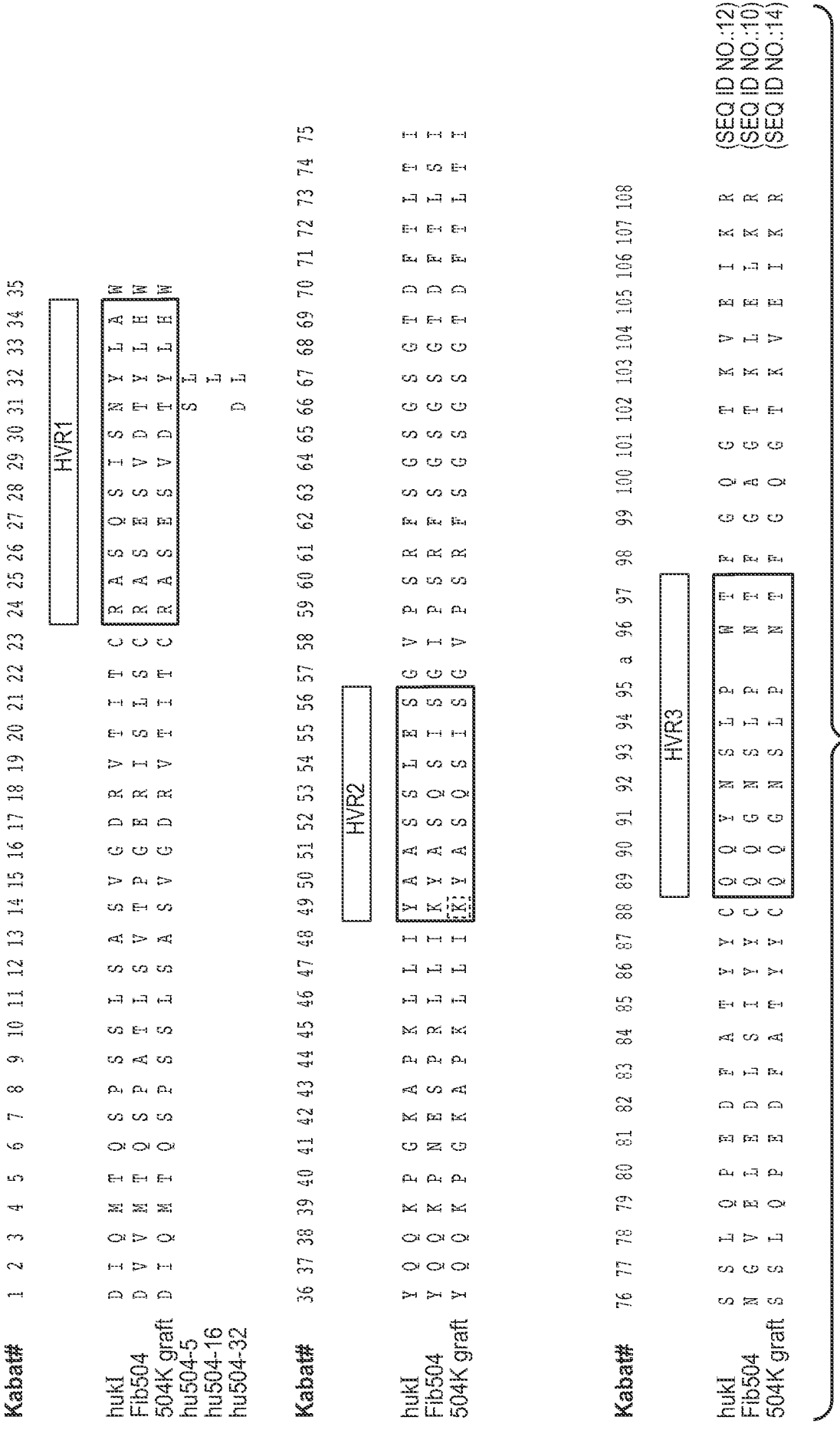

Kabat# 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35
HVR1
hukI D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q S I S N Y L A W
Fib504 D V V M T Q S P A T L S V T P G E R I S L S C R A S E S V D T Y L H W
504K graft D I Q M T Q S P S S L S A S V G D R V T I T C R A S E S V D T Y L H W
hu504-5 S L
hu504-16 L
hu504-32 D L
Kabat# 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75
HVR2
hukI Y Q Q K P G K A P K L L I Y A A S S L E S G V P S R F S G S G S G T D F T L T I
Fib504 Y Q Q K P N E S P R L L I K V A S Q S I S G I P S R F S G S G S G T D F T L S I
504K graft Y Q Q K P G K A P K L L I K V A S Q S I S G V P S R F S G S G S G T D F T L T I
Kabat# 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 a 96 97 98 99 100 101 102 103 104 105 106 107 108
HVR3
hukI S S L Q P E D F A T Y Y C Q Q Y N S L P W T F G Q G T K V E I K R (SEQ ID NO.:12)
Fib504 N S V E L E D L S I Y Y C Q Q G N S L P N T F G A G T K L E L K R (SEQ ID NO.:10)
504K graft S S L Q P E D F A T Y Y C Q Q G N S L P N T F G Q G T K V E I K R (SEQ ID NO.:14)

FIG. 1A

Kabat#	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
																										HVR1																		
humIII	E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	S	W	V	R	Q	A	P	G
Fib504	E	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	Q	S	L	S	L	T	C	S	V	T	G	F	F	I	T	N	N	Y	W	G	W	I	R	K	F	G	G
504K graft	E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	F	I	T	N	N	Y	W	G	W	V	R	Q	A	P	G

Kabat#	43	44	45	46	47	48	49	50	51	52	a	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	a
humIII	K	G	L	E	W	V	S	V	I	S	G	D	G	G	S	T	Y	Y	A	D	S	V	K	G	R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N
Fib504	N	K	M	E	W	M	G	Y	I	S		Y	S	G	S	T	S	Y	N	P	S	L	K	S	R	I	S	I	T	R	D	T	S	K	N	Q	F	F	L	Q	L	N
504K graft	K	G	L	E	W	V	G	Y	I	S		Y	S	G	S	T	S	Y	N	P	S	L	K	S	R	F	T	I	S	A	D	T	S	K	N	T	A	Y	L	Q	M	N
hu504-5																														R							F						
hu504-16																														R							F						
hu504-32																														R							F						

Kabat#	b	c	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	a	k	101	102	103	104	105	106	107	108	109	110	111	112	113	
														HVR3																							
humIII	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R	G							F	D	Y	W	G	Q	G	T	L	V	T	V	S	S	(SEQ ID NO.:13)
Fib504	S	V	T	T	E	D	T	A	T	Y	Y	C	A	M	T	G	S	S	G	Y		F	D	F	W	G	P	G	T	M	V	T	V	S	S	(SEQ ID NO.:11)
504K graft	S	L	R	A	E	D	T	A	V	Y	Y	C	A	M	T	G	S	S	G	Y		F	D	F	W	G	Q	G	T	L	V	T	V	S	S	(SEQ ID NO.:15)

FIG. 1B

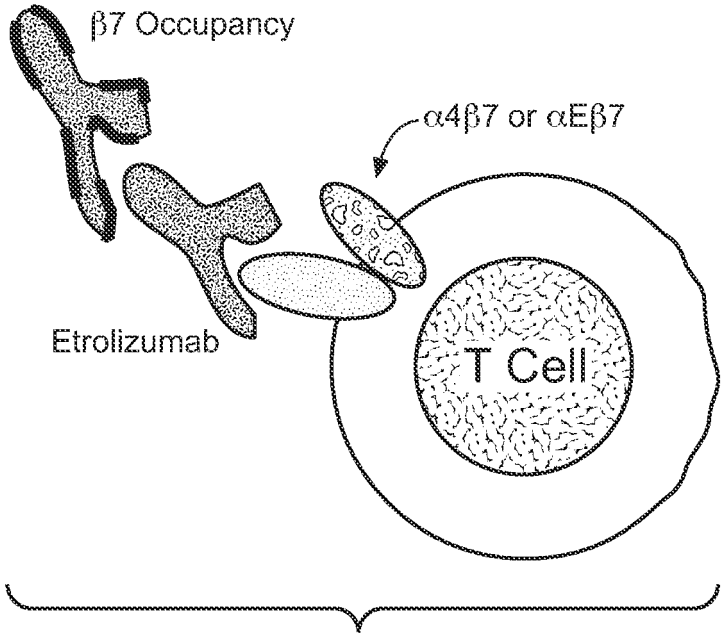

β7 Occupancy
α4β7 or αEβ7
Etrolizumab
T Cell

FIG. 2A

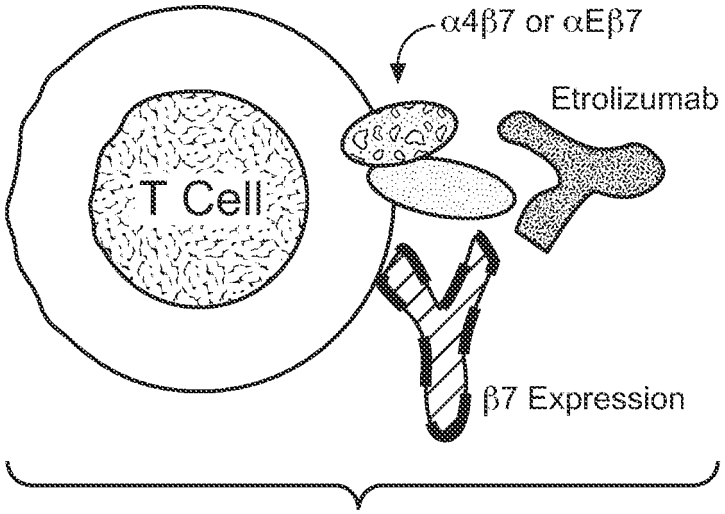

α4β7 or αEβ7
Etrolizumab
T Cell
β7 Expression

FIG. 2B

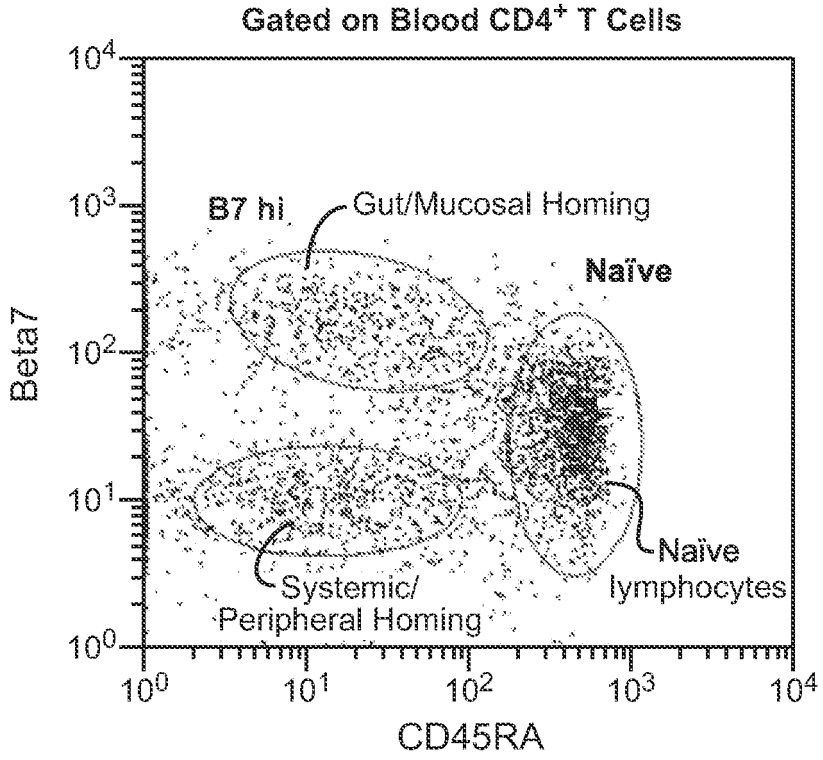

Gated on Blood CD4+ T Cells
B7 hi
Gut/Mucosal Homing
Naïve
Naïve lymphocytes
Systemic/ Peripheral Homing
Beta7
CD45RA
10^0
10^1
10^2
10^3
10^4

