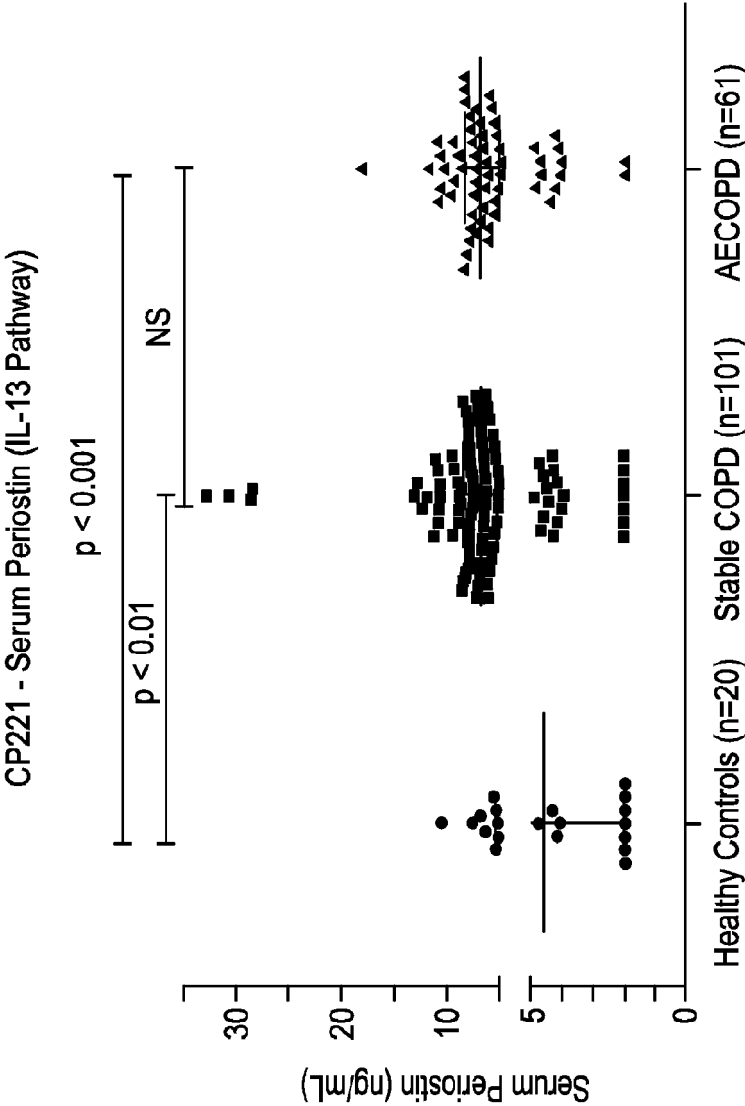


FIG. 37

CP221 - Serum DPP4 (IL-13 Pathway)