FIG. 3A

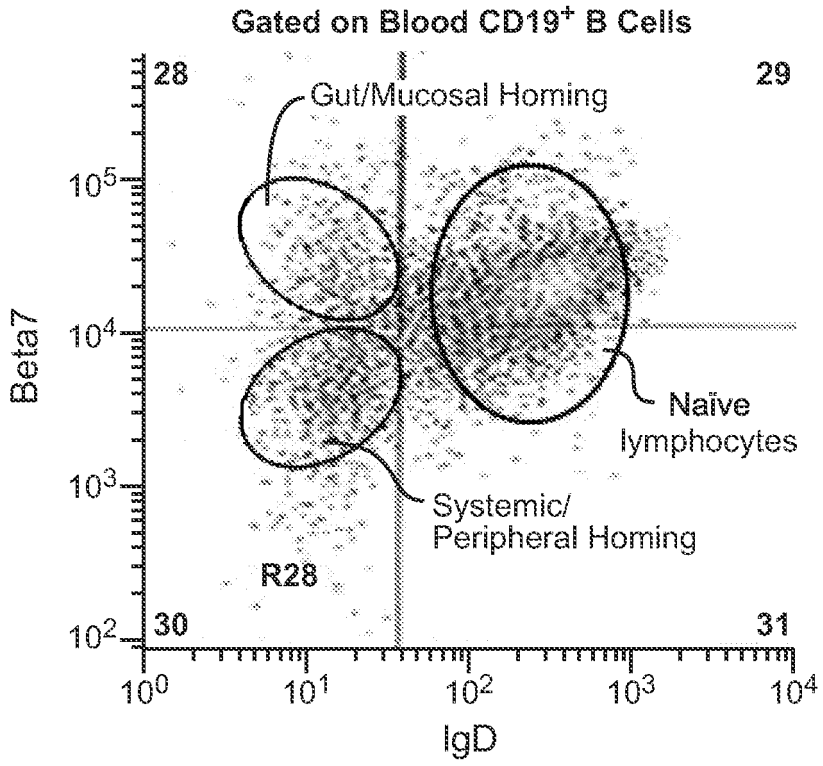

Gated on Blood CD19+ B Cells
28
29
30
31
R28
Gut/Mucosal Homing
Naïve lymphocytes
Systemic/ Peripheral Homing
Beta7
IgD
10^0
10^1
10^2
10^3
10^4
10^5

FIG. 3B

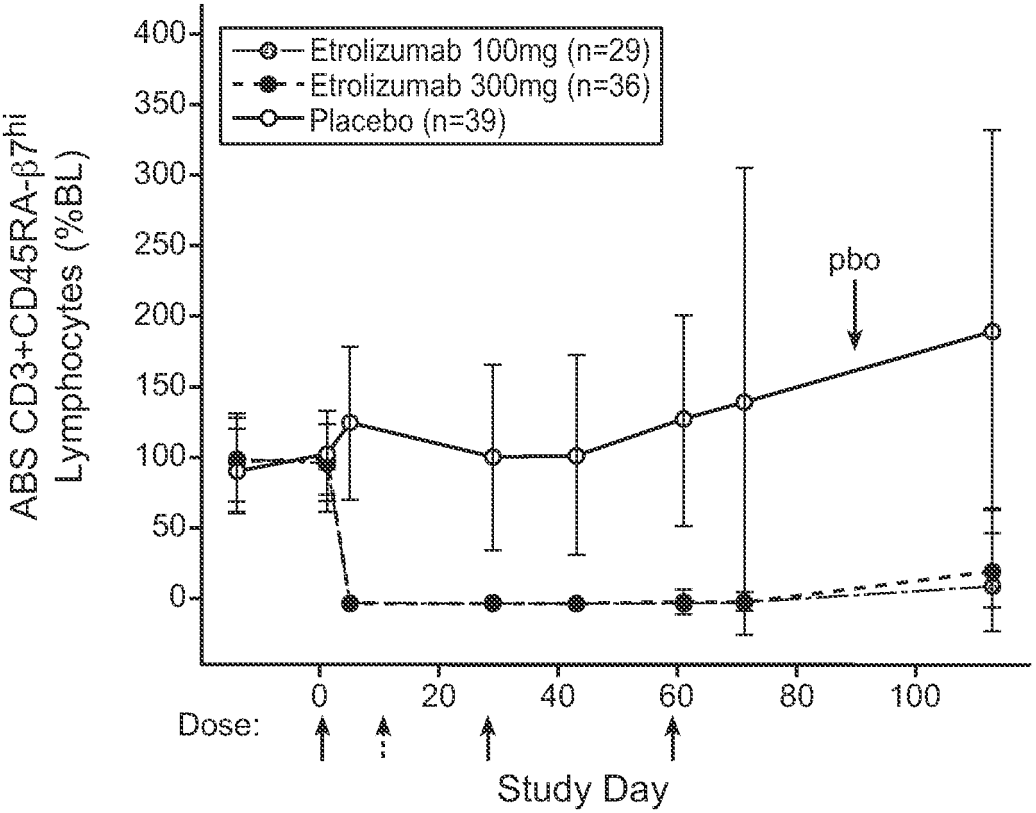

ABS CD3+CD45RA-β7hi Lymphocytes (%BL)
400
350
300
250
200
150
100
50
0
Etrolizumab 100mg (n=29)
Etrolizumab 300mg (n=36)
Placebo (n=39)
pbo
0
20
40
60
80
100
Dose:
Study Day

FIG. 4A

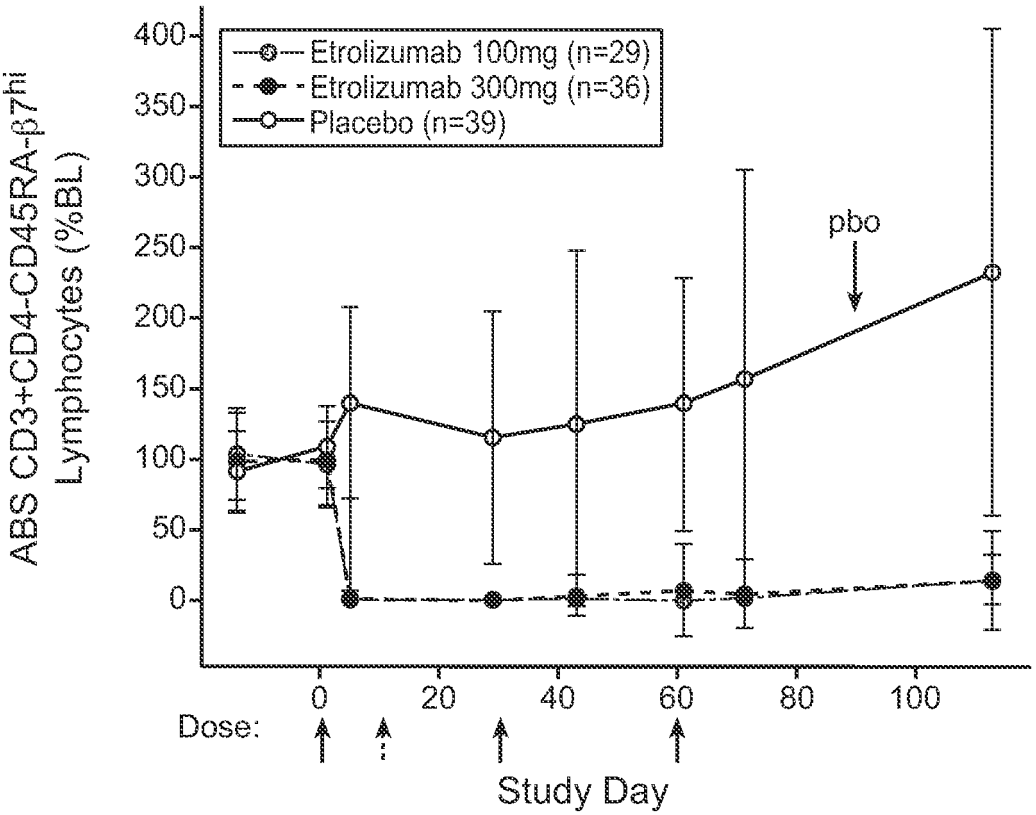

ABS CD3+CD4-CD45RA-β7hi Lymphocytes (%BL)
400
350
300
250
200
150
100
50
0
Etrolizumab 100mg (n=29)
Etrolizumab 300mg (n=36)
Placebo (n=39)
pbo
0
20
40
60
80
100
Dose:
Study Day

FIG. 4B

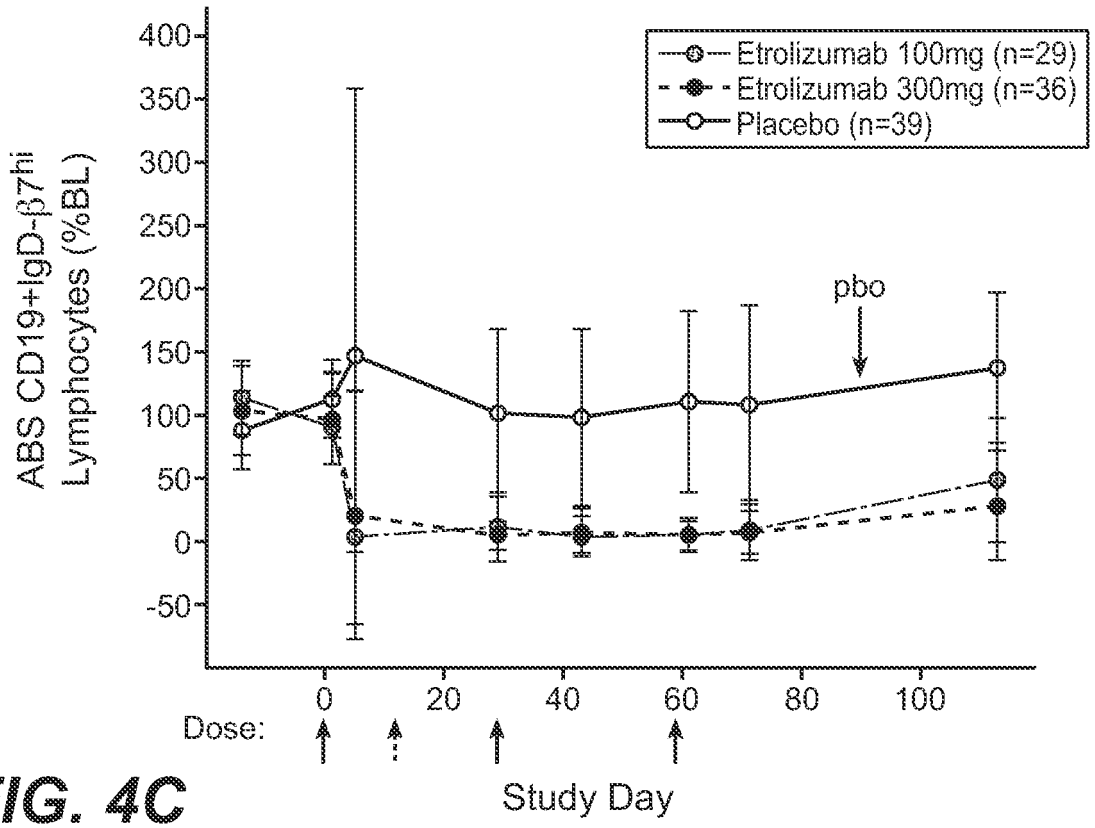

Etrolizumab 100mg (n=29)
Etrolizumab 300mg (n=36)
Placebo (n=39)
ABS CD19+IgD-β7hi Lymphocytes (%BL)
400
350
300
250
200
150
100
50
0
-50
pbo
0
20
40
60
80
100
Dose:
Study Day

FIG. 4C

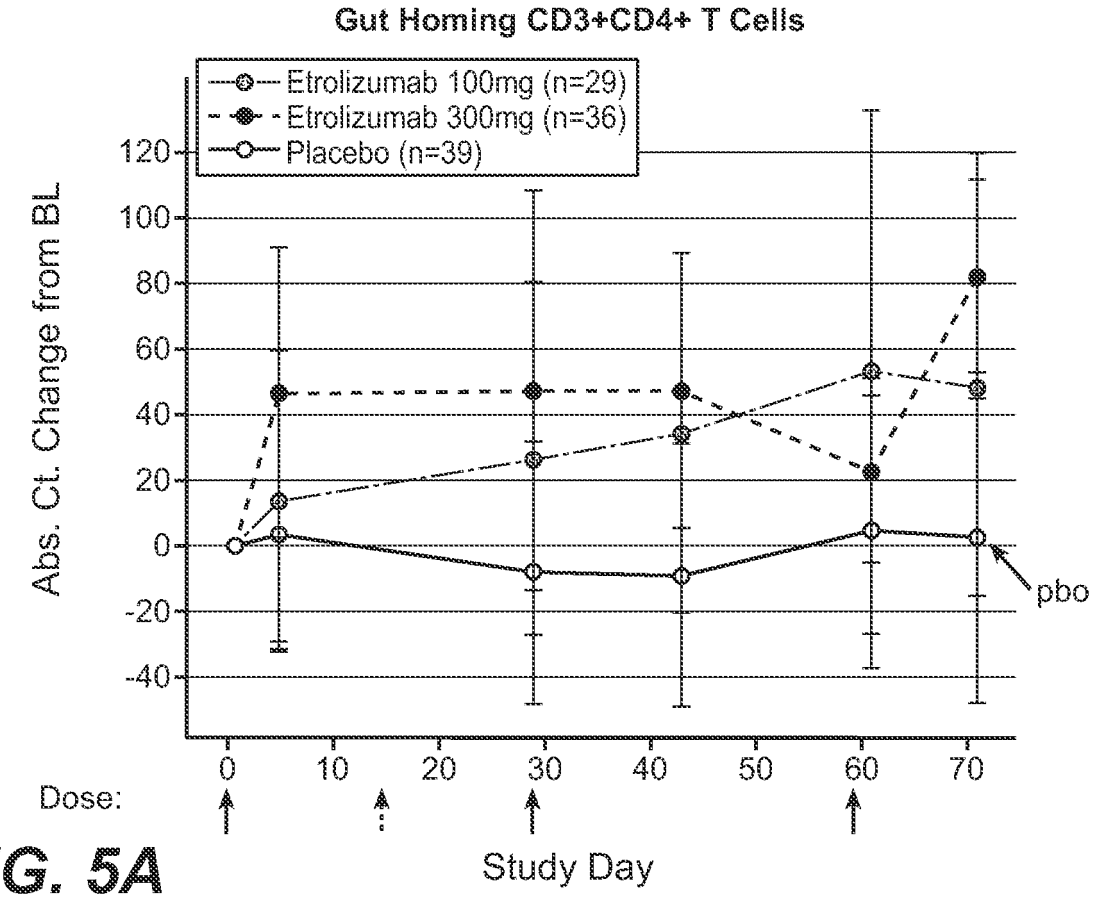

Gut Homing CD3+CD4+ T Cells
Etrolizumab 100mg (n=29)
Etrolizumab 300mg (n=36)
Placebo (n=39)
Abs. Ct. Change from BL
120
100
80
60
40
20
0
-20
-40
pbo
0
10
20
30
40
50
60
70
Dose:
Study Day

FIG. 5A

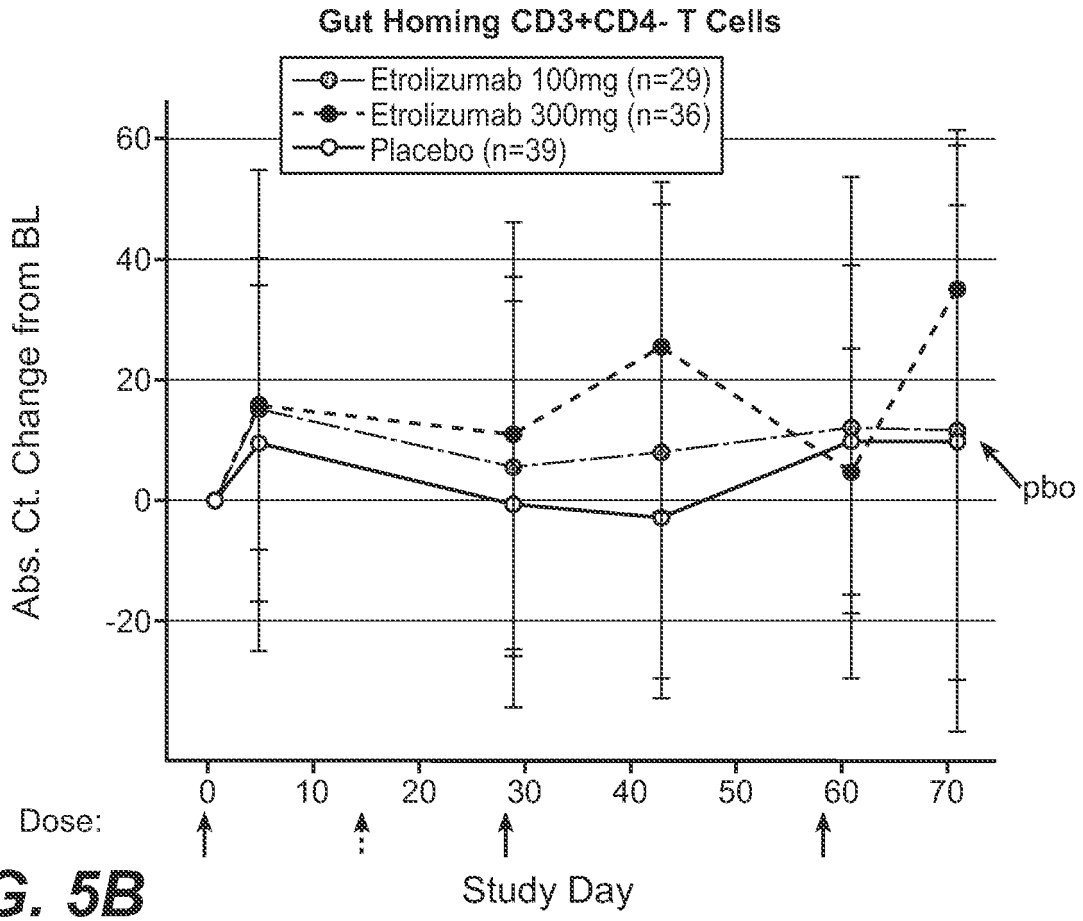

Gut Homing CD3+CD4- T Cells
Etrolizumab 100mg (n=29)
Etrolizumab 300mg (n=36)
Placebo (n=39)
Abs. Ct. Change from BL
60
40
20
0
-20
pbo
0
10
20
30
40
50
60
70
Dose:
Study Day

FIG. 5B

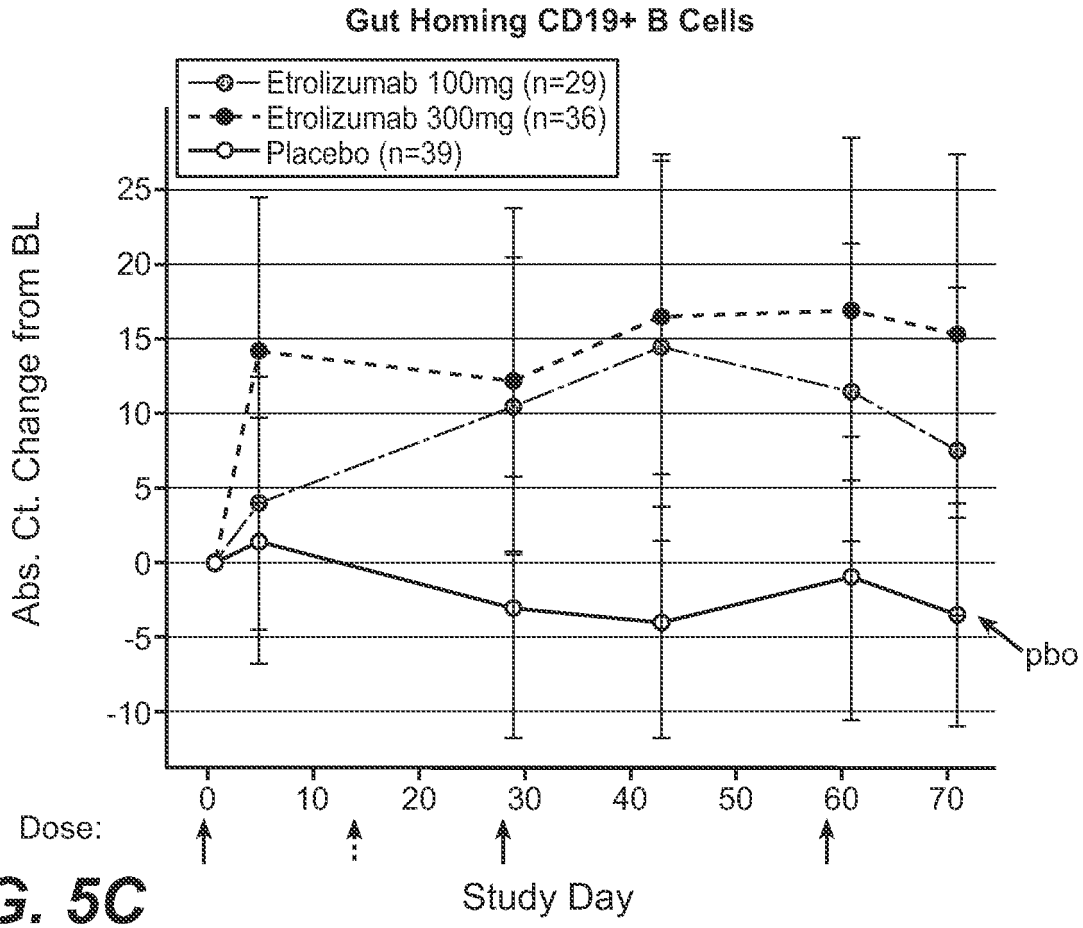

Gut Homing CD19+ B Cells
Etrolizumab 100mg (n=29)
Etrolizumab 300mg (n=36)
Placebo (n=39)
Abs. Ct. Change from BL
25
20
15
10
5
0
-5
-10
pbo
0
10
20
30
40
50
60
70
Dose:
Study Day

FIG. 5C

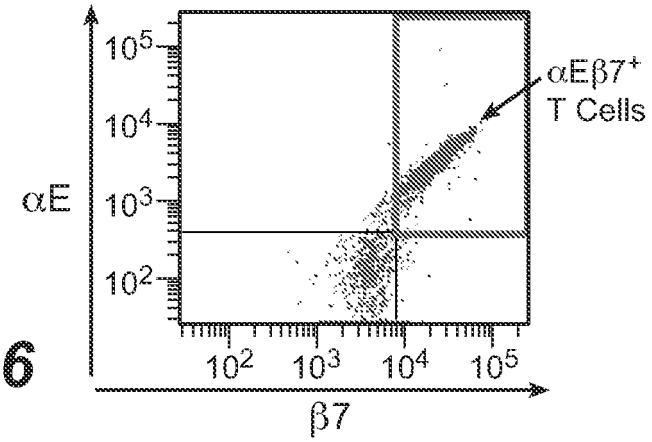

αEβ7+
T Cells
αE
β7

FIG. 6

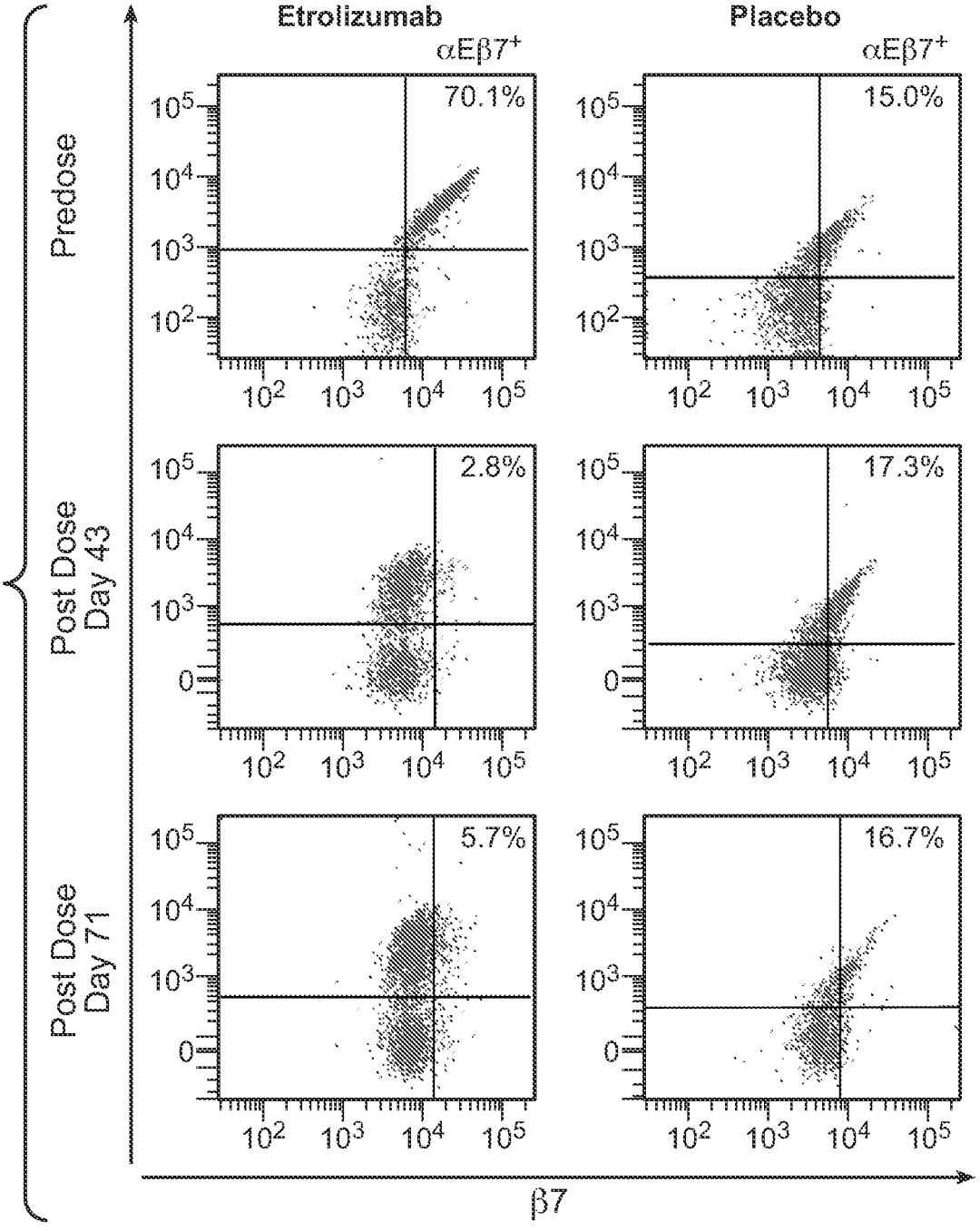

Etrolizumab
Placebo
αEβ7+
70.1%
15.0%
2.8%
17.3%
5.7%
16.7%
Predose
Post Dose Day 43
Post Dose Day 71
β7

FIG. 7

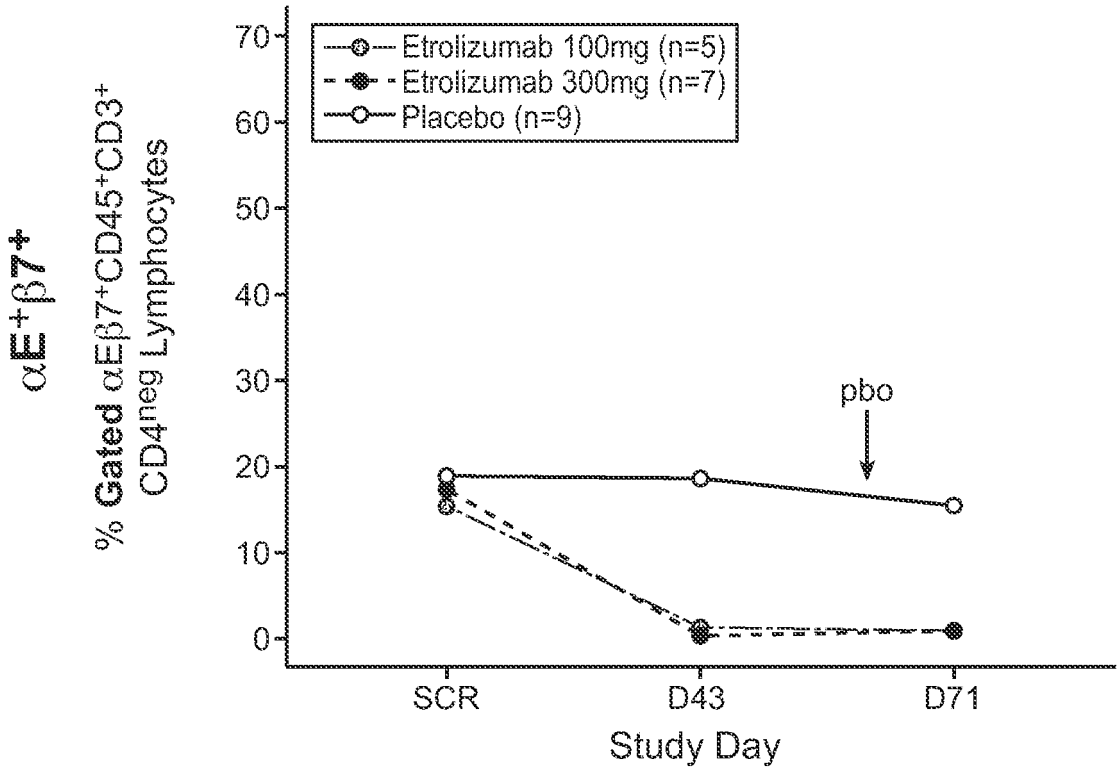

αE+β7+
% Gated αEβ7+CD45+CD3+ CD4neg Lymphocytes
Etrolizumab 100mg (n=5)
Etrolizumab 300mg (n=7)
Placebo (n=9)
pbo
70
60
50
40
30
20
10
0
SCR
D43
D71
Study Day

FIG. 8A

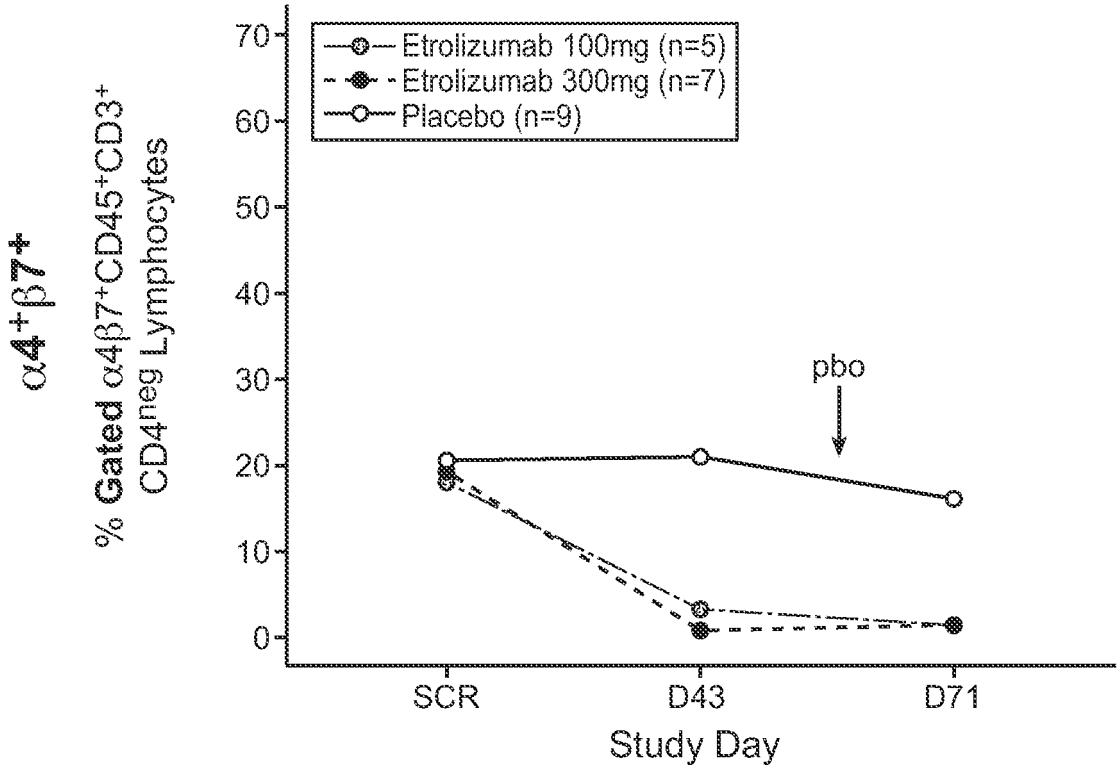

α4+β7+
% Gated α4β7+CD45+CD3+ CD4neg Lymphocytes
Etrolizumab 100mg (n=5)
Etrolizumab 300mg (n=7)
Placebo (n=9)
pbo
70
60
50
40
30
20
10
0
SCR
D43
D71
Study Day

FIG. 8B

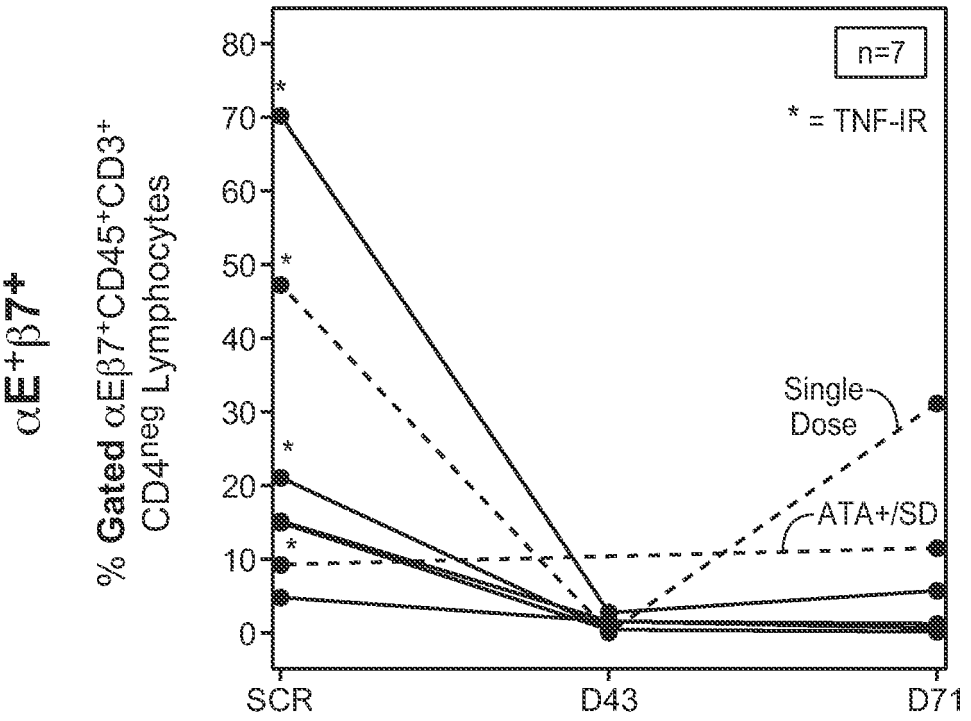

αE+β7+
% Gated αEβ7+CD45+CD3+ CD4neg Lymphocytes
80
70
60
50
40
30
20
10
0
n=7
* = TNF-IR
Single Dose
ATA+/SD
SCR
D43
D71

FIG. 8C

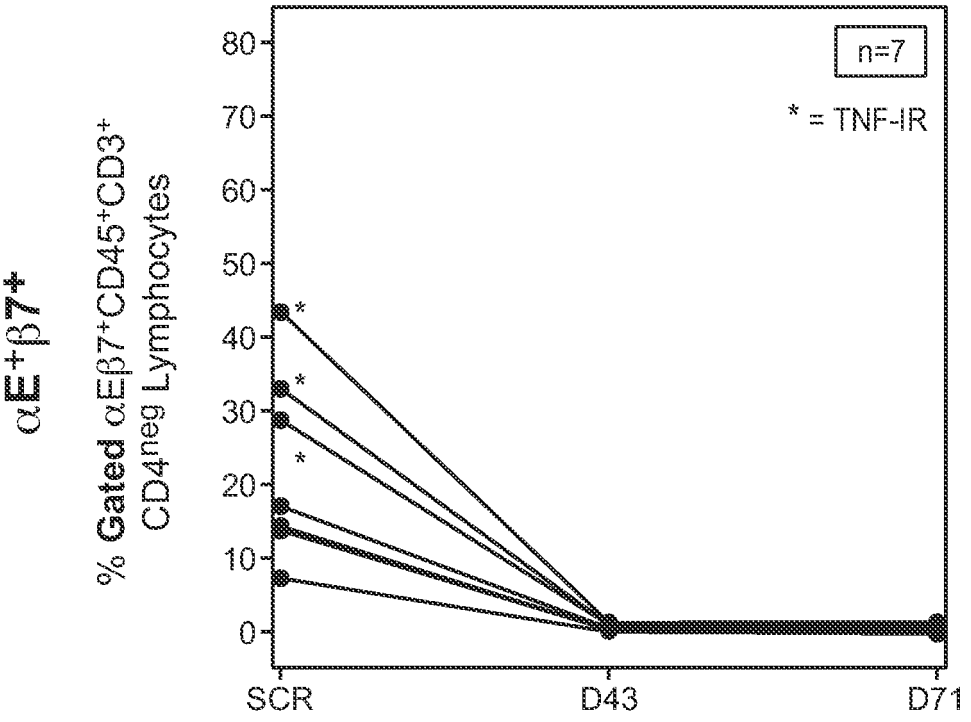

αE+β7+
% Gated αEβ7+CD45+CD3+ CD4neg Lymphocytes
80
70
60
50
40
30
20
10
0
n=7
* = TNF-IR
SCR
D43
D71

FIG. 8D

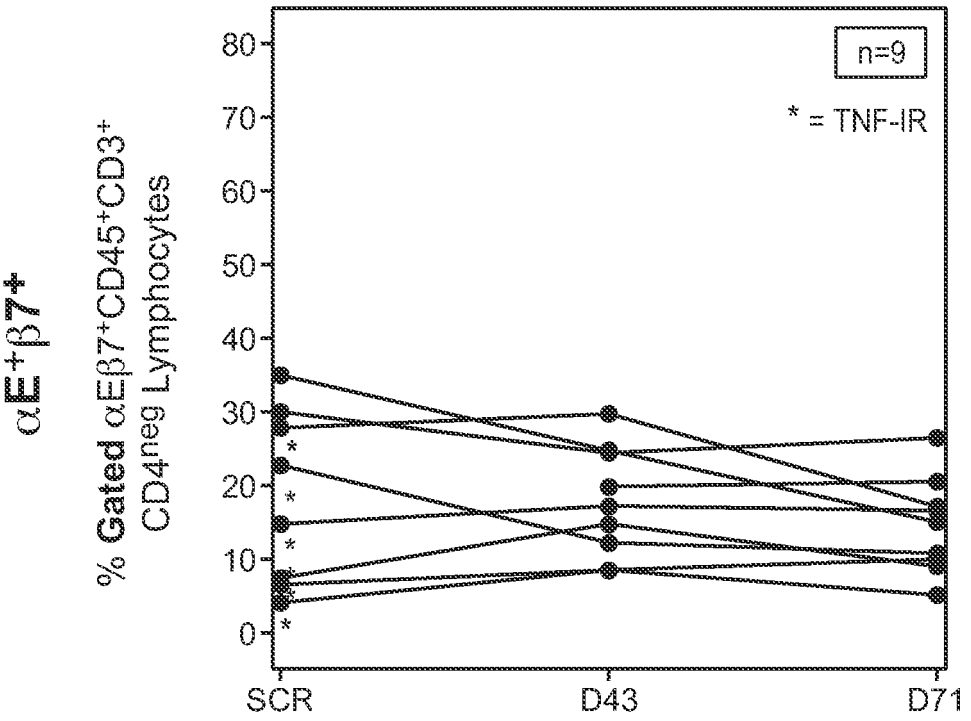

αE+β7+
% Gated αEβ7+CD45+CD3+ CD4neg Lymphocytes
80
70
60
50
40
30
20
10
0
n=9
* = TNF-IR
SCR
D43
D71

FIG. 8E

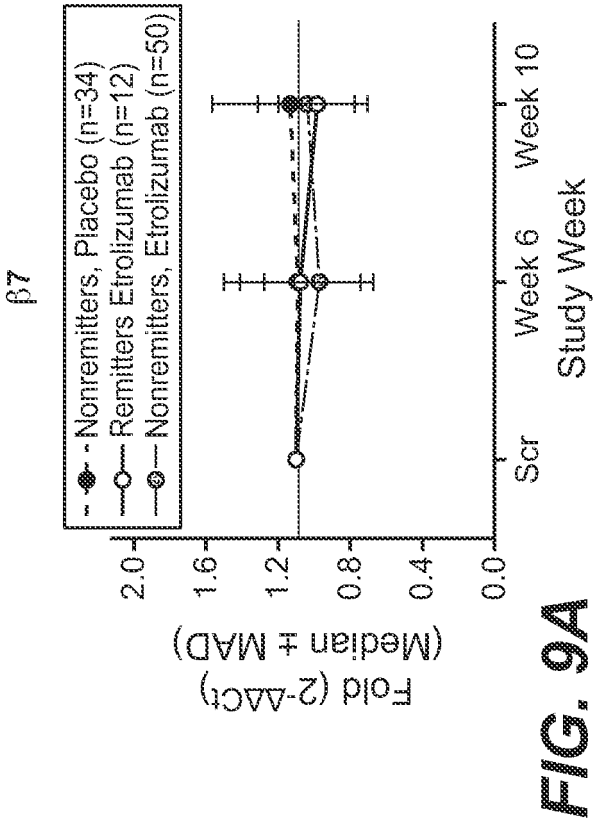


FIG. 9A

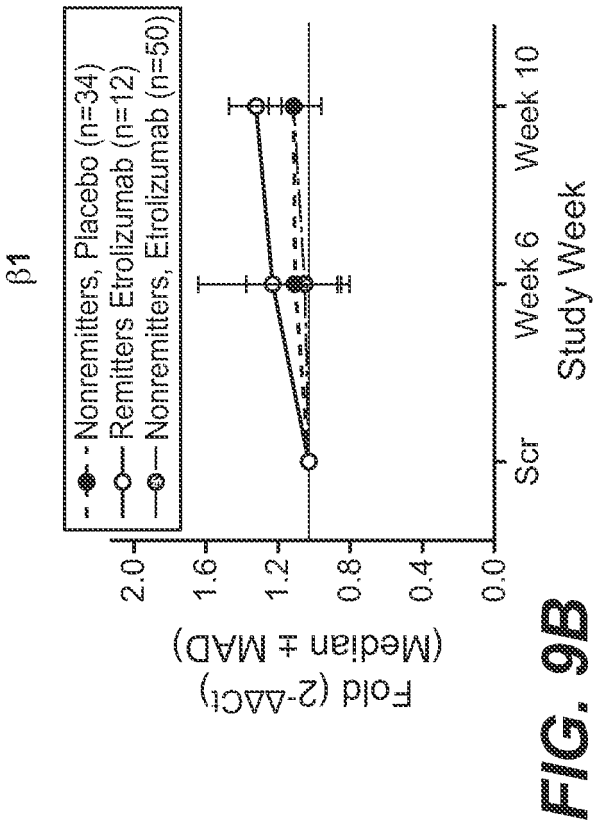


FIG. 9B

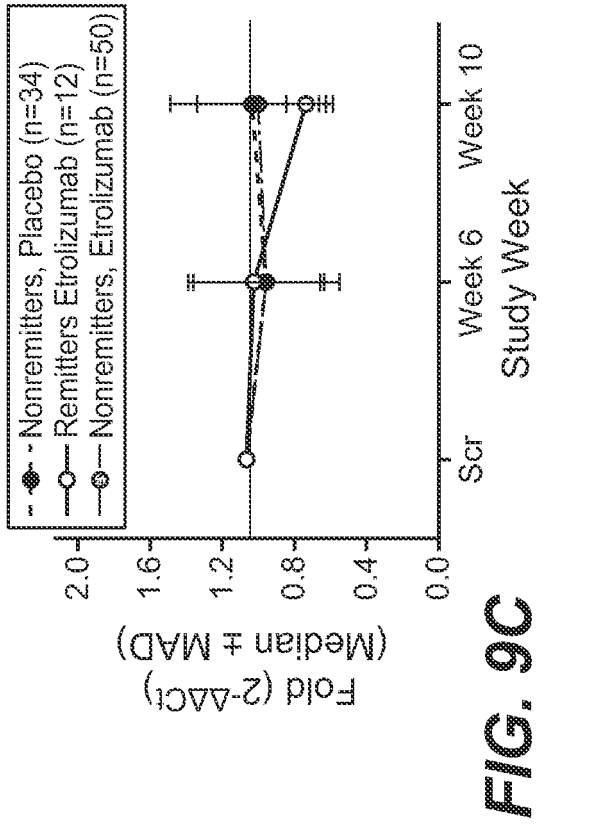


FIG. 9C

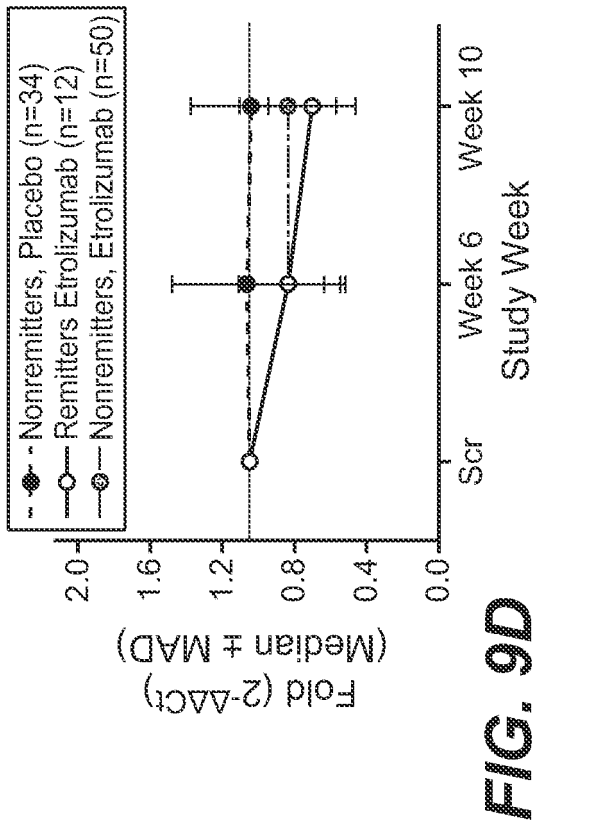


FIG. 9D

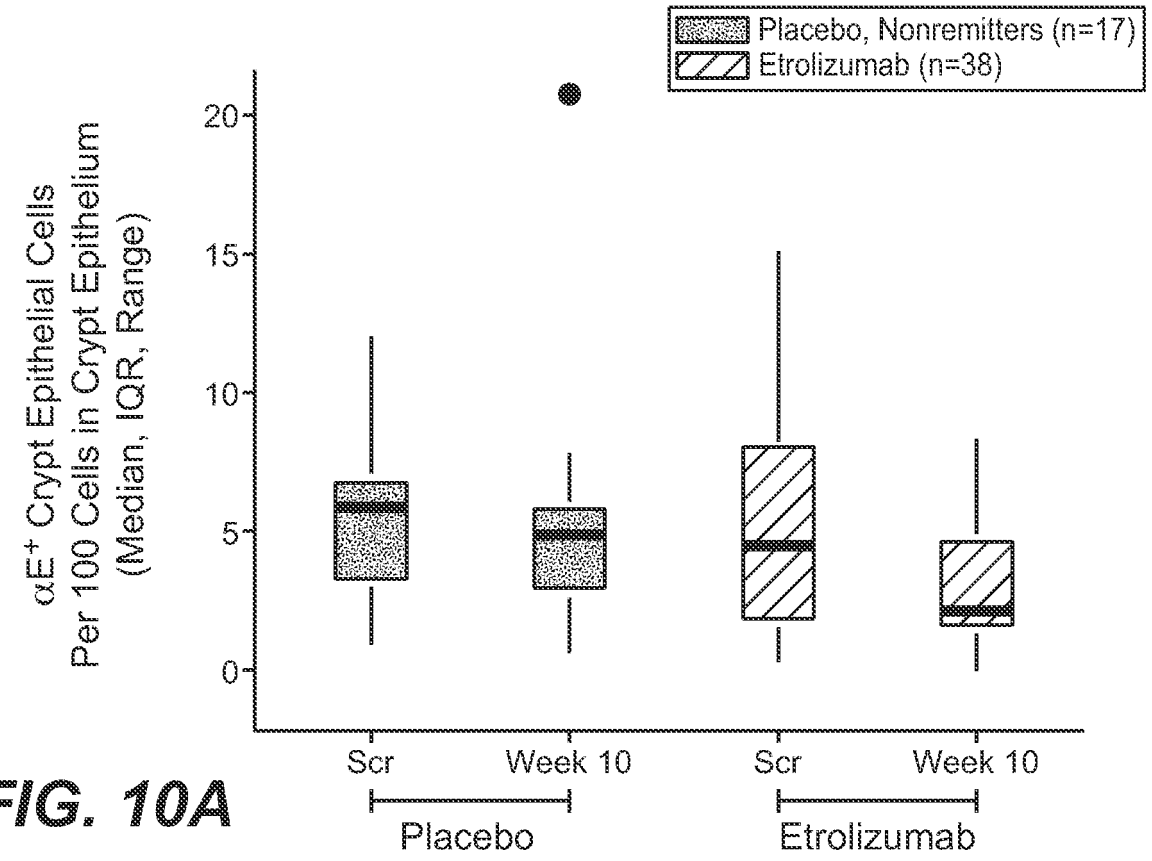


FIG. 10A

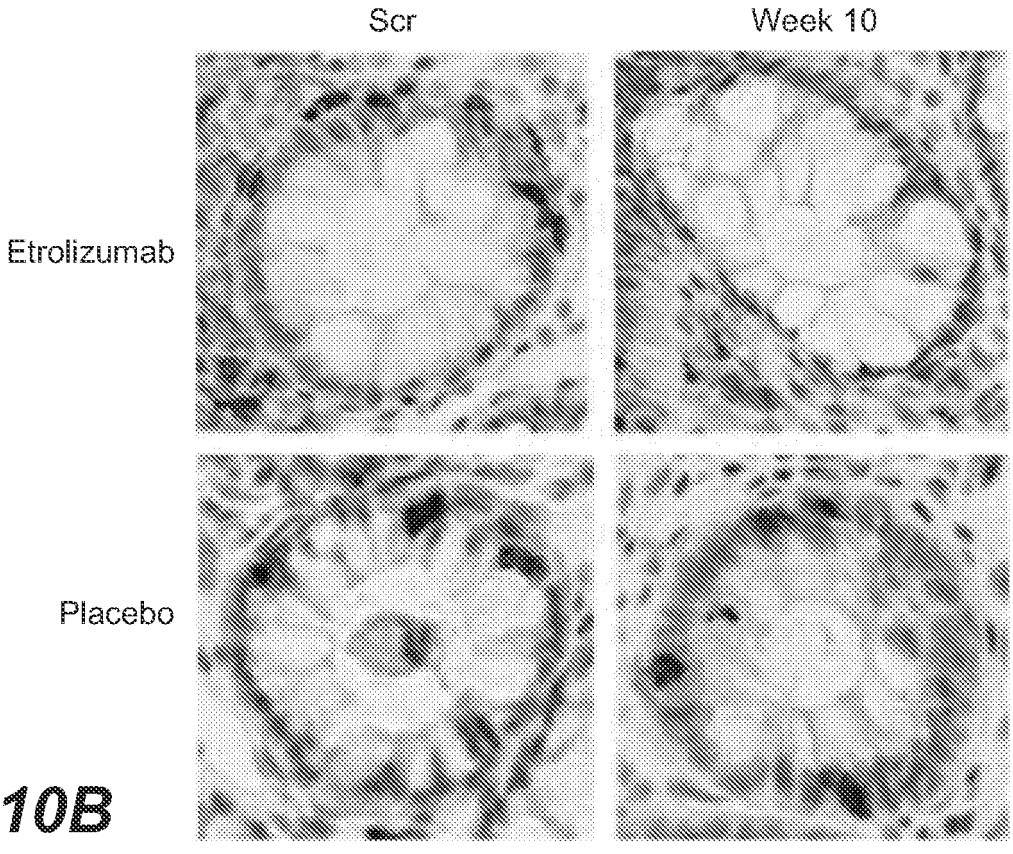


FIG. 10B

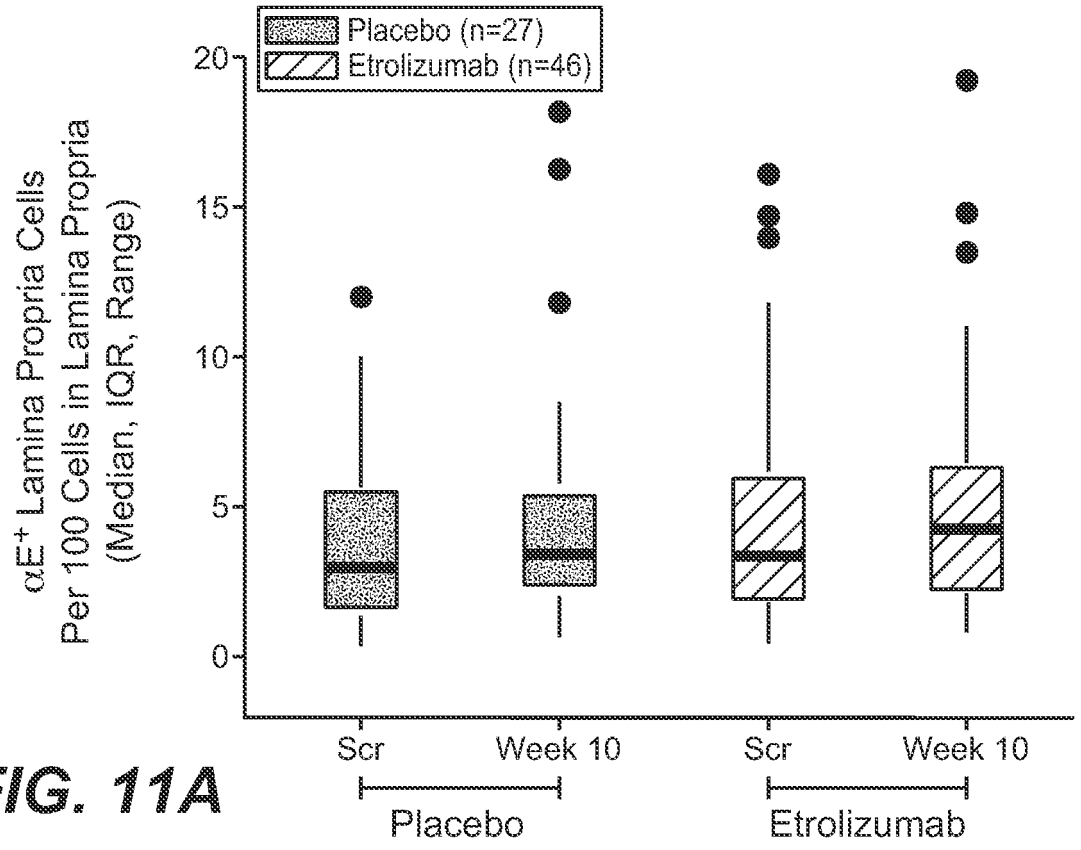


FIG. 11A

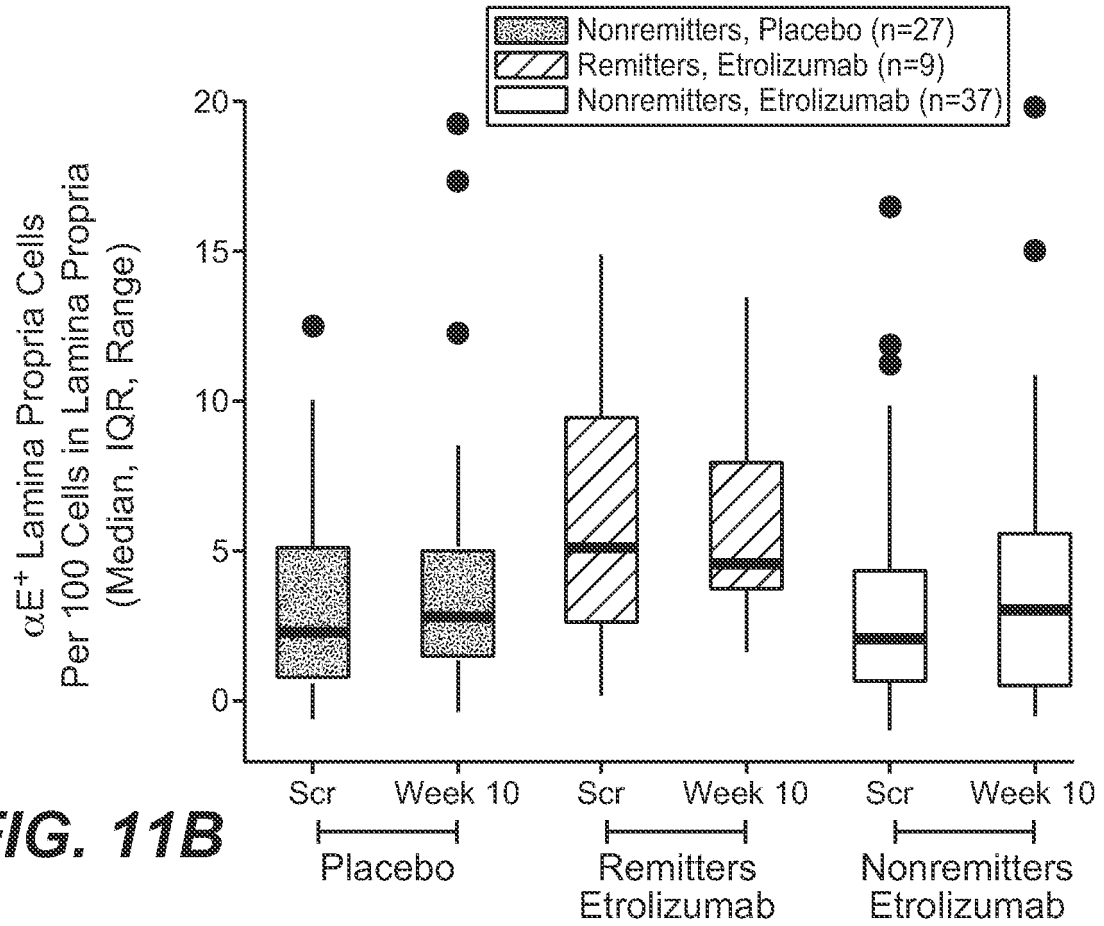


FIG. 11B

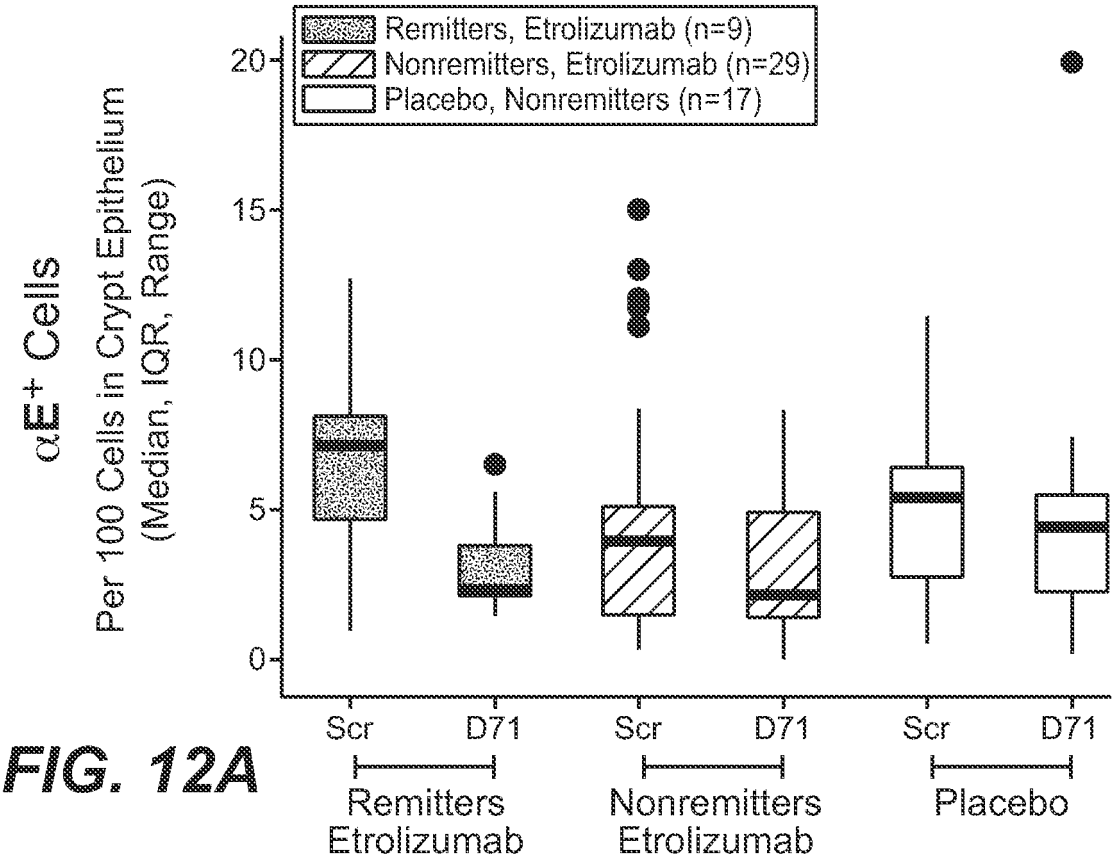


FIG. 12A

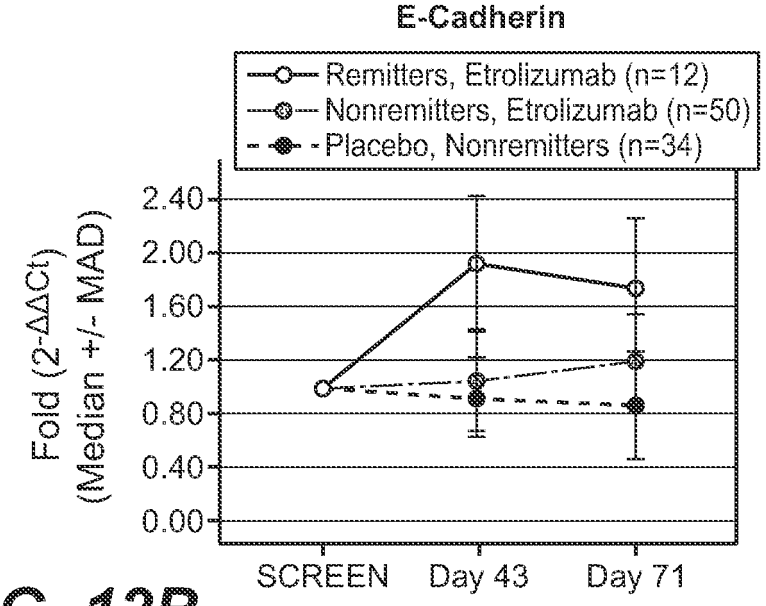


FIG. 12B

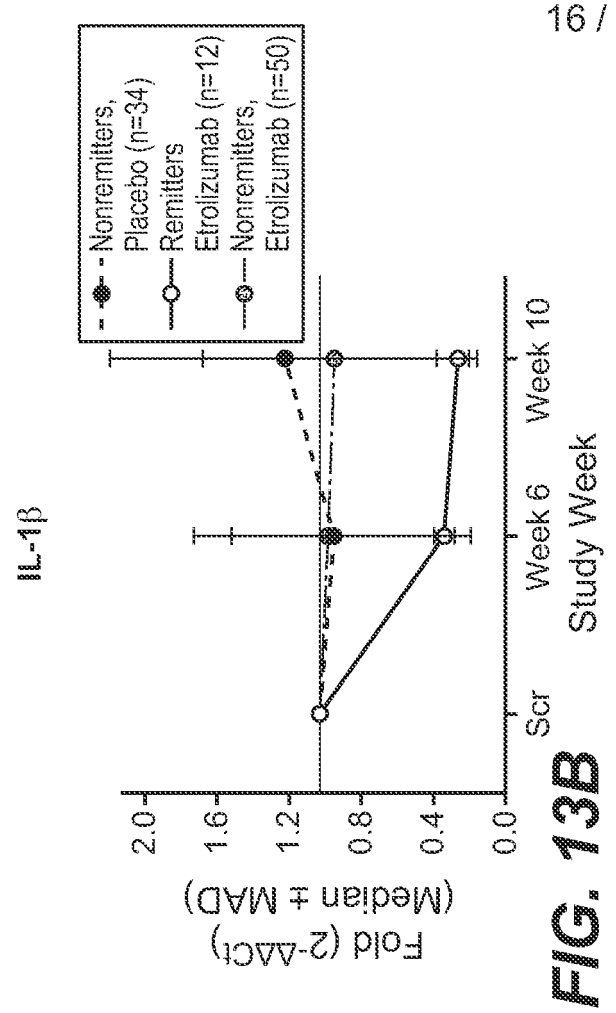


FIG. 13B

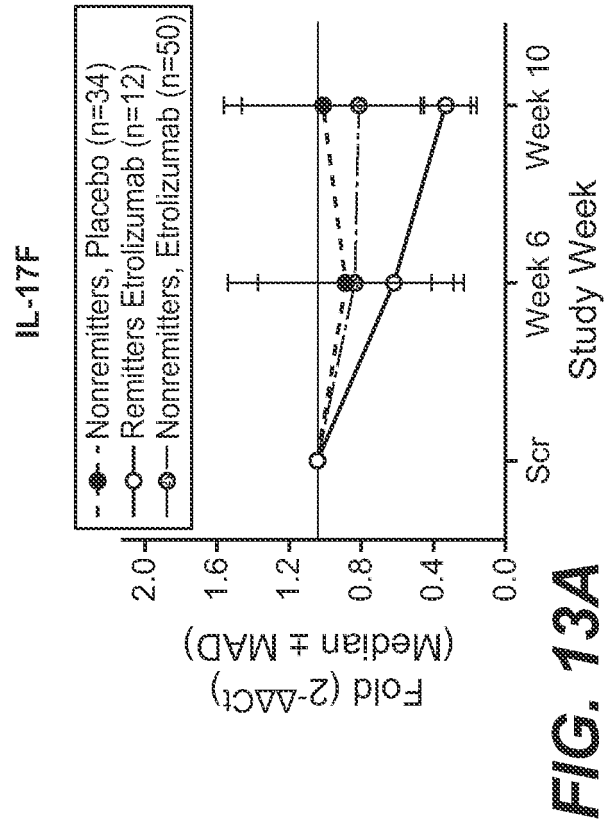


FIG. 13A

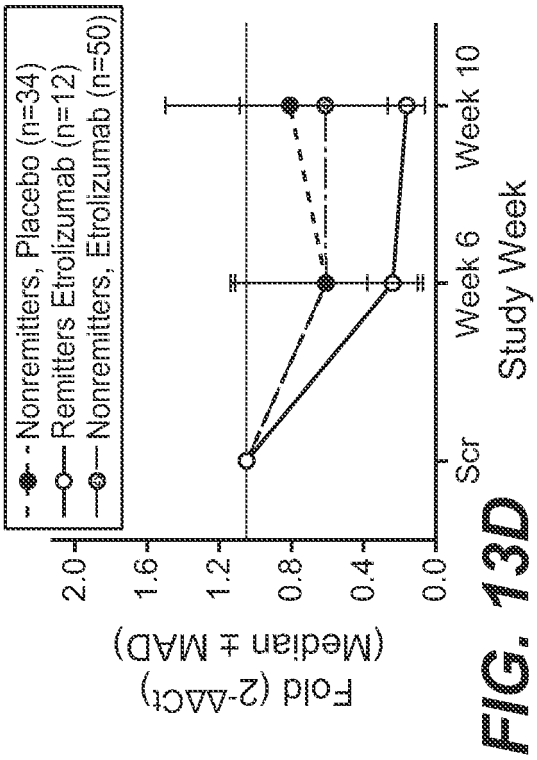


FIG. 13D

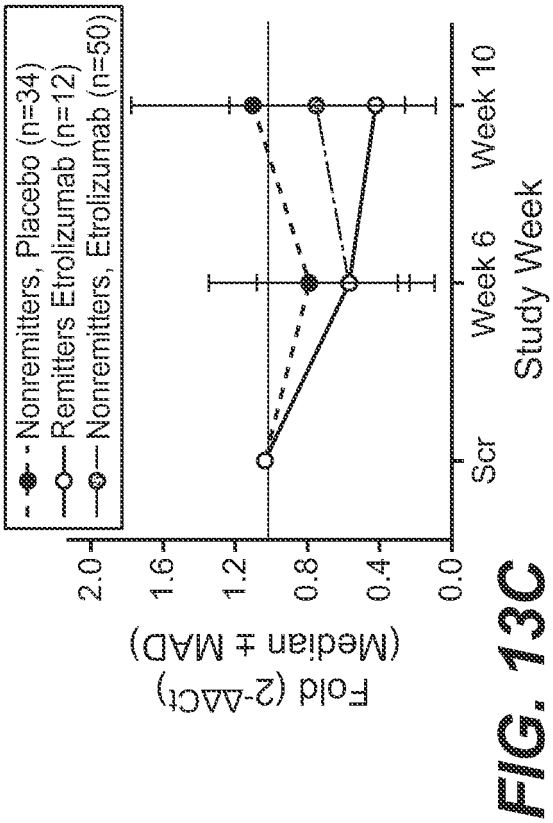


FIG. 13C

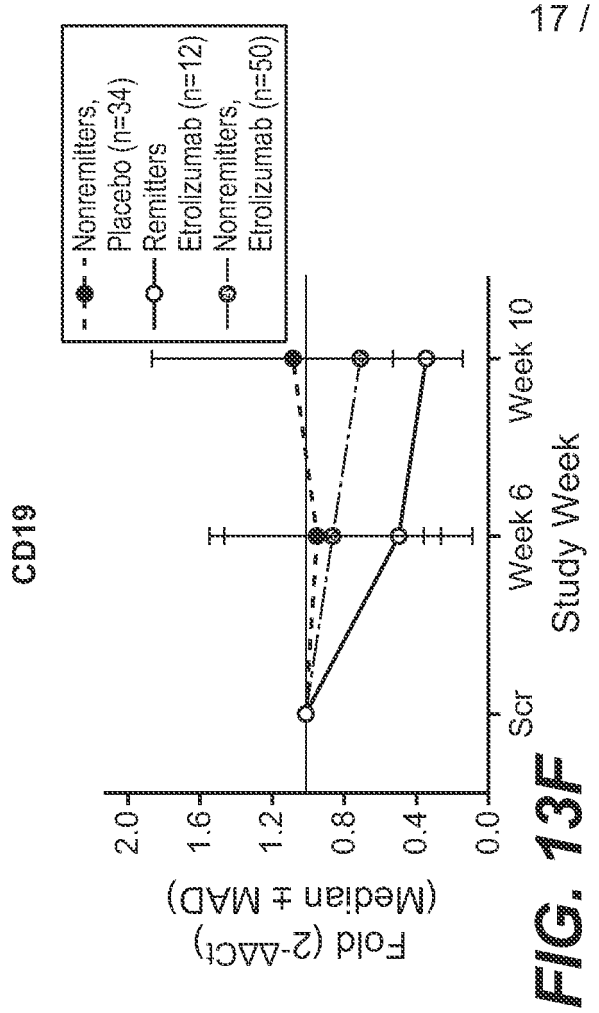


FIG. 13F

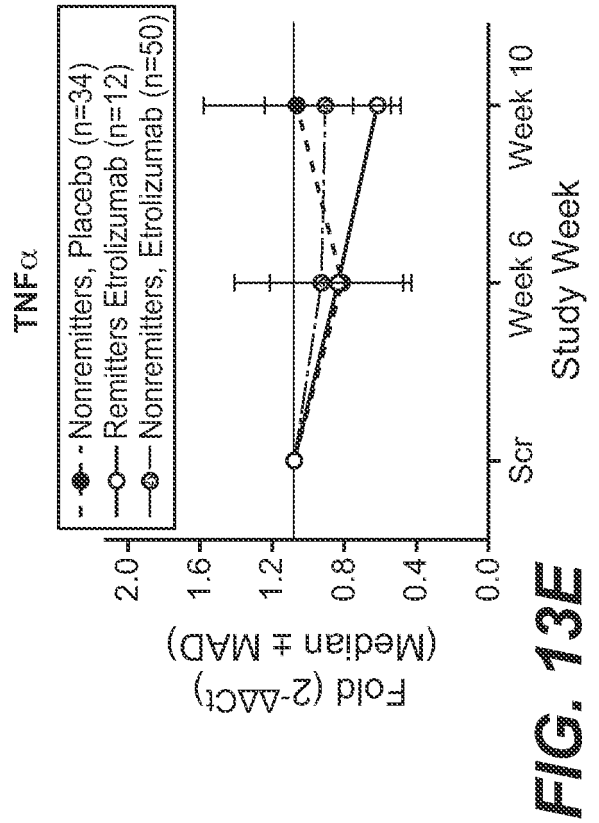


FIG. 13E

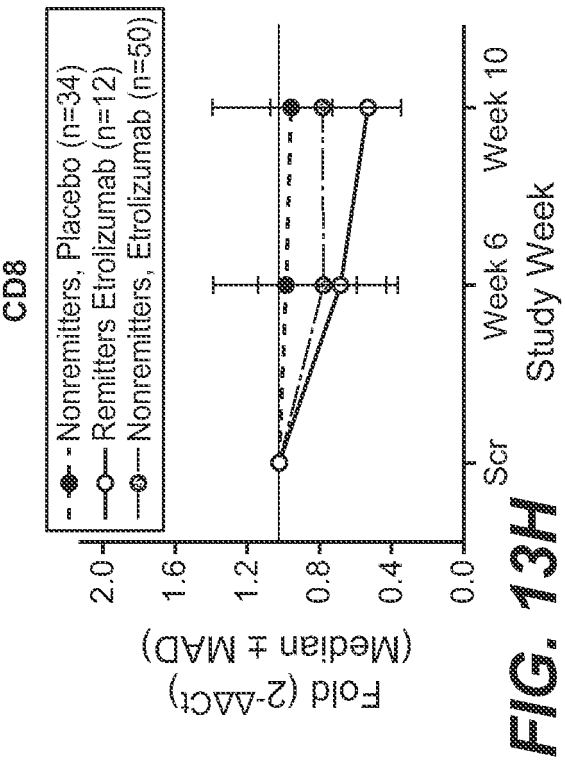


FIG. 13H

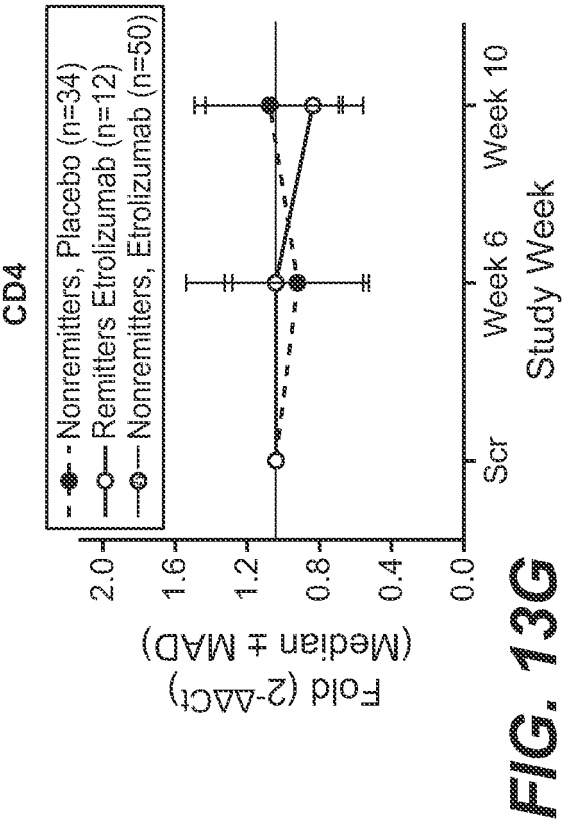


FIG. 13G

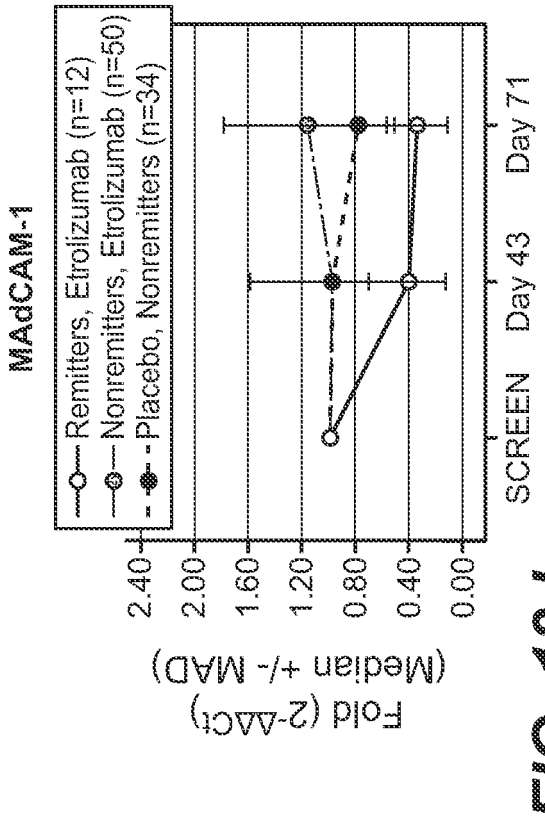


FIG. 13J

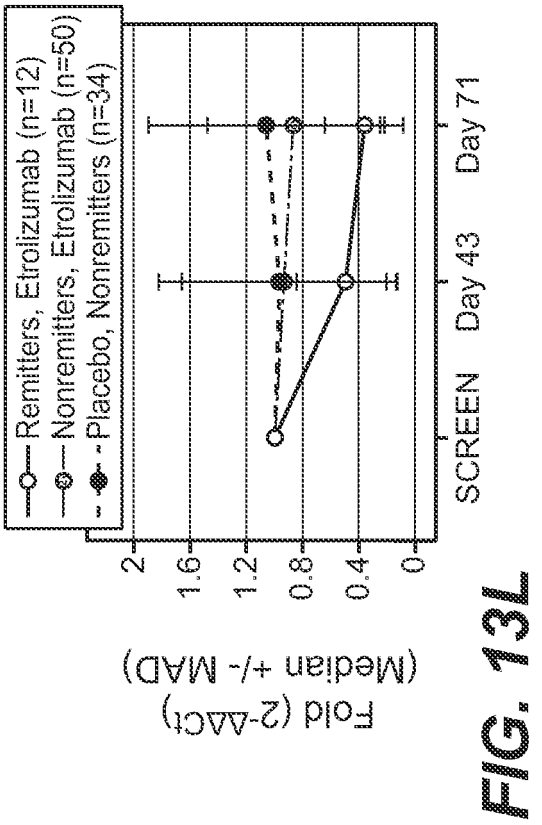


FIG. 13L

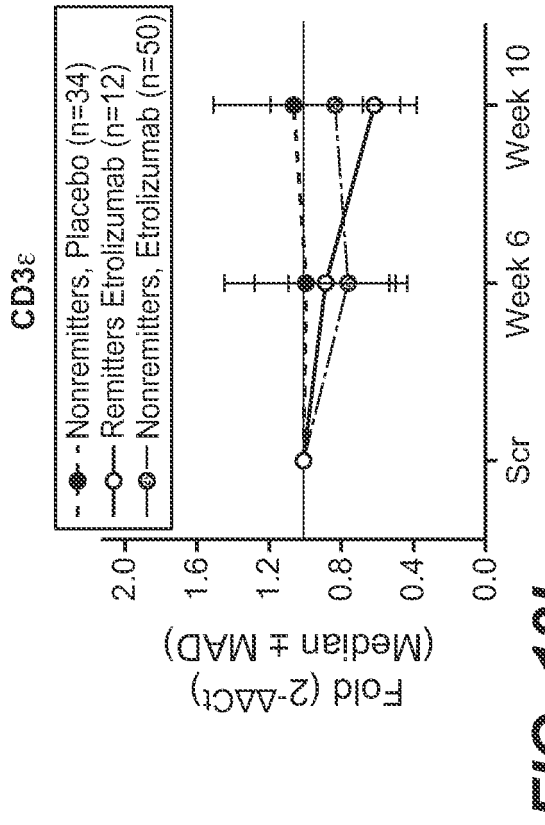


FIG. 13I

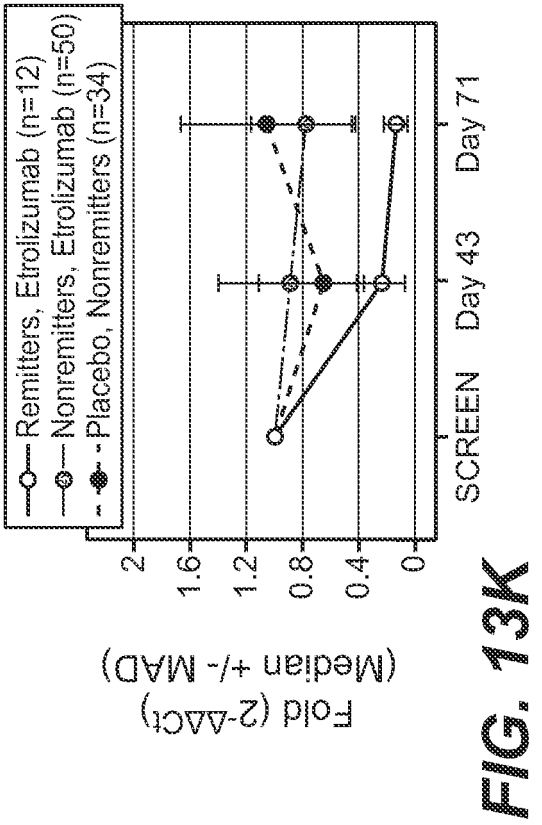


FIG. 13K

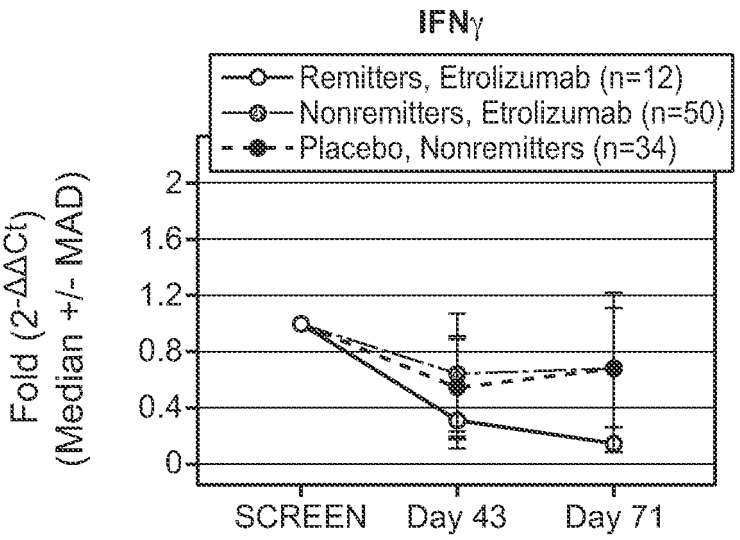


FIG. 13M

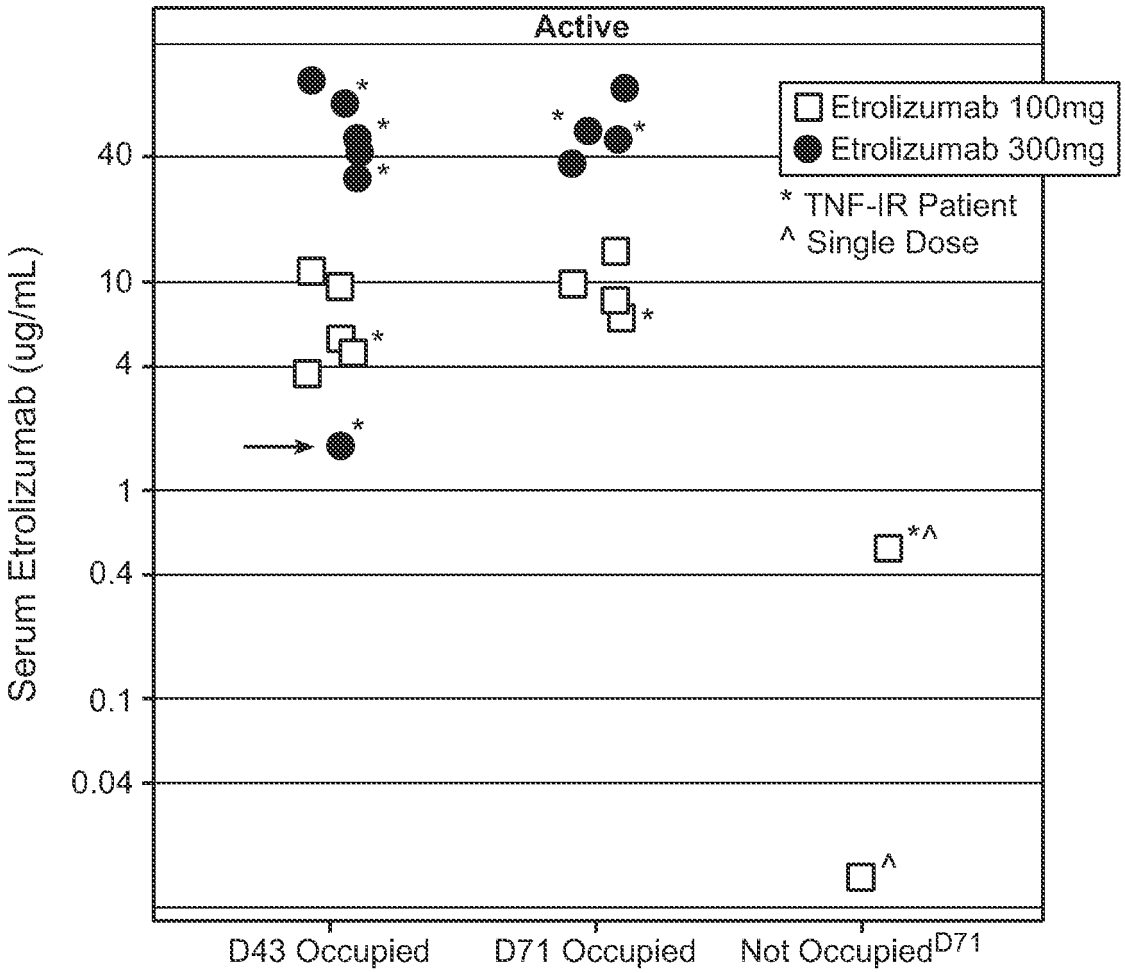


FIG. 14

```
1       10        20        30        40        50        60
|       |         |         |         |         |         |
DIQMTQSPSSLSASVGDRVTITCRASESVDDLLHWYQQKPGKAPKLLIKYASQSISGVPS

        70        80        90        100
        |         |         |         |
RFSGSGSGTDFTLTISSLQPEDFATYYCQQGNSLPNTFGQGTKVEIKR (SEQ ID NO.:31)
```

FIG. 15A

```
1       10        20        30        40        50        60
|       |         |         |         |         |         |
EVQLVESGGGLVQPGGSLRLSCAASGFFITNNYWGWVRQAPGKGLEWVGYISYSGSTSYN

        70        80        90        100       110
        |         |         |         |         |
PSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARTGSSGYFDFWGQGTLVTVSS
                                                (SEQ ID NO.:32)
```

FIG. 15B